Abraham H. Dachman
Andrea Laghi
Editors

Atlas of Virtual Colonoscopy

Second Edition

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(Editors)

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I dedicate this book to my wife, Yisraela and to my children, Toby, Yitzchak, Laya and our daughter Eliana, for their love and encouragement

Abraham H. Dachman

To my loving wife Isabella and to our wonderful child Massimo

Andrea Laghi

Foreword I

When U.S. president Barack Obama decided in February 2010 to personally undergo a virtual colonoscopy (VC) as part of his own routine health check-up, the 15-year development of this new imaging technique for detecting colon neoplasia can be said to have reached maturity. The saga has been as grand and as breathtaking as any in modern medicine, including new, futuristic, and still advancing technology, deluges of research publications, challenges to conventional clinical wisdom, broad public policy and hence cost implications, political lobbying, full-fledged turf antagonisms, and much of the drama played out in the pages of the world's most prestigious medical journals, to say nothing of the lay media.

Among the community of both American and worldwide radiologist researchers drawn to the excitement of these events, Abe Dachman of the University of Chicago was one of the earliest and has remained throughout one of the most creative and productive. His first edition of this atlas, published in 2003, for which I was kindly asked to prepare the Foreword, was the very first book ever published on the then still new topic of virtual colonoscopy. There are now several. This second edition reflects the coming together of global efforts to validate VC by the addition of a leading European proponent, Andrea Laghi of the University of Rome, "La Sapienza," as coeditor.

The format is identical to that of the first edition and is quite well suited for an atlas, with an initial section of text chapters followed by chapters of sparkling illustrative material. The content is entirely new, however, with clinical images of superb quality, many in full color, and effectively supplemented by cine movie loops of "fly-through" 3D VC studies accessible through the Springer website. The text chapters offer a remarkably rich and energetic survey of modern VC highlights, including fresh details of its historical development; natural history of polyps, especially the controversial "flat lesion"; insightful analysis of clinical trial results; and real-world, practical advice on conducting a clinical exam, reporting the study, and setting up a clinical VC service. Particularly compelling is the collection of brief international status reports from 13 leading VC advocates around the world on the current local role of VC for colon cancer screening in their own countries. Nowhere, it seems, is the ultimate goal—reimbursement for screening—yet achieved. But as many as a hundred thousand or more patients may now have had this procedure worldwide, including a president. The goal is in sight.

Drs. Dachman and Laghi are to be congratulated. Their fine new Atlas has surely aided the cause.

August 2010 Joseph T. Ferrucci

Foreword II

It is with immense pleasure that I have accepted the invitation to write a foreword to the second edition of the *Atlas of Virtual Colonoscopy*; a milestone among publications in its field and the very first book, in 2003, treating this exciting and innovative technology. Modern and up to date at the time of its publication, yet clearly "vintage" if compared to the work object of discussion. In fact, a comparison of the two editions suffices to testify the extremely quick development of Virtual Colonoscopy.

Following the rapid advancement in technology of CT scanners and informatics in Medicine, Virtual Colonoscopy has in parallel made greatly significant progress in terms of image quality, exam reliability, robustness and overall accuracy. But mostly, it is thanks to Virtual Colonoscopy that Radiologists have re-discovered the colon; forgotten in recent years due to the poor performance of barium enema in comparison to the outstanding development of optical colonoscopy. And now, Radiologists have become leading actors in the field of colorectal cancer screening, initiating discussions at various levels with policy makers and stakeholders, in order to implement Virtual Colonoscopy as a screening method for the general population. And though we are not there yet, we are very close.

An important strength of the second edition of the *Atlas* is found in the strict collaboration between Radiologists from across the world; with contributions ranging from North and South America, to Europe, to the Middle and Far East. Virtual Colonoscopy was born in the USA in 1994, but since then it has rapidly developed worldwide, and particularly in Europe, where some of the most important multicenter trials have been conducted and where pilot projects using Virtual Colonoscopy as a screening method on the general population have been put in place.

The format – *an atlas including texts and numerous images supported by cine-movies available through the Springer website* – is another winning point of this work. Texts are not limited singularly to important technical issues (i.e. bowel cleansing and tagging, colon distention, scanning parameters, image reviewing and reporting), but they also address significant epidemiological and clinical problems of colorectal cancer, polyps and nonpolypoid ("flat") lesions, whose knowledge by Radiologists is usually poor. There is also space for a critical analysis of the results of major clinical trials; the discussion of the significance and economic impact of extra-colonic findings; and finally, a view of the future represented by the development and implementation of Computed Aided Detection (CAD) software and the role of Magnetic Resonance Colonography. Unique and of extreme interest for those who wish to confront with the rest of the world is the tracking shot on the experiences of different countries. Historical background, leading researchers, turf battles with clinicians until acceptance and implementation is achieved in each single country will be discussed.

The second part is devoted to images. Plenty of cases studied with different technical approaches are presented, testifying to the strong clinical experience of the authors necessary to collect such a large selection of usual and unusual cases.

Finally, I would like to congratulate Dr. Dachman and Dr. Laghi for their great effort to co-edit this book and for the myriad of outstanding leading experts they were able to convince to join the project. I am personally sure that this work will vaunt at least the same success as the first edition, if not more.

September 2010 Roberto Passariello

Preface

Since the publication of the first book on virtual colonoscopy, the first edition of the *Atlas of Virtual Colonoscopy* in 2003, researchers and advocates of virtual colonoscopy around the world have made considerable progress. Virtual colonoscopy is being done in many countries and its acceptance by the public and by the medical community at large has gained substantial footing. The practice of virtual colonoscopy has spread beyond academic centers to private practice. Many, but not all, exams are now reimbursed by insurance companies. Notably, in 2010, the president of the United States opted to be screened for colorectal cancer with virtual colonoscopy rather than conventional optical colonoscopy.

In approaching the task of compiling material for the first edition, I approached everyone I knew who was conducting research on virtual colonoscopy to contribute to the project. The collective effort helped bring together information and case material showing examples and teaching points from all experts, regardless of whether those teaching points had been presented previously in the peer-reviewed literature. In carrying out the task of creating a second edition, such an inclusive approach was no longer necessary or feasible. Yet, it was important to garner the knowledge and experience of experts from around the globe. I therefore enlisted the assistance of Andrea Laghi to coedit the work. I took primary responsibility for Part I and Andrea and his colleague Franco Iafrate took primary responsibility for the images in Part II.

Part I remains a text-based collection of chapters on key topics with a liberal use of images, including the history of virtual colonoscopy, clinical background information, review of clinical trial data separated by the United States and by other countries, patient preparation and tagging, performance and reporting of virtual colonoscopy (with all my best tips on how to do great exams and efficient interpretations), viewing methods, flat lesions, magnetic resonance colonography, extracolonic lesions, and computer-aided detection. I would like to bring attention to the unique chapter on "Global Implementation of Computed Tomography Colonography" (Chapter 2), in which contributors from countries around the word tell the "story" of virtual colonoscopy research and clinical development in their country. This affords the opportunity to document historical information not found in the peer-reviewed literature and will be of interest to a wide international audience. Part II remains primarily image-based with detailed explanations of the teaching point in each caption, divided into chapters on normal anatomy and sessile, pedunculated diminutive, and flat lesions, masses, stool, and diverticula. A most interesting chapter on pitfalls (and how not to fall into them!) and miscellaneous topics are included in chapter 20. In all, there are about 700 images in the book.

A new feature is the use of movie files for several figures. The movies, i.e., endoluminal fly-throughs and teaching videos, are posted on the publisher's Web link: http://extras.springer.com/2011/978-1-4419-5851-8. The use of movie loops in radiology textbooks, in the form of either a CD, a DVD, or a Web link, is beginning to gain acceptance and adds a wonderful dimension to the book beyond the printed words and images.

We thank the countless individuals who have contributed to the advancement of virtual colonoscopy since 1993. We are particularly grateful for the opportunity to bring this timely contribution to the radiology, gastroenterology, and medical community at large.

Chicago — Abraham H. Dachman
Rome — Andrea Laghi

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This work would not be possible without the help of countless individuals. The authors would like to acknowledge the invaluable assistance of all our colleagues and support staff.

Dr. Dachman acknowledges the support staff for the clinical virtual colonoscopy program at the University of Chicago Medical Center: Vanessa De La Rosa, Rosalyn Hughes, LaQuisha Fleming, Sandra Brown and my secretary Paula Martinez. Our program's research in the computer aided detection was dependant on the efforts of Kenji Suzuki and his predecessor Hiro Yoshida and all the post-doctoral researchers and members in their labs and numerous medical students who participated in research projects. My research assistant Ila Sethi, MD was invaluable in working on all aspects of the book. I also thank my gastroenterology colleagues, particularly David Rubin. I thank Mark Klein for proofreading portions of the manuscript.

Dr. Laghi and Dr. Iafrate acknowledge the CT colonography team at the University of Rome "Sapienza" for the valuable contribution in clinical practice, research and education. Without the help of such an enthusiastic group also the collection of the images for this book would have not been possible. In particular, we would like to thank Maria Ciolina, Paolo Baldassari, Alessandro Pichi, Marcella Iannitti and Andrea Stagnitti for the many hours spent with us in preparing the image data.

We thank other radiologists who contributed some cases in the Atlas, particularly Philippe Lefere, Tanya Chalwa, Amy Hara, Jacob Sosna, Stuart Taylor, Roberto Fiori, Professor Giovanni Simonetti, Gabriella Iussich and Daniele Regge. Contributors are also acknowledged in the caption for the cases they provided.

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Part I

Text

Virtual Colonoscopy: From Concept to Implementation

1

Elizabeth G. McFarland, Kathryn J. Keysor, and David J. Vining

Virtual colonoscopy (VC, aka computed tomography [CT] colonography, or CTC) was introduced in 1994 as a minimally invasive screening technique for the detection of colorectal polyps and cancer [1]. It is a CT examination of the colon, cleansed of stool and distended with gas, in which the images are interpreted on a workstation using two-dimensional (2D) and three-dimensional (3D) techniques. After early work by several academic groups, VC soon gained the public's attention for its potential to be a minimally invasive colorectal screening option. This chapter provides an overview of its early development, challenges to gain insurance coverage, and key factors that will impact its broader implementation in the United States. Implementation in several other countries is discussed in Chapter 2.

Early Development and Clinical Trials

CT technology advanced rapidly in the 1980s from single slice scanners to helical imaging which permitted the acquisition of a contiguous volume of anatomy during a single breath-hold. At the same time, computer technology was rapidly advancing to allow virtual reality simulations. Intravenous contrast enhanced CT had already been well established as a means of staging colorectal cancer, and inflation of the colon with gas to improve visualization of the colon wall for staging colorectal cancer was done as early as 1981 [2]. Researchers at New York University reviewed the value of CT for detection and staging of known lesions by CT and reported that when the colon was distended with air, the detection rate was 95% versus 68% if no special attempts were made to promote visualization of the colon wall [3]. In a little-known presentation, the father and son team of Coin and Coin [4] suggested the idea of distending [5] the colon and using CT for polyp detection.

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The key invention for creating the 3D endoluminal flythough method and bringing the idea to the attention of the gastrointestinal radiology community was the work of David J. Vining. His inspiration for creating VC as we know it was brought about by combining the advances in helical CT scanning technology with virtual reality computing. It occurred to him that the computer technology used in flight simulator games could be used to navigate the volume of data generated by helical CT. Combining these two technologies enabled him to literally travel inside a simulation of the human body.

With startup funds granted by his chairman, Dr. Douglas Maynard, at the Wake Forest University School of Medicine in 1993, Dr. Vining purchased a Silicon Graphics Crimson computer and began his research program. The essential steps of VC that he devised included cleansing a patient's bowels, distending the colon with gas, scanning the abdomen and pelvis with spiral CT, and generating a 3D flight simulation through the colon.

One of Dr. Vining's colleagues, Dr. David Gelfand, volunteered to be the first to undergo the VC examination in September 1993. The single-slice spiral CT scanner that was used took approximately a minute to scan the patient during an attempted breath-hold, and the VC flight required more than 8 h for the computer to process. Today, multidetector CT scans the body in a matter of seconds, and 3D processing occurs in real time on laptop computers. Vining's first flight through a colon was presented at the 1994 Society of Gastrointestinal Radiologists (SGR) meeting held in Maui, Hawaii.

Dr. Maynard's investment in his young faculty member eventually led to significant research funding and an extensive patent portfolio covering the technology, but more importantly, it launched an industry and gave the public a less-invasive option for colorectal cancer screening.

Some of the earliest peer-reviewed publications following Vining's presentation include data on 20 patients from his research group [6] and work in the United Kingdom comparing barium enema and "CT pneumocolon" in four patients [7]. The earliest clinical trials for screening appeared in the peer-reviewed literature in 1997 and 1998 [8, 9]

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(Editor's note: The term "2D with 3D problem solving" was coined by University of Chicago medical student Jeremy Kunioshi [9]). In October 1998 the First International Symposium on Virtual Colonoscopy, a 2-days multidisciplinary meeting hosted by Boston University and co-directed by Drs. Ferrucci and Fenlon [10], was attended by more than 120 registrants from 12 countries. Since then, this international symposium has continued to meet and remains a key event of political and research updates in the field.

Subsequent early clinical trials of VC yielded promising results; however, mixed messages arose as the technology evolved. Some pioneering researchers reported high sensitivities exceeding 90% for the detection of polyps ≥1 cm [11, 12], but these results were countered by other, less appealing results [13–15]. One of the successful trials by Dr. Helen Fenlon and colleagues at Boston University was highlighted as a lead article in the *New England Journal of Medicine* in 1999 [11]. Differences among the various studies were attributed to multiple factors, including the type of patient cohort, training and experience of readers, and 2D versus 3D image analysis techniques [16].

Public awareness of virtual colonoscopy was raised by the activism of noted talk show host Katie Couric, who underwent a virtual colonoscopy on television in 2002 on her *Today* show [17]. The status of virtual colonoscopy by May 2001 and the political issues related to its national implementation were set forth by Joseph T. Ferrucci in a visionary presentation titled "Colon Cancer Screening with Virtual Colonoscopy: Promise, Polyps, Politics" at the American Roentgen Ray Society's "Caldwell Lecture" [18].

Near the end of the first decade following its introduction, another landmark article in the *New England Journal of Medicine* once again put CT colonography in the news. This study, led by Dr. Perry Pickhardt, represented the largest screening trial to date with the evaluation of over 1,200 patients in the military [16]. New technological breakthroughs were introduced, including stool tagging and subtraction, use of segmental unblinding to improve the reference standard beyond colonoscopy, and use of 3D as a primary image display review. Pickhardt's study set a benchmark of 90% sensitivity for the detection of polyps ≥1 cm and 80% for 6–9 mm polyps in asymptomatic patients at low risk. As the first decade closed, the stage was set for another string of successful trials to emerge using newer technologies in both screening and high-risk patient cohorts [19–22].

Challenges to Gain Reimbursement

Following a decade of innovation and clinical validation, efforts to establish VC's clinical role focused on achieving reimbursement by the major private insurers and the government through Medicare. VC faced reimbursement hurdles despite the continued success of larger validation trials in screening cohorts, as well as the development of practice guidelines and quality metrics to help its implementation in community settings.

Reimbursement decisions for new medical technologies are based on many factors, including level of clinical validation, cost effectiveness, quality assurance, and the potential of a new technology to improve patient health outcomes. Regarding validation, Dr. Daniel Johnson led a key multi-institutional clinical trial funded by the American College of Radiology Imaging Network (ACRIN) involving over 2,500 asymptomatic patients and performed in 15 private and academic centers [19]. The performance characteristics of the ACRIN trial published in 2008 and the 2003 Pickhardt trial would later be used in the cost-effectiveness analysis initiated by the Centers for Medicare and Medicaid Services (CMS) in 2009.

In an effort to establish a VC quality assurance program, an updated version of the American College of Radiology (ACR) Practice Guideline for the Performance of CT Colonography in Adults was published in 2009 [23, 24]. Important elements included hands-on workstation training required for radiologists, new dose limits (i.e., values of CT dose index per volume [$CTDI_{vol}$] of 12.5 millisieverts [mSv] or less for screening VC), and the definition of appropriate cohorts for VC based on family risk and/or symptoms. In the preceding year, an ACR committee led by Dr. Johnson developed six key quality metrics for CTC, including both process and outcome metrics. Process measures included rates of adequacy of bowel cleansing and insufflation, rate of adequacy of VC screening exams, and rate of adequacy of VC diagnostic exams. Outcome metrics include rate of bowel perforation, positive predictive value for polyps ≥10 mm, and rate of extracolonic findings which lead to further imaging examinations. These metrics have since been incorporated into the National Registry of Diagnostic Radiology's CT Colonography registry, with data for over 2,000 patients entered since 2008.

Another key factor that has influenced VC reimbursement decisions was the 2008 release of screening guidelines from two national health care policy groups: the American Cancer Society (ACS) and the U.S. Preventative Services Task Force (USPSTF) [25, 26]. The guidelines resulting from these two groups were diametrically opposed with respect to VC. The ACS guidelines were developed with the cooperation of the U.S. Multi-Society Task Force on Colorectal Cancer (comprising representatives from the American Gastroenterological Association, the American Society of Gastrointestinal Endoscopists, and the American College of Gastroenterology) and the ACR [25]. The new ACS guidelines created two tiers of colorectal screening tests, namely tests used to detect colorectal cancer (i.e., stool guiac and stool DNA) and tests

used to prevent cancer by the detection of polyps (i.e., colonoscopy, sigmoidoscopy, barium enema, and VC). VC was included in the latter group as one of the tests used to prevent colorectal cancer, provided that state-of-the-art VC technology is used and rigorous quality assurance instituted [25]. On the other hand, the USPTF performed a systematic review of VC using the expertise of economic modelers with an emphasis on cost-effectiveness analysis [26]. The result was that VC was given an "I" rating for having insufficient evidence, largely due to the potential risks associated with radiation exposure and the work-up of extracolonic findings. The USPSTF decision would later influence CMS's denial of coverage for screening VC in the Medicare population.

In 2008, CMS called for a national coverage decision for VC. This process included a meeting of the Medicare Evidence Development and Coverage Advisory Committee that was held in November 2008. The Committee reviewed the report of the Agency for Healthcare Research and Quality from three modelers using data from the 2008 ACRIN trial and the 2003 Department of Defense trial. Despite coordinated efforts by the ACR, the American Gastroenterological Association, ACS, and industry, CMS released a final non-coverage decision in May 2009 [27].

Despite the negative CMS decision, several private payors have subsequently decided to cover VC for screening and following failed colonoscopy. In September 2008, the Blue Cross Blue Shield Association Technology Evaluation Center endorsed VC for screening, reversing an earlier position against the technology [28]. It is important to note that this evidence-based review does not represent a Blue Cross Blue Shield coverage decision – however, it does carry weight with many local Blue Cross Blue Shield plans, such as Anthem, Wellmark, Empire, and Horizon, which offer coverage of diagnostic and screening VC. In 2008–2009, other national private payors that have passed positive coverage decisions for screening VC include Cigna and United Healthcare [29, 30]. These early coverage decisions are promising, and individual payors are expected to continue evaluating and updating their decisions about VC coverage.

Contrary to coverage for screening VC, coverage for diagnostic VC for specific indications is still prominent across the United States. CMS continues to support local coverage decisions in 48 states, largely for the indications of history of prior failed optical colonoscopy and risk to undergo colonoscopy [31]. Similarly, many private payors have also followed these trends for indications for diagnostic CTC. Efforts to expand VC coverage by both Medicare and private payors are continuing. With respect to CMS, coverage with evidence development is being proposed by the ACR, the American Gastroenterological Association, the Colon Cancer Alliance, the ACS, and other industry leaders. In spite of these reimbursement issues, VC gained public attention in February 2010 when President Obama opted to have a VC as part of his first routine physical exam as commander-in-chief, at the National Naval Medical Center in Bethesda, Maryland [32]. In May 2010, a bill was introduced into the U.S. Congress called the Virtual Screening for Colorectal Cancer Act of 2010, which would require CMS to provide coverage for screening CTC.

Other important elements in the reimbursement process include the development of Level I CPT codes, followed by the assignment of relative value units. In 2004, the American Medical Association (AMA) approved Level III codes in Current Procedural Terminology (CPT) for VC (VC Screening and VC Diagnostic), but these were used primarily for tracking and not billing purposes [31]. As the Level I codes for CTC were being considered in 2007, an AMA workgroup was formed to help facilitate discussions between gastroenterologists and radiologists over a 2-years period. At a February 2009 AMA meeting, three Level I codes were approved: 74263 for VC screening (without contrast), 74261 for VC diagnostic (without contrast), and 74262 for VC diagnostic (with and without contrast). These Level I CPT codes went into effect on January 1, 2010. Following the approval of the Level I CPT codes, assignment of relative value units was voted on and became effective on 1 January 2010. These relative value units were set at 2.28 for CTC screening and CTC diagnostic without contrast, and 2.50 for CTC diagnostic with and without contrast and were subsequently increased.

Future Challenges for Broader Implementation

Several factors will greatly impact VC's future implementation in general practice, including the role of screening in the era of health care reform and government regulations aimed at reducing radiation exposure and reimbursements. The reluctance of patients to undergo bowel cleansing remains a major hurdle for both VC and conventional colonoscopy. Acceptance, pricing, reimbursement, and competing technologies are all major hurdles. Affordable pricing for the VC procedure, especially to make it competitive against other available colon screening methods, will require consensus among radiology practices. Evolving technologies, such as proteomics and stool screening for DNA markers, could also greatly impact the value of VC as a screening tool. Nevertheless, VC continues to contribute in the fight against colorectal cancer.

Patient-related issues for VC may be among the most influential factors affecting broader use. One of the greatest barriers to colorectal cancer screening is the bowel preparation. Future development of more patient-friendly innovations in the bowel preparation could improve compliance with colorectal screening recommendations. In addition, patient advocacy will be important to translate appropriate

use to patients and understand their perspectives. In today's health care environment, a better understanding of what drives patient choices will be important.

Technical improvements in VC may largely involve innovations in bowel contrast agents and radiation dose reduction. Development of molecular imaging techniques for mucosal contrast agents may allow improved sensitivity and specificity of identifying colorectal lesions. New scanner technology and software are producing VC radiation dose levels lower than those of annual background radiation (less than 3 mSv). Dual-energy CT scanners that are emerging on the market today promise to better characterize bowel wall abnormalities and reduce artifacts.

Quality assurance efforts with broader implementation of quality metrics will continue to expand. The continued validation of dose-efficient VC protocols will be important to follow. The currently developed quality metrics may set the stage for third-party pay-for-performance. The use of structured reporting with C-RADS (the CT Colonography Reporting and Data System) to report both colorectal and extracolonic findings will be invaluable to future data analysis efforts [33]. Similar to mammography, the use of structured reporting is essential for clear communication of findings and to guide patient management.

Finally, success of VC will require a multidisciplinary approach and cooperation among radiologists, gastroenterologists, surgeons, and other health care professionals involved in the early detection and treatment of colorectal cancer and its precursor polyps. Given the fact that positive VC screening examinations occur in about 10% of cases which will necessitate a follow-up colonoscopy for polyp biopsy and/or removal, a close working relationship between radiologists and endoscopists will be needed for patients to undergo same-day procedures.

Efforts not only to define appropriate use and evaluate quality, but also identify future areas of research to advance the technology will be important. One recent example of this was the ACS workshop on small polyps which began in the fall of 2009. In this effort, ACS invited gastroenterologists, radiologists, and pathologists to help review important topics, including the prevalence and incidence of advanced pathology in small polyps, the different pathological pathways for colorectal cancer, and natural history data. Hopefully a clinical consensus of how to manage small polyps, as well as topics for future research efforts, will result from this shortly. This process of literature review combined with expert consensus in areas of debate or knowledge gaps will become increasingly important to advance technologies into clinical practice.

Virtual colonoscopy is a rapidly evolving technology that has gone from innovation to implementation in less than 2 decades. Future developments will continue to expand its utilization and contribute to VC's role in the fight against colorectal cancer.

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Global Implementation of Computed Tomography Colonography

2

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Editor's Introduction

This chapter is a series of short essays composed by key researchers and advocates of computed tomography colonography from several different countries. I hope this will help document some important historical information regarding the development of computed tomography colonography on a global scale. This information is not available in print in any single source and often incorporates a historical perspective never before appearing in print. Each section has its own style, content, and references. The essays are listed in alphabetical order of the country discussed: Argentina, Austria, Belgium, Canada, France, Germany, Ireland, Israel, Italy, Japan, Korea, Sweden, and the United Kingdom. Authors provided photographs of themselves and/or their research team, which are provided in an appendix at the back of the book.

Virtual Colonoscopy in Argentina

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About Colorectal Cancer in Argentina

In Argentina, colorectal cancer (CRC) is a common disease with high morbidity and mortality. While we do not have statistical data from the National Cancer Registry, the incidence of cancers was estimated by the International Agency for Research on Cancer (IARC) based on the World Health Organization from mortality records obtained from the Ministry of Health of the Nation. In 2000, the IARC estimated that in Argentina there were approximately 10,300 new cases of CRC, second in incidence after breast cancer and lung cancer.[1]

The latest available data for different causes of mortality in Argentina were published in the *2002 Yearbook* from the Bureau of Health Statistics and Information of the Ministry of Health of the Nation. In the December 2003 publication, it was noted that the number of CRC deaths reached 5,700 in 2002, placing it fifth after breast, prostate, stomach, and lung cancer, in that order. This information allows us to calculate about 15 deaths per day from CRC in Argentina. The analysis of the distribution by gender shows that in men, the cancer mortality is led by lung cancer, then prostate cancer; colorectal cancer is slipped to the third place. For women, breast cancer produces the largest number of deaths, followed by CRC, lung cancer, and cervical cancer.

In 2000, the Argentine Society of Gastroenterology, the Argentine Society of Coloproctology, the Argentine Federation of Gastroenterology, the Argentine Association of Clinical Oncology, and the Argentine Federation of Associations of

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Digestive Endoscopy presented the first jointly authored guide of recommendations for the prevention of CRC. These recommendations were presented and subsequently published as *Argentine Consensus 2000,* which was disseminated in publications and scientific events by the sponsoring companies, but, unfortunately, there were insufficient public venues of dissemination to significantly impact implementation of the guidelines. For those reasons, it was proposed that the National Academy of Medicine, through its Institute of Oncology, in conjunction with the Ministry of Health of the Nation, reconvene the scientific societies that participated in *Argentine Consensus 2000* and other interested societies, for the purposes of making a new "Argentine Consensus 2004."[2] In this statement, the following specific objectives were proposed: (a) Develop recommendations for primary prevention of disease; (b) develop recommendations for prevention and early detection of CRC; (c) set standards of individualized inquiry as the risk group; (d) actively participate in medical education programs; and (e) establish the basis for discussion and elaboration of a national program. There were also three general objectives: (1) reduce the incidence of CRC; (2) decrease the morbidity and mortality for CRC; (3) improve the quality of life of the patients.

In this consensus, virtual colonoscopy (VC) was mentioned as only a promising technique undergoing further development and progress, with a sensitivity for the detection of lesions greater than 6 mm, similar to optical colonoscopy. It was noted in the consensus statement that VC was not widely available, that there is a long learning curve to understand and interpret its results, that the test still requires a bowel cleansing preparation (albeit without the need for sedation), and, in case of a pathologic finding, that an optical colonoscopy must nevertheless be performed. It was also mentioned that the sensitivity for the detection of flat lesions was not yet well established. Finally, it was emphasized that there was an absence of published guidelines that included VC as an option for CRC screening.

About Virtual Colonoscopy

A few years after the first stunning presentation of a VC fly-through video in 1994 by Vining and Gelfand at the annual meeting of the American Society of Gastrointestinal Radiology in Latin America, CT colonography (CTC), better known in this part of the world as virtual colonoscopy, took the first steps toward broader investigation by the academic radiology community. The beginning of this new area in the examination of the colon was challenging and difficult, particularly in Argentina. Among the important limitations that most countries of the region have to deal with are the high cost of state-of-the-art CT technology, the absence of economic capabilities to invest quickly in emerging technology, and the lack of good health policies.

In Argentina, the first display of this nascent CT diagnostic modality was performed by our group in August of 1998 during a scientific session of the Argentine Society of Coloproctology.[3] Since then, our group has performed more than 2,500 examinations both for research and for diagnostic purposes. Starting with single-slice helical CT technology and then with a four-row multidetector CT scanner, Carrascosa et al. [4] published in 2003 a large, single-institution experience in an increased-risk population. The study enrolled 500 patients (264 women, 236 men; mean age 52 years old) over a 4-year period. Patients underwent both VC and conventional optical colonoscopy (OC) within the same day, with the latter serving as the reference standard where segmental unblinding was not used. The study protocol was carried out with the basic technique for that time, including 300 patients evaluated with single-slice helical CT scanning protocol, with 4 mm collimation, 2 mm reconstruction interval, and 150 mA; the remaining 200 patients were studied using a four-row multidetector CT scanner, with 2.5 mm collimation, 1.3 mm reconstruction interval and 50 mA. All patients underwent the same cathartic preparation without fecal tagging; colonic distention using manual insufflation of room air; and a primary 2D interactive analysis, reserving 3D virtual endoscopic imaging for problem resolving only. At the ≥9 mm threshold, the sensitivity for polyps at VC was 100% (140 of 140 lesions); at the 5–9 mm threshold, sensitivity was 95.6% (108 of 113 lesions); and for polyps ≤5 mm, sensitivity was 87.8% (108 of 123 lesions).

To understand the evolution of the modality in our country, it is important to remember that 12 years ago, the majority of CT equipment comprised conventional CT scanners, and only a small number of helical CT scanners were available in the federal district and its neighborhood. Of the institutions with helical CT scanners, only a few had also a dedicated workstation with navigation software capable of performing VC fly-through interpretation. From those developmental years to now, the CT community has increased, there are newer multidetector CT scanners, and different virtual endoscopy products for image post-processing have been introduced. Indeed, currently there are in our country more than 40 diagnostic imaging centers and hospitals that perform VC, either with 16-row or 64-row CT scanners, most of them with appropriate, last-generation 3D post-processing software. However, only a minority of sites are performing colonic distention with automated CO_2 delivery. Unfortunately, there are also sites performing VC studies using outdated techniques such as single-slice helical CT scanners and a primary 2D interpretative approach. This broad spectrum of CT technology in combination with a widespread dissemination of the VC technique raised another concern: the absence of adequate, local training courses and

well-established VC guidelines to certify the level of expertise in the field.

Professional and also patient acceptance is also variable. As in the rest of the world, the road to widespread clinical acceptance has been and remains hard. However, the method is in part well accepted for the gastroenterology and coloproctology community, and the topic is included in the annual meeting programs of internal medicine, gastroenterology, and coloproctology societies, as well as being part of postgraduate scholarship programs. But the use of VC in the daily practice is related not only to acceptance by professionals but also to the policies adopted by the national health systems, including cost/benefit matters of the different countries.

In Argentina the health system is complex, though not original. It is regulated by the state, but the effective provision of services is divided into three main levels[5–7]:

1. The public health care system, which access is universal and egalitarian, funded by national, provincial, and municipal governments, supports 22% of the expenditure on public health care. In this system, access to high complexity imaging exams is limited.
2. The social labor system, which includes, compulsorily, people who work and receive a formal salary or who receive a state pension or retirement benefits. In this case, services are provided under the administration of entities regulated by labor unions. Personal contribution to the funds of each entity is required by law. Their relative weight in the system is 33%. This system also has limitations in high complexity studies, which are approved only under specific indications.
3. Finally, there are private services at civilian institutions or commercial enterprises or provided by nonprofit foundations that contract with independent institutions or individuals, funded through the payment of a fee. Each affiliate chooses the institution and the coverage plan that it is able to afford. Relative spending of this sector is 45%.

Another interesting fact is that 51.9% of the population (18.8 million) has coverage of health insurance or private social coverage, while the remaining 48.1% must be covered by the public system with only just over a fifth of spending on health.[8] Unlike the public system, the other two systems have similar benefits of high complexity examinations to the rest of the world. However, in Argentina, a developing country, such services are cheaper than in other countries. For this reason and because of the availability of advanced technology and professionals with international experience, many patients are coming from abroad to have their screenings done. In Argentina, the cost of a VC examination in private practice is about US$330, two-thirds of the cost of an optical colonoscopy in the same setting.

The main indications of the procedure, which are accepted by the vast majority of social health insurance plans and private health systems, are: (a) complement of an incomplete optical colonoscopy; (b) patients with an indication for optical colonoscopy who have risks for complications from sedation or anesthesia; (c) currently in concordance with the latest revision of the American Cancer Society guidelines for CRC screening.[9]

Conclusions

In Argentina, as in the other countries of the region, the road to widespread clinical acceptance for VC has not been smooth. The availability of the procedure is still limited and has a large spectrum of technical variations. Nevertheless, the medical community, particularly clinicians, abdominal surgeons, and a growing number of gastroenterologists and coloproctologists, have appreciated the benefits of this new diagnostic imaging examination, and there is an encouraging positive growth rate.

The need for adequate, local training courses is of paramount importance, along with well-established VC local guidelines to certify the level of expertise and competency in VC interpretation, as well as to set standards for the performance of the procedure to ensure the maintenance of quality as this diagnostic modality becomes more commonly applied for screening purposes.

Computed Tomographic Colonography in Austria

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Introduction

Austria is a landlocked country of roughly 8.3 million people in central Europe. Published data from the Federal Statistical Institute of Austria, *Statistik Austria,* reported that 4,462 cases of colorectal cancer were diagnosed in Austria in 2007 and that 2,210 people died of colorectal cancer in this year. Notably, the risk of dying from colorectal cancer before the age of 75 years has decreased in the last 20 years, from 1.9% to 1.2%, indicating the potential success of colorectal cancer prevention programs.[10]

Implementation of Computed Tomographic Colonography in Austria

For many years, imaging of the colon and rectum has traditionally been a major part of both scientific and routine clinical work at the Medical University of Vienna.[11–13] When the first images from virtual colonoscopy appeared in the scientific media, the radiologists at the Department of Radiology at the Medical University of Vienna were very excited and enthusiastic about a new advanced technique for imaging the colon, and began to work on the clinical implementation of this novel technique. Apart from the initial experience at the Medical Universities of Innsbruck[14,15] and Graz, advanced computed tomographic colonography (CTC) began, in Austria, at the Medical University of Vienna in 2000, with the acquisition of a four-detector-row CT scanner at the Department of Radiology. With the improvements in multidetector CT technology, "single-breath" examinations were possible, for the first time, with high spatial resolution, enabling high quality examinations suitable for advanced 2D and 3D rendering. The CTC program was initiated by Professor Lechner, then head of the Department of Radiology at the Medical University of Vienna**.** The first steps in this field were taken by Mathias Prokop, Ewald Schober, and Andrea Maier. In 2000, Thomas Mang joined the team as a Research Fellow, and in 2003 Wolfgang Schima became substantially involved in this project. However, as always at the inception of a new technique, endoscopists were slightly skeptical about this entirely digital examination, and the referral rates remained relatively low in the first year. However, after the initial skepticism, the inherent benefits of this new colonic imaging technique over double-contrast barium enema, and its feasibility after incomplete optical colonoscopy, became obvious. Since then, the number of referrals has constantly increased. Thus, CTC subsequently replaced the double-contrast enema for diagnostic colonic imaging at our department. Interest in CTC has also grown outside of academic centers, and CTC programs were initiated in several other hospitals and private imaging departments. At present, CTC is offered as a diagnostic modality by many radiological facilities all over the country, although widespread application is limited because of lack of financial reimbursement.

Research

Initial scientific work was based on mainly image reconstruction and interpretation modalities. The majority of these studies were performed on cadaver models. The initial work on image reconstruction was performed in a cadaver study by a working group at the Medical University of Innsbruck.[14] Comparing various CT scanning protocols in an explanted pig's colon with several artificial lesions, the authors concluded that the image quality and the reconstruction artifacts were affected less by pitch values than by beam collimation. Another group from the Medical University of Graz evaluated a very early stage of virtual dissection and computer-aided diagnostics in a cadaver model.[16] Virtual dissection was found to be feasible for CTC by overcoming the disadvantages of standard virtual endoscopic views. At the Medical University of Vienna, baseline work on spatial resolution and image interpretation was performed in anthropomorphic porcine models. The authors concluded that multidetector CTC also enables the detection of polyps less than or equal to 5 mm in size with high sensitivity and specificity and that additional 3D image tools improve the diagnostic accuracy even more, especially for detection of flat and small polyps.[17] Another study focused on interreader variability with different imaging methods. It showed a significant decrease of interreader variability when using 3D rather than 2D interpretation methods.[18] Currently, research on CTC is performed mainly at the Medical University of Vienna, with a focus on imaging modalities and computer-aided detection.[19,20] In a retrospective study on 52 symptomatic patients, computer-assisted

detection, used as a second reader, showed a significant improvement in sensitivity for polyp detection for nonexpert readers and a modest increase in reading time.[19] Further studies on computer-assisted detection are in progress. Focusing on different image display techniques for 3D CTC, so-called "advanced image displays" were evaluated in cooperation with the Klinikum Großhadern of the University of Munich. The main conclusion of this study was that advanced panoramic displays increase the amount of visualized mucosa and allow time-efficient unidirectional 3D evaluation of the colon.

Training and Education

After the incorporation of CTC into the academic and clinical workflow, we soon realized that dedicated training and expertise is a prerequisite, not only for performing CTC examinations, but also for correctly interpreting image data. At the same time, radiologists and technicians, in nonacademic centers and private radiological departments as well, were increasingly interested in learning this technique. Consequently, we established dedicated teaching courses at the Medical University of Vienna. This was achieved in cooperation with a commercial vendor who supported the CTC education program with hardware and software. The course is currently held in a dedicated teaching facility at the Medical University of Vienna, equipped with six CTC workstations. The first hands-on courses were held in 2003. To date (2010), the course has been held 22 times. Altogether, 220 radiologists have been trained. Presently, the course extends over 2 full days. The first section consists of lectures on background, indications, techniques, and evaluation strategies. The second section focuses on morphological criteria of normal anatomy and of colonic lesions and pseudolesions. Fifty validated CTC examinations of different pathologies are prepared for extensive, practical, hands-on training. Since 2006, another course has been held in Linz, by Gernot Böhm, in cooperation with another vendor.

Based on the local experience in teaching CTC, several review and teaching articles and book chapters were published, focusing on the interpretation of colonic lesions and pseudolesions.[21–26] To further support education in CTC apart from hands-on courses, the authors published a textbook on CTC in 2008, in German.[27] In addition, the authors are actively involved as tutors in dedicated international CTC teaching programs, such as the CTC course of the European Society of Gastrointestinal and Abdominal Radiology (Fig. 2.1), and in dedicated workshops of the International Cancer Imaging Society. To further improve CTC education, the local CTC workshop program is ongoing.

Distribution and Reimbursement

Austria has a high-standard public health insurance system. However, CTC, as a "relatively new" technique, is currently not generally reimbursed, as is also the case in some other

Fig. 2.1 Group photograph from the first ESGAR CTC course in 2003. From *left* to *right*, *lower row*: Stefaan Grijspeerdt, David Burling (in between Stefaan and Stuart), Stuart Taylor, Roger Frost, Jaap Stoker, Steve Halligan, Philippe Lefere, Wolfgang Luboldt, Robert Donderlinger (Chair ESGAR 2003), Andrea Laghi. *Upper row*: Yung Nio, Frans Vos (image processing), Jasper Florie, Rogier van Gelder

European countries, especially for screening purposes. CTC is generally accepted and is indicated and requested after incomplete optical colonoscopy and for evaluation of symptoms. However, although optical colonoscopy is accepted and reimbursed for screening of colorectal cancer, CTC is presently not accepted as a primary screening tool for colorectal cancer. If performed at academic, governmental, or general hospitals for research or for clinical indications, CTC examinations will generally be covered by the health insurance. Patients who request a CTC examination as a screening test or in nongovernmental, private medical facilities will usually have to pay for the additional costs of this examination. This prevents widespread application outside academic centers in smaller nonacademic hospitals or dedicated private imaging centers. Notably, double-contrast barium enemas are still reimbursed and accepted as a valuable method for colonic imaging.

Consequently, for clinical indications, such as incomplete colonoscopy or evaluation of symptoms, the majority of examinations are performed in general hospitals or in academic centers. In the authors' department, the main reason for referral is incomplete colonoscopy, contraindications of optical colonoscopy, or presurgical or postsurgical evaluation, as well as the evaluation of abdominal symptoms. The majority of patients are referred from the surgical or gastrointestinal department. Outside the public health system, CTC is offered as a screening test by different private hospitals, some of them operating at a high quality level and with a moderate examination frequency, with more than 1,000 screening CTC examinations per year.

CTC Consensus Statement of the Austrian Radiological Society and the Austrian Society of Gastroenterology and Hepatology

The Austrian Society of Radiology (ÖRG), the Austrian Society of Gastroenterology and Hepatology (ÖGGH) and the Austrian Society of Surgery (ÖGC) have jointly developed a consensus statement on indications and reporting of CTC which is currently being evaluated by both societies. In addition, the working group on gastrointestinal radiology of the ÖRG established recommendations on best practices for the CTC examination and evaluation technique, in accordance with the consensus statement of the European Society of Gastrointestinal Radiology. The aim was to provide structured guidelines for clinicians, advising them about which indications necessitate a referral for CTC, and for radiologists, informing them about best practices for performing CTC.

Conclusion

CTC has become a valuable diagnostic tool for the examination of the entire colon, replacing the double-contrast studies for colonic imaging. Accepted indications in Austria are incomplete colonoscopy, contraindications against optical colonoscopy, and evaluation of symptomatic patients or patients with suspected or known diseases – but primary screening with CTC still needs to be evaluated. Although CTC is available in many radiological facilities, widespread application is limited because of the lack of financial reimbursement.

Computed Tomographic Colonography: Implementation in Belgium

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Introduction

The authors discuss several aspects: history with an overview of the main publications in international literature, accepted indications, screening for colorectal cancer, and the issue of education.

History: The Enthusiasm for a New Technique

The authors started with computed tomographic colonography (CTC) in 1998. In that period CTC was still performed using a single-slice CT scan. Using a slice collimation of 5 mm and a reconstruction index of 3 mm, the acquisition of the entire abdomen was covered in only 60–70 s. Frequently, the supine and prone aspects were scanned with two acquisitions, respectively, with some overlap. They worked with dedicated CTC software needing manual path tracking to perform a 3D fly-through of the colon. Despite the single-slice technology, good 3D image quality was obtained using a radiation dose of 120 kV and 100 mAs. This resulted in adequate polyp detection with a sensitivity of 100% and 89% for lesions ≥1 cm and 6–9 mm, respectively.[28] Quite rapidly the authors focused on the important issue of preparation. In an attempt to improve both patient compliance and specificity for polyp detection, they developed a preparation method based on fecal tagging.[28] By the patient's drinking of positive-contrast material, the residual stool in the colon was labeled, facilitating the differentiation between true polypoid lesions and residual stool. Using a 2.1% barium suspension as sole tagging agent, they could demonstrate improved specificity for polyp detection: 88% for tagged data sets versus 77% for nontagged data sets. Although not deemed necessary by the international CTC community of experts at that time, fecal tagging is now used by the majority of centers and is considered the state-of-the-art preparation. This acceptance as essential part of the technique was achieved after the publication of the landmark study of Perry Pickhardt in 2003.[29] In that study, fecal tagging was part of the preparation. Gradually most experts agreed that fecal tagging is efficient. In that way, fecal tagging was applied in the major recently published trials.[30,31] Besides improving specificity for polyp detection, the authors conceived a method of reduced cathartic preparation with a colonic cleansing based on a reduced dose of Magnesium citrate.[28,32] This resulted in a significant improvement of patient compliance compared with patients prepared with a full dose of laxatives.

Further concentrating on the issue of patient compliance, the authors tried to decrease the volume of barium to drink. This was achieved by administering a 40% barium suspension.[33] Indeed, by increasing the concentration of the barium suspension, it was possible to obtain efficient tagging with a significant decrease of the barium volume to drink: The volume decreased from 750 to only 60 mL. This highly concentrated barium was used in the American College of Radiology Imaging Network 6664 trial.[30] The authors performed also considerable research in the field of laxative-free CTC.[34] The concern of patient comfort also played an important role in development of scanning the patient, in replacing the prone acquisition by an acquisition in left lateral decubitus.[35] This method is particularly useful when examining the elderly, frail, or obese patient. This enthusiasm for CTC was gradually taken over by other departments. At the Catholic University of Leuven, the technique also gained importance. This was underscored in the publication of some important studies and in the development of a proprietary computer-assisted detection (CAD) system. In an early study, Thomeer et al.[36] focused on the importance of issues related to patient compliance. Besides the importance of fecal tagging, they concluded that CTC was more attractive for the patient compared with optical colonoscopy because of the faster CTC procedure, the lower physical challenge, and the lack of sedation.[36] In another study, Thomeer et al.[37] demonstrated the important influence of the CTC learning curve on the results of polyp detection. In this study of 150 patients, polyp detection significantly improved between the first and the last group of 75 patients: Sensitivity improved from 50% to 90% for polyps >9 mm. Besides work on magnetic resonance colonography,[38] Bielen et al. also worked on developing a laxative-free CTC method using iodinated contrast as tagging agent.[39]

Important research on CAD CTC was developed by Kiss, Van Cleynenbreugel, et al.[40] Using a combination of surface normal and sphere fitting methods to distinguish polyps from normal colonic wall, they were able to obtain promising results and could demonstrate the usefulness of CAD in CTC. In the meantime, several centers in Belgium started CTC, and at the time of writing this text, the technique is available in most radiological departments of the country. This enthusiasm for CTC has been confirmed by the participation of numerous Belgian radiologists in the CTC workshops held by the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) (Fig. 2.1), with more participations than larger countries, such as Germany, France, and Spain.

Current Status: The Period of Validation

Although accepted by the Ministry of Social Security and Health as an examination, there is no official coding for CTC in Belgium. A committee has been started to solve this issue. Currently CTC is accepted as indication after incomplete optical colonoscopy by both the gastrointestinal and the radiological community. At this moment there is no acceptance of CTC as a screening tool for colorectal cancer. Population screening for colorectal cancer does not depends on only the performance of the examination used. Indeed, the main criteria for acceptance as a screening tool are defined by cost-effectiveness. In a Health Technology Assessment of December 2006, the Federaal Kenniscentrum voor de Gezondheidszorg,[41] an independent multidisciplinary center of experts in public health, concluded that only a fecal occult blood test (FOBT) could be considered a valuable test for CRC screening:

> This [Health Technology Assessment] report shows that CRC screening using a biennial guiac FOBT screening followed by colonoscopy in case of a positive FOBT in individuals aged 50 years and older (exact age range to be defined) can be a cost-effective mass screening program when properly organised. Therefore, we recommend introducing such a screening program in Belgium. However, before such a program can be successfully implemented, a series of key issues need to be addressed and resolved. We recommend the implementation of a few pilot screening programs to investigate these issues. A political decision on whether to implement a CRC screening program can be made based on the existing information to date in consultation with the competent authorities on the federal and regional levels and in collaboration with the stakeholders. This decision should also address organizational issues including quality control and setting up a screening registry, the scope of the screening such as age groups to be included, target goals such as minimal participation and compliance rates, the timeframe for full implementation (presumably within two to four years, allowing the pilot projects to deliver the necessary information), and the funding of CRC screening. …
>
> Together with this process, a screening management organization should be defined and implemented, preferably not only for CRC screening but conjointly for different mass screening programs, and international (European) cooperation might be considered. This screening management organization should also take care of the indispensable quality assurance and organize the most cost-efficient way to deliver FOBT screening. Whether this screening management organization would be located at the federal or at the community level is a political decision. To address the uncertainties surrounding the implementation of a FOBT based screening program we recommend the implementation of a few pilot screening programs. We estimate that these pilot programs should run for two to four years with intermediate evaluations. Those pilot programs should address and test the design of the program, the organisation and implementation of a screening registry, negotiations with suppliers on the price of test kits to be used in a screening program, and the colonoscopy capacity as well as quality assurance. The pilot programs should also specifically address the following uncertainty issues: participation rates, compliance and acceptance of the screening program in Belgium, prevalence of increased CRC risk, positivity rates and sensitivity/specificity of FOBT in real world circumstances, CRC and adenoma detection rates. A first report should be ready soon.

What about the gastrointestinal community? At this moment there is no official statement on CTC by the gastrointestinal community. In the monthly journal *Acta Gastroenterologica Belgica*, the last published paper on CTC goes back to 2005 in a report of the Belgian Consensus Meeting on Colorectal Cancer Screening.[42] In a recent publication by Professor Urbain, head of the gastroenterology department of the University Hospitals of Brussels, it was concluded that CTC is inefficient unless performed and interpreted by experienced "hyper-performing" CTC teams and that currently not all radiologists are motivated enough.[43]

The Future: Need for Structured Education

The article by Urbain[43] underscores the need for CTC education. In 2005 the authors were able to edit a book on virtual colonoscopy. This book was the result of an international collaboration, with the contribution of numerous CTC experts from all over the world. Recently the second edition was released.[44] Indeed, despite a large interest in the ESGAR CTC workshops (Fig. 2.1), there is currently no official or accredited CTC education. CTC is not included in the education of radiology residents. To meet this need for CTC education, the authors started the Virtual Colonoscopy Teaching Centre in 2006 (VCTC; www.vctc.eu). To our knowledge this is the first private initiative in the world to promote CTC and to offer structured education. Four times a year the VCTC organizes a CTC workshop in both Dutch and French languages for Belgian radiologists. These workshops are organized in collaboration with the Catholic University of Leuven (D. Bielen). They are dedicated to small groups (a maximum of ten participants) of radiologists and focus on the interpretation of cases with discussion of practical and imaging aspects of the technique. In this way they can be considered an additional and different approach compared with the technique of the ESGAR CTC workshops.

Besides the workshops, the VCTC provides structured CTC education based on teleradiology. Several approaches are considered. Besides second reads, the main activity of the VCTC focuses on remote education in several steps: theoretical introduction with a web-based CTC course and supervision of 75 CTC examinations performed by the novice department with technical and interpretational advice, followed by a test of 20 cases. In this test, the novice radiologist has to obtain a sensitivity and specificity of >80% for lesions >6 mm. This educational activity is officially recognized by the Belgian health authorities and receives continuing medical education credits. The first results are encouraging and are being presented at major international meetings.[45,46] So far, 15 VCTCs have been or are being educated. The centers are also active outside of Belgium.

It is clear that work should be done to educate radiology residents on a regular and structured basis. This can be done

only with the support of the universities from both languages (Dutch and French) of the country. This would be the first step toward an efficient implementation of the technique. Only at that moment will both the authorities and the gastrointestinal community start considering CTC as a useful, efficient, and ultimately invaluable technique when screening the colon for colorectal cancer.

Conclusion

Started in 1998 in Belgium, the technique has since developed considerably and is now performed by many centers throughout the country. There is an obvious need for structured education to achieve widespread implementation of CTC. Only at that moment will good performance be obtained on a large scale, and CTC will establish itself as an invaluable technique accepted by the medical community.

Implementation of Computed Tomographic Colonography in Canada

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Introduction

Canada is in close geographic proximity to the United States – however, the course of computed tomographic colonography (CTC) implementation in the two neighbors has been very different. This can be explained in part by the disparity in how the health care systems are funded and in turn how that influences funding for CTC.

Although Canadian radiologists at academic centers have been involved in CTC since its inception, we have been slower to obtain widespread acceptance amongst the radiological and gastroenterological community at large. We could speculate that this may be due in part to lack of a Canadian multi-institutional study looking at CTC performance. This may have helped at the political level to obtain credence; however, there is no dearth of studies that have emerged in the US and elsewhere within the radiological literature that makes such a study redundant at this point in time.

It would be more appropriate at this point to address the growing concerns leveled at CTC in the wider radiological community with regard to radiation burden imposed on a screening population. Despite ample data showing its greater acceptability to a patient population as well as cost-effectiveness compared with some of the other methods of screening, there are still misconceptions that need to be addressed. There are also manpower and training considerations, within both the radiological and gastroenterological communities.

This contribution aims to put CTC in the context of colorectal screening in Canada at large and put into perspective our current role as well as future aims and aspirations.

Canadian Health Care System

The Canadian health care system (also known as Medicare) was set up in 1966 and is designed to ensure that all residents have reasonable access to medically necessary hospital and physician services on a prepaid basis without direct charge at the point of service.

There is no single national plan; instead there are 13 interlocking provincial and territorial health insurance plans, all

of which share some common features and basic standards of coverage. The roles and responsibilities for the health care system are shared between the federal and provincial territorial governments. In order to receive its full share of funding from the federal government, each province or territory must show compliance with criteria laid out in the Canada Health Act (CHA).[47] As health care is administered at the provincial level in Canada, this can create dissent with the federal government, whose interest it is to promote uniformity and universal standards of health care across the country. Both impact policymaking, although the provincial governments are required by fiscal controls to have federal input.

The CHA states that the primary objective of the health care policy is to "protect, promote and restore the physical and mental health being of residents of Canada and to facilitate reasonable access to health services." There are therefore five components to the health care system: comprehensive coverage of a menu of services, universal care, portability (such that citizens have access to the services anywhere in Canada, even when temporarily absent from their own province), public administration (government control), and, finally, accessibility. Accessibility is defined as freedom from financial or other barriers and stipulates that this specifically discourages private payment by patients either through user charges or through extra billing for services covered under provincial health care insurance plans.

With the exception of native Canadians who are funded directly by the federal government, the CHA guarantees health care that is funded by the provincial government.

Income tax provides the major source of revenue for Medicare in most provinces, with three of the provinces levying an additional fixed monthly premium, which may be waived for those in low-income situations. There are no deductibles on basic health care, and co-pays are also negligible or nonexistent. Typically excluded are dental and pharmaceutical costs, but there is considerable individual variation across the provinces and territories in terms of coverage for services such as long-term care, ambulances, and out-of-hospital prescription medication.

In addition, there are a few private clinics in Canada that provide diagnostic and surgical services. The number of private diagnostic imaging clinics has risen steadily in recent years in Canada, with a growth of 74% between 2001 and 2005, or an average annual increase of 15%.[48–50] The term "private," however, is a misnomer, as most of these clinics are in fact publicly funded but are simply situated in private facilities and therefore are still within the umbrella of the Medicare system.

In reality, Medicare covered approximately 70% of health care costs across Canada in 2009. Although public monies fund the system, health services are provided by the private sector. An estimated 65% of Canadians have additional private health insurance, often received as an employee benefit.

Funding for Physicians and Radiological Equipment

All doctors are independent practitioners (with the ability to incorporate) and bill the government directly on a fee-per-service basis. This fee is usually locally determined after negotiations between the provincial government and provincial medical associations. Diagnostic imaging equipment is hospital based and paid for by hospital budgets. A recent federal transfer of funds to the provinces was earmarked to upgrade imaging equipment infrastructure and resulted in a much needed boost to this area. The numbers of CT scanners in Canada as of 2007 increased to 419 from a baseline of 325 scanners in 2003. Canada therefore falls below the median determined by the Organisation for Economic Co-operation and Development of 15 CT scanners per million population in 2005. As per the most recent available data, Canada has 12 CT scanners per million population.[48] The rapid increase in the number of new installations means that Canadians have benefited from the advent of newer technology, with 64-slice scanners representing more than 70% of the new installations (Fig. 2.2).

With regard to CT, the numbers of exams per 1,000 of the population in the United States was almost twice that in Canada. However, the numbers of scans performed per scanner was almost 46% higher in Canada than in the United States. The data indicate that even though the United States has more scanners per million of the populations than Canada, the scanners are used more intensively in Canada. In contrast to the United States, very few CT scanners are installed in free-standing (i.e., private) facilities. Only four provinces (Quebec, Ontario, Alberta, and British Columbia) have privately funded CT scanning facilities. As of January 2007 only 5% of all CT scanners were in private facilities (compared with 3% in 2003).

Epidemiological Importance of Colorectal Cancer in Canada

Colorectal cancer (CRC) is the most common cause of cancer-related death in nonsmokers in Canada.[51] Each year, approximately 21,500 Canadians are diagnosed with colorectal cancer, with 90% of the cases occurring in the over-50 age category. An estimated 4,800 Canadian men and 4,100 Canadian women die each year from the disease.

Ontario has one of the highest incidences of colorectal cancer in the world, exceeding all 50 U.S. states for both genders[52] and exceeded by only New Zealand and the Czech Republic. There were 8,000 new cases diagnosed in the province alone during 2008 (Canadian Cancer Society

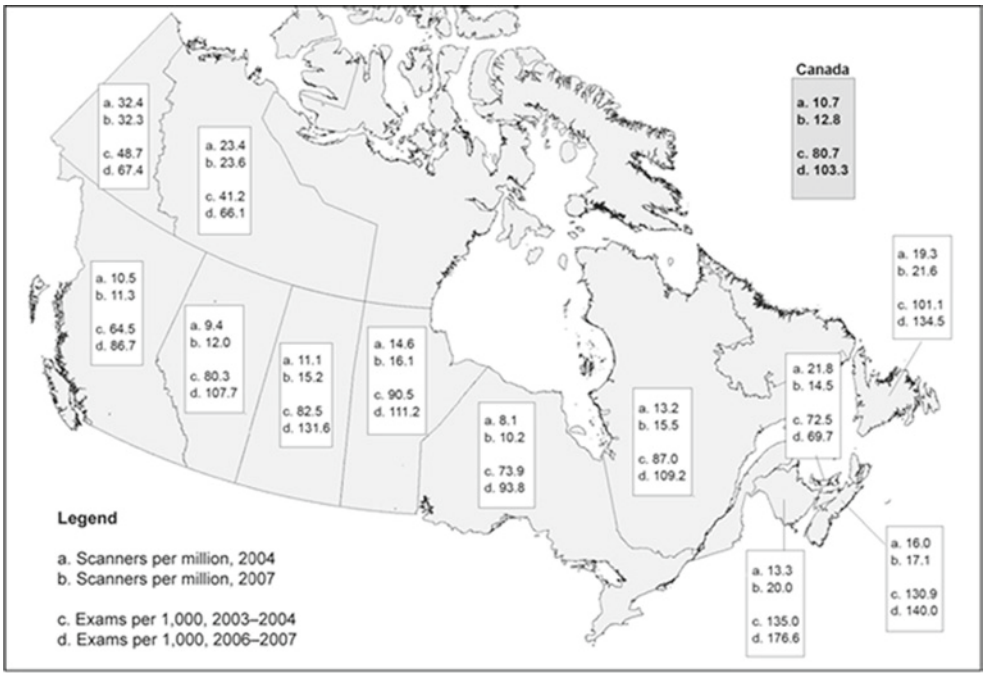

Fig. 2.2 Computed tomography (CT) scanners per million provincial populations and exams per 1,000 provincial population, 2004 and 2007 (Figure reproduced from National Survey of Selected Medical Imaging Equipment, Canadian Institute for Health Information. With permission)

statistics, 2008). In Ontario alone, an estimated 7,800 people (total population >13 million) were diagnosed with colon cancer in 2007, with 3,250 dying in the same year).

In the 15- to 29-year age group, the incidence is around 0.3% or 20–30 cases per year; however, the incidence in this age category has been steadily rising. Since 1992 there has been a rise of 5.6% on average per annum in the adolescent/young adult age group.

There are approximately 44 cases per 100,000 for women and 64 cases per 100,000 for men (Fig. 2.3).

Screening Initiatives Canada Guidelines

The Canadian Task Force on Preventive Health Care in 2001 and the Canadian Association of Gastroenterology/Canadian Digestive Health Foundation in 2004 have released guidelines in Canada in respect to CRC screening.[53] The Canadian Task Force on Preventive Health Care is an independent panel funded through a partnership of the federal and provincial/territorial governments, and their statements are based on the technical report *Preventive Health Care, 2001 Update: Screening Strategies for Colorectal Cancer.* It recommends that average risk asymptomatic individuals over the age of 50 undergo annual or biennial fecal occult blood testing (FOBT). It concluded that there was fair evidence for flexible sigmoidoscopy in this category of individuals but deemed that there was insufficient evidence about whether one or both tests should be performed. It also concludes that there is insufficient evidence to include optical colonoscopy as an initial screening tool in the asymptomatic average risk category.

The Canadian Association of Gastroenterology issued Guidelines on Colon Cancer Screening in 2004 whose summary appears below for both average and high-risk patients[54]:

- FOBT every 2 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy combined with FOBT every 5 years
- Double contrast barium enema every 5 years
- Colonoscopy every 10 years

Screening of Individuals at Higher Risk

Colonoscopy is the recommended screening test for high-risk patients with the following indications:

- A first-degree relative with the disease diagnosed before age 60 (colonoscopy every 5 years to begin at age 40, or 10 years earlier than the youngest diagnosis of polyp or cancer in the family; if diagnosed after the age of 60, then employ average risk screening to begin at age 40)
- A family history that suggests a genetic abnormality capable of causing the disease, such as hereditary non-polyposis colorectal cancer (colonoscopy every 1 or 2 years beginning at age 20, or 10 years younger than the earliest case in the family)
- Familial adenomatous polyposis (sigmoidoscopy annually to begin at ages 10–12 years)

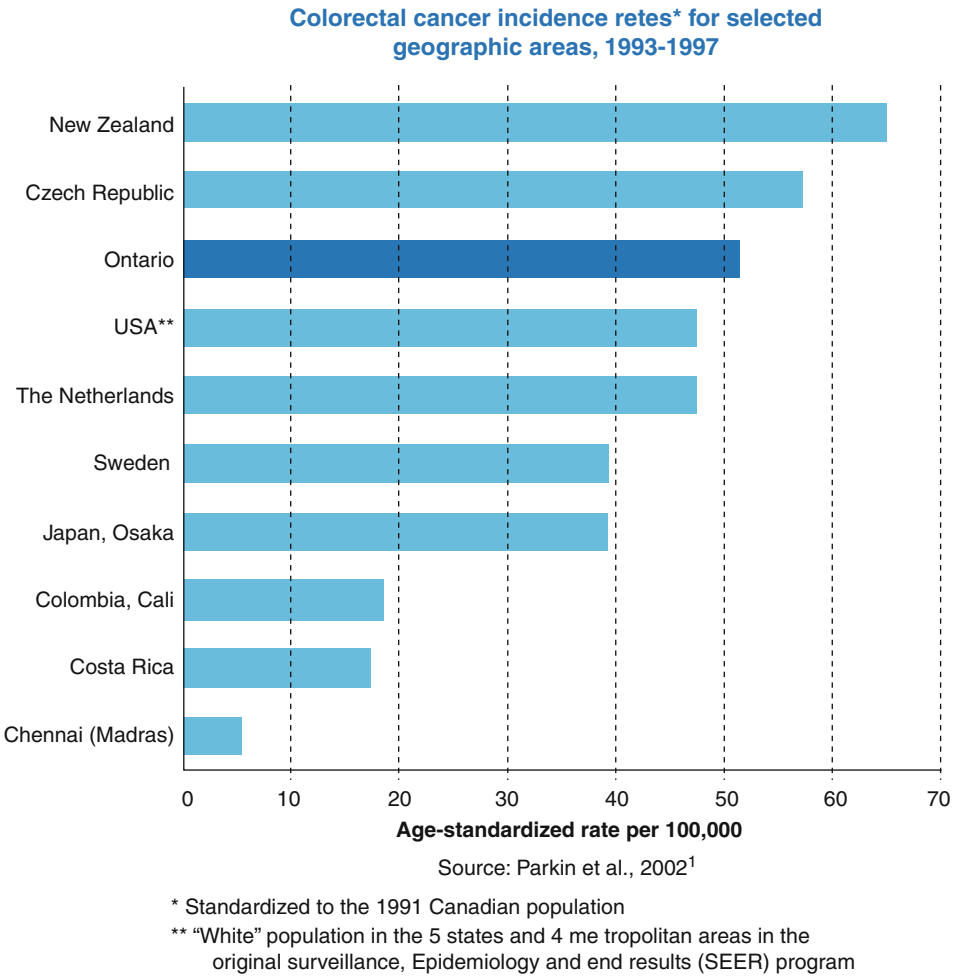

Fig. 2.3 Colorectal cancer incidence rates for selected geographic areas, 1993–1997 (From Cancer Care Ontario and the Canadian Cancer Society. Insight on Cancer, News and Information on Colorectal Cancer. Toronto: Canadian Cancer Society (Ontario Division). With permission)

- Long-standing colonic inflammatory bowel disease, such as Crohn's or ulcerative colitis (for pancolitis, i.e., colitis that involves the entire colon, begin screening at 8 years after onset of disease, continue with colonoscopy every 3 years in the second decade, colonoscopy every 2 years in the third decade, and colonoscopy every year in the fourth decade; for left-sided colitis, begin screening at 15 years after onset)

Due to the layout of Medicare, implementation of population-based screening for colorectal cancer has not occurred as a uniform rollout across the country. The majority of provinces and territories have now made commitments to establishing organized colorectal cancer screening programs, in hopes of increasing compliance rates. There are thus multiple provincial initiatives that will be briefly discussed.

Ontario

In January 2007 the Ontario Ministry of Health and Long-Term Care (OHLTC) in collaboration with Cancer Care Ontario (the provincial cancer agency) launched the first of the population-based CRC screening programs in Canada. [55–57] This is a two-stage program with the primary aims of increasing uptake amongst the screening population and. in the long term, reducing CRC mortality. The government is investing C$193 million over 5 years in an FOBT-based program aimed at the 50+ age group in the population.

High-risk individuals (those with family or personal histories of polyps or colon cancer and inflammatory bowel disease) are being triaged directly to optical colonoscopy. There is funding for approximately 100,000 additional colonoscopies over the 5-year period. Average risk asymptomatic patients positive for fecal occult blood will be referred to optical colonoscopy, whilst those who are negative will be screened by FOBT every 2 years. Additional components of the program include a public awareness campaign, a single provincial lab for FOBT analysis, a central registry to tabulate participation and results, and easy access to the kits for primary care practitioners.

Manitoba and Alberta

At the time of writing, Manitoba and Alberta were the only other two provinces besides Ontario with CRC screening

programs. Both of these provinces are targeting a similar audience as Ontario, including average risk individuals in the 50–74 year age group.

In Alberta the health care region has recognized the inadequacy of current endoscopic provision by opening a dedicated center for colorectal screening in 2008. In addition to increasing endoscopic capacity by 50%, it is offering alternative methods of screening such as virtual colonoscopy and fecal immunochemical test (FIT). Alberta has the highest gross domestic product and economic growth of any region in Canada, and its CRC screening program is being funded by Alberta Health and Wellness and coordinated with the Alberta Cancer Board. It is being implemented from 2007 to 2012, with the goal of screening 67% of the target population within 5 years. There has been an additional cash injection of C$500 million from the Alberta Cancer Prevention legacy fund to kick-start an intensive education campaign to increase awareness and encourage participation.

The Manitoba screening project aims to emulate the model initiated in the United Kingdom. A pilot commenced in 2007 and sent FOBT kits to 10% of the screening population between 50 and 74 years of age of average risk. An additional 5,000 kits were distributed to women in the breast cancer–screening program. The pilot was intended to assess the practical issues and capacity of the system to assimilate the FOBT-positive referrals to colonoscopy.

Saskatewan, Quebec, and British Columbia

Saskatchewan has a pilot with FIT-based screening, and Nova Scotia launched a pilot FIT-based program in spring 2009, to be continued through 2011. Quebec is still putting together plans for its provincial screening strategy. The British Columbia FIT-based pilot was launched in Penticton in January 2009.

Remaining Provincial Initiatives

Newfoundland, Labrador, and Prince Edward Island have pilots in place, but as an interim measure are offering CRC screening on an ad hoc basis. New Brunswick aims to start a pilot project in 2010–2011 to run for 3 years.

Uptake for Screening Across Canada

In Canada as a whole, less than 15% of individuals over the age of 50 get an FOBT screen (Fig. 2.4).[58–60]

There are provincial strategies to increase adherence, and many provinces are now tracking participation and making

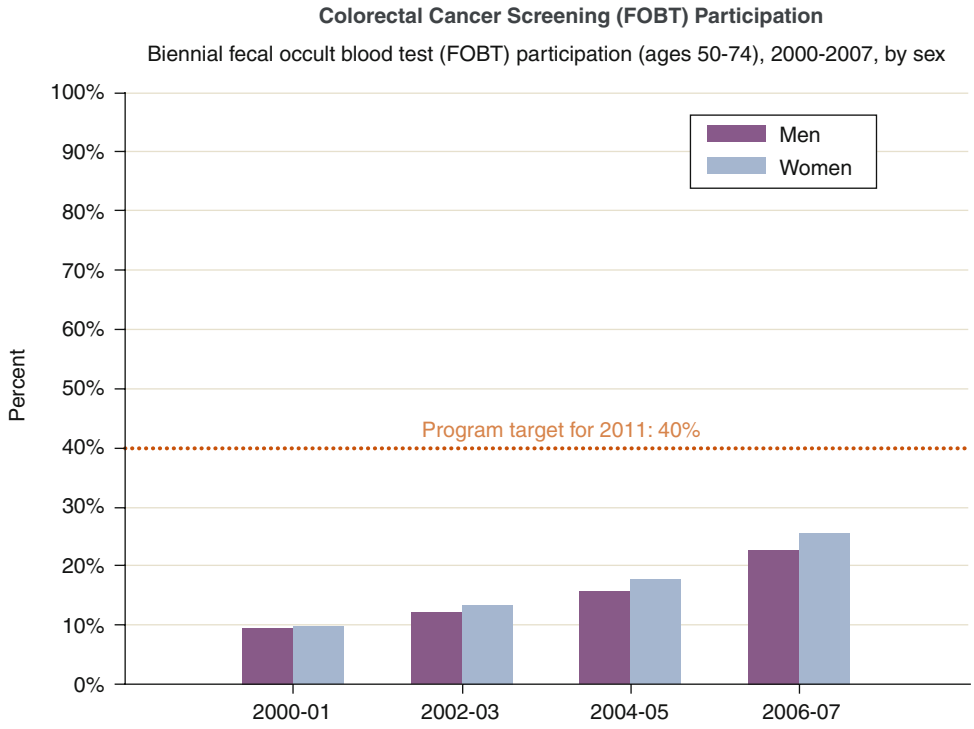

Fig. 2.4 FOBT participation by sex across Canada (Reproduced from Cancer Care Ontario. With permission)

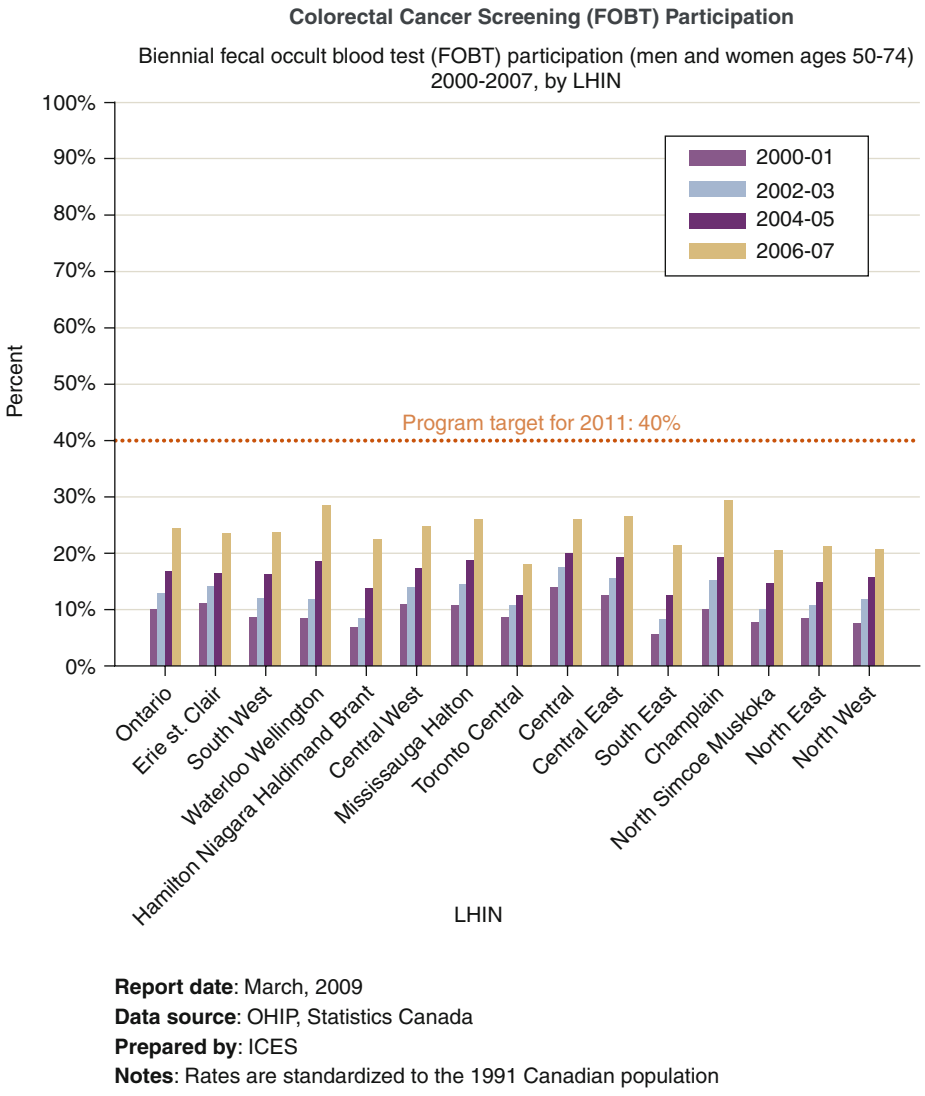

Fig. 2.5 Colorectal screening participation subdivided by Local Health Integration Network (Reproduced from Cancer Care Ontario. With permission)

these statistics available for public consumption. The most recent data for Ontario show a gradual increase in the numbers of screened individuals to 24% in 2006–2007. This reflected a 30% increase over the previous period but still below the target of 40% uptake set by the ColonCancerCheck initiative of the province. These uptake rates compare unfavorably with other countries – for instance, Australia achieved 45% participation among its invited population in its initial round of screening. In the United States, the Veterans Administration screened about 75% of its plan members for colorectal cancer, of whom 90% were screened by FOBT (Fig. 2.5).

Inclusion of CTC in the Screening Guidelines for CRC

To date no published Canadian guidelines recommend CTC for screening of asymptomatic adults at average risk of developing CRC. The Canadian Agency for Drugs and Technologies in Health (CADTH) and the Ontario Health and Technology Assessment Centre (OHTAC) are both evidence-based agencies used to aid policymaking with regard to effectiveness of pharmaceutical and new health technologies. They independently issued technology reports on CTC in December 2008 and September 2009, respectively.

The CADTH[62] expressed concern with regard to the clinical utility and impact of CTC on population-based screening as compared with other screening tests. They performed an economic evaluation comparing CTC with colonoscopy and found CRC screening with CTC to be more costly and less effective compared with colonoscopy. Depending on which screening method was adopted, the CADTH estimated that if the entire current screen-eligible population participated in colorectal screening, the numbers of available gastroenterologists in Canada would need to increase 12-fold compared with the current provision. If CTC were adopted as the primary screening strategy, there would be a need for five times the number of current radiologists practicing in Canada. The referrals from CTC to OC would require two and a half times

the current number of gastroenterologists to effectively implement a joint strategy of CTC/OC.

The economic evaluation was an incremental cost utility analysis comparing CTC with the most widely utilized CRC screening strategies (OC and FOBT) with no screening in average risk patients. The modalities were rank ordered by cost and outcomes evaluated included costs, quality adjusted life years (QALYs), life years gained, number of cancers and cancer deaths, and the cost per QALY gained.

The review concluded that CTC was on a par with OC for evaluation of polyps larger than 5 mm but that colonoscopy outperformed CTC for diminutive polyps (<5 mm).

In addition it speculated that CTC would have to have an adherence rate of 90% or greater to be equal to or superior to colonoscopy.

Ontario Health and Technology Assessment Centre Recommendations

The OHTAC issued a comprehensive report on screening methods for detection of colorectal cancers and polyps.[61–66] It distinguished between population-based screening and opportunistic screening. FOBT was the only recommended modality for population-based screening in asymptomatic average risk individuals over the age of 50, as it was felt to be the only modality for which evidence existed for a reduction in colon cancer mortality. For opportunistic screening, the OHTAC recommended that colonoscopy, flexible sigmoidoscopy, or FOBT could be utilized in asymptomatic average risk individuals over the age of 50. It suggested however that colonoscopy when performed every 5–10 years led to a significant improvement in detection rates for polyps and cancers compared with FOBT.

CTC and magnetic resonance colonography were recommended for patients who have had an incomplete colonoscopy or where performing a colonoscopy is technically infeasible or medically contraindicated.

When specifically comparing optical colonoscopy with CTC, the OHTAC report expressed concerns with regard to "significantly increased costs associated with colonography, radiation exposure to ionizing radiation (especially in the context of increasing cumulative lifetime exposure to multiple radiation emitting diagnostic tests) and increased burden on existing CT and MRI machines in Ontario which are already operating at a high capacity."[3]

Implementation of CTC in Canada

Canadian radiologists have been involved in performing CTC since its inception in 1994. The rollout occurred predominantly at the academic level in significant numbers, although many community radiologists also perform CTC to a high standard.

The more widespread dissemination of CTC has and will remain a unique challenge in the Canadian radiological community. This is a multifactorial issue. Geographically, Canada is a vast country, and the distribution of radiologists is by no means uniform. Many radiologists in the community work single-handedly in practice, and this can make adoption and widespread dissemination of a new technology challenging. In this setting, building up a high-volume service of CTC can be difficult when radiologists are servicing large communities and offering multiple general radiological skills and modalities.

At present the substantial numbers of barium enema examinations performed in the provinces are in some part due to the lack of CT scanner availability in private practice, imposing constraints on service delivery in the private practice setting. The data for Ontario alone (see Fig. 2.6) show how the numbers of barium enemas in the province have declined over the last decade but still remain at a sizable number.[67–71]

As in many communities that are embracing CTC, there will be a period of overlap when there are still insufficient numbers of radiologists who are fully versed in the newer technology such that barium enemas are replaced entirely. This issue is being addressed at multiple levels. The board examination for diagnostic radiology in Canada does not at present have a mandatory requirement for training in CTC; however, this is under review and is anticipated to change in the very near future. As a preemptive measure, the Canadian Association of Radiologists (CAR) is embarking on training in this area, aimed specifically at residents and community radiologists.

Not only is it important to receive adequate training in CTC, but for historical reasons we recognize that maintaining credibility can occur only if new recruits to this technology practice the technique to a high standard and routinely employ mechanisms such as audit to maintain those standards.

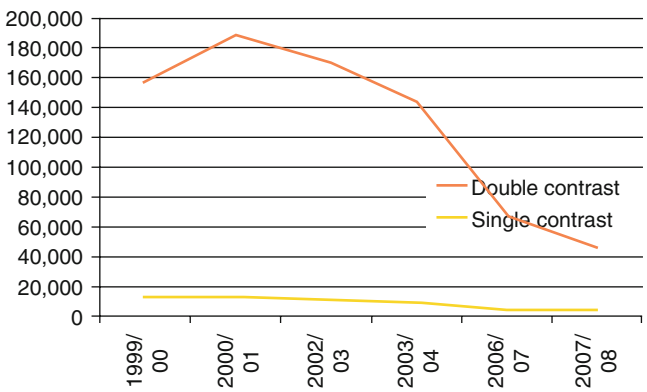

Fig. 2.6 Numbers of barium enema examinations performed in the province of Ontario between 1999 and 2007 (Data as per personal communication from the Ontario Medical Association)

Interface with Gastroenterology in Canada

As radiologists practicing CTC, we know from the results of multiple trials that CTC is a credible alternative to diagnostic OC. FOBT is a relatively inexpensive test and has been proven to reduce mortality in those screened by between 24% and 39%.[72–74] Moreover, we recognize that FOBT as a screening tool is flawed. Of the 2% of screening FOBT exams that are positive, only 20% will have an intermediate adenoma, an advanced adenoma, or carcinoma, and up to 80% of subsequent colonoscopies will be negative. The opportunity for CTC to circumvent a technique that will result in unnecessary polypectomies is an attractive one. OC is not without its risks and complications, and we are currently lobbying the Ministry of Health and Cancer Care Ontario to receive appropriate recognition.

Uptake statistics for FOBT remain dismal. Quoted rates range from 5% in Newfoundland to about 13% of the eligible population in Ontario, British Columbia, and Saskatchewan.

There is a relative shortage of gastroenterologists in Canada. Most recent statistics show 1.8 gastroenterologists per 100,000 population in Canada compared with 3.9 in the United States, 3.48 in France, 2.1 in Australia, and 1.4 in the United Kingdom. There is a higher prevalence of the over-55 age group, and up to a third are anticipated to retire in the next decade.[77] Data show that gastroenterologists perform only 35% of total optical colonoscopy procedures. Surgeons perform up to 45%, with family physicians and other internists performing the rest.[75]

The Canadian Association of Gastroenterology (CAG) has published a Canadian consensus on medically acceptable wait times and has set benchmarks that recommend that a colonoscopy be completed within 2 months for those with a positive FOBT and 6 months for a screening colonoscopy. These benchmarks ("Canadian Consensus on Medically Acceptable Wait Times for Digestive Health Care") were published in the *Canadian Journal of Gastroenterology* in 2006. ColonCancerCheck's program guidelines (adapted from the CAG benchmarks) are 8 weeks for those with a positive FOBT and 26 weeks for those with a family history of colorectal cancer. Mirroring trends elsewhere, the current wait list for OC in the setting of a positive FOBT far exceeds the recommended CAG targets. In a recently published study, the average wait time (Fig. 2.7) was 229 days, and 78.6% of the patients did not meet the expected target.

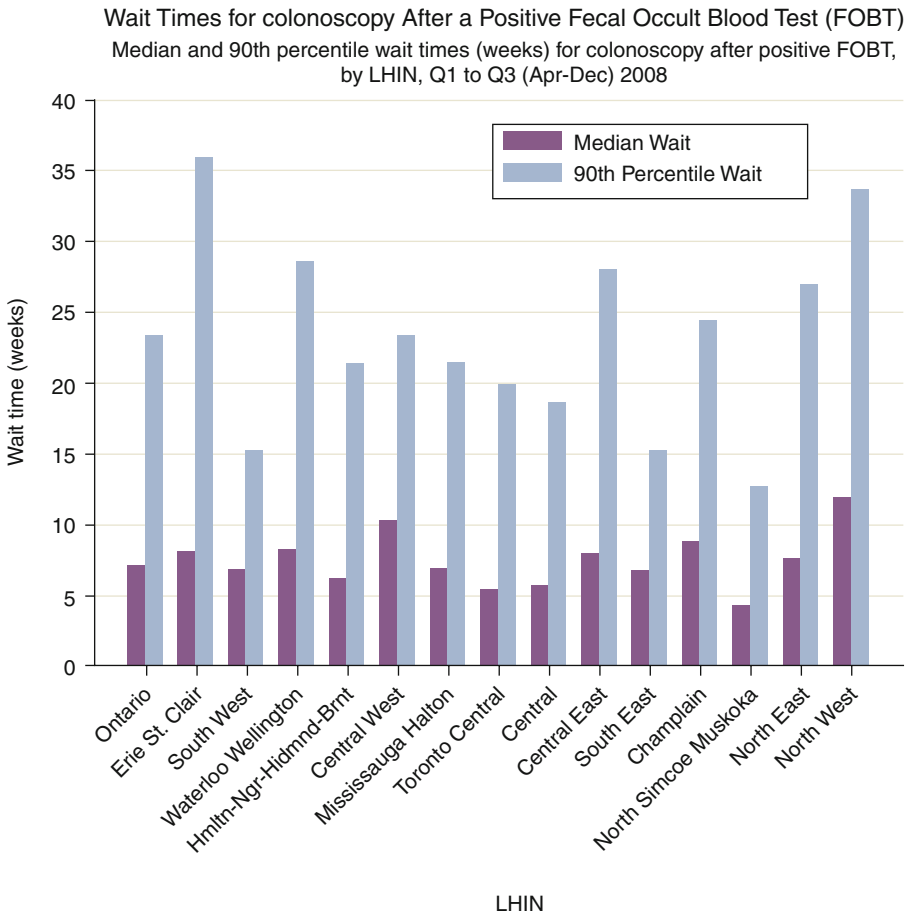

Fig. 2.7 Average waiting times for colonoscopy

As an interim measure, nurse-led flexible sigmoidoscopy[76] was introduced to diminish the wait for those on a long OC wait list. This procedure was sited at a colonoscopy hub with a 10–15% referral rate on to optical colonoscopy. The most current wait times published by the Cancer Care Ontario website, however, show that those for colonoscopy after positive FOBT are decreasing and that median wait times are steady.

Current median wait times in Ontario are at 7.1 weeks for colonoscopy following positive results for fecal occult blood. The 90th percentile wait times are, however, much longer, with an average of 23.3 weeks in Ontario (range 12.8–35.9 weeks).

We face our own challenges in terms of patient acceptance and obtaining gastroenterologist buy-in for same-day OC in those patients whose CTC yields significant positive findings. There remains concern within the radiology community about our ability to cope with increased numbers of CTC if there is an opportunity to be part of the armamentarium of population screening tests.

Reimbursement

Other than in Quebec, where there is a specific fee code for reimbursement of CTC, the procedure specifically is not part of the schedule of medical benefits in any province in Canada. It is, however, usually compensated at the standard rate for a CT of the abdomen and pelvis. An additional 3D interpretation fee in part reimburses for the additional time incurred in reading these studies as compared with a routine abdominal CT.

Current Clinical Status of Computed Tomographic Colonography

The CTC Program at the Joint Department of Medical Imaging in Toronto

The Joint Department of Medical Imaging is the largest medical imaging department in Canada and has a multisite practice encompassing the Toronto General Hospital, Toronto Western Hospital, Mount Sinai Hospital, Princess Margaret Hospital, and the Women's College Hospitals. It is affiliated with the University of Toronto and is the largest residency and fellowship program in Canada. Although there are gastroenterology services at all sites, we have centralized our CTC program at Mount Sinai to maintain expertise and streamline patient referrals.

The hospitals are centered in the downtown core of the Greater Toronto area (GTA). The GTA is the eighth largest metropolitan area (population 5.5 million) in North America and covers 7,125 km^2. The majority of our examinations are drawn from the GTA population, with a minority of our referrals originating elsewhere in the province due to our reputation.

Our program has been in place since 2000. Since 2005, the Joint Department of Medical Imaging at the University of Toronto has been performing CTC on an average of four lists per week. We have performed over 4,500 studies in that time period. The majority of our referrals have had remote incomplete colonoscopy (33%) – however, an increasing number of patients are referred due to background medical contraindications (22%) or because they have self-selected to undergo CTC as their primary screening method.

We also offer a same-day service for failed OC performed by in-house clinicians at any of the four main hospital sites that we serve. Our experience in obtaining same-day OC correlation for patients with significant positive findings at the time of CTC has been less favorable. A constraint on the gastroenterology waiting list (discussed above) and demands for urgent inpatient and emergency work have resulted in many of our positive referrals having no immediate OC feedback. Our referral rate to OC has been around 8%. Our other findings compare with other major screening programs and are as follows:

Category	Percent
Polyps 6–9 mm	7
Polyps >1 cm	5.6
Neoplasia	3.5
Significant extracolonic findings	11

We have highly trained technologists who are fully versed in the technique of CTC and rely on radiologist input for safety issues and problem solving. They are trained in administering hyoscine (Buscopan®) when necessary and provided there are no medical contraindications. Our technologists have led workshops in training other radiological technologists to perform CTC.

At the local level we have been heavily involved in educating other radiologists and disseminating the technique into the wider community. We have run workshops both alone and with organizations such as the CAR and the Ontario Association of Radiologists. The CAR is making attempts to provide local training at the provincial level by having a regional workshop in each province that is supported by local expertise.

Our Advanced Imaging Education Centre has also trained radiologists at the national level but is aiming to address the deficiency in CTC training at the resident level by offering the courses to residents routinely in their third and fourth years of training. As yet CTC training is not a requisite of the Royal College of Physicians examination at the end of the residency program, but this oversight seems to be the next logical target for improvement.

In British Columbia the Innovation Fund helped to shorten the 2-year-long waiting list for conventional colonoscopy

and provided the additional impetus to create a high-volume CTC service as well as comparing diagnostic performance by the two techniques. Enrollment for this project was completed in March 2008[78]; 2,005 patients were recruited over a 12-month period.

The mean age of participants was 62 years and the patients were equally recruited from the screening and symptomatic population groups. Some of the screening patients had waited up to 2 years for their test. In 1,462 patients CTC completely obviated the need for subsequent OC. Of the 430 definite or equivocal lesions seen on CT and subsequently investigated, 327 (76%) were found to be true positives. Of the 387 definite calls, 305 (78.8%) were true positives and 43 were equivocal on imaging, and of these 22(51.1%) were true positives. In terms of significant extracolonic findings, 175 (7%) were recommended for further work-up.

Future Directions

This is an exciting time for the radiological community in Canada with regard to the widespread dissemination of CTC. The numbers of radiologists who have embraced this technique by performing examinations and attending formal workshops continues to grow daily.

The CAR has acknowledged this interest and the need for formalization of training and performance standards by issuing a standards document[79] in collaboration with counterparts in the United Kingdom, Europe, Korea, and Australia. This comprehensive document provides guidance to those considering embarking on CTC as well as providing minimum standards for those who are already involved in performing and interpreting CTC. At the political level, although we do not face the reimbursement issues of our American counterparts, we are facing equivalent criticisms leveled at CTC with regard to performance in detecting flat polyps. In the wider radiological community, the issue of radiation has also come to the forefront and will remain one of our biggest issues in the screening population.

We continue to strive to get wider acknowledgement from government and regulatory bodies to get CTC accepted as a formal method for screening in colorectal cancer.

Computed Tomographic Colonography in France

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With almost 37,500 new cases and 17,000 deaths per year, colorectal cancer represents a major public health problem in France. In 2000, the Advisory Committee on Cancer Prevention of the European Commission recommended the national implementation of colorectal cancer screening. This recommendation led to the incorporation of colorectal cancer screening in the "European Code Against Cancer," and to the release of a statement from the European Commission itself. In France, pilot studies were implemented in 21 districts in 2003, and the decision to generalize screening took place in 2005. This decision became effective by the end of 2008 with the widespread implementation of a colorectal cancer screening program over the entirety of France. This population-based screening program targeted a potentially eligible population of 16 million people. (Note that biennial fecal occult blood tests (FOBTs) were proposed for individuals aged 50–74.) The results of the first-round and second-round performance indicators released in 2007 are described below.

The overall participation rate after a complete first round reached 42%. For the first round, overall positive test rate was 2.6% (n=37,903/1,457,799 subjects). For the second round, 2.9% of tests were positive when people performed the test for the first time, and 2.7% for the second time. A total of 3,289 people with cancer (0.22%) and 10,884 (0.78%) people with adenomas were diagnosed. The rate of adenomas larger than 1 cm was 0.38%. Among the 2,504 cases of invasive cancer, 33% were stage I and 18% stage II.

In April 2010, Pickhardt and Kim et al.[80] published in *Radiology* the results of colorectal and extracolonic cancers detected at computed tomographic colonography (CTC) in 10,826 asymptomatic adults (50–74 years). A total of 22 people with invasive cancer (0.21%) among the 54% had stage I and 13.6% stage II. It is interesting to notice that this result was similar to the French evaluation with the invasive cancer rate detected by FOBT being 0.22% versus 0.21%, while the stage I detected by CTC was 54% versus 33% by FOBT. Moreover, the CTC performance for ≥10 mm polyp detection was 4% (approximately 500 subjects), whereas the FOBT performance in France was 0.38%, a "10-fold difference in advanced adenoma detection between CTC and FOBT" (Pickhardt[80]). Also, CTC detected in an extracolonic cancer in 36 patients.

The author started his experience in 1999 when Fenlon et al.[81] published their first results in the *New England Journal of Medicine* with adequate >10 mm lesion detection. They used the dual slice CT scanner (Elscint CT Twin, United Medical Technologies, Fort Myers, FL) with 3 mm slice

collimation and reconstruction index of 2 mm. Both prone and supine acquisitions were performed with 30–45 s per acquisition. The manual colonic distension was performed initially using a barium enema catheter with a balloon with room air for inflation. They used polyethylene glycol (PEG) for bowel preparation the day before the examination. The patients had to drink 4 L of PEG over 3 h. This choice seemed logical because same-day optical colonoscopy was performed to validate the CTC findings.

The author used dedicated CTC software, first with a 3D approach requiring manual path tracking to perform a 3D fly-through of the colon. Virtual dissection was also used when it became available. In 2003, the author participated in the 2-day CTC workshop conducted by Dr. Michael Macari, using a primary 2D read with multiplanar reconstruction and 3D view for problem solving. That group was experienced in that method of interpretation. However, in the beginning, the correlation between the 3D and 2D images was tedious, and careful correlation between the prone and supine acquisitions was also necessary to properly characterize polyp candidates. Despite these barriers which made the interpretation time-consuming, good 3D image quality was achieved using a technique with 120 kV peak (kVp) and 250–350 mAs (abdominal CT protocol parameters). The positive feedback from gastrointestinal endoscopists regarding CTC diagnostic performance for lesions ≥10 mm allows the author to continue with the encouragement of gastroenterologists.

In 1999–2000 the majority of French radiologists started performing virtual colonoscopy in both private and academic centers. The use of CTC was limited, however, by the necessity to acquire dedicated CTC software not available to the majority of radiologists, the need for training, and the time-consuming (1 h) interpretation time, which in practice limited the case volume to one examination per day. Most radiologists then were reluctant to use the technique. Furthermore, radiologists switched slowly from room air to water enema as a distension agent. This choice seemed logical because the images were more familiar for interpretation, along with use of intravenous contrast media as part as water enema CT to improve cancer detection.

Maybe because the author is addicted to video games, he continued using the available CTC software and presented several papers on the topic.[82–91] To improve the technique, he switched from wet preparation to dry preparation by introducing Phospho-soda (C. B. Fleet Company, Lynchburg, VA) as a laxative solution. To improve the comfort of colonic distension, he switched to a thin rectal catheter without balloon. After Pickhardt et al.'s publication in the *NEJM* in 2003 with the excellent results for ≥6 mm polyp detection, the combination of a dietary and cathartic preparation of the colon combined with fecal tagging was and is still considered the state-of-the-art method of preparing the colon for CTC. The actual bowel preparation consists of a low-fiber meal the day before the examination with a clear liquid diet. This is combined with 30 mL of Prepacol (Guerbet GmbH, Sulzbach, Germany) (Fleet Phospho-soda equivalent) and 20 mg bisacodyl tablets as laxative solution. Patients are also instructed to drink 100 mL of a 2% fluid barium suspension for solid stool tagging and 50 mL of Gastrografin for fluid tagging. Finally in 2005, the author started exploring the V3D-Colon software (Viatronix, Inc., Stony Brook, NY) which is considered one of the 3D flythrough state-of-the-art workstations.

Since then, the author has refined the CTC protocol by introducing in 2006 the automated CO_2 insufflation for better distension quality and patient acceptance. During the French radiology annual meeting in 2006, the author presented his first results for ≥10 mm and 6–9 mm polyp detection with 94% and 80%, respectively. From this date, CTC yielded a renewed interest from the French radiologist. The CTC workshop organized every trimester at the Pitiè Sâlpetriere hospital (Paris) has facilities for training more than 200 radiologists. This workshop is based on the classical scheme including a theoretical course and hands-on sessions by using V3D-Colon software.

Despite the earlier experience with gastroenterological encouragement, the relationship with the gastroenterologists changed from the moment the author's CTC performance became equal to that of optical colonoscopy for the relevant lesions. However, in 2007–2008, the author started a partial private activity, located very far from his hospital. The initial experience started with only one CTC exam per week and the patient was referred for a double contrast barium enema which was converted to CTC. Unfortunately the results of the first CTC examinations were positive, with ≥10 mm lesion confirmed by the endoscopists. At the end of the year, the CTC number exceeded 10 per week. It is interesting to note that the major referring physician was a first-year gastroenterologist.

Seven hundred thirty seven asymptomatic (73%) patients were enrolled in the French STIC (Sciences et Technologies de l'Information et de la Communication) study between January 2007 and April 2008. Twenty-six centers with 28 radiologists participated in this study. Participants had an average (41%) or with high risk (58%) for CRC (personal or family history of polyps or cancer). Concerning the radiologist training, they all achieved a detection rate above 30% for polyps of any diameter and median detection rates of 61% and 65% for polyps ≥ 5 mm or 10 mm, respectively. The detection rate for polyps ≥ 5 mm varied from 51% to 72% and was related to the radiologist's experience and case load.

Conclusion

The CTC technique has undergone considerable development in France and is now performed by many centers throughout the country. The need for local guidelines to certify the level and competency of CTC as well as to set procedure standards to maintain excellent quality may allow this technique to grow in the French medical community.

Screening and Computed Tomographic Colonography: The German Experience

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Geography and Demography

Germany has the second largest population in Europe, covering a territory of 357,021 km^2 in central Europe stretching from the Alps, across the North European Plain to the North Sea and the Baltic Sea, consisting of 349,223 km^2 of land and 7,798 km^2 of water. The highest elevation represents the "Zugspitze" at 2,962 m. Since reunification in 1989, the City of Berlin has become again the capital of Germany. Because of its central location, Germany shares borders with nine European countries: Poland, Czech Republic, Austria, Switzerland, France, Belgium, Luxembourg, the Netherlands, and Denmark. The population of the Federal Republic of Germany, monitored by the Statistisches Bundesamt, amounts to approximately 81,880,000, making it the 14th most populous country in the world. Germany's population is characterized by zero or declining growth, with an aging population and smaller cohort of youths. The largest ethnic group of non-German origin are the Turkish; more than 16 million people are of non-German descent in the first or second generation. Since the nineteenth century, there has been a long history of east-to-west migration within Germany. Germans from East Germany (the former German Democratic Republic) tried to flee to West Germany during the partition of the country until 1989, mainly for political reasons. Moreover, migration is still ongoing within the reunified Germany for economic reasons.

Germany has one of the world's highest levels of education, technological development, and economic productivity. It represents a broad middle class society with an average income of about $27,000 per capita. The social welfare system includes universal health care and unemployment compensation among many other social programs. Germany's aging population and struggling economy since the 1990s has forced the government to push through belt-tightening and labor market reforms.

Germany's climate is temperate and marine. The greater part of Germany lies in the temperate climatic zone in which humid westerly winds predominate, whereas in the northwest and north the climate is extremely oceanic and rain falls all the year round. The climate in the east is clearly characterized by continental features. Winters can be very cold for long periods, and summers can become very warm.

Health Care System

The number of physicians in Germany ranges between 370 and 380 per 100,000 inhabitants. Health care is funded by a statutory contribution system that ensures free health care for all via sickness funds. Insurance payments are based on a percentage of income, almost evenly divided between employee and employer and currently ranging between 12.9% and 15.0%. Two principal types of insurance exist; the statutory health insurance, the so-called Gesetzliche Krankenversicherung (GKV), occupies a central position in the health care system in Germany, as about 90% of the population are covered by this insurance type. It is obligatory for everybody who earns less than €3862.50 (normalized to the year 2004) before tax. Private health care insurance can either provide additional coverage to individuals who are covered by the statutory insurance or provide full coverage for individuals who opt out of the statutory insurance.

In Germany, the provision of health care can be broadly separated into ambulatory and inpatient sectors. Outpatient services supplied to the public are largely the responsibility of independent physicians practicing on freelance bases under contract to the statutory health insurance. Physicians caring for patients insured by the statutory health insurance must be registered by the regional association of Statutory Health Insurance of Physicians (Kassenärztliche Vereinigung).

Hospitals in Germany are grouped into three main types:

- Public hospitals run by the local authorities (usually city or state governments), including all university affiliated hospitals
- Voluntary nonprofit hospitals run by religious organizations or nonprofit organizations such as the German Red Cross
- Private hospitals run as free commercial enterprises

Medical Education

Medical school takes a minimum of 6 years. After graduating with a state examination, the student is licensed as a physician (approbation) and may practice medicine. To obtain a medical doctor degree, a doctorial thesis must be successfully completed. Postgraduate education takes between 4 and 6 years, depending on the specialty, more precisely 5 years in radiology. Continuing medical education is mandatory for all physicians practicing in Germany. The German Medical Association has issued a Regulation Framework for Continuing Medical Education which serves as a model regulatory procedure for all State Medical Chambers in Germany.

Radiation Protection

The long tradition of radiation concerns in Germany, mirrored in a framework of laws (Strahlenschutzgesetz), has induced the establishment of the Federal Office for Radiation Protection (Bundesamt für Strahlenschutz, BfS, http://www.bfs.de/en/bfs). The BfS aims at safety and protection of humans and the environment against damages due to ionizing and non-ionizing radiation. The area of activity encompasses all fields of ionizing radiation, including X-ray diagnostics in medicine, safety in the handling of radioactive substances in nuclear technology, protection against enhanced natural radioactivity, and very recently heated issues around X-ray scanning of cabin baggage and of travelers for air traffic security. The work in the field of non-ionizing radiation includes protection against ultraviolet radiation and the effects of mobile communication.

Without negating the positive effect of a central institution overlooking the use of radiation with the aim of reducing its utilization, concerns have arisen in recent years as to the complicated process, overcritical appraisal, and time delays in application processes of more than 6 months, leading to a slow-down of medical research. Most recent attempts aiming at acceleration of application processes have not been overwhelmingly successful. Especially in multicenter trials, German institutions are faced with a lengthy and detailed procedure which relevantly prolongs ethics approval. Furthermore, concerns have been expressed that focusing only on potential side effects of radiation would subsequently lead to an underestimation of benefits of diagnostic procedures, particularly of computed tomography (CT). The compilation of one of the world's first X-ray images, the hand of Röntgen's wife, next to a picture of an exploding atomic bomb (http://www.bfs.de/en/ion) has been critically perceived as an unnecessary and unrealistic comparison.

However, there is a regulatory framework (in the category of Radiology: Röntgenverordnung as part of the Strahlenschutzgesetz) and general agreement among the public and official bodies that any medical procedure is regarded as a violation of an individual's integrity and therefore requires a legitimate indication: In a screening scenario with healthy individuals being exposed to ionizing radiation, the medical indication is replaced by the "screening" indication necessitating an especially high level of justification. The potential benefit to the individual screened must clearly outweigh potential risks involved with the procedure. By law, the BfS must be consulted before a screening program can be established and must approve the entire process. To this date, the only country-wide screening program in Germany involving utilization of ionizing radiation is X-ray mammography, for which a particular law was implemented. From this perspective, it appears highly unlikely that further screening programs will be approved in the near future.

Screening Optical Colonoscopy

Since October 2002, enrollees in the statutory health insurance plans have been entitled to undergo a screening colonoscopy beginning at age 56, and a second colonoscopy 10 years later (twice in a lifetime). From the beginning of the screening initiative, quality assurance issues have played an important role because individuals likely to be healthy are exposed to a substantial risk for adverse events. As part of quality assurance, only experienced endoscopists are allowed to perform the screening colonoscopy after approval. The minimum standards for approval are a license as an internist or gastroenterologist and profound experience in at least 200 total colonoscopies and 50 polypectomies performed during the last 24 months. Documentation of the procedure is mandatory for later quality evaluation of the screening performance. The forms have to be sent to the Central Research Institute of Ambulatory Health Care in Germany. With this program, Germany represents the only country that offers free screening colonoscopy with participation by invitation to the general public. Enrollees in private health care insurance have been able to take the liberty to undergo procedures whenever deemed necessary by a general or specialized physician; however, recent budget developments at a few insurance companies have forced closer looks into the medical necessity of examinations and procedures. Some restrictions to the rampant access to medical services have been recently invoked.

Alternatively, all enrollees may participate in a colorectal cancer screening program comprising an annual fecal occult blood test (FOBT) from the age of 50 and biennial FOBTs after 55 years of age. FOBT and digital rectal examination have been offered in Germany since 1971. With

Table 2.1 Summary of the screening results using optical colonoscopy in Germany. Source: Zentralinstitut für die kassenärztliche Versorgung (ed.), 6. Jahresbericht 2008, Berlin 2009 (p 44)

	2003–2004		2005–2006		2007		2008	
Diagnoses	*n*	%	*n*	%	*n*	%	*n*	%
Men	349,280	100	464,969	100	221,378	100	217,551	100
Polyps	56,479	16.2	74,689	16.1	39,647	17.9	39,873	18.3
Adenoma	73,771	21.1	112,333	24.2	63,755	28.8	63,854	29.4
Advanced adenoma	27,687	7.9	40,536	8.7	20,326	9.2	19,627	9.0
Women	490,965	100	571,336	100	256,874	100	248,702	100
Polyps	56,695	11.5	71,156	12.5	36,510	14.2	35,650	14.3
Adenoma	63,568	12.9	85,119	14.9	46,130	16.0	45,751	18.4
Advanced adenoma	22,343	4.6	28,516	5.0	13,380	5.2	12.720	5.1

accompanying tremendous efforts in advertising, including ads on public TV channels, radio, and print media, participation and results of the optical colonoscopy screening program have been quite inspiring and might serve as a model for alternative examination techniques, in particular CT colonography. Between 2003 and 2008, 3.3 million Germans underwent optical screening colonoscopy – the cumulative participation rates (corrected for the natural mortality rate) of those 55–74 years old are 15.5% for men and 17.2% for women.[92] In addition, 4.5 million Germans have undergone FOBT screening in the same period of time. Table 2.1 summarizes the screening results by gender and age. Noteworthy is the low complication rate: 2.7 complications per 1,000 participants have been documented, consisting of 1.6 bleedings, 0.8 cardiopulmonary complications, and 0.2 perforations. A total of 27,060 colorectal cancers were found in individuals with an average age of 69 years; 47.3% of the detected cancers were in stage I of the Union Internationale Contre le Cancer criteria; 22.3% in stage II; 20.7% in stage III; and 9.7% in stage IV.

CT Colonography

Early reports using CT as the imaging modality to examine the colon date back to the year 1999[93] and have paved the way for the largest CT colonography (CTC) trial in Germany recently published.[94] In the light of the health care structure and the regulatory framework in Germany described above, CTC has, however, remained a specialized examination technique offered predominantly in a handful of university and larger community hospitals where clinical trials can be organized and conducted.[95–97] Some private institutions offer CTC but almost exclusively for individuals with private insurance. Aside from persistent and institutionalized radiation concerns, it appears unlikely that regulatory bodies in Germany will approve CTC as an alternative imaging test to optical colonoscopy anytime soon, or that statutory health insurance companies will reimburse CTC on the basis of their regular health care plans in the near future. This situation sheds light on a growing apprehension in Germany about the fact that access to innovative medical services will become patchy and in the future increasingly dependent on individual income levels rather than medical evidence.

CTC has lived a shadowy existence in Germany to date, despite obvious craving in the public for alternative imaging tests for complete colon evaluation. The working group for gastrointestinal and abdominal imaging under the auspices of the German Radiological Society has released guidelines for the indication and technical implementation of CTC in order to standardize the examination procedure, guide novices to the field,[98] and promote CTC as the second best test for complete colon evaluation after optical colonoscopy. At the same time, it has become overwhelmingly clear that CTC in conjunction with the dominating role of optical colonoscopy has nearly scrubbed out the few remaining indications for conventional double-contrast barium enema (DCBE). With the exception of practice in some institutions, mostly in community hospitals with restricted access to latest CT technology, DCBE has virtually vanished from the scene and the armamentarium of diagnostic tests in radiology. It is hoped that with further continuing medical education in teaching hospitals and by means of dedicated training courses as have been offered for several years at annual assemblies of the German Radiological Society, CTC will hoist anchor and raise radiologists' interest in colon imaging. Attracting younger trainees in medical imaging will eventually lead to broader acceptance of CTC amongst medical professionals as well as administrative and regulatory bodies.

The German public and academics are open-minded and remain enthusiastic about medical innovation and technical advances, and will undoubtedly master the challenges of health care budget constraints and structural roadblocks that have hampered an innocent passage of CTC into statutory health care insurance plans.

Computed Tomographic Colonography: The Irish Experience

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Introduction

The population of the Republic of Ireland is approximately 4.5 million. Published data from the National Cancer Registry of Ireland reported that 2,174 new cases of colorectal cancer were diagnosed in Ireland in 2007, with a predicted increase in incidence of the disease to approximately 3,300 new cases by 2020 given the aging population.[99] Colorectal cancer represents 10% of all invasive cancers in Ireland. Furthermore 60% of people diagnosed with colorectal cancer in Ireland present at stage III and IV, when the disease is more difficult to treat. Ireland also has the highest mortality rate for bowel cancer in western Europe and the fourth highest rate among men worldwide, with over 900 people dying from the disease each year. Over the past 15 years, the incidence of colorectal cancer has increased by 20%.

The National Cancer Screening Service is currently implementing an Irish Colorectal Cancer screening program based on a biannual fecal immunochemical test and plans to enroll men and women aged 60–69 years in 2012. It is estimated that a national colorectal cancer screening program will save 330 lives every year and prevent a further 320 people from developing colorectal cancer annually. Overall, it is estimated that the lives of 650 people will be dramatically improved every year with the implementation of this colorectal cancer screening program.

Since the first computed tomography colonography (CTC) was performed in Ireland in 1999, it has been embraced by the Irish radiology, medical, and surgical communities and has now replaced barium enemas in many centers throughout the country as the completion test of choice following incomplete colonoscopy or in patients who are judged too frail to undergo colonoscopy. It is estimated that 2,000–2,500 CTC examinations are currently performed each year in Ireland and interpreted by consultant radiologists appointed over the past 10 years who have trained in academic centers in North America and the United Kingdom. While access to CTC still remains patchy throughout the country, its recent inclusion as one of five major criteria of the selection process for national colorectal cancer screening centers underscores how far this technology has evolved in Irish clinical practice in the past 11 years.

The Boston Link

Irish medicine has long benefited from strong clinical and research links with American academic centers. The introduction of CT colonography into Ireland came in 1999 when Professor Helen Fenlon returned from Boston University to take up her position as a consultant radiologist at the Mater University Hospital in Dublin. Professor Fenlon had performed seminal research on the accuracy of CT colonography in detecting colorectal polyps as part of her clinical research as a Radiology Fellow at Boston Medical Center under the guidance of Professor Joseph Ferrucci. Her clinical research at Boston University culminated in the publication in the *New England Journal of Medicine* of November 1999 of the first ever prospective comparison of CT colonography and conventional colonoscopy in detecting colorectal polyps in 100 patients at high risk for colorectal cancer, demonstrating that both "virtual and conventional colonoscopy had similar efficacy for the detection of polyps that were 6 mm or more in diameter." [100] Professor Fenlon's subsequent collaborative CT colonography work includes studying the effect in a multicenter setting of observer experience on polyp measurement and size categorization, as well as the effect of reader experience, fatigue, and scan findings on CT colonography interpretation times.[101,102]

Following her return to Dublin, Professor Fenlon collaborated with Professor Paul Whelan, director of the Vision Systems Laboratory at Dublin City University, on research assessing ways of optimizing computer-aided diagnostics in CT colonography (CAD-CTC). The research was funded by a grant from Science Foundation Ireland and recruited patients at the Mater University Hospital.[103]

In 1997, I commenced my radiology fellowship at Beth Israel Deaconess Medical Center in Boston and subsequently began my interest in CT colonography under the guidance of Professor Vassilios Raptopolous. Our research group was the first to publish on the role of CT colonography as a completion examination in patients with incomplete colonoscopy.[104] My research in Boston also included assessing the utility of glucagon hydrochloride as an antispasmolytic agent to aid colonic distention during CT colonography[105] and the benefit of intravenous contrast in enhancing polyp detection, particularly in patients with suboptimal bowel preparation.[106] I also received funding from the General Electric Radiology Research Academic Fellowship to assess the utility of 1.5 and 3.0 T magnetic resonance colonography.[107] Following my return to Beaumont Hospital in Dublin as a consultant radiologist in 2005, I introduced CT colonography to our hospital, where it has replaced barium enema as the completion test of choice following incomplete colonoscopy. My current research interests include assessment of

different bowel preparations and the utility of a limited-preparation CT colonography in the frail elderly population.[108] In recent years Helen and I have published on CT colonography in collaboration with North American and European colleagues as part of the Working Group on Virtual Colonoscopy.[109,110]

Access to CT Colonography in Ireland

Current access to CT colonography in Ireland remains patchy, with its availability limited mainly to a handful of teaching centers in the large cities of Dublin, Cork, Galway, and Waterford. In more recent times, CT colonography is being performed in regional centers in Mullingar and Drogheda. There are 37 public acute hospitals and 19 private medical hospitals in the Republic of Ireland. Currently, CT colonography is available in ten public hospitals and five private hospitals, and it is estimated that approximately 2,000–2,500 CT colonography examinations are being performed annually throughout the country. An important advance in the past 2 years has been the designation by our Health Services Executive of eight national centers for cancer care, and to date CT colonography is performed in all but three of these centers.

While access to CT colonography remains patchy throughout the country, the recent inclusion of "completion" CT colonography by the National Cancer Screening Service as one of five major criteria of the current selection process to determine suitable colorectal cancer screening centers underscores how far this technology has evolved in Irish clinical practice since the first examination was performed in 1999.

CT Colonography and Ireland: 2010 and Beyond

Following on from our involvement with CT colonography workshops run by the Society of Gastrointestinal Radiologists and the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) (Fig. 2.1), Professor Helen Fenlon and I are running the first Irish-based CT colonography workshop in Dublin in October 2010. The interest in CT colonography and this workshop has been heightened by the introduction of the national colorectal cancer screening program. In 2011 we will host the first ESGAR CT colonography workshop, and through these and future efforts we anticipate that the number of centers and radiologists performing CT colonography will continue to go from strength to strength throughout the country.

Computed Tomographic Colonography in Israel

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The State of Israel was established in 1948, and the current population is approximately 7.2 million.[111] Colorectal cancer is a leading cause of cancer morbidity and mortality in Israel, with 3,200 new cases and 1,800 deaths attributed to CRC each year.[112] Colorectal cancer screening is being promoted by the Israeli Ministry of Health, with annual fecal occult blood testing offered as the preferred screening mode.

Computed tomographic colonography (CTC) has been performed in Israel since 2000 and has gained popularity – thousands of examinations have been performed in multiple centers. A recent survey by the Israel Radiological Association and the Israeli Association of Abdominal Imaging assessed CTC availability, as well as technical and professional standards of practice for the examination in comparison with guidelines.[113] The survey showed that a large number of examinations had been performed given the small national population. Most studies are performed at private clinics, for several reasons. Private institutions have invested more in marketing and advertising and were able to recruit a sufficient number of radiologists. Since patients pay out-of-pocket in private clinics, there is more incentive to perform the study. Public hospitals, on the other hand, are mostly understaffed with radiologists who are able to perform the examination. In addition, Israeli radiologists carry a relatively heavy workload, and those working at public hospitals who have sufficient training do not have the time to perform CTC studies, which are time-consuming.

CTC availability is not equal throughout the country – in the central, heavily inhabited area, the examination is readily available at multiple public and private centers, while in the north and south of the country it is not as available.

Overall, up to a third of patients had CTC performed due to an incomplete colonoscopy, but when only public hospitals are evaluated, the percentage jumps to as much as 80% in some hospitals. This is because of the close cooperation between gastroenterologists and radiologists where CTC and colonoscopy complement each other. Another third of patients had CTC examinations because of various contraindications to endoscopic colonoscopy, and a third had them as a screening study, usually self-referred.

Although CTC reimbursement is not provided as part of the basket of services covered by the national health funds, some medical providers cover expenses for patients after incomplete colonoscopy, and those with high risk for conventional colonoscopy. Some other insurance funds provide partial coverage for CTC, leaving a reduced cost of about 400 NIS ($110) for the patient.

All institutions performing CTC in Israel are very well equipped, with state-of-the-art multidetector CT scanners, of which over 70% are 64-slice scanners. Technical parameters used for the CTC examinations, including collimation, slice thickness, and slice increment, are in accordance with published international standards. Slice thickness of 1 mm is used in most institutions, enabling near isotropic data, and dual positioning is used in all institutions as required.

Radiation exposure is one of the major drawbacks of CTC, and it is therefore important to use low radiation protocols. In Israel all institutions were found to use low radiation protocols. Most use 100 mAs in one position and 50 mAs in the second position, and some even reaching 15 mAs.[113]

Intravenous contrast is used mostly for problem solving in selected groups of patients: those who have colonic masses; those who present for assessment of pericolonic spread, lymphadenopathy, and distant metastases; and those who have suboptimally prepared colon. Stool tagging is not used routinely in most centers, and only a third of institutions use fluid tagging. Barium suspension or diluted iodine is given to patients before CTC examination is performed.

Insufflation is performed in Israel by radiologists or by general physicians who are employed for contrast injections to increase CT productivity. All facilities inflate the colon manually with room air; unfortunately carbon dioxide pumps are not used. Because the market price for CTC has recently dropped as low as $140, investing in carbon dioxide pumps and using the required equipment is not economical in Israel.

About 20 of 500 radiologists (5%) throughout the country perform and interpret CTC studies, with a majority performing the examination at more than one center. Most of these radiologists are well trained and very experienced. In most institutions, radiologists read up to 5 CTC studies per session, but in a few institutions up to 30 CTC examinations per session are read by a single radiologist.

CTC research in Israel has focused on meta-analysis of reported sensitivity and specificity, and on the safety of the procedure. One of the first documentations of colon perforation at CTC was published by an Israeli multicenter group.[114] Factors related to the pressure within the colon have also been analyzed, and safety precautions are now used to reduce the risk for perforation.[115] Recent research has focused on the use of reduced purgation at CTC.[116]

In conclusion, CTC examinations in Israel are performed by well-trained and highly experienced radiologists, using state-of-the-art CT scanners and workstations, with CTC protocols in conformance with accepted guidelines. Future improvements in CTC should focus on using carbon dioxide pumps to lower patient discomfort, more frequent use of stool and fluid tagging, and the inclusion of CTC as a reimbursed imaging study in the basket of nationally approved health services.

Computed Tomographic Colonography in Italy

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It is now 15 years since Vining and Gelfand[117] presented the first virtual images of the colon at the meeting of the Society of Gastrointestinal Radiology in Hawaii in 1994, marking the birth of computed tomographic colonography (CTC). Only 3 years later, in 1997, the first Italian researchers coming from a few academic (University of Rome "La Sapienza," Prof A. Laghi; University of Pisa, Dr. E. Neri; and University of Trieste, Dr. A. Morra) and nonacademic centers (Valduce Hospital in Como, Dr. G. Belloni; and Institute for Cancer Research and Treatment in Candiolo, Turin, Dr. D. Regge) began to explore this new imaging technique, producing virtual endoscopic images with the technology available at that time. Over the subsequent decade, not only have extensive research studies been performed, but the development of an intense educational activity has been implemented.

Research

From 1997 to 2001, studies were focused on the optimization of CTC technique, with particular attention to refining imaging protocols applicable to new multidetector scanners.[118] The advantages of thinner collimation and the impact of the other technological advances in scanning were also explored. The first published series comparing CTC and optical colonoscopy (OC) reported interesting preliminary results[119–122] and served to lay the foundations for future studies. In 2001, thanks to a close collaboration between radiologists and gastroenterologists, the first Italian authored paper in an international peer-reviewed journal was published.[123] The main message of the study was the recognition of a clear learning curve for readers interpreting CTC examinations.

In this first period, CTC was still confined within the radiological community, primarily in academic and research centers; only those few gastroenterologists and endoscopists actively participating in the comparative research studies were involved.

A major impetus to research was due to the preseason of a series of papers published between 2002 and 2004, beginning with the first Italian paper in the journal *Radiology*[124] and continuing with several other studies which focused mainly on scanning protocols and bowel preparation.[125] An interesting cluster of contributions made by Italian researchers are those studies pioneering low-dose CTC scanning protocols. Excellent results were obtained in terms of lesion detection despite the use of low radiation dose exams. At that time it was possible to optimize a study protocol delivering a dose of radiation below that of the annual radiation exposure of the population.[126,127] Another significant contribution involved the minimization of patient discomfort by implementing a reduced bowel cathartic preparation, combined with fecal/fluid tagging.[128] The first results using a hyperosmolar iodinated contrast agent as the sole agent for bowel preparation paved the way for further optimization of the technique and for the use of tagging agents, now an internationally widely accepted method for performing CTC.

Following the first years of developments, the Italian Society of Radiology (SIRM) in 2004 sponsored the first multicenter study performed in Europe: the so-called IMPACT (Italian Multicenter Polyp Accuracy CT Colonography Group) trial (principal investigator: Dr. D. Regge), whose results were recently published.[129] This constituted the first attempt to involve several Italian centers on a head-to-head comparison between CTC and OC. Two major strengths characterized the study: (1) This was the first study on a population at risk higher than average, confirming excellent results obtained by CTC in average risk individuals; and (2) no special bowel preparation was mandated by the research, and interpretation of the CTC did not require specific reader training or testing, but rather, the investigators were free to use the interpretation methods (2D or 3D) that they routinely used in their daily clinical practice. In other words, this study provided an excellent "snapshot" of the real situation of CTC performances in different academic and nonacademic centers, as well as in both large and small community hospitals.

After the success of the IMPACT (Italian Multicenter Polyp Accuracy CT Colonography Group) trial, a second multicenter study was designed in 2007: the Computer-Aided Detection (CAD)-IMPACT trial, whose primary aim was to assess the added value of a CAD-assisted reading in CTC diagnostic workflow. Results are under peer review (preliminary data presented at the 2009 meeting of the European Society of Gastrointestinal and Abdominal Radiology by Dr. D. Regge).

Between 2007 and 2009, thanks to a strict collaboration between an enthusiastic Italian gastroenterologist, Dr. C. Hassan, the group of radiologists of the University of Rome "La Sapienza," and Dr. P. J. Pickhardt of the University of Wisconsin, the research was aimed toward the analysis of cost-effectiveness of CTC in colorectal cancer screening.[130] Based on the use of mathematical models, the investigators were able to demonstrate a favorable cost-effectiveness ratio, especially if diminutive (<5 mm) lesions were dismissed.[131–133] Another important area of research was, in fact, the analysis

of histopathological and gastroenterological data, in order to demonstrate the clinical insignificance of diminutive polyps in CRC screening programs.[134]

The next natural step was the design of a screening project on a real population in order to assess, first, the adhesion rate of normal individuals at a minimally invasive screening examination; and then, the performance of CTC in comparison with flexible sigmoidoscopy. This project, known as PROTEUS (principal investigator, Dr. D. Regge), will commence in the beginning of 2011.

Education and Training

Educational activity has been developed in parallel with research studies. The first meetings on CTC were organized in an attempt to diffuse CTC among radiologists and to promote internal discussions, particularly about technical issues. Historically, the first residential course on "Virtual Endoscopy in Clinical Practice" was held at the University of Rome "La Sapienza" in December 1998 (local organizers, Prof. R. Passariello and Dr. A. Laghi), followed 2 years later by two international meetings: the International Workshop on 3D Imaging and Virtual Endoscopy, Parma, February 3–5, 2000 (local organizer, Prof. P. Pavone), and the first residential workshop on Virtual Colonoscopy, Candiolo, March 23, 2001 (local organizer, Dr. D. Regge). The first refresher course at the national meeting of SIRM was held in Rimini in May 2002 (presenter, Dr. E. Neri). The educational activity has since been implemented over the years and is now structured as a single hands-on workshop, under the patronage of SIRM, organized three times a year in Rome, Pisa, and Candiolo, home of the three centers of the country with the largest experience in CTC. It is structured as a 3-day full immersion course, where the attendees are requested to read cases under the supervision of expert tutors.

The development of an advanced residential course dedicated to readers involved in screening programs has been organized for the first in July 2010 in Turin, as part of the preliminary phase of the Proteus trial.

Political Situation

General radiologists, despite an initial skepticism, are now always more interested in the technique. This is clearly demonstrated by the enthusiastic participation registered during the training workshops (usually fully booked several weeks in advance). There still remains, however, some resistance to the learning curve and long reading time, as well as sometimes a difficult approach to the workstation. SIRM is supporting research and education and is also promoting relations with gastroenterological and endoscopic societies. In fact, in the last few years, meetings between SIRM and the Italian Society of Digestive Endoscopy (SIED) were organized during the National Gastroenterological Congress in the attempt to diffuse clear information about CTC to gastroenterologists and endoscopists.

Gastroenterologists recognize CTC as a useful method for colon imaging and they often refer cases of incomplete colonoscopies as well as difficult patients (elderly and frail) to CTC. Endoscopists are not fully convinced about the potential role in CRC screening, and an increased concern is arising in regard to the level of accuracy obtained in the detection of nonpolypoid lesions.

Primary care physicians (PCPs) remain a group to be addressed, since they are the real prescribers of diagnostic examinations. At the moment there is a clear lack of information about CTC. In addition to organizing a course dedicated to PCPs, efforts are aimed toward the publishing of papers in PCP journals as well as the use of new media platforms (such as web TV).

If we consider the Italian market dynamics, there still prevails a great difference in resources between CTC and OC. In fact, while there can be found about 1,000 endoscopic centers, there exist less than 100 sites offering CTC: 41 "qualified centers" (www.colonscopiavirtuale.it/centri_qualificati.html), participants of the IMPACT trials and thus well trained in CTC, and another unknown number of private centers, whose expertise is unknown. Thus, there still remains a great difference in the number of examinations performed with the two procedures. The lack of CTC centers as well as radiologists trained in CTC prevents the possibility to offer CTC today as a screening test for the general population.[135]

Procedural reimbursement is another important issue. In fact, in a public, region-based national health service, where access to medical services is free for the population, the possibility of a specific code for CTC would help in the development of the technology. Unfortunately, at the time of the writing of this chapter, only 2 out of 20 regions have a specific code and reimbursement for CTC, whereas in the other regions CTC is coded as a simple non–contrast-enhanced CT of the abdomen and pelvis, with net reduction of the theoretical reimbursement.

While private insurances do reimburse for CTC, the majority do so only in the case of symptomatic patients, or as a part of a whole-body contrast-enhanced scan. No procedure of certification or quality assessment is in place, thus virtually any radiological center with a CT scanner can start its own CTC program without any preliminary training.

In conclusion, CTC has become an active area of research and has a significant clinical role which continues to grow in the Italian medical community.

Computed Tomographic Colonography in Japan

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Introduction

In Western countries, computed tomographic colonography (CTC) has been intensively investigated for its application in colorectal screening since the era of single-slice computed tomography (CT). The usefulness of CTC in the diagnosis of colorectal polyps has been reported in many articles.[136,137] The image quality of CTC was dramatically improved with the advent of multi-slice CT (MSCT), and the diagnostic use of CT for colorectal lesions has drawn attention. Many hands-on training courses using imaging workstations have been held in Europe and the United States, demonstrating that colorectal image diagnosis has become a widely accepted concept throughout the world. New technologies, such as computer-aided detection (CAD,[138] which utilizes the advantages of digital CTC image data) and "tagging" (which labels feces and liquid remains in the bowel to delete their signal as high density areas using oral contrast agents, e.g., barium and Gastrografin), have been developed.[139,140] Recently, a U.S. multicenter study conducted by the American College of Radiology Imaging Network (ACRIN) evaluated colorectal screening using CTC.[141] However, no new findings were obtained compared with previous studies. CTC is still not included in the medical fee structure as an accepted colorectal examination method. The goal of early-stage colorectal lesion diagnosis in Europe and the United States is the identification of colorectal polyps, based on the theory of an adenoma-carcinoma sequence pattern. As a result, CAD and digital preprocessing for CTC have been developed for colorectal polyps. After some recent Japanese reports regarding the diagnosis of early-stage superficial tumors by colonoscopy,[142,143] such diagnoses have come to be recognized as "flat lesions" also in Europe and the United States.[144,145] To position CTC as a reliable colorectal examination method in the future, understanding the development and progression of colorectal cancers, including their relationship with superficial tumors, and conducting research and development concerning the limitations and benefits of CTC diagnosis in early-stage colorectal lesions are required.

Current Status of CTC in Japan

The National Cancer Center has pursued CTC research for several years and has established a preoperative colorectal diagnosis system for the daily clinical setting with the introduction of the 64-slice MSCT. The National Cancer Center is currently promoting the development of CAD and digital preprocessing for colorectal cancer examinations and an automatic CO_2 insufflation system,[146] which has attained the level of practical applicability (Fig. 2.8). With the wider use of

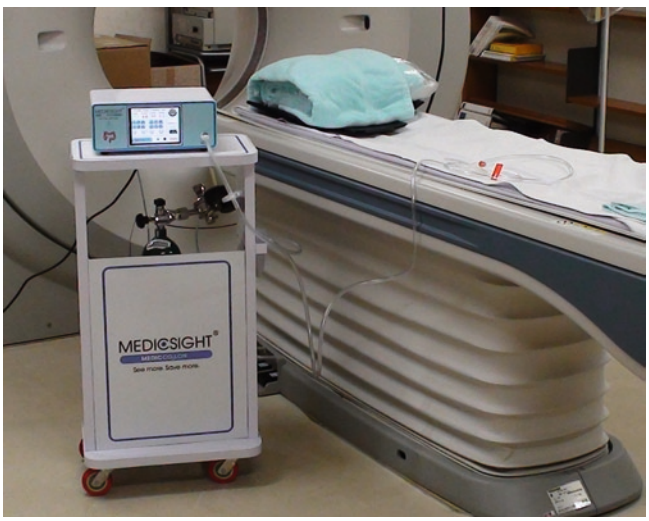

Fig. 2.8 Automatic CO_2 insufflation system for CTC examination. Automatic CO_2 insufflation system developed at the National Cancer Center. Gas insufflation pressure and the rate of insufflation can be adjusted to obtain favorable bowel gas inflation. Safe CTC examination can be performed without pain or suffering for the patient.

Fig. 2.9 The fourth JRC-CTC training course. (**a** and **b**) At JRC2010, held on April 15, 2010, in Yokohama, over 100 people participated in the CTC training course. A total of 40 imaging workstations were provided by four supporting companies

MSCT, the use of CTC has been reported at academic conferences and symposia. A steadily increasing number of facilities are using CTC, not only for preoperative colorectal diagnosis but also for complete medical checkups and outpatient practices. Hands-on CTC training was first provided at the Japan Radiological Society conference in 2007 (JRC2007) and has subsequently been provided as one of the regular events at the conference (Fig. 2.9a, b). As mentioned above, CTC has drawn increasing attention as a colorectal examination method, but automatic CO_2 insufflation systems and contrast tagging agents, which are important in such examinations, have not received governmental approval. Meanwhile, the National Cancer Center is playing a central role in promoting clinical trials and application for the approval of CTC and CAD preprocessing in collaboration with other medical institutions. The National Cancer Center has also formed a joint task force with facilities that have already begun using CTC in colorectal cancer screening and with facilities that are planning to introduce it. Moreover, the National Cancer Center has begun promoting the use of CTC in general clinical practice. In the future, a multicenter study specifically aimed at listing CTC and related items in the medical fee structure will be planned by the National Cancer Center together with JRC and other related academic societies and companies.

Diagnosis of Superficial Colorectal Tumors Using CTC

CTC is generally inferior to colonoscopy in the detection of superficial colorectal lesions. CTC reveals lesions by the density contrast between intestinal gas and the mucosal surface, whereas colonoscopy reveals lesions by direct observations of changes in color or fine irregularities in the mucosa (Fig. 2.10a, b). Our experience with preoperative evaluation has shown the difficulties in diagnosing IIa- or IIc-type lesions with CTC, which have less mucosal irregularity (Fig. 2.11a, b). Our experience using CTC with 4-slice or 16-slice MSCT at the Central Hospital of the National Cancer Center has shown that visualization of superficial type tumors tends to be affected by remaining liquid or residue remnants, and the tumors are often difficult to delineate although the presence of the lesions is known. The introduction of 64-slice MSCT, however, has improved the resolution of CTC images, thus allowing the possibility of obtaining images free from artifacts caused by intestinal peristalsis, an improvement attributable to the high-speed scanning ability of 64-slice MSCT. Additionally, CTC image quality has significantly improved with gas inflation of the intestinal tract, which is constantly maintained within an appropriate range with the use of an automatic CO_2 insufflation system. Through advances in image processing methods, an image display method suitable for diagnosing superficial type tumors and which allows the observation of fine mucosal irregularities was developed. As a result, the diagnostic performance for superficial type tumors has greatly improved. Meanwhile, CAD and digital preprocessing are being developed in Europe and the United States for the purpose of diagnosing colorectal polyps. Thus, to establish a truly reliable CTC diagnostic system, the promotion of research on CAD and digital preprocessing also for use in diagnosing superficial tumors will be required in the future[147] (Fig. 2.12a, b). CTC diagnosis is likely to become superior to colonoscopy for colorectal screening of superficial tumors[148] by (a) utilizing the advantages of digital CTC images, (b) developing a display method that allows efficient observation of the entire bowel without blind spots,[149,150] and (c) improving the accuracy of CAD and digital preprocessing methods.

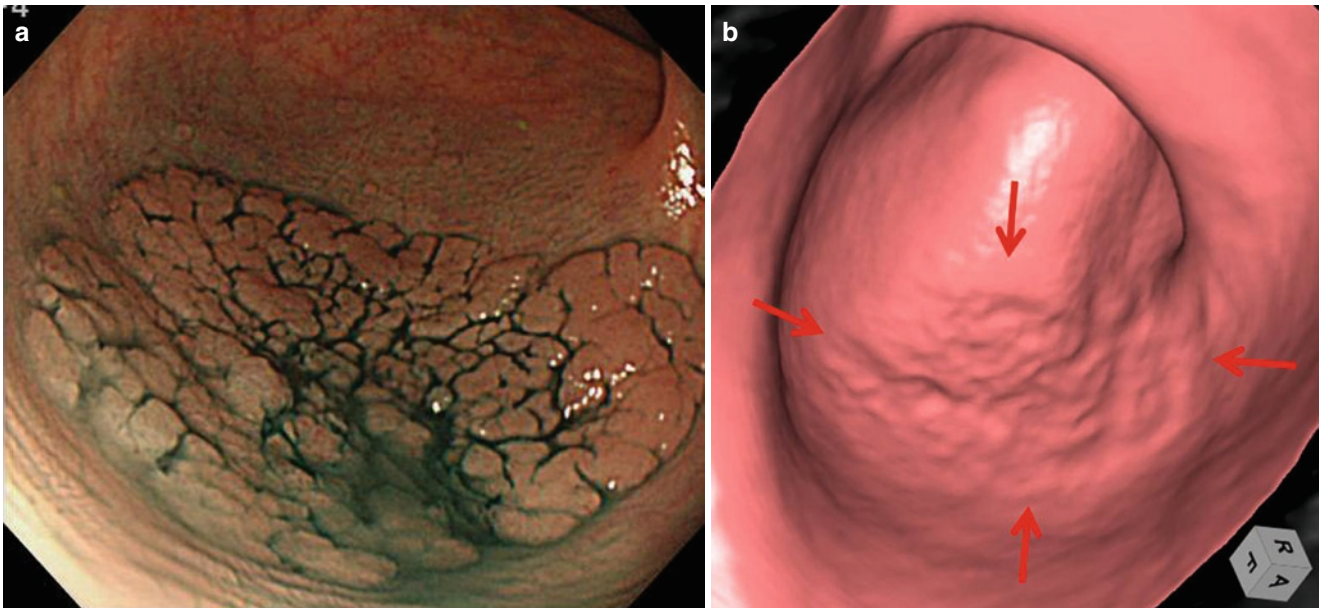

Fig. 2.10 Rectal IIa (LST-G) type adenoma (35 mm). (**a**) Colonoscopic view (dye sprayed). A flat elevation is observed as an aggregation of extremely low homogeneous nodules in the upper part of the rectum. (**b**, *arrows*) It can also be recognized with CTC as a low flat elevation with an irregular surface

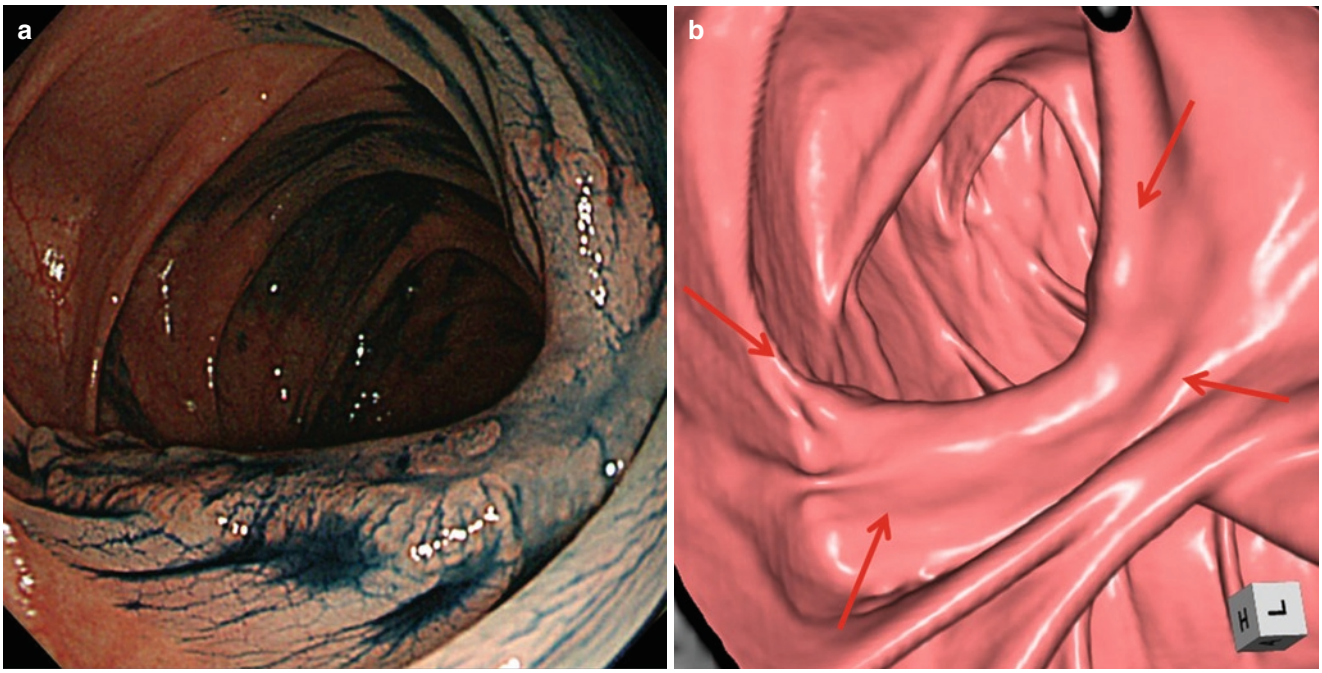

Fig. 2.11 IIc-type early-stage invasive cancer in the ascending colon. (**a**) Colonoscopic view (dye sprayed). A shallow irregular depression is shown on the semilunar fold of the ascending colon. Nodules can be seen in some parts of the depression. (**b**, *arrow*) It can be recognized with CTC as an irregular thickening of the semilunar fold

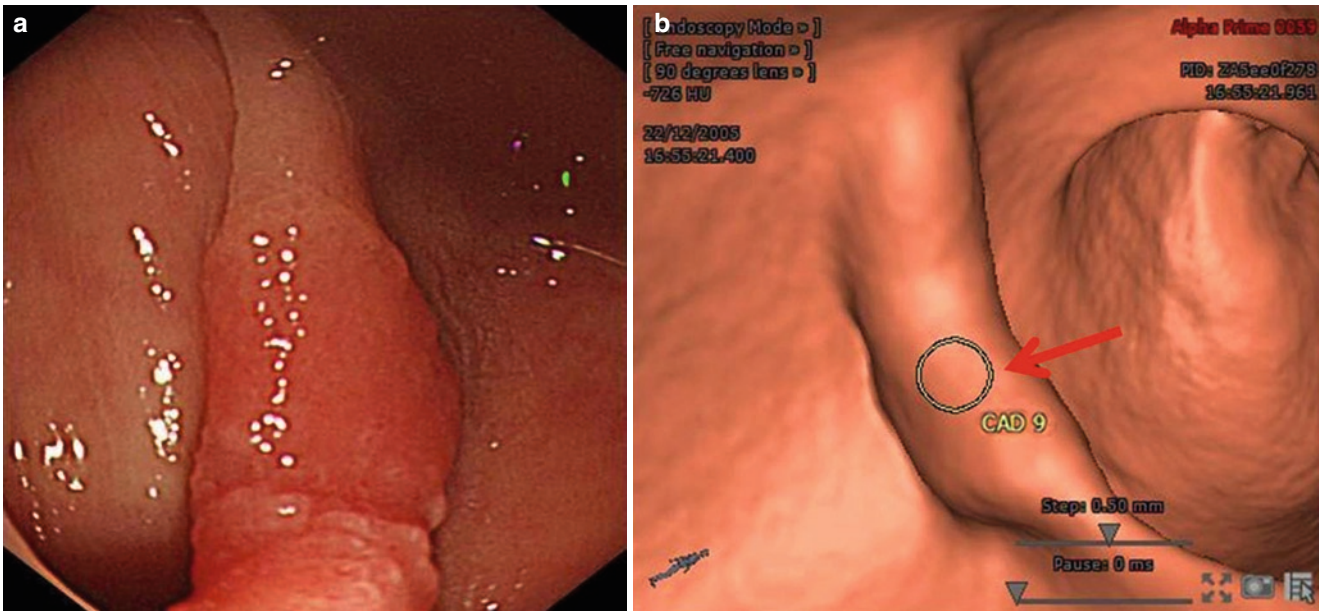

Fig. 2.12 IIa + IIc-type early-stage invasive cancer in the descending colon detected by CAD. (**a**) A low flat reddened elevation 20 mm in size with a central depression is shown in the descending colon with ordinary colonoscopy. (**b**, *arrow*) The lesion can be detected by yellow labels by CAD

Future Prospects of CTC Diagnosis in Japan

Compared with colonoscopy, CTC can be performed more safely and easily and has excellent examination processing capacity. Objective and reproducible diagnostic images have a high likelihood of becoming standardized. In colorectal examinations, in which the burden for preprocessing is especially high, digital preprocessing of CTC will revolutionarily change the examination system for colorectal examinations (Fig. 2.13a, b). With widespread use of MSCT as an infrastructure, CTC will inevitably be applied in clinical practice as a colorectal examination method. In Europe and the United States, the usefulness of CTC in diagnosing colorectal polyps has been reported in numerous studies, but difficult-to-diagnose lesions clearly exist when superficial type tumors are included. Thus, understanding the limitations of diagnostic performance is also important. Colorectal cancer proliferates locally from the early stages of development. Once the cancer invades the submucosal layer, it forms elevations[151] as a result of the cancerous lesions, which can be adequately diagnosed by CTC. Flat superficial lesions, which are difficult to diagnose with CTC, are also difficult to diagnose with colonoscopy. The beneficial contribution of CTC to colorectal cancer screening will be extremely great with future improvements in diagnostic accuracy. The prognosis for colorectal cancers is relatively better than for other gastrointestinal cancers and is expected to improve if these cancers are efficiently detected at early curable stages. The present modality used in Japan for colorectal screening is the fecal occult blood test (FOBT). Although the effectiveness of FOBT in improving prognoses has been verified,[152] its sensitivity for detecting early-stage cancer is low, and more accurate methods are needed. Thorough colonoscopy examinations are also associated with pain and suffering for the patient with additional preprocessing burdens. The resultant low rate of patients who undergo detailed examinations, among those who need such screening, is an issue of concern. CTC is highly likely to solve these current issues in colorectal screening, positioned between FOBT and colonoscopy.

The National Cancer Center will begin providing colorectal cancer screening with CTC beginning in July 2010. We have already established a tagging method that uses barium and special test meals for CTC and a diagnostic system with Band View[150] combined with CAD (Fig. 2.14a, b). We expect to disseminate a highly reliable colorectal cancer screening system with CTC from Japan to the world by optimizing CAD and digital preprocessing for superficial type tumors through actual practice of colorectal cancer screening and improvements in diagnostic accuracy.

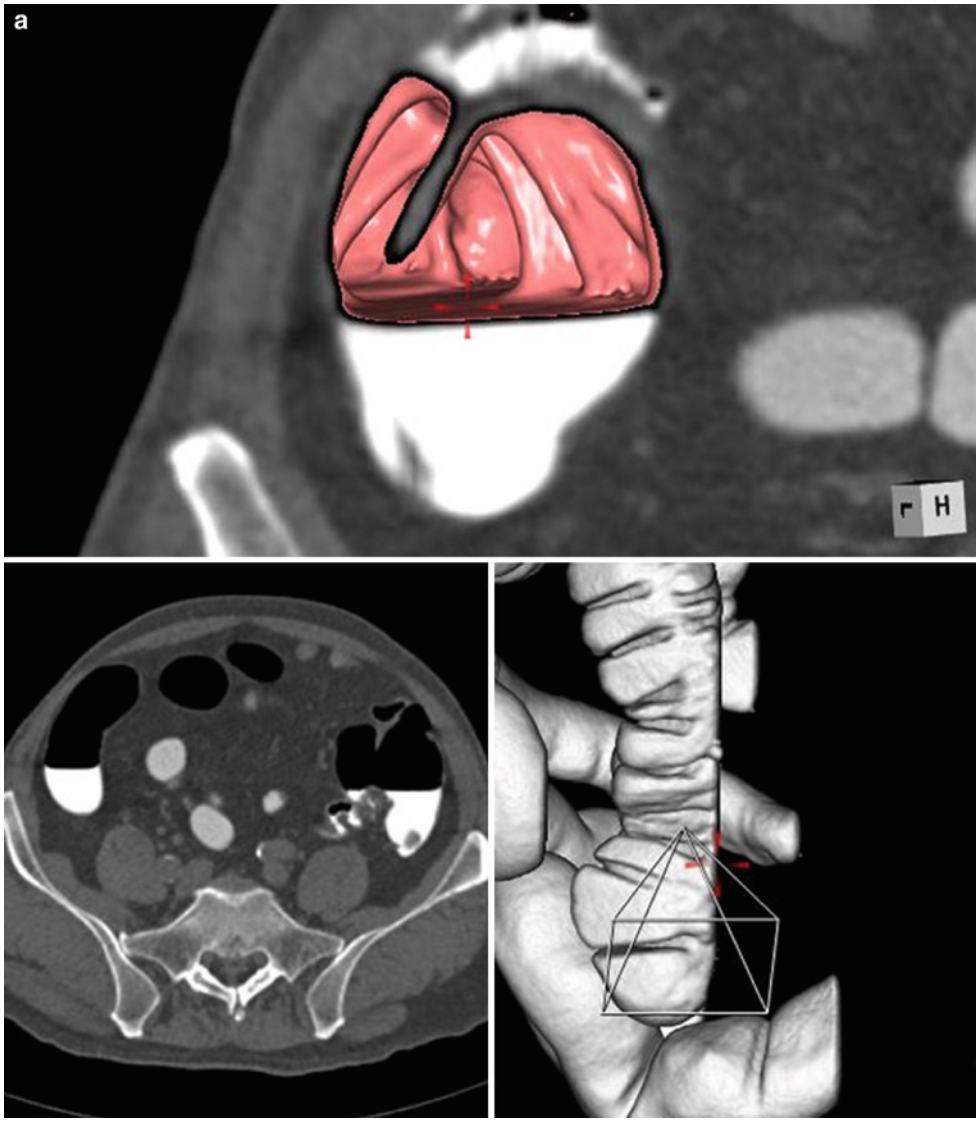

Fig. 2.13 Tagging with barium and digital pre-processing. (**a**) By tagging with barium, fecal and liquid remnants in the bowel inflated with CO_2 are labelled as high density areas. (**b**, *arrow*) By electronic cleansing or digital image processing, polyp lesions hidden in the remaining liquid can be diagnosed

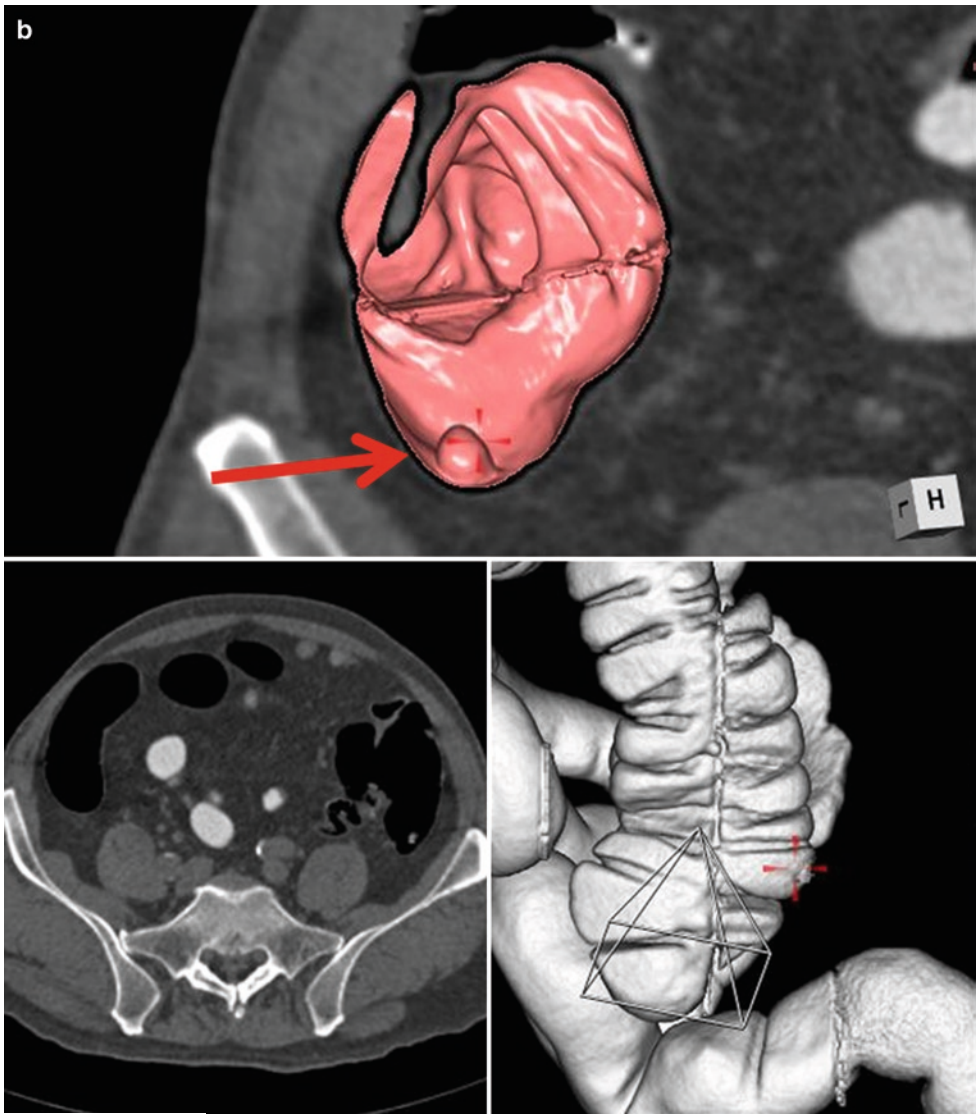

Fig. 2.13 (continued)

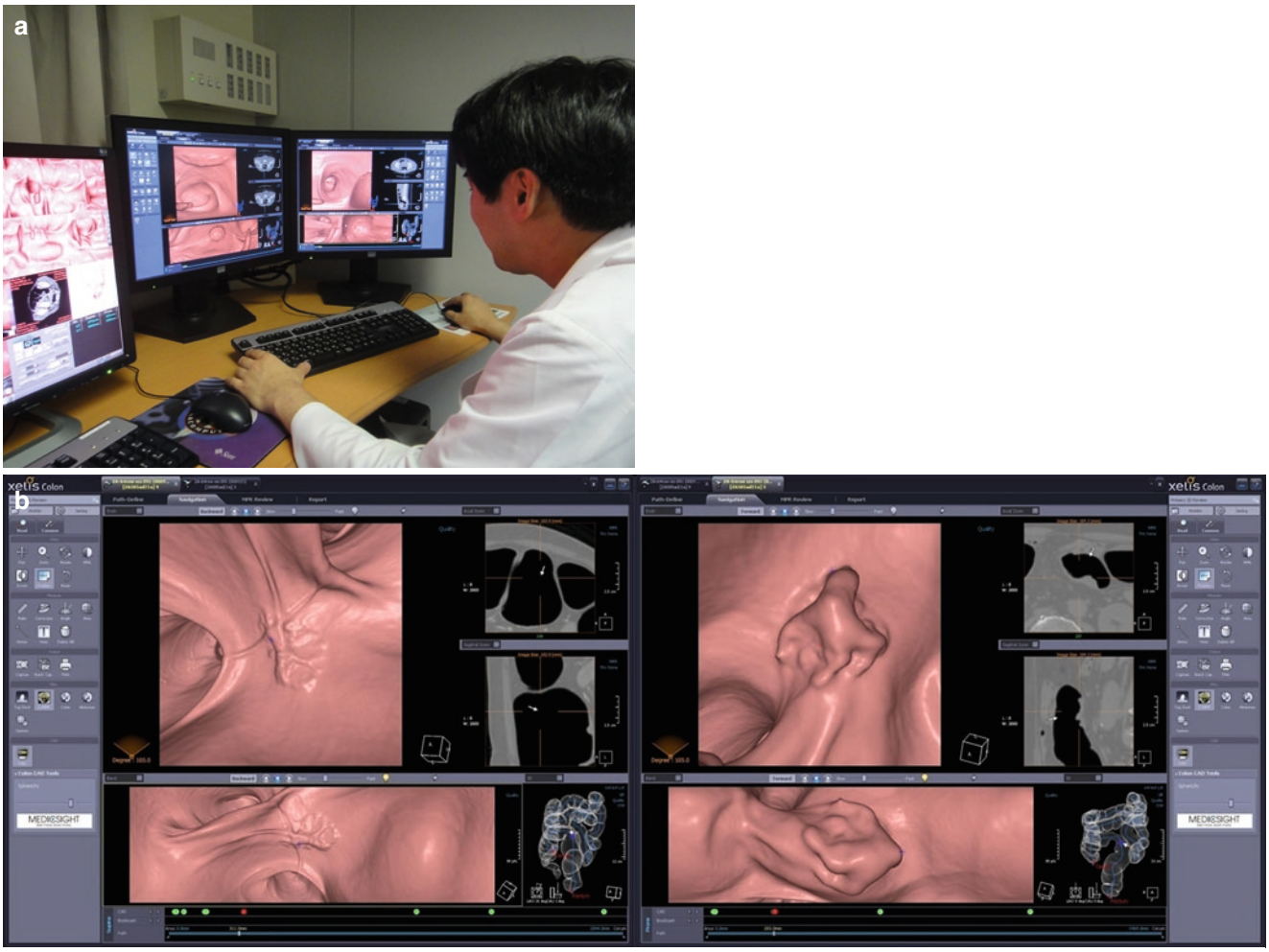

Fig. 2.14 Actual practice of CTC diagnosis with Band View combined with CAD. Band View (INFINITT Korean Co., Ltd.) displays a 360° spread view from the viewpoint positioned along the center line of the bowel and allows the observation of the entire mucosa without blind spots. It can effectively show the result of CAD (Medicsight K.K.) and performs efficient CTC diagnoses without overlooking lesions

Acknowledgments

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Additional Note on Categorization of Superficial Tumors

In the General Rules for Clinical Pathological Studies on Cancer of the Colon, Rectum, and Anus, early cancers are grossly categorized into two large types: protruded type (type I) and superficial type (type II). The protruded lesion is divided into three subtypes: (1) *Ip*, or pedunculated type, (2) *Isp*, or subpedunculated type, and (3) *Is*, or sessile type. Superficial lesions are further divided into three subtypes: (1) IIa, or elevated type, (2) IIb, or flat type, and (3) IIc, or depressed type. For a lesion with multiple morphologic types, applicable types should be connected with "+" in the order of the prominence of findings, such as IIa+IIc or IIa+Is. The laterally spreading type (LST) is divided into a granular type (LST-G) and a nongranular type (LST-NG). LST-G is further subdivided into a uniform type that comprises homogeneous nodules, and the nodule mixed type that comprises large nodule(s) within the lesion. A significant number of studies reported characteristic histopathological findings of these types, which are effectively utilized for clinical colonoscopic diagnosis.

Global Implementation of Computed Tomographic Colonography in Korea

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Computed tomographic (CT) colonography was first introduced into Korea in the early 2000s. Then, it took several years thereafter until this examination started being used as a colorectal cancer screening tool.

The obstacles we faced in the clinical implementation of CT colonography for colorectal cancer screening in Korea were somewhat different than those in the United States, where the lack of reimbursement is cited as a key barrier. Korea has a single medical insurance system operated by the Korean government, called National Health Insurance. It provides universal coverage for virtually all Koreans residing in Korean territory (96.4% [over 47 million] as of 2006). Screening CT colonography has yet to be covered by National Health Insurance. However, colorectal cancer screening itself is generally not covered by the National Health Insurance regardless of the screening methods. Therefore, the lack of reimbursement for CT colonography was not a major issue in the clinical implementation of CT colonography for colorectal cancer screening in Korea. In addition, the general shortage of gastroenterologists who could perform colonoscopy in the country and the resultant colonoscopy overload for gastroenterologists diluted any "political" antagonism by the gastroenterology community against adoption of CT colonography. Fortunately, the most important factor that determined the acceptability of CT colonography as a colorectal cancer screening examination was its medical value. Regarding this issue, the Department of Defense trial by Pickhardt et al.[153] published in the *New England Journal of Medicine,* played a pivotal role. This study was the one by which the medical value of screening CT colonography was clearly made known to nonradiologist physicians as well as to radiologists in Korea.

Ironically, the major hindrance factors to widespread adoption of CT colonography in Korea arose on the radiology side. One of the critical factors was the generally low interest in CT colonography among Korean radiologists (which still exists in some areas and institutions). One of the unique aspects of the Korean medical environment, including medical insurance, is that it requires an exceedingly rapid turnover and high throughput of CT exams (the details are beyond the scope of this chapter). Therefore, Korean radiologists are generally overloaded with CT examinations, probably no less than the radiologists in most other countries. Hence, the time-intensive nature of CT colonography for both scanning and interpretation is a deterrent. Additionally, the interpretation pattern of CT colonography, which involves meticulous evaluation of the complete luminal surface of the colon by scrolling through hundreds of images (particularly when one uses the primary two-dimensional review method), searching for small lesions on the order of 6 mm and larger, can be perceived as tedious and unsatisfying, especially in many screening patients who have no lesions. Another hindrance factor has been the limited resources for CT colonography training, which is now partially resolved. Although occasional lectures or seminars were held, it was not until late 2007 that we had any hands-on training programs for CT colonography in the country. The Korean Society of Radiology (KSR) organized a CT colonography hands-on workshop in 2007 with the purpose to promote CT colonography education. This program has been successfully held annually since then. We designed the program as a fee-free training course with contributions made by KSR. The purpose was to remove economic burden, particularly for radiology residents, and thus to encourage them to participate in the workshop. This was because we believed that educating trainees in CT colonography would be crucial and effective down the road in increasing the interest in CT colonography among radiologists as well as in propagating the interpretation skills.

Korea has seen a rapid increase in the incidence of colorectal cancers in the past decade, and colorectal cancer has become the third most common cancer in Korea (as of 2008). However, public awareness of colorectal cancer screening has not increased as much and is still at a low level. CT colonography is slowly but increasingly being implemented in clinical practice in Korea. With the growing utilization of and interest in CT colonography in the medical community, public awareness of CT colonography is also gradually increasing. Hopefully, CT colonography can play an increasing role in improving the colorectal cancer screening rate and, eventually, in decreasing mortality from colorectal cancers in Korea in the coming years.

Computed Tomographic Colonography in Sweden

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While in the United States computed tomographic colonography (CTC) is promoted as a screening test in asymptomatic individuals, in the Nordic countries CTC has attracted attention primarily for detection of symptomatic colon cancer. In Sweden, this is due to the fact that general screening for colon cancer is presently not part of the national screening program.

CTC was first introduced into Sweden at the Sahlgrenska University Hospital in Gothenburg in 1998, using single-slice CTC technology. Initial interest was primarily in research on the technique, which resulted in a series of publications on the technical aspects of CTC, diagnostic efficiency, patient acceptance, and extracolonic findings[154–157] and the first Scandinavian doctoral thesis in the field in 2002,[158] followed by a second thesis in 2009.[159–164] For several years after the introduction of CTC, only a few centers used it on a large scale, barium enema remaining the primary radiological modality for routine use on symptomatic patients in most centers. National[165] and regional[166] health technology assessments (HTAs) of CTC have thereafter helped radiologists and clinicians to assess and increase its acceptance. The HTA report of 2009 clearly recommends that barium enema should be abandoned and replaced by colonoscopy and CTC.

The introduction of a new technology such as CTC may be complex and is influenced by factors other than scientific evidence regarding its diagnostic accuracy and proper utilization. The implementation of CTC as a replacement for double-contrast barium enema (DCBE) or as a complement to optical colonoscopy may affect costs for the referring clinic, as well as investments for the radiology departments and, indirectly, the selection of patients for optical colonoscopy. In order to assess the status of CTC in Sweden, we performed a national survey in 2004–2005 and a survey update in 2009.

In the first survey in 2004–2005, we evaluated the availability of CTC in Sweden and the reasons for its implementation or lack thereof, as well as indications, technical performance, and opinions of radiologists on the procedure.[160] A structured questionnaire was mailed to all radiology departments in Sweden in May 2004 and nonresponders were contacted by telephone in June 2005. The survey showed relatively limited diffusion of CTC practice in Sweden, with approximately one-third of radiology departments offering a CTC service, mostly on a small scale. Since then, multi-slice CT scanners and software suitable for CTC have been introduced on a larger scale, and several workshops have been organized in Europe offering the opportunity to learn CTC and foster its utilization. In order to evaluate which factors still limit the diffusion of CTC into general practice, and whether any action should be taken to further implement CTC, a survey update was performed in 2009.[161] The results of that survey showed an increased CTC availability in Sweden over a 4-year period, with 18 additional departments performing CTC compared with the number in 2005, and CTC was available in 50 of 119 (42%) centers that were contacted. Furthermore, 38% (23/60) of the responding departments stated that they intended to start to perform CTC in "the near future." The survey update also showed a parallel reduction of DCBE availability, although DCBE was still more widely available than CTC, being performed in 65% of the departments.

In both national surveys, about 40% of the responding radiology departments reported non-availability of a multi-slice CT scanner as the major reason for not implementing CTC. Although good CTC results have been obtained with single-slice CT equipment, the limited speed of image acquisition and cumbersome image postprocessing are arguments for non-implementation of CTC using older equipment. In Sweden most single-slice scanners have been replaced by multi-slice scanners with appropriate software, providing a much wider platform for CTC implementation in the near future.

In those departments with CT equipment, lack of CTC training and expertise was the most stated reason for the non-implementation of CTC in 2005. Unlike many other new applications of CT, CTC includes several technical and interpretative aspects not previously handled by most radiologists. Since 2003, several workshops on CTC have been offered throughout Europe and the United States. The availability of training courses is reflected in our survey update in 2009, where the most stated reason for non-implementation of CTC in those departments, where CT was available, was lack of doctors' time. In Sweden, "doctors' time" for CTC usually corresponds to "specialists' time," while DCBE is commonly performed by residents. While the survey update showed an increasing role of radiology nurses/radiographers in performing CTC examinations, radiologists still have to invest time in learning and reading CTC. The indications for CT examinations have increased dramatically over the past decade and now include acute abdomen, flank pain/renal colic, pulmonary embolism, and more. This means increased competition for CT scanner time, thus affecting the availability of CT for colorectal imaging and increasing the workload of the radiologist. In order to further implement CTC in Sweden, a sufficient number of radiologists with interest in CTC should be recruited and trained. Also, reading of a certain number of CTC examinations is needed to obtain and maintain a high quality diagnostic level. CTC reading therefore tends to be

concentrated among a limited number of radiologists in Sweden, as indicated in our survey update (median three radiologists per department). It seems desirable that radiology residents undergo basic training in CTC, by attending courses and by reading CTC in those centers where a high number of CTC examinations are performed. A reasonable compromise between educational demands and clinical efficiency might be achieved by primary reading by a resident and final reading by an experienced CTC specialist. New technical developments, such as computer-aided detection (CAD), may in the future improve the accuracy of inexperienced readers and limit the need for double reading, although CAD cannot substitute for training.[163]

Noteworthy is that in 2009, compared with 2005, fewer departments claimed "awaiting further scientific documentation on CTC" as a reason for not implementing it (3% in 2009 vs. 26% in 2005). This could be explained by the fact that while earlier CTC studies on symptomatic patients have shown mixed results for large and medium-sized lesions, recent large CTC trials on screening populations[167,168] have shown good results for detection of large lesions with sensitivities approaching those of colonoscopy. The attitudes of Swedish radiologists seem, in fact, to have changed dramatically in favor of CTC. The majority of departments in 2009 believe that CTC will replace DCBE in the future, while a similar answer was given by only half of the responding departments in 2005.

In the first survey, DCBE was stated by nearly half of the departments offering a CTC service as being the first-line colon imaging method in patients with clinically suspected colon cancer, despite the fact that this technique has been shown to be less accurate than both colonoscopy and CTC.[169,170] Although these figures may be biased because only radiologists were asked, it is apparent that DCBE is still a common examination in Sweden. In fact, even in 2009 DCBE is still largely available, probably because of insufficient availability of endoscopists and insufficient large-scale experience in CTC. As suggested by the literature and experts, DCBE should be replaced by colonoscopy and/or CTC. In Sweden, traditions and local imaging cultures among radiologists do not seem to be major obstacles for the transition from DCBE to CTC.

The most common indications for CTC both in 2005 and in 2009 were failed total-colon examination (colonoscopy or DCBE) and old age or physical disability, i.e., frail or immobile patients. These indications are in accordance with those of a national survey in the United Kingdom[171] and other published recommendations.[172] Noteworthy is that an increased proportion of departments perform CTC as "alternative to colonoscopy regardless of history," probably as a consequence of the long waiting lists for colonoscopy.

In 2009, compared with 2005, a larger number of Swedish departments perform CTC with state-of-the-art techniques such as the use in all centers of multi-slice CT with thin collimation, the use of carbon dioxide for bowel distension in 90% of the centers, and intravenous contrast medium in 86%. In over 90% of CTC centers, a combination of 2D and 3D views are used for CTC interpretation. The technical parameters are thus in agreement with guidelines for CTC performance suggested by the consensus of experts from the European Society of Gastrointestinal Radiology (ESGAR) in 2007.[173] Recent developments in CTC techniques, such as fecal/fluid tagging and CAD, have been suggested to improve CTC performance but are at present used by only a minority of Swedish centers, according to our survey.

Based on the results of the surveys, one may consider centralization of CTC to departments with the most experience performing the procedure, in order to ensure high-quality diagnostic performance. However, the examination is easy to perform, and the expected further spread of multi-slice CT scanners makes it suitable for decentralized performance. Nevertheless, it is mandatory that radiologists perform a defined number of CTCs per year, in order to maintain CTC skills at an acceptable level. For centers with a limited number of CTC examinations, double reading by digital communication networks with more experienced centers could be helpful. Close collaboration with gastroenterologists and colorectal surgeons is also necessary for feedback and follow-up.

In contrast to the situation in the United States, where the lack of reimbursement is cited as a key factor preventing widespread adoption of the exam, the decision to perform CTC in Sweden is not affected by the availability of funding.[174] As long as referring doctors are acknowledged by the general health insurance system, they can spend their money on any type of radiological imaging, including new techniques such as CTC.

In conclusion, Sweden is in a transition process from DCBE to CTC, but the transition has been mostly rather slow and requires both human and economic resources.

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UK Implementation of Computed Tomography Colonography

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Introduction

Over a relatively short time in the United Kingdom, computed tomography colonography (CTC) has grown from a test limited to a few specialist research centers to a widely implemented technique being practiced across much of the National Health Service. This chapter will describe how this happened, focusing on those events which have most shaped current UK practice.

Early Research and Implementation

One of the first technical descriptions of CTC was published in *Clinical Radiology,* the journal of the UK Royal College of Radiologists[175] 2 years after the initial description by David Vining. The paper described spiral computed tomography (CT) performed after bowel cleansing, administration of a smooth muscle relaxant, and rectal air insufflation. Rapid dynamic scanning was undertaken with intravenous contrast enhancement, and 5–10 mm contiguous slices acquired with 2.5 mm image reconstruction. The authors called the technique "CT pneumocolon" (a term still in use in some centers in the UK) and compared the results in four patients with the results of barium enema and surgery. The key difference was that the authors grounded interpretation firmly in the 2D axial review domain, stressing that acquisition and interpretation could be practiced immediately on the then current helical CT scanners. At that center (University College Hospital, London), radiological imaging of the colon rapidly transferred from barium enema to CTC using 2D interpretation and was essentially predicated on examination of older symptomatic patients, i.e., those with symptoms of colorectal cancer. At approximately the same time, trainee radiologists on fellowships in the United States returned to the UK and "imported" the technique of CTC back with them; for example, Dr. Clive Kay had worked with Dr. Peter Cotton, an endoscopist in South Carolina, and brought CTC to his practice at Bradford Royal Infirmary.

At that time, CTC was limited to a handful of academic centers, much like the rest of Europe and the United States, which increased their experience in the technique,[176,177] but whilst initial technical developments and clinical results were published,[178–187] little further UK dissemination occurred. However UK interest was markedly raised by the landmark paper from Helen Fenlon, a trainee radiologist from Ireland working on a fellowship with Joe Ferrucci and colleagues in Chicago. Published in 1999,[188] her work stimulated considerable interest in the UK (as it did elsewhere), prompting the *British Medical Journal* to publish a review of the technique in the same year in the "Science, Medicine, and the Future" section of the journal.[189]

Further Development of CT Colonography Research in the UK

By 1999 it was becoming clear to the UK academic radiological community working in gastrointestinal radiology that CTC was not only here to stay but potentially likely to replace the barium enema, which at the time was the most commonly performed colonic diagnostic examination, exceeding colonoscopy. This precipitated research activity in the area, aided by the UK government's New Opportunities Fund, which aimed to replace older National Health Service (NHS) equipment with new helical CT scanners. At the same time, clinician demand for the technique was high because of ever-increasing numbers of patients referred with symptoms of bowel cancer (e.g., abdominal pain, change in bowel habit, rectal bleeding) and because of government initiatives that required such patients to be examined within 2 weeks. Work from Cambridge University using conventional abdomino-pelvic CT scanning to diagnose colorectal cancer in older, frail patients also helped fuel clinicians' perceptions that "CT" was appropriate to examine this type of patient.[190,191] Most initial work came from researchers then working at St. Mark's Hospital, a subspecialist hospital for bowel disease, and focused on technical aspects of CTC, such as optimization of CT acquisition parameters, bowel preparation, effect of spasmolytics, and rectal catheter type[192–194] but preliminary work investigating a role in symptomatic NHS patients soon appeared.[195,196]

It is important to stress that throughout the history of CTC implementation in the UK, the emphasis has been overwhelmingly on investigation of patients with symptoms of colorectal cancer. Most UK patients are seen in the NHS, and clinicians' salaries are dependent upon their seniority and not upon their discipline or the number of patients they examine. Thus a radiologist is paid the same amount as a gastroenterologist, and there is no fee-per-item system (i.e., procedural fee). The result is that clinicians' incomes are not directly related to the procedures they perform, which contrasts with many other countries in Europe and the United States. "Turf wars" in this area are less apparent and probably result in a less biased view of how competing procedures

should be implemented. In general, UK academics believed that CTC was best reserved for older symptomatic patients for two reasons: These patients are most at risk from colonoscopy-related adverse events, and cancers are large and generally easier to detect. Since colonoscopy is better suited than CT for detection of small polyps and better tolerated by younger patients, there is a tendency in the UK to stream symptomatic patients toward CT and screening patients toward colonoscopy.

UK academics working in the field of CTC became regular presenters at the highly influential International Virtual Colonoscopy Symposium in Boston, and also regularly presented their work at other international radiological meetings, such as those of the Radiological Society of North America, the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) (Fig. 2.1), and the European Congress of Radiology (ECR). A systematic review by UK researchers (funded by ESGAR) attempted to determine point estimates for sensitivity for diagnosis of symptomatic colorectal cancer by CTC, since the vast majority of published primary studies at that time had actually examined symptomatic patients but chose to emphasis a role in screening. Preliminary data from this systematic review suggested that CTC was highly effective for diagnosis of symptomatic cancer.[197] Other research also suggested that barium enema was very unpopular with patients,[198,199] and likely becoming less sensitive.[200] The UK Department of Health, via the Health Technology Assessment (HTA) program, commissioned research to determine the likely future role of CTC within the NHS. The HTA is a UK government-funded program whose remit is to investigate the efficacy and cost-effectiveness of new health technologies. The HTA was also influenced by early data from a survey of UK NHS hospitals that revealed that approximately one-third were already practicing CTC, albeit to a variable degree.[201] A second survey was also influential. This aimed to determine the procedural complication rate across all UK centers practicing the technique, not just those at academic centers (whose complication rate is likely to be lower as a result of greater experience). The survey of 50 hospitals and an estimated 17,067 procedures revealed only 13 potentially serious adverse events, i.e., a rate of 0.08%, with symptomatic complications approximately one-quarter that estimated for colonoscopy.[202]

The HTA stipulated a randomized controlled trial (RCT) design, and Professor Steve Halligan (a radiologist) and Professor Wendy Atkin (a colorectal epidemiologist), along with collaborators from many other disciplines, were awarded nearly £2 million to perform the research. The resultant SIGGAR trial was named after the UK Special Interest Group in Gastrointestinal and Abdominal Radiology (now the British Society of Gastrointestinal and Abdominal Radiology; BSGAR), since radiologists in this group were fundamental to the success of the study – the investigators believed strongly that any trial of the new technology should be led by those practicing it rather than gastroenterologists, who could be accused of bias.[203] Radiologists, surgeons, and gastroenterologists in 21 centers participated, with the first patient randomized in April 2004 and accrual completed by November 2007. SIGGAR registered 9,012 patients and recruited 3,838 to the RCT comparing CT with barium enema and 1,610 to the RCT comparing CT with colonoscopy. The results were orally presented in late 2009 and early 2010, and the fact that the trial found CT significantly superior to barium enema and not significantly different from colonoscopy will have a major effect on implementation of CTC in the UK.

Current Implementation

Now that the SIGGAR results have paved the way for structured implementation of CTC in the UK (and phased withdrawal of barium enema), thoughts are turning toward education and training. Indeed, these issues have concerned UK researchers for some time. An early UK study of three radiologists of differing general experience revealed interesting results; performance varied and one observer deteriorated after training.[204] The authors concluded that there was considerable variation in the ability to report CTC and that competence cannot be assumed even after directed training. The authors extended this work to a multicenter European setting, funded by ESGAR, investigating the effect of administering a directed training schedule of 50 cases to novice readers and then comparing their performance with that of experienced observers. Again the authors found that there was considerable variation, that competence could not be assumed after training, and that some so-called "experts" were in reality pretty poor![205] The effect of fatigue and experience on reading time and performance was also assessed in subsequent analyses.[206] Further observer studies have investigated the performance of those readers who are in a non-academic setting, finding some excellent and some very definitely not.[207]

The latter study was performed in an NHS setting typical of centers that will need to provide CTC in the near future if they are not doing so already. Implementation has also been accelerated by the fact that CTC has been recognized by the National Institute for Health and Clinical Excellence (NICE) for both symptomatic and screening indications (http://guidance.nice.org.uk/IPG129). NICE is an independent organization responsible for providing national guidance on promoting good health and preventing and treating ill health. In line with this, CTC is now also stipulated as part of core training for the Fellowship of the Royal College of Radiologists (FRCR), the postgraduate UK examination for specialty training in radiology.

It is clear that implementation should not happen in a haphazard and piecemeal fashion. Two related components are necessary if patients are to receive the highest quality care: High quality images must be acquired and they must be interpreted correctly. The UK has extensive experience in structured provision of high-quality colonoscopy services. In particular, national training centers for colonoscopy were established in preparation for the roll-out of the National Bowel Cancer Screening Programme, which is based on fecal occult blood tests with colonoscopy for those testing positive (http://www.cancerscreening.nhs.uk/bowel). The result has been very high completion rates and very low complication rates. Recognizing their expertise in the realm of standards development, UK proponents of CTC began work in 2009 on developing a set of standards for performing and interpreting CTC. Under the chairmanship of Dr. David Burling and with the help of the UK National Lead for Endoscopy Services, Dr. Roland Valori, a group of key stakeholders developed guidelines for best practice intended to guide and support radiology teams implementing the procedure by promoting methods to improve the technique, interpretation, and patient experience (CT colonography standards).[211] ESGAR, the Canadian Association of Radiologists, and the Abdominal Radiology Group of Australia and New Zealand have subsequently adopted the standards.

UK Training Courses

The efforts of ESGAR in promoting CTC research should not be underestimated (Fig. 2.1). Obviously, many members are active researchers in this field, but ESGAR has actively funded studies described in the sections above,[205,208,209] with the aim of promoting cross-European academic collaboration. Most obviously, ESGAR has made its presence felt via its European training courses. UK radiologists have a strong presence on the committee and faculty for these courses, and on two occasions the ESGAR CTC workshop has been held in the UK (in Edinburgh in 2006 and in Harrogate in 2009), running back-to-back with the annual BSGAR meeting and training approximately 120 attendees on each occasion. Even when held on the continent, UK delegates form a significant proportion of those attending the ESGAR workshops, confirming the strong UK appetite to learn how to interpret CTC correctly. The ESGAR consensus statement published in 2007[210] has informed best practice in the UK and elsewhere but will soon be updated by the new standards document described above.

The UK also has its own training courses, but these have lagged a little behind those of the United States, where several leading CTC researchers have been running courses for some time. Recognizing a need, in 2005 Drs. Stuart Taylor and David Burling ran the first of a series of 2-day UK training courses based in London, which have been running since. The workshops are made possible by generous support from industry and provide training for 20 delegates, with access to their own CTC workstations. The courses are based on recommendations from the Boston virtual colonoscopy symposium and consist of a series of short lectures interspersed with hands-on training. To date, this UK course has trained over 200 radiologists. New courses are being developed outside London, notably in Leeds (Dr. Damian Tolan, Dr. Andy Lowe, and Dr. Clive Kay), and training has extended to radiographic technicians (radiographers), who increasingly perform the examination in many UK centers.

Conclusion

UK researchers have contributed much to the development of CTC, and the technique is firmly established in the National Health Service. The transition from barium enema to CT will continue apace, and its complementary role in comparison to colonoscopy will remain at the forefront of implementation.

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Epidemiology and Screening of Colorectal Cancer

3

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Epidemiology of Colorectal Cancer

Colorectal cancer (CRC) represents an important health problem in Western countries. In 2009, there were 147,000 newly diagnosed cases of CRC and nearly 50,000 deaths associated with this disease [1]. In Europe, almost 413,000 individuals are newly diagnosed with CRC, and about half of these patients will die of the disease, making CRC the second leading cause of cancer deaths in both Europe and the United States [2].

Different trends in CRC incidence and mortality have been observed between the United States and Europe. During the 10-year period between 1985 and 1995, the long-term CRC incidence in the United States decreased 1.8% per year and then stabilized through 2000 [3]. The American CRC death rate has been declining since 1980, due to a synergistic effect of a CRC incidence reduction and an improvement in 5-year CRC survival rate of up to 60%. Both of these effects are believed to be due to primarily the emphasis placed on early diagnosis of CRC [2, 3]. On the other hand, the trend in CRC incidence from 1960 to 2006 has steadily increased in all European countries. In particular, a recent estimate based on 19 general cancer registries in Italy has computed an annual increase of 2.5% and 0.9% in men and women, respectively, between 1986 and 1997 [6]. The increased death rate in Europe due to CRC not only reflects an increase in CRC incidence, but also a European average 5-year survival rate of less than 50% [7]. Although the primary reasons for this vast difference in survival rate are unclear, a greater use of hormone replacement therapy and more diffuse implementation of screening procedures have been proposed to account for this discrepancy.

A brisk increase in CRC incidence has been seen in Japan, as the age-standardized incidence rate has passed from 12.3 to 76 per 100,000 individuals [9]. It is speculated that this sixfold raise is related to a Westernization of life, and specifically the consumption of a high-fat diet. A similar trend has also been identified in the developing countries of eastern Europe and several other Asian countries [10, 11].

CRC is a tremendous burden on society worldwide, not only due to its incidence and mortality rates, but also due to its costs. In 2005, the annual CRC-associated expenditure in the United States was estimated to be $8.4 billion, assuming a mean CRC treatment cost of $45,000 [12]. However, such values likely underestimate the true cost because of the recent implementation of costly chemotherapy regimens for late stages of CRC [13]. The application of resources for cancers that may have been prevented through appropriate screening is of great importance because it could be diverted to finance more widespread CRC screening, which can detect cancers at an earlier and more curable stage. Such distribution of existing resources would result in a net savings of both life and expense.

Screening guidelines and recommendations have been based on stratification of risk for different groups within the population. More sensitive and more invasive tests are recommended for high-risk groups to minimize the number of false-negative results. On the other hand, safer and more specific tests are recommended when a low prevalence of disease is expected, in order to avoid the possibility of false-positive results.

CRC Pathogenesis

Extensive studies have been performed to identify the natural history of CRC. In the adenoma–carcinoma sequence, CRC is believed to develop from nonmalignant precursor lesions called *adenomas,* which take the form of discreet mucosal elevations, or polyps. Adenomas can occur anywhere in the colorectum after a series of mutations that cause dysplasia of the epithelium. Although adenomas are often polypoid, they can also be flat. Small adenomas are exceedingly common, and their prevalence increases with age. Only a small

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percentage of adenomas will increase in size and undergo histological alterations manifested by increased villous components and marked cellular dysplasia, which may progress to frank adenocarcinoma [23].

The strongest evidence in favor of the adenoma–carcinoma (polypoid-cancer) sequence arises from both cohort and case-control studies. In the National Polyp Study, over 1,400 patients with adenomatous polyps underwent complete colonoscopy with removal of all polyps. At 6-year follow-up of this cohort, a reduction of CRC incidence between 76% and 90% was achieved when compared with historical or population-based controls [24]. A similar study performed in Italy has shown a 64% CRC reduction in patients who underwent polypectomy as opposed to surveillance alone [25]. Stryker performed a radiological follow-up of 130 patients with evidence of a large polyp at barium enema. After 20 years, 24% of these lesions evolved into CRC, accounting for the vast majority of malignancies observed in this cohort of patients [26]. In a post-hoc case-control study based on a large cohort of post-polypectomy patients, Atkin et al. showed that 11 of the 14 incident rectal cancers arose from large sessile polyps which were incompletely removed [27]. Case-control studies have shown CRC incidence reductions of between 50% and 60% in patients who underwent endoscopic screening as compared with those who did not [28]. Interestingly, these studies have also demonstrated the protective effects of endoscopy to last 10 years, suggesting a slow progression of polyps to neoplasia. It is this evidence that informed screening intervals in subsequent guidelines.

The wide discrepancy between the high prevalence of polyps (50–60% of individuals over age 50 have polyps) and the low prevalence of CRC (0.1–1%) implies that only a tiny fraction of all adenomas progress to cancer. Since the early 1970s, the relationship between polyp size and the presence of unfavorable histology has been demonstrated [30–33]. In particular, high-grade dysplasia (HGD) or malignancy appears to be more prevalent among lesions ≥1 cm, unveiling a major role for this threshold in clinical practice. This critical threshold has been confirmed by the pre-colonoscopic radiological study by Stryker et al., in which the 24% cumulative CRC risk at 20 years in patients with a ≥10 mm polyp was several-fold higher than that expected in the general population [26]. More recently, Vogelstein demonstrated that polyps larger than 10 mm are more likely to accumulate oncogenic mutations than are small lesions, offering a genetic rationale for their more aggressive behavior [34].

Aside from dimension, some histological features of polyps have been related to prognosis. After the incomplete excision of sessile rectal polyps, Atkin demonstrated a five-fold increased risk of rectal cancer in patients with HGD in the index polyp as compared with the general population [27]. A mathematical simulation suggests a conversion rate in CRC of 17% for polyps with HGD as compared with 0.25% risk in those with more favorable histology [35]. More recent evidence suggests adopting an even more stringent critical threshold for polyp size. A meta-analysis of four colonoscopy screening studies that totaled 20,562 subjects showed that over 95% of advanced adenomas appear to be represented by polyps >6 mm, supporting the adoption of a 6 mm threshold for posttest referral to polypectomy [39, 40].

Although CRC most often develops according to the adenoma–carcinoma sequence, a minority of malignancies arise directly from the mucosa without an adenomatous precursor, the so-called de novo pathway. In particular, it has been estimated that 20–30% of the all CRC cases stem de novo from the mucosa without a polypoid intermediate [29]. Such alternative pathways seem to be more frequent in the right colon (which is also where lesions with microsatellite instability are more often located), explaining the less pronounced efficacy of polypectomy in preventing right-side CRC.

CRC Screening

A prevention program for CRC targets disease morbidity and mortality. It is initiated by screening at-risk individuals in order to identify those whose risk for developing and dying from CRC is high enough to warrant intervention. Screening should be undertaken only in people without significant health comorbidities, in order to minimize the potential risks associated with screening, and who have a sufficient life expectancy so that early detection will substantially increase life duration. Secondary prevention of CRC is based on two major tenets: (1) The removal of premalignant lesions reduces the incidence of CRC and, therefore, its related mortality; (2) early diagnosis of CRC is associated with better survival when compared with detection at an advanced stage. It is worth noting that despite the introduction of effective chemotherapeutic agents for CRC treatment, the 5-year survival difference between early and late stages is still considerable. The 5-year survival difference between Dukes' stages A–B is 60–95%, but less than 50% for the more advanced neoplasias [41].

The evidence that CRC mortality was significantly reduced by fecal occult blood testing in large randomized control studies, as well as flexible sigmoidoscopy/colonoscopy in well-designed case-control or cohort studies, has led the US Preventive Services Task Force to give a grade A recommendation for CRC screening to all men and women older than 50 [42]. Moreover, cost-effective analysis has shown that CRC prevention compares favorably with other screening strategies, such as those of breast and cervical cancers [43]. More controversial, however, is the debate regarding which screening technique should be used, specifically stool-based tests versus endoscopic or radiological

procedures. According to the World Health Organization, a screening test should be inexpensive, rapid, simple, and not intended to be diagnostic, since further evaluation is required in those who test positive. As of now, no such test for CRC is available, meaning that a compromise among accuracy, safety, and cost is necessary.

Fecal Occult Blood Test

Three systematic reviews have found a significant reduction in CRC mortality with guaiac (g)-based fecal occult blood test (FOBT) screening. All three reviews included randomized control trials comparing g-FOBT with no screening [44–46]. Combining the results of four trials including 329,642 participants, the Cochrane Review found a relative risk of death of 0.84 (CI: 0.78–0.90) in the screening arm [47]. Such a result has been achieved primarily through detection of CRC in early stages. FOBT is therefore not intended to prevent cancer, but only to detect developed neoplasia at an early stage. Sensitivity and specificity of g-FOBT for CRC have been shown to be 40% and 97%, respectively, with a positive predictive value of 7.4%. Unfortunately, its accuracy for detecting advanced adenomas is lower than 20% [46]. Subjects with a positive FOBT are recommended to undergo colonoscopy, a procedure with 96.5% sensitivity for lesions detected by g-FOBT.

More recently, an immunochemical-based (i)-FOBT (or fecal immunochemical test, FIT) has been proposed as a screening test. This test is specific for human hemoglobin and has the advantage of increased accuracy. Three Japanese case-control studies evaluated the efficacy of i-FOBT on CRC mortality and show an odds ratio of death from CRC for those screened to be between 0.2 and 0.54 [48–50]. There have also been 13 population-based screening studies comparing performance characteristics of g-FOBT and i-FOBT, which consistently show that i-FOBT has a higher sensitivity for advanced adenomas and cancer than g-FOBT [51].

Flexible Sigmoidoscopy

Flexible sigmoidoscopy (FS) is a simple, safe, and relatively painless endoscopy of the distal part of the colon. It requires a minimal bowel preparation and is better tolerated by patients overall. Preparation consists of only two enemas in the morning, and endoscopy lasts 4–5 min. The procedure has a very low complication rate (<1:50.000) and occurs without the need for sedation.

The strongest evidence to support the use of FS for CRC screening comes from case-control and cohort studies. In the Kaiser Permanente–Northern California study, screening with a rigid sigmoidoscope was associated with a 70% reduction in mortality for cancers in the rectum and sigmoid colon, and a 30% reduction in overall CRC mortality [52]. Such mortality benefits persist uniformly over the entire 10-year postprocedure period. A population case-control study performed by Newcomb et al. showed a 76% CRC incidence reduction after FS [53]. Recent studies comparing FS with colonoscopy have shown the ability of FS to correctly identify more than 70% of advanced neoplasias throughout the colon in male patients when performing a colonoscopy for any adenoma detected in the distal colon [54]. However, such results have not been repeated by the authors in female subjects, in which no more than one-third of all advanced neoplasias were detected with the same strategy [55]. Four large, randomized trials comparing an FS screening arm with a nonscreening arm are ongoing in Norway, the United States, the United Kingdom, and Italy [56–59]. The Norway trial did not reduce the incidence of CRC and did not find a mortality benefit for FS [59]. However, the most recent randomized controlled trial by Atkin and colleagues at 14 UK centers of over 170,000 people did demonstrate in the intention-to-treat analyses a reduction in incidence of CRC by 23% (hazard ratio = 0.77; 95% CI = 0.70–0.84), and mortality by 31% (0.69; 0.59–0.82) [60]. Despite this impressive trial and the obvious benefit of FS, it remains a concern that right-sided lesions, which may have more aggressive malignant potential, are not seen with flexible sigmoidoscopy.

Colonoscopy

Colonoscopy is a more definitive procedure for CRC screening, being both diagnostic and therapeutic. Unfortunately, colonoscopy has the highest complication rate and requires the most preparation of all screening procedures. Patients at average risk for CRC who are screened with colonoscopy have a 0.5–1.0% chance of colon cancer; 5–10% have advanced neoplasia that can be removed during this procedure. A case-control study on more than 30,000 US military veterans comparing FS and colonoscopy showed an overall reduction in CRC incidence of more than 50%, with colonoscopy being regarded as the superior modality (60% reduction compared with 40% for FS) [28]. In the National Polyp study, colonoscopy with polypectomy achieved a 76–90% reduction of CRC incidence as compared with three historical and population control groups [24]. Moreover, the reduction of CRC incidence in the rehydrated FOBT study was attributed to the high rate of colonoscopy performed [47]. A recent report from the United States on a baseline colonoscopy screening in 13 Veterans Affairs Medical Centers has shown colonoscopy screening to be feasible, to have high

completion rates to the cecum, and to provide a manageable outcome for more than 10% of advanced neoplasias [54]. Around 3% of the subjects had an advanced proximal neoplasia without associated distal polyps, which would have been missed by FS.

CT Colonography

Computed tomographic colonoscopy (CTC), or virtual colonoscopy, is the only noninvasive (or minimally invasive) modality that allows for a systematic evaluation of both the right and left sides of the colon. CTC uses helical computerized tomographic imaging to create standard axial and reformatted images of the colon (novel tests for CRC screening and beyond). CTC, compared with FS, is expected to substantially reduce the false-negative rate for advanced neoplasia in the right colon, especially in females. Moreover, CTC allows both CRC prevention through the identification of polyps and early CRC diagnosis. CTC currently plays a role in the evaluation of patients with incomplete colonoscopy due to technical difficulties, patient discomfort, or obstructing lesions. Fenlon evaluated 29 patients with occlusive CRC and found that CTC identified the obstructing lesion in all cases and synchronous lesions in 18/20 patients, and visualized the proximal colon in 26/29 patients (18 on novel tests for CRC screening and beyond) [61].

The debate concerning the performance of CTC is ongoing and is extensively discussed in other portions of this text. In 2004, Cotton reported a study involving 615 patients at nine sites at increased risk for neoplastic lesions. A total of 284 lesions were found on 308 participants. The sensitivity and specificity of CTC detection of lesions >10 mm was 55% and 96%, respectively, while colonoscopy showed a sensitivity and specificity of 100% for similar lesions. As the size of the lesions decreased, so did the sensitivity and specificity for CTC detection of lesions [62]. A similar trial performed by Rockey [63] had to be halted early due to the statistical superiority of optical colonoscopy. Improvements in technology and software continue to augment this approach to screening.

High-Risk Individuals

Age and family history are by far the most important risk factors used to stratify CRC risk in asymptomatic individuals. CRC risk is rare in asymptomatic individuals younger than 40 years, as less than seven incident cases per 100,000 people are reported in this population [14]. At age 50, CRC incidence rises exponentially from 50 cases per 100,000 people screened to 340 per 100,000 cases at age 80 years. It is during this "age window" that screening is strongly advised. The importance of age 50 years as a screening cutoff is also strengthened by evidence which indicates that the prevalence of advanced adenomas increase with age. In the study by Imperiale and colleagues, there was a prevalence of advanced neoplasia in 3.5% of 906 asymptomatic subjects aged 40–49. The prevalence increases to 4.5% and 7.8% in those older than 50 and 60 years, respectively [15].

Knudsen's two-hit hypothesis of carcinogenesis is evident in the hereditary CRC syndromes. In these syndromes, the first "hit" is a germline mutation, while the second is a somatic mutation. In sporadic cancers, both hits are somatic mutations and are much less likely than the occurrence of one single somatic mutation in hereditary cancer syndromes, although it is one that still occurs in approximately 5% of the population worldwide. Patients at high risk for CRC include those with a family history or personal history of the disease, familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNPCC), Peutz–Jeghers syndrome (PJS), inflammatory bowel disease (IBD), and other rare syndromes.

Family/Personal History

A family history of colon cancer is defined by CRC or adenomatous polyps in a first-degree relative by age 60, or in multiple first-degree relatives after the age of 60. It has been recently estimated that 9.4% of the American population has a positive family history for CRC, with 3.1% having a first-degree relative diagnosed at age 60 or younger [16]. A meta-analysis involving 26 studies has shown a pooled relative risk for CRC of 2.25 (95% CI = 2–2.5) when a family history for CRC is reported [17]. Moreover, an association between the age of diagnosis in the first-degree relative and CRC was also demonstrated. The relative risk is highest when the age of diagnosis in a relative is <45 years (3.87) and lowest when it is >60 years (1.8).

It is recommended that patients with a family history undergo screening colonoscopy either at age 40 or 10 years prior to the age at which their youngest relative was diagnosed with CRC, whichever is youngest. It is believed that the shared genetic/environmental factors in family members lead to cancerous events at younger ages and at increased rates, and for that reason patients with a familial history of CRC are to be followed up with subsequent colonoscopies every 5 years. This interval may even be reduced to 3 years in patients with particularly strong family histories. Currently, a family history of CRC or adenomatous polyps in second- or third-degree relatives does not merit early CRC surveillance.

Patients with colorectal adenomas are deemed to be at higher risk for subsequent neoplastic processes. Patients at high risk include those found to have three or more adenomas, a single adenoma larger than 1 cm, or an adenoma in combination with a family history of CRC. If all adenomas are resected, patients should undergo subsequent surveillance every 3 years until the patient has a negative colonoscopy, at which point screening can be pushed back to 5-year intervals [22]. Patients with hyperplastic polyps are not at increased risk for the development of CRC.

Familial Adenomatous Polyposis

FAP is an autosomal dominant condition characterized by the development of hundreds to thousands of adenomatous polyps throughout the colon, in patients as young as their teens. If prophylactic surgery is not performed, nearly 100% of these patients will develop CRC by the time they are 40. The pathophysiology of this disease involves a germline mutation in the adenomatous polyposis coli (APC) gene, a tumor suppressor. Loss of function of APC allows for stimulation of unregulated cell growth and the development of adenomas. As time progresses, enough genetic mutations occur for these adenomatous polyps to become cancerous. This process is similar to what happens in sporadic adenomas, and as a result, APC is considered a gatekeeper of colonic neoplasia.

FAP occurs once in every 6,850 people, and results in less than 1% of all colon cancers. Patients with FAP should undergo elective annual colonoscopy at ages 10–12 and continue annually until a prophylactic proctocolectomy can occur, as well as testing for the APC gene mutation. A partial colectomy can be considered if the patient is willing to have yearly flexible sigmoidoscopic surveillance. The screening guidelines for patients with FAP stress the need for prophylactic colectomy by age 20. If surgery is to be postponed, annual colonoscopy should be performed. Extracolonic screening by upper endoscopy is also recommended every 1–3 years to aid in early detection of gastric polyps, which are found in 26–61% of patients [22–25]. While usually benign in the general population, diffuse gastric polyps may be a risk for gastric cancer [27–29]. Also, annual thyroid exams and ultrasounds should be performed, as well as periodic ultrasounds for pancreatic cancer and desmoid tumor screening.

Hereditary Nonpolyposis Colorectal Cancer

HNPCC, or Lynch syndrome, is an autosomal dominant syndrome which accounts for 2–5% of all CRC. It is the most common of the heridtary colon cancer syndromes and carries an 80% lifetime risk for CRC. HNPCC is defined by the Amsterdam Criteria or Bethesda Criteria. It must be noted that not all patients with the HNPCC gene mutation meet family history criteria, yet fulfillment of this criteria is sufficient for the screening/surveillance guidelines. Patients with HNPCC have inherited a mutation in one of the DNA mismatch repair genes (MLH1, MLH2, MSH6, PMS2), which causes the accumulation of mutations and increases the risk for malignant transformation. HNPCC patients develop adenomas at the same rate as the general population, but these adenomas are more likely to progress to cancer, and at a quicker rate in these individuals (2–3 years compared with 8–10 years) [19]. It is characterized by earlier onset of CRC, a right-sided predilection (70% of HNPCC cancers are found proximal to the splenic flexure), and a mucinous histopathology with infiltrating lymphocytes [5].

Patients diagnosed with the HNPCC mutation should have annual colonoscopies beginning at age 25. Patients with the specific MSH6 mutation may delay surveillance until age 30 [18]. The British Society of Gastroenterology allows annual FOBT with biannual flexible sigmoidoscopy if colonoscopy is not available. Currently, no guidelines recommend prophylactic surgery. Yet, individuals with HNPCC who do not undergo a partial/total colectomy after the first diagnosis of cancer have an estimated 30–40% risk for developing a metachronus tumor within 10 years and a 50% risk within 15 years, compared with 3% and 5% risks, respectively, in the general population.

Due to the high risk of gynecological malignancies, annual transvaginal ultrasounds, CA-125 measurements, and endometrial aspirations should be performed beginning at age 30 years in female patients. Once females are finished bearing children, prophylactic salpingo-oopherectomy and prophylactic hysterectomy are recommended.

Peutz–Jeghers and Juvenile Polyposis Syndrome

PJS is an autosomal dominant disorder characterized by hamartomas of the gastrointestinal tract, mostly in the small bowel, and pigmented mucocutaneous lesions. The pathophysiology of this syndrome involves a mutation in the STK11 gene (a tumor suppressor gene), whose protein plays a role in cellular growth inhibition. Hamartomas have extensive smooth muscle arborization, which gives the appearance of pseudo-invasion. Approximately 50% of PJS patients develop and die from cancer by age 50 [8]. The overall cumulative risk for colon cancer is as high as 39%. The Dutch surveillance guidelines recommend a colonoscopy every 2–5 years beginning at age 25, as well as video capsule enterography beginning at age 10 and continuing every 2–3 years, due to the high risk of polyps in the small intestine. The high risks of extra intestinal tumors involving the breast and gynecological

system in women mandate yearly mammography and transvaginal ultrasounds as well [4].

Inflammatory Bowel Disease

Patients with Crohn's disease (CD) or ulcerative colitis (UC) have an increased risk for cancer due to dysplasia in flat mucosa. The risk for colon cancer increases with duration of disease, extent of colonic involvement, presence of dysplasia, backwash ileitis, stricturing disease, and the presence of primary sclerosing cholangitis (PSC) [34, 36–38]. The risk for CRC in inflammatory bowel disease patients with UC is 2% at 10 years, 8% at 20 years, and 18% after 30 years [72]. Patients with CD of the colon have cumulative risks of 2.9% at 10 years, 5.6% at 20 years, and 8.3% at 30 years [20]. More recently, the degree of inflammatory activity over time has been shown to be associated with a higher risk for malignancy as well [64, 65].

Many of the lesions in patients with inflammatory bowel disease are flat, yet recent studies have shown that they are visible to most operators during colonoscopy [21]. Unfortunately, many of these lesions remain invisible, thus four quadrant biopsies every 10 cm are still recommended. It is also recommended that colonoscopic surveillance begin 8 years after diagnosis. If the screening is initially negative, subsequent colonoscopies can be performed at 1- or 2-year intervals. Following two negative colonoscopies, the interval between screenings can be increased to 1–3 years. Patients with disease limited to the rectum may follow the guidelines of the general population [66]. There has been interest in the use of chromoendoscopy, which has been demonstrated to increase the detection of dysplasia [67, 68], but this has not yet been adopted in screening guidelines.

Resectable lesions of low-grade dysplasia may be managed by polypectomy and repeat colonoscopy within 3–6 months if the surrounding mucosa is free of flat dysplasia. Lesions classified as indefinite dysplasia require close follow-up at 3- to 6-month intervals. Unresectable polypoid lesions, multifocal flat dysplasia, and spreading flat lesions confer a high risk for CRC and total proctocolectomy is recommended. If the patient (and physician) decides against colectomy, colonoscopy should be performed every 3–6 months until two consecutive colonoscopies are negative for dysplasia.

CRC Screening Guidelines

The advent of new techniques for CRC screening in recent years, coupled with the increased incidence and mortality of CRC in many parts of the world, arouses considerable interest in an optimal prevention of this disease. In particular, the approval of i-FOBT by Medicare (in the United States), the increasing accuracy of CTC, and the further validation of colonoscopy in average-risk populations have expanded the choices of available screening strategies. Such evidence has led scientific societies to upgrade the previous versions of the guidelines on CRC screening. Two independent position statements were released in a short time. The first was the result of a joint commission formed by the American Cancer Society, the US Multisociety Task Force on Colorectal Cancer, and the American College of Radiology [69], while the second was prepared by the US Preventive Services Task Force (USPSTF) [70]. Although based on similarly designed systematic reviews of the literature, the two guidelines came to substantially different conclusions, leaving some uncertainty on the optimal approach to CRC screening. This discrepancy is due to a different interpretation of analogous data and the lack of direct evidence correlating the new screening techniques with an effective reduction in CRC incidence or mortality. The primary difference between the two screening guidelines is that the USPSTF does not recommend stool testing or CTC, two tests that until now were still associated with varying degrees of uncertainty.

Position Statement of the American Cancer Society, US Multisociety Task Force on Colorectal Cancer, and American College of Radiology

Unlike previous versions of these guidelines, the authors have clearly distinguished tests capable of identifying both CRC and adenomatous polyps (structural examinations) from those primarily able to identify only cases of previously developed CRC (stool tests) (Table 3.1) [69]. According to these guidelines, the structural examinations accepted for CRC prevention are represented by endoscopy (colonoscopy and flexible sigmoidoscopy) and radiology (CTC and barium enema). The stool tests (g-FOBT, i-FOBT, and tests detecting oncogenic mutations in stool) have a high sensitivity and are used primarily to detect already developed carcinomas at an earlier stage (Table 3.1).

The options included in this position statement are based on simple inclusion criteria, which accept only the tests that are able to identify at least 50% of prevalent cancers and/or advanced adenomas (≥10 mm or <10 mm with HGD or rich villous component). The authors assume that there is too much uncertainty in subject compliance to repeat testing (programmatic compliance), so that each test should be associated with a high sensitivity, even when offered only once.

Table 3.1 Options for colorectal cancer screening recommended by the position statement of the American Cancer Society, US Multisociety Task Force on Colorectal Cancer, and American College of Radiology for asymptomatic people aged over 50 years at average risk for CRC

(a) Tests that Detect Adenomatous Polyps and Cancer
Flexible sigmoidoscopy every 5 years
Colonoscopy every 10 years
Double contrast barium enema every 5 years
CT colonography every 5 years
(b) Tests that Primarily Detect Cancer
Annual g-FOBT with high sensitivity for cancer
Annual i-FOBT with high sensitivity for cancer
Stool DNA test with high sensitivity for cancer (interval uncertain)

Regarding CTC, the authors used the American College of Radiology Imaging Network (ACRIN) study as adequate proof for acceptance of this screening method for large polyps. This decision was in line with selecting tests based on high sensitivities, marginalizing other variables such as specificity and issues related to risk-benefit analysis or cost-effectiveness ratios. This position also recommends 10-year repetition intervals for those aged between 50 and 80 years for colonoscopy, and 5-year intervals for sigmoidoscopy, CTC, and barium enema. Both g- and i-FOBTs should be repeated annually. These guidelines are important in that they acknowledge that not all patients are willing to undergo invasive tests or have access to invasive testing, and provide other acceptable alternatives.

Position Statement of the US Preventive Task Force

The authors of the USPTF conducted a systematic review of published articles since their previous position statement of 2002 to assess the implementation of tests that had already been adopted, namely colonoscopy, flexible sigmoidoscopy, g-FOBT, and the combination of the last two tests [70]. Note that barium enema had already been excluded as a screening option in 2002.

This review focuses mainly on the level of evidence available for the efficacy of any screening strategy in reducing CRC incidence and mortality. Unlike the position statement of the American Cancer Society, the authors evaluated other aspects of a screening program, such as simplicity, acceptability, safety, specificity, and the use of colonoscopy in the follow-up of noninvasive tests.

The authors argued that there is sufficient evidence to recommend the following options for CRC screening: g- or i-FOBT, FS with FOBT, and colonoscopy. The interval between two consecutive tests should be annual for FOBT, 5 years for FS, and 10 years for colonoscopy. The window screening should also be limited to patients aged 75 or younger, although it may be extended to those 80 years of age after an individual assessment of the subject. Unlike the previous position statement, the representatives of USPTF have found inadequate evidence to support CTC, genetic stool tests, and FS without FOBT.

The decision not to include CTC was based largely on the low positive predictive value shown by CTC in the ACRIN study, acceptability of the study, the inability to adequately detect polyps <10 mm, the risks of radiation, and extracolonic findings.

Unlike the high values of specificity shown by CTC in previous studies conducted in referral centers, the ACRIN study showed a disappointing specificity of CTC. In particular, the specificity for lesions ≥10 mm was only 86%. Taking into account the low prevalence of advanced lesions in an asymptomatic population, such low specificity would translate into an unsatisfactory positive predictive value, namely slightly above 20% for larger lesions.

In regard to CTC acceptability, the authors highlighted the lack of compelling evidence to suggest that the addition of CTC to the previously implemented screening options would increase overall population screening. In fact, studies that have compared the tolerability (a substitute for exam acceptability) of CTC have led to mixed results. In fact recent studies show a greater tolerability for colonoscopy with sedation than for CTC without sedation. Both CTC and colonoscopy require an uncomfortable procedure preparation and intra-procedural dilation with gas. Unlike colonoscopy, CTC does not require sedation, which may not be viewed favorably by all patients.

The adoption of a policy of nonreferral for CTC-detected diminutive polyps, together with CTC reduced sensitivity for 6–9 mm polyps compared with colonoscopy would risk a synergistic effect in decreasing CTC efficacy in preventing CRC compared with colonoscopy. Further studies on the natural history of small polyps are still needed.

The risk of ionizing radiation is particularly important when a technique is proposed to asymptomatic people with low prevalence of advanced neoplasia. A recent study by Brenner estimated a lifetime risk for cancer induced by radiation of 0.14% when a person undergoes full-dose CTC. Despite the evidence that such risk may be attenuated by at least ten times when adopting a low-dose protocol, it is unclear whether this protocol would be widely used by the radiological community.

Fifteen to thirty percent of CTC-screened subjects would need further follow-up for the identification of extracolonic findings, resulting in major surgery for suspected cancer or abdominal aortic aneurysm in 3–4% of the population. Hara et al [71]. studied 264 consecutive virtual colonoscopies using two observers and found 30/264 (115) had important

extracolonic findings. Six patients underwent surgery, and two underwent subsequent imaging. The impact of these extracolonic findings is largely unknown. Although these incidental discoveries may be important, the cost-effectiveness of this screening is still up for debate.

The diversity of the two guidelines is vast. In particular, the American Cancer Society has set a high priority for the reduction of CRC incidence by any means, while emphasizing the role of sensitivity over all other variables. This view is well justified when taking into account the low level of uptake of CRC screening in Western countries. In contrast, the USPTF position attaches more importance to the specificity of techniques and is careful not to accept uncertainty in its guidelines due to the lack of accepted literature on specific screening methodologies.

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Implementation and Clinical Trials in the United States

4

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Introduction

With any emerging medical imaging technology, there will be those who embrace and attempt to refine a potentially revolutionary modus operandi and those who hesitate to change the status quo. The history of computed tomographic colonography (CTC), also known as virtual colonoscopy, in the United States is no different. From the birth of the concept of "noninvasive, virtual colonoscopy" in 1994 [1], CTC has taken many steps forward and a few steps back on the way to becoming an indisputable alternative to optical colonoscopy for colon cancer screening.

In the not too distant past, many had serious doubts about the future of CTC altogether. Superimposed on a potential turf war with gastroenterologists, as well as political and reimbursement/payment implications, CTC continues to have its doubters and detractors. With continued advances in technology, however, CTC will only take more steps forward. The accuracy of CTC will no doubt only increase as techniques such as automated colonic distension, multidetector row CT technology, electronic stool subtraction, and computer-aided detection are further developed. The potential for a clinically proven, minimally invasive colorectal cancer (CRC) screening tool that may not require bowel prep, while simultaneously screening for abdominal aortic aneurysm and bone density, makes CTC a very attractive option when compared with optical colonoscopy (OC).

This chapter summarizes the data from US-based multi-institutional prospective studies and screening programs that have studied the accuracy of CTC versus OC. This chapter aims to answer the question: How good is CTC?

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Colorectal Cancer: Screening Options

In the United States, CRC ranks third in incidence and second in cause of death among all cancers for both women and men [2]. Approximately 150,000 new cases and 60,000 deaths are reported every year secondary to CRC [3]. Despite recommendations from national cancer organizations and increased media attention, CRC screening rates are low and only slowly increasing [4–6]. Of special concern is CRC screening disparity across ethnic and economic lines, with lower screening rates among nonwhite and Hispanic populations and among the poor [4, 7].

It is hoped that giving patients multiple options for CRC screening will increase present screening rates. Current available methods for CRC screening include (1) *indirect* tests that detect CRC via fecal tests, e.g., fecal occult blood tests (FOBTs), fecal immunochemical tests (FITs), and stool DNA and (2) *direct* imaging tests that can detect both cancer and advanced lesions, e.g., proctosigmoidoscopy, barium enema, OC, and CTC.

FOBTs have been the mainstay for inexpensive, widely available CRC screening. And while there is some evidence to support the mortality benefit from FOBT [8–10], other studies show no significant effect on mortality [11]. Recently, FIT demonstrated better sensitivity and similar specificity and is considered a rational substitute for FOBT [12]. Currently, the American Cancer Society recommends annual FOBT or FIT starting at age 50 [13].

Proctosigmoidoscopy, aka flexible sigmoidoscopy, as a screening tool for CRC is flawed for multiple reasons. Proctosigmoidoscopy evaluates only the left colorectum, entirely excluding the right and transverse colon; thus, half of CRCs are not identified with this screening tool. Although there are clinical trials which have shown flexible sigmoidoscopy to decrease colon cancer mortality [14–16], the invasiveness and lack of sedation inherent to this screening method make it unpopular for potential patients [17]. Nevertheless, flexible sigmoidoscopy remains one of the four recommended options for CRC imaging tests, recommended

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every 5 years after the age of 50. The other three imaging choices include OC, barium enema, and CTC [13].

OC is considered the de facto gold standard for colorectal cancer screening [18]. Historically, however, OC has been thought of more as a diagnostic procedure than as a screening procedure, secondary to its invasiveness, expense, need for sedation, and small (but real) risk for morbidity and mortality. Prospective studies have meanwhile demonstrated that colorectal screening with OC among high-risk patients reduces CRC mortality [19]. Some, however, believe that many screening OCs are being performed unnecessarily given the low yield of OC in detecting cancer in a large cohort of asymptomatic adults [20, 21]. Finally, CTC trials have shined the light on shortcomings of OC – a topic to be discussed later in this chapter.

Clinical Background: Polyp Histology, Size, and Management

A basic understanding of the histology and natural history of a colorectal "polyp," an all-encompassing term that includes a wide range of benign to malignant entities, is required to understand why CTC clinical trials are designed the way they are and why attention is paid to the particular size of a colonic lesion. As CTC (or OC for that matter) cannot determine histologic features on virtual or true visual inspection, the *size* of a polyp has become the primary feature that drives clinical management.

Many studies have demonstrated that polyps measuring less than 5 mm have little if any malignant potential. In a cohort of greater than 10,000 patients, Rex et al [22]. recently found the incidence of advanced adenomas and cancers in polyps ≤5 mm to be 0.87% and 0.05%, respectively. Although there is no complete consensus, there are a growing number of gastroenterologists and radiologists who argue that polyps less than 5 mm should be ignored [23–25], given that the prevalence of advanced histologic features in small polyps is less than 2% [26]. On the other end of the spectrum, a polyp measuring greater than 10 mm is generally considered an *advanced adenoma* and is at increased risk for future progression to carcinoma [27]. The long-term cancer risk of polyps measuring 6–9 mm lies somewhere in between the other two categorizations. This 6–9 mm subset (and how to handle these polyps in terms of OC versus interval follow-up) is the source of current research, to be discussed later in this chapter.

Stratifying polyps according to size (and therefore risk) is very important, as it helps guide clinicians in clinical management decisions, i.e., when a patient can undergo interval CTC surveillance versus immediate OC for removal of a polyp or polyps. Similar guidelines exist in other subspecialties, such as the Fleischner criteria for follow-up of pulmonary nodules [28].

Early CTC

After the introduction of CTC in the early 1990s, a number of studies were published that provided the first steps toward determining whether there was any prospect for CTC to one day be considered a valid alternative to OC. Study designs focused simply on demonstrating the comparability between CTC and OC. When the entire course of CTC research is examined, it is important to remember that many of these early trials did not attempt to establish CTC as a potential screening tool. Instead, their questions were much more basic. They simply wanted to demonstrate that if a polyp could be detected on OC, could it be demonstrated on CTC and, if so, was there a definable size threshold? For this reason, they sought out a cohort that was likely to provide them with material to image, either patients with known polyps, patients at high risk for developing neoplasia, or patients undergoing CRC surveillance. Following several encouraging results, a number of subsequent publications were also aimed at refining the technique of CTC.

The 2003 Sosna et al [29]. metaanalysis is a nice synopsis of early (pre-2003) CTC trials and their results. The authors reviewed results from 14 prospective studies, which evaluated the accuracy of CTC. They stratified the results according to polyp size and reported sensitivities per patient and per polyp. For polyps 10 mm or larger, the pooled per patient sensitivity was 88%; the per polyp sensitivity was 81%. For polyps measuring between 6 and 9 mm, the pooled per patient and per polyp sensitivities were 84% and 62%, respectively. For polyps 5 mm or smaller, the per patient sensitivity dropped to 65% and the per polyp sensitivity was only 43%. Overall specificity was high at 95%. They concluded that both CTC sensitivity and specificity were high for polyps measuring 10 mm or larger.

In their analysis, Sosna et al. made some keen observations. First, they pointed out the limitations imposed by the patient populations included in these early trials. The majority of the trials included in their analysis involved only high-risk patients, which may have artificially increased the positive predictive value. Additionally, the size of the studies significantly limited the extrapolation to larger populations for the purposes of screening. The summed total of all 14 studies was 1,324 patients, and the largest of the studies was only 300 patients. Further examination of two of the larger early studies, Fenlon et al [30]. and Yee et al [31],. reveals some valuable lessons learned along the way and some important points of caution.

Fenlon et al [30]. studied 100 patients from a single center who were determined to be high risk for colorectal neoplasm. The results revealed a similar efficacy of CTC to OC for detecting polyps measuring 6 mm or larger in diameter. Sensitivity of CTC was reported at 90% for polyps 6 mm or larger and 67% for those measuring 5 mm or less. The

researchers observed that frequent causes of false positives included residual stool, diverticular disease, poor colonic distention, and thickened haustral folds. They also suggested that the smaller, undetected polyps may become effaced in the air distended colon. Advantages of CTC included reduced study time, lack of need for sedation, and removal of operator-dependent results. Although encouraged, the authors in part concluded that the validity of their results would need to be reexamined in a larger-scale screening population involving multiple centers. Remaining questions included whether the low detection rate of polyps was clinically acceptable.

Yee et al [31]. also suggested excellent sensitivity of CTC in detecting clinically significant polyps and cancer in a slightly larger study group of 300 patients. The overall sensitivity was 90.1% (164 of 182) and overall specificity 72.0% (85 of 118). They also reported a sensitivity of 100% for the detection of carcinomas. Of note, the study selected patients from both average- risk asymptomatic and high-risk symptomatic groups and demonstrated comparable performance of CTC in the two groups. This finding encouraged further investigation into CTC as a screening tool.

In the end, the few early trials specifically considering the potential of CTC as a *screening* tool were heralding sensitivity values of 84–94% in the detection of polyps with a threshold of 6 mm, and 85–100% in the detection of polyps greater than 10 mm [21, 30–32]. These studies, however, were primarily from single center institutions with experienced, dedicated CTC radiologists. The next logical step would be for large-scale trials to verify these promising results.

CTC Takes a Couple of Steps Backward

In addition to the Department of Defense CTC trial (discussed in the next section), there were three other large-scale, multi-institutional trials [33–35] that set out to test whether CTC was ready for widespread clinical application.

Cotton et al [34]. enrolled 615 asymptomatic adults, aged 50 years and older, who were evaluated with CTC followed by OC. The results were disappointing. CTC sensitivity was 39% for polyps measuring at least 6 mm and 55% for polyps greater than 10 mm. CTC specificity for detecting trial participants without a lesion of at least 6 mm and without a lesion of at least 10 mm was 91% and 96%, respectively.

There are some noteworthy study design considerations with the Cotton et al. study that may help explain the suboptimal results. First, the prerequisite number of CTC cases for interpreting radiologists was set at only 10, with little opportunity for continued improvement/learning during the clinical trial. Initial CTC interpretation was read using 2D technique, while 3D CTC reconstruction was reviewed only at a later date/time (although sensitivity/specificity using the 3D technique primarily did not dramatically improve results, which were 45% and 93%, respectively). Additionally, oral contrast was not administered, thus the soon to be developed fecal tagging technique was not employed.

Rockey et al [35]. similarly investigated the accuracy of CTC for widespread application, comparing it not only with OC but also with air contrast barium enema (ACBE). Six-hundred and fourteen patients were evaluated prospectively with all three of these imaging tests. Initial ACBE was followed 7–14 days later by CTC with follow-up same-day OC.

The sensitivity of ACBE, CTC, and OC for polyps greater than 10 mm was 48%, 59%, and 98%, respectively. Sensitivity of these same three tests for polyps 6–9 mm was 35%, 51%, and 99%, respectively. As with the Cotton et al. study, interpretation was primarily with 2D technique with 3D problem solving; fecal tagging with oral contrast was not performed.

The study by Johnson et al [33]. was a third attempt to evaluate the sensitivity and specificity of CTC on a larger scale. Seven-hundred and three asymptomatic, patients at higher than average risk for CRC were evaluated prospectively with CTC compared with same-day OC. Noting high interobserver variability among three experienced CTC readers, the study found that per patient sensitivity for the detection of polyps greater than 10 mm and 5–9 mm ranged from 35% to 72% and 41% to 69%, respectively. Per patient specificity for these two groups of polyps ranged from 97% to 98% and 88% to 95%, respectively. The authors cited technical errors as a significant cause for missing 46% of polyps sized 5–9 mm and 37% of polyps greater than 10 mm. Suboptimal colon preparation, CT technique, and software capability were some of the technical limitations mentioned.

Department of Defense Trial Sets the Bar

But just as these multiple large-scale trials and soon to be published large-scale metaanalyses doubted the efficacy of CTC, the future and viability of CTC as a screening tool for CRC received a substantial boost when a 2003 US Department of Defense (DoD) multicenter study not only showed very promising results, but also introduced innovative CTC techniques and documented novel methods to better assess the true accuracy of CTC.

Prospective CRC screening of 1,233 asymptomatic adults, with CTC followed by same-day OC, resulted in impressive sensitivity and specificity values. For detecting colonic polyps measuring greater than 10 mm, CTC per patient sensitivity and specificity were 93.8% and 96%, respectively. This compared with an 87.5% calculated sensitivity of OC for detection of 10 mm or greater colonic polyps in the same

patient population. CTC per patient sensitivity and specificity for polyps measuring between 8 and 10 mm were 93.9% and 92.2%, respectively. OC sensitivity for these 8–10 mm polyps was 91.5%. Finally, CTC per patient sensitivity and specificity for polyps between 6 and 8 mm were 88.7% and 79.6%, respectively. OC for similar sized polyps was 92.3%.

The DoD study was different from previous clinical validation studies in multiple ways. Most importantly, it utilized two very important novel CTC techniques: fecal tagging and primary use of 3D "fly-through" polyp detection (as opposed to the 2D technique). Previous larger studies [34–39] had used a primary 2D polyp detection approach, with 3D views reserved for only problem solving. Fecal tagging, the technique whereby oral contrast "tags" residual stool and fluid in the colon, was also not routinely employed in these same studies.

During the same-day follow-up OC, colonoscopists were blinded to the results of the CTC. Results of the CTC were revealed with "segmental unblinding," whereby a study coordinator sequentially revealed the CTC results of a particular colonic segment during the patient's colonoscopy. The colonoscopists could therefore account for potential false negative polyps on OC, which would have otherwise been documented as false positives on CTC.

The segmental unblinding technique therefore allowed for identification and investigation of the adenoma miss rate of OC. Up until that point, the only way to estimate the miss rate of OC was either retrospective analysis or prospective "tandem" colonoscopy; these two techniques resulted in estimated miss rates of 10% and 0–6%, respectively [40–42]. Segmental unblinding, on the other hand, allowed for direct assessment of OC. The DoD trial was the first time a different exam with comparable sensitivity was used to assess the performance characteristic of conventional colonoscopy. Results showed that OC missed 55 pathologically proven polyps of 511 polyps identified prospectively on CTC; 21 of the 55 polyps measured greater than 6 mm [43]. In the end, the OC miss rate for large adenomas (>10 mm) was 12% [43]. A more recent study again confirmed an estimate of 11% for OC in detecting advanced adenomas [44].

The *location* of the missed, clinically significant adenomas with respect to a colonic fold was likely the most important clinical inference gleaned during detailed examination of the polyps missed on OC. The areas of the colon most likely to harbor a missed adenoma on prospective colonoscopy included the proximal sides of folds, the inner aspect of the colonic flexures, and the distal rectum [43].

Thus the DoD trial not only showed the potential of CTC as a CRC screening tool in an average risk population, it also pointed out that the hitherto gold standard of CRC screening, optical colonoscopy, had its limitations. OC "lost some of its glitter," [45] while CTC was positioned for prime time.

2005 Meta-analyses Muddy the Waters

Two large-scale CTC meta-analyses [46, 47] published in 2005 continued to cloud the waters for determining CTC efficacy. As with the only previous large-scale meta-analysis concerning CTC [29], these two more up-to-date meta-analyses again included older CTC studies which had not incorporated the multiple technical advancements used in the 2003 DoD trial [48]. As with Sosna et al [29],. the majority of the included studies for these two new meta-analyses evaluated symptomatic or high-risk patients: 23 of the 24 studies of the Halligan et al. meta-analysis [46] included symptomatic or high-risk patients.

A 2005 meta-analysis from Mulhall et al [47]. reviewed the results of 6,393 patients from 33 prospective CTC studies spanning 1999–2005. The wide variance among results, what the authors termed "heterogeneity," was not surprising. The combined sensitivity of CTC for detection of polyps measuring less that 6 mm averaged 48% (95% confidence interval [CI], 25–70%). Sensitivity for detection of larger polyps was better, but the heterogeneity of the results persisted: 70% (95% CI, 55–84%) for polyps measuring between 6 and 9 mm, and 85% (95% CI, 79–91%) for polyps greater than 9 mm.

In addition to compiling a very complete meta-analysis reviewing the up-to-date clinical performance of CTC, the authors addressed the wide variance among results from clinical trials up to that point. Mulhall et al. listed three main potential sources for explaining the diverse results of the 33 studies. First, studies that used thinner slices for collimation resulted in better sensitivity for polyp detection. Second, studies that used multidetector CT scanners versus single detector CT scanners also reported higher sensitivity. Lastly, there seemed to be improved sensitivity whenever 2D imaging was not the primary interpretative technique used. Although only two of the 33 investigated studies employed the fly-through technique [31, 48] these studies resulted in a pooled polyp detection sensitivity of 99%, as opposed to a pooled sensitivity of 82% for ten studies using 2D imaging with use of 3D imaging only when considered necessary.

The authors submitted that these three considerations were not the only sources of heterogeneity. Among other potential sources to explain the varied sensitivity values, they also mentioned poor bowel preparation, software limitations, experience level of readers, and misinterpretation of stool or folds.

Acknowledging the push for across-the-board consensus for CTC technique and interpretation, Halligan et al [46]. attempted to be more discriminating, using consensus documents from the fourth International Symposium on Virtual Colonoscopy to create minimum inclusion criteria. These criteria included the need for full bowel prep, the acquisition of prone and supine images, and the use of helical scanners. Important to note, either 2D or 3D image interpretation was permitted.

Only 24 of 1,398 initially identified studies met these inclusion criteria; these 24 studies investigated a total of 4,181 patients. Large (≥1 cm), medium (6–9 mm), and small (<6 mm) were the three polyp categories evaluated for sensitivity and specificity. Averaged sensitivity for large and medium polyps was 93% and 86%, respectively. As with the Mulhall et al. study, heterogeneity of small polyp testing resulted in a heterogeneous sensitivity range of 45–97%. Specificity of the large and medium polyps averaged 97% and 86%, respectively. Heterogeneous evaluation of the specificity of small polyps resulted in a range of 26–97%.

Definitive CTC Clinical Validation

ACRIN I/II

In 2005, the American College of Radiology Imaging Network (ACRIN) embarked on a large two-part multi-institutional trial funded by the National Cancer Institute to address the conflicting evidence of effectiveness of CTC. The primary aim was to examine the potential of CTC as a screening tool for colon cancer in a diverse, asymptomatic population, specifically calculating the sensitivity of CTC in detection of clinically significant large colonic lesion, defined as a lesion measuring at least 10 mm. Secondary analysis documented both the sensitivity of detecting 5–10 mm polyps and proven polyps at least 5 mm and at least 10 mm containing high-grade dysplasia, invasive carcinoma, and/or villous features.

Known as ACRIN I, a preliminary CTC investigative study examined 93 positive OC studies from eight institutions. Eighteen blinded independent readers retrospectively reviewed the CTC exams from these same patients. Average sensitivity and specificity for detection of OC proven polyps measuring greater than 10 mm was 75% (range 50–100%) and 74% (range 38–100%), respectively [49].

The larger ACRIN II trial, results of which were published by Johnson et al [50],. involved 15 institutions and 2,600 asymptomatic patients and employed many of the same techniques that had proven so effective in the DoD trial: oral contrast fecal tagging, colonic distention with automated CO_2 delivery, and the use of more technically advanced multidetector row CT scanners (>16 slices). In terms of image acquisition, meticulous and reproducible specifications were adhered to, such as 0.5–1 mm collimation, 0.98 to 1.5 pitch, 50 effective mAs, and 120 kV peak voltage. And for the first time in a large multicenter CTC trial, interpreting radiologists had to complete a qualifying exam consisting of established cases; the candidate radiologists had to identify 90% or more polyps measuring 10 mm or greater. Establishing uniform criteria and imaging protocols for this large multicenter trial was essential. If CTC was to become a clinically accepted colorectal screening modality, there needed to be increased standardization of image acquisition and radiologic interpretation. Of note, one important variable of the ACRIN II trial was the utilization of both 2D and 3D polyp detection techniques.

The ACRIN II results were convincing and reinforced the DoD study results. Sensitivity and specificity for detection clinically significant large (≥10 mm) colonic lesions that turned out to be adenomas or adenocarcinomas were 90% and 86%, respectively. There was lower, but respectable, sensitivity and specificity for CTC identification of colonic lesions less than 10 mm. Sensitivity for adenoma or cancer detection for lesions ≥9, ≥8 ≥7, and ≥6 mm were 90%, 87 %, 84%, and 78%, respectively. Specificity for these same sized lesions were 86%, 87%, 87%, and 88%, respectively. Most of all, an impressive high negative predictive value of 99% for any adenomas or cancers measuring greater than 6 mm confirmed the power of CTC as a powerful screening tool.

University of Wisconsin

Further evidence supporting CTC as a viable CRC screening method came in a University of Wisconsin study that directly compared the success of a CTC screening program versus an OC screening program. While previous and contemporaneous studies at that time looked at the accuracy of CTC itself, these investigators were not asking whether CTC was as good as OC in detecting polyps. They wanted to better understand the *clinical* impact of screening patients with CTC versus with OC.

Kim et al [51]. followed two arms. In the first, they used CTC as a primary screening tool in 3,120 consecutive patients over a 25-month period. In the second group, OC served as the primary screening method for 3,163 patients over 17 months. All patients were recruited from the same general screening population. Those patients currently being followed for polyp surveillance, with a history of inflammatory bowel disease, polyposis syndromes, or hereditary nonpolyposis CRC syndrome were excluded from the study so as to ensure a true low-risk screening pool of patients.

Their outcomes were measured by the detection of advanced neoplasia and the total number of polyps removed. The authors defined advanced neoplasia as either adenocarcinoma or advanced adenoma, which includes any adenoma greater than 10 mm in diameter, containing a significant villous component or containing high-grade neoplasia. They pointed out that most polyps measuring less than 10 mm are not adenomatous and that only a small fraction of all adenomas are advanced. The authors argued that these facts suggest a need for a more selective alternative to the practice of universal polypectomy.

A similar prevalence of advanced neoplasms was found in both the CTC and OC groups. There was also no significant difference in the number of large or small advanced adenomas that were removed. There was, however, a significant difference in the number of polypectomies required to achieve this similar outcome, with four times as many polyps being removed in the OC group. From the CTC group, 7.9% (246/3,120) of patients were referred for therapeutic OC.

Serious adverse events were demonstrated to be significantly less in the CTC group. Colonic perforation occurred in 0.2% of the OC patients compared with zero in the CTC group.

An additional interesting finding was the detection of extracolonic cancers on CTC. Eight extracolonic cancers were found in the 3,120 patients. This prevalence of 0.3% is certainly comparable to the 0.4% and 0.1% prevalence of invasive colon carcinoma found on CTC and OC, respectively.

The researchers also defend the proposition that diminutive polyps (≤5 mm) are likely clinically insignificant. They go further to suggest that diminutive polyps should not even be reported, as the rate of polypectomy and potential complication would be reduced without sacrificing cancer prevention. Of 2,006 small polyps removed in the OC group, only four advanced lesions were found, resulting in a yield of only 0.2%. Using size as a discriminating characteristic in a total of 6,283 patients studied, not a single subcentimeter cancer was observed. One question that does remain concerns the clinical management of polyps measuring between 6 and 9 mm. Two options are suggested. In one, all polyps falling into this category found on CTC are referred to OC for polypectomy. Alternatively, short-term follow-up with CTC allows only enlarging lesions to proceed to polypectomy, thereby providing a more selective filter.

These findings support the suggestion that CTC be used as a safe, clinically effective, and cost-effective filter to OC. Reduced complication rate and the potential to detect extracolonic cancers are additional benefits of CTC.

National Naval Medical Center Colon Health Initiative

In 2004, a congressionally funded grant authorized the commencement of the Colon Health Initiative at the National Naval Medical Center (NNMC). Since the opening of the center, 8,265 adults have been primarily screened for colon cancer with CTC. Provided they meet the American Cancer Society's recommendations for screening colonoscopy and fall into a "low" or "average" screening risk, each individual patient ultimately decides whether he/she will undergo CTC or OC.

Continued statistical analysis of the 8,265 screened patients demonstrates the efficacy of the program as an alternative to OC for CRC screening. NNMC's per patient CTC sensitivity and specificity for polyps measuring between 6 and 8 mm are 89.7% and 85.2%, respectively. Sensitivity and specificity for polyps measuring between 8 and 10 mm are 92.1% and 95%, respectively. Sensitivity and specificity for polyps measuring greater than 10 mm are 90% and 96.9%, respectively. NNMC's per patient CTC sensitivity and specificity for adenomatous polyps measuring 6 mm or larger are 93.9% and 82.2%, respectively. Sensitivity and specificity for adenomatous polyps measuring between 8 and 10 mm are 97.2% and 93.1%, respectively. Finally, sensitivity and specificity for adenomatous polyps measuring greater than 10 mm are 100% and 96.2%, respectively (Drs. D. Barlow, B. Cash of NNMC, February 4, 2010, confirm permission to publish "personal communication").

Walter Reed Army Medical Center

Since the landmark DoD funded multi-institutional study exploring the potential of CTC to screen for colon cancer, Walter Reed Army Medical Center continues to have a very robust CTC program. In addition to the CTCs being performed at Walter Reed, radiologists also interpret CTC exams sent remotely from two hospital sites in the US Army health care system.

Since the opening of the Walter Reed CTC program, 8,040 patients have been primarily screened for colon cancer with CTC. Of these, 740 patients (9.2%) were categorized in the CT Colonography Reporting and Data System (C-RADS) as modified C3 (having one polyp ≥8 mm or three or more polyps between 6 and 7 mm in diameter) or C4 and referred for conventional colonoscopy (Dr. M. Frew of Walter Reed Army Medical Center, personal communication, February 3, 2010). As patients are no longer enrolled in a clinical study and receive only conventional colonoscopy when needed, sensitivity and specificity cannot be measured. However, the referral rates for conventional colonoscopy for screening populations fall within the expected range based on both the DoD clinical trial and subsequent trials at both NNMC and the University of Wisconsin.

Non-US-Based Clinical Trials

While CTC clinical trials and research continue in the United States, large-scale, prospective studies have been taking place all over the world. Multi-institutional trials similar in

design to the ACRIN trials include the Italian IMPACT (Identification of Men with a genetic predisposition to ProstAte Cancer: Targeted) trial [52], which enrolled 1,103 participants, and the Munich Colorectal Cancer Prevention Trial [53], which enrolled 311 patients. These trials consistently confirmed the efficacy of CTC as a screening tool, both recording greater than 90% sensitivity for the detection of advanced neoplasias measuring 10 mm or larger. The European-based clinical validation for CTC is discussed in detail in Chap. 5 of this book.

Future Clinical Trials

As briefly discussed earlier in the chapter, the *size* of a polyp is the most important defining characteristic that helps guide patient management decisions. Current CTC guidelines from the American College of Radiology and the Working Group on Virtual Colonoscopy do not advocate reporting of polyps measuring 5 mm or less, which are categorized as C1 in the C-RADS classification scheme [54, 55]. Consensus opinion from the Working Group on Virtual Colonoscopy further recommends OC for patients with three or more polyps (each measuring 6–9 mm) or with a single polyp measuring more than 10 mm [53]. This is category C3 in the C-RADS classification.

The proper handling of intermediate polyps, those measuring ≥6 and ≤9mm, is the one area where mixed recommendations exist. The Working Group on Virtual Colonoscopy offers either 3-year surveillance or OC for intermediate polyps, also known as the C2 categories; patients can actually have up to two of these intermediate-sized polyps and still fall in the C2 classification [54]. However, a joint recommendation from the US Multisociety Task Force on Colon Cancer, the American Cancer Society, and the American College of Radiology recommends that polypectomy should be offered for patients with any polyp measuring 6 mm or greater [56]. Regardless of the consensus group or specialty society, most agree that follow-up CTC for intermediate lesions versus polypectomy should be based on clinical contexts such as a patient preference, comorbidities, and risk factors.

One of the main thrusts of current CTC research, therefore, is to examine these intermediate polyps, their natural history, and how aggressively they should be followed. An ongoing clinical trial being performed dually at the University of Wisconsin and the NNMC directly addresses these concepts. In an excellent review article discussing the prevalence, size, histology, morphology, and natural history of polyps [57], Pickhardt and Kim describe the framework of this novel prospective natural history study tracking 6–9 mm polyps. In the study, intermediate polyps identified on an initial CTC are followed either at 1- to 2-year intervals with CTC surveillance, with potential expansion to 3- to 5-year CTC follow-up (the University of Wisconsin arm) or 1-year follow-up CTC surveillance with immediate follow-on OC with polypectomy (the NNMC arm). The University of Wisconsin arm therefore allows researchers to track the natural history and progression/regression of the 6–9 mm polyps, while the NNMC arm results in correlative histologic data.

Initial interim results from 128 intermediate-sized polyps in 100 patients supports the growing belief that not all polyps measuring greater than 6 mm need to be removed on OC. Of the 128 polyps, 116 (90.6%) showed no interval growth in size, including 73 polyps stable in size, nine polyps smaller in size, and 34 polyps not identified at follow-up (polyps having either totally regressed or been false positives on the initial CTC). There were no cancers among the histologically proven lesions, and only one of the 128 polyps reached the 10 mm threshold.

In addition to research into handling of 6–9 mm polyps, there are two additional areas of CTC study, which are exciting and promising. The possibility of a no bowel prep CTC and computer-aided detection will be covered in detail in Chaps. 6 and 11, respectively.

Conclusion

The question today is no longer whether CTC is "good enough" when compared with OC in the detection of clinically significant colonic polyps. The answer is a resounding "yes." Bolstered by the numerous large-scale clinical trials discussed in this chapter and outlined in Table 4.1, the American Cancer Society and multidisciplinary societies have even labeled CTC as an acceptable screening modality for colorectal cancer screening [55]. The question instead becomes how CTC will fit into the role of a screening modality, thereby reserving OC for high-risk patients or patients with large polyps noted on CTC necessitating removal.

The future will see the increasing capability of multidetector rows in the performance of CTC, while at the same time requiring less and less total radiation exposure. Advances with respect to 3D modeling and computer-aided detection techniques will also become more and more refined. Patients will be the eventual winners, as the minimally invasive CTC exam will play an increasing role in CRC screening, preventing potentially unnecessary biopsies. Instead of a potential screening tool, OC will likely take on more of a diagnostic role.

Table 4.1 CTC trials for polyp detection per patient analysis

Authors/Institution	Patient Number	Sensitivity (%)		Specificity (%)	
		≥6 mm	≥10 mm	≥6 mm	≥10 mm
Early CTC Trials					
Fenlon et al.	100	94	96	92	96
Yee et al.	300	93[a]	100	NA	NA
Pre-DoD Large-Scale Trials					
Cotton et al.	615	39	55	91	96
Rockey et al.	614	51	59	89	96
Johnson et al.	703	65[a]	64	86	95
DoD Trial and Beyond					
Pickhardt et al.	1,233	89[b]	94[b]	80[b]	96[b]
ACRIN II	2,600	78[c]	90[c]	88[c]	86[c]
NNMC CHI	8,265	94[b]	100[b]	82[b]	96[b]

[b]Evaluating for adenomatous polyps

[c]Evaluating for adenomatous polyps and/or adenocarcinoma

[a]Value is for polyps measuring 5–9 mm as opposed to 6 mm

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Clinical Trials in Europe

5

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Introduction

To have some insight into the present and future role of computed tomographic colonography (CTC) in Europe, one must keep in mind that there are significant differences between Europe and the United States in their approaches to the early diagnosis of colorectal cancer (CRC) [1]. The main difference is that in the United States, screening costs are mainly covered by insurers, while in Europe, screening programs are sustained by national health services. In 2003 the European Union Commission officially recommended CRC screening by means of fecal occult blood test (FOBT) [2, 3]. Since then, several European nations have implemented state-sponsored screening programs aimed at anticipating diagnosis of CRC in the average-risk individual by targeting subjects over 50 years [4–7]. Flexible sigmoidoscopy (FS) and colonoscopy programs have also been proposed for screening in some European countries but, as of today, have a limited territorial coverage [8, 9]. FS will probably pick up momentum in view of new data from the UK Flexible Sigmoidoscopy Trial, showing a reduction of mortality of up to 43% in people attending screening [10]. Subjects at increased risk for developing CRC due to personal or family history or who have alarm symptoms (i.e., rectal bleeding, weight loss, change in bowel habit, presence of severe anemia) and/or an FOBT-positive test have a higher probability of carrying CRC (e.g., 21% in individuals over 50 with severe anemia have CRC) and should undergo colonoscopy [11, 12]. Since 2000, several CTC trials have been performed in Europe, initially with the aim of testing the performance of CTC by applying different protocols and instrumentation and subsequently to understand which group of subjects could benefit from the test. Ongoing trials are aimed mainly at comparing CTC performance with that of other CRC screening tests in terms of detection rate and participation.

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This review presents the results of the European trials of CTC and attempts to give insight into the future trends of research in the field.

Trials Aimed at Assessing Performance of CTC with Different Protocols and Instrumentation

Single center CTC trials were conducted in Europe – mainly in Belgium, Italy, the Netherlands, and the United Kingdom– starting in the late 1990s [13–17]. In order to have an adequate number of positive cases, these studies included mostly high-risk and/or symptomatic subjects. In fact, in a selection of the most relevant trials, the prevalence of abnormality (i.e., excluding small polyps) was between 31% and 54% [18]. In most cases, the reference standard was same-day colonoscopy and the main endpoint per polyp sensitivity, which ranged from 67% to 95% cumulatively for intermediate-sizes and large lesions [19].

Preparation was mostly laxative based (e.g., polyethylene glycol [PEG], Phospho-soda), and the preferred reading mode was primary 3D. Large multicenter studies were first planned in Italy, starting in 2003 [20], and in the United Kingdom [21]. Results of these trials will be discussed in sections that follow.

Trials Targeting Average-Risk Individuals

Opposite to the United States, as of today no multicenter trials targeting average-risk patients have been performed in Europe. One large single center study, the Munich Trial, reported the results of 307 average-risk symptomatic individuals over 50 years of age undergoing a fecal immunochemical test (FIT), colonoscopy, and CTC [22]. FS performance was deduced from colonoscopy, by considering for analysis only the rectum and sigmoid colon. In the trial, all individuals underwent conventional laxative preparation;

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iodinated contrast agent was added to the last liter of PEG, which was drunk the morning prior to scanning. Patients underwent scanning with a low-dose protocol on a 64-channel multirow scanner at a collimation of 0.6 mm and a reconstruction interval of 0.75 mm. Mean radiation dose was 4.3 mSv. Sensitivities of colonoscopy, CTC, FS, and FIT for detecting advanced adenomas were respectively 100%, 96.7%, 83.3%, and 32%. Specificity and positive predictive value were low for all tests, as they were affected by the low prevalence of advanced lesions in relation to the total number of polyps (9% overall and 35.5% considering only lesions of at least 6 mm). In their conclusions the authors suggest that CTC might be included in CRC screening guidelines as an alternative to colonoscopy.

In European countries where national screening programs are ongoing, national policy makers require that CTC be confronted with existing tests. Randomized trials have been designed and financed and are on their starting blocks, comparing the performance of CTC with those of FS (PROTEUS Trial, Piedmont, Italy), FIT (SAVE Trial, Tuscany, Italy) and colonoscopy (CoCoS Trial, The Netherlands) [23].

The main aim of the trials will be to compare the detection of advanced neoplasia of the tests and the participation rate with the program. Cost-effectiveness of programs will also be assessed to establish whether it will be affordable for governments to perform screening with CTC. The PROTEUS and SAVE studies will also evaluate the role of computer-aided diagnosis and the impact of reporting extracolonic findings. The results of these trials will be available starting in 2012.

Trials Targeting Individuals at Increased Risk for CRC by Family History

A positive family history of CRC is defined as the presence of advanced neoplasia (i.e., advanced adenoma or invasive cancer) in any first-degree relative aged younger than 60 years, or in at least two first-degree relatives at any age [24].

In such cases the relative risk for developing CRC is two to four times that of the general population [25]. Due to their increased risk for developing CRC, individuals with a family history should have their entire colon examined with colonoscopy [26]. CTC may be an appealing alterative to optical colonoscopy in view of the dismal participation rate of these subjects in screening programs [27].

The IMPACT Stands for Italian Multicenter Polyp accuracy CTC Study trial includes a group of 373 individuals with a family history for CRC with a median age of 51 years (range 41–65). In this group of subjects the prevalence of advanced neoplasia was 7.5%, similar to figures reported elsewhere [27, 28], including four patients with invasive carcinoma (1.1% prevalence) and 24 with advanced adenomas (6.4% prevalence). Per patient sensitivity for individuals with at least one 6 mm or larger lesion was 82.1%; negative predictive value, positive predictive value, and specificity were 98.5%, 51.1%, and 93.6%, respectively.

At the end of 2008 the Italian Health Ministry sponsored a study aimed at establishing whether CTC could sort out low-risk individuals, aged 40–70 and with a family history of advanced neoplasia, who could avoid undergoing colonoscopy. The proposed colon preparation includes a low laxative regimen and iodine-based fecal tagging. To date, 350 of the expected 1,500 subjects have been enrolled in four Italian academic Institutions.

Trials Targeting Individuals at Increased Risk by Personal History (Surveillance)

Patients undergoing polypectomy are recommended to undergo surveillance colonoscopy at <1–10 year intervals, according to number of adenomas and histology [29]. However, the yield in terms of polypectomy is very low, and surveillance colonoscopy accounts for approximately one-fourth of all endoscopic procedures [30, 31]. If CTC performance is adequate, it could be used to reduce the workload of endoscopic units by targeting individuals whose index lesion is a low-risk adenoma, while ensuring an efficient detection rate of clinically relevant lesions. Unfortunately, very few studies worldwide have addressed this issue. Van Gelder et al [17]. assessed CTC performance in 249 subjects, including 158 (64%) who performed the test for surveillance. Per patient sensitivity and specificity for patients with large polyps (i.e., diameter of at least 1 cm) were 84% and 92%, respectively. However, in the trial, four of the 14 (29%) large flat lesions, including one cancer, were overlooked. The authors conclude that CTC and colonoscopy have a similar ability to detect large colorectal polyps.

The IMPACT trial includes 266 postpolypectomy patients who were analyzed separately [20]. In the study, per patient sensitivity, specificity, positive predictive values, and negative predictive values for postpolypectomy patients with at least one advanced neoplasia 6 mm or larger were 84.2%, 85.3%, 41.6%, and 97.7%, respectively. The authors conclude that CTC is feasible to enhance follow-up in postpolypectomy individuals, especially those carrying a lower risk for recurrence, and to reduce burden of surveillance colonoscopy. The issue of the appropriateness of CTC in subjects with a personal history of colorectal lesions needs to be addressed by other, larger, and more effective trials that should be aimed at assessing the opportunity of performing CTC in relation to patient risk for developing new lesions. To our knowledge, no such trials are ongoing or planned in Europe for the near future.

CTC in FOBT Positives

Approximately 55–65% of FOBT-positive subjects do not have advanced colorectal lesions [4, 32, 33] These patients undergo colonoscopy unnecessarily, which adds to patient anxiety and to the cumulative risk for complications. CTC could be used as a triage instrument to select patients for colonoscopy, thereby reducing the number of unnecessary exams. To avoid sending individuals who have no lesions to endoscopy, it will be necessary for CTC to have a high negative predictive value in addition to good sensitivity and specificity profiles. Liedenbaum et al. recently addressed this issue by inviting FOBT-positive patients scheduled to undergo colonoscopy to undergo CTC before colonoscopy [34]. CTC was performed in 302 FOBT-positive subjects, with positive predictive value, negative predictive value, and diagnostic accuracy of the CT test as the main determinants. The authors report negative predictive values for lesions ≥10 and ≥6mm of 84% and 77%, respectively, and they conclude that CTC is probably not cost-effective as a triage technique in FOBT positives. The IMPACT trial included 221 FOBT positives from regional FOBT screening programs [20] who were also evaluated separately. In the trial, per patient sensitivity, specificity, and negative predictive and positive predictive values for advanced adenoma ≥6 mm were 86.5%, 76.4%, 78.7%, and 84.9%, respectively . The authors conclude that results do not support the use of CTC as a first-line strategy in FOBT positives because of the high prevalence of advanced neoplasia, of the low specificity, and of the low negative predictive value. However CTC could be proposed to patients who refuse colonoscopy, which may occur in up to one-third of FOBT-positive cases [35], or who could not complete colonoscopy. On this point, Sali et al [36]. performed CTC in 42 subjects with incomplete colonoscopy from the population-based screening program of Tuscany. CTC identified significant colorectal lesions in 21 patients (50%), including two colonic masses and 20 large and intermediate polyps; the positive predictive value was 87.5%. The authors conclude that CTC is useful for the evaluation of the nonvisualized part of the colon after incomplete colonoscopy.

Further research in the field should focus more on the cost-effectiveness of using CTC as a triage technique and on its value in individuals who refuse or have incomplete colonoscopy.

CTC in Patients with Alarm Symptoms

CTC is indicated in individuals with alarm symptoms who refuse or have incomplete colonoscopy [37, 38]. Patients at increased risk for complications from optical colonoscopy because of age, coagulation disorders, increased sedation risk, and known diverticular disease should also undergo CTC instead of colonoscopy [38, 39]. On this point it must be remembered that in the elderly and/or frail, the target of imaging is to identify gross colonic and extracolonic abnormalities; finding a small lesion will probably not impact patient survival rate. Iafrate et al. report on 136 subjects with a mean age of 81 years undergoing CTC with reduced bowel preparation following incomplete colonoscopy [40]. No major side effects were reported in the study, and 25% of patients referred diarrhea following bowel preparation. Overall 83% of exams were of excellent quality and 76% of subjects replied to the interview that they would be willing to repeat the test if necessary. Similar findings were reported by Keeling et al [41]. on 67 patients with a reduced functional status who were deemed unfit for optical colonoscopy. Also in this study, exam quality was good or excellent in 84% of cases; colon and extracolonic abnormalities were detected in 18% and 43%, respectively, of subjects.

One large UK trial, the SIGGAR (Special Interest Group in Gastrointestinal and Abdominal Radiology) study, will soon report its results [21]. The aim of the SIGGAR study is to compare the detection rate of CTC versus barium enema and CTC versus colonoscopy for CRC and colonic polyps measuring 1 cm or larger. SIGGAR targets individuals aged 55 years and older with symptoms or signs considered suggestive of CRC by the referring physician. Over 5,000 patients had been randomized in the study by the end of 2007. A second multicenter trial, involving 26 centers for a total of 845 patients, has just completed recruitment in France (Mehdi Cadi, May 13, 2010, personal communication).

Conclusions

The large number of clinical trials conducted in Europe over the last decade testifies to the interest of European radiologists and clinicians in CTC. Started as studies needed to explore the potential of the technique, they are now aimed at assessing the possible role of CTC as a CRC screening method. At least three randomized trials are about to start, in order to compare CTC performance with that of existing screening tests (FS, FIT, and colonoscopy). Among the targets of study, participation rate and cost-effectiveness are extremely important, since they are the key issues needed for European governments to support CRC screening with CTC.

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Patient Preparation and Tagging

6

Dipti K. Lenhart, Rocio Perez Johnston, and Michael E. Zalis

Introduction

Computed tomographic colonography (CTC) has become widely used over the past decade as a complementary method for colorectal cancer screening. Achieving consistently high performance with the examination depends on the quality of a number of factors, including: patient preparation prior to the examination, colonic distension, computed tompgraphic (CT) scanning parameters and data acquisition, postprocessing of data, 2D and 3D navigation workstations, and interpretation by the radiologist. This chapter will focus on patient preparation for the examination, including cathartic colonic cleansing as well as fecal and fluid tagging.

There is currently no consensus on the single best preparation or tagging method to achieve optimal colonic cleansing, although there has been convergence of technique among different centers internationally. Variation persists in regard to diet and type, timing, and duration of bowel preparation, although most centers now combine cathartic, purgation cleansing with some form of fecal tagging, and this combination has been associated with high performance in large clinical trials of CTC [1, 2]. There have also been proposals to eliminate the need for cathartic colonic cleansing altogether, opting instead for only fluid/fecal tagging with postprocessing subtraction of the tagged residue; these reduced- or noncathartic techniques have been demonstrated in pilot and small clinical trials but as of this writing are not yet fully validated.

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Diet

Fiber-Restricted Diet

Fiber is a carbohydrate that passes through the gastrointestinal tract undigested and unabsorbed by the body. Dietary fiber restriction prior to CTC consequently reduces the amount of stool in the colon. Fiber-containing foods include legumes, nuts, and seeds. Some centers recommend a fiber-restricted diet and/or liquid diet for 24–48 h before CTC. The impetus and evidence for implementing fiber reduction prior to CTC derives from clinical experience with barium enema and optical colonoscopy, for which diet modification has a long clinical history. To our knowledge, there have been no prospective clinical trials specifically evaluating the benefit of fiber restriction as part of the bowel preparation for CTC.

Liquid Diet

Limiting the diet to clear liquids (including water, juice, broth, popsicles, and Jell-O) further reduces the amount of solid fecal material present in the colon. Given the restricted nature of this diet, this is limited to at most 1 day prior to the examination. Again, evidence for liquid diet in preparation for CTC derives from standard clinical practice with barium enema and optical colonoscopy preparation and the association with good performance observed in large clinical trials of CTC.

Cathartic Preparation

Polyethylene Glycol-Based Electrolyte Solution

The polyethylene glycol (PEG) formulation is an orally ingested colonic lavage solution that functions by physically

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clearing the colon with a large volume of iso-osmolar non-absorbable solution [3]. In contrast to the saline cathartics, which leave the colon relatively free of fluid, PEG is considered a "wet preparation" because it leaves a large amount of fluid in the colon. If this residual fluid is not further modified, as with a contrast tagging agent, it can potentially compromise a CTC examination if administered in sufficient quantity, because soft tissue polyps may be submerged and hence obscured by iso-attenuating residual fluid. In addition to PEG, the formulation contains potassium chloride, sodium bicarbonate, sodium chloride, and sodium sulfate in concentrations that are isotonic to the circulating volume. In contrast to certain osmotic loading cathartic preparations (principally Phospho-soda), PEG solutions are not associated with clinically significant electrolyte or volume shifts and are considered safely ingestable by individuals with renal or cardiac deficiencies.

There are several different formulations of PEG solution commercially available, most of which require a patient to ingest 2 or 4 L [4]. PEG solution is typically used for optical colonoscopy because it is safe and rigorously cleanses the colon. However, the large volume (especially with 4 L preparations) is a deterrent to patient compliance and comfort [5]. It can be particularly unpleasant for incontinent patients and those with limited mobility because of the associated cramping and diarrhea [6]. Experience at our own institution indicates that adequate preparation for CTC can be achieved with the 2 L variant of PEG that combines cathartic lavage with bisacodyl sodium, an ancillary agent discussed below. The smaller volume of this preparation has been associated with improved patient comfort.

NuLytely (Braintree Laboratories, Braintree, MA) is a similar solution which does not contain sulfates (PEG sulfate-free electrolyte lavage solution), also requiring 4 L of volume.

HalfLytely (Braintree Laboratories) is similar to NuLytely, but requires only 2 L of administration, which is better tolerated by patients. HalfLytely is available in a commercially available kit that also includes 10 mg of bisacodyl, discussed next.

Bisacodyl Sodium

This product is a stimulatory cathartic often used in conjunction with other cathartics such as PEG, sodium phosphate, and magnesium citrate. Its cathartic effect is achieved by stimulating parasympathetic reflexes to induce evacuation of stool [4]. Because of this additional stimulation, there is increased diarrhea with bisacodyl use [5]. Bisacodyl comes in a 5 mg tablet form, with a total administered dose usually of 10 or 20 mg.

Sodium Phosphate

Sodium phosphate solution (Phospho-soda; Fleet Pharmaceuticals, Lynchburg, VA) was a saline cathartic previously available in an over-the-counter commercially available kit. Saline cathartics share a common mechanism of action in that the relative hypertonicity of the cathartic agent draws fluid from the circulation into the bowel lumen. The resultant expanded fluid volume in the colon then stimulates peristalsis and is eventually expelled, along with retained fecal material [3]. A relatively small volume of sodium phosphate solution is consumed: either a normal dose of 45 mL or a double dose of 90 mL. Kim and colleagues found that the smaller 45 mL dose was comparable to 90 mL in achieving colonic cleansing [7, 8]. Because the relatively high sodium content had been found to cause transient electrolyte disturbances and renal toxicity [4], the US Food and Drug Administration issued a warning in December 2008 concerning the specific adverse effect of acute phosphate nephropathy, and the manufacturer voluntarily removed sodium phosphate solution from the US market shortly thereafter. However, sodium phosphate is still available by prescription in a tablet form (Visicol and OsmoPrep, Salix Pharmaceuticals, Morrisville, NC).

Magnesium Citrate

Magnesium citrate (LoSo Preparation; E-Z-EM Inc., Westbury, New York) is a hyperosmolar saline cathartic, typically containing 18 g of magnesium citrate with a very low sodium content (less than 35 mg) and usually administered in a total volume of approximately 250 mL [4] or less. Because of its low sodium content, it is preferable to sodium phosphate in patients susceptible to electrolyte imbalances from fluid shifts. Magnesium citrate can be given alone or with a stimulatory cathartic such as bisacodyl [9].

Current Practice

Studies that have addressed patient preference with regard to colorectal cancer screening have found that a cathartic bowel preparation is one of the most unpleasant portions of the examination [10, 11]. In current CTC practice, PEG 4L is rarely used as a cathartic agent. Macari and colleagues demonstrated that compared with sodium phosphate, PEG left a significantly higher amount of fluid in the colon [12]. Another study directly comparing PEG with magnesium citrate plus ioxehol found that magnesium citrate was significantly better tolerated by patients with comparable CTC image quality [9]. Borden and coworkers found that magnesium citrate and

sodium phosphate solution both provided excellent image quality without significant differences [13]. Most centers therefore use either sodium phosphate, magnesium citrate, or a reduced PEG solution such as HalfLytely, rather than a full 4 L PEG preparation.

Fecal and Fluid Tagging

Fecal and fluid tagging was initially conceptualized as a technique to spare the patient from an uncomfortable cathartic preparation. By selectively tagging retained stool and fluid in the colon, this residue could potentially be distinguished from polyps. The use of tagging alone without a cathartic prep is still under investigation, but tagging currently is incorporated into routine CTC practice in conjunction with the cathartic preparation to improve polyp detection and reduce the number of false positive findings.

CTC examinations can be evaluated either with or without digital subtraction (electronic cleansing [EC]) of the tagged fecal or fluid material, but studies have shown increased sensitivity for polyp detection with the use of digital subtraction [1].

Patients typically consume a small amount of either barium- or iodine-based contrast material with each meal 24–48 h prior to their CTC examination. The radioopaque contrast then mixes with the ingested foodstuff and remains fixed to the undigested retained material and residual fluid while the nutrients are absorbed. In combination with a cathartic prep, some of the tagged material is evacuated, while the rest remains in the colon and appears hyperdense [4]. A common feature of the tagging agents is that their absorption from the bowel in negligible. In particular, the contrast agents are not incorporated into polyps found along the bowel mucosa such that polyps remain largely soft tissue attenuation in cross section, whereas feces and fluid demonstrate a distinctly higher mean attenuation.

The dilution of the contrast material is important in achieving appropriate digital subtraction and minimizing artifacts. For example, if the solution is too dilute, it may not meet the software's attenuation threshold for subtraction and will remain on the data set, thereby making 3D visualization more difficult and potentially inhibiting detection of real lesions. Conversely, if the contrast concentration is too high, this could create beam-hardening artifacts that would interfere with accurate interpretation by obscuring portions of the colon. The optimal contrast concentration was addressed in a 2001 study utilizing an anthropomorphic colon phantom, which found that the optimal range of contrast attenuation was between 200 and 560 Hounsfield units (HU) (with 200 representing the software's threshold for subtraction). This yielded a dilution ratio of approximately 1:30–1:20 of 300 mg organically bound iodine/mL iodinated contrast to water [14]. At our institution, we mix 10 mL of 300 mg I/mL iodinated contrast in 8 oz of water (approximately 240 mL), for a ratio of just under 1:20.

Another study found the optimal contrast attenuation to be 700 HU in order to optimize polyp conspicuity [15].

There are two categories of tagging agents: barium and iodinated contrast.

Barium-Based Agents

Barium sulfate suspensions may be used in concentrations of 2% or 2.1% administered in a relatively large volume (~250 mL per dose) or 40% weight/volume administered in a relatively low volume (20–40 mL). Barium sulfate normally has limited water solubility and requires emulsifiers in order to remain in aqueous solution; therefore, it appears most effective for tagging solid fecal material, while its ability to uniformly tag liquid stool is more limited [2, 14]. For this reason, barium is almost always used in combination with an iodinated agent to achieve adequate tagging of both fluid and solid stool. Of note, barium is considered an extremely safe agent, with a negligible allergy profile.

Ionic Iodine-Based Agents

Iodine agents are ideal for tagging liquid material[2] and arguably are useful for tagging solid material as well [14]. Ionic iodine-based agents consist of diatrizoate meglumine and diatrizoate sodium (Gastrografin, Bracco Diagnostics, Princeton, New Jersey). In addition to their tagging properties, they also soften and emulsify adherent fecal material [16]. Ionic iodine agents tend to be hypertonic relative to their nonionic counterparts and are therefore associated with more diarrhea and cramping because of osmotic effects [5]. One study found that a 1-day ionic iodine prep had improved patient acceptability compared with a longer, 2-day administration, with comparative image quality [17].

Non-ionic Iodine-Based Agents

Non-ionic iodine-based agents include iopromide (Ultravist, Bayer HealthCare Pharmaceuticals, Wayne, New Jersey), iohexol (Omnipaque, General Electric Healthcare, Princeton, New Jersey), and iodixanol (Visipaque, General Electric Healthcare). These non-ionic formulations have a lower osmolarity than ionic iodine-based agents and may be better

tolerated and safer due to reduced diarrhea and reduced fluid shifts. The limited anecdotal experience of Pickhardt and colleagues suggests that ionic agents may be more effective than non-ionic agents in emulsifying residual stool in the colon [16], though there are no formal comparisons of ionic versus non-ionic agents in combination with cathartic, tagging-based CTC prep.

Electronic Cleansing

EC combines pre-examination tagging of ingested food material with post-acquisition electronic removal of the tagged material on the subsequent CT data set [19]. This postprocessing step occurs at a dedicated 3D workstation equipped with software for EC.

In EC, the patient ingests high-density oral contrast material as a fecal tagging agent prior to undergoing CTC. The contrast material mixes with and opacifies retained colonic contents. Following the CT acquisition, a postprocessing step is performed in which the high-density contrast is digitally subtracted from the image. The software identifies and modifies the attenuation of opacified regions of the bowel with attenuation values of greater than a predetermined HU (200 HU at our institution) and renders them translucent, leaving behind soft tissue elements, including the colonic wall and polyps [9] (Figs. 6.1 and 6.2).

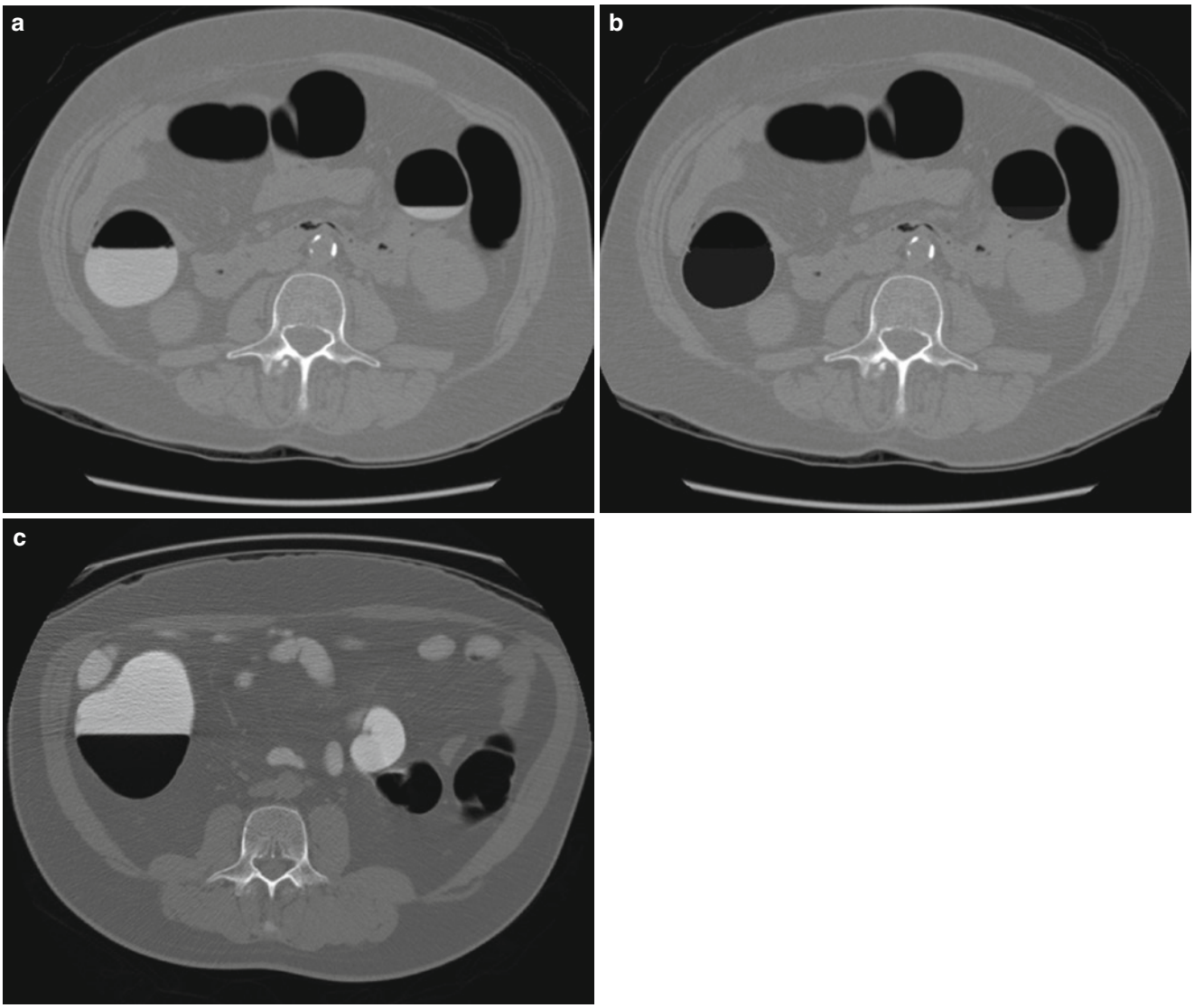

Fig. 6.1 (**a**) 2D CT colonography (cathartic: HalfLytely; tagging: ioxehol) demonstrates homogenous pools of oral contrast material within the colon. (**b**) 2D CT colonography in the same patient with electronic cleansing demonstrates good digital subtraction of the oral contrast material. (**c**) 2D colonography in another patient (cathartic: magnesium citrate; tagging: barium) demonstrates a well-prepped colon

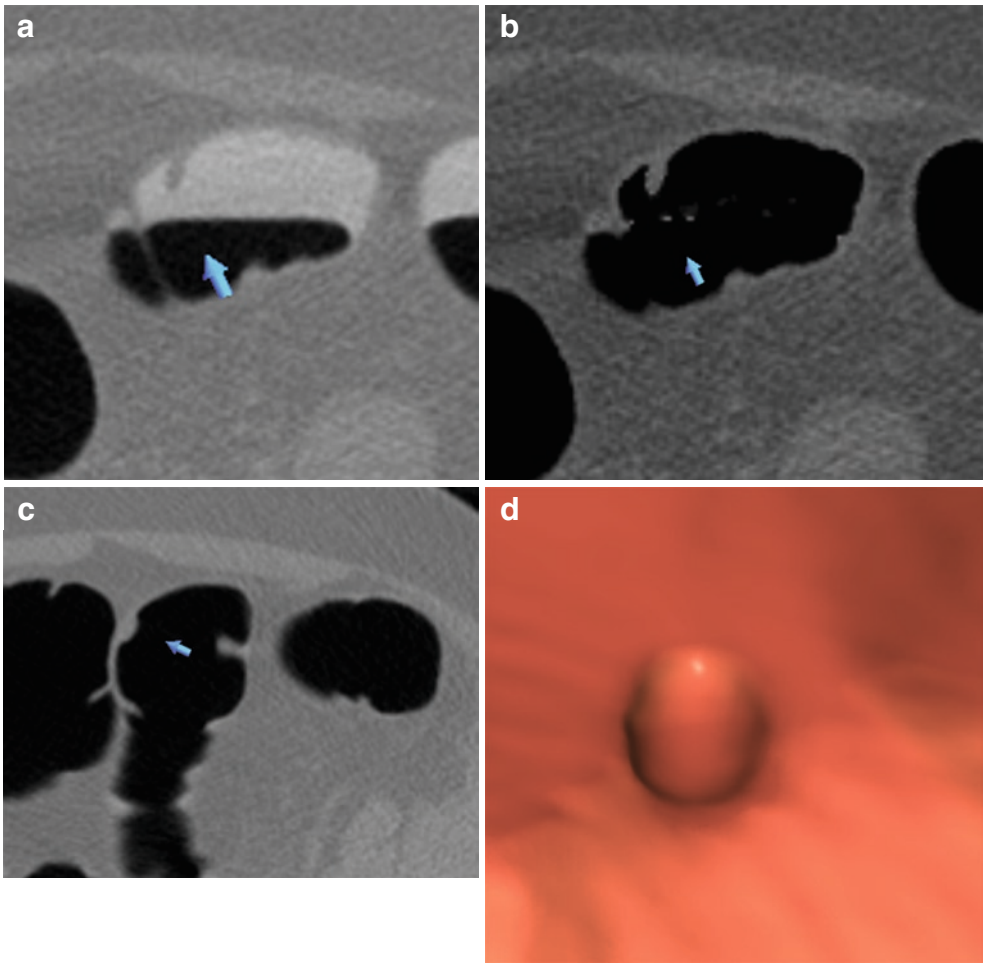

Fig. 6.2 (**a**) 2D CT colonography (cathartic: HalfLytely; tagging: ioxehol) with patient in the prone position demonstrates a polyp submerged in a pool of contrast material. (**b**) 2D CT colonography of the same patient with electronic cleansing of contrast material demonstrates the same polyp, which no longer appears submerged in the pool of contrast. (**c**) 2D CT colongraphy with the patient in the supine position demonstrates the same polyp surrounding by air due to movement of contrast material. (**d**) 3D CT colonography with electronic cleansing demonstrates the same polyp protruding from the colonic mucosa

Artifacts

A potential pitfall to the use of tagging with EC is the occasional 3D artifact that is produced when fluid or solid stool is incompletely or nonuniformly tagged. The entirety of the retained material will not meet the threshold for subtraction, and only portions of the retained stool will be subtracted. This results in bizarre jagged "pseudopolyps" on the cleansed display. These are usually easily recognizable by their irregular outlines, distinguishing them from the smooth outlines of polyps [2] (Fig. 6.3). In current practice, mucosal reconstruction algorithms are applied to digital subtraction bowel cleansing to smooth out unnatural edges [18].

If the administered contrast material is too diluted, it may not be adequately subtracted from the dataset. On the other hand, if the contrast material is not sufficiently diluted, beam hardening may produce a streak artifact across the image, which could preclude adequate evaluation of the colon and surrounding structures (Fig. 6.4).

A "bathtub" artifact may also be produced at the interface between colonic wall and subtracted fluid on the 3D images, which is an easily recognizable linear artifact of subtraction [2] (Fig. 6.5).

Another 3D polypoid artifact results from partial volume averaging of contrast and air where they interface with the colonic wall or haustral fold. In this situation, it is important to evaluate the 2D uncleansed image to exclude a true polyp [2].

Different Cathartic Preparations and Tagging Protocols

ACRIN Trial

In the multicenter American College of Radiology Imaging Network (ACRIN) National CT Colonography Trial, a cathartic colonic preparation was utilized in which patients took one of three cleansing agents on the day prior to the examination: PEG 4L, magnesium citrate 300 mL, or Phospho-soda 45–90 mL, plus bisacodyl 10 mg. For fecal tagging, patients consumed 16 g of high-density 40% weight/volume barium (Tagitol V, EZ-EM Inc., Lake Success, New York) in

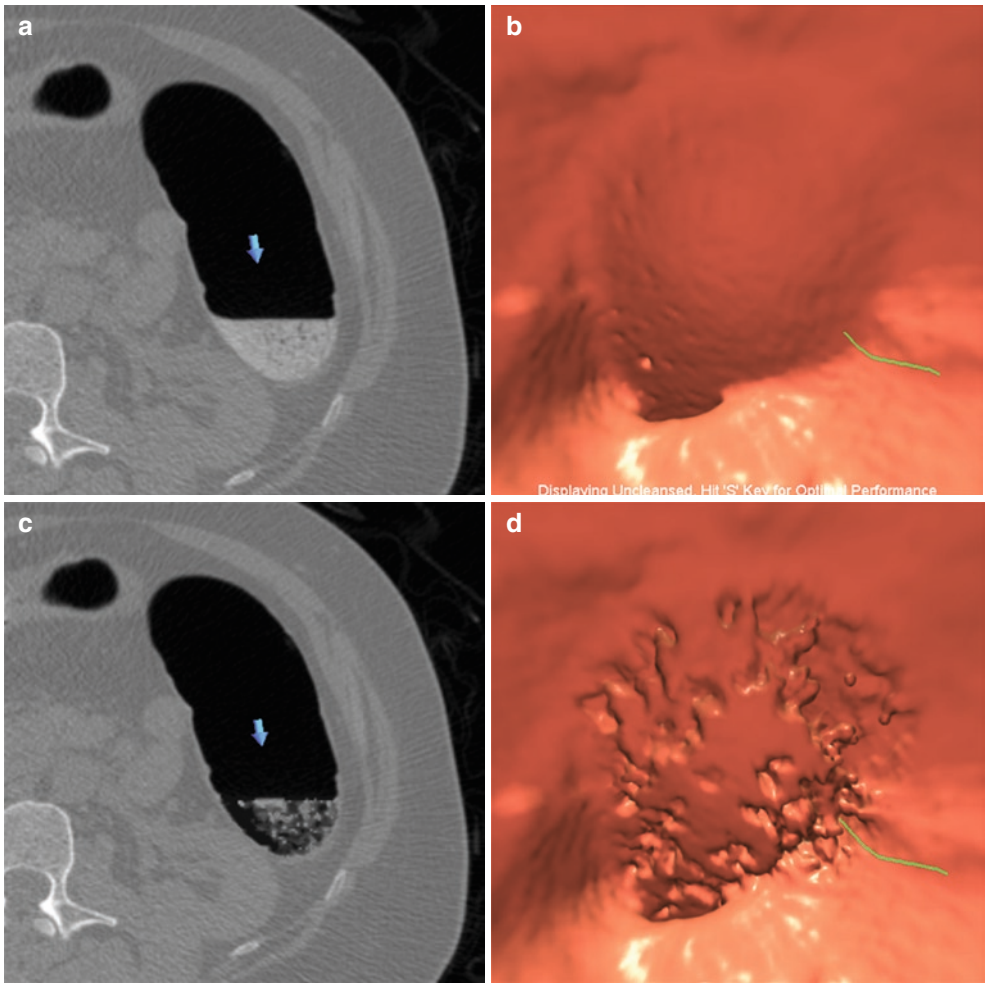

Fig. 6.3 (**a**) 2D CT colonography (cathartic: HalfLytely; tagging: barium) demonstrates a relatively heterogeneous pool of contrast material in the descending colon, reflecting non-uniform tagging of fecal material/fluid. (**b**) 3D CT colonography in the same patient demonstrates the pool of contrast material in the colon. (**c**) 2D CT colonography in the same patient with electronic cleansing demonstrates incomplete subtraction of contrast material due to non-uniform tagging. (**d**) 3D CT colonography in the same patient with electronic cleansing demonstrates irregular "pseudo-polyps" from incomplete subtraction of contrast material

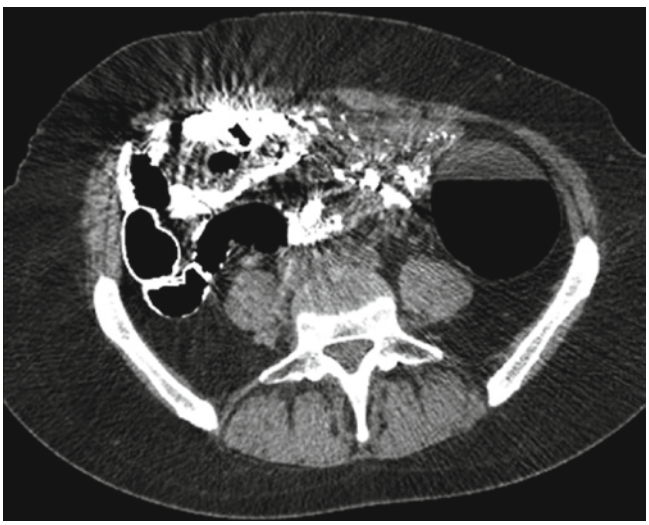

Fig. 6.4 2D CT colonography (cathartic: HalfLytely; tagging: barium) demonstrates streak artifact from undiluted barium in the bowel

three divided doses 4–6 h apart approximately 24 h prior to laxative administration. For fluid tagging, they took 60 mL diatrizoate meglumine and diatrizoate sodium (Gastroview, Mallinckrodt Imaging, St. Louis, Missouri) in three divided doses mixed with 8 oz of water orally the evening before the examination. These combinations of tagging plus cathartic were validated in this large, multicenter trial.

University of Wisconsin

Pickhardt and colleagues [16] instruct patients to prepare for colonography with a clear liquid diet the day before the study. Patients take 45 mL of sodium phosphate the day prior to CTC. Three hours after ingesting the sodium phosphate, they take 250 mL of 2% barium followed by 60 mL of diatrizoate 3 h later. In patients with renal insufficiency, a magnesium citrate alternative is used in lieu of sodium phosphate in which a patient drinks two 296 mL magnesium citrate bottles 3 h apart.

In their experience, using both barium and water-soluble iodinated contrast material is useful; the barium tags residual fecal material, while diatrizoate decreases the amount of adherent fecal material. Their limited experience with non-ionic iodinated contrast material found increased adherent

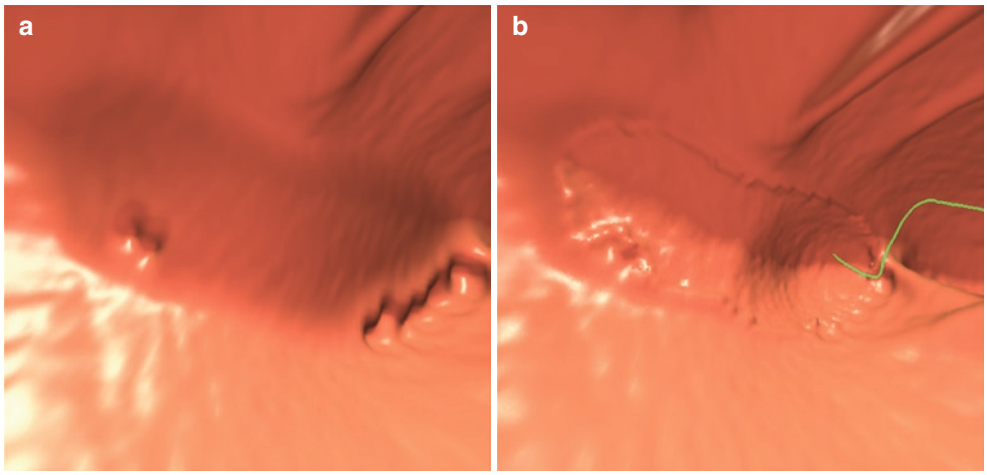

Fig. 6.5 (**a**) 3D colonography (cathartic: HalfLytely; tagging: ioxehol) demonstrates a pool of contrast within the colon, without electronic cleansing. (**b**) 3D colonography demonstrating linear "bathtub artifact" produced at the interface between colonic mucosa and contrast material after electronic subtraction

fecal material compared with diatrizoate [16]. These investigators also validated the use of tagging with cathartic agents as a standard CTC preparation in prospective clinical experience in over 3,000 patients [21].

Massachusetts General Hospital

In our experience, we have found a good balance between patient adherence to the preparation and quality of CTC by utilizing a HalfLytely catharsis and non-ionic water-soluble iodinated contrast material for tagging. Patients are instructed to assume a clear liquid diet the day prior to CTC. Bisacodyl 10 mg (which comes in the HalfLytely kit) is taken at noon. Patients mix 50 mL of iohexol 300 (Omnipaque) with 2 L of HalfLytely and drink the solution over the course of the next 5 h. On the day of the examination, patients drink 10 mL of iohexol 300 with 8 oz of drinking water. We have found that this additional bolus of contrast material achieves good opacification of the cecum [9].

Conclusion

There is no consensus on the single best preparation for CTC in terms of colon cleansing and fecal and fluid tagging; many combinations of agents permit high quality preparation and exam performance. Various centers use PEG, sodium phosphate, or magnesium citrate for catharsis and barium and/or water-soluble iodinated contrast material for tagging. It is clear, however, that the quality and interpretation of a CTC study are extremely dependent on a well-cleansed colon. Therefore, an optimal cleansing protocol will balance patient adherence to the prescribed preparation and effectiveness in achieving adequate catharsis, tagging, and electronic cleansing.

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Scheduling, Performing, and Reporting Computed Tomographic Colonography

7

Abraham H. Dachman

Introduction

The purpose of this chapter is to provide a practical guide for setting up a computed tomographic colonography (CTC) practice commencing with processing the initial request by a potential patient or clinician, selecting the patient cathartic and tagging agent (these issues are detailed in Chap. 6, "Patient Preparation and Tagging"), training technologists in performing the actual CTC exam (scanning and insufflation), training radiologists in interpreting the exam, and concluding with guidelines for communicating the results. Table 7.1 is a checklist that is helpful for radiologists and administrators in organizing the process.

Screening CTC Requests

The first component of a successful program is the proper education of scheduling personnel [1]. The usual training of scheduling personnel must be supplemented with additional education related to scheduling CTC exams. A dedicated nurse is best suited to manage a large-volume screening program (and take on the additional function of gathering follow-up information on patients referred to optical colonoscopy [OC]), but with proper training, any scheduling personnel can learn to screen CTC requests. Taking a "cold call" from a patient involves answering questions that require knowledge of the exam indications and contraindications, insurance issues, and logistics of referring patients with polyps to OC, and discussing the advantages and limitations of CTC. Occasionally, prospective screening patients misunderstand CTC, confusing it with OC. Patients may not recognize that colon cleansing and rectal tube insertion is necessary or that the exam may cause pain and is not designed to detect extracolonic findings. Scheduling personnel must be trained to explain these issues, and respond to billing questions.

In order for practitioners in the United States to obtain reimbursement, CTC cases must be properly categorized as 74263 for screening (without contrast), 74261 for diagnostic (without contrast), and 74262 for diagnostic (with contrast). The Relative Value Units for the CTC codes became effective on January 1, 2010, and were set at 2.25 for CTC screening and CTC diagnostic without contrast, compared with 2.50 for CTC diagnostic with and without contrast. Some codes in the *International Classification of Diseases,* 9th revision, associated with a diagnostic exam or increased risk for bleeding during OC (which may affect insurance approval) are shown in Table 7.2.

The colon cleansing regimen must be selected and tailored to the patient [2]. Patient-related factors that might affect the proper cleansing regimen must be known (i.e., age, known medical renal disease, or risk factors for renal damage such as long-standing diabetes or hypertension). Our questionnaire (Table 7.3; the full questionnaire in the Appendix is at the end of this chapter) comprises questions that will help correctly identify the exam as screening or diagnostic. The questionnaire will help select the appropriate cleansing regimen: saline cathartic, gavage, or limited prep for patients who may refuse or not tolerate a standard cathartic. Knowing the patient's colorectal cancer risk factors and prior screening history may help the interpreting radiologist optimize the recommendations made in the exam report's final "impression."

In addition to understanding and working with the initial questionnaire, the scheduling personnel interact with the radiologist and the billing office. Table 7.4 summarizes the sequential actions taken by these personnel. The details of the process should be tailored to institutional policy and guidelines.

Documenting Site Quality Assurance

Insurance companies may eventually require proof that CTC exams were properly performed and interpreted by adequately trained radiologists. Just as certification or continuing

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DOI: 10.1007/978-1-4419-5852-5_7,

Table 7.1 Checklist for setting up a CTC screening program

Training scheduling and billing staff
Creating a questionnaire and scheduling procedure
Creating patient information packets
Creating preparation options
Offering a same-day optical colonoscopy option
Training CT technologists
Initial and follow-up training
Training radiologists
Building skills and confidence and documenting training or "certification"
Selecting equipment and supplies
CT scanner, scanning protocols, insufflator, and supplies
Quality assurance measures

Table 7.2 Codes of the international classification of diseases, 9th revision

A. Associated with a diagnostic rather than screening CTC
787.99 change in bowel habits
787.91 Diarrhea
787.7 Abnormal feces
787.5 Abnormal bowel sounds
789.00 Abdominal pain, unspecified
783.21 Loss of weight
578.1 Blood in stool; melena
798.1 Abnormal stool color, fat, mucus or occult blood in stool
B. ICD-9 Codes associated with an increased risk of bleeding during OC or risk of sedation
569.3 Hemorrhage of rectum and anus
578.9 GI bleeding
286.9 Other and unspecified coagulation defects
V58.61 Long-term (current) use of anticoagulants
519.9 Unspecified disease of respiratory system
C. ICD-9 Codes associated with an increased risk of perforation or failed OC
562.10 Diverticulosis of colon
562.11 Diverticulitis
560.9 Obstruction or stricture
569.2 Stenosis of rectum and anus
751.5 Congenital; tortuosity
751.4 Congenital; malrotation

Table 7.3 Key elements of the patient questionnaire we use when taking cold calls (The full questionnaire is appended to the end of this chapter)

Patient age and risk factors for colorectal cancer (personal and family history, prior colon exams)
Risk factors for cathartic agents (renal, long-standing hypertension or diabetes) or known difficulty to prep
Risk factors for tagging agents (hyperallergic, known iodine allergy)
Billing and scheduling issues (Medicare, same-day optical colonoscopy option)

Table 7.4 Scheduling process

1. Summarize response to questionnaire in an email to the radiologist. Include patient information and pharmacy information. If same-day OC option is desired, additional steps are needed (see Table 7.5).
2. Radiologist confirms exam as screening or diagnostic and calls in preparation to pharmacy (or for over-the-counter preparations, confirms which one the patient should use in reply to scheduling personnel). We often use HalfLytley®, since it is safe for patients with renal impairment. If the patient's insurance does not pay for HalfLytley®, we may substitute GoLytley® or a saline cathartic.
3. Scheduling personnel assess insurance. Medicare patients are sent a waiver form to sign or must sign this form prior to commencing the exam. An information packet is sent to the patient, including the oral tagging agent and instructions for taking the preparation and tagging agent.
4. Self-pay patients are instructed to either mail payment or arrive with payment on the day of the exam. Patients are reminded to call if they have a problem with the preparation. Patients should not come in if they are still having formed stool on the morning of the exam, but rather call for instructions for an additional preparation day and reschedule for the following day. Patients should still come in if they have not received or completed the oral tagging agent, since the agent can be given on the morning of the exam if necessary or the exam can be done without tagging.
5. Scheduling personnel email a monthly or weekly schedule to the radiologist. This may be important in a new practice if only one radiologist is knowledgeable in CTC and wishes to be available for every exam. Scheduling personnel should know the radiologist's schedule to avoid scheduling exams during extended vacation or absence of the interpreting radiologists.

recertification by the American Board of Radiology may be required by some carriers for participation in their plans, CTC providers may be required to show quality metrics similar to those used in mammography screening programs. In the case of CTC, quality metrics may include documentation of the proper training and experience of the radiologist, e.g., an American College of Radiology (ACR) certificate of participation or the equivalent. These requirements have been stated in the ACR white paper on CTC [4] and are discussed later in this chapter.

In the United States, the ACR manages the National Radiology Data Registry (NRDR) to aid facilities with their quality improvement programs and to improve patient care by comparing facility data with those of others in the same region and with the nation as a whole. The NRDR is exempted by institutional review boards. For a small fee, CTC practices can participate in the ACR NRDR CTC database (http://nrdr.acr.org/) to document adherence to quality metrics summarized in Table 7.6. Participation in the NRDR CTC

Table 7.5 Process for patients desiring same-day optical colonoscopy option

1. Call the Gastroenterology business representative (insert name/phone #) with the patient information (including the history showing the reason for the virtual colonoscopy, e.g., screening, diagnosis, signs/symptoms) and explain the purpose of the call.
2. Tell the patient to expect a call from the Gastroenterology business representative for pre-approval of insurance information should an optical colonoscopy be needed. Remind the patient that optical colonoscopy involves sedation and requires that he be accompanied.
3. Have the patient call her doctor to formally fill out an order for "optical colonoscopy to evaluate abnormality seen on virtual colonoscopy." You should fax the order form to her doctor in advance of that call with an explanatory cover letter.

Table 7.6 American College of Radiology, National Registry CTC Metrics

- Process measures
  - Rate of adequate bowel cleansing and distension
    - Is one or more segment non-diagnostic? If yes, list cause
  - Rate of adequacy of diagnostic CTC examination
    - For non-obese patients (<40 cm width on scout view): scanner # rows, detector row size, supine/prone/decubitus acquisitions, reconstruction thickness and interval, confirm entire colon imaged.
    - For non-obese patients (<40 cm width on scout view): scanner # rows, detector row size, supine/prone/decubitus acquisitions, reconstruction thickness and interval, confirm entire colon imaged.
  - Rate of adequacy of screening CTC examination
    - For non-obese patients (<40 cm width on scout view): scanner # rows, detector row size, CTDIvol, supine/prone/decubitus acquisitions, reconstruction thickness and interval, confirm entire colon imaged.
- Outcomes measures
  - Rate of colonic perforation
  - True positive rate
    - For polyps >10 mm, number of polyps confirmed at OC
  - Extracolonic findings
    - Only list clinically significant findings not otherwise known based on history provided or prior imaging

database has been approved by the American Board of Radiology as an acceptable Practice Quality Improvement project for fulfilling requirements of board certification.

Selecting a Cathartic and Oral Tagging Agent: Educating Radiology Personnel

Chapter 6 covers the topic of colon preparation and tagging in greater detail. Here it is summarized from the perspective of considerations when setting up a new CTC practice, showing the option I prefer and information to educate program personnel. If a nurse is communicating with prospective patients, then medical information relating to both the exam and the preparation can be discussed. If the individual communicating with the patient is not a nurse, then medical-related questions should be referred to a physician. Know the policy of your department when deciding how much of this information may be communicated between the scheduling personnel and the patient. It is important that all scheduling personnel and the CT technologists have a general appreciation of the process. Patients sometimes call the CT work area directly with questions or arrive at the reception area without having followed the preparation instruction perfectly. It is, therefore, important that the radiology reception and CT personnel are aware of factors that preclude proceeding with the exam, such as the patient still having formed stool on the morning of the exam. This is in contrast to factors that do not preclude proceeding with the exam, such as the patient reporting passing only tiny particles of stool, or not having taken the tagging agent (which can then be given upon arrival and waiting an appropriate duration of time). Radiology personnel should also know how to deal with same-day requests for CTC after a failed OC. For these patients, factors that must be considered are recovery from anesthesia and the need to tag residual fluid with oral contrast.

Colon cleansing is still the standard of care even though minimal preparatory or so-called "prepless" (meaning no cathartic combined with an oral contrast tagging agent) procedures are feasible [2, 5]. The two categories of cleansing agents are saline cathartics (e.g., magnesium citrate, sodium phosphate if available) and gavage with polyethylene glycol (e.g., GoLytley® or HalfLytley®). Generally, gastroenterologists favor a gavage. However, for CTC this has the disadvantage of leaving a large volume of residual fluid. If oral contrast is not used, then residual fluid will hide polyps (Fig. 7.1). For this reason, both supine and prone scans are performed to move the fluid (in addition to the reason of moving gas to improve colonic distention and move stool to help differentiate stool from polyps). In fact, all the early CTC clinical trials (before tagging was routine and both CTC and OC were done on the same day) were performed with a gavage, putting the CTC interpretation at a disadvantage. Now we routinely recommend that every patient ingest a positive oral contrast agent that will help opacify (or "tag") any residual fluid or stool. Nearly every visualization software package for CTC has an option for "electronic subtraction" of opacified residual fluid. Since it is ideal to minimize the volume of residual fluid in the colon, saline is normally the preferred cathartic.

Saline cathartics (magnesium citrate and sodium phosphate) are osmotic agents that draw fluid into the bowel lumen and induce peristalsis. They, therefore, cause electrolyte shifts and will induce hypovolemia unless the patient

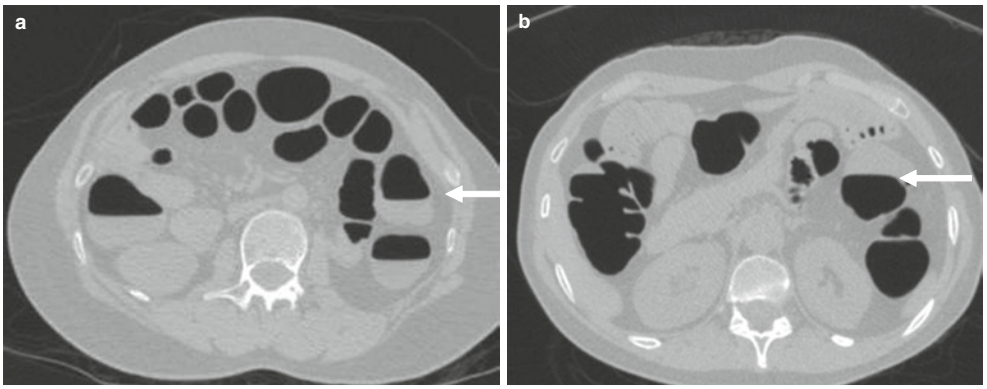

Fig. 7.1 Axial images from a CTC without oral contrast. (**a**) Supine view shows excessive residual fluid in the ascending and descending colon filling about 50% or more of the estimated luminal diameter. (**b**) Prone view. In this case, it is important to check if the fluid moved sufficiently on the prone view or if a decubitus view is needed. Note that in one portion of the descending colon (*arrow*) excessive fluid is present on both views. The fastest solution is to add a right side down decubitus view. In extreme cases, the patient can be asked to void and oral contrast can be administered. A limited repeat study is done after 2 h to allow oral contrast to reach the rectum

ingests sufficient volume of fluids, either water or fluids with electrolytes, such as sports drinks (e.g., Gatorade®). Saline cathartics are excreted by the kidney and may cause transient impairment of renal function in a patient with diminished glomerular filtration rate. They are relatively contraindicated in patients with underlying conditions associated with impaired renal function (e.g., age over 70 years, long-standing diabetes or hypertension). (In the United States, some forms of sodium phosphate have been removed from the market, and it is possible that this drug will not be available.)

Any regimen can be supplemented with bisacodyl to stimulate rectal emptying. Bisacodyl can be given orally (two 10 mg pills, for a total of 20 mg) in the evening. There is a variable time to onset of effect for the orally administered agent. Therefore, if bisacodyl is also given the morning of the examination, it should be given as a suppository. We currently omit the morning suppository, since we have found it will dilute the orally administered positive contrast agent in the rectum.

A common regimen is the same as was used in the Department of Defense clinical trial by Pickhardt et al. [6]. and subsequently used in the University of Wisconsin CTC screening program [7, 8] (Table 7.7). Note that Phospho-soda *solution* is no longer available, since a warning by the Food and Drug Administration (FDA) related to some deaths (particularly for use of double dose Phospho-soda), and the company removed the product from the market. However sodium phosphate is still available in *pill form* (e.g., Osmoprep), but manufacturers might nevertheless discontinue use due to several lawsuits. The FDA statement indicated that one of the risk factors for acute phosphate nephropathy with the use of oral sodium phosphate was age 55 and older. Since magnesium citrate is available over the counter, many radiologists now use single- or double-dose magnesium citrate as the cathartic for virtual colonoscopy.

The main reason for using a saline cathartic is to minimize the volume of retained fluid that can hide polyps. However, when fluid is adequately tagged, the exam is easily interpreted either in 3D by electronically subtracting the tagged fluid or by using "bone windows" to view the mucosa submerged in tagged fluid for polyps in 2D. Another advantage of saline cathartics is improved patient compliance compared with large-volume gavage. GoLytley® is a 4 L polyethylene glycol preparation. Patients may have difficulty ingesting the entire volume. HalfLytley® is a 2 L volume preparation that we have used extensively (Table 7.8) in combination with

Table 7.7 University of Wisconsin regimen

Clear liquid diet day prior (electrolyte sports drinks, e.g., Gatorade®)
Bisacodyl tab 5 mg p.o.×2 (11 am)
One bottle (295 cc) magnesium citrate (2–6 pm)
At least 3 h later (5–9 pm), a second bottle of magnesium citrate
250 mL 2% barium
60 mL diatrizoate (Gastrografin ®) (8–11 pm; at least 2–3 h after barium)

Table 7.8 University of Chicago low volume polyethylene glycol regimen

HalfLytley®
Omnipaque® tagging
One teaspoon mixed in 10 oz cold beverage (one dose)
One dose dinner 2 days prior
One dose mealtime×3 on day prior
Bedtime 3 teaspoons in 22 oz beverage
Remainder in morning ~4 h prior to exam
Alternate protocol: One-half bottle tagging agent near bedtime and the remainder in the morning.

oral tagging agents (either hypertonic, such as Gastrografin®; hypo-osmotic, such as Omnipaque®; or inert, such as barium in the form of Tagitol® or 2% barium) (Table 7.9).

Table 7.9 Tailored "Limited Preparation" regimen

Same day after optical colonography
Wait for recovery from sedation
40 cc diatrizoate or 60 cc Omnipaque p.o.
Wait about 2 h for contrast to reach colon (1.5 h minimum)
Frail patients who cannot tolerate a standard cathartic
Limited prep or low fiber diet cathartic-free tagging protocol

Training CT Technologists

Radiologists promoting the CTC program must be sufficiently knowledgeable to train the technologists under their supervision [9, 10]. Technologists must learn not only how to scan and insufflate the colon, but how to confirm that the exam is of diagnostic quality, in addition to evaluating the need for additional decubitus views. Table 7.10 below is the information sheet we provide to our technologists. Notice the importance of confirming that patients successfully completed their cathartic, ingested the tagging agent, and went to the restroom shortly prior to the exam.

Table 7.10 Technologist CTC information sheets

A

Equipment: Plug in insufflator (should have two tanks of CO_2) (Fig. 7.2), E-Z-EM (Westbury, NY) tubing, tube of jelly. Use either the 265- or 64-slice scanner

After introducing yourself, these are the key questions and information needed to perform the exam:

- Did you complete your colon cleansing preparation and ingest the tagging agent?
- Are you having any formed stool?
  - If patient has brown liquid but no solid stool, you may proceed.
  - If patient is having tiny pieces, ask if "stool tagging" was performed by drinking contrast agent mailed to the patient. If yes, proceed. If not, ask radiologist's advice.
  - If patient has solid stool, reschedule the exam.
- Did patient sit on the toilet in the last hour? If not, have patient go to the toilet before starting.

B

After the patient is in a gown and ready for the examination, review the procedure with the patient (even though this was explained to the patient previously and he/she received a written information sheet).

- I'm going to explain the procedure to you.
- I'll put a small catheter in your rectum and inflate a small balloon to help keep it from falling out.
- I'll use this mechanical insufflator to fill your colon with carbon dioxide gas. You need to "squeeze down" to hold the gas in, in order for the test to work. You may feel some crampy pain. It usually takes a couple of minutes to fill the colon.
- Then I will do a preliminary view that takes 5 s. If the colon looks full, I will continue; it takes a minute for me to program the computer and then perform a 10-s scan of your abdomen and pelvis while you hold your breath.
- Then I will relieve the pressure a little bit and turn you onto your stomach. After a few minutes, I'll start the flow of gas again and repeat a preliminary view and a scan.
- All together, you'll be uncomfortable holding in the gas for 5–7 min, and the test will be over in 15 min.
- Do you have any questions?
- In a few patients, I need to do an extra view lying on one side if some bowel is collapsed or has a lot of retained fluid. Remember, polyps can hide in collapsed bowel or fluid, so it's real important that you try to hold the gas in, and that's also why we scan you twice, once on your back and once on your belly.
- Do you have any questions?

C

Technologist CTC reconstruction and networking instructions (this can be tailored for your scanner and network).

- Reconstruct only supine to 3 mm thick axials and 4 mm coronals soft tissue window.
- Source images (1.25 mm) in lung windows
- Send the ENTIRE CASE *(including the source images, scout views and dose page)* to the Picture Archive Communication System.
- Send only the source supine and prone (and decubitus views if done) images (1.25 mm) to the CTC workstation (specify the icon or file name for your particular scanner console).

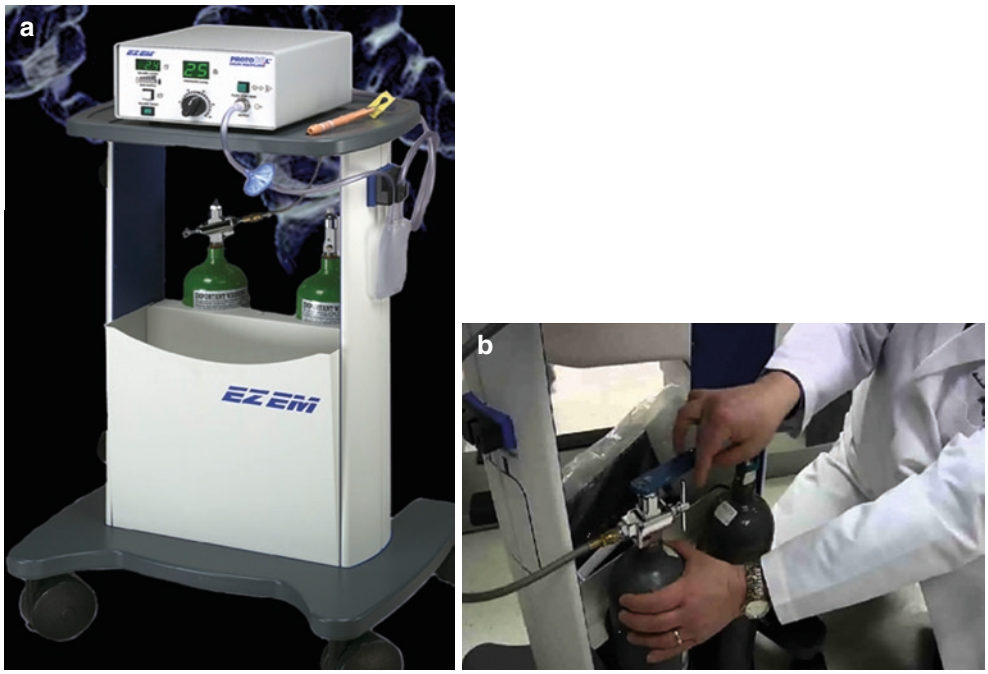

Fig. 7.2 CTC Insufflator showing two tanks of CO_2 in storage compartment. (**a**) View from the front of the insufflator on a wheeled cart. Fluid catch bag is on the side of the stand. (**b**) Close-up view from the rear while opening the CO_2 tank valve

Technologist Training in Colonic Insufflation

To minimize patient discomfort and possibly the risk of perforation due to traumatic insertion of the rectal tube, the external anus, the anal canal, and the catheter tip should be sufficiently lubricated with jelly. If the patient has an extremely tender anus due to the preparation and/or external hemorrhoids, Lidocane jelly can be substituted (or use a spray can of Lidocane to mix some with standard jelly. This is the least costly method). If there is good visualization of the anus, it may be unnecessary to perform a digital rectal application of lubricant. However, if the anatomy of the buttocks prevents good visualization, it is important to perform a limited rectal exam to learn the optimal direction of catheter insertion as well as to lubricate the anal canal. Improper direction of the catheter tip and excessive force contribute to traumatic insertion of the rectal tube. Another way to minimize the risk of perforation of the rectum upon rectal tube insertion is to choose a thin, soft catheter. While any catheter designed for rectal use is acceptable, my choice is always a thin, soft tip, such as the E-Z-EM/Bracco Diagnostics "thin catheter with small balloon" (E-Z-EM Inc., Westbury, NY) (Fig. 7.3). A small-gauge Foley catheter is similar in size and can be used if manual insufflation, which is less desirable, is performed (Fig. 7.4).

I prefer a catheter with a small inflatable balloon, rather than a red rubber Robinson catheter that has no balloon. The E-Z-EM catheter is equipped with a small balloon (Fig. 7.3b) and a bag (Fig. 7.5) to trap excess fluid from the patient's rectum. Prior to use of this catheter, when barium enema catheters were used, overdistension of the balloon was implicated in some cases of rectal perforation at barium enema and at CTC. This should not occur if the balloon is properly positioned and

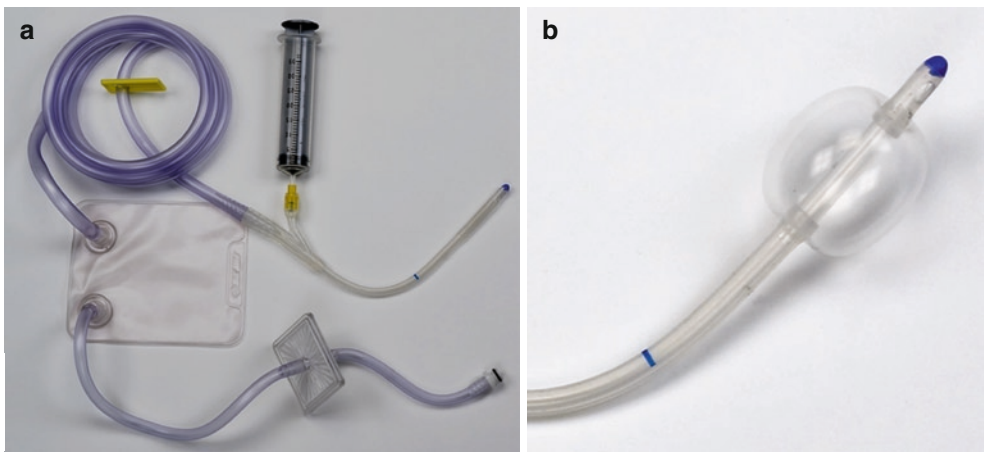

Fig. 7.3 Thin catheter administration set for use with E-Z-EM insufflator. (**a**) Full set. (**b**) Close up of tip with inflated balloon

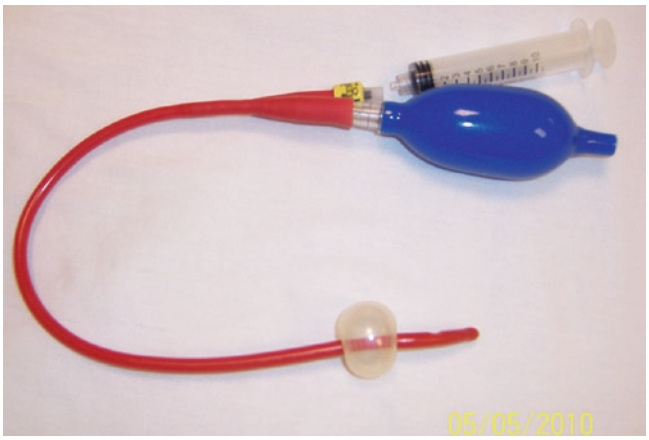

Fig. 7.4 Foley catheter with blue puffer attached for manual room air insufflation method

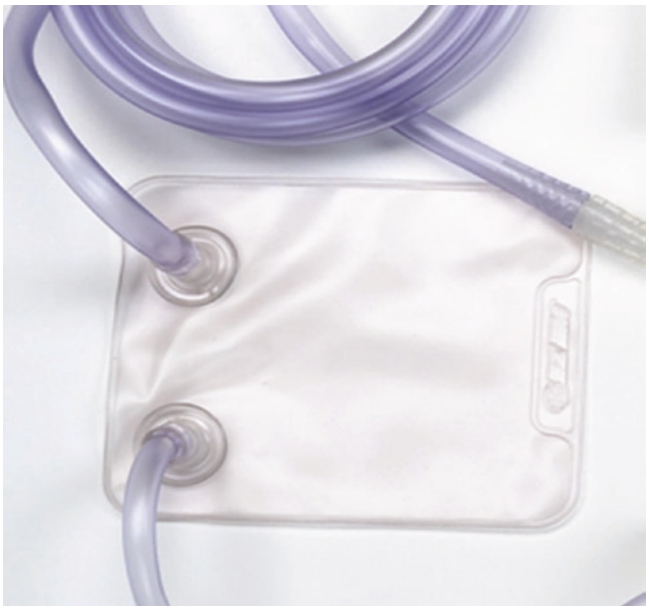

Fig. 7.5 Bag to trap excessive fluid exiting from rectum into tubing. A large amount of fluid could block the flow of gas. The tubing can be manipulated to gather the fluid into the bag

inflated. The deflated balloon should be advanced well into the capacious rectal vault. It is inflated to less than its capacity by using only about 25 cc of air to achieve a diameter of less than 1.34″ (compared with a standard double contrast barium enema tip balloon inflated with 100 cc to a diameter of 2.7″). If a Foley catheter is used for manual insufflation, typically 5–10 cc is used to inflate the balloon. Regardless of which balloon catheter is used, let the patient know you are inflating the balloon. The patient should not feel the balloon inflation. After inflating the balloon, tug gently on the catheter to seat the balloon against the anal verge. This will help prevent the catheter from dislodging during the exam, particularly when the patient turns from the supine to the prone position. Inserting the catheter too far could contribute to obscuring a rectal lesion even if no balloon is used [11]. The alternative to not inflating the balloon requires that a 10″ strip of perforated plastic tape be placed in a butterfly fashion around the tube at the anus to secure the catheter to the buttocks. If the tape is not placed as close as possible to the anus, it may serve as a fulcrum and actually cause the tube to dislodge as the patient turns.

How to Insufflate

Although manual insufflation and even patient self-insufflation have been successful, I strongly prefer mechanical insufflation of carbon dioxide gas because it is the most time-efficient for a technologist working alone. The tube is placed into the rectum and the patient is positioned in the right side down decubitus position. Insufflation of gas should commence in the same position. The theoretic advantage of starting with the right side down position is that it facilitates filling of the sigmoid and descending colon with gas. We administer the first 1 L of gas with the patient in the right side down decubitus position. We then instruct the patient to turn prone for 15 s, then left side down for 15 s, and then again supine to be positioned by the technologist for the scout view (Fig. 7.6). (Others

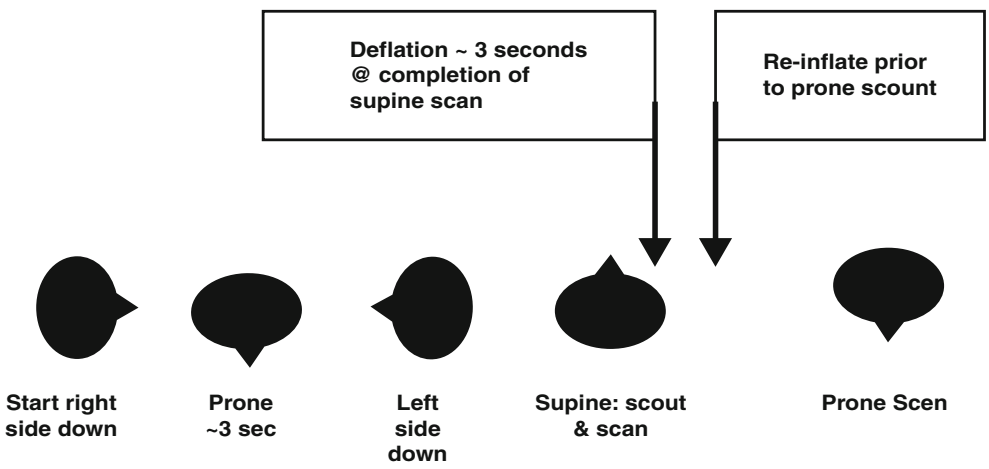

Fig. 7.6 Turning maneuver during insufflation using right side down starting position. Some others prefer to turn first to the supine position and continue to turn 360°, or just stop in the supine position

suggest turning supine from the initial right side down position. It is probably not critical, but turning is strongly advised unless the patient is immobile, e.g., with hip pain.) An initial pressure setting of 20–25 mmHg is recommended.

Minimizing Perforation Risk

Nearly all of the perforations reported to date [12–21] have been associated with manual insufflation, although 2 of 16 reported cases occurred with mechanical insufflation of carbon dioxide. A causal relationship to manual insufflation cannot be inferred, since it is unknown how many patients received mechanical versus manual insufflation. Carbon dioxide is more rapidly resorbed than room air, and this may improve patient comfort after completion of the exam, particularly if there is abundant reflux of gas into the small bowel. It also is more suitable for a single CT technician working alone, since insufflation can commence mechanically while other tasks, such as entering the patient protocol into the scanner, are completed.

The technician should monitor the patient closely during insufflation and remain in constant communication with the patient, either in the CT suite or from the console. The insufflator is designed for patient comfort by starting at 1.0 L/min for the first half liter, then 2 L/min for the second 0.5 L and then maximizing at a flow rate of 3 L/min. Insufflation automatically ceases when a pressure of 25 mmHg is reached. If pressure exceeds 50 mmHg for more than 5 s, an alarm sounds and gas is vented into the room until the pressure drops below 50 mmHg. (There is a back-up mechanical release valve at 75 mmHg; however, this pressure is never encountered in practice.) The model insufflator currently in use also turns off automatically after delivering 4 L and at every 2 L thereafter. Flow must be restarted by the person performing the exam. These safety features may help minimize, but not eliminate, the risk of perforation.

It is unknown whether any of the documented perforations were due to the generation of high pressures. It is possible to monitor pressures with the insufflation pump to employ a strategy to avoid high pressures yet deliver optimal insufflation and maximize patient comfort. In my experience the highest pressures – 40–50 mmHg – are generated when the patient turns from supine to prone. To avoid these high pressures, the pump should be turned off after completing the supine series, and the rectum should be deflated by disconnecting the tubing from the pump for 3 s. This will not deflate the entire colon but will allow sufficient collapse of the rectum to make the patient comfortable and prevent the generation of high pressures in the rectum (Figs. 7.7 and 7.8). We use the same "decompression maneuver" during any part of the exam if a patient is in extreme pain (which is rare) and states that he or she cannot continue the exam. In every case in which we used this maneuver, there was sufficient insufflation for a diagnostic exam.

Fig. 7.7 Deflation maneuver. The pump is turned off (note round green button is not lit) before disconnection. Then the tubing is disconnected from the mechanical insufflator for 4 s and immediately reconnected prior to resuming flow

When to Scout

The decision of when to proceed with the scout view is based on three factors: the patient's level of discomfort, the pressure achieved, and the volume of gas administered. If little or no gas is being pumped because the pressure is nearly always over 25 mmHg, then a scout is obtained (Figs. 7.9 and 7.10) regardless of the volume administered (but if this happens within the initial 30 s of insufflation, check that the tubing is not clamped). We generally wait for at least 2 L of gas to be pumped. (If room air is used, the rate of inflation can be modified based on patient discomfort and a scout obtained after about 50 puffs or when the patient experiences constant moderate pain.) Patients are asked to rate their pain on a three-point scale: mild, moderate, or severe. Practitioners should look for signs of pain in stoic patients (e.g., grimacing, toe wiggling). If there is no pain and the pressures vary such that gas is slowly entering the colon, wait for an additional 0.5–1 L to flow before obtaining a scout. Conversely, even if little or no gas entered the patient, but the pain level is severe, obtain a scout view immediately. Sometimes these patients are post same-day OC and have moderately distended colons from the carbon dioxide (or air) administered during the colonoscopy. If they did not have same-day colonoscopy, these may be patients at risk for perforation due to a distal mechanical obstruction to retrograde flow of gas.

Several patients with reported perforations had obstructing masses. Masses may produce obstruction to retrograde flow of gas (or barium on barium enema) even though they do not produce obstruction to antegrade flow. Thus the patients do not have clinical signs of colonic obstruction. We encountered

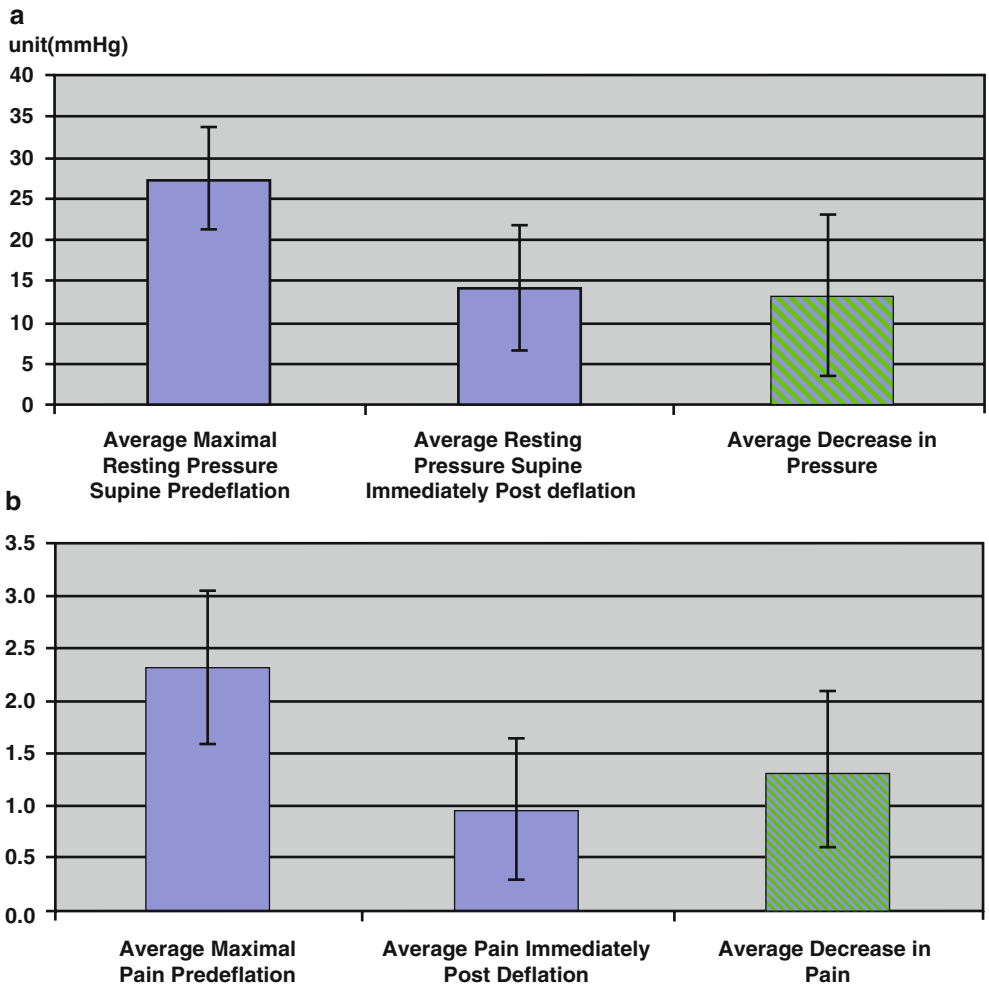

Fig. 7.8 (**a**) From a study of 38 patients who underwent monitoring of colon pressure and pain level during CTC performed with the turning and deflation maneuvers. All patients experienced a decrease in pressure with deflation. Average decrease in pressure = 13.2 mmHg (Dachman AH, Saldanha D. Presented at the 7th Annual Symposium on VC, Boston, Oct 2006).(**b**) During the entire exam pain was monitored on a subjective four point scale: none = 0, mild = 1, moderate = 2, severe = 4. All patients experienced a decrease in pain after deflation. Average decrease in pain score = 1.3

one such case, where pain was immediate after insufflation of 0.2 L. We applied the rule: "When in doubt—scout." The scout view is a low radiation view and it can help assess the status of colonic distension. The same can be accomplished in CT units equipped with CT fluoroscopy (biopsy mode). In our case, a distal obstruction was found due to an incisional hernia (Fig. 7.11) containing colon in a patient with a penile prosthesis. Caution should be exercised in men with a known or suspected inguinal hernia. If there is obvious increase in size of a hernia during insufflation, consider performing a scan at that point to assess the anatomy without obtaining optimal insufflation. Several of the men who perforated also had left-sided inguinal hernias [22]. Extra caution should also be exercised for elderly and frail patients.

When to Scan After Scout View

The decision as to when to proceed with the scan depends on the same factors described above for obtaining the scout view plus the appearance of the colon on the scout view. If the colon is not well distended on the scout view but the patient is in pain and gas continues to flow, encourage the patient to tolerate the discomfort. If the pain is severe and the colonic distension is adequate but not optimal, proceed with the scan. Our scans are accomplished with a 10-s breath hold. As with any CT, be sure the patient actually stops breathing before scanning so as to avoid motion artifact. During scanning, the technologist should view the preview images to be sure that no portions of the colon were cut off from the scan field of view. The patient's pain can be relieved by turning off the insufflator and disconnecting the tubing for about 4 s (our so-called "deflation maneuver") (Fig. 7.7).

What to Do If Colonic Distension Is Suboptimal on the Scout View

If the pain is not severe and gas is not flowing because the pressure is nearly always above 25 mmHg and the colonic distension is not optimal (this is rare, but more common in obese patients, particularly in the prone position), we convert

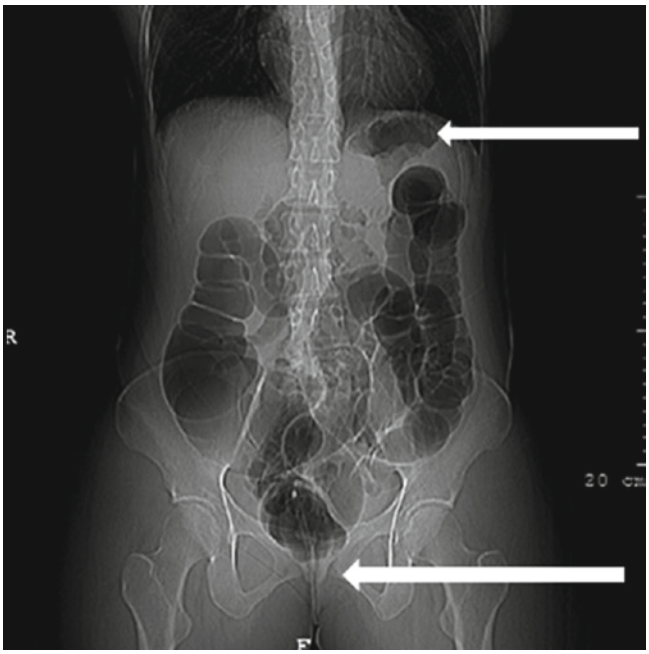

Fig. 7.9 Scout view, selection of scan field range. The entire colon is well-distended on this optimal scout view. The scanning range should be at least a finger breath or more above the colon and below the rectum (*arrows*) to avoid accidentally cutting off either structure. The technologist must recognize colonic flexures and the stomach gas bubble and be able to differentiate them. When uncertain, scan more, rather than less, to avoid omitting any colon

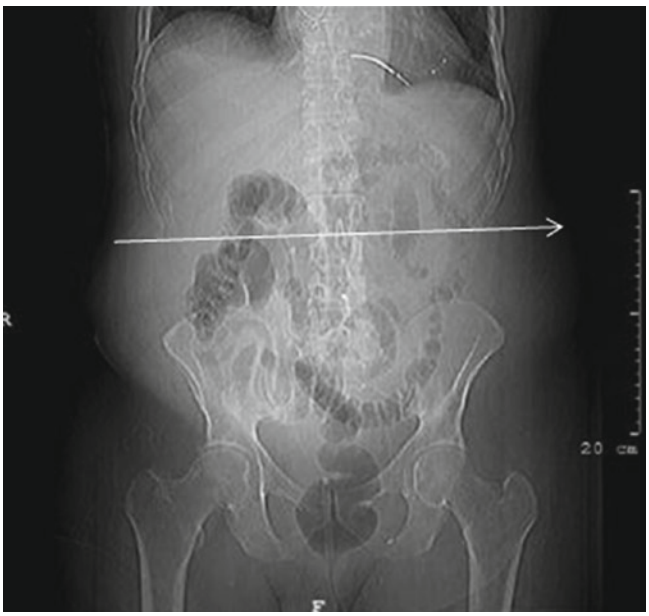

Fig. 7.10 Scout view showing method for measuring transverse dimension of body as seen on scout view. The largest transverse dimension is measured (*arrow length*). If over 40 cm, we adjust the technique

to supplemental manual insufflation. This can be done with carbon dioxide by rigging a pump with a one-way valve into the tubing, the so-called "bag-maneuver" (Fig. 7.12), or simply by clamping the tubing to prevent escape of gas, disconnecting the tubing from the machine (shut off the machine), cutting off the tip that clips to the machine with a scissors, and forcing a manual insufflation bulb known as a "blue puffer" into the end of the tubing (Fig. 7.13). Then unclamp the tubing and proceed with slow manual insufflation of room air. Query the patient for his pain level and slow down or stop pumping if the patient experiences cramping. If pain is constant and moderate (not severe), stop pumping and scout. Do not try to achieve maximal inflation yet. If distension is optimal, proceed with the scan. If distension is adequate, proceed with the scan but pump additional air (usually about 10 puffs) immediately prior to the scan (after the table has been positioned for the scan). In this manner optimal insufflation will be achieved and the patient will need to tolerate moderate to severe pain for only a few seconds (our scans are done on a 40-slice scanner in less than 10 s).

We have experimented with a breath hold in expiration rather than inspiration to help straighten out the splenic flexure – but this is of doubtful value with current visualization software. Immediately after the scan, use the "deflation maneuver" by disconnecting the blue puffer for 3 s to partially deflate the rectum and diminish the pain level (Figs. 7.7 and 7.8).

After Completion of the Supine Scan

After completing the scan and performing the deflation maneuver, the patient can be turned into the prone position. By time the patient is turned into position, the reconstructed images should be read and can be checked in more detail for quality of distention, coverage of the colon, and field of view. In particular, tortuous areas of the sigmoid colon should be checked for adequate distension, since the overlap is hidden on the frontal projection on the scout view [22].

After turning the patient into the prone position, use one to three pillows in a wedge-like fashion under the chest and the pelvis (more so in obese patients) to minimize pressure of the abdomen against the table (Fig. 7.14). This will improve distension of the transverse colon and possibly diminish colonic intraluminal pressure slightly. Some investigators suggest deflating the rectal balloon just prior to obtaining the prone scan (or removing the tube) to prevent obscuring rectal lesions. I believe that the small air-filled balloon is unlikely to hide lesions and that deflation of the balloon is optional; leave the catheter in place.

When the supine and prone scans are completed, do not rush to remove the catheter. Rather, disconnect the tubing

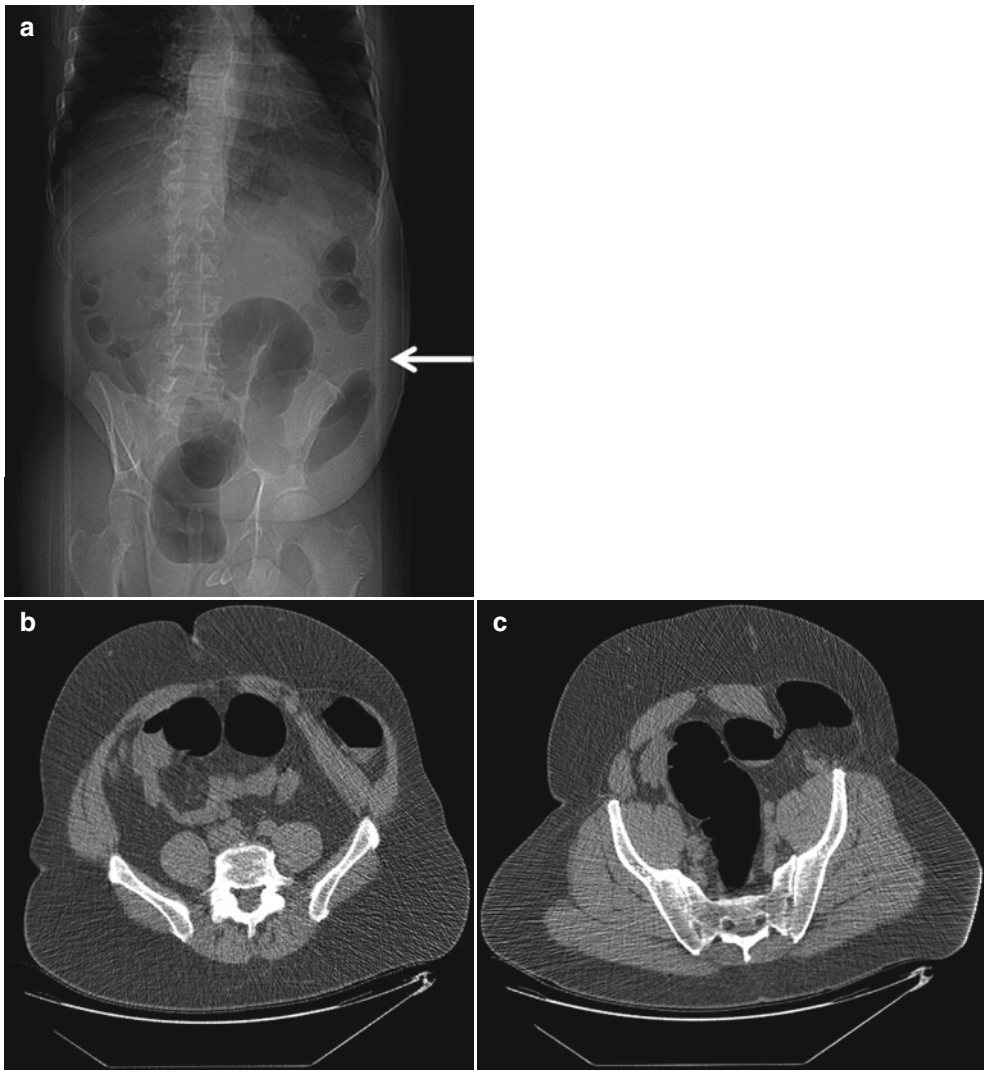

Fig. 7.11 CTC on an asymptomatic patient with a previously unrecognized incisional hernia causing obstruction to retrograde flow of gas during insufflation. After only 30 s the patient experienced severe pain. A scout (**a**) was obtained showing marked distension of the rectum and sigmoid colon to a point of relative obstruction. Limited axial views through the pelvis were then obtained (**b**, **c**) showing an incisional hernia containing descending colon. This was the site of insertion of the tubing for a penile prosthesis (*short arrow* on **a**)

from the pump or blue puffer and remove the pillows from under the chest. Allow the tubing to remain in place for 30–60 s. At this point most of the gas will evacuate via the tubing into the room and the patient will feel comfortable. The technologist can take a few minutes to check the prone view (as was already done for the supine view) for collapsed areas to determine whether additional views are needed. If the right colon is not well distended, the study can be supplemented with a left side down decubitus view (Fig. 7.15).

If there is a large amount of retained fluid, the exam can be supplemented with either a right or a left side down decubitus view to maximize visualization of the colonic mucosa [9]. I perform this extra view if 50% or more of the diameter of a well-distended segment contains fluid. In my experience about 5% of patients require an extra scan. I ask the technologist to page me to see if I am available to check the scan myself, either in person or remotely on the Picture Archiving and Communication System (PACS). Once technologists are experienced, they will nearly always make the correct decision.

If a perforation is suspected during a CTC (Figs. 7.16 and 7.17), decompress the colon, deflate the rectal balloon, gently remove the rectal tube, and obtain a scan to document the extent and location of gas. Intravenous fluid access should be established, and a surgery consult should be obtained immediately.

Then the balloon is collapsed (if not done prior to scanning), the tube removed, and the jelly wiped from the rectum with a soft tissue. Be sure the patient has no dizziness or vasovagal symptoms before she sits up and before being allowed to stand.

Along with my colleague Mike Vannier, I have developed a software-based training simulator that can be used to train technologists and radiologists in the entire process of insufflating and scanning (Figs. 7.18 and 7.19).

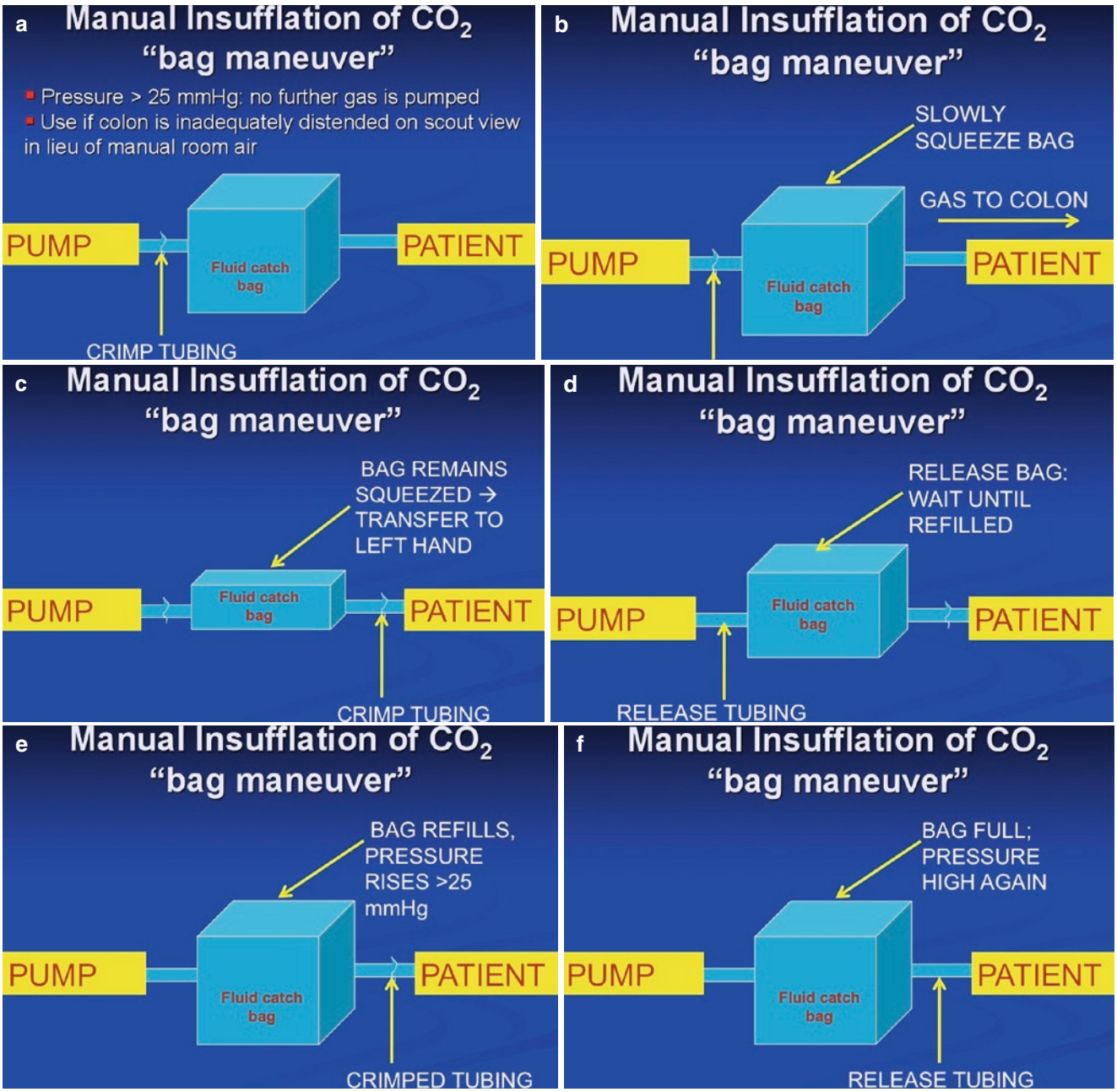

Fig. 7.12 Use of the "bag maneuver" to overcome mild spasm and pressures exceeding 25 mmHg. The maneuver is shown in movie loop and illustrated diagrammatically in steps (**a**–**f**) above

Post–Optical Colonoscopy Cases

If the patient is referred for CTC after same-day OC [23–26], an asymptomatic perforation which may have resulted from the colonoscopy should be excluded prior to performing the CTC. I recommend performing a radiological exam to check for free intraperitoneal gas. If this search is not performed before placing the rectal tube, any subsequent demonstration of perforation will be attributed to the CTC. In order to search for perforation due to OC, perform either a left side down decubitus radiograph (before bringing the patient to CT) or a limited low radiation dose CT of the abdomen and pelvis with a wide interslice gap. The scout image from the CTC may be helpful but is not likely to be sensitive for small amounts of extraluminal gas.

A same-day CTC after colonoscopy is contraindicated if the patient has undergone a snare biopsy (since it might draw colon wall into the snare) or a "well biopsy," where multiple

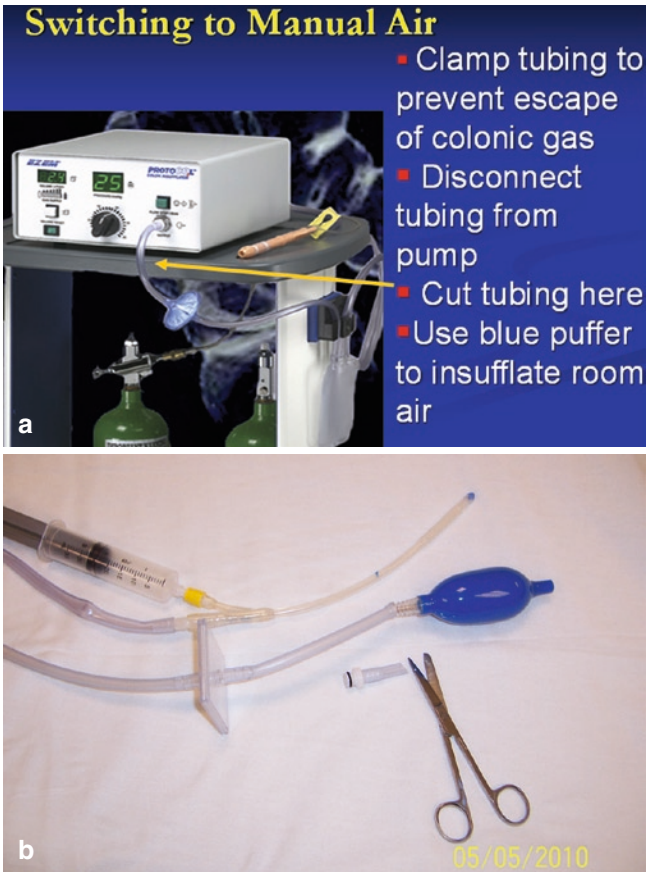

Fig. 7.13 An alternate to the "bag maneuver" is switching to manual insufflation of room air by turning off the insufflator, cutting the tubing where shown (**a**), and without removing the catheter from the patient, attaching a blue puffer to instill room air. This is shown on a catheter set in (**b**). The same method can be used if the insufflator or CO_2 is not available

Fig. 7.14 Use of pillows for the prone view. Decreasing pressure on the transverse colon is accomplished using a pillow folded over under the chest and thighs. (**a**) common error is placing the lower pillow too high. The lower pillow should not touch the pelvis and the upper pillow should not touch the abdomen

samples are taken from the same site. A routine biopsy obtains only superficial mucosal tissue and is not a contraindication to CTC. If one chooses to wait for healing after a colonoscopic biopsy, it is best to allow sufficient time for the wall to heal. Although the literature suggests that a wait of 1 week is sufficient [27], I prefer to wait longer to be safe. Note that waiting 1 week is not a rational approach, since granulation tissue is maximal in most surgical wounds at 1 week and the wall is paradoxically weakest and most susceptible to perforation at this time.

Summary of Potential Complications of CTC

Several potential complications have been discussed above and in the chapter on CTC colon cleansing; however, it is useful to summarize these risks and put them in perspective (Table 7.11).

A few points deserve emphasis. Patients should not stop their medications because of a CTC preparation; however, they should take the medications either well before or a few hours after completing the cathartic. As noted above, if a patient has a known allergy to iodine, has multiple (i.e., four or more) drug allergies, or a history of a life-threatening allergic reaction, we prefer to give barium rather than an iodinated agent for tagging. Brittle diabetics may need to alter their dose of insulin or oral hypoglycemic agents due to the reduced food intake during the preparation period.

The incidence and factors surrounding bowel perforation and methods to minimize the risk were discussed above. Some data from the literature deserve comment. Overall, perforation due to CTC is rare and much less common than in OC. The perforation rate at OC is 0.1–0.2% [28]. In a large survey, the total perforation rate of 0.009% was reported [16]. The higher rates of perforation in surveys from the United Kingdom and from Israel range from 0.06% to 0.08% [9, 17–29]. Their higher rates may have been related to factors such as population age, catheter tip type, manual air insufflation and might have unknowingly included cases of asymptomatic pneumatosis. Caution should be used in patients with left-sided hernias or known partial obstructions. CTC-related asymptomatic pneumatosis may occur in 0.001% of CTC exams, does not require a hospital admission, and has a benign course [30].

Addressing Radiation Dose Concerns

Much has been written in the lay press and other media on the radiation effects of CT. It is incumbent upon radiologists to be knowledgeable so that they may address such concerns.

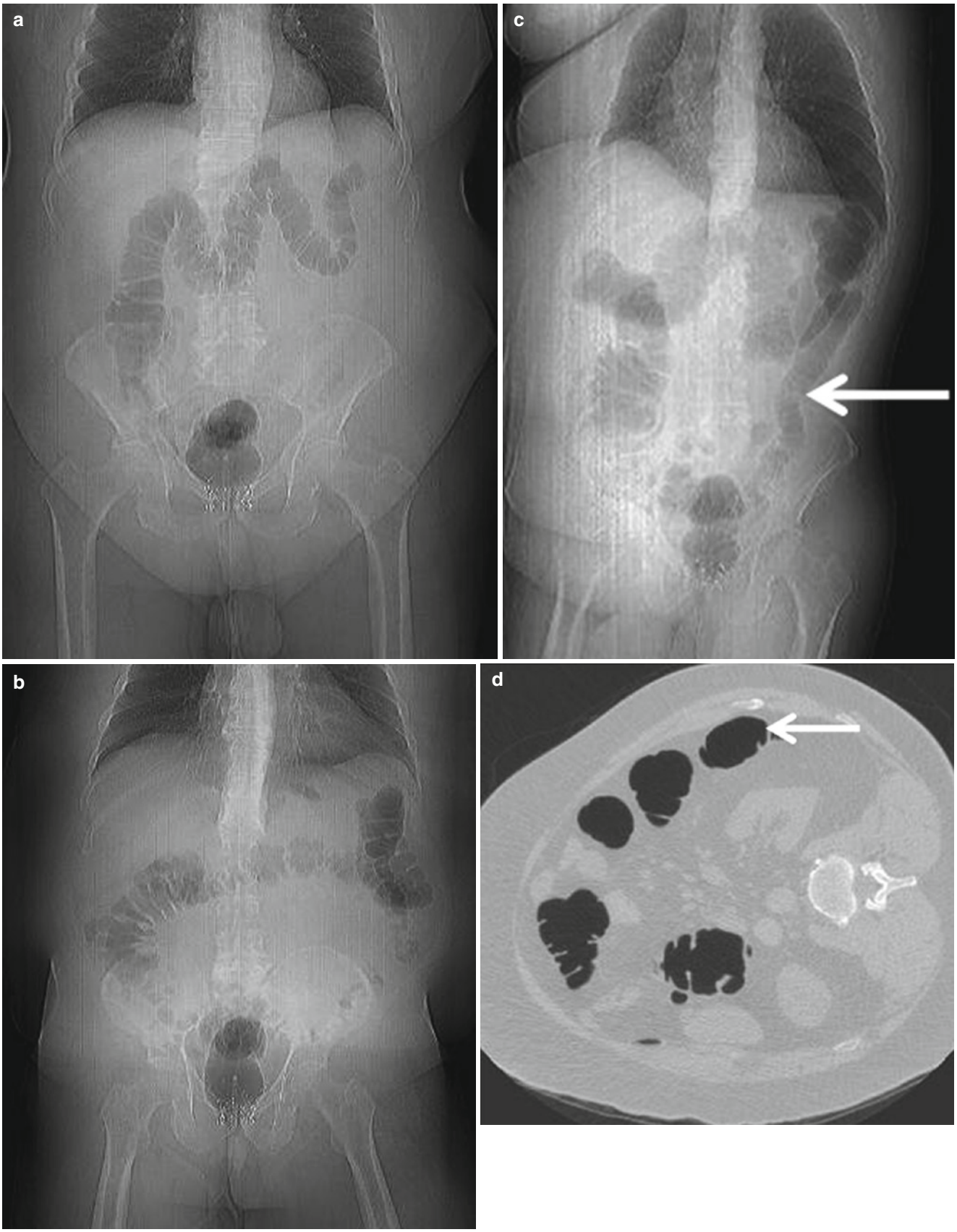

Fig. 7.15 Suboptimal distention on both supine and prone views requiring a decubitus view. (**a**) Supine scout view and (**b**) prone scout view both show collapse of the descending colon. After performing a quality check, the technologist added a right side down decubitus view, (**c**) scout and (**d**) axial images show excellent distension of the descending colon (*arrows*)

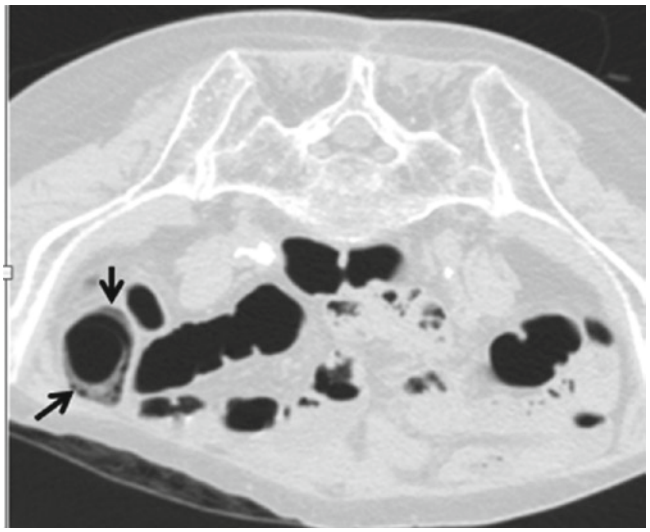

Fig. 7.16 (**a**) CTC technologist training simulator. Sample 3, monitor set up option. Multiple simultaneous display monitors are required to provide real-time simulation of the interactions between the CT scanner, insufflator, and the patient. The technologist (student) can set up and monitor the exam, leading to high quality data acquisition. Allows technologist to attend to the numerous required details and progress through the necessary steps in correct order. (**b**) Opening page of a test version of the simulator. Nearly 200 screen shots and movie loops can be accessed in linear, sequential or random order. (See sample movie). (**c**) Screen shots and movie loops can be accessed in linear, sequential or random order. This is a sample screen shot of the Philips technologist console during programming of the scanner

CTC experts consider this a highly theoretical domain [31–38]. Radiologists should be familiar with two key points. First, CTC doses are much lower than conventional CT. Second, the relative theoretical risk of the low radiation doses of CTC in the >50-year-old population is dwarfed by the known risk of colorectal cancer. This perspective is supported by the position statement of the Health Physics Society [39]. Young adults, whose long-term radiation risk is more significant, are not subjected to CTC.

The head, neck (exposing the thyroid), and chest (except possibly the lung bases) are excluded from the scan field of view for CTC. In this section, some data and key references will be discussed. The radiation dose of CTC is lower than the ambient radiation in many locations [3, 40–42]. It is interesting to note that in locations such as Guarapari, Brazil; Yangjiang, China; Kerala, India; and Ramsar, Iran, the average background dose (including cosmic and terrestrial sources, but excluding radon and internal radiation) ranges from 4 to 10 millisieverts (mSv)/year, with peak measurements in Ramsar at 260 mSv/year. Compare this with the 0.7 mSv average in the United States (Fig. 7.20).

In a survey of research institutions performing CTC, Liedenbaum et al. [33]. reported that the median effective dose for a screening CTC was 5.8 mSv (2.5–2.8 mSv/position) and that use of automatic exposure control did not result in a decline in overall radiation dose compared with 2004 [33]. However, these data reflect older techniques that are no longer state of the

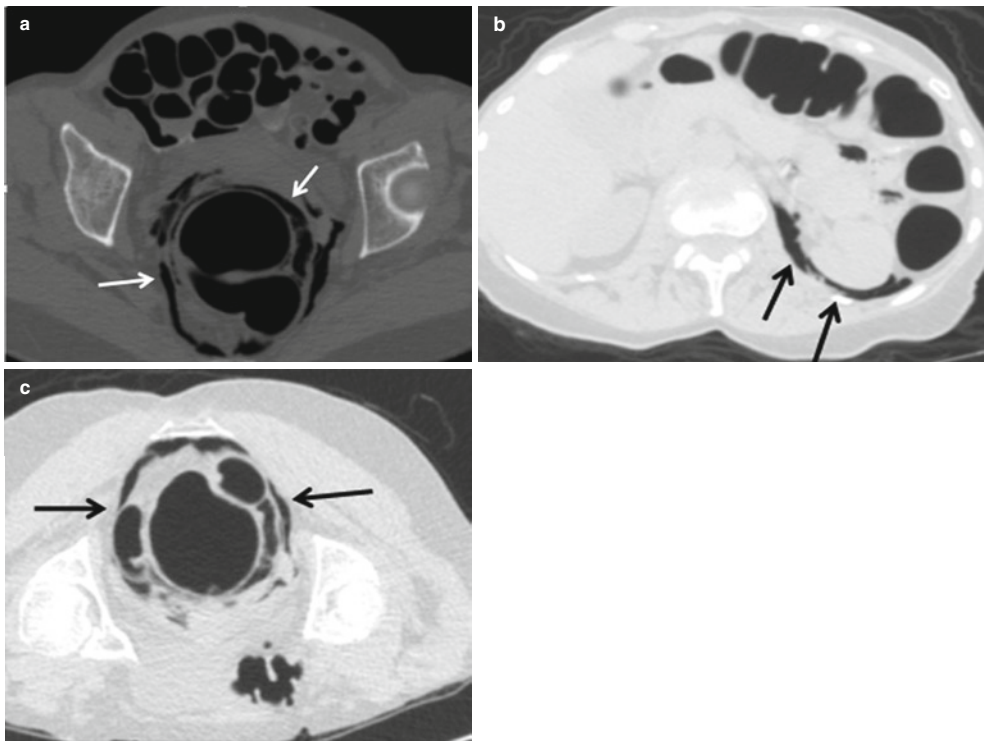

Fig. 7.17 (**a**) CTC Simulation software for training technologist. A small portion of the logical hierarchy and sequencing of the simulator pages. Screen shots and movie loops can be accessed in linear, sequential or random order. (**b**) Screen shot from the simulator demonstrating images and teaching points regarding suboptimal distension

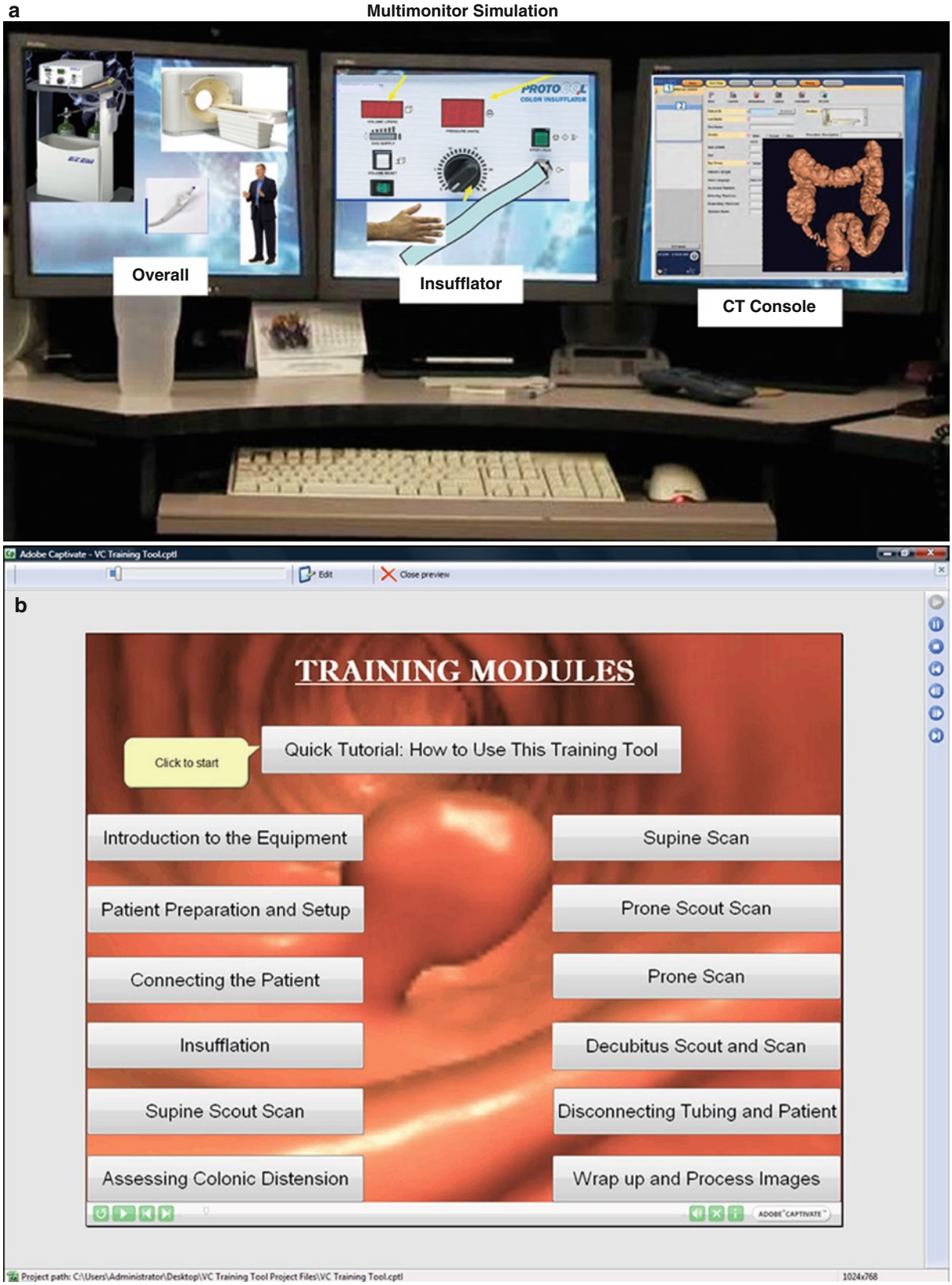

Fig. 7.18 (**a**) CTC Technologist training simulator. Sample 3-monitor set up option. Multiple simultaneous display monitors are required to provide real-time simulation of the interactions between the CT scanner, insufflator, and the patient. The technologist (student) can set up and monitor the exam, leading to high quality data acquisition. Allows technologist to attend to the numerous required details and progress through the necessary steps in correct order. (**b**) Opening page of a test version of the simulator. Nearly 200 screen shots and movie loops can be accessed in linear, sequential or random order. (See sample movie, Figure 7.18C). (**c**) Screen shots and movie loops can be accessed in linear, sequential or random order. This is a sample screen shot of the Philips technologist console during programming of the scanner

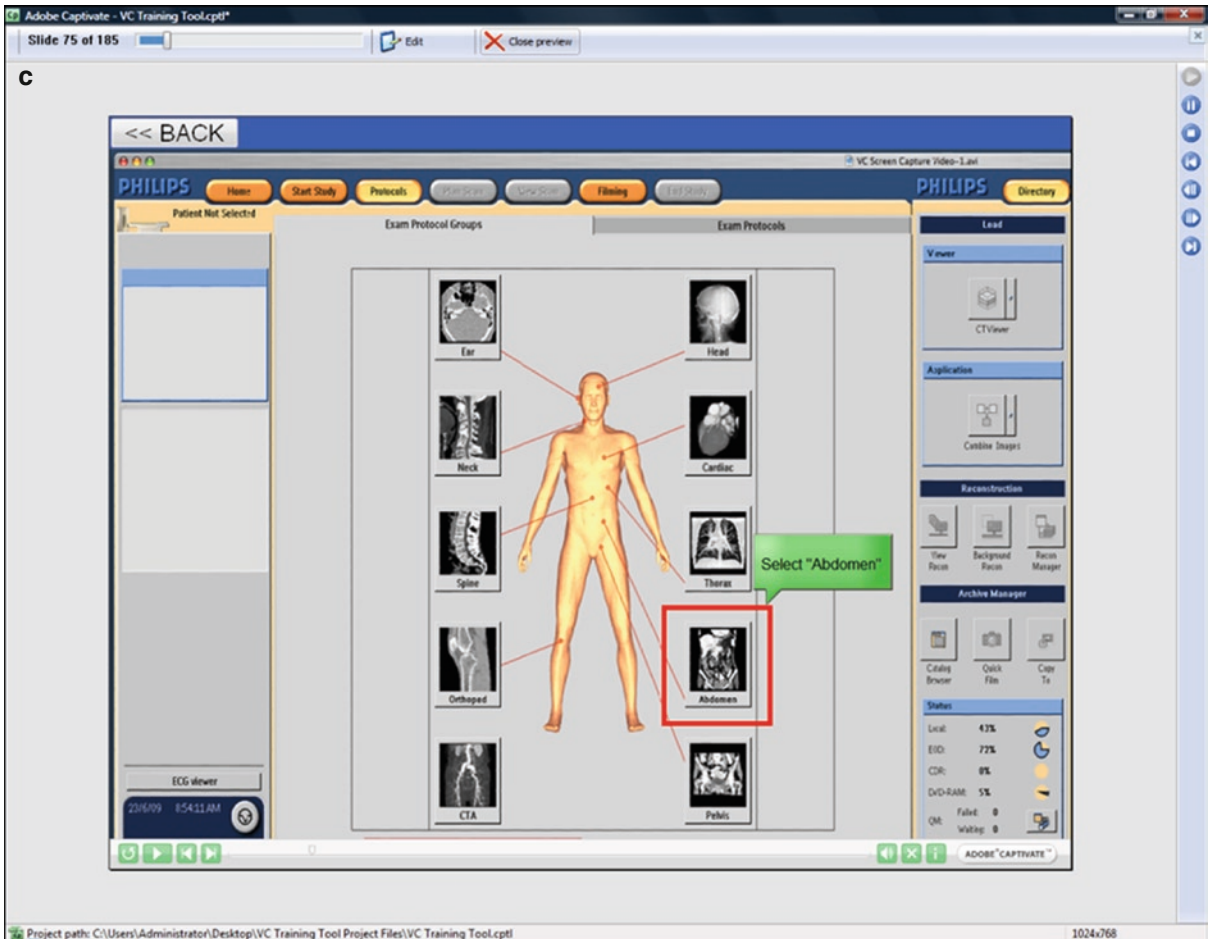

Fig. 7.18 (continued)

art. The 2009 ACR practice guidelines are written to be acceptable to a broad spectrum of radiologists who use a wide range of equipment. These guidelines recommend that the dose index by volume for CTC be 50% that of routine abdominal pelvic CT (which has an upper limit of 25 milligray [mGy]). Thus, for CTC, a CT dose index by volume of 6.25 mGy/position or 12.5 mGy for the entire examination is recommended. In fact, much lower doses can be achieved. In the CTC National Colonography Trial of the American College of Radiology Imaging Network (ACRIN), the effective milliamperes/s (mAs) was 50. For large patients the effective mAs was doubled. (Large patients were defined as having a >40 cm transverse dimension as measured on the frontal CTC scout view; Fig. 7.10).

As CT scanners improve, techniques change, which may result in either an increased or a decreased radiation dose. In general, the trend is to much lower doses than those reported by ACRIN or the Leidenbaum survey [23]. The slice interval, overlap, and table speed are adjusted to yield high-quality images. The number of images must be appropriate to the workstation used for visualization. Some 3D visualization programs are better suited than others in processing low radiation dose studies.

As an example, we use a Phillips 256 iCT at 15 or 30 mAs/slice, resulting in volume CT dose index ($CTDI_{vol}$) doses 1–2 mGy/series. Obese patients can be defined subjectively by the technologist and a slightly higher dose can be used. I believe that similar doses can be achieved in most state-of-the-art scanners using 16 or more channels.

Radiologist Training Requirements

The ACR recommendations are detailed in the white paper by McFarland et al. [4]. Besides education regarding patient preparation, colon insufflation, and image acquisition, the key elements of interpretation include hands-on experience in primary 2D or primary 3D CTC interpretation to search for colonic

polyps. Individuals experienced in abdominal CT should read 50 cases, and those unskilled in abdominal CT at least 75 cases. The abnormal cases should be endoscopically confirmed. The cases should be carefully selected to demonstrate the gamut of morphologic appearances on colorectal neoplasia and known reading pitfalls, and should be acquired using a variety of acquisition techniques. Ideally, mentored supervision or double reading should initially be performed [43–47], Watching an expert demonstrate the findings is not sufficient. Readers should be adept at using the specific software package of their choice. For maintenance of competence, 50 CTC cases should be reviewed every 2 years with either endoscopically confirmed cases in individual practice or by participating in a continuing medical education activity with interpretation of CTC by the reader preceding unblinding.

A more comprehensive discussion dealing with research on CTC reader training can be found in the ACR white paper [4]. Training as it relates to computer-aided detection is discussed in Chap. 11.

Reporting the CTC Exam Results

Communication of CTC results has elements in common with any radiology report. Timely effective communication, particularly of abnormal results (ACR practice guidelines for communication and for CTC), is critical. However, clinicians may not understand the follow-up recommendations or the limitations of visualizing extracolonic findings. CTC reports should be succinct yet provide meaningful results and impressions. Some workstation software will integrate images into the report. This is an attractive feature. Three-dimensional images and movie loops of key parts of the exam can also be networked from the workstation to the PACS to become part of the patient's permanent record. This can be accessible to anyone within the network (e.g., a gastroenterologist performing a follow-up OC). The report should be sufficiently detailed to permit someone reviewing the CTC Digital Imaging and Communications in Medicine images to locate the reported abnormalities.

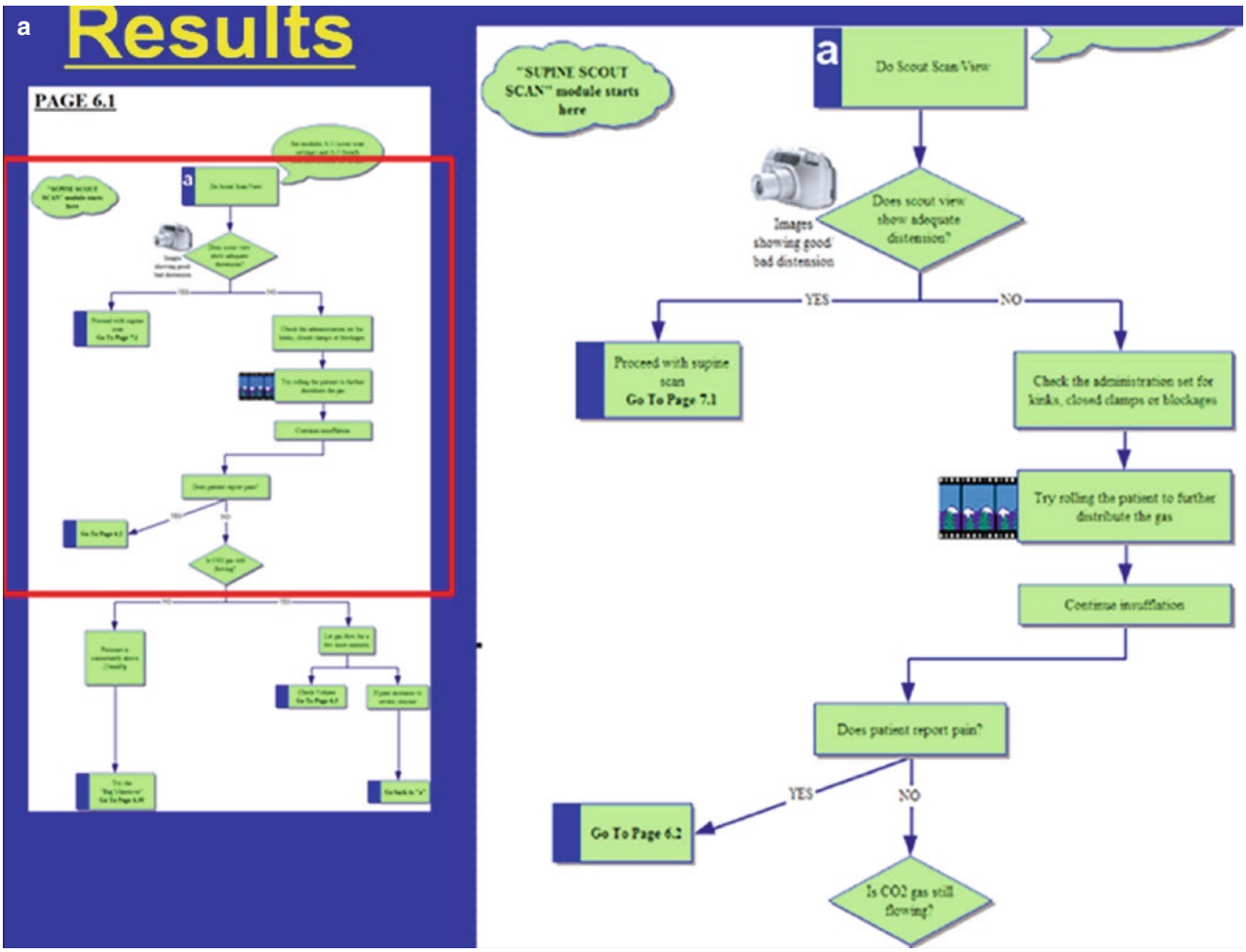

Fig. 7.19 (**a**) CTC Simulation software for training technologist. A small portion of the logical hierarchy and sequencing of the simulator pages. Screen shots and movie loops can be accessed in linear, sequential or random order. (**b**) Screen shot from the simulator demonstrating images and teaching points regarding suboptimal distension.

b

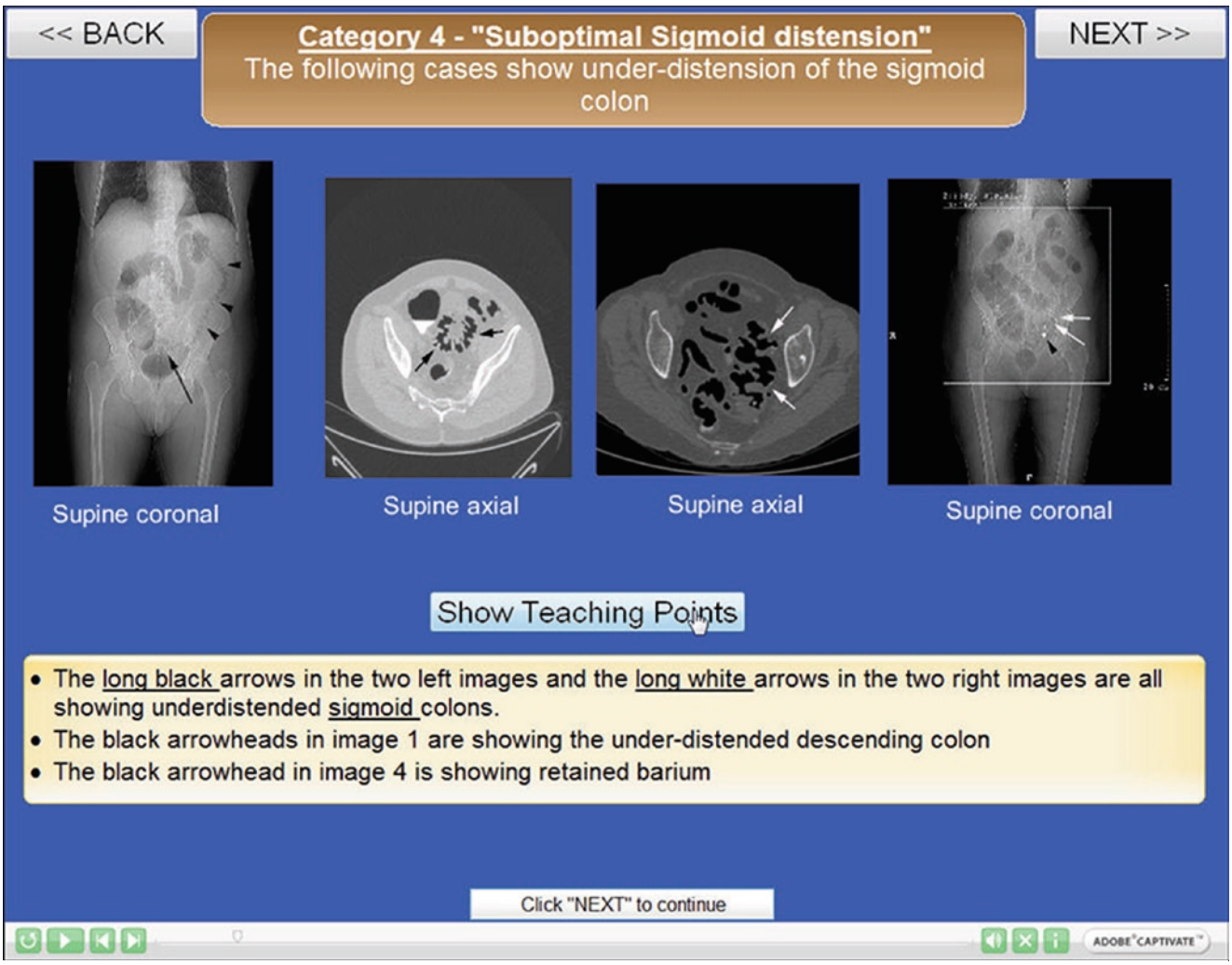

Fig. 7.19 (continued)

Table 7.11 Potential complications of CTC

Bowel preparation related
Hypovolemia (e.g., hypotension; dizziness)
Electrolyte shifts (e.g., hypocalcemia, hyperkalemia)
Cardiac, renal or other systemic effects
Exacerbation of co-morbidities (e.g., diabetes)
Tagging agent related
Rare allergic reactions (iodinated agents, barium even less likely)
Bowel distension related
Pneumatosis intestinalis
Perforation
Vasovagal reaction (due to distention or spasmolytic if used) (e.g., hypotension, diaphoresis, nausea, vomiting

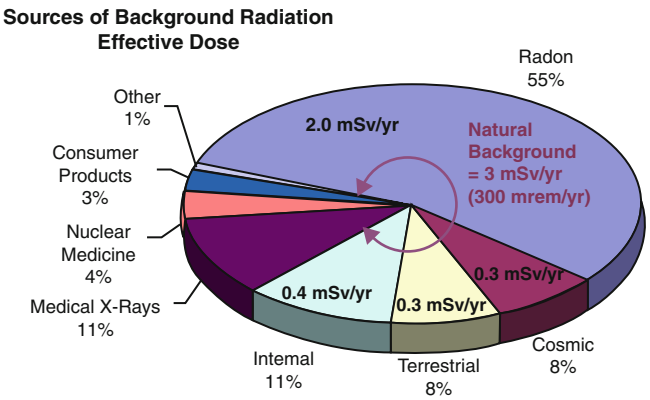

Fig. 7.20 Pie chart showing sources of background radiation contributing to the average 3 mSv/year. Many locations have background radiation as high as 10 mSv/year however (e.g., Denver, Co.) (Courtesy Dr. Frank Ranallo, Ph.D., DACR, Associate Professor of Medical Physics and Radiology, Univ. of Wisconsin School of Medicine and Public Health ranallo@wisc.edu)

Reports should contain these seven sections: History/Indications, Technique, Comparison, Colon Findings, Extracolonic Findings, Impression, and Optional C-RADS [the CT Colonography Reporting and Data System] Classification, along with a "disclaimer." [51] A template we use is shown in Table 7.12, and a few sample reports with images are appended to the end of this chapter. The components of these sections and some sample reports are discussed below. These should be sufficiently detailed to allow tracking of institutional data should that be desired, without the need to look at the scans or other records. Many workstations can generate reports that integrate 2D and 3D images. Others now incorporate pull-down menus to automatically generate the findings.

History/indications. Besides age, gender, and race of the patient (which may affect colorectal cancer risk; see Chap. 3), specify the indications for the exam that justify classifying it as "screening" or "diagnostic." Indicate if the exam is a follow-up for a prior CTC finding. Additional information that might indicate known risk factors for colorectal cancer should be included. These might include a prior history of colon polyps (and, if known, their histology), history of blood in the stool (specify if gross or by a test for occult blood), anemia, pain, constipation, etc. If the patient had a prior complete or incomplete OC, CTC, or barium enema, this should be stated, including the date and findings, if known. The colon cathartic and oral tagging agent should be specified.

Technique. If an information sheet or a consent form was provided to the patient, consider mentioning this. This will document that the limitations of the exam were revealed and explained to the patient (e.g., reporting polyps only ≥6 mm, limitations for some small or flat lesions, small complication rate including perforation). The rectal tube (e.g., "E-Z-EM/Bracco Diagnostics small rectal catheter") and the method of insufflation are given, e.g., "mechanical insufflation to patient tolerance using carbon dioxide" or "manual insufflation using room air." Next indicate that the patient was scanned supine and prone and specify if additional decubitus views were done. Indicate the scanner model and number of channels (e.g., 64 slice), the kilovolt peak, mAs (or mAs/slice depending on the scanner's nomenclature), for some scanners the table speed, the reconstruction interval, and kernel (or algorithm). From the dose page, we like to give the dose per series in mGy and the $CTDI_{vol}$ in mGy*cm for each series. The workstation model or version and interpretation method (normally 3D and 2D) should be specified. Since methods may change over time even within a particular radiology practice, having this degree of detailed documentation in the report may be valuable later when retrospectively tabulating data.

Comparison. If there is a prior CTC, give the date and compare the results in the impression. If there was a prior routine CT, mention it would have been done with a higher radiation dose and possibly with intravenous contrast and therefore would be more sensitive for the detection of extracolonic findings.

Colon findings. The first sentence should address the quality of the exam, including the effectiveness of the cathartic, the presence of residual fluid, the quality of the tagging of the residual fluid and stool, and the degree of colon distention. This may be simple or detailed depending on whether the exam is limited by any of these factors. For example: "The colon was well distended and well cleansed with minimal residual fluid which was well tagged." Or: "The colon was well distended except for the sigmoid colon, which is poorly distended but adequately evaluated on the right side down decubitus view. There is minimal residual particulate stool, all under 10 mm in size. There is minimal fluid in the left colon and a moderately large amount of fluid in the right colon which is well tagged with oral contrast."

Any unusual aspects of the colon anatomy can be described in this paragraph, e.g., an unusually tortuous sigmoid colon (which might explain why OC was incomplete) or a mobile

Table 7.12 University of Chicago CT colonography reporting template/sample dictation

HISTORY/INDICATION: ____ year old male/female. CTC for colorectal cancer screening.
TECHNIQUE: Informed consent was obtained. Patient was prepared using HalfLytley and oral tagging with oral Omnipaque. E-Z-EM catheter placed per rectum. Insufflation to patient tolerance using CO2 and a mechanical insufflator. Patient scanned supine and prone on a Phillips 256 iCT scanner, (kVp = 120, mA = 15, CTDIvol = supine, __ Prone, DLP [dose length product] = ___supine, ___ prone). Images were interpreted using 2D and 3D techniques on a _____ (workstation).
COMPARISON:
COLON FINDINGS: The colon was adequately cleansed and adequately distended. A small amount of residual fluid is seen and is well tagged with oral contrast.
No polyps 6 mm or larger were seen anywhere in the colon. A few scattered sigmoid diverticula are seen with no evidence of diverticulitis. No strictures.
EXTRACOLONIC FINDINGS: CTC is not sensitive for detection of findings outside the colon due to the low radiation dose and lack of intravenous contrast. Given those limitations, the following extracolonic findings are seen:
IMPRESSION: _____ _____.
Note: CTC is not sensitive in detecting polyps under 6 mm in size, which rarely contain advanced neoplasia.[a]
C-RADS CLASSIFICATION[a]:
C _
E_

[a]Zalis et al. [46]

segment (e.g., a floppy right colon which might predispose to an interpretive pitfall of confusing movement of stool with colonic rotation causing a stationary polyp to appear to have moved). If there are limitations due to artifacts, these should be specified. For example, streak artifact in the pelvis due to hip prostheses limit the quality of the 3D views in the pelvis. Rarely, respiratory, peristaltic, or patient motion (check the appearance of the skin on the coronal views for this) may limit the examination.

All polyps should be described per C-RADS [46] including size, morphology (sessile, pedunculated or flat, surface lobulations), relationship to folds, and colon segment. The images showing the polyp should be given by series number and image number (e.g., "supine images #45–50 corresponding to prone images #253–260"). Since supine or prone images might be reconstructed more than once – for example, at 3–4 mm for evaluation of extracolonic findings – be sure the series is clearly stated by number or description. Optionally, if the software shows the distance on the automated centerline, this can be given, but since it alone is not reliable without a correction factor, never rely on only that metric.

Each polyp should be described in a separate sentence. Note that size of the polyp is measured using the single longest dimension regardless of whether this is seen on 2D or 3D images. When specifying the polyp size I often add how the measurement was obtained (e.g., "based on prone 3D views"). The location of the colonic segment should use the designations of rectum, sigmoid, descending, transverse, ascending, and cecum as detailed in C-RADS [46].

If a mass or a stricture is present, describe its location, length, the presence of pericolonic fat infiltration, associated adenopathy or signs of metastatic disease, or unexpected inflammation from diverticulitis or inflammatory bowel disease. Since CTC would be relatively contraindicated if there were any clinical signs of acute inflammation, these findings are rarely encountered. An obviously benign fatty mass indicating a lipoma should be described as such and does not need further evaluation with OC.

Extracolonic findings. Our template includes the following statement: "Virtual colonoscopy is not sensitive for detecting lesions outside the colon due to the low radiation dose and lack of intravenous contrast. Given those limitations, the following observations are made." The extracolonic findings are then given as seen on the thick axial and coronal images reconstructed for that purpose. Soft tissue, liver, and bone window settings should be routinely used in searching for extracolonic findings (see Chap. 11). Comparison to any relevant prior exams should be made. The C-RADS "E-classification" can optionally be used.

Impression. A final impression should summarize the findings, document personal communication of the important positive findings that might require referral to OC or follow-up CTC, and, optionally, make a recommendation for the interval to the next CTC exam. If there are any limitations to sensitivity of the exam, these are reiterated in the impression. Polyps 10 mm or larger or patients with three or more 6–9 mm polyps should be referred to colonoscopy. While the guidelines specify discrete size cutoff points, in actual practice, polyp measurements are subjective. I personally recommend colonoscopy if the polyp size is close to but less than 10 mm, particularly if I find features such as lobulations or irregular shape to the polyp surface. A flat carpet lesion, with an irregular surface, suggests a "frond-like" appearance characteristic of villous histology and would be another indication to consider colonoscopy even if the lesion were under 10 mm. Age and other colorectal cancer risk factors are also taken into consideration. A patient with a family history of colorectal cancer or is age 70 or older should probably be referred to OC for polyps 8 mm or larger.

If the exam is abnormal, I document to whom the results were communicated. This is one reason I require a physician of record from all patients. It is becoming increasingly accepted to communicate directly to patients that an exam is abnormal and that the patients should discuss their results with their physicians [47].

Our template includes the C-RADS classification (Table 7.13) for the colonic and extracolonic findings, a short table explaining their definition, and the literature reference.

We follow the ACR Practice Guidelines for Communication of Diagnostic Imaging Findings [1]. There are factors which inherently limit the sensitivity of the exam that are explained in the "disclaimer" (CTC is designed to detect polyps 6 mm or larger). If there are other limitations due to retained stool or partial collapse of a segment, this is explained both in the body of the report and in the impression (see sample reports).

When making a recommendation, consider the patient's risk factors (see Chap. 3) and know the information contained in the C-RAD recommendations [46] and ACR white paper [4]. We also work closely with our gastroenterologist in offering a same-day OC option and sometimes (e.g., in executive health screening programs when a patient is undergoing multiple exams all day) immediate reporting of unexpected extracolonic findings that might necessitate a routine intravenous contrast enhanced scan (e.g., to evaluate a renal mass or adenopathy suspicious for extracolonic malignancy). A normal exam may include a recommendation for 5-year follow-up CTC or alternatively may be silent on a recommendation. Finding a polyp at or near 10 mm necessitates referral to OC. Three or more 6–9 mm polyps also require referral to OC. One to two polyps 6–9 mm in size may be evaluated in 1–3 years with a follow-up CTC. These are merely guidelines, and the final decision should be made by the patient in consultation with his or her personal physician. For this reason, we require that *all patients* provide a name and contact information for a personal physician.

Table 7.13 C-RADS Classification[a]

Colonic findings
C0 Inadequate study
Preparation insufficient to rule out polyps 10 mm or larger
Collapse of one or more segments on both views
Need prior studies for comparison
C1 Normal colon or benign lesions (screening continues every 5–10 years)
No visible colonic abnormalities
No polyps 6 mm or larger
Lipoma or inverted diverticulum
Non-neoplastic lesions (e.g., diverticulosis)
C2 Intermediate (small) polyp or indeterminate finings (1–3 year surveillance)
Fewer than three polyps 6–9 mm in size
Indeterminate fining, cannot exclude polyp 6 mm or larger
C3 Polyp, possible advanced adenoma (suggest OC correlation)
Polyps 10 mm or larger
Three or more polyps 6–9 mm in size
C4 Colonic mass, likely malignant (i.e., CTC sufficient to get surgical consult)
Semi annular or annular mass, possible extracolonic invasion
Extracolonic findings
E0 Limited examination
Compromised by artifact, severely limited
E1 Normal examination or normal variant
E2 Clinically unimportant finding, no work up indicated
E3 Likely unimportant finding, incompletely characterized
Subject to local practice and patient preference, workup may be indicated (e.g., complex ovarian cyst)
E4 Potentially important finding
Communicate to referring physician (e.g., aortic aneurysm, mass, marked lymphadenopathy)

[a]Adapted from Zalis ME, Barish MA, Choi JR, et al. [46]. CT colonography reporting and data system: A consensus proposal. *Radiology* 2005;236:3–9

Summary

The entire process of scheduling, billing, informing the patient about the preparation, tagging, and scanning has been covered in detail incorporating advice based on our experience at the University of Chicago. Radiologist and technologist education are also critical to a successful program. Innovative methods of education such as "simulators" may help in educating large numbers of individuals in a rapid and reliable fashion.

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Computed Tomographic Colonography: Image Display Methods

8

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Introduction

High reader performance (high sensitivity levels with low false-positive rates) and time efficiency are the two main goals sought during interpretation of computed tomographic colonography (CTC) examinations. As CTC continues to grow as a valid screening test for colorectal neoplasia, one concern is that, as currently proposed by most authorities in the field, interpretation of CTC examinations can be perceived as time-consuming and potentially impractical for some radiologists. Thus, it is mandatory that radiologists (and others interpreting the examinations) familiarize themselves with the various paradigms available to display the CT data. In the past decade, vendors and independent researchers have devoted time, effort, and resources to develop image display tools that ease the interpretation of CTC studies.

Interpretation of CTC examinations is a complicated process comprising two separate but equally important components: detection of a possible lesion, followed by characterization. Regardless of the reading paradigm preferred (primary 2D, primary 3D or other), the critical importance of a well-cleansed, well-tagged and especially well distended colon cannot be overemphasized. All technological innovations aimed at improving reader efficiency rely on excellent colonic preparation and distention for optimal performance. These topics are covered in other chapters of this atlas. It should also be kept in mind that although much emphasis has been given to using either a 2D or 3D approach for primary evaluation of CTC exams, good skills at both 2D and 3D reading are necessary in order to detect the smaller and often elusive polyps and to problem-solve various common and uncommon pitfalls.

Although subtle differences exist among the various vendors, all workstations currently available for CTC interpretation have dedicated software that allows a real-time interaction with the CT datasets. Also, even though there is some debate in the literature concerning CTC reading times, an experienced reader utilizing state-of-the art software can expect to complete the evaluation of the colon and the other soft tissues of the abdomen and pelvis in 15–20 min and often in much less time. This chapter describes the methods most commonly used in practice to display CTC datasets, as well as newer tools that are likely to gain popularity in the near future (including some that are currently approved for only investigational use). We also discuss how the implementation of these novel display methods could lead to successful and more time-efficient CTC interpretations.

Primary 2D Interpretation

Evaluation of the directly acquired axial supine and prone CT images is an approach to CTC that is easily accessible to most radiologists, especially those first starting to read CTC. Cine-mode scrolling through axial datasets is a familiar workflow for those accustomed to reading abdominal CT and generally requires less training than interacting with a 3D workstation. This primary 2D approach to CTC involves less postprocessing and potentially lesser computational requirements than a primary 3D read where a centerline needs to be tracked through the colonic lumen to generate "fly-through" movies in antegrade and retrograde directions. In a survey published in 2005, the primary 2D approach to reading CTC was preferred by 80% of experienced CTC readers at that time [1].

Workflow

Most primary 2D readers advocate a workflow which involves magnifying axial CT images to focus on the colonic segment of interest and tracking the colonic lumen on axial images from the rectum retrograde to the cecum, including scrolling through the top and bottom of each turn

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and flexure of the colon [2]. Often, this primary axial read is supplemented by multiplanar reformations (MPRs) in the coronal and sagittal planes, with most interfaces also including 3D correlation (endoluminal, cube, or one of the other "novel" 3D techniques described later in this chapter) of select target areas for problem solving. This approach is repeated for the prone and/or decubitus dataset, which is often linked to the supine images for improved segment-to-segment correlation. A variety of window/level settings have been advocated for use in 2D image evaluation, with most readers using "lung," wide soft-tissue, and/or "bone" windows, an option that should be user configurable and variable at the workstation. An example of a 2D multiplanar display with 3D correlation is illustrated in Fig. 8.1. A 2D multiplanar display with a 3D rendered cube for correlation is illustrated in Fig. 8.2.

Advantages

There are many potential advantages to using a primary 2D workflow for CTC interpretation. The full extent of colonic wall thickness is better visualized depending on the window

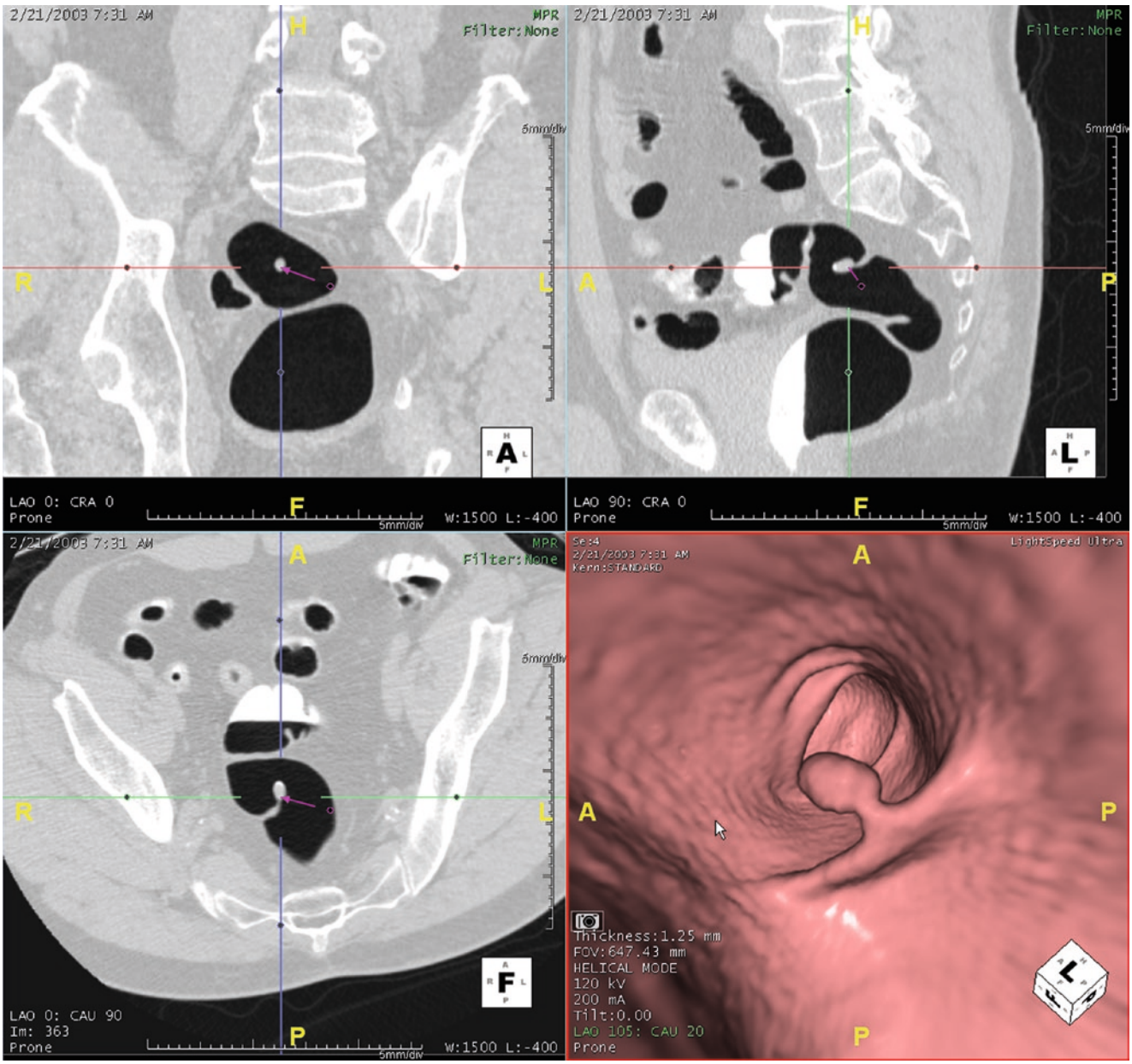


Fig. 8.1 2D multiplanar view of a pedunculated polyp on a fold with coronal reformat (*top left*), sagittal reformat (*top right*), and axial source data (*bottom left*). 3D endoluminal view for correlation (*bottom right*)

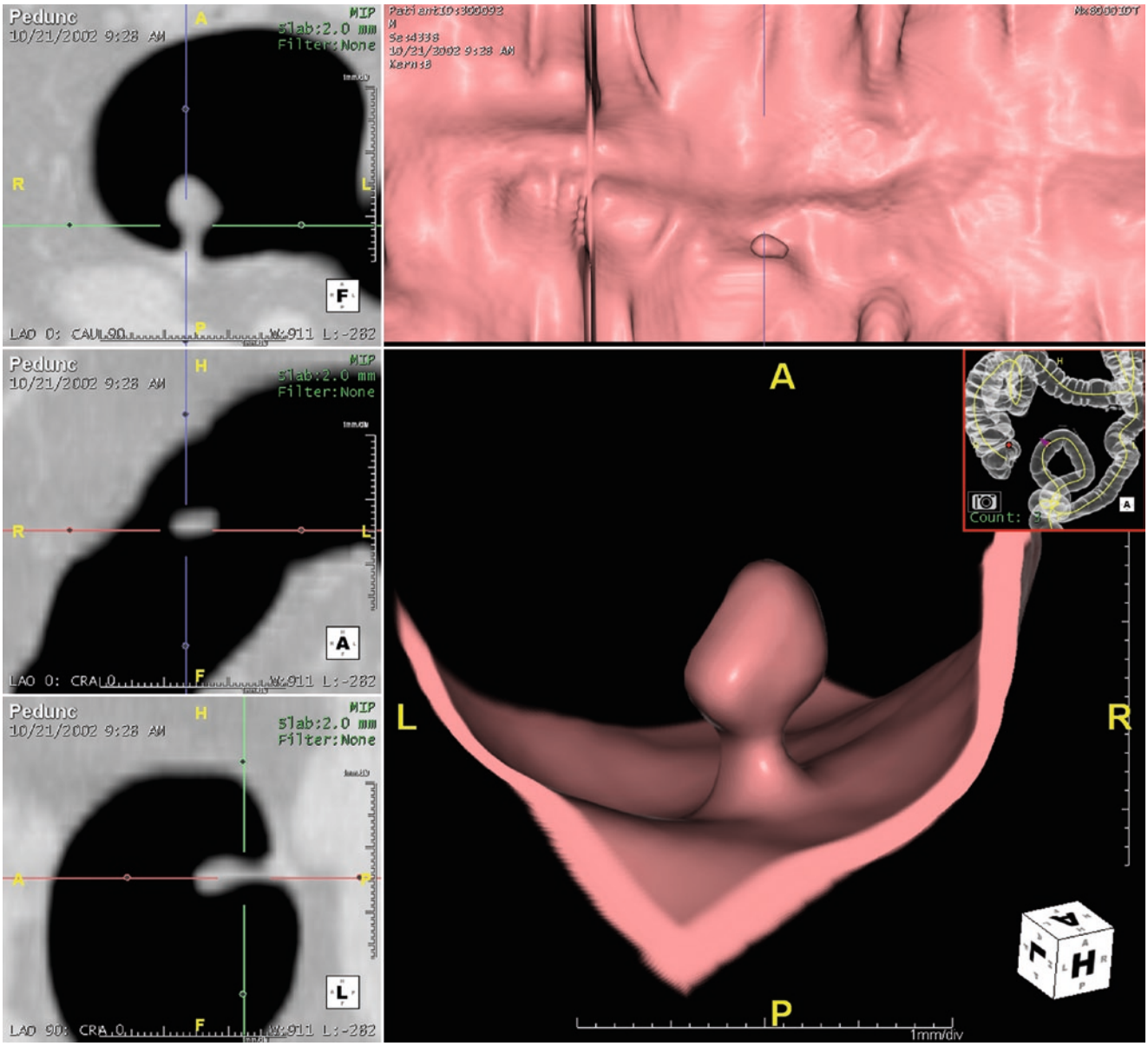


Fig. 8.2 2D/3D correlation for a pedunculated polyp with 2D axial, coronal, and sagittal reformats along the left, 3D "cube" in the lower right, and a virtual dissection or "filet" view in the top right strip

and level settings used. A 2D approach is also necessary if extracolonic findings are to be evaluated. As the 2D source images allow the reader to visualize what is beyond the mucosal surface, the attenuation and homogeneity of polypoid lesions is better demonstrated, allowing a more specific distinction of homogeneous soft-tissue density polyps from more heterogeneous residual stool. Density differences between stool and residual oral contrast (particularly if fecal/fluid tagging is used) is also more easily appreciated. Other polypoid-appearing findings such as inverted diverticula, stool-impacted diverticula, a prolapsed appendix, and ingested materials/pills are also easier to recognize on 2D images. Rapid identification of the ileocecal valve is also easier when the terminal ileum can be tracked to the valve. Colonic "pseudo-masses" caused by extrinsic impression from adjacent solid organs, adjacent loops of bowel, and ribs are more easily dismissed with 2D evaluation [3, 4].

In addition, simultaneous evaluation of axial supine and prone images also better allows the reader to incorporate the evaluation of lesion mobility to distinguish mobile stool from an immobile polyp, recognizing that a pedunculated polyp with a long stalk or a polyp within a mobile segment of colon may appear to move with changes in patient position. The morphology of a pedunculated polyp on a stalk, however, may be better recognized on 3D evaluation [5]. Simultaneous supine and prone image evaluation also allows for detection

of polyps which may be submerged in a pool of fluid on one or both positions. In cases where fecal/fluid tagging is utilized, submerged polyps may be visible on only 2D images viewed with appropriate window settings (Fig. 8.3). Polyp visualization on 2D and 3D images may be improved with the use of electronic subtraction; however, this type of image postprocessing is prone to leaving image artifacts related to incomplete subtraction, particularly at the meniscus of air/fluid levels and in areas of heterogeneous tagging such as residual stool (Fig. 8.4) [6, 7].

Primary 2D interpretation may also better detect polyps hidden directly behind haustral folds, which may be obscured

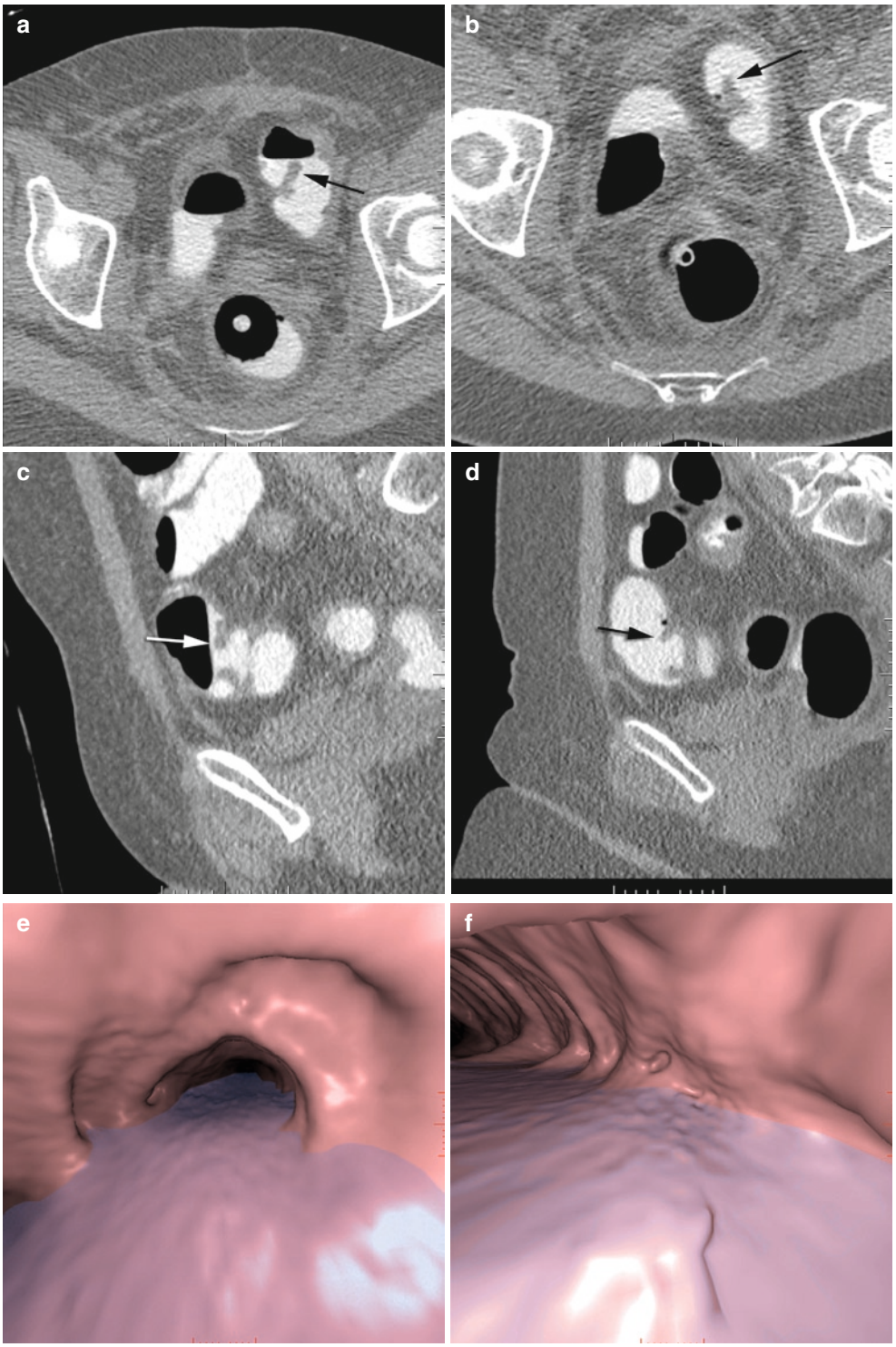


Fig. 8.3 Submerged polyp visible only through tagged fluid on 2D views. Axial supine (**a**), axial prone (**b**), sagittal reformat supine (**c**), sagittal reformat prone (**d**), 3D endoluminal view supine (**e**), 3D endoluminal view prone (**f**), fluid level highlighted in blue on 3D endoluminal views obscuring visualization of the submerged polyp. This polyp might be visible if electronic subtraction of tagged fluid was utilized

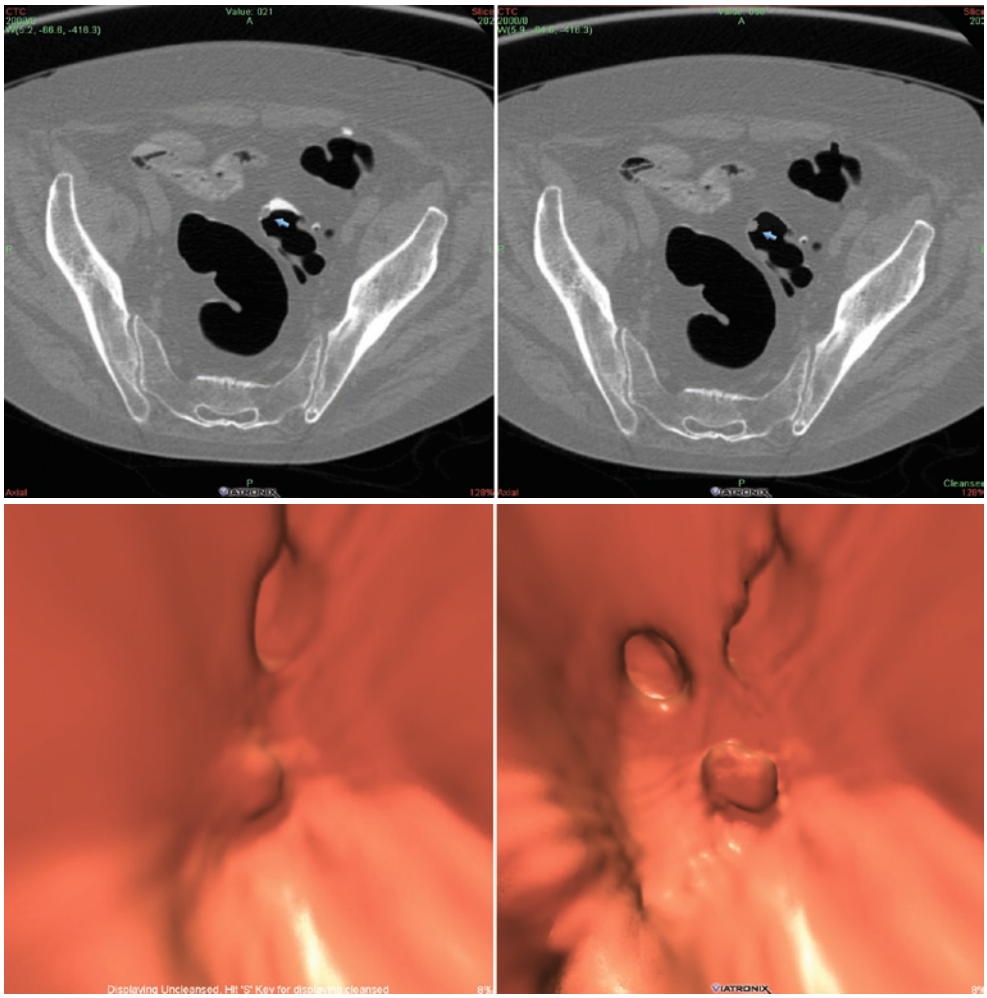


Fig. 8.4 Partially submerged polyp better viewed on 2D axial images (*top*) and 3D endoluminal views (*bottom*) before (*left*) and after (*right*) electronic subtraction

on 3D fly-through endoluminal images (Fig. 8.5). Flat lesions are difficult to detect with either primary 2D or 3D interpretation but may be more conspicuous on 2D images due to the ability to see areas of focal wall thickening which may be more subtle on 3D endoluminal images (Fig. 8.6).

Many studies have demonstrated that a primary 2D approach to CTC interpretation takes less time than a primary 3D approach, which usually incorporates bidirectional endoluminal fly-through in both supine and prone positions [1, 4, 8–11].

Disadvantages

Disadvantages that have been cited with the use of a primary 2D approach include greater interobserver variability as well as a possible lower sensitivity for polyps, particularly for those under 1 cm in diameter [8, 12–15]. This may be due, in part, to the constant vigilance required in scrutinizing axial cine-mode images for small polyps, which may appear in the reader's field of view for only a fraction of a second. This relative constant attention and focus needed to succeed as a 2D reader may result in increased reader fatigue and eye strain compared with 3D approaches [10, 12, 16].

2D polyp size measurements have shown less accuracy and more interobserver variability than 3D measurements compared with optical colonoscopic measurements. Sizes measured on axial or MPR images tend to underestimate the true size of the polyp. This may be due to the obliquity that an oblong or irregularly shaped polyp may have in relation to the traditional orthogonal axes used on 2D evaluation, whereas an interactive 3D view using linear calipers may more reliably confirm and measure the longest axis of a polyp [5]. Overall, however, size measurements made on either primary 2D or primary 3D CTC are reproducible and show less interobserver variability than optical colonoscopy size measurements [17, 18].

Primary 3D Interpretation

A primary 3D approach to CTC interpretation generally involves a greater amount of user training and a working familiarity with a dedicated 3D workstation. The 3D technique

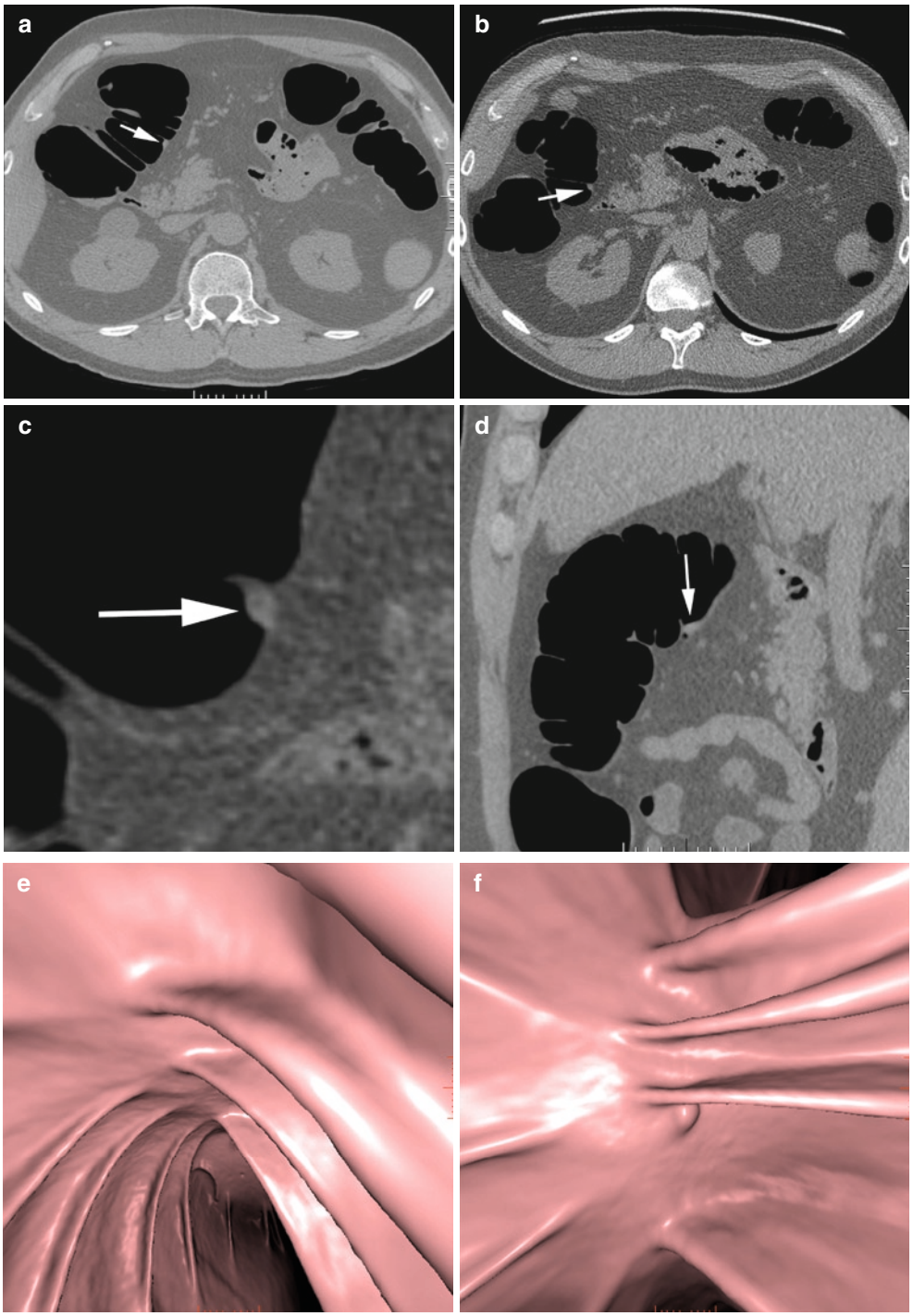
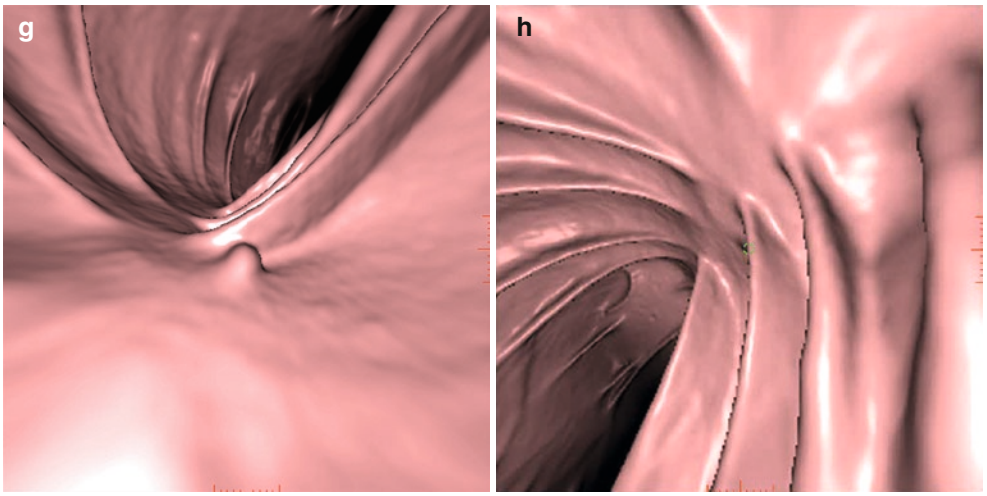


Fig. 8.5 Six millimeter polyp behind fold. Supine (**a**) and prone (**b**) CT images show a 6 mm polyp located directly behind a haustral fold at the hepatic flexure (*arrows*). Magnified axial (**c**) and coronal reformatted images (**d**) better illustrate the relationship of the polyp to the fold. 3D endoluminal views from a retrograde (**e**), perpendicular (**f**), and antegrade (**g**) vantage point, as well as a fly-through movie (**h**, video can be accessed online at http://extras.springer.com/2011/978-1-4419-5851-8) show that the polyp is only visible from an antegrade point of view

Fig. 8.5 (continued)



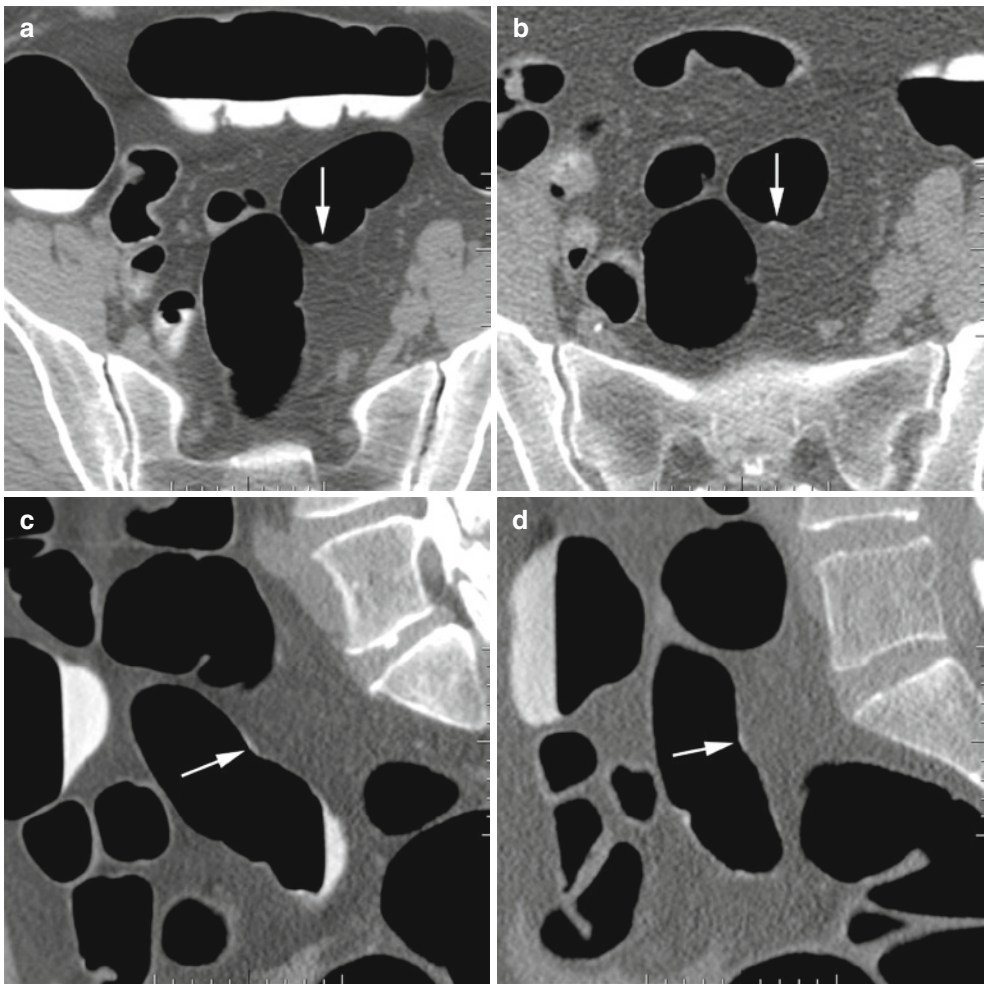
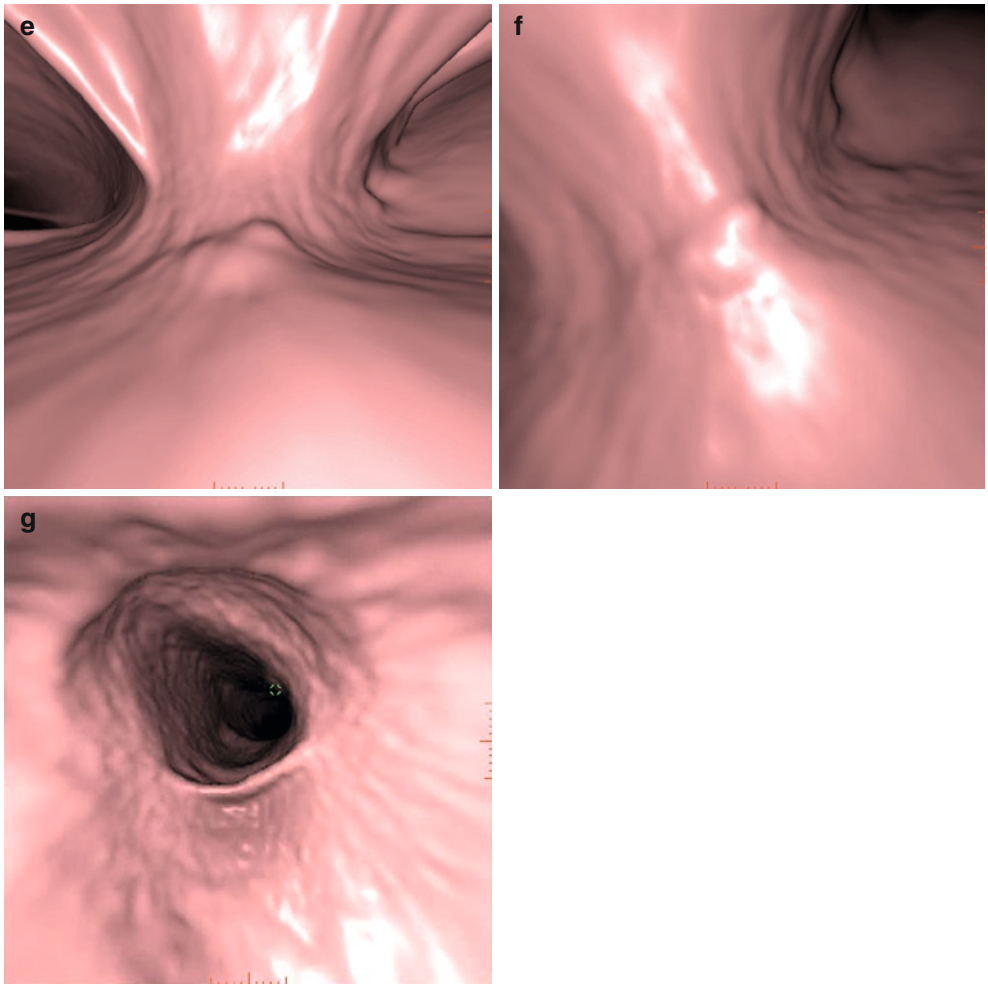


Fig. 8.6 Flat lesion. Supine (**a**) and prone (**b**) CT images as well as supine sagittal reformatted (**c**) and prone sagittal reformatted images (**d**) of a flat lesion in the sigmoid colon. 3D endoluminal views in supine (**e**) and prone (**f**) positions as well as a 3D fly-through movie (**g**, video can be accessed online at http://extras.springer.com/2011/978-1-4419-5851-8) confirms the flat but slightly raised appearance of this lesion

Fig. 8.6 (continued)



is more intuitive for gastroenterologists and other clinicians who perform optical colonoscopy. In general, some amount of postprocessing time is necessary in editing or confirming a centerline traced through the lumen of the colon from rectum to cecum. Significant computational requirements are also necessary to render the 3D endoluminal fly-through, although newer hardware and current 3D software applications are more robust, responsive, and affordable than in the past.

Workflow

There are a wide variety of software packages allowing different approaches to 3D interpretation. Most of these interfaces allow the reader to perform an automated or semi-automated endoluminal fly-through in antegrade and retrograde directions for both the supine and prone/decubitus datasets for a total of four complete fly-throughs per patient examination. These fly-throughs may be played as a fully automated movie but usually involve a variable amount of user-directed navigation. Some software packages have a "paint" function, which assigns a color to the patches of colonic mucosa that are not inspected after the fly-throughs are completed (Fig. 8.7). This function allows the reader to gauge how much of the colonic surface has been visualized after each pass. However, this tool does not distinguish between residual fluid and colonic mucosa and may overestimate the fraction of true mucosa that has been inspected. Careful review of fluid-covered areas on 2D images is critical.

As many polypoid-appearing lesions in the colon may in fact represent residual stool or sources of false-positive findings, direct correlation to 2D and MPR images is still necessary to determine lesion attenuation, mobility, and relationship to the colonic wall. Some vendors also include a "translucency" tool, which permits evaluation of polyp density directly within the 3D viewing pane to help differentiate true polyps from heterogeneous stool or fatty structures such as lipomas and inverted diverticula without having to refer back to the 2D source data (Fig. 8.8). Lesions on supine and prone images can often be directly correlated with each other using the distance from the anus tool and/or endoluminal landmarks, but this correlation is usually easier with 2D axial datasets due to variable endoluminal orientation and lack of extracolonic positional clues on 3D images. Use of "colon maps" (resembling a double-contrast

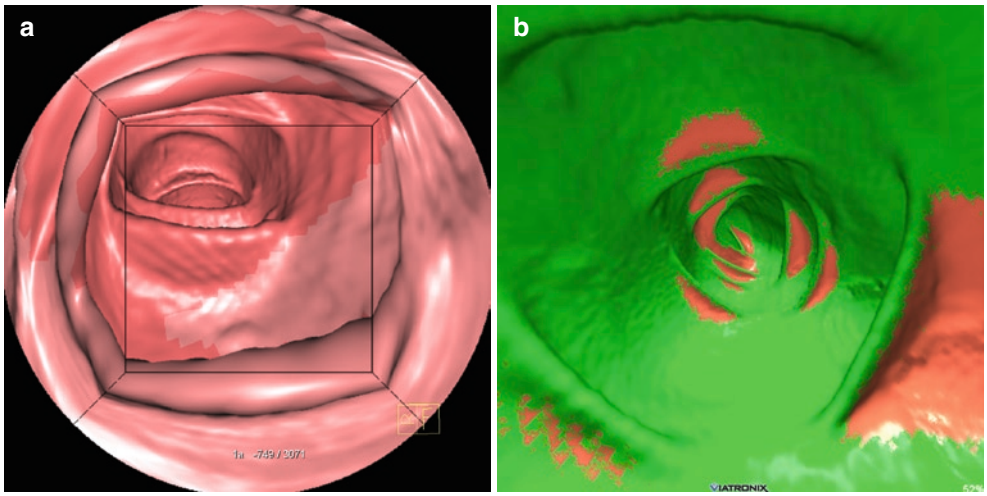


Fig. 8.7 (**a**) 3D endoluminal "panoramic" view on antegrade fly-through with "paint" function illustrating not yet visualized mucosal surfaces. Darker color represents surfaces not visualized on initial retrograde fly-through. (**b**) Another 3D software package demonstrating the "paint" function. Here, viewed surfaces are painted green while unviewed surfaces (especially behind haustral folds) are pink

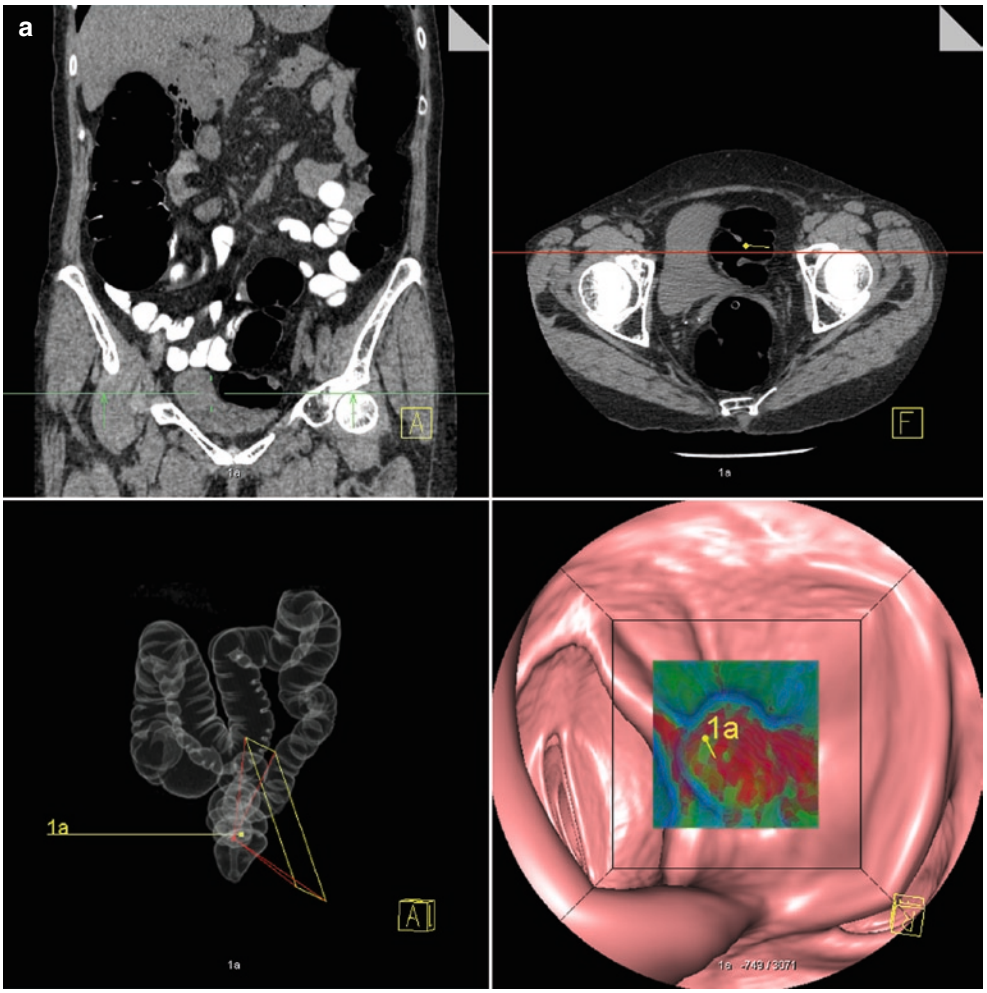
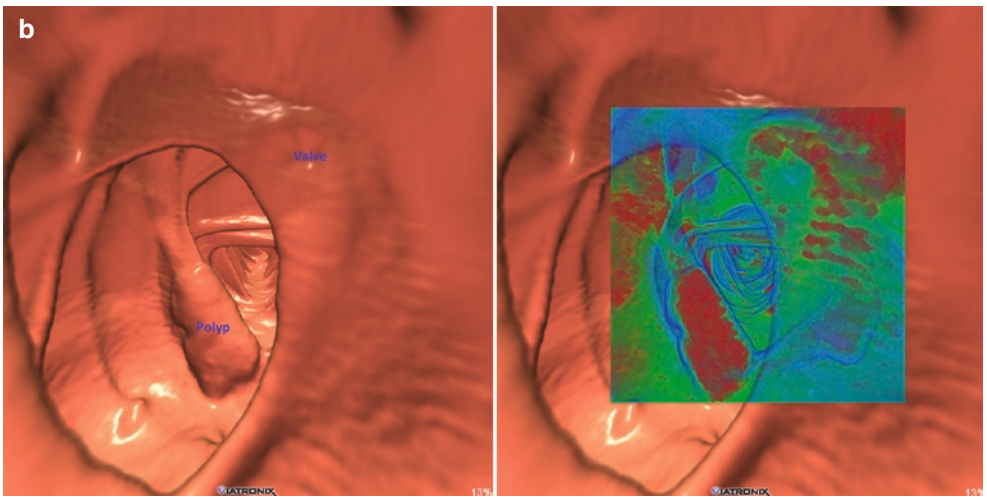


Fig. 8.8 (**a**) 3D "translucency" tool permits evaluation of polyp density directly within the 3D viewing pane (*lower right*). Red represents soft tissue density. **(b)** 3D endoluminal views on another software package demonstrating the "translucency" tool on the right showing a soft tissue density polyp as red and the fatty ileocecal valve as green

Fig. 8.8 (continued)



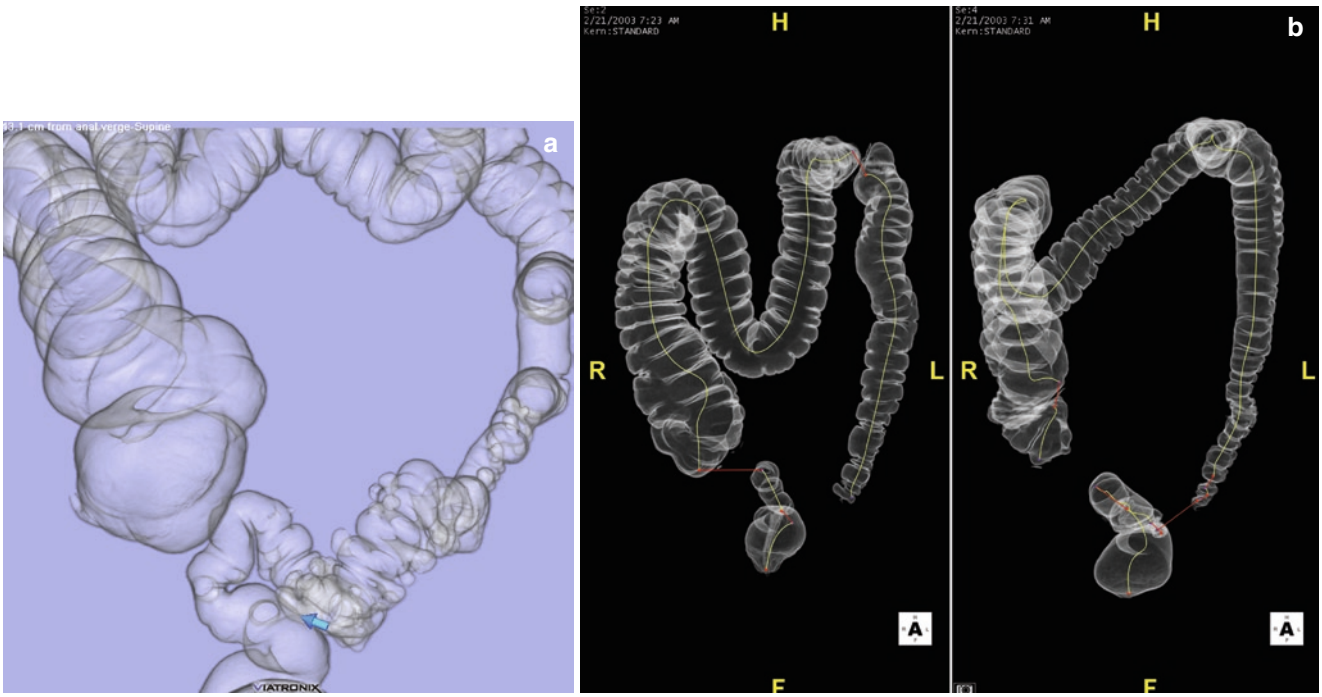


Fig. 8.9 Colon maps display an overview of colonic anatomy through surface rendering of the air-mucosal interface at the colonic wall. Direct correlation with 3D endoluminal views aids in localization and orientation during 3D fly-through cine navigation

barium enema) can be helpful in gauging colonic location on 3D fly-throughs (Fig. 8.9). Various approaches, including normalizing the distance along the centerline to the overall colon length and multiplying polyp distance from the anus or cecum by a conversion factor, have also been shown to be fairly reproducible [19–21].

Advantages

One of the most important advantages to a primary 3D workflow is less reader fatigue and eye strain. As polyps are rendered three-dimensionally and are presented in the reader's field of view for a longer period of time than when using a primary 2D cine-viewing mode, this additional "dwell time" tends to make polyps more conspicuous on 3D fly-through than on axial images. In addition, polyps are more easily distinguished from adjacent haustral folds when viewed as a 3D rendering as opposed to a primary 2D read where a polyp may appear identical to a fold on a static axial image (Fig. 8.10). Recent studies have suggested that this may result in higher 3D sensitivity for polyps, particularly subcentimeter polyps than with a primary 2D approach [8, 12–15]. In fact, this has been cited as one of the main reasons that some recent larger trials have showed significantly more success than others [12, 22, 23].

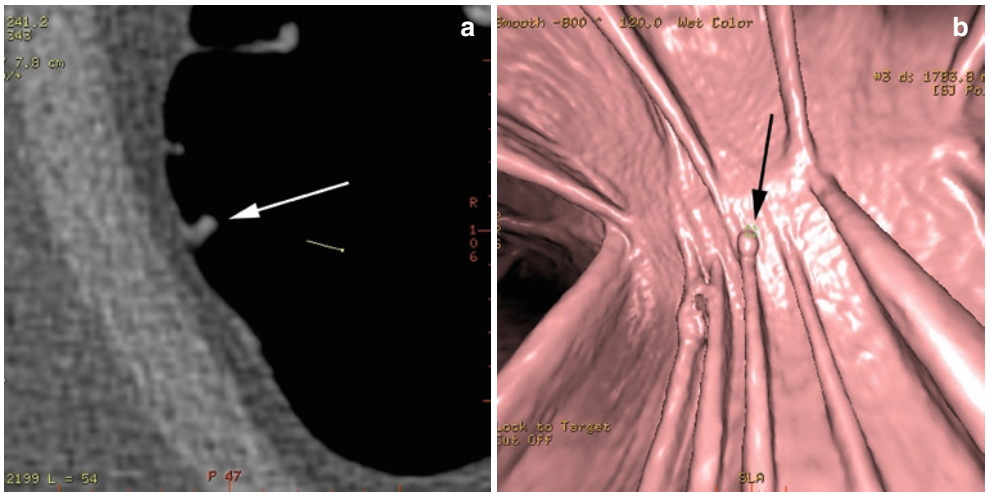


Fig. 8.10 6 mm sessile polyp on a haustral fold. This polyp may be more difficult to distinguish from a haustral fold on a 2D axial image (*left, arrow*) than on the corresponding 3D image (*right, arrow*)

3D techniques have also shown significantly less interobserver variability than 2D techniques [8, 12, 14, 15]. This may also reflect an increase in reader confidence when detecting and confirming colonic polyps. The morphology of polyps may also be more easily recognized as sessile, pedunculated, or flat. The stalk of an elongated pedunculated polyp is more easily recognized and excluded from the polyp size measurement, as is recommended in practice.

As previously mentioned, polyp size is more accurately and reproducibly measured on 3D endoluminal views than on 2D MPRs. Three-dimensional measurements show less interobserver and intraobserver variability, as well as a trend toward less underestimation of size than 2D measurements, when optical colonoscopic measurements are used as the gold standard [5]. Accurate polyp measurement is especially important, as size is the main criterion dictating patient management recommendations and, in any given case, can help the radiologist decide between recommending a short-term follow-up CTC versus referring a patient for optical colonoscopy for confirmation and polypectomy. This is especially true for polyps nearing the 1 cm size range, where each fraction of a millimeter is important. As the longest axis of a polyp can be more easily determined on a 3D view than on a 2D view, 3D size measurements are more accurate and reproducible for oblong and irregularly shaped polyps such as pedunculated polyps on a stalk or flat lesions. In addition, while some flat lesions may be less conspicuous on a primary 3D evaluation than on 2D, when seen, they are generally better measured on the 3D view [24].

Disadvantages

As a primary 3D evaluation usually involves four complete fly-through passes for full evaluation of the colon, an endoluminal approach tends to result in longer reading times compared with a primary 2D approach. A single unidirectional fly-through is usually insufficient for full evaluation of the colon, as over 20% of the mucosal surface is not visualized on a single pass [25, 26]. This is partially alleviated with use of a wider viewing angle (e.g., 120º) resulting in a larger field of view (Fig. 8.11b, d) [12, 27]; however, even a bidirectional fly-through evaluation may still miss up to 5% of the colonic mucosa (Fig. 8.11) [25, 26].

While smaller polyps may be more readily detected with a primary 3D approach, some studies comparing a primary 3D versus 2D reader approach have shown a higher false-positive rate with the 3D method [8, 28, 29]. A higher false-positive rate can significantly affect CTC management recommendations, as more patients may be inappropriately sent to optical colonoscopy for further evaluation. However, as the use of fecal and fluid tagging becomes more widespread, newer generation multi-detector scanners are used, and the latest versions of the 3D software interfaces are incorporated into clinical practice, it is likely that the false-positive rate of primary 3D evaluations is decreased. A higher false-positive rate may also reflect the higher sensitivity of the 3D approach for detection of diminutive polyps and the well-known imperfections of the standard of reference used (optical colonoscopy).

When visualized on 3D views, polyps tend to be more conspicuous than on axial images and more easily differentiated from haustral folds – however, endoluminal fly-through approaches to polyp detection may miss polyps obscured behind haustral folds or situated deeply within a sacculated haustra between high folds (Fig. 8.5). In addition, flat lesions may be less conspicuous on 3D views than 2D views, as the full wall thickness is not accounted for endoluminally.

Combined 2D/3D Approach

All readers and current consensus guidelines acknowledge the complementary role of both 2D and 3D visualization methods, and point-to-point correlation between the two is

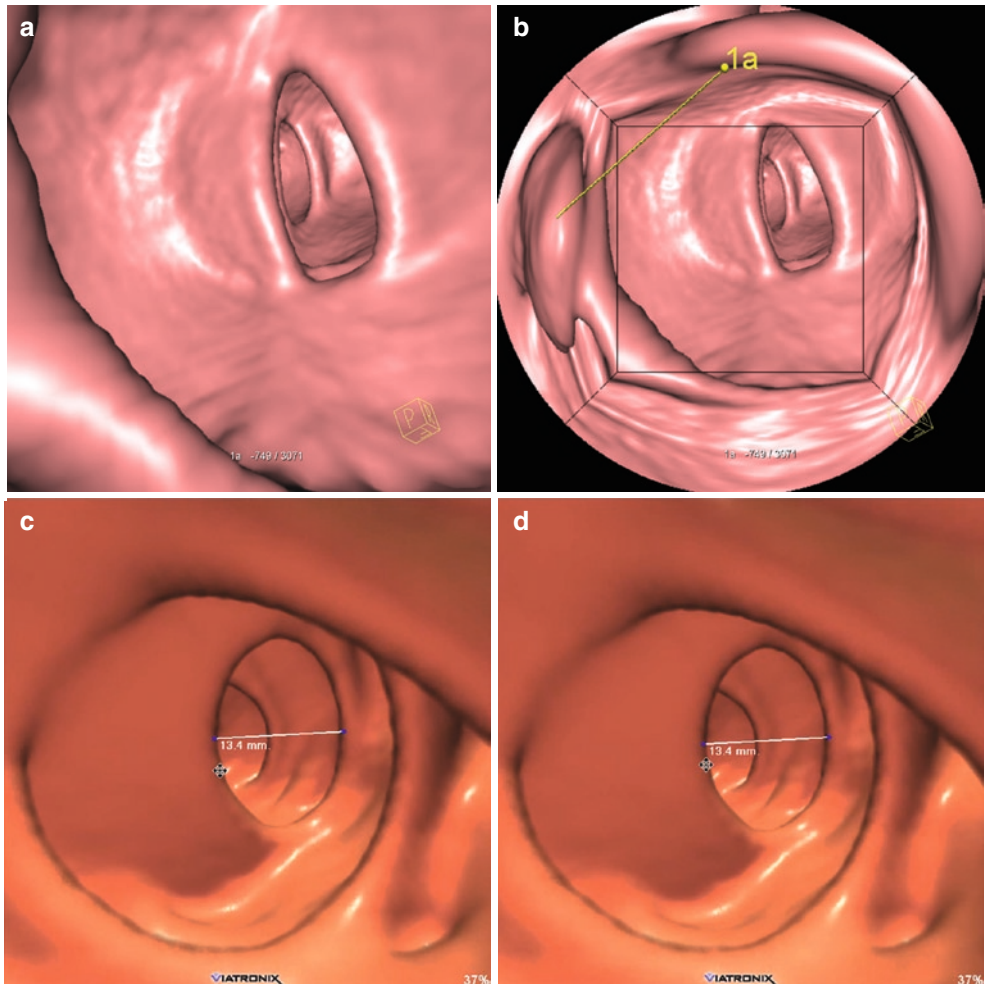


Fig. 8.11 Increasing the field of view (FOV) on 3D endoluminal fly-through images permits visualization of more of the mucosal surface, particularly in the periphery of the images and behind haustral folds and around colonic flexures. (**a**) 90º FOV. (**b**) 120º FOV better visualizes a polyp ("1a") adjacent to a haustral fold in the periphery of the image. Similarly, in a second patient, a polyp seen in the periphery of a fly-through movie using a 90º FOV (**c**, video can be accessed online at http://extras.springer.com/2011/978-1-4419-5851-8) is more readily seen using a 120º FOV (**d**, video)

favored. Whether a primary 2D approach with 3D correlation for problem solving or a primary 3D approach with 2D correlation is used is up to each individual reader and often depends upon the particular software package chosen. Nonetheless, a trend toward a more generalized use of the primary 3D approach has been recognized lately among authorities in the field. In practice, many CT colonographers begin as primary 2D readers with many moving toward a primary 3D approach as they gain more experience.

Novel Display Methods

Although primary 2D and primary 3D are the two widely accepted methods for CTC data interpretation, both have limitations. The primary 2D approach may be suboptimal for detecting some polyps because the total amount of time that each finding remains in the field of view of the radiologist tends to be shorter when compared with the primary 3D approach. On the other hand, the primary 3D method has a stigma of being more time-consuming than the primary 2D method because in order to allow a complete (or near complete) visualization of the colonic mucosa, it demands four fly-through passes: antegrade and retrograde fly-through of both the supine and prone datasets. This difference in interpretation times is supported by the results of the ACRIN II trial [11]. In an attempt to improve reader efficiency while still maintaining adequate performance levels, many investigators and vendors have developed novel methods to display the mucosal surface of the colon and facilitate interpretation. These methods are likely to be more time-efficient because only a single review is performed, compared with the bidirectional review that is recommended for a primary 3D endoluminal interpretation.

Early work on the potential benefits of these alternative display methods began in the late 1990s [10, 30], such as the "panoramic technique" described by Beaulieu et al. [10]. Others followed, including the "filet view," "unfolded cube," "band view," and "virtual dissection." Most of these methods combine elements of the 2D and 3D paradigms, such that an endoluminal view of the colon is displayed in a 2D image. The main advantage of these alternative display algorithms is that more colonic mucosa is displayed per unit of space. The main drawbacks, however, are the inevitable distortion

associated with many of these methods and a limited depth perception. However, as readers of CTC examinations continue to gain experience and confidence, it is possible that for some readers, these novel display paradigms will become the preferred approach and result in some time savings.

Virtual Pathology

In the virtual dissection mode [31–34], the 3D model of the colon is stretched out and sliced open and the full circumference is displayed as a flat 3D rendering of the mucosal surface in rectangular segments. This flattening method uses a mathematical algorithm to straighten the colon, sectioning it longitudinally across an arbitrary plane and flattening the lumen such that large surface areas of the colon are displayed in a manner that resembles gross pathology specimens. The entire mucosal surface of the colon can be displayed as a series of segmented strips on a single monitor (Fig. 8.12), but the length of the strip can be adjusted to meet the readers' preferences. There is overlap at the edges of the plane of "dissection," ensuring that lesions that abut the cut surface of the colon on the virtual dissection image extend into the area of overlap (Fig. 8.13). With a dual-monitor system, interactive interpretation can be performed by displaying 2D images in any plane, 3D endoluminal renderings, and virtual images of the supine and prone acquisitions simultaneously. Robust software applications allow immediate point-to-point correlation of findings between the virtual dissection images and the corresponding 2D and 3D images (Fig. 8.14).

In a well-distended colon without significant residual fluid, the virtual dissection algorithm also allows display of the entire mucosal surface, unlike 3D endoluminal display, which may result in some blind spots. Thus, this technique has the potential to reduce evaluation time (and reader fatigue) by providing a more rapid assessment than is possible with a traditional fly-through.

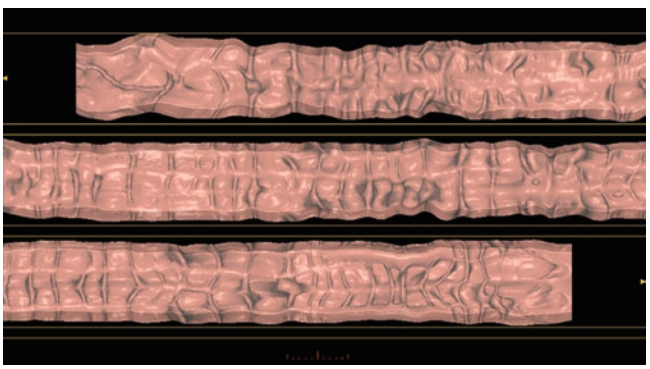


Fig. 8.12 Flattened view. The complete colon (divided into three stripes) is displayed in the monitor for inspection and interpretation

The flattened view introduces potential sources of error that are not present with the 2D mode or more traditional 3D endoluminal fly-throughs. For example, the virtual dissection approach may yield severe distortion, causing lesions to appear elongated (or "stretched out") (Fig. 8.15). This is inevitable given that the colon is virtually straightened and flattened, especially the sections that are curved (flexures, redundancies). As a result, some lesions may be displayed more than once in some areas. Vendors are developing and testing numerous rendering algorithms to diminish the severity of distortion. With careful attention and experience, it generally is possible to differentiate these areas of distortion from true lesions, which often tend to be oriented perpendicular to the transversely oriented folds (Fig. 8.16). Perceived distortion on virtual dissection images may be

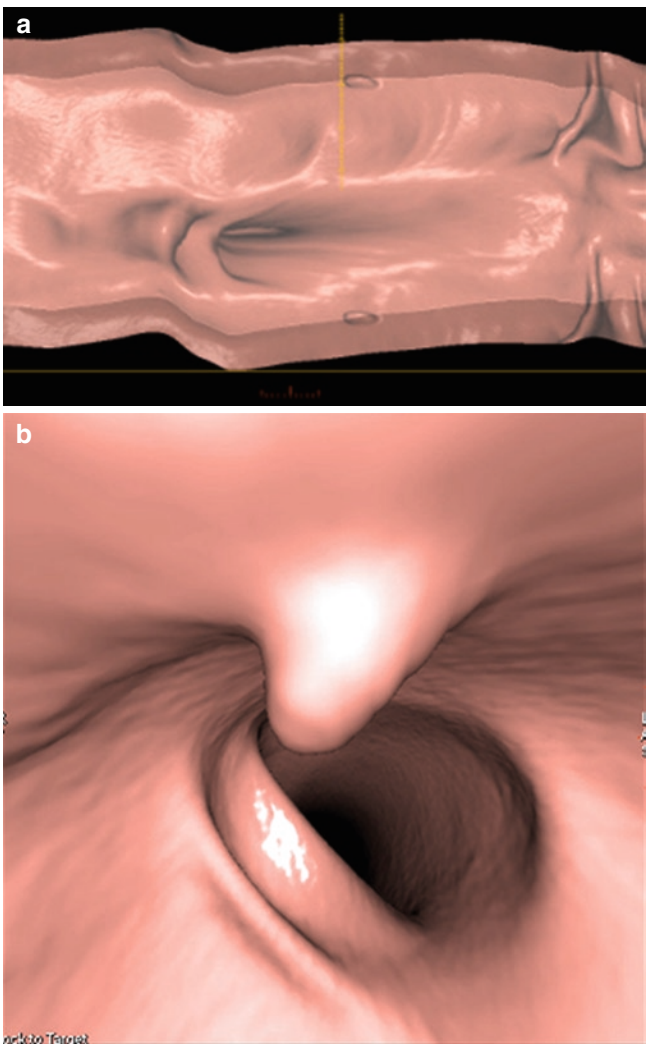


Fig. 8.13 Overlapping tissue at the plane of dissection in a flattened view (**a**). Notice that a small sessile polyp (*arrows*) is displayed on both sides of the plane of dissection, thus ensuring that a potential lesion will not be overlooked because of the dissection. The same polyp is well demonstrated on the 3D endoluminal image (**b**)

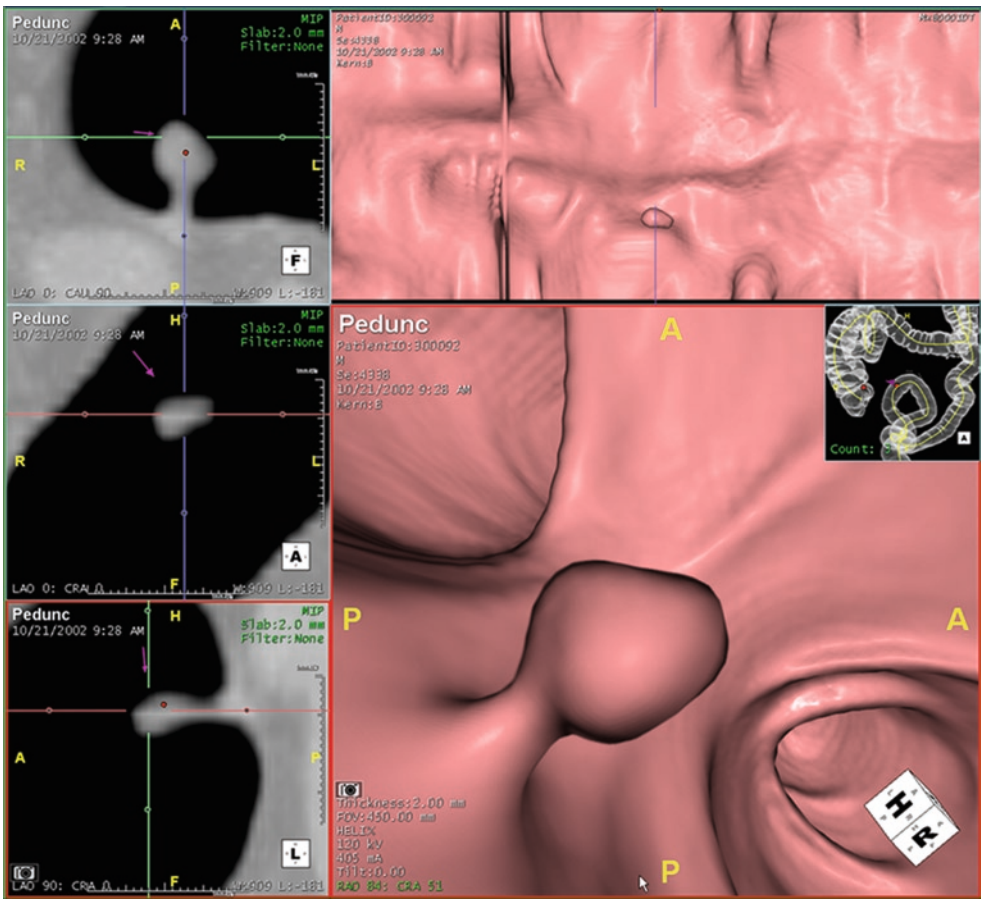


Fig. 8.14 Point-to-point correlation between flattened view and 2D/3D images. A cursor placed over the pedunculated polyp on the flattened view (*top right image*) allows immediate point correlation with the orthogonal plane 2D images (*left column*) and 3D endoluminal image (*bottom right image*)

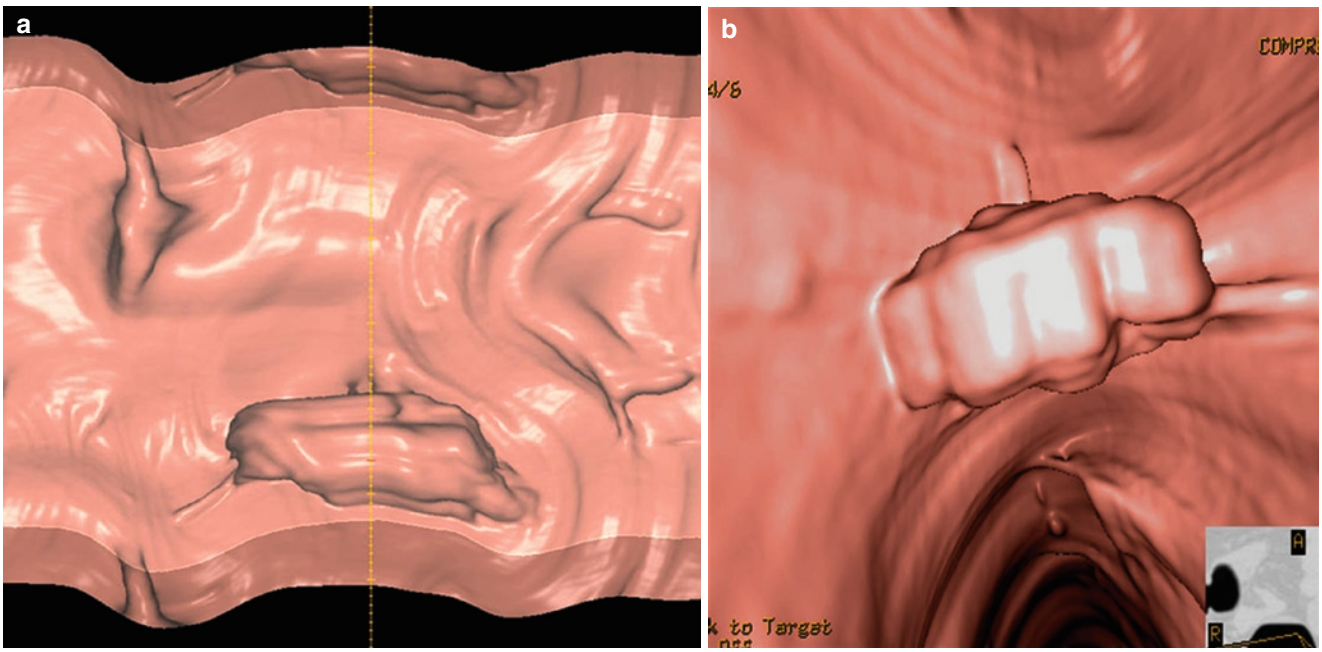


Fig. 8.15 Large polypoid mass seen on flattened view (**a**) and 3D endoluminal image (**b**). The mass, subsequently proven to be a villous adenoma, appears distorted and "stretched out" on the flattened view. This limitation that is inherent to flattening display techniques can be overcome with proper reader training and experience

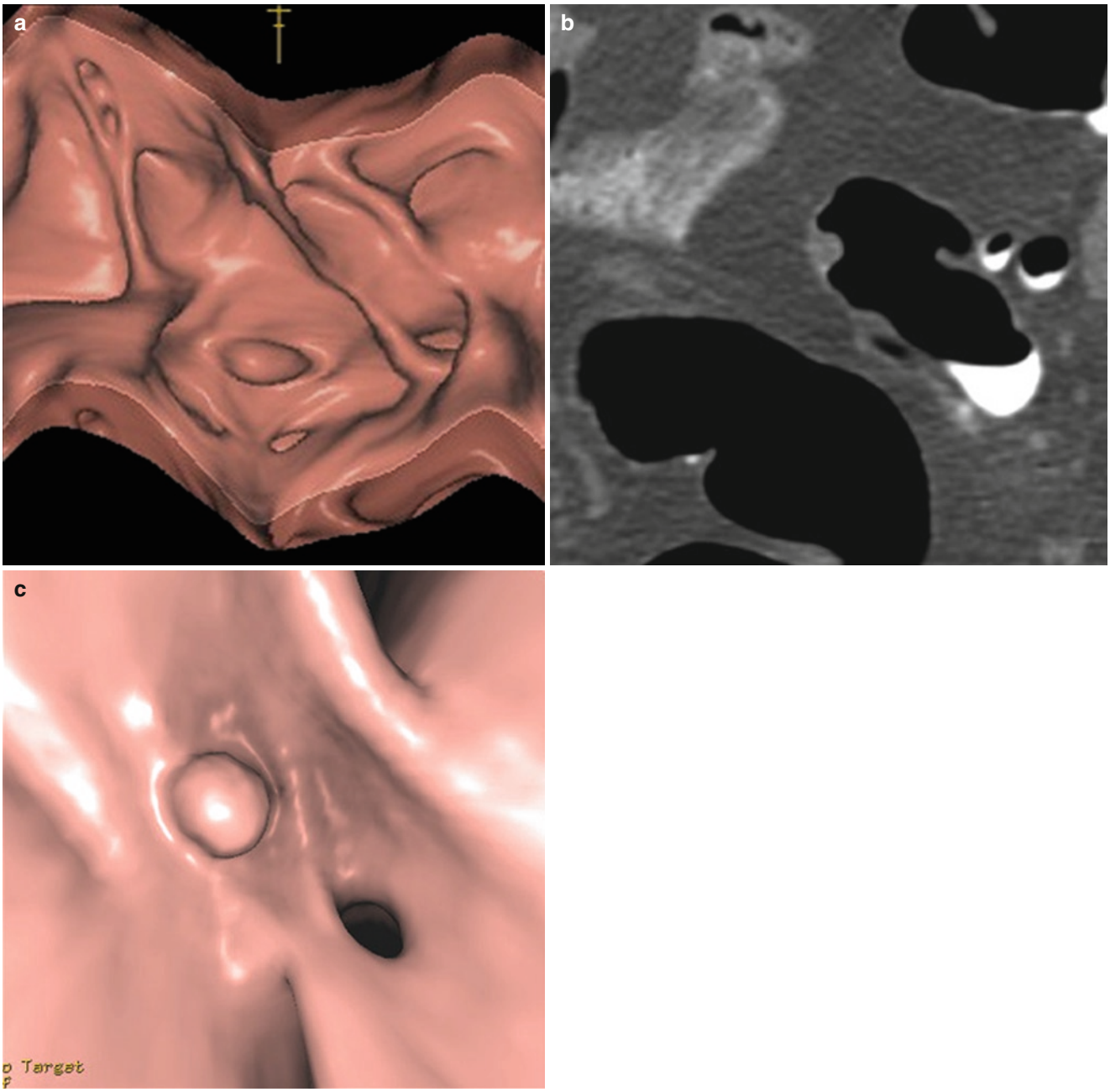


Fig. 8.16 Distortion of sessile polyp. Flattened (**a**, *arrow*), axial 2D (**b**, *arrow*) and endoluminal 3D (**c**) images demonstrate a 7 mm sessile polyp. On the flattened view, the polyp is distorted and appears "stretched out," perpendicular to the orientation of the transverse folds

influenced by polyp morphology: with sessile lesions tending to have an elongated or rounded shape (Fig. 8.17), whereas pedunculated polyps are less predictable (Fig. 8.18). Thus, with proper training, it is possible that radiologists will find that distortion does not necessarily compromise polyp detection and that a more rapid review is indeed possible because there are fewer images to interpret. When evaluating flattened views, it is also important to inspect all segments where the colon appears to be interrupted, to avoid potentially devastating pitfalls. Gaps occur whenever there is little or no gas in the lumen of the colon. Collapse secondary to spasm or poor distention or a completely fluid-filled colon are potential causes of interruption of the colon in the flattened view. However, an annular carcinoma can have the same appearance. Thus, it is imperative that the 2D images be scrutinized very carefully to identify the characteristic signs of a malignant narrowing (Fig. 8.19). Similarly, retained fluid limits evaluation of the mucosal surface of the colon. On flattened views, residual fluid is identified as a featureless, flat surface that effaces several contiguous folds in a segment of the colon (Fig. 8.20). When fluid is tagged with positive contrast material, some software packages highlight

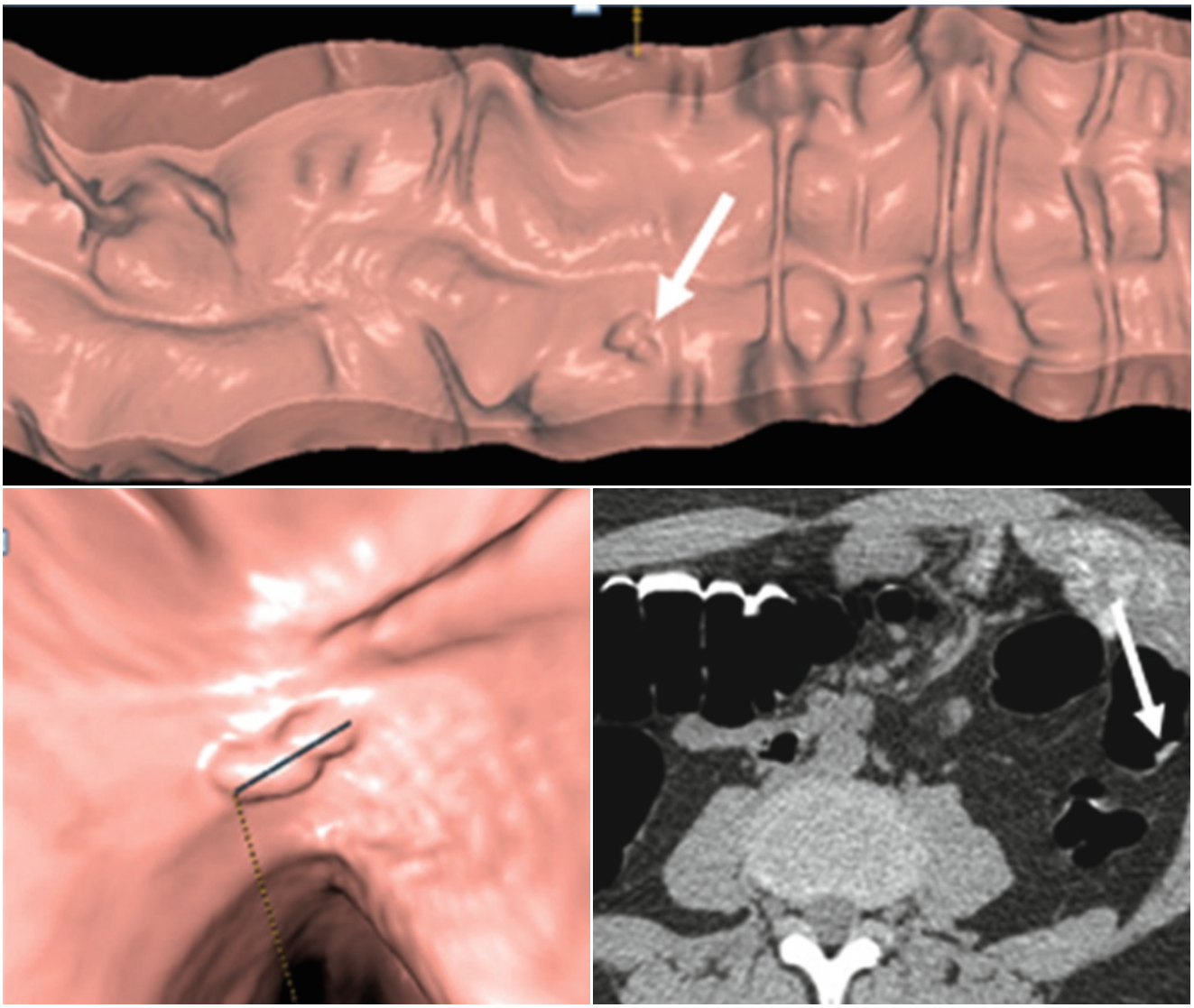


Fig. 8.17 Lobulated sessile polyp seen on flattened (upper image), 3D endoluminal (*lower left*) and 2D axial (*lower right*) images (*arrows*). The sessile polyp has a rounded shape on the flattened view

the air/fluid levels and direct the attention of the observer to the 2D images (Fig. 8.21). There is growing literature suggesting that the virtual dissection display mode may be a viable alternative to traditional 2D and 3D renderings [31, 33, 35]. In a large study that enrolled over 4,300 subjects, Hock et al. used the flattened view for primary interpretation and found a high sensitivity of 98.7% for polyps >6 mm, at the expense of a limited positive predictive value of 79.1% (Hock D, unpublished data, personal communication).

Unfolded Cube Projection

The unfolded cube projection shows the full visible field around a point within the lumen of the colon and avoids some of the deformation of structures that is seen with typical dissection algorithms [36, 37]. Six images, representing each side of the imaginary cube surrounding the point of view in the center of the colon, are placed on a single plane such that the complete field of view is represented on those six images. The six images of the unfolded cube include the forward and backward views, as well as the superior, inferior, and lateral walls (Fig. 8.22). The sequence of unfolded cubes is then shown as a series of cine images during interpretation, in a manner similar to a traditional fly-through paradigm. If a suspicious finding that requires further evaluation is identified, the cine review can be stopped to allow the operator to manipulate the 2D and 3D reformatted images for closer inspection and characterization. During real-time interpretation, the operator can also modify the position and orientation of the virtual camera. Although experience with this display method

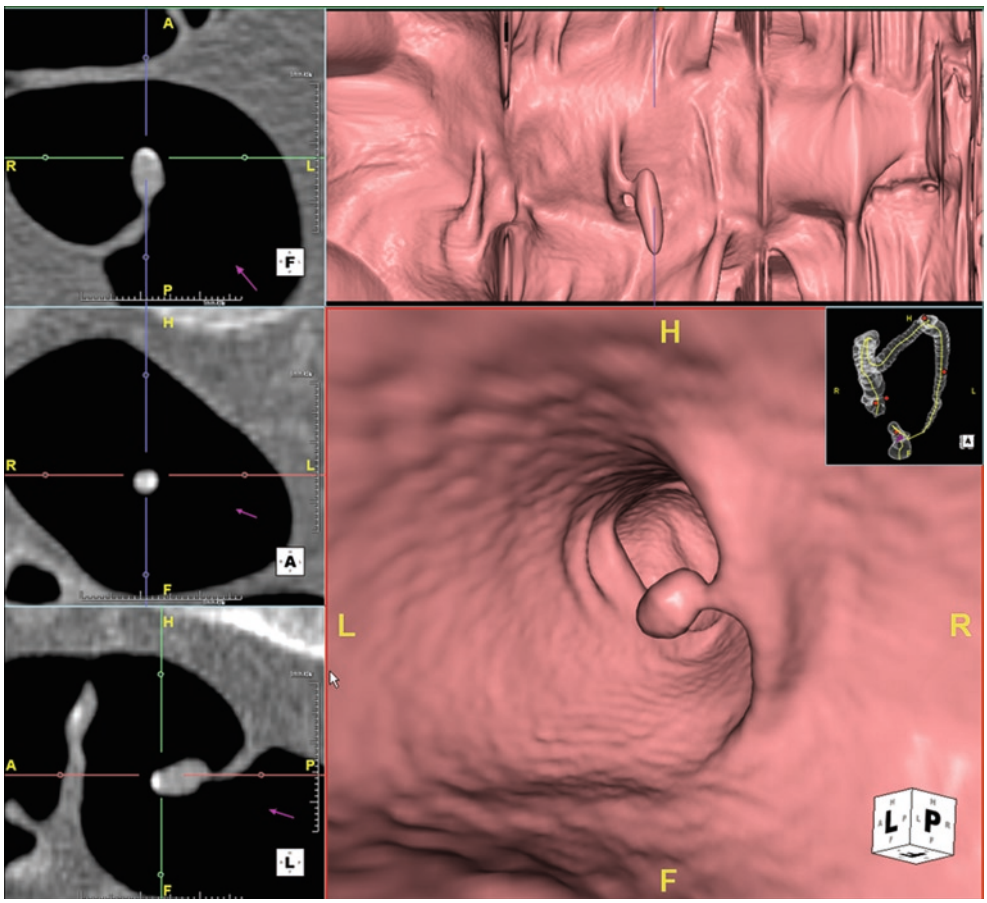


Fig. 8.18 Pedunculated polyp on virtual dissection. A 9 mm polyp with a short stalk is well seen on the 2D images (*left column*) and the endoluminal 3D image (*bottom right*). On the flattened view (*top right*), the polyp has a slightly elongated appearance in the vertical direction (along the axis of the folds). This elongation represents distortion of polyp morphology

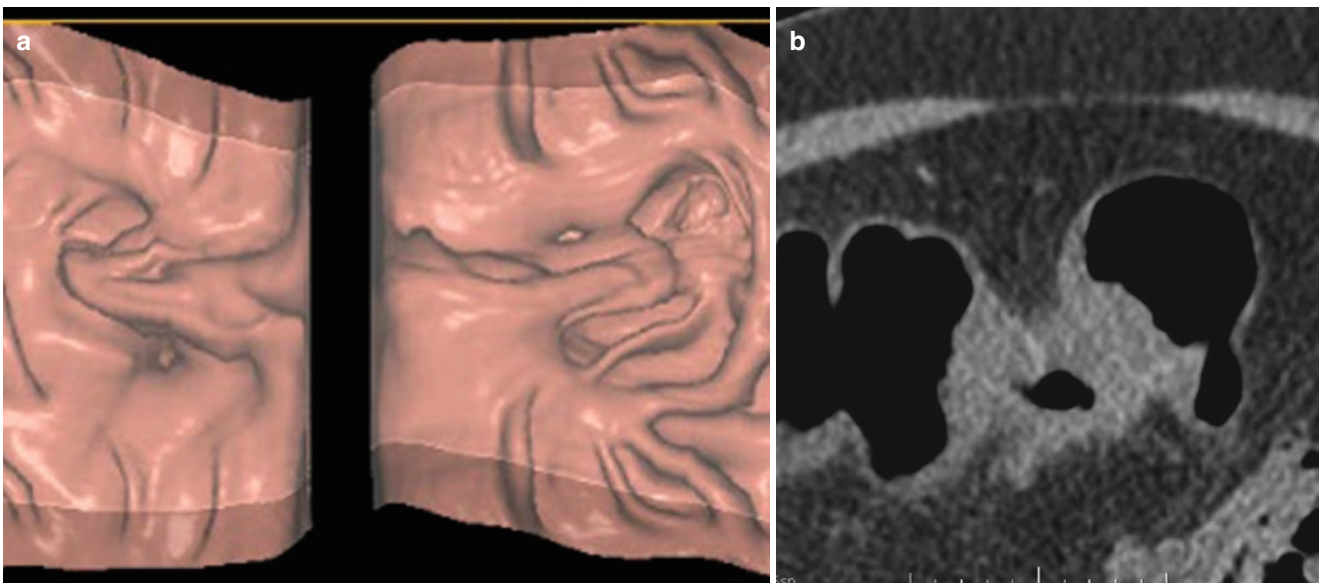


Fig. 8.19 Annular constricting mass on flattened view. The single short segment of interruption of colon continuity (**a**, *arrows*) should be viewed with suspicion and mandates careful evaluation of the 2D images. This appearance can be caused by collapse, excessive retained fluid or an annular tumor. The 2D image (**b**) shows definite signs of a malignant stricture, with an annular carcinoma

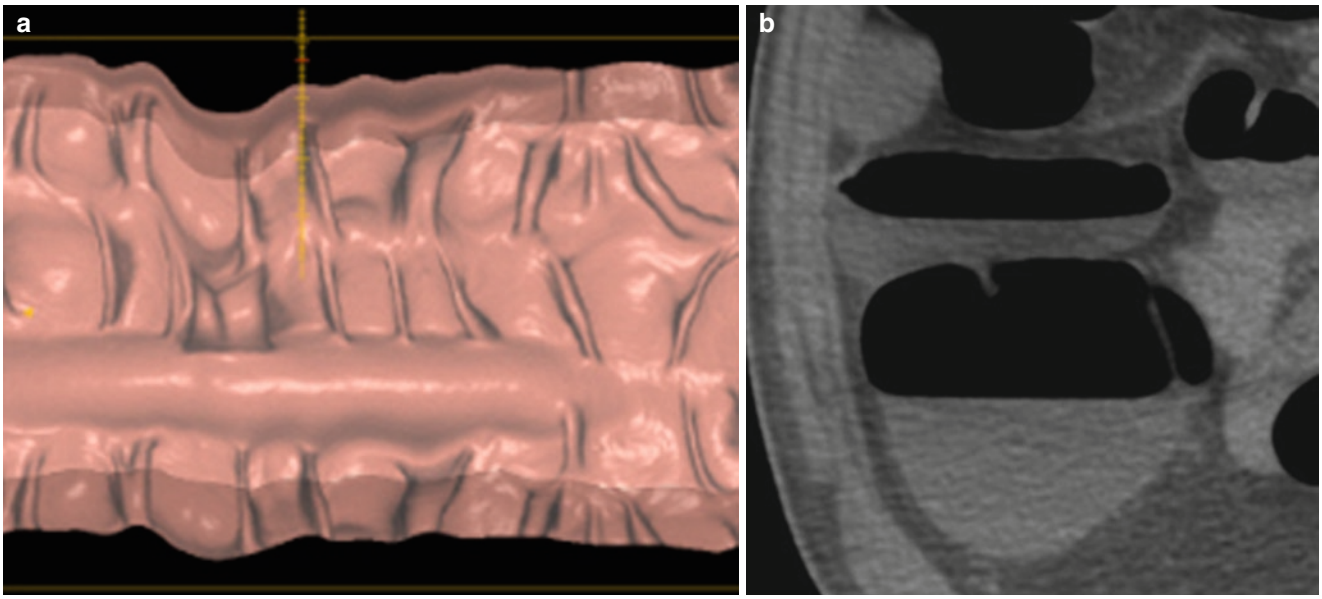


Fig. 8.20 Residual fluid in flattened view. On the flattened view (**a**), there is a segment where the colonic surface are obscured by a featureless, flat surface (*arrows*) that effaces several contiguous folds. On the 2D image (**b**), this surface is noted to correspond to an air/fluid level (*arrow*)

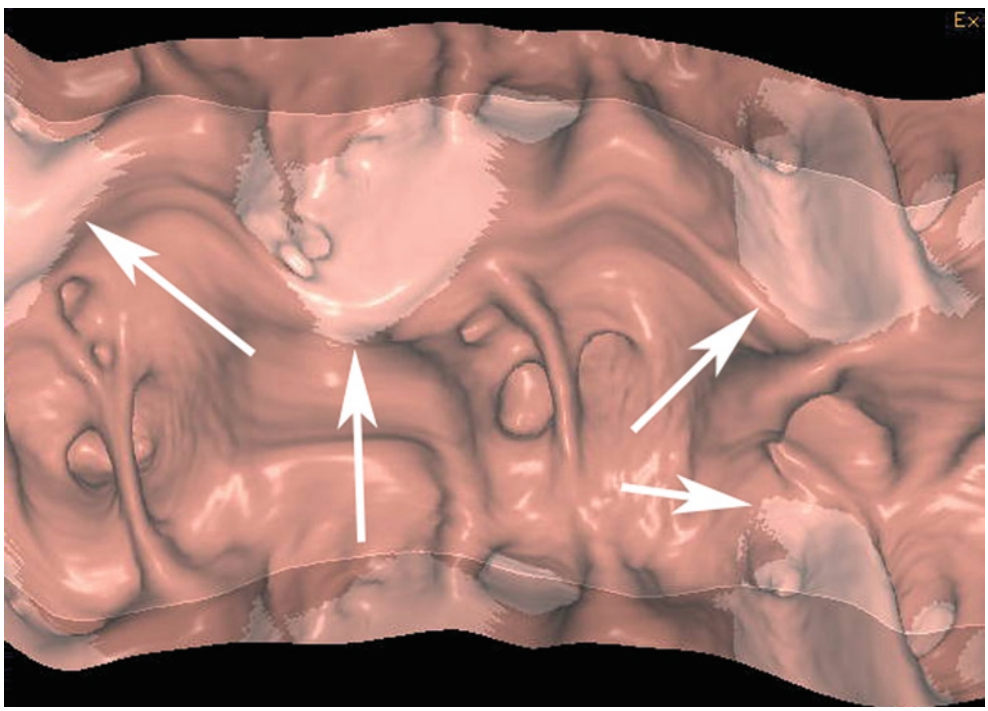


Fig. 8.21 Tagged residual fluid in flattened view. Multiple contiguous flat surfaces obscuring the colonic wall are present (*arrows*). The slightly lighter coloring indicates that these surfaces represent air/fluid levels created by residual fluid tagged with orally administered iodine and/or barium

is limited, some studies report adequate sensitivity and specificity values at a polyp threshold size of 5 mm, with adequate time-efficiency (about 15–20 min per patient) [36]. In the same study, interpretation times using the traditional 3D endoluminal display were significantly longer (31–39 min). Another potential advantage of the unfolded cube projection is the large percentage of mucosal surface displayed during evaluation (up to 99.5% in the study by Vos et al. [36]).

Filet View and Panoramic Endoluminal Display ("Band" View)

The concept underlying the filet view is similar to other methods that dissect the colon along its longitudinal axis. However, the main difference is that the filet view creates a movie loop of the opened colon, and each segment is displayed for a short period of time in the center of the screen [38]. There is little to

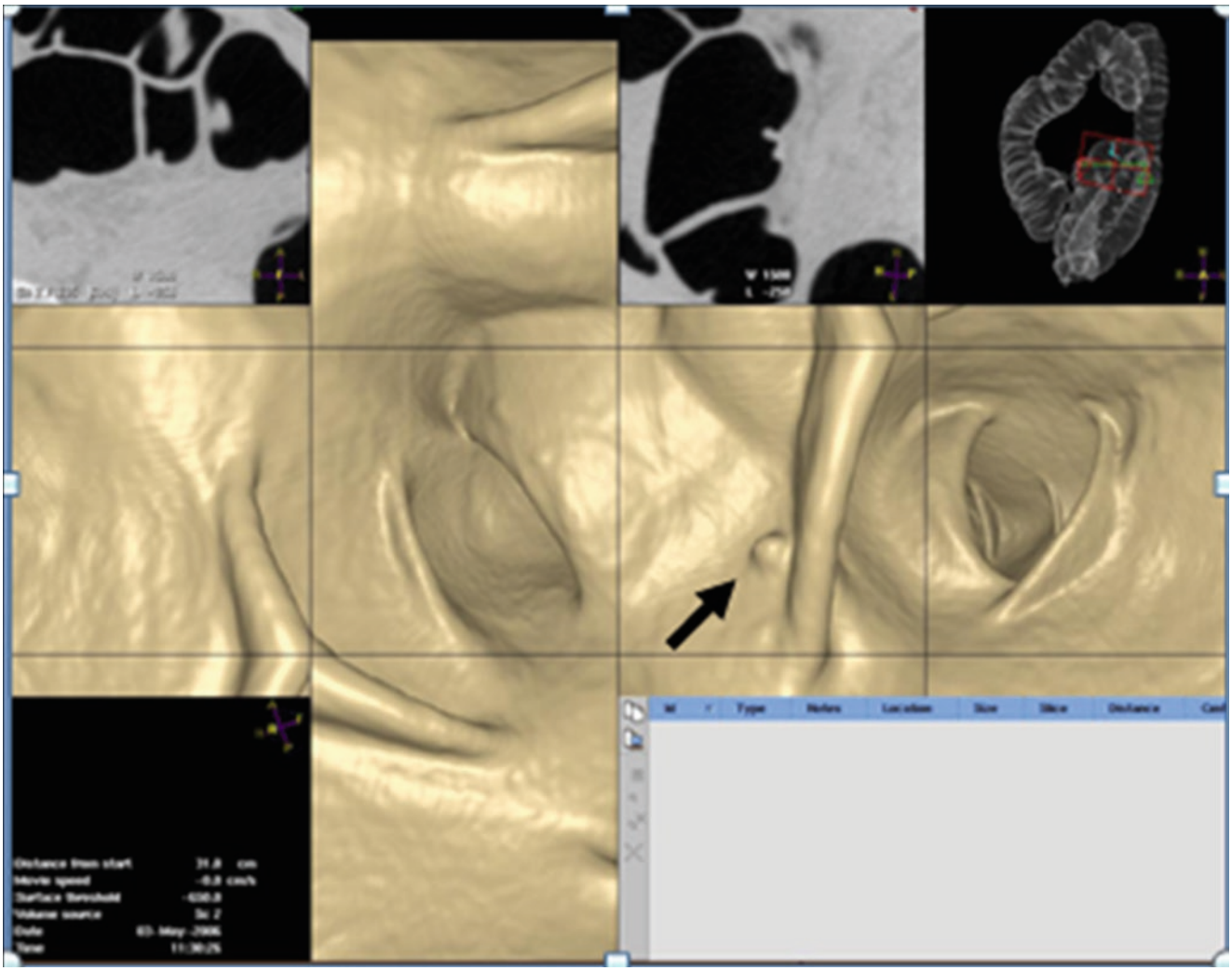


Fig. 8.22 Unfolded cube projection. This display method opens ("unfolds") the segment being evaluated from the center of an imaginary cube. The six images of the unfolded cube include the forward (F) and backward (B) views, as well as the superior (S), inferior (I) and right (R) and left (L) lateral walls. Note the small sessile polyp (*arrow*)

no appreciable distortion affecting the segment located in the exact center of the screen (Fig. 8.23). Therefore, for the primary interpretation, the reader can concentrate on inspecting one short segment at a time while still using 2D and/or traditional endoluminal 3D views for correlation. As each fold moves through the screen during the movie loop, each side of the fold is well displayed either immediately before or immediately after the fold occupies the center of the screen.

The panoramic endoluminal display method ("band" view) also produces less distortion of folds and polyps than the traditional filet view. The 3D reconstruction algorithm used for the band view displays the inner surface of the colon by projecting imaginary rays from the center line to the lateral walls. This technique is similar to the one described initially by Beaulieu et al. [10]. The band view allows visualization of both sides of the haustral folds and the intervening mucosa located between two adjacent folds. As the camera navigates along the center line, review of the entire colon is achieved with unidirectional navigation (Fig. 8.23). In addition, limited published results using this method suggest that interpretation time is significantly shorter than conventional 3D endoluminal fly-throughs while still maintaining adequate diagnostic accuracy for polyp detection [39, 40].

Supine-Prone Image Synchronization

Efforts and resources have also been invested in the development of automated methods for matching lesions found on the two CTC acquisitions (supine and prone). These methods, although still experimental, have a strong potential for reducing interpretation times. It is well known that certain segments of the colon (most notably the sigmoid, transverse,

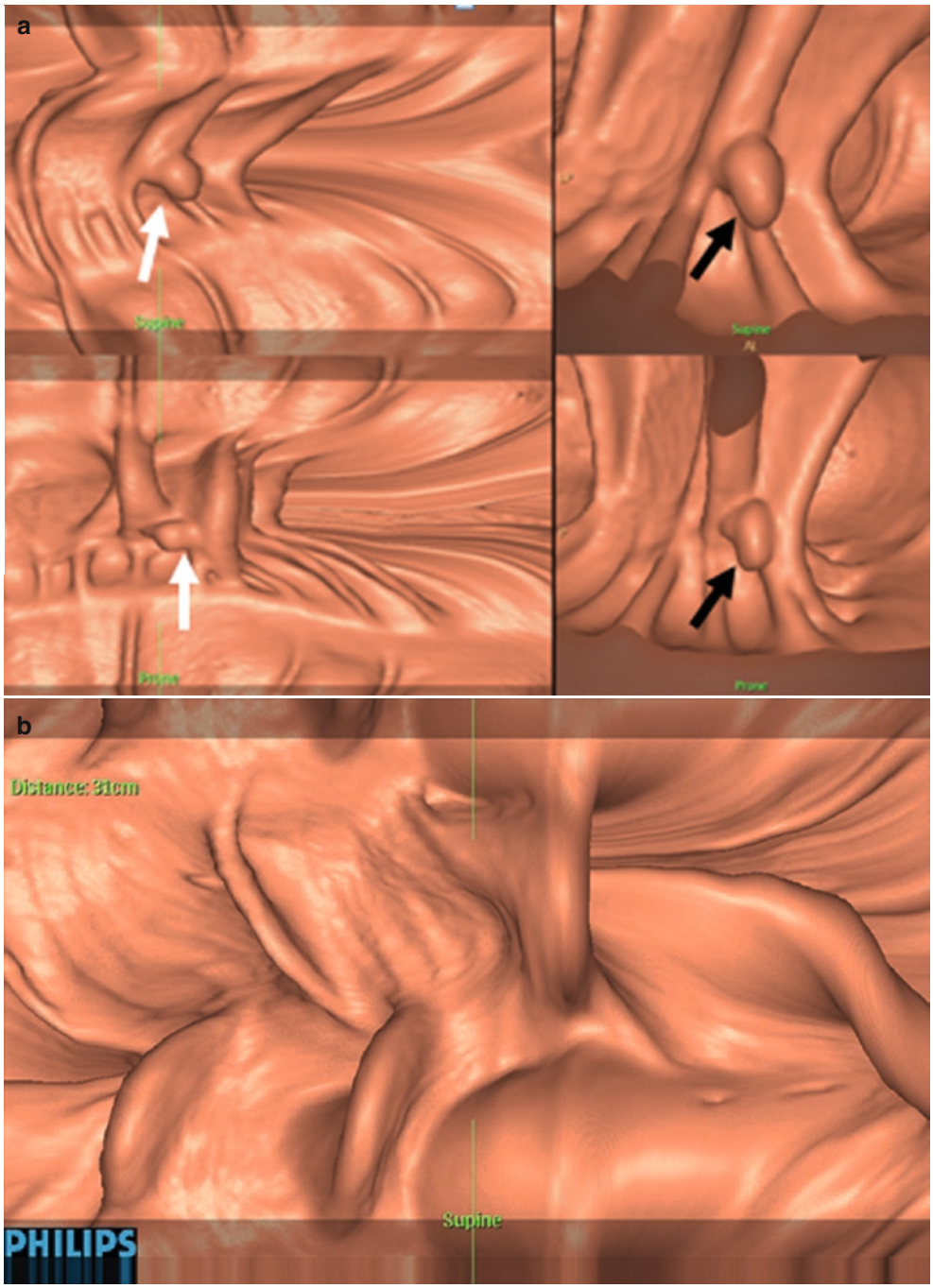


Fig. 8.23 Panoramic endoluminal display ("band" view), supine views on the top and prone views on the bottom (**a**). The segment located in the middle of the screen of the band view shows little to no distortion. However, the folds located proximal and distal to the central segment are markedly distorted. The 8 mm pedunculated polyp is well seen on both band views (*white arrows*) and both 3D endoluminal views (*black arrows*). On the cine display (**b**, video can be accessed online at http://extras.springer.com/2011/978-1-4419-5851-8), as a fold moves through the screen during the movie loop, each side of the fold is well displayed either immediately before or immediately after the fold occupies the center of the screen

and cecum) can rotate considerably within the abdomen with changes in patients' positions. When a polyp is located within such a segment, the radiologist may spend significant time deciding whether the findings represent one polyp, two separate polyps or mobile fecal residue inside the colonic lumen. Methods that use the internal or external topographical features of the colon (such as the teniae coli) may help with co-registration of polyps. Early results of the work by Huang et al. [41] are encouraging, and suggest that this may be a feasible and helpful tool.

Electronic Cleansing and Computer-Aided Detection

Other chapters in this atlas cover these two very important and current topics. However, from the perspective of data display methods, it is important to note and emphasize that most, if not all, vendors have incorporated these two novel tools into their software platforms (Fig. 8.24). The aim is to facilitate image interpretation and maximize reader performance. In particular, when used in combination (and once the regulatory hurdles are

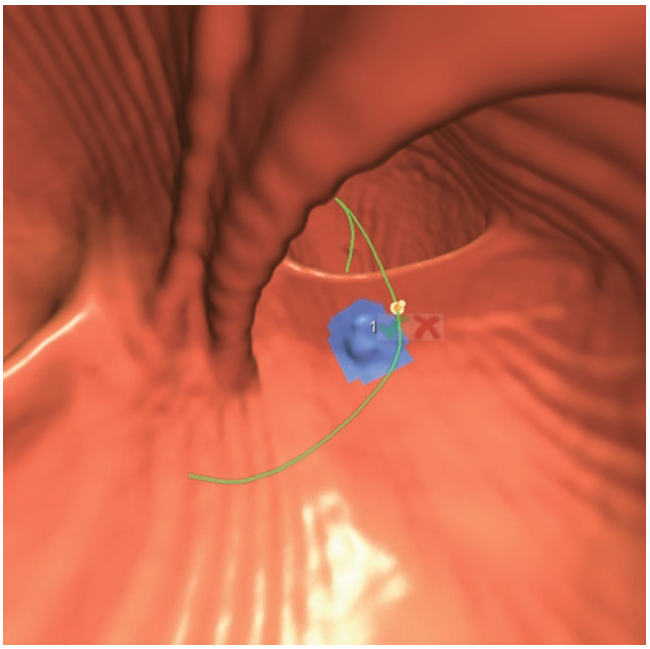


Fig. 8.24 Integration of computer-aided detection (CAD) marks with endoluminal display method. The CAD software correctly identified a sessile poly and is displayed as a blue painting of the surface of the polyp on this 3D endoluminal display mode

overcome), electronic cleansing and computer-aided detection have the potential to significantly reduce interpretation times.

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Nonpolypoid Colorectal Neoplasia

9

Seong Ho Park

Introduction

Since Muto et al. reported the first "small flat adenoma" of the colon in 1985 [1], the importance of nonpolypoid colorectal neoplasia is increasingly being recognized. In the past, all colorectal cancers were assumed to arise slowly from polypoid adenomas through the adenoma–carcinoma sequence in combination with the accumulation of genetic alterations and environmental changes. However, it is now widely accepted that a substantial proportion of colorectal cancers are attributed to nonpolypoid colorectal neoplasms.

The accuracy of computed tomography (CT) colonography for detecting colonic neoplasms has been validated in multiple large-scale clinical trials [2–6], and as a result, CT colonography has recently been added to the joint guideline for colorectal cancer screening by the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology [7]. However, the high diagnostic performance of CT colonography shown in these trials was obtained mostly with polypoid colorectal lesions. On the other hand, the diagnostic performance of CT colonography for detecting nonpolypoid colorectal lesions is relatively less well established, although nonpolypoid lesions are generally considered to be more difficult to detect with CT colonography than polypoid lesions.

For CT colonography to be more effective, it is important for interpreting radiologists to be knowledgeable of nonpolypoid colorectal lesions and to be able to recognize both polypoid and nonpolypoid lesions on CT colonography.

Definition and Terminology

Definition of Nonpolypoid Colorectal Neoplasia

There are several definitions of nonpolypoid colorectal lesions. Histologic definitions include a lesion height no more than twice the height of the adjacent normal mucosa and a lesion thickness 1.3 mm or less [8]. These histologic definitions are limited in that they are not practical, although they are scientific, as they can be applied only after a lesion is excised and examined with a microscope. Endoscopic definitions are easier to apply than histologic definitions and thus are more widely used. A commonly used endoscopic definition is a mucosal elevation with the lesion height less than half the greatest lesion diameter. This definition has been used in many epidemiologic studies because of its simplicity [9–13]. However, this endoscopic definition may be too crude to characterize the flatness of a lesion and too generous, as lesions of various heights will be grouped into the same nonpolypoid category on the basis of their width. The recent Paris endoscopic classification proposes a more refined endoscopic definition [14]. In the Paris classification, the height of a lesion is measured in comparison with the 2.5-mm height of closed jaws of biopsy forceps [14]. Lesions protruding above the level of the closed jaws of the biopsy forceps are classified as polypoid, whereas those below this level are classified as nonpolypoid [14]. Compared with the definition of "a lesion height less than half the greatest lesion diameter," the Paris classification is a better definition, as it more clearly characterizes the flatness of a lesion and includes only those genuinely nonpolypoid lesions.

Morphologic Subtypes of Nonpolypoid Colorectal Neoplasia

According to the Paris endoscopic classification [14] and the Japanese Research Society classification, colorectal

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neoplasms are classified into polypoid and nonpolypoid types according to the lesion height in comparison with the height of the closed jaws of biopsy forceps, as previously explained. The polypoid type consists of sessile and pedunculated morphology. The polypoid type is designated as type I (I*s* for sessile morphology and I*p* for pedunculated morphology), whereas the nonpolypoid type is referred to as type II. The nonpolypoid type is further divided into various morphologic subtypes (Fig. 9.1). Type IIa lesions are nonpolypoid with a slightly elevated plaque-like shape (Fig. 9.2), type IIb represents completely flat lesions, and type IIc refers to slightly depressed lesions compared with the surrounding mucosa. There are also mixed morphologic types, including type IIa + IIc and type IIc + IIa. Type IIa + IIc (Fig. 9.3) is a lesion that is mostly slightly elevated (i.e., IIa component), with an area of central depression (i.e., IIc component), whereas type IIc + IIa (Fig. 9.4) is mostly a depressed lesion with an elevated peripheral rim.

Many endoscopists and radiologists use "nonpolypoid" and "flat" synonymously for the morphologic description of nonpolypoid colorectal lesions. However, the synonymous use of these two words may be inappropriate, as the term "flat" gives the impression of a completely flat morphology, i.e., IIb morphology, although most nonpolypoid colorectal neoplasms actually have slightly elevated shape, i.e., IIa morphology.

A laterally spreading tumor (LST), also referred to as "carpet lesion," is a large nonpolypoid colorectal lesion. Endoscopic literature, including the Paris classification and the Japanese Research Society classification, defines LTS as a type IIa nonpolypoid lesion 10 mm or greater in diameter [14, 15]. However, LST is typically used to describe larger lesions, e.g., several centimeters in widths. LST is subdivided into granular-type (LST-G) and nongranular or flat type (LST-F) according to the surface structure of the lesion [16, 17]. LST-G has an uneven granulonodular surface (Fig. 9.5), whereas LST-F has a smooth surface (Fig. 9.6).

Epidemiology and Malignant Potential

The results of selected large epidemiologic studies regarding nonpolypoid colorectal neoplasia are summarized in Table 9.1.

Prevalence/Frequency of Nonpolypoid Colorectal Neoplasia

The prevalence/frequency of nonpolypoid colorectal neoplasia is highly variable across studies due to multiple

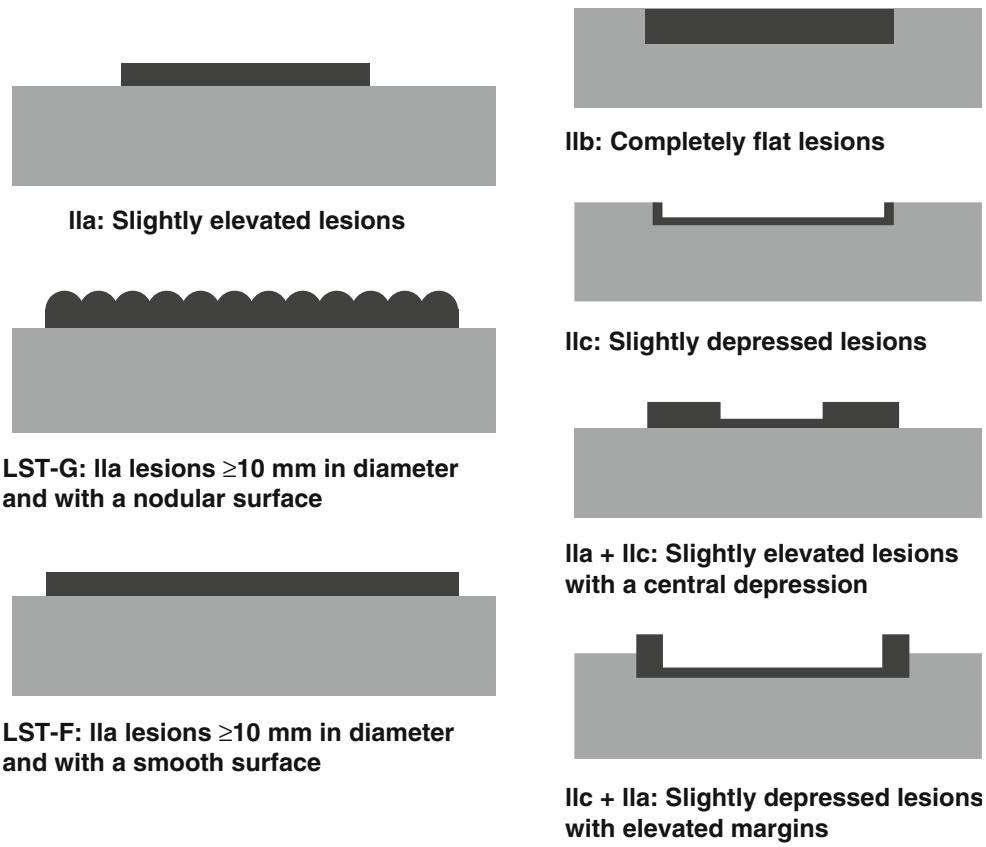

Fig. 9.1 Morphologic subtypes of nonpolypoid colorectal neoplasms according to the Paris endoscopic classification (participants in the Paris Workshop 2003) and the Japanese Research Society classification

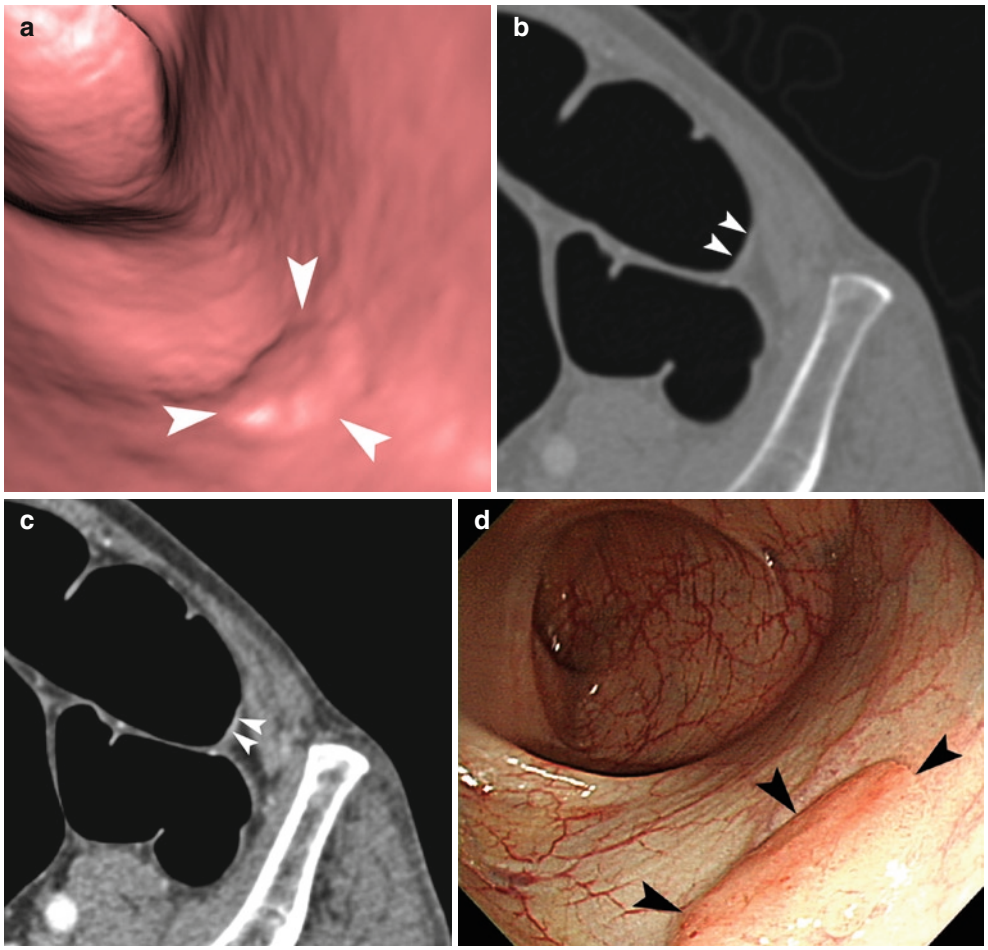

Fig. 9.2 A 15-mm-wide type IIa nonpolypoid tubular adenoma in the sigmoid colon. (**a**) Three-dimensional endoluminal CT colonography image shows a slightly elevated nonpolypoid lesion (*arrowheads*). (**b**) Transverse two-dimensional CT colonography image at colon window setting barely shows slight change in colonic contour by the lesion (*arrowheads*). (**c**) Transverse two-dimensional CT colonography image at soft-tissue window setting more clearly shows localized thickening of the colon wall (*arrowheads*). (**d**) Colonoscopy image shows corresponding nonpolypoid lesion (*arrowheads*) (From Park et al.[27] Reprinted with permission from the *American Journal of Roentgenology*)

factors. The reported frequency of nonpolypoid colorectal neoplasms among all colorectal neoplasms detected at colonoscopy ranged from approximately 6% to 40% [8, 9, 11–13, 18, 19]. One of the reasons for the heterogeneous prevalence/frequency is the use of different definitions of the nonpolypoid morphology. The prevalence/frequency was generally higher when the definition of "lesion height less than half the greatest lesion diameter" was used [9, 11, 12] compared with when stricter criteria were used [19], as the former is a quite generous definition. Interestingly, a retrospective analysis of the National Polyp Study data by O'Brien et al [8]. revealed a fairly high 31% frequency of nonpolypoid colorectal neoplasms among all colorectal neoplasms, even though the study used a strict definition of the nonpolypoid morphology, which was a histologically measured lesion thickness of 1.3 mm or less or a lesion thickness no more than twice the height of adjacent normal colonic mucosa. However, the majority of the nonpolypoid neoplasms in the National Polyp Study were actually 5 mm or smaller in diameter. Classifying these diminutive lesions into sessile or nonpolypoid categories would only be a technical distinction and would not be clinically meaningful. The rate of nonpolypoid colorectal neoplasms in the National Polyp Study would become much lower if the diminutive nonpolypoid lesions were excluded.

It is uncertain whether nonpolypoid colorectal neoplasms occur in different frequencies in different patient risk groups for colorectal cancer, and there are yet limited data regarding the prevalence of nonpolypoid colorectal neoplasia in screening patients with an average risk for colorectal cancer. According to one study from the United States by Soetikno et al [13], the per patient prevalence of nonpolypoid colorectal neoplasia and nonpolypoid colorectal carcinoma in screening patients was 5.84% and 0.32%, respectively. Similarly, another study from Taiwan, by Chiu et al [18],. reported a 4.2% per patient prevalence of nonpolypoid colorectal neoplasia in a screening population. On the other hand, in the National CT Colonography Trial [3], the per patient prevalence of nonpolypoid neoplasms 5 mm or greater in diameter (defined as both mucosal elevation of 3 mm or less compared with adjacent normal mucosa and lesion height less than half the greatest lesion diameter) was only 0.75% (19/2,531 patients).

Regarding the frequency of various morphologic subtypes of nonpolypoid colorectal neoplasms, most nonpolypoid colorectal neoplasms have IIa morphology in both the Paris

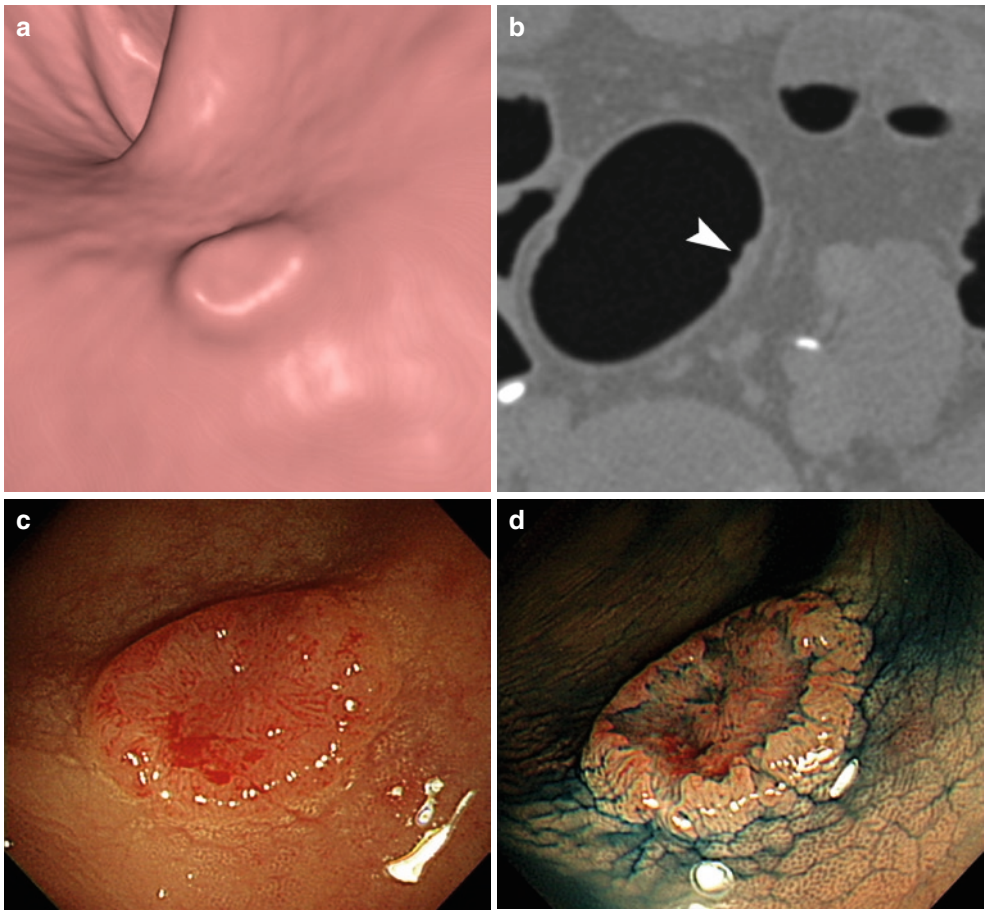

Fig. 9.3 A 10-mm-wide type IIa + IIc nonpolypoid adenocarcinoma with submucosal extension in the sigmoid colon. (**a**) Three-dimensional endoluminal CT colonography image shows a slightly elevated lesion with central depression. (**b**) Lesion seen on transverse two-dimensional CT colonography image at colon window setting (*arrowhead*). (**c** and **d**) Lesion seen on routine colonoscopy (**c**) and chromoscopy (**d**), i.e., colonoscopic examination after mucosal spraying of methylene blue dye. Surface topography of lesion is more clearly visualized on chromoscopy as dye pools in mucosal grooves, crevices, and depressions

classification [14] and the Japanese Research Society classification. IIb lesions and depressed lesions, including IIc, IIa + IIc, and IIc + IIa types, are reported to be uncommon [10, 11, 13, 18]. In particular, IIb lesions, i.e., completely flat lesions, are exceedingly rare [13, 18, 20].

Malignant Potential of Nonpolypoid Colorectal Neoplasms

The cancer risk of nonpolypoid colorectal adenomatous lesions compared with that of polypoid adenomatous lesions is controversial. Some epidemiologic studies have reported higher risks of malignancy in nonpolypoid adenomatous lesions [9, 13, 19]. On the other hand, one study from the United States [8] and another study from Korea [10] reported similar risks of malignancy regardless of the lesion morphology, when adjusted for other risk factors for colorectal cancer, such as lesion size and villous component, using multivariable analysis [8, 10]. Despite this controversy, most studies agree that nonpolypoid adenomatous lesions with a depressed component, i.e., IIc, IIa + IIc, and IIc + IIa types, have a particularly high risk of containing malignancy [9, 11, 13, 18, 19]. Some of the discrepancies regarding the malignant potential of nonpolypoid colorectal neoplasia in various studies can probably be explained in part by the differing prevalence/frequency of depressed lesions in their study populations. For example, the Korean study [10], which reported no increased risk of malignancy in nonpolypoid neoplasms compared with polypoid neoplasms, did not include any lesions with a depressed component. The differing prevalence/frequency of morphologic subtypes of LST is another factor that may explain the discrepancies between studies. Compared with LST-F with a smooth surface, LST-G with an uneven granulonodular surface has a lower risk of malignancy [10, 16, 17]. Histologically, LST-G often shows a growth pattern similar to that of polypoid adenomas [10]. Unlike LST-F, a significant number of LST-Gs were not classified as nonpolypoid lesions in most of the Japanese reports [10] because the size-adjusted malignancy rate of LST-G is not higher than that of polypoid lesions.

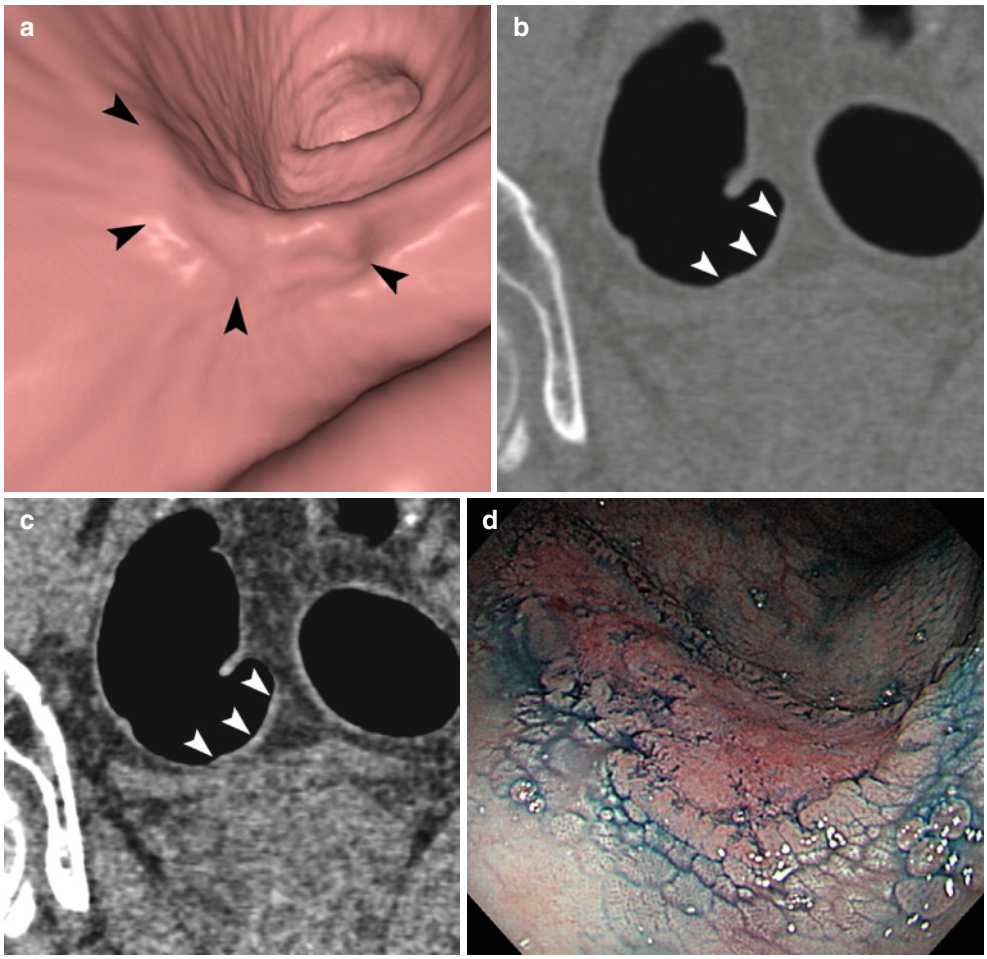

Fig. 9.4 A 35-mm-wide type IIc + IIa nonpolypoid adenocarcinoma with submucosal extension in the sigmoid colon. (**a**) Three-dimensional endoluminal CT colonography image shows a slightly depressed nonpolypoid lesion with slightly elevated peripheral rim (*arrowheads*). (**b**) Coronal two-dimensional CT colonography image at colon window setting shows slight change in colonic contour by the lesion (*arrowheads*). (**c**) Coronal two-dimensional CT colonography image at soft-tissue window setting shows localized thickening of the colon wall (*arrowheads*). (**d**) Lesion seen on colonoscopy after mucosal spraying of methylene blue dye

Detection with Colonoscopy

Nonpolypoid colorectal lesions are more difficult to detect on colonoscopy than polypoid lesions. Therefore, special techniques have been developed to help with the detection of nonpolypoid lesions using colonoscopy. First, chromoscopy is a technique used to endoscopically examine the colonic mucosa after spraying dyes such as indigocarmine or methylene blue (Fig. 9.7) [20]. As the dye pools in the mucosal grooves, crevices, and depressions, it highlights the border and surface topography of the lesion, which may not be clearly visible before staining. Narrow band imaging (NBI) is a new endoscopic technique that may potentially help to detect and/or characterize nonpolypoid colorectal lesions (Fig. 9.7) [21–24]. NBI uses special narrow-band filters placed in front of the light source of an endoscope. Of the three color components (red, green, and blue lights) that constitute the white light of an endoscope, only blue and green lights can pass through the filters and illuminate the mucosa. Images are generated from the reflections of these lights, and the images are then integrated into a single color image using a videoprocessor. The blue light cannot penetrate into deeper layers of the mucosa and is absorbed by the hemoglobin in the superficial mucosal microvessels, making these vessels appear accentuated in brown color on NBI. As a result, nonpolypoid colorectal neoplasms with a high density and/or abnormal patterns of intralesional superficial microvessels may appear distinguished from adjacent normal colonic mucosa on NBI. Additional studies will still be necessary to prove the usefulness of NBI for detecting nonpolypoid colorectal lesions.

Detection with CT Colonography

CT Colonographic Appearance of Nonpolypoid Colorectal Neoplasms and Mimickers

Nonpolypoid colorectal lesions typically appear as plaque-shaped slightly elevated mucosal elevations with a smooth or granular/nodular mucosal surface. When the lesions are

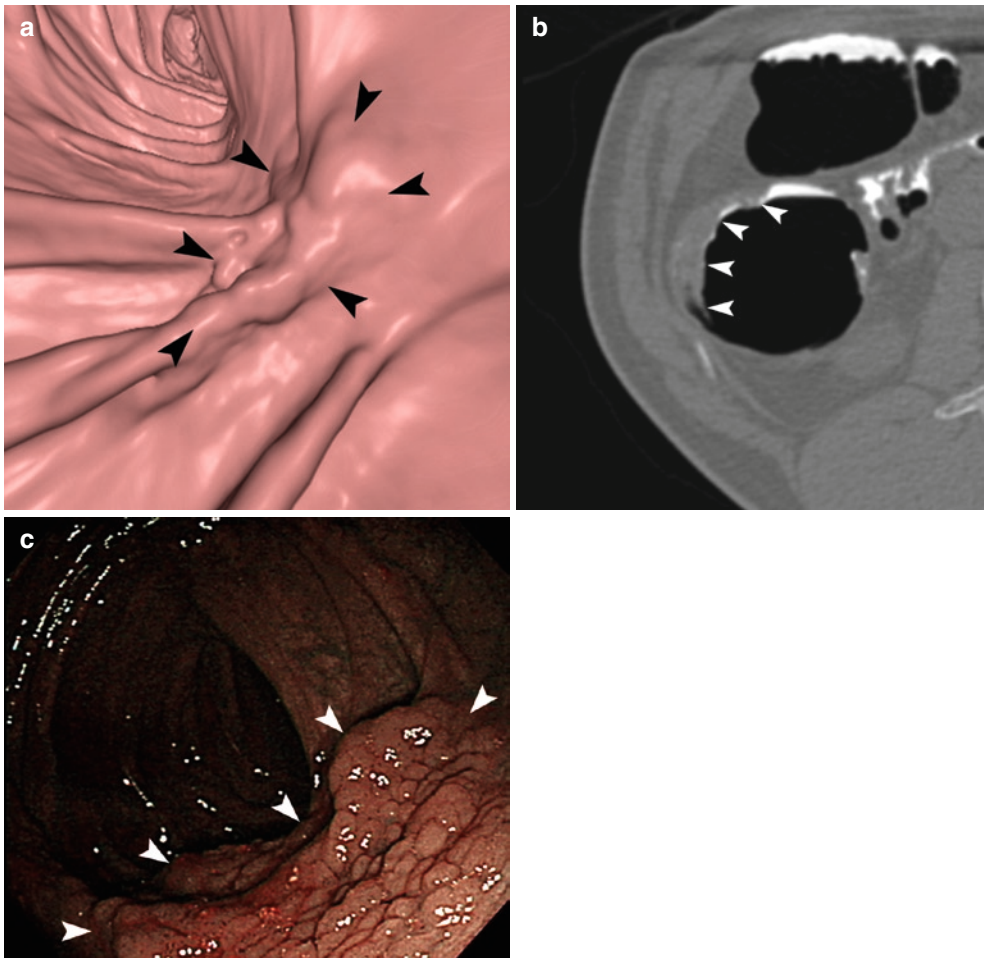

Fig. 9.5 A 45-mm-wide granular-type laterally spreading (LST-G) tubular adenoma with high-grade dysplasia in the ascending colon. (**a**) Three-dimensional endoluminal CT colonography image shows an area of nodularity in the colonic surface (*arrowheads*). (**b**) Transverse two-dimensional CT colonography image at colon window setting shows nodular thickening of the haustral fold (*arrowheads*). (**c**) Lesion seen on colonoscopy (*arrowheads*)

located on the haustral fold, they may present merely as slightly thickened haustral folds and would therefore be difficult to detect. An area of central depression which is known to suggest a high probability of harboring carcinoma [9, 11, 13, 18, 19] may be clearly depicted on CT colonography (Figs. 9.3 and 9.4). Several studies have suggested that two-dimensional view using an intermediate soft-tissue window (such as width = 400 HU and level = 20 HU) may be helpful in detecting and confirming nonpolypoid lesions [25–27]. On soft-tissue window two-dimensional views, nonpolypoid lesions typically present as areas with a perceptible thickness in the colonic wall, whereas the normal colonic wall is barely perceptible if the colon is optimally distended (Figs. 9.2, 9.4, and 9.6). However, the perceptible colonic wall should be carefully interpreted using a correlation with three-dimensional endoluminal views in order to avoid false-positive diagnosis, as this finding is also commonly found in the normal colonic wall unless the colon is fully distended.

Small plaque-like stool pieces adhering to the colonic wall can closely mimic the CT colonographic findings of nonpolypoid colorectal lesions. These types of stool pieces, as opposed to rather large polypoid stool pieces, are often extremely difficult to distinguish from a true lesion unless fecal tagging or intravenous contrast enhancement is used, as they typically do not have internal air density and do not move during positional change by the patient because of their strong attachment to the colonic wall. Air bubbles present on the colonic mucosal surface during CT scanning can also mimic flat lesions (Fig. 9.8) [28]. The fluid shell of a bubble is generally too thin to be visualized on CT, and the base of a bubble, i.e., the bubble's attachment to the mucosa, may resemble a depressed lesion with a slightly elevated border when visualized on the three-dimensional endoluminal view. This pseudo-lesion can be distinguished from a true nonpolypoid lesion by noting the bubble's characteristic morphology of a smooth, thin, ringlike peripheral elevation and the lack of colonic wall thickening on the soft-tissue window view and also by noting the disappearance of the pseudo-lesion on the other scan.

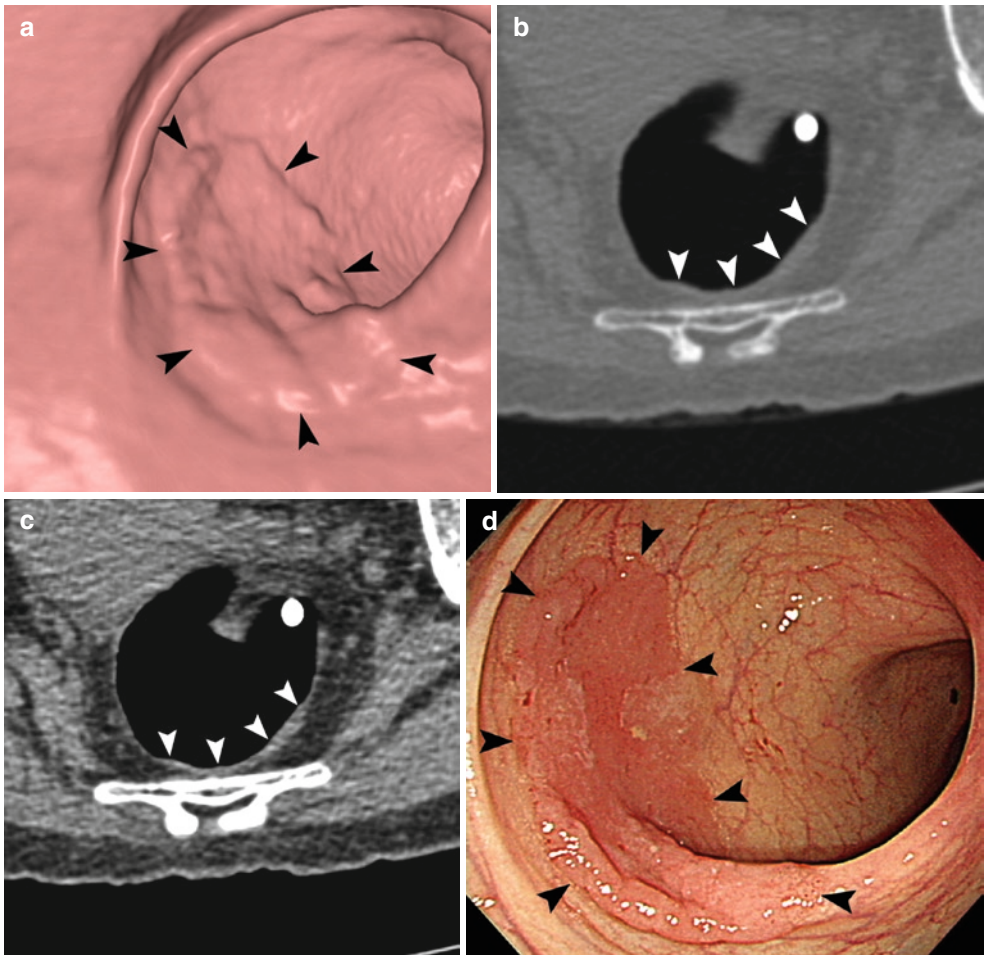

Fig. 9.6 A 40-mm-wide flat-type laterally spreading (LST-F) adenocarcinoma in the rectum. (**a**) Three-dimensional endoluminal CT colonography image shows a large slightly elevated nonpolypoid lesion (*arrowheads*). (**b**) Transverse two-dimensional CT colonography image at colon window setting shows slight elevation in the colonic wall by the lesion (*arrowheads*). (**c**) Transverse two-dimensional CT colonography image at soft-tissue window setting shows localized thickening of colon wall (*arrowheads*). (**d**) Lesion seen on colonoscopy (*arrowheads*)

Sensitivity of CT Colonography for Detecting Nonpolypoid Colorectal Neoplasms

It is generally accepted that nonpolypoid colorectal lesions are more difficult to detect than polypoid lesions using CT colonography. However, the sensitivity of CT colonography for detecting nonpolypoid colorectal lesions has not been clearly determined. Although there have been some relevant studies [25–27, 29–32], most studies unfortunately included only a small number of nonpolypoid lesions. In addition, it is difficult to compare or combine the reported results due to the heterogeneity of the studies regarding CT colonography techniques and the target lesion definition. However, several studies included relatively large numbers of nonpolypoid lesions and used current techniques of CT colonography [27, 31]. These study results are summarized below.

Pickhardt et al [31]. reported an additional analysis regarding nonpolypoid colorectal lesions from their original screening CT colonography trial that included 1,233 asymptomatic patients with an average risk for colorectal cancer [5]. They used cathartic cleansing, fecal and fluid tagging, 4- or 8-row multidetector CT scanners, and primary three-dimensional review. The definition for nonpolypoid lesions was a lesion height less than half the greatest lesion diameter, and the lesion heights were generally 3 mm or less but were higher for some larger lesions. This study demonstrated a CT colonography sensitivity of 82.2% (24/29) for nonpolypoid adenomatous lesions 6 mm or greater in width. The sensitivity did not differ significantly from that for polypoid lesions in the same size range (86.2% [156/181]).

Park et al [27]. reported a study using cathartic cleansing, fecal and fluid tagging, a 16-row multidetector CT scanner, and primary three-dimensional interpretation. In their study, all nonpolypoid lesions were very thin, as they met the definition of the Paris classification, which is a lesion height below the height of the closed jaws of biopsy forceps, i.e.,

Table 9.1 Summary of selected epidemiologic studies on nonpolypoid colorectal neoplasia

Authors and year of publication	Country	Patient characteristics and colorectal cancer risk	Number of patients studied	Definition of nonpolypoid lesions	Number of nonpolypoid neoplasms/all neoplasms (%)	Relative risk of malignancy of nonpolypoid neoplasms compared with polypoid neoplasms
Rembacken et al. 2000	UK	Symptomatic	1,000	Lesion height <1/2 of lesion width	37.6	Higher risk in depressed lesions
Saitoh et al. 2001	US	Symptomatic	211	Lesion height <1/2 of lesion width	39.7	Not clearly stated
Tsuda et al. 2002	Sweden	Mixed risks (mostly symptomatic)	337	Lesion width greater than several times its height	6.8	Higher risk
Hurlstone et al. 2003	UK	Symptomatic	850	Lesion height <1/2 of lesion width	36.9	Higher risk
O'Brien et al. 2004	US	Mixed risks (generally average risk)	938	Histologic Lesion thickness ≤1.3 mm or ≤twice the height of normal mucosa	31 (Although the majority of nonpolypoid lesions were ≤5 mm in diameter)	Same risk
Park et al. 2008	Korea	Mixed risks (mostly higher-than-average risk)	3,360	Lesion height <1/2 of lesion width or histologic lesion thickness ≤twice the height of normal mucosa	Not clearly stated	Same risk (but no depressed lesions in the study population)
Soetikno et al. 2008	US	Mixed risks	1,819	Lesion height <1/2 of lesion width	14.8	Higher risk
Chiu et al. 2009	Taiwan	Average risk	8,327	Not clearly stated	17.4	Same risk in slightly elevated lesions but higher risk in depressed lesions

2.5 mm [14]. Their study included 8 nonpolypoid adenomas measuring 9–30 mm in width (median, 15 mm), ten nonpolypoid carcinomas in situ (Tis; involvement of only the mucosa) or T1 (extension into the submucosa but not beyond) adenocarcinomas measuring 10–25 mm in width (median, 14 mm), and five nonadenomatous lesions measuring 8–20 mm in width (median, 10 mm). Their sensitivities for nonpolypoid adenomatous lesions (i.e., both adenomas and adenocarcinomas), adenocarcinomas, and nonadenomatous lesions were 66.7% (12/18), 90% (9/10), and 0% (0/5), respectively. Although CT colonography missed a 10-mm T1 adenocarcinoma, this was apparently due to a reader perception error and was clearly visualized on retrospective review of the CT colonography. Therefore, this could have been easily detected with a more careful interpretation.

The National CT Colonography Trial [3] data contained 19 nonpolypoid colorectal neoplasms, including eight advanced adenomas (1 cm or greater in diameter and the presence of high-grade dysplasia or villous component). The 19 lesions measured 5–25 mm in width (median, 8 mm) and met the definition of a lesion height 3 mm or lower and less than half the greatest lesion diameter. The trial used cathartic preparation, fecal and fluid tagging, and 16-row (or higher) multidetector CT scanners. The CT colonography sensitivity for the 19 nonpolypoid neoplasms was 68.4% (13/19) when interpreted using combined two-dimensional and three-dimensional techniques and 47.4% (9/19) and 31.6% (6/19) when interpreted using either the individual two-dimensional or individual three-dimensional method, respectively. Retrospective analysis identified four additional lesions, and therefore technically 89.5% (17/19) could be seen on CT colonography.

In both Pickhardt's [31] and Park's [27] studies, the CT colonography sensitivity for nonadenomatous nonpolypoid lesions was lower than that for adenomatous lesions. One plausible explanation for this finding may be the tendency of nonadenomatous lesions to efface with air distention of the colon [33]. This low sensitivity of CT colonography for nonadenomatous nonpolypoid lesions is actually an advantageous feature of CT colonography, as it will decrease

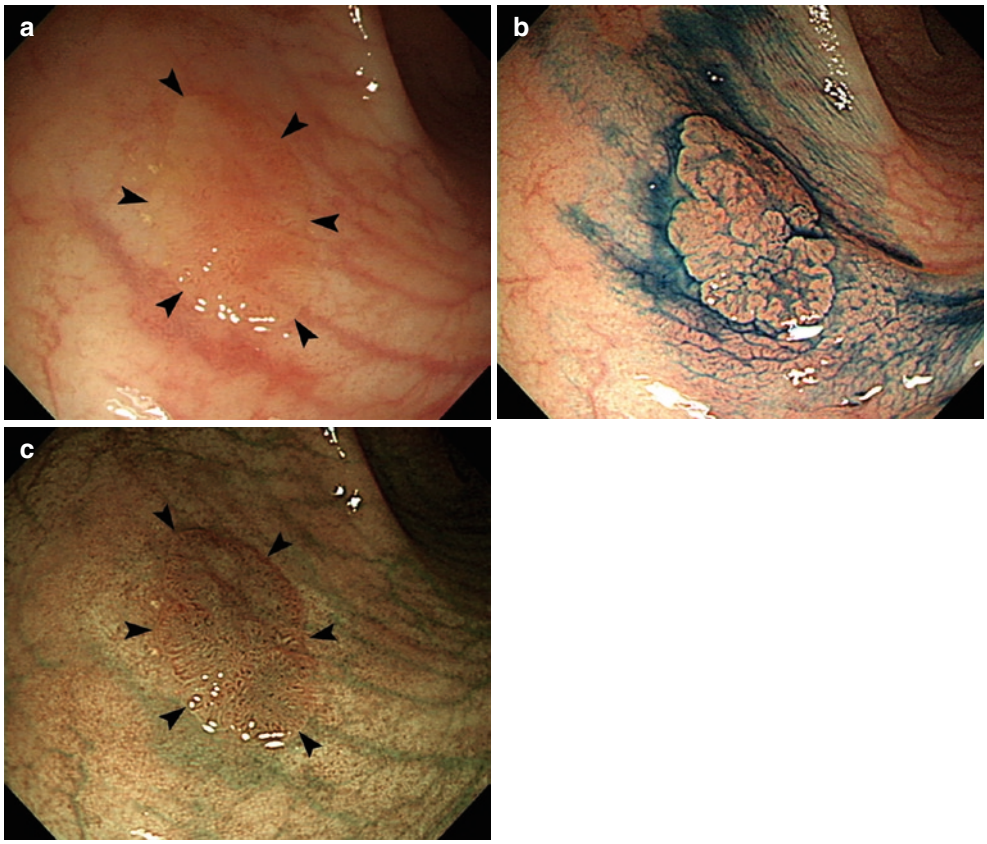

Fig. 9.7 A 10-mm-wide type IIa nonpolypoid tubular adenoma in the sigmoid colon. (**a**) A slightly elevated lesion (*arrowheads*) is suspected on routine colonoscopic view using white light colonoscopy. (**b**) Chromoscopy after spraying indigocarmine reveals the lesion and the surface pattern of the lesion more clearly. (**c**) Narrow band imaging (NBI) highlights tubulogyral pattern of the microvessels in the nonpolypoid tubular adenoma and thus improves the lesion visibility (*arrowheads*) (Case courtesy of Jeong-Sik Byeon, MD, Asan Medical Center, Seoul, Korea)

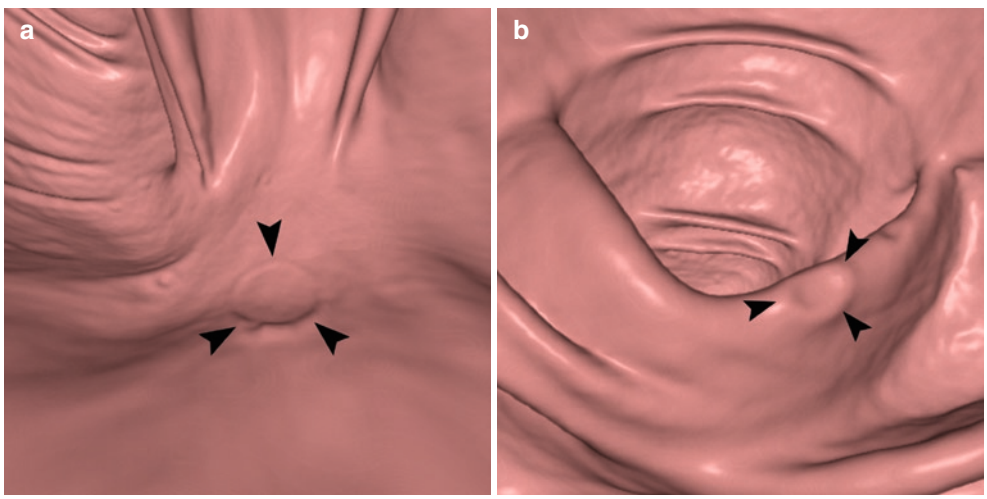

Fig. 9.8 Air bubbles that mimic nonpolypoid lesions with a central depression on the haustral surface (*arrowheads* in **a**) and on the haustral fold (*arrowheads* in **b**)

unnecessary referrals for colonoscopy prompted by the detection of nonadenomatous nonpolypoid lesions on CT colonography. According to the literature, a substantial fraction of colorectal lesions with nonpolypoid morphology consists of nonadenomatous lesions. In two large epidemiologic colonoscopic studies [9, 12], 18% and 37.8% of colonoscopically detected nonpolypoid colorectal lesions were nonadenomatous. In Pickhardt's screening CT colonography trial [5, 31], 50.8% of nonpolypoid colorectal lesions 6 mm or greater in diameter were nonadenomatous.

Suggestions for Better Visualization of Nonpolypoid Colorectal Neoplasms on CT Colonography

The importance of using proper techniques in achieving high diagnostic accuracy with CT colonography cannot be overemphasized [34, 35]. This is probably even more important for detecting nonpolypoid colorectal lesions, as nonpolypoid lesions cause even more subtle changes in the colonic

contour and are more easily obscured by suboptimal colonic distention or residual fecal matter. Therefore, adequate colonic cleansing, good fecal tagging, and optimal colonic distention are all necessary for successful lesion detection. Fecal tagging also allows avoidance of false-positive interpretations which could be caused by plaque-like adherent untagged stool pieces. Some institutions may be performing "cathartic-free" or reduced cathartic CT colonography as an alternative technique to the standard CT colonography performed with full cathartic preparation. Although several studies have already demonstrated the high diagnostic accuracy of reduced cathartic CT colonography [36], its diagnostic accuracy has yet to be validated in a large population. Moreover, the visibility of nonpolypoid lesions submerged under tagged fecal matter has yet to be clearly addressed. Unlike polypoid lesions, there is a potential risk that nonpolypoid lesions submerged under tagged fecal matter may not be as easily identified due to their morphologic subtlety even if the overlying stool is homogeneously well tagged. This issue must be resolved in future studies. Intravenous contrast enhancement is not routinely used for screening CT colonography but is helpful for distinguishing true nonpolypoid lesions from plaque-like adherent feces [26, 30].

There is uncertainty regarding the optimal viewing methods for detecting nonpolypoid colorectal lesions [37, 38]. Several studies have suggested that two-dimensional view using a soft-tissue window may be helpful for detecting some nonpolypoid lesions (Figs. 9.2, 9.4, and 9.6) [25–27]. However, it is uncertain if the two-dimensional review using a soft-tissue window should be routinely added to the clinical interpretation of CT colonography, as it will increase the interpretation time substantially.

Conclusion

Nonpolypoid colorectal neoplasia is present both in the Eastern and the Western countries. Despite the variable reported prevalence/frequency of nonpolypoid colorectal neoplasia and the lack of a uniform lesion definition, it is clear that a substantial proportion of colorectal cancers are attributed to nonpolypoid colorectal neoplasia. Although their malignant potential is controversial, nonpolypoid colorectal neoplasms have at least a similar risk for colorectal cancer as polypoid lesions and should, therefore, not be neglected. Moreover, most studies agree that nonpolypoid adenomatous lesions with a central depressed area have a particularly high risk of containing malignancy. Although "flat" is colloquially used synonymously with "nonpolypoid," completely flat lesions with no elevation above the mucosal surface are extremely rare. Most nonpolypoid colorectal neoplasms are slightly elevated lesions which are, therefore, likely to be visible on CT colonography if the examination is performed using proper techniques. A combination of both two-dimensional and three-dimensional interpretation techniques is likely to lead to the greatest sensitivity of CT colonography for detecting nonpolypoid colorectal lesions. Knowledge of nonpolypoid colorectal lesions and familiarity with their appearance on CT colonography will help with lesion detection and will serve to enhance the diagnostic effectiveness of CT colonography.

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Magnetic Resonance Colonography

10

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Introduction

Colorectal cancer (CRC) is a major cause of morbidity and mortality in Western societies. The majority of CRC arises from adenomas over a period of time, and development into CRC is related to size and histology [1]. Hyperplastic polyps are considered to have very low risk of malignant transformation in contrast to adenomas.

Computed tomographic colonography (CTC) has been accepted as an alternative to colonoscopy in patients with symptoms of CRC and for screening and surveillance [2, 3]. Advantages of CTC over colonoscopy is the reduced burden of both the bowel preparation (when using a limited bowel preparation) and the procedure itself. The disadvantage of CTC is the associated ionizing radiation exposure, which has been reported as an essential point of concern, especially in a screening setting [3]. Colonography with the use of magnetic resonance (MR) imaging obviates the radiation issue and has consequently emerged as an alternative colonography modality over the last decade [4]. Similar to CTC, MR colonography is considered a noninvasive tool in which the complete colon and extracolonic organs can be radiologically evaluated [5, 6].

Still, studies evaluating imaging features (e.g., bowel preparation, colonic distension methods), imaging analysis (e.g., methods of interpretation), and diagnostic accuracy of MR colonography are largely outnumbered by the body of knowledge concerning CTC. Due to the relatively small amount of available research and a major diversity in reported imaging features, in this field a standardized consensus statement, similar to that for CTC [7, 8], has not been established to date.

In this chapter, the current status of MR colonography for detection of (precursors of) CRC will be described by its technical aspects and clinical applications. Finally, the future perspectives for imaging of the colon by MR colonography will be discussed.

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MR Colonography Requirements

Technique

A high magnetic field is required for an adequate signal-to-noise ratio (SNR) for MR colonography. In general, field strengths of 1.5 T are preferred, as the prevalence of artifacts is low and acquisition times are short [9]. Phased array coils are necessary to ensure high signal reception (in terms of SNR) and coverage of the anatomical area of interest [10]. In addition, parallel imaging enables increase of spatial resolution or decreased scan times [9].

To avoid respiratory artifacts in colorectal imaging, data should be collected under breath-hold conditions. The advantage of short acquisition times in high field strength imaging is that it allows coverage of a large imaging volume during one single breath-hold. The acquisition times in general, therefore, are between 15 and 20 s. As in CTC, supine and prone positioning is important for an optimal distension of the colon [11] and subsequent accurate assessment of colorectal lesions.

Several imaging sequences are employed for optimal abdominal imaging in MR colonography, depending on the applied approach to prepare the bowel.

Fast imaging with steady-state precession (FISP) images provide both T1 and T2 contrast. This sequence benefits from its low susceptibility for motion artifacts. Furthermore, it allows detection of inflammatory changes, as seen in inflammatory bowel disease [12]. Single-shot T2-weighted sequences with fat saturation are applied to demonstrate adjacent bowel wall structures and pathologic lesions [9]. T1-weighted images are obtained by 3D T1-weighted spoiled gradient sequences after administration of intravenous gadolinium. It allows high spatial resolution with isotropic voxel size [9]. Imaging is performed pre- and post-contrast administration, enabling diagnostic assessment of tissue perfusion [10].

Tesla MRI

MR imaging at 3 T has proven to be advantageous in musculoskeletal and brain imaging, but application to gastrointestinal

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imaging is more cumbersome [13]. The increased SNR at 3 T is tempered by other effects that decrease the positive effect on SNR. At 3T MRI, longitudinal relaxation times (T1) increase, therefore diminishing the SNR. In addition, the increase of T1 relaxation times is tissue dependent, therefore contrast imaging at high field strength varies from that at lower magnetic field strengths. Furthermore, with a twofold increase of magnetic field strength, the specific absorption rate (SAR) increases fourfold [13]. SAR describes the depositing of energy by the radiofrequency pulses and, as a result of that, the potential heating of the tissue [14]. At 3T, protocols require adjustments to not exceed SAR approved limits. Usually this is achieved by increasing total repetition times, reducing the number of slices, and decreasing the flip angle. However, SNR decreases as a result of that [9].

To overcome chemical shift artifacts, bandwidth can be augmented. Yet, this decreases the SNR as well. Chemical shift artifacts are more prominent in high field strength imaging, due to difference in the resonant frequency between water and fat, which increases proportionally to the increase in magnetic field strength [14]. Artifacts caused by chemical shifting appear as a hyper- or hypointense zone, usually best seen around the kidneys. To overcome these consequences of bandwidth increase, one could apply chemical shift fat saturation, inversion nulling, or water excitation. In addition, due to the augmented difference in resonant frequency between fat and water, the separation of the MR-spectroscopic peak of water and fat is improved at 3 T MR imaging, which improves fat suppression [14].

Susceptibility artifacts are caused by small heterogeneities in the magnetic field and are generally seen at interfaces of soft tissue and air [9]. Susceptibility artifacts increase with the rise in magnetic field strength [9]. In MR colonography, the susceptibility artifacts are most explicit at the interface of residual gas in the colon and bowel wall [14].

Imaging artifacts particularly seen at high field strength are known as standing wave artifacts [13]. Water reduces the speed and wavelength of electromagnetic energy, which creates variations in signal appearing as bright and dark gaps in the images. In distended abdomen (e.g., in obese persons), these artifacts are more explicit.

In addition, circulating electric currents in conductive tissue can act as an electromagnetic field opposing the main magnetic field, causing signal attenuation [13].

Patient Preparation and Impact on Accuracy and Acceptance

The general contraindications for MR imaging have to be considered. Patients with pacemakers, heart defibrillators, and other electrical implants have to be excluded. Relative exclusion criteria like hip prosthesis, metal implants, and claustrophobia have to be evaluated [15].

Equally to CTC, the prerequisites of MR colonography for sufficient visualization of the bowel are adequate bowel preparation (by bowel cleansing or fecal tagging) and colonic distension.

Bowel Cleansing

Fecal residue in the bowel lumen can impede the evaluation of the large bowel, as fecal material can mimic and conceal colorectal pathology. As in colonoscopy, the colon can be cleansed using purgatives. Generally both polyethylene glycol (PEG) electrolyte solutions and sodium phosphate solutions are used for that purpose [16]. Sodium phosphates are generally more efficient and better tolerated than PEG solutions [17]. In contrast to PEG solutions, sodium phosphates can lead to electrolyte imbalances, so application must be handled with care in pediatric patients and elderly. In addition, renal failure was described in patients with previously normal renal function after the use of sodium phosphate [17]. The examination should preferably be done in the morning after bowel preparation in order to reduce patient discomfort. Residual fecal material can hamper diagnostic evaluation – therefore, optimal cleansing is essential.

Although bowel cleansing is generally accepted in colonoscopy, patients consider cleansing as burdensome and one of the most unpleasant elements of the examination. This has also been reported for both CTC and MR colonography [18, 5]. So far in most MR colonography studies, performed with the use of cathartic bowel cleansing, the examination has been followed by conventional colonoscopy the same day [19–21].

Fecal Tagging

Other preparation methods were introduced, as elimination of bowel purgation would ultimately lead to better patient acceptance of MR colonography [22]. Contrary to colonoscopy, MR colonography does not require that the bowel be cleansed, as long as there is sufficient contrast between bowel wall (and lesions) and bowel content. Similar to fecal tagging in CTC, this contrast can be obtained by ingestion of contrast agents with regular meals, thereby homogeneously labeling stool (“fecal tagging”) [23]. Prerequisites for fecal tagging in MR colonography are easy ingestion of the contrast agent (volume, taste), no or limited reabsorption of the fecal tagging agent by the bowel, and adequate mixture with fecal material [24].

Preliminary research was effectuated by gadolinium-based fecal tagging, providing for a high signal intensity of the bowel lumen (bright lumen; see Sect. Bright Lumen and

Dark Lumen MR Colonography). Nevertheless, the high costs of the gadolinium-based tagging agent hampered clinical application [23]. Highly concentrated barium sulfate was studied as a tagging agent; this contrast agent results in low signal intensity on both T_1- and T_2-weighted imaging (dark lumen) of the bowel lumen. Differentiation of bowel lumen and wall proved to be excellent when 200 mL of barium-based contrast agent with each of four meals starting 36 h prior to the examination was used and applied in combination with contrast enhancement of the bowel wall [24, 25]. MR colonography demonstrated high sensitivity (89.3%) and specificity (91.7%) for any size of colorectal lesion [24]. However, Goehde and colleagues demonstrated limited patient acceptance for barium-based substances (6 × 150 mL barium sulfate) [26]. Patient acceptance proved to be in favor of bowel cleansing for conventional colonoscopy in this study. Stool thickening and constipation were reported as uncomfortable side effects. In fact, 18% of the scans proved to be of poor image quality, as this fecal tagging approach did not provide adequate stool darkening. Accordingly, moderate results in lesion detection were found. Overall sensitivity for detection of polyps was 20.7%. On a lesion-by-lesion basis, sensitivities were demonstrated at 100% for polyps larger than 20 mm and at 50% for polyps larger than 10 mm [26].

Other fecal tagging strategies were evaluated in order to improve both bowel content homogeneity and patient acceptance. A combination of 5% Gastrografin, 1% barium, and 0.2% locust bean gum was evaluated for patient acceptance. Ingestion of the tagging agent was considered less burdensome than bowel cleansing for conventional colonoscopy, but still no significant difference in overall acceptance for both procedures was noted [27]. Using this barium-based tagging solution, a sensitivity of 70% and specificity of 100% were demonstrated for detecting patients with colorectal polyps >10 mm [28].

Achiam and colleagues explored the feasibility of fecal tagging with the use of ferumoxsil, a contrast agent resulting in decreased stool signal intensity [29]. Significantly better tagging results were obtained using barium sulfate/ferumoxsil compared with barium sulfate alone. In addition, acceptable per-patient sensitivity and specificity rates for detection of polyps >10 mm of 100% and 91.4% were demonstrated [30].

A prospective feasibility study in a surveillance group applied three different preparation strategies to compare image quality and patient acceptance [31]. Two barium-based strategies and one gadolinium-based tagging preparation were studied. Image quality was evaluated best for the gadolinium-based strategy and demonstrated better diagnostic confidence. The accuracy for polyp detection could not be validated given the limited number of patients in that study [31]. The gadolinium-based strategy was subsequently used in a prospective study with 209 surveillance patients comparing MR colonography with conventional colonoscopy, regarding patient preparation acceptance and accuracy of polyp detection. For polyps of 10 mm or larger, the per-patient sensitivity was 75% (9/12) and specificity was 93% (175/188). A per-polyp sensitivity of 77% (17/22) was demonstrated for polyps 10 mm or larger [22] (Fig. 10.1). The study demonstrated that bowel preparation for MR colonography was significantly less burdensome in comparison with the extensive preparation for colonoscopy and moreover that the MR examination was preferred to colonoscopy [5].

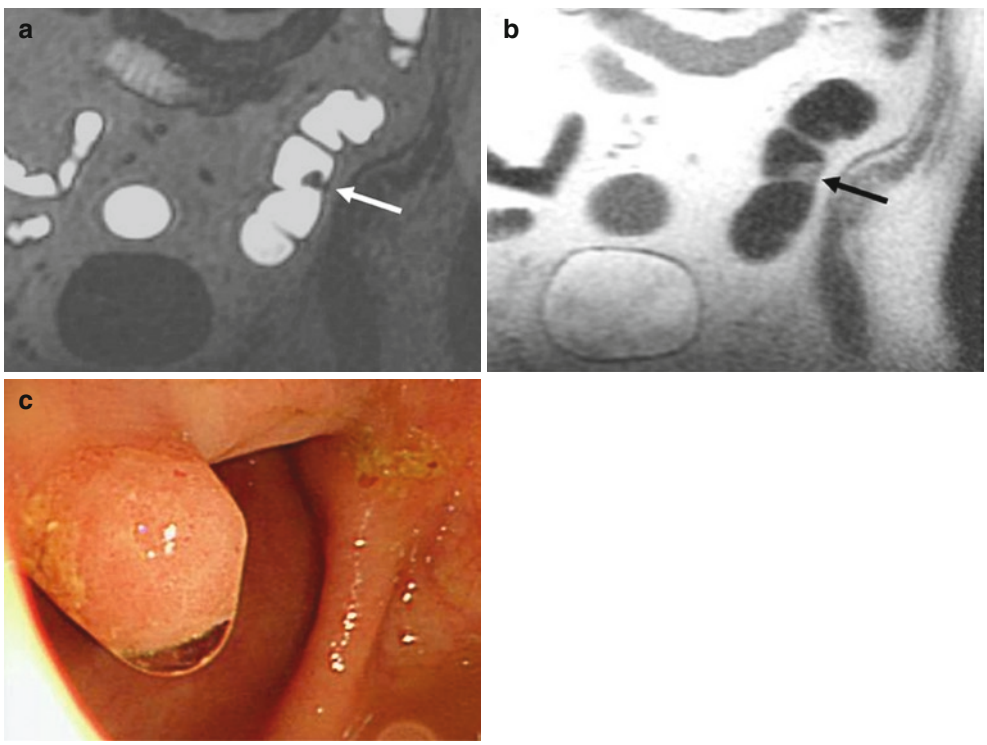

Fig. 10.1 Bright-lumen MR colonography in a 61-year-old female patient who was suspected for CRC. (**a**) Coronal 3D T_1-weighted fast field echo (FFE) sequence visualized a lesion in the descending colon (*white arrow*). (**b**) On the corresponding T_2-weighted 2D fast spin echo (FSE) image, the polyp is demonstrated as a hyperintense lesion (*black arrow*). (**c**) Conventional colonoscopy confirmed the presence of a 12 mm polyp in the distal aspect of the descending colon

Immediately after both examinations, 69% of participants preferred MR colonography and 22% colonoscopy, and 9% were indifferent. After 5 weeks, 65% preferred MR colonography and 26% preferred colonoscopy.

A limitation of bowel preparation with fecal tagging is that no immediate colonoscopy after MR colonography is practicable, as the colon is insufficiently cleansed.

Bowel Distension

Collapsed colonic bowel segments may be interpreted as bowel wall thickening, as seen in inflammation, or be mistaken for tumor [32, 33]. On the other hand, pathology may be masked, leading to false negative findings [34]. Consequently, for accurate diagnostic evaluation of the bowel, adequate differentiation of the bowel wall from the bowel lumen is required, thus colonic distension is an absolute prerequisite for MR colonography.

Imaging in two positions is necessary for optimal bowel distension [35]. As in CTC, prone positioning improves distension of specific bowel segments, such as the rectum; the transverse colon is better distended in supine positioning [36].

Conventionally in MR colonography, water-based enemas are frequently used for bowel distension, consisting of either warm tap water [16, 25, 27, 29, 31, 37–40] or a mixture of gadolinium plus tap water [19–22]. The initial water-based method was performed with a water/barium mixture; however, as the signal intensity proved to be similar to that for tap water alone, this method was abandoned [16]. Water-based distension has the advantage of maintaining a constant distension of the colon, while CO_2 insufflation is under the influence of ileocecal reflux and to a greater extent reabsorption by the bowel, and consequently the intracolonic pressure might vary [40]. In MR colonography, usually 1–3 L of tap water is used for water-based distension [4], administered under hydrostatic pressure by a rectal canule. Water has high signal intensity on T_2-weighted sequences and low on T_1-weighted sequences. The high signal in T_2-weighted sequences enables bowel lumen differentiation from the bowel wall, as the latter demonstrates low signal intensity. Furthermore, water can be labeled with a gadolinium-containing contrast agent [5, 21, 41], allowing a "bright lumen" on T_1-weighted sequences (Fig. 10.2).

Importantly, enemas are associated with soiling and spill of the large volume of fluid in the colon [23] and are therefore considered the most burdensome part of an MR colonography examination [35]. Replacing enemas with insufflation of room air or carbon dioxide for bowel distension in MR colonography – as is common practice in CTC – would be an important development. Morrin et al. reported patients who underwent MR colonography to be in favor of air-based distension in comparison with that by water, as air insufflation was better tolerated than a fluid enema. Limited studies have explored the feasibility of air- or CO_2 -based distension in MR colonography [35, 40, 42–44] compared with water-based MR colonography. Preliminary results were unsatisfactory due to susceptibility artifacts at interfaces of air and tissue. The availability of high-performance gradients permitting data acquisition with very short echo times improved susceptibility [40], and MR colonography with gaseous luminal distending agents proved to be feasible [42]. In this study, results were promising, as all colon carcinomas in seven patients were correctly identified.

Although most experience in MR colonography concerns air insufflation, the use of carbon dioxide (as in CTC) is advantageous: Reabsorption is faster than with room air, resulting in less postprocedural discomfort. Administration of carbon dioxide can be performed manually, but automated carbon dioxide insufflation is preferred in CTC. Advantages are the monitoring of intracolonic pressure and of constant intracolonic pressure as carbon dioxide can be reinsufflated in case of ileocecal reflux and gas incontinence. Automated insufflation can be considered for MR colonography as well. To our knowledge, no MR-compatible insufflator is available, but a CTC insufflator outside the MR imaging suite and long tubing are adequate in our experience (Fig. 10.3).

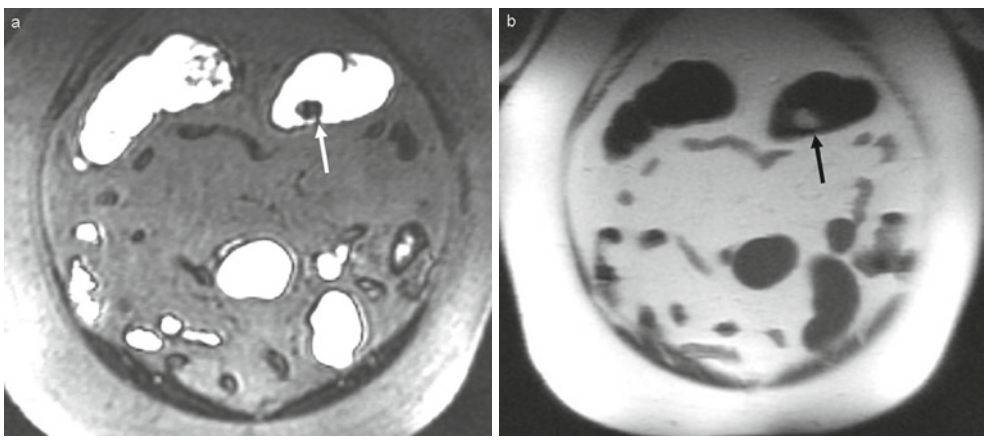

Fig. 10.2 Bright lumen MR colonography in a 61-year-old female patient who was suspected for CRC. (**a**) Axial 3D T_1-weighted FFE sequence visualized a lesion in the transverse colon (*white arrow*). (**b**) On the corresponding axial T_2-weighted 2D FSE image, the lesion is demonstrated as hyperintense (*black arrow*)

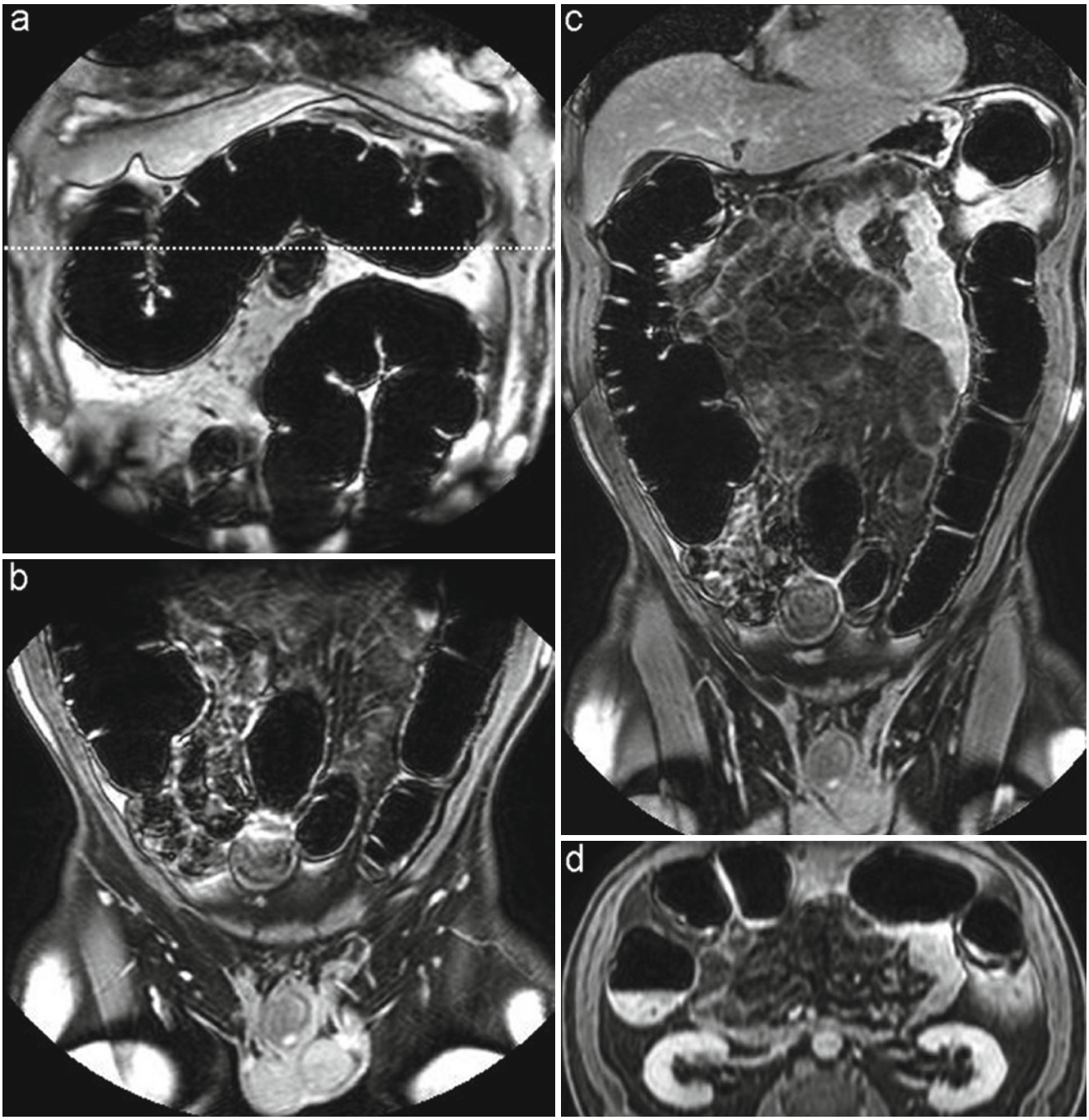

Fig. 10.3 Supine T_1-weighted 3D coronal fat saturated FFE in a 53-year-old male receiving carbon dioxide for colonic distension. Coverage of the complete colon includes the breath-hold acquisition of linked upper-abdominal (**a**) and lower-abdominal (**b**) image stacks by the use of automatic table movement. Using the MR imaging system postprocessing software, both image stacks can be fused (**c**). Acquisition of isotropic voxel volumes enables multiplanar reconstruction (MPR) on each desirable level (**d**) (level of MPR indicated in the upper-abdominal image stack by *dotted line* (**a**))

Bowel distension by air or CO_2 insufflation in MR colonography results in low signal intensity of the bowel lumen at T_1- and T_2-weighted sequences.

Nonuniformity in diagnostic performance has been reported for MR colonography using insufflation of gaseous distending agents. Moderate results for MR colonography with insufflation of room air were reported by Leung et al [44]. as a result of poor bowel distension and physiological artifacts. In 156 patients at average or increased risk for CRC, only 4 out of 31 patients with colorectal polyps were identified. Ajaj and colleagues [40] randomly performed air-based and water-based methods for distension in 50 patients

and in five volunteers and demonstrated comparable patient acceptance, but concluded that both strategies performed equally well in colon distension. As for image quality, both methods were comparable, although contrast-to-noise demonstrated to be significantly better with air-based insufflation [40]. In a study comparing three patient preparation strategies, using water-based and air-based distension [19], one of the two observers rated bowel distension significantly better in the water-based strategies. No statistically significant differences regarding pain were found between the strategies; patient preference was reported to be equal for all.

As for air compared with CO_2, one study in colonoscopy showed that both air and CO_2 performed equally well in distension, but CO_2 resulted in better patient acceptance [45].

Spasmolytic Agents

To decrease motion artifacts and bowel distension, intravenously administered spasmolytic agents should be administered when performing MR colonography. In addition, patient discomfort is reduced with administration of spasmolytics [46]. Glucagon and butylscopolamine are the most frequently used agents. Glucagon, though generally more effective in the small bowel compared with the colon, relaxes smooth muscles. Butylscopolamine is not approved by the Food and Drug Administration but is regularly used in Europe. It also relaxes smooth muscle and is believed to be more efficient for bowel distension. Administration of spasmolytic agents should be carefully planned, as half-life time of the agents is short [46]. In our experience it should be administered directly prior to data acquisition.

Bright Lumen and Dark Lumen MR Colonography

Bright lumen imaging refers to the high signal intensity of the bowel lumen on T_1-weighted sequences, while the bowel wall remains low in signal intensity. At T_2-weighted series, colonic pathology is visualized with high signal intensity, whereas the bowel lumen is low in signal intensity. The bright lumen approach is based on visualization of filling defects (Fig. 10.4). As previously mentioned, the colonic lumen is prepared with a mixture of water and gadolinium, which is rectally administered [5, 21, 22, 47]. As the bright lumen method is dependent on evaluation of hypointense filling defects at T_1, diagnostic accuracy of bright lumen MR colonography is hindered by residual air, low signal intensity, or heterogeneous stool leading to false positive findings [23, 47]. To overcome this problem, data acquisition has to be performed in supine and prone position – gravity leads to movement of residual air and fecal material, while bowel lesions are not subjected to gravity (except stalked polyps) [47] (Fig. 10.5). Initial research was executed to assess diagnostic accuracy of bright lumen MR colonography for detection of colorectal polyps and malignancies [21, 47]. Although preliminary results were promising, only lesions exceeding 10 mm could be accurately diagnosed [21, 47]. Additionally, subsequent studies [19, 22] demonstrated mediocre results in diagnostic accuracy of bright lumen MR colonography due to false positive and false negative findings, and costs of the contrast agents diminished the use of the bright lumen approach even further [26].

Dark lumen MR colonography shows a homogeneously dark bowel lumen on T_1-weighted series, whereas the colonic wall is enhanced by an intravenously administered paramagnetic contrast agent [26] (Fig. 10.6). In contrast to the bright lumen approach, wall-related pathology in dark lumen MR colonography is not detected by low signal filling defects but by enhancement after administration of paramagnetic contrast medium [26, 42]. Bowel wall distension is achieved by water-based or air-based enemas, providing low signal intensity on T_1-weighted sequences [26, 42]. Although preliminary experiments stated that supine and prone imaging in the dark lumen approach would no longer be required, as colonic lesion enhancement was achieved [16], imaging in two positions is in fact required for optimal bowel distension [35].

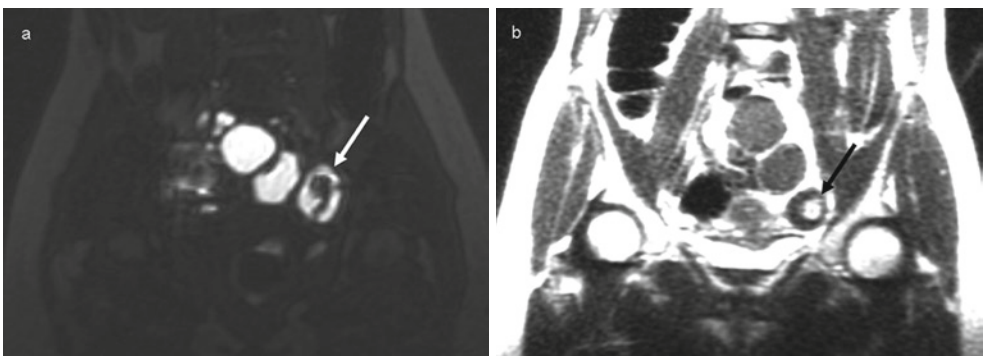

Fig. 10.4 Bright lumen MR colonography achieving colonic distension by the rectal administration of a mixture containing water and gadolinium in a 42-year-old female patient. (**a**) Coronal T_1-weighted 3D FFE image visualized a pedunculated lesion (*white arrow*) in the sigmoid colon, appearing as a large hypointense "filling defect" in a hyperintense colonic lumen.Colonoscopy confirmed the presence of the 3 cm pedunculated adenomatous polyp in the descending colon. (**b**) The polyp is also visualized on the corresponding T_2-weighted 2D FSE image, showing a relative high signal intensity (*black arrow*)

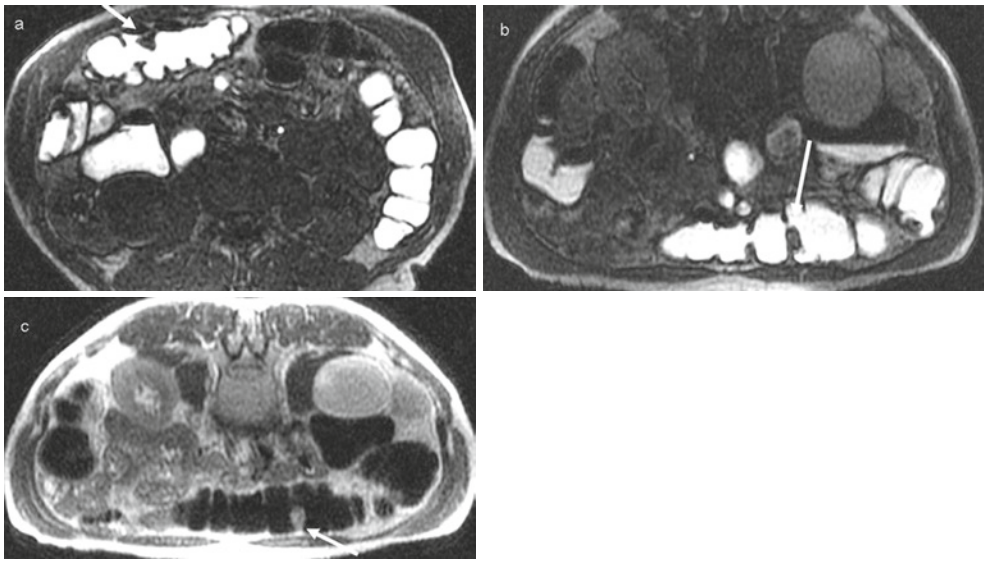

Fig. 10.5 (**a**) Supine T_1-weigthed 3D axial FFE image of an 84-year-old male suspected for CRC. Bright lumen MR colonography demonstrated a lesion at the proximal aspect of the transverse colon (*white arrow*). The lesion is also demonstrated in prone position on T_1-weighted (**b**) and corresponding T_2-weighted 2D FSE images (**c**). Colonoscopy confirmed the presence of a pedunculated polyp of 10 mm in size in the transverse colon

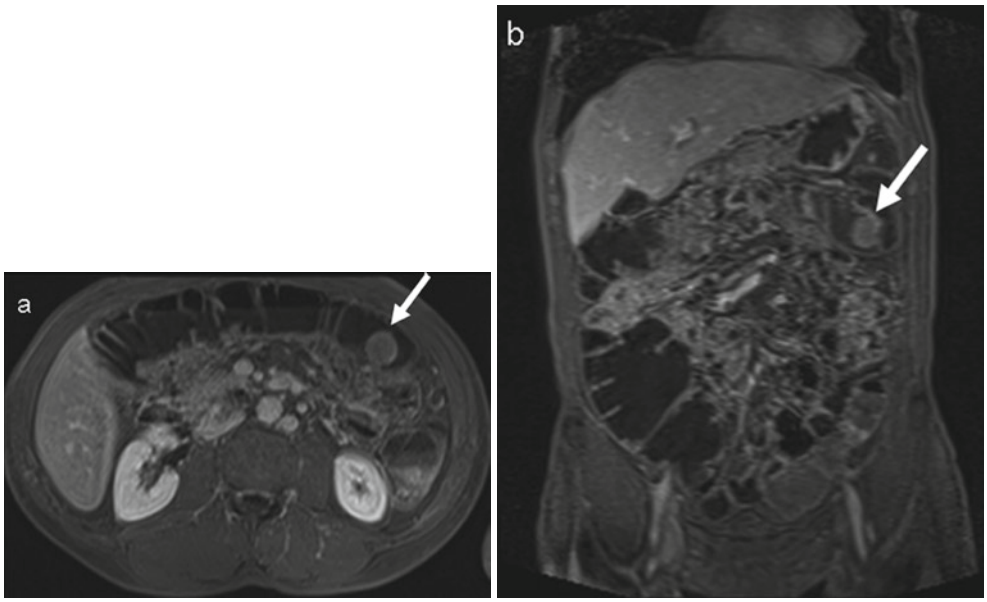

Fig. 10.6 (**a**) Supine transverse T_1-weighted 3D volumetric interpolated breath-hold examination (VIBE) of a 57-year-old male patient. Dark lumen MR colonography visualized a round, broad-based lesion with increased enhancement after the intravenous administration of paramagnetic contrast, at the distal aspect of the transverse colon (*white arrow*). (**b**) On the corresponding coronal T_1-weighted 3D VIBE image, the lesion is visualized as well (*white arrow*)

Furthermore, pre- and post-contrast imaging is performed to confirm true positive findings; lesions enhance after contrast administration; if not, it represents stool residue or residual air [26, 42].

MR Colonography Results

Large lesions detected at MR colonography are likely malignant, especially when this concerns masses or obstructive lesions. For polypoid lesions, this is not so obvious, and it is in fact not really possible without colonoscopy verification. Hyperplastic polyps and adenomas without or with cancer cannot be discriminated. However, size is a surrogate for histopathology. The prevalence of advanced neoplasia in polyps 6–9 mm is 6.6%, with a range of 4.6–11.7%. The prevalence of advanced histology in 1–5 mm polyps is 1.7%, with a range of 1.2–2.0% [48].

By consensus, polyps are classified in three sizes: large polyps of no less than 10 mm, intermediate polyps between 6 and 9 mm, and small polyps of less than 6 mm [1]. In CTC, patients are generally referred for colonoscopy for polyps with sizes of 6 mm and larger.

Most MR colonography research is performed in patients at increased risk (either symptomatic or surveillance) with favorable results. A systematic review by Zijta et al. demonstrated that the sensitivity for the detection of CRC, observed in five studies, was 100%. On a per-polyp basis, polyps of 10 mm and larger were detected with a sensitivity of 84% (95% confidence interval [CI]: 66–94). Furthermore, per-patient

sensitivity of MR colonography for the detection of large polyps (10 mm and larger) was 88% (95% CI: 63–97), and specificity 99% (95% CI: 95–100) [4]. Only one study [29] has focused primarily on asymptomatic individuals with average risk for CRC, with an overall prevalence of 6.3% for polyps larger than 10 mm (20/315). This prospective study compared dark lumen MR colonography with colonoscopy. In this study, patients were prepared with fecal tagging (5% Gastrografin, 1% barium, 0.2 % locust bean). For intermediate-sized lesions, sensitivity was 60.0% and increased to 70.0% and specificity was 100% for lesions larger than 10 mm. However, overall patient-based accuracy was limited (sensitivity 36.0%, specificity 90.2%).

MR colonography has proven to have favorable results for detection of CRC and large polyps. However, both dark and bright lumen strategies were taken into account, and due to the heterogeneous data, no conclusions could be drawn for the application of MR colonographic patient preparation strategy and technique [4].

Conclusions and Future Perspectives

The continuous technological developments in the MR imaging field, with faster imaging protocols generating images with improved image quality and optimal resolution, might facilitate the clinical implementation of MR colonography. However, in the current status, MR colonography is relatively far from optimized and standardized – to date no consensus has been established regarding important technical aspects of the examination [4]. Consensus statements such as we see proposed for CTC can serve as templates in this context and consequently might lead to more homogeneity in MR colonography literature [2].

MR colonography provides colonography without ionizing radiation exposure, which can be regarded as its main important strength compared with CTC. Additionally, the excellent soft-tissue contrast permits a wide range of fecal tagging strategies, potentially leading to less preprocedural burden and ultimately satisfactory overall patient acceptance [5]. Nonetheless, substantial limitations of this modality include its limited availability, higher costs, and procedural length, and the limited evidence in literature.

The primary role of MR colonography is to detect (precursors of) CRC. A recently conducted systematic review demonstrated an acceptable average per-patient sensitivity of nearly 90% for detecting large polyps (≥10 mm), and the sensitivity in detecting colorectal carcinoma was 100% [4]. Although the body of evidence for CTC is substantially larger than for MR colonography, these findings indicate that MR colonography has comparable diagnostic accuracy to CTC in detecting CRC and colorectal polyps of clinical importance.

Results of MR colonography are poorer for the intermediate-sized polyps. Apparently, an optimal evaluation of these modalities in terms of diagnostic accuracy and procedural burden would entail a direct prospective head-to-head comparison study between state-of-the-art CTC and a potential state-of-the-art MR colonography protocol. Although reported once to date, this study recognizes substantial methodological limitations which prevent drawing consequential interpretation of the results [49].

The developments toward a consensus for the technical performance of MR colonography are under way. Albeit the use of dark lumen MR colonography is favored, the distension method is under debate. Present technology permits the use of carbon dioxide distension, which can be expected to increase the acceptance of MR colonography. Further, a wide range of fecal tagging approaches for dark lumen MR colonogaphy have been proposed and focus mainly on the application of barium-based elements. Although results are not unambiguous, the type of applied bowel preparation certainly needs further investigation. Finally, the role of MR imaging in diagnosing gastrointestinal conditions continues to develop, and so does the application of colonography using this modality. Other applications studied are for inflammatory bowel disease and diverticulitis [50].

Although CTC currently is the most evaluated and preferred imaging modality in colonography, the use of MR colonography certainly deserves further exploration. At present, MR colonography is not widely used in clinical practice; its role is as an alternative to CTC when the latter is contraindicated. Its potential role in detecting colorectal pathology, especially in a screening setting, might be advantageous to CTC.

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Extracolonic Findings

11

Abraham H. Dachman and Ila Sethi

Introduction

CTC is not intended to be sensitive for detecting extracolonic findings (ECFs), particularly in the solid organs. This is due to the low radiation dose used and the lack of intravenous contrast. Nevertheless, many ECFs are detectable, some of which may be potentially clinically significant. If the ECF was previously unknown, its detection may result in additional diagnostic or therapeutic procedures. The cost-effectiveness of CTC is therefore altered by the additional cost (including patient anxiety) resulting from the detection and reporting of the ECFs. Criticisms raised in the opinion rendered by the United States Public Service Task Force (USPSTF) and by the Center for Medicare Services (CMS), include the concern regarding the effect of ECFs [1–3]. The detection of ECFs has both advantages and disadvantages. For most patients, there are no clinically important ECFs and CTC may provide some reassurance. For other patients, an abnormality may be found that results in beneficial therapeutic options, and for others the finding results in a work up that is ultimately, unnecessary with no therapeutic option. The purpose of this section is to review data on ECFs and to show why ECFs are ultimately a beneficial corollary of CRC screening using CTC [4–25].

Detection and Reporting of ECFs on CTC

A directed search for ECFs will reduce errors of detection. Since CTC images are noisy due to the low radiation dose and thin slice thickness, we reconstruct the supine images using 4 mm thick axial slices and coronal reconstructions for interpretation of ECFs. Those thicker images are read in soft tissue, bone and narrow ("liver") window/level settings, usually at our PACS workstation. When reading the thin CTC images at the CTC workstation, it is convenient to search for lesions in the lung bases, since CTC window/level settings are sufficiently similar to "lung" windows.

The CT Colonography Reporting and Data System (C-RADS) [8] contains an "E" classification for ECFs (Table 11.1).

In practice, we do not use the E0 category and most patients have normal exams. The use of E0 might mistakenly imply that additional imaging is necessary. The application of the E1–E4 categories is subjective and generally means that the finding is potentially of very low (E2), moderate (E3) or high (E4) clinical significance. The actual significance will depend on patient-related factors and whether the finding was previously known or unknown. A patient may or may not be personally aware of this finding even if one of several clinicians who have seen the patient may be aware of the finding, and may have already dismissed the finding as unworthy of follow up. In our research we often lump E1 and E2 together as "not important to patient management" and E3 and E4 as "potentially important" findings that need to be considered by the patient and their physician. Care should be taken in deciding if a lesion belongs in the E2 vs. the E3 category. A useful way of understanding the categories is by way of some examples provided below, Table 11.2–11.4, with the accompanying discussion (see Figs. 11.1–11.3).

E2 findings include some that are self-explanatory without follow up or comparison to prior exams, such as granulomata, mild vascular calcifications without associated aneurysm, uncomplicated hernias, and small adrenal adenomas (nodules measuring about 10 HU or less). Other E2 findings deserve clinical correlation and even if asymptomatic, could become symptomatic at some future time, e.g., cholelithiasis (seen in up to 10% of asymptomatic adults), nephrolithiasis (seen in 5% of asymptomatic adults) or mild fatty liver (that could become more severe and concerning for steatohepatitis). It is important that the patient and their doctor be aware of these ECFs since they could become symptomatic in the future.

E3 findings are "likely unimportant" but some physicians will choose to obtain further diagnostic tests to better characterize them. Complex adnexal lesions, complex renal

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Table 11.1 C-RADS classification, modified from [8]

E0 – incomplete or limited by artifact
E1 – normal/anatomic variant
E2 – benign/incidental
E3 – likely unimportant
E4 – potentially important finding

Table 11.2 Examples of E2 lesions

Atherosclerosis
Hiatal hernia (small)
Degenerative disk disease
Renal hypodensity or homogeneous hyperdensity
Gallstones
Liver hypodensity (non-specific)
Splenic granuloma
Disk space narrowing
Degenerative joint disease
Spondylolithesis (grade 1–3)
Liver granuloma
Uterine lesion (small, non-specific)
Adrenal nodule <3 cm
Ventral hernia without bowel
Bone islands
Emphysema
Lung granuloma
Inguinal hernia without bowel
Angiomyolipoma
Ascites (minimal)
Pleural effusion (small)
Pericardial effusion (small)
Adrenal calcification
Uterine calcification
Testicular calcification
Lipoma
Ovarian cyst <3 cm

Based on a previously published analysis of 376 CTC exams [15]

Table 11.3 Examples of E3 lesions

Nephrolithiasis
Renal, complex cyst
Pancreatic calcification
Hepatic lesion (complex/suspicious for metastasis)
Fatty liver
Hiatal hernia (large)
Aortic focal bulge <3 cm
Ascites (moderate)
Ovarian cyst ≥3 cm
Splenomegaly (mild)

Based on a previously published analysis of 376 CTC exams [15]

Table 11.4 Examples of E4 lesions

Abdominal aortic aneurysm ≥3 cm
Renal, solid mass concerning for carcinoma
Liver, solid mass, concerning for metastases or primary neoplasm
Bone, blastic (suspicious for metastasis)
Bone, lytic
Ovarian mass, solid or complex
Hydronephrosis
Lung nodule ≥ 1 cm or mass
Splenomegaly (moderate or marked)
Artery aneurysm – splanchnic (e.g., splenic artery)

Based on a previously published analysis of 376 CTC exams [15]

lesions (with solid and cystic components), liver lesions that are not fluid density are such examples. In non-obese patients, these could be evaluated with ultrasound. Other patients may require CT. In the vast majority of patients, these ultimately turn out to be benign lesions. Newly discovered micronodules in the lung require correlation with risk factors for lung cancer (e.g., smoking history) and nodule size, in order to triage the patient to 6 or 12 month follow up exam. We suggest judicious use of this category and minimizing recommendations for follow up exams. As we have lowered our CTC radiation dose, we find that the density measurement of many non-specific hypo-attenuating lesions in the solid organs are less reliable and have wide standard deviations. We tend to categorize many of these as E2 (statistically likely cysts) unless their features are strongly concerning for a solid mass.

E4 lesions represent findings that usually deserve a personal communication to the physician and/or patient. Marked adenopathy concerning for lymphoma or metastasis or a large aortic aneurysm are some examples. Even E4 lesions may not generate further work up. For example, a large aortic aneurysm may have been a previously known finding that was stable for several years. For this reason, simply looking at the E-classification of ECFs in the literature is not a good surrogate for cost-effectiveness analysis of ECFs. Only actual work up data should be used in cost-effectiveness studies.

As discussed in Chap. 7, when we report CTC exams, the template contains a qualifier for the ECFs stating that "the exam is not sensitive for detection of findings outside of the colon due to the low radiation dose and lack of intravenous contrast. Given those limitations the following observations are made". This helps both patients and clinicians understand the limitation of the exam. We do issue a C-RADS classification for ECFs as well. Note that the ACR National Radiology Data Registry (NRDR) data base (see Chap. 7 for a more complete description) logs information

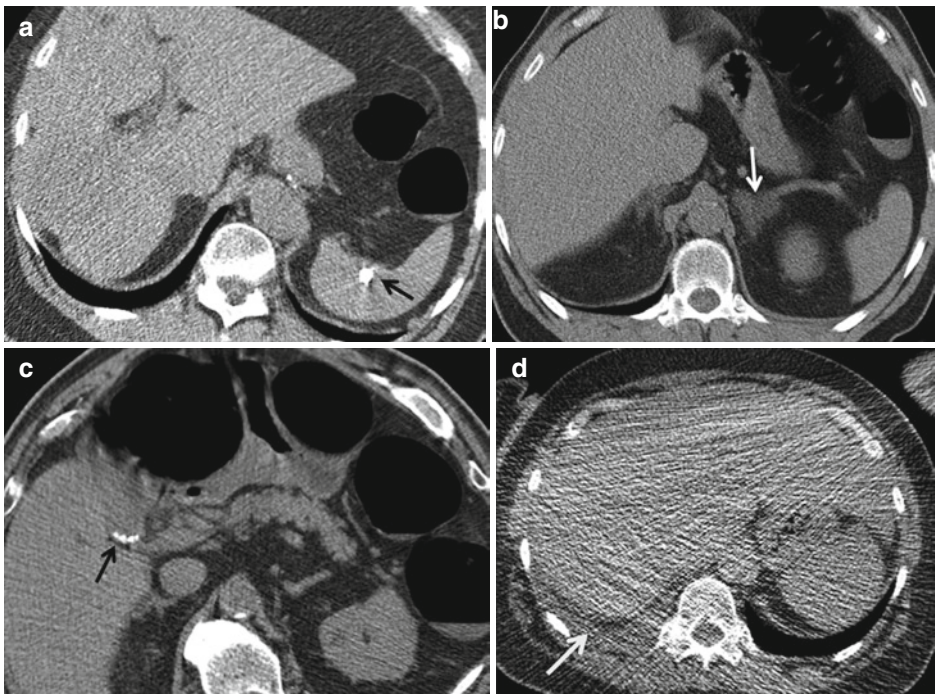

Fig. 11.1 Examples of E2 lesions. (**a**) Supine, axial image shown in soft tissue window setting. Shows a single, large calcific granuloma (*black arrow*) in the spleen. (**b**) Supine, axial image shown in soft tissue window setting. Shows enlarged left adrenal gland measuring 1.4 cm (*black arrow*) suggestive of adrenal adenoma. (**c**) Supine, axial image shown in soft tissue window setting. Shows multiple small gall stones in the dependent portion of gall bladder (*black arrow*). (**d**) Supine, axial image shown in soft tissue window setting. Shows a small right sided pleural effusion (*white arrow*)

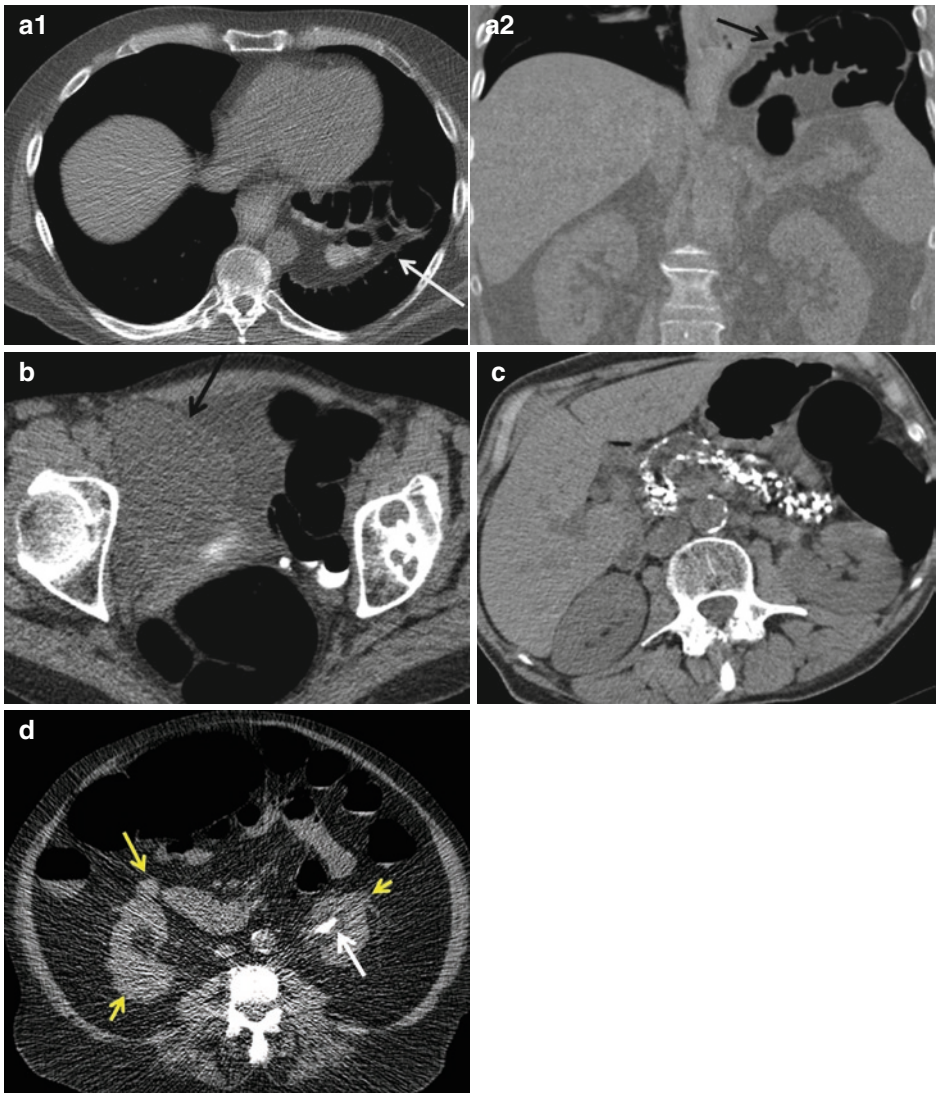

Fig. 11.2 Examples of E3 lesions. (**a.1**) Supine, axial image shown in soft tissue window setting. Shows large post operative diaphragmatic hernia containing proximal transverse colon (*white arrow*). (**a.2**) Same patient. 3 mm coronal reconstruction scan shows a wide-necked post operative hernia containing proximal transverse colon. (**b**) Supine, axial image shown in soft tissue window setting. Shows a hypoattenuating fluid density (15–20 HU) lesion measuring 7.7×6.1 cm in right adenexa consistent with an ovarian cyst (*black arrow*). (**c**) Supine, axial image shown in soft tissue window setting. 3 mm reconstructed axial image shows multiple pancreatic calcifications in an atrophic pancreas consistent with chronic pancreatitis. (**d**) Supine, axial image shown in soft tissue window setting. Shows multiple hypoattenuating lesions (yellow *arrows*) with fluid density in both kidneys suggestive of cysts in left kidney (*white arrow*). In the left kidney a staghorn calculus is also seen

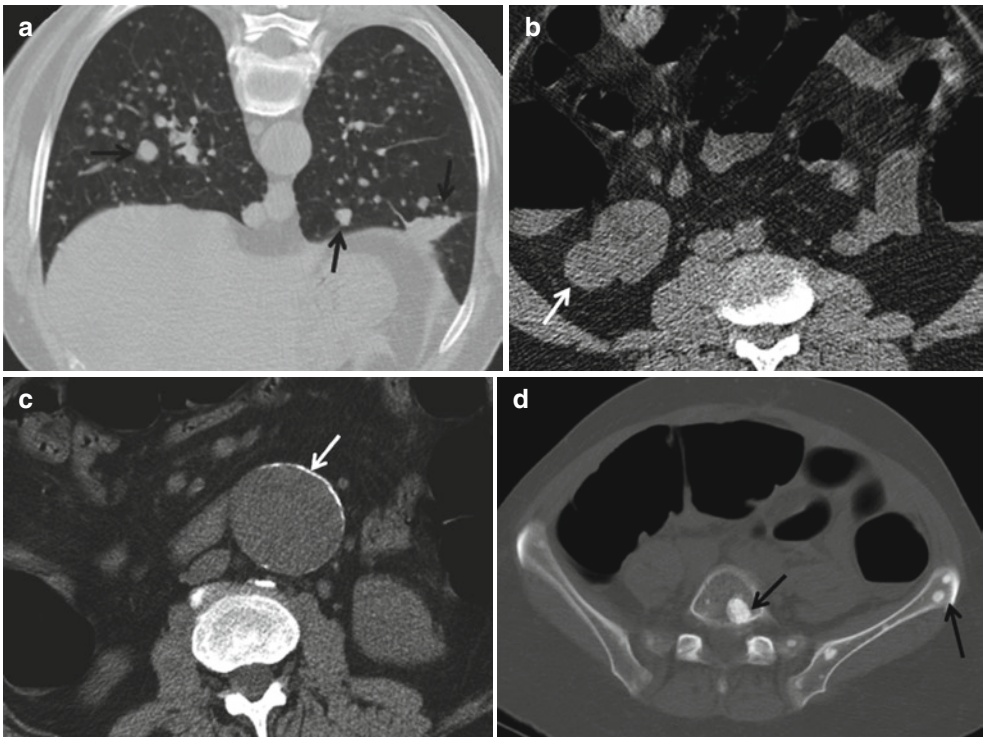

Fig. 11.3 Examples of E4 lesions. (**a**) Prone, axial 5 mm scan shown in lung window setting. Shows multiple varying sized lung nodules (*black arrows*) not known previously, suggestive of metastasis. The patient was found to have a cecal mass and multiple polyps on CTC. (**b**) Supine, axial image shown in soft tissue window setting. Shows solid renal lesion (*white arrow*) measuring 2.6 cm,discovered on CTC which was found to be papillary renal carcinoma on surgery. (**c**) Magnified, supine, axial 5 mm image in soft tissue window setting. Shows a 5.3 cm abdominal aortic aneurysm (*white arrow*) of which was previously unknown. The patient underwent surgical repair because of its discovery on CTC. (**d**) Supine, axial image in bone window setting depicting multiple blastic metastasis in lumbar vertebrae and left iliac wing (*black arrows*). Patient known case of ovarian carcinoma with metastasis

about significant ECFs as well. Others prefer to avoid using the C-RADS categorization for ECFs. Either way, ACR communication guidelines should be adhered to when significant findings are present.

Incidence and Cost Effectiveness of ECF Reporting

A limited chart of ECF incidence and cost effectiveness data is summarized in Tables 11.5 and 11.6. Consideration should be given to the nature of the cohort: screening asymptomatic patients vs. symptomatic or mixed cohorts, the age of the patients – older patients are more likely to have ECFs, the data based on CTC reporting vs. data reflecting actual follow and correlation with all medical records on the patient.

Reports on asymptomatic screening cohorts have demonstrated that the incidence of ECFs requiring medical or surgical treatment, or further investigation, ranges from 5% to 9% [4–10]. Older patients, ages 65–79 (i.e., the Medicare aged population), were found to have a 15.4% (89 of 577) incidence of potentially important ECFs and a work up rate of 7.8% (45 of 577) in one study in which the majority of important diagnoses were vascular aneurysms [23]. The ACRIN National CT Colonography Trial found that 16% of its patients had ECFs categorized as potentially requiring additional test or treatment, but the impact on patient management, and cost has not yet been studied [23]. The incidence of "significant" ECFs increases not only in symptomatic cohorts, but also those with known colorectal lesions, and if the CTC is performed using intravenous contrast or higher radiation dose [4, 7, 11, 12, 21, 25]. Detection of unsuspected malignancies on CTC at an early stage may lead to increased survival rates and favorable outcomes as shown in a retrospective analysis of a cohort of more than 10,000 patients undergoing screening CT Colonography. This study reported an overall detection rate of unsuspected cancer to be 1 per 200 (58 of 10,286) in asymptomatic adults [24]. Of these, at least 26 were identified in Stage I. One report in a mixed screening and symptomatic

Table 11.5 Extracolonic findings in screening or asymptomatic patients

Author	Research subject population	Sample size	Risk for colon CA	Risk categorization of ECF severity	Subjects with ECFs[a] (%)	Mean ECFs/ patient	% with highly important ECFs	Subjects with any further treatment based on an ECF	Surgical intervention based on an ECF	Mean add'l cost per subject
Kim et al.	Asymptomatic screening	577	Average/high risk	Yes	NA	NA	15.4%	7.8%	NA	NA
Pickhardt et al. [6].	Asymp-tomatic screening	1,253	Average or increased risk	Yes	NA	NA	5%	NA	0.2%	NA
Gluecker et al. [5]	Asymp-tomatic screening	681	Increased risk	Yes	469/681 (69%)	1.8	10%	1.3%	1%	$34
Yee et al. [10]	Asymp-tomatic screening	500	Average or increased risk	Yes	315/500 (63%)	1.9	9%	2.6%	1%	$28
Chin et al. [9]	Screening	432	Average risk	Yes	118/432 (27%)	1.2	7%	NA	NA	$24
Johnson et al. [14]	Asymp-tomatic screening	2,531	Average or increased	Yes	(66%)[b]	NA	16%	NA	NA	NA
Pickhardt et al. [17]	Asymp-tomatic screening	2,195	NA	Yes	NA	NA	9%	6.1%	22/2195 (1%)	$31 (non-surg) $67 (surg)

[a] Includes both subjects who underwent treatment as well as those who underwent subsequent imaging follow-up

[b] Number of patients in each category not reported

Table 11.6 Extracolonic findings in CT colonography in surveillance or symptomatic patients

Author	Research subject population	Sample size	Risk for colon CA	Categorization of ECF Severity	Definition of significant ECFs	Subjects with ECFs (%)	Mean ECFs/patient (total ECFs/# of patients)	Subjects with highly important ECFs (%)	Subjects with any further treatment based on an ECF	Surgical intervention based on an ECF	Mean cost per subject for further work-up
Hara et al. [4]	Screening/ surveillance	264	Asymptomatic (high risk)	High, moderate and low potential	Require surgical or medical treatment or further investigation	109/264 (41%)	1.4(151/109)	30 (11%)	20/264 (8%)[a]	6 (2.3%)	$28
Edwards et al. [26]	Diagnostic	100	Symptomatic or high risk	Significant/ insignificant	Require further investigation	15/100 (15%)	1.1 (16/15)	8 (8%)	6/100 (6%)[a]	2 (2%)	NA
Khan et al. [11]	Diagnostic	225	Symptomatic or high risk	Two groups	Further action taken (investiga-tion/hospital visit/treatment)	116/221 (52%)	1.8 (211/116)	24 (11%)	NA	12 (5.3%)	$153
Flicker et al. [15]	Screening/ symp-tomatic	376	Average or high	High, moderate, low potential & normal finding	Potentially significant finding that should be communicated	272/376 (72.3%)	1.9 (520/272)	16 (4%)	NA	? 2 (0.5%)	$13
Spreng et al. [12]	Referred to evaluate symptoms by	102	Symptomatic or high risk	Two groups	Finding that will either lead to further work-up	91/102 (89%) 75% IV 25% no IV	3.3 (303/91)	26 (25%)	19/102 (19%)	15 (15%)	NA
Hellstorm et al. [7]	Referred to evaluate symptoms by colonoscopy	111	Known or suspected colorectal disease	Major, moderate and minor	Finding that has a definite or potential major clinical importance	94/111 (85%)	2.5 (232/94)	26 (23%)	14/111 (13%)	NA	NA

[a] Includes both subjects who underwent treatment as well as those who underwent subsequent imaging

wpopulation found that only 4% of patients had significant ECFs, but half of those were known previously by their referring physicians [15]. In a retrospective study on a mixed population of 749 female patients, the incidence of gynecologic ECFs was found to be 9.5%. Additional work up was done in 20% of these [18].

One meta-analysis found that the incidence of resectable extracolonic neoplasms found on CTC was 0.9%, which interestingly, is similar to the frequency of non-metastatic colon cancers detected by colonoscopy in asymptomatic adults [13]. Since surgery is invasive and costly, it is useful to know how often ECFs result in surgical intervention. Some studies have found that 0.2–2% of asymptomatic patients will undergo surgery for ECFs [4–6, 17]. The mean cost of additional workup incurred as a result of potentially significant ECFs (not including surgical expenses) have been estimated at $24–34 per patient [4, 5, 9, 10, 17], however, the costs for any individual patient, is high.

Hassan et al. modeled the benefit and cost of detecting extracolonic neoplasms and abdominal aortic aneurysms into CTC screening, and compared this strategy with optical colonoscopy and one-time screening ultrasound for visualization of the abdominal aorta (a test which is reimbursed by Medicare), in addition to the screening for adenomatous polyps [20]. The CTC model resulted in slightly more life years gained, but an incremental cost effectiveness ratio (ICER, as measured in quality life-years) that dominated the optical colonoscopy-ultrasound model. The additional cost-savings of the CTC approach were mostly due to the detection of aortic aneurysms (not cancers), and the colonoscopy-ultrasound model was more cost-effective only when the sensitivity of CTC for large polyps dropped to <61% [20].

In summary, ECFs are inevitable part of performing CTC, the majority of which will not require for further work up. The incidence of clinically significant (and previously unknown) findings warranting further evaluation ranges from 5% to 9% and the incidence of surgical intervention in the subset of patients with significant findings is about 2%. Overall, the average cost generated by reporting ECF is very low, but for the individual patient with an unwanted detection, the cost may be considerable. Cost-effectiveness studies are complex and additional analyzes are expected. However, we believe that the lower radiation doses currently in use diminish the detection of hypoattenuating lesions in the solid organs and thus improve the cost-effectiveness of reporting ECFs.

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Computer-Aided Diagnosis in Computed Tomographic Colonography

12

Kenji Suzuki and Abraham H. Dachman

Introduction

Computed tomographic colonography (CTC) is gaining acceptance as a method to screen the colon and rectum for polyps and masses, but there is a substantial learning curve [1, 2] and sensitivity remains variable [3]. Computer-aided diagnosis (CAD) has recently been referred to more often as "computer aided detection" and abbreviated CADe as distinct from CADx, which refers to features which differentiate benign from malignant lesions. CADe reflects the fact that the software is not making any histologically specific feature analyses, but only looking for polyp candidates. In this chapter the generic term "CAD" will be used with the understanding that it refers to CADe.

CAD has been proposed as a way to help readers [4–6] – particularly novice readers [7–9] achieve a high sensitivity without unduly reducing specificity or adversely impacting reading time [7–10]. Since many polyps missed by readers are often visible in retrospect [11], CAD is expected to help readers improve sensitivity. CAD has been shown in standalone studies to be sensitive for detecting polyps. A standalone study refers to analyzing how well the software detects polyps when compared with some standard of truth (e.g., an expert reader's opinion and/or optical colonoscopy). A standalone trial does not involve human readers reinterpreting the CTC exam with CAD. However, such reader studies are critical to demonstrate the practical value of CAD, since readers may accept or reject CAD marks and there is a potential for sensitivity and specificity to improve or deteriorate. Multiple-reader/multiple-case (MRMC) CAD trials to date have generally been either small patient cohorts or small numbers of readers often addressing a specific narrow question [4, 6, 8, 12–20], e.g., cost-effectiveness of CAD [21]. Only a few have been in low-prevalence cohorts [22] or large cohorts [10], although data from larger trials are only now becoming available and we believe CAD will gain acceptance in routine clinical practice. When looking at data on CAD, note that different CAD systems function differently and sensitivity and false positive rates of CAD cannot be "generalized" amongst fundamentally different software programs.

This chapter will cover CAD from both technical and clinical perspectives. This is a fast-moving field with new advances constantly emerging. This discussion will help provide an understanding of the issues surrounding CTC CAD. We will provide more detailed information about the CAD schemes developed in our department at the University of Chicago, and highlight important data from published trials using all available commercial and research software.

Why Should CTC Readers Use CAD and How Should It Be Used?

Most errors in CTC interpretation are related to failure to detect a polyp that is visible in retrospect [12]. CAD can be particularly helpful in finding polyp candidates ≥6 mm (the size threshold normally reported per guidelines of the CT Colonography Reporting and Data System [C-RADS]). Other errors of interpretation are related to mischaracterizing a polyp candidate as stool or fold. While CAD also employs classifiers to reduce false positive hits, polyp candidates which the human observer will find difficult to correctly characterize will often be difficult for CAD as well. Thus stool which lacks bubbly gas or homogenous tagging, is likely to be classified as a polyp by CAD. Thus the main value of CAD is to improve reader sensitivity, but without unduly reducing specificity or markedly increasing reading time.

Most researchers recommend that CAD be used in second-reader mode, i.e., read the case fully and then reveal the CAD hits. This will permit a less biased interpretation of the exam as compared with first revealing and evaluating the CAD hits and then reading the remained of the exam. Some vendors have advocated a "concurrent" CAD read, i.e., allowing the CAD hits to be revealed but suggesting that the

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reader perform a full read with the CAD marks showing. A "primary CAD read" means first looking only at the CAD hits, deciding which are true-positive (TP) hits and which are false-positive (FP) hits, after which the case is read to detect additional polyps. Either approach introduces some bias, but the primary read introduces the most bias and there is concern that it might discourage a genuine full read of the case. The reader using a secondary read mode is also aware that the CAD hits will be revealed shortly and thus might not perform a genuinely thorough read. One school of thought claims that it is important that a full read independent of the CAD output, be performed, in order to maximize the by-polyp sensitivity of the CTC exam. The incidence of synchronous polyps is significant and since some polyps are missed on optical colonoscopy as well, the radiologist reading CTC cannot simply rely on the fact that one polyp candidate ≥10 mm was found and that the patient will undergo OC. In our opinion, a full read of the CTC exam should be done, regardless of the CAD output.

CAD Schemes for Detection of Polyps in CTC

Several CAD schemes for the detection of polyps have been developed for improving the diagnostic performance of radiologists in CTC [23–25]. A CAD scheme automatically detects polyps in CTC and displays the locations of suspicious polyps for radiologists' review. CAD has the potential to (a) increase radiologists' diagnostic accuracy in the detection of polyps, (b) decrease reader variability, and (c) reduce radiologists' interpretation time when CAD is used as a first reader [20] or a concurrent reader [26]. An improvement in radiologists' detection performance can be achieved because CAD can reduce perceptual errors during the detection of subtle polyps. A decrease in inter- and intrareader variability can be achieved because CAD provides objective and consistent results, whereas the performance of a human reader may be influenced by skill and experience. In addition, a variety of circumstances, including distraction, fatigue, and time constraints in a busy clinical practice, may influence human diagnostic performance. Use of CAD can potentially overcome this lack of consistency by human readers and, potentially, decrease variability among readers in the identification of polyps on CTC. Observer studies on CAD in mammography [27, 28], chest radiography [29], and thoracic CT [30, 31] have demonstrated such a trend, especially by improving the performance of inexperienced radiologists. Some of these studies demonstrated an improvement in residents' performance with CAD to the level of attending radiologists [29]. Also, a reduction in the interpretation time can be achieved if radiologists focus only on the regions indicated by the CAD scheme (i.e., a first reader), or if radiologists focus mainly on the small number of regions indicated by the CAD scheme, and quickly review the large portion of the colon that is likely to be normal (i.e., a concurrent reader). A CAD scheme with a clinically acceptable level of performance is expected to improve radiologists' polyp detection performance and reader variability in CTC.

Technical Development of CAD Schemes

A diagram of a standard CAD scheme for the detection of polyps in CTC is shown in Fig. 12.1. The University of Chicago developed a fully automated CAD scheme for this purpose. The CAD scheme consists of knowledge-based extraction of the colon, shape-based detection of polyps [32], an initial reduction of FPs by use of quadratic discriminant analysis based on geometric and texture features [33, 34] and a mixture of expert 3D massive-training artificial neural networks (MTANNs) [35, 36] for further reduction of FPs. As a fundamental preprocessing technique for CAD of the colon, a method for segmenting the colon was developed. The colon segmentation method consisted of (1) anatomy-based extraction for masking of air and bone in CTC volumes, and (2) colon-based analysis for tracing the colon from the rectum to the ileum [32]. After the colon is segmented, polyp candidates in the colonic wall are identified by extraction of geometric features that characterize polyps. Polyps adhering to the colonic wall tend to appear as relatively small, bulbous, cap-like structures, and the colonic wall itself appears as a large, nearly flat, cup-like structure. For characterizing these shape differences, the volumetric shape index (SI) [37] was used [32]. The SI is calculated by using the Hessian matrix. This index determines to which of the following five topologic shapes an object belongs: cup, rut, saddle, ridge, or cap, as shown in Fig. 12.2. Polypoid polyps can be identified with the SI as a cap shape. Haustral folds can be identified as a saddle

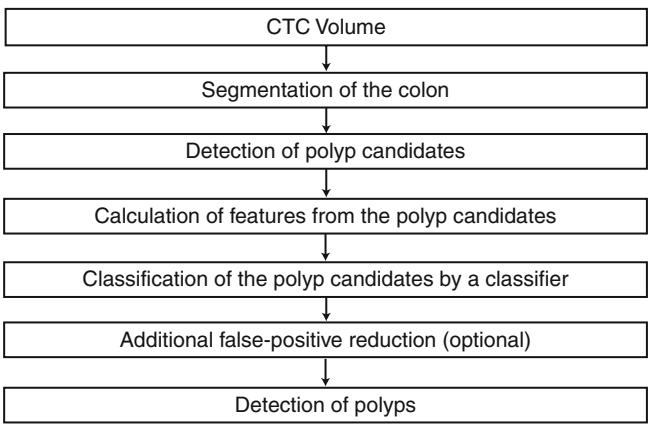

Fig. 12.1 Diagram of a standard CAD scheme for the detection of polyps in CTC

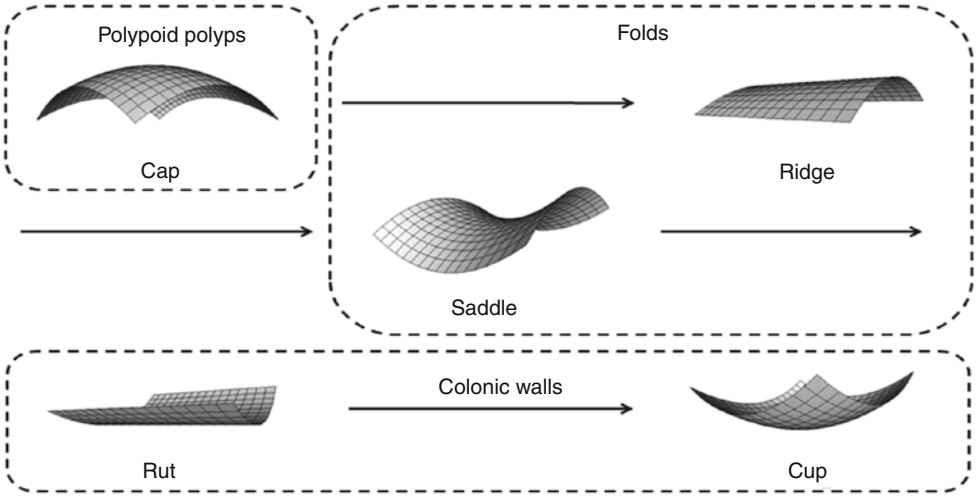

Fig. 12.2 Shape index (SI) for characterizing five different shapes. Polypoid polyps can be identified with the SI as a cap. Haustral folds can be identified as a saddle or ridge. Colonic walls can be identified as rut or cup

or ridge. Colonic walls can be identified as rut or cup. Quadratic discriminant analysis [38] with 3D geometric and textural features was used for classifying lesion candidates as polyps or nonpolyps. Quadratic discriminant analysis generates a decision boundary that optimally partitions the lesion candidates into a lesion class and a nonlesion class in feature space.

Researchers in other institutions have developed CAD schemes for polyp detection in CTC. Summers et al. [39] developed a CAD scheme based on the curvature of the surface of the colonic wall and a rule-based filter. Gokturk et al. [40] developed a CAD scheme based on statistical pattern recognition, and they applied a 3D pattern-processing method for reduction of FPs. Kiss et al. [41] reported on a CAD scheme based on convexity and sphericity and used a standard artificial neural network (ANN) for the reduction of FPs. Acar et al. [42] used edge-displacement fields to model the changes in consecutive cross-sectional views of CTC data and quadratic discriminant analysis for FP reduction. Jerebko et al. [43] used a standard ANN to classify polyp candidates in their CAD scheme and improved the performance by incorporating a committee of ANNs [44] and a committee of support vector machines [45]. Paik et al. [46] reported on a CAD scheme that employed a surface normal overlap method. Thus, most CAD schemes follow the framework of the standard CAD scheme shown in Fig. 12.1.

False-Positive Reduction in a CAD Scheme

Although current CAD schemes could be useful for the detection of polyps, some limitations still exist in CAD development. Some lesions will always be difficult for CAD to detect, so some CAD false negatives will always be found (Fig. 12.3). One of the major limitations with current CAD schemes is a relatively large number of FPs, which could adversely affect the clinical application of CAD for colorectal cancer screening. A large number of FPs is likely to confound the radiologist's task of image interpretation and thus lower the radiologist's efficiency. In addition, radiologists may lose their confidence in CAD as a useful tool. Therefore, it is important to reduce the number of FPs as much as possible while maintaining a high sensitivity.

Overview of FP Reduction Techniques

Various methods have been developed for the reduction of FPs. Gokturk et al. [40] developed a 3D pattern-processing method for reduction of FPs. Näppi et al. [33] developed a method for FP reduction based on volumetric features and another method based on supine-prone correspondence [47]. Acar et al. [42] used quadratic discriminant analysis for FP reduction in their CAD scheme. Jerebko et al. [43] used a standard ANN to classify polyp candidates in their CAD scheme and improved the performance by incorporating a committee of ANNs [44] and a committee of support vector machines [45]. Iordanescu et al. [48] developed an image-segmentation-based approach for the reduction of FPs due to rectal tubes. A method for the reduction of FPs caused by the ileocecal valve was developed by Summers et al. [49, 50] Wang et al. [51] described an FP reduction method based on internal features of polyps, whereas Suzuki et al. [35, 36] used an FP reduction technique called a mixture of expert 3D MTANNs to reduce various types of FPs such as rectal tubes, stool, haustral folds, and the ileocecal valve.

FP Reduction with 3D MTANNs

To reduce various types of FPs produced by a CAD scheme, Suzuki et al. developed a mixture of expert 3D MTANNs [35, 36]. The architecture of a mixture of expert 3D MTANNs is shown in Fig. 12.4. Each expert 3D MTANN

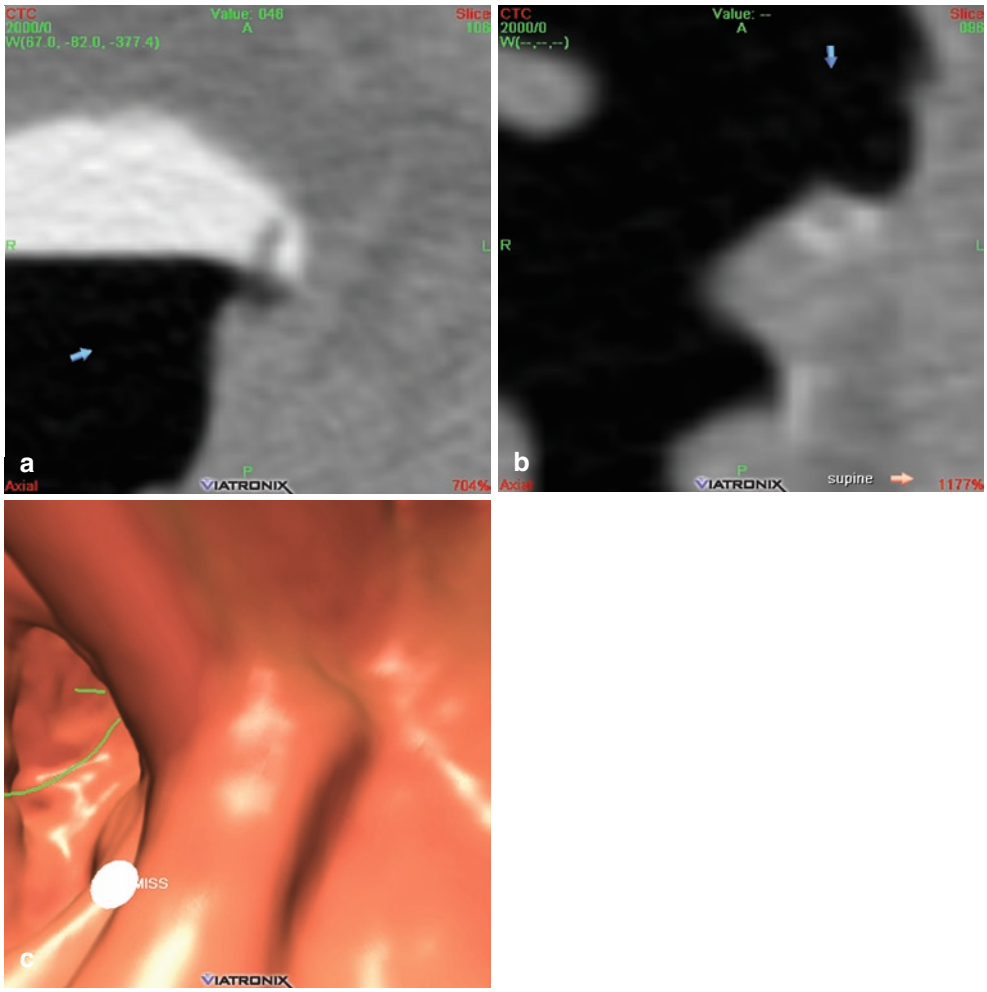

Fig. 12.3 Example of a CAD false negative. Prone axial image (**a**) from a CTC done with oral contrast tagging shown in soft tissue window setting, shows a small, linear filling defect (*arrow*) representing an endoscopically proven polyp. This polyp is seen on the supine view (**b**) coated with contrast (*arrow*).The contrast appears to coat the polyp circumferentially due to partial volume effect. The accompanying supine 3D view (**c**) shows this small polyp (*arrow*) on a fold. It was missed by CAD on both views due to its size

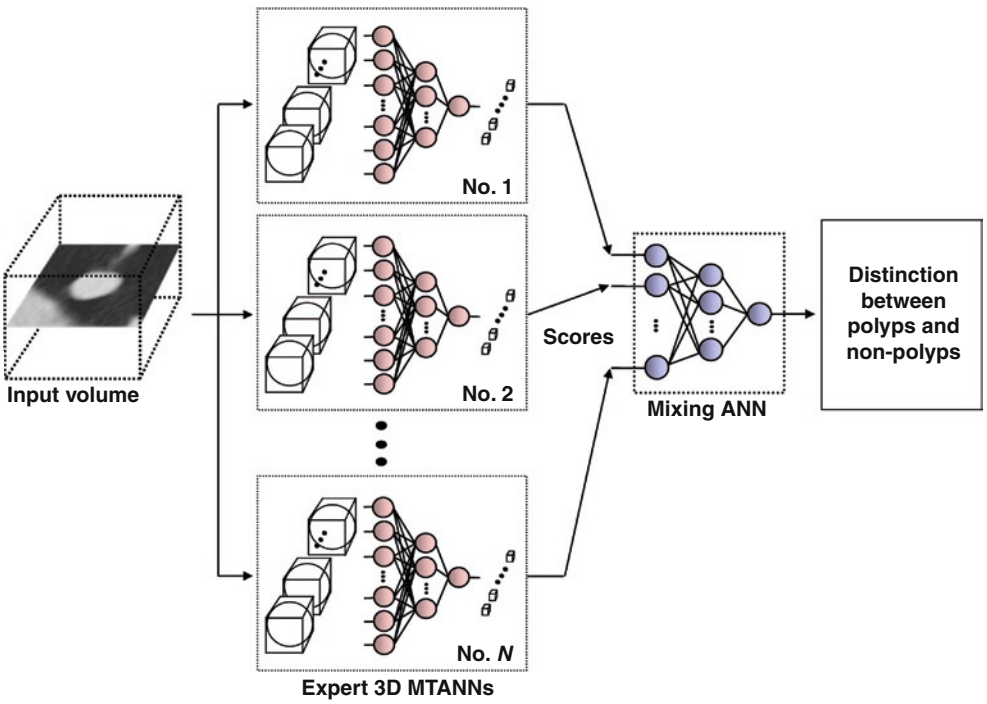

Fig. 12.4 A mixture of expert 3D MTANNs for distinguishing lesions (polypoid and flat lesions) from various types of FPs. Each expert 3D MTANN consists of a linear-output regression ANN model. Each MTANN is an expert for distinguishing lesions from a specific type of FP. The outputs of the expert 3D MTANNs are combined with a mixing ANN so that the mixture of expert 3D MTANNs can remove various types of nonlesions

[52] consists of a linear-output regression ANN model [53, 54]. The 3D MTANN is trained with input CTC volumes and the corresponding teaching volumes for enhancement of polyps and suppression of nonpolyps. The input of the 3D MTANN is the voxel values in a subvolume extracted from an input CTC volume. The output of the 3D MTANN is a continuous value, which corresponds to the center voxel in the subvolume. For enhancement of polyps and suppression of nonpolyps in CTC volumes, the teaching volume contains the 3D distribution for the "likelihood of being a lesion." The teaching volume for a polyp contains a 3D Gaussian function. The teaching volume for nonpolyps contains all zeroes. The structure of each MTANN may be designed by a method for determining the optimal structure of an ANN [55, 56]. The mixture of expert MTANNs consists of several 3D MTANNs, each of which is specifically designed for removing a specific type of FP, as show in Fig. 12.4. Each of the 3D MTANNs is trained independently with a different type of FPs and typical polyps. The 3D MTANNs are combined with a mixing ANN such that all major sources of FPs such as haustral folds, stool with bubbles, colonic walls, bulbous-shape folds, stool and blunted folds, and solid stool can be removed.

Suzuki and colleagues at the University of Chicago applied their CAD scheme without 3D MTANNs to 73 CTC cases, including 15 patients with 28 polyps ≥5 mm. This CAD scheme achieved a 96.4% by-polyp sensitivity (100% by-patient sensitivity) with an average of 3.1 FPs per patient. The trained expert 3D MTANN was then applied to the polyps and to 224 FPs identified by our initial CAD scheme. The output volumes for these testing cases are shown in Fig. 12.5. Various polyps are represented in the output by distributions of bright voxels, whereas various types of nonpolyps appear as darker voxels, indicating the ability of the expert 3D MTANNs to enhance polyps and suppress different types of non-polyps. To distinguish between polyps and FPs, the scores from the four individual expert 3D MTANNs were merged with a mixing ANN. The overall performance of the mixture of expert 3D MTANNs was evaluated for FP reduction by use of free-response receiver operating characteristic (FROC) analysis [57]. The FROC curve of the trained mixture of expert 3D MTANNs is shown in Fig. 12.6. This FROC curve indicates that the mixture of expert 3D MTANNs was able to eliminate 63% of nonpolyps (FPs) without removal of any of the polyps, i.e., a 96.4% overall by-polyp sensitivity (100% by-patient sensitivity) was achieved at an FP rate of 1.1 per patient. Therefore, the MTANN was able to remove FPs substantially without reduction in the number of true positives. Thus, this CAD scheme achieved a by-polyp sensitivity of 96% with a FP rate of 1.1 per patient.

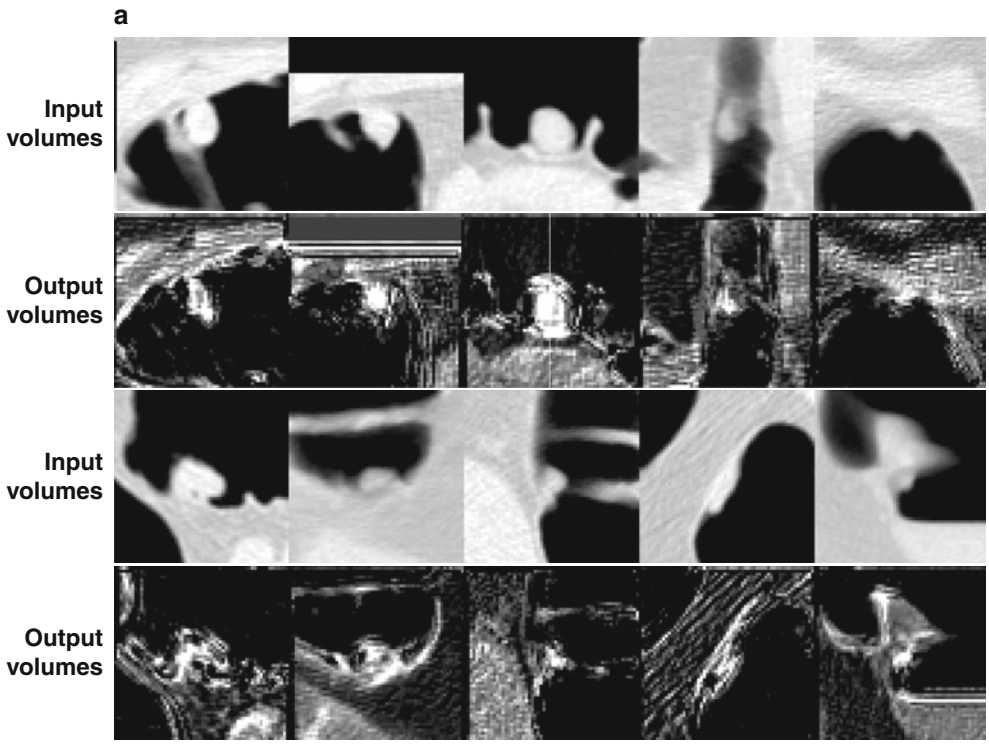

Fig. 12.5 Illustrations of (**a**) various testing polyps and the corresponding output volumes of four trained expert 3D MTANNs, and (**b**) four different categories of testing FPs and the output volumes from the corresponding expert 3D MTANNs. In the output volumes, polyps appear as distributions of bright voxels (i.e., they are enhanced), whereas different types of FPs appear as dark voxels (i.e., they are suppressed)

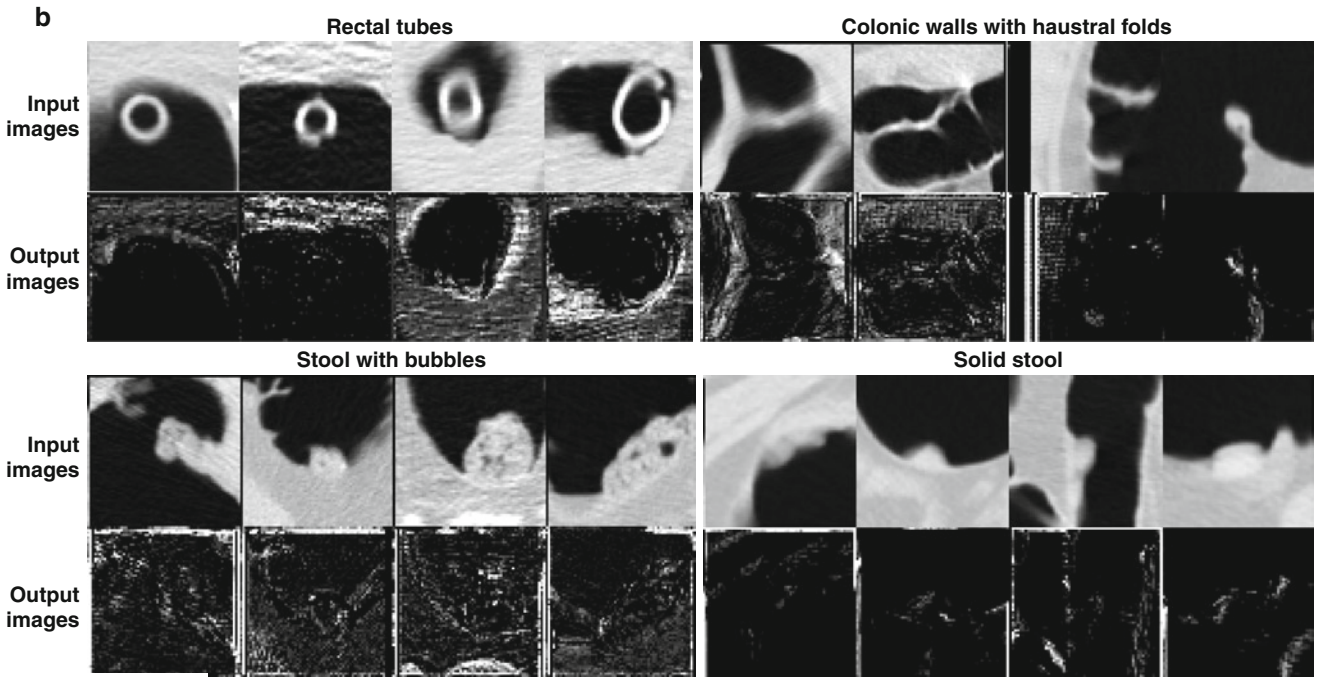

Fig. 12.5 (continued)

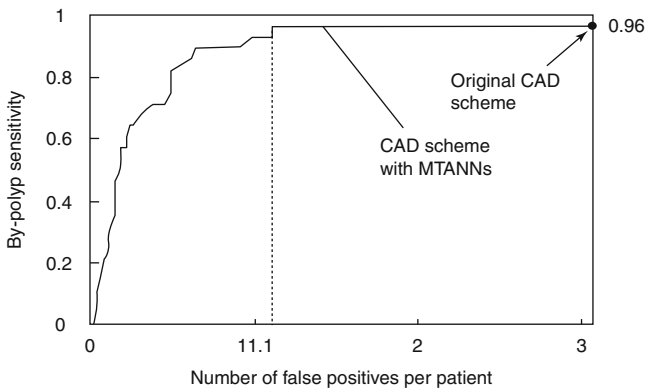

Fig. 12.6 The FROC curve that shows the overall performance of the mixture of expert 3D MTANNs when it was applied to the entire database of 27 polyps and 224 FPs. The FROC curve indicates that the mixture of expert 3D MTANNs yielded a reduction of 63% of nonpolyps (FPs) without removal of any true positives, i.e., it achieved 100% classification performance

Stand-Alone Performance of CAD Schemes

CAD Schemes Developed in Academia

Academic institutions have developed prototype CAD schemes and reported their stand-alone performance. Summers et al. [39] reported a curvature-based CAD scheme applied to both simulated polyps [58] and actual polyps [39]. Their CAD scheme yielded a sensitivity of 64% with a FP rate of 6 per colon in the evaluation of a 20-patient database with 28 polyps ≥10 mm. Summers et al. [59] applied their improved CAD scheme to a screening cohort of 792 patients including 95 patients with 119 adenomas ≥6 mm. Their scheme yielded by-polyp sensitivities of 61.3%, 80.8%, and 89.3% (by-patient sensitivities of 75.8%, 87.2%, and 89.3%) for adenomas at the 6, 8, and 10 mm size thresholds with FP rates of 7.9, 6.7, and 2.1 per patient, respectively. More recently, Summers et al. [60] tested their CAD scheme on a cohort of 86 adenomas in 75 patients. Their CAD system yielded by-polyp sensitivities of 91.5% for adenomas ≥10 mm and 82.1% for adenomas 6–9 mm (by-patient sensitivities were 97.6% and 82.4%, respectively). The mean and median false-positive rates were 9.6 and 7.0 per patient, respectively. Kiss et al. [41] reported that their convexity-and-sphericity–based CAD scheme yielded a by-polyp sensitivity of 80% with 8.2 FPs per patient for a database of 18 patients, with 15 polyps ≥5 mm in nine patients. Jerebko et al. [43] found that their CAD scheme based on a committee of ANNs yielded a sensitivity of 90% with 30.4 FPs per patient, based on 40 patients, with a total of 39 polyps ≥3 mm in 20 patients. In a separate study, the same investigators noted that the use of multiple ANNs improved the sensitivity by an average of 6.9% and decreased the FP rate by 36% [44]. Paik et al. [46] reported that their surface-normal-overlap-based CAD scheme yielded a sensitivity of 100% with 7.0 FPs per data set based on eight patients (supine scans only), which included a total of seven polyps ≥10 mm in four patients. Kim et al. [61] reported a Hessian matrix-based algorithm in a well-described cohort in which data were stratified by size and histology. When retrospective review by radiologists'

consensus was used to define truth in that cohort (similar to the approach in our study), 40 polyps ≥6 mm were evaluated and the CAD was 92.5% sensitive by polyp and 91.7% sensitive by patent with 5.5 FPs per patient [61].

Thus, the stand-alone performance of CAD schemes in academia ranges between by-polyp sensitivities of 60% and 96% (by-patient sensitivities of 70% and 100%) for polyps ≥6 mm, with 1 to 31 FPs per patient, based on 7–119 polyps in 8–95 patients.

Industry (Nonacademic) CAD Software

Peer-reviewed stand-alone performance data in patient cohorts which include all polyp morphologies are known for only a few CAD systems [5, 59, 61]. Bogoni et al. used the Syngo Colonography Polyp Enhanced View (PEV) system (Siemens Healthcare, Inc.) and a test set of 62 cases with 39 polyps but the data were not stratified by histology and the FP rate was 3 per series. The same software was tested on a small specialized cohort of only nonpolypoid lesions [6], in small clinical observer trials [7, 62] and in anthropomorphic phantom studies [63]. Fletcher et al. [62] compared the performance of a commercial CAD system (PEV, Siemens Healthcare, Inc.) with that of an academic CAD system (developed by Summers et al. at the National Institutes of Health) on the same cohort of 65 patients, including 31 positive cases with 36 polyps ≥6mm and 34 negative cases. The commercial CAD system yielded a sensitivity of 56% with 1.2 FPs per patient, whereas the academic CAD system yielded a sensitivity of 83% with 5.2 FPs per patient. Another system that has undergone several clinical investigations is ColonCAD™ (Medicsight, Inc.) [26], which has only limited stand-alone data described in small or specialized cohorts [13, 19]. Non-peer reviewed recent reports describe the current version of this system to have a 6–9 mm and ≥10 mm by polyp sensitivity of 90% and 92%, respectively, and a by patient mean FP rate of 6.5 [64]. One CAD-like system (i.e., without detailed claims of sensitivity and specificity), Virtual Colonoscopy Computer Assisted Reader (CAR® by Philips Medical Systems, Inc.), has partial reporting of stand-alone data incorporated into an observer trial in a cohort of 170 patients in which CAD detected 72% (42/58) of the 6–9 mm polyps and 60% (18/30) of the polyps ≥10 mm; however, the data were not stratified by histology or morphology and number of false positives was not reported [65].

In evaluation of iCAD, Inc. VeraLook version 1.0, Dachman et al. [66] reported an overall patient level sensitivity of 91.8% and an overall polyp level sensitivity of 86.3% with an average of 4.59 FP marks per view based on testing 355 patients, including 184 patients with 271 polyps ≥6 mm. The average number of false marks was 4.08 per view for all 171 negative patients with no polyps >6 mm. These high sensitivities were maintained for small and large polyps, adenomas, and nonadenomas. This system detected 93.2% of adenomas that are most clinically relevant at ≥10 mm in size.

Evaluation of a CAD Scheme with Reader Trial False-Negative CTC Cases

One of the limitations of current CAD research is a lack of evaluation of "difficult" polyps, particularly those which radiologists failed to detect by using standard techniques. Most previously reported studies used polyps detected by radiologists in CTC (i.e., human true-positive polyps). CAD benefits cannot be fully evaluated based on such TP polyps because these polyps are likely to be detected by radiologists without CAD.

To evaluate the stand-alone performance of a CAD scheme with FN polyps, Suzuki and colleagues collected a database consisting of CTC scans obtained from a previous multicenter clinical trial [67] that included an air-contrast barium enema, same-day CTC and colonoscopy, and segmental unblinding for each subject, followed by robust reconciliation of all lesions by utilization of the data from all three imaging examinations. Six hundred and fourteen high-risk subjects participating in the original trial were scanned in both supine and prone positions with a multidetector-row CT system. The reference standard was a final reconciliation of the unblinded lesions identified on all of the three examinations. In the original trial, 155 patients had 234 clinically significant polyps ≥6 mm. Among them, 69 patients had FN interpretations (i.e., the by-patient sensitivity was 55%). These patients had 114 "missed" polyps/masses which were not detected by reporting radiologists during their initial clinical reading. Causes of errors included observer errors, i.e., perceptual and measurement errors (51%), technical errors (23%), and nonreconcilable (26%) [11]. The perceptual errors are associated with polyps that failed to be detected by observers. The measurement errors refer to the errors associated with undermeasurement of polyp size compared with colonoscopy findings as the reference standard. In the studies detailed below, Suzuki and colleagues focused on FN cases with observer errors, because the aim of CAD is to prevent such errors.

The inclusion criterion for this study required that each case had at least one "missed" polyp due to the perceptual error. As a result, we obtained 24 FN cases with 23 polyps and one mass. An experienced radiologist reviewed CTC cases carefully and determined the locations of polyps with reference to colonoscopy reports. Polyp sizes ranged from 6–15 mm, with an average of 8.3 mm. The mass size was 35 mm. Among them, 14 lesions were adenomas. The

radiologist determined the difficulty of detection for each polyp/mass as difficult, moderate, or easy. The radiologist also determined the morphology of each polyp.

CAD Stand-Alone Performance for Reader Trial False-Negative Cases

The initial polyp-detection scheme yielded a sensitivity of 63% with 21.0 FPs per patient. The 3D MTANNs [35, 36] removed many FPs, and our CAD scheme achieved a sensitivity of 58% (14/24) with 8.6 (207/24) FPs per patient for the 24 "missed" lesion cases, whereas the conventional CAD scheme with linear-discriminant analysis (LDA) instead of the MTANNs achieved a sensitivity of 25% at the same FP rate. There were statistically significant differences [57] between the sensitivity of the MTANN CAD scheme and that of the conventional LDA CAD scheme. Therefore, our MTANN CAD scheme has the potential to detect 58% of "missed" polyp/mass cases with a reasonable number of FPs [68].

Among the 24 polyps/mass, 17 polyps, 6 polyps, and 1 mass were classified as difficult, moderate, and easy, respectively. Among the 23 polyps, 12, 9, and 2 were categorized as sessile, sessile on a fold, and pedunculated, respectively. Figure 12.7 illustrates FN polyps detected by our MTANN CAD scheme. All three examples were graded as difficult to detect. It was expected that the MTANN CAD scheme would be helpful in the detection of "difficult" polyps.

Analysis of Stand-Alone CAD FP Sources

FPs were reviewed and identified the sources of error, as summarized in Table 12.1. Forty percent of the FPs were related to flexural pseudotumors or folds comprising converging folds, haustral folds, and tenia coli. Thirty-two percent of the FPs were considered to be related to stool artifact. Six percent of the FPs were located in the small bowel and were therefore attributed to segmentation error and were not analyzed further. Collapsed colon segments and rectal tubes accounted for 5% each. The ileocecal-valve FPs accounted for 3%. The remaining 10% of the FPs were grouped in the miscellaneous category, which included respiratory motion, extrinsic compression, streak artifact, and compression by or interface with the rectal catheter retention balloon. Figure 12.8 illustrates examples of the FPs produced by our CAD scheme.

Stand-Alone Detection of Flat Neoplasms by CAD

Morphologically Flat Neoplasms (Flat Lesions) in CTC

Current efforts to prevent colorectal cancer focus on the detection and removal of polypoid polyps (i.e., polypoid neoplasms). Recent studies, however, have shown that colorectal cancer can also arise from flat colorectal neoplasms (also known as flat lesions, non-polypoid lesions, superficial elevated lesions, or depressed lesions) [69]. Flat lesions are more likely than polypoid polyps to contain in situ or submucosal carcinoma. One study has shown that flat lesions contributed to 54% of superficial carcinomas [62]. Flat lesions are also a major challenge for current "gold-standard" optical colonoscopy, because the subtle findings of these lesions can be difficult to distinguish from those for the normal mucosa [70]. Compared with the surrounding normal mucosa, flat lesions appear to be slightly elevated, completely flat, or slightly depressed. Although flat lesions were believed to exist primarily in Asian countries such as Japan [71, 72], recent studies have shown their significance in other parts of the world [73] such as the European countries [69] and the United States [74]. Flat lesions in the Western population, thus, may have been missed in current "gold-standard" optical colonoscopy

Table 12.1 Summary of the performance of CAD schemes by different institutions

Institution	No. of cases	No. of polyps	By-polyp sensitivity	By-patient sensitivity	No. of FPs/patient
U. of Chicago	73	28	96%	100%	1
Institution A	8	7	—	100%	14
Institution B	40	39	90%	—	31
Institution C	62	21	90%	—	6
Institution D	25	21	81%	—	13

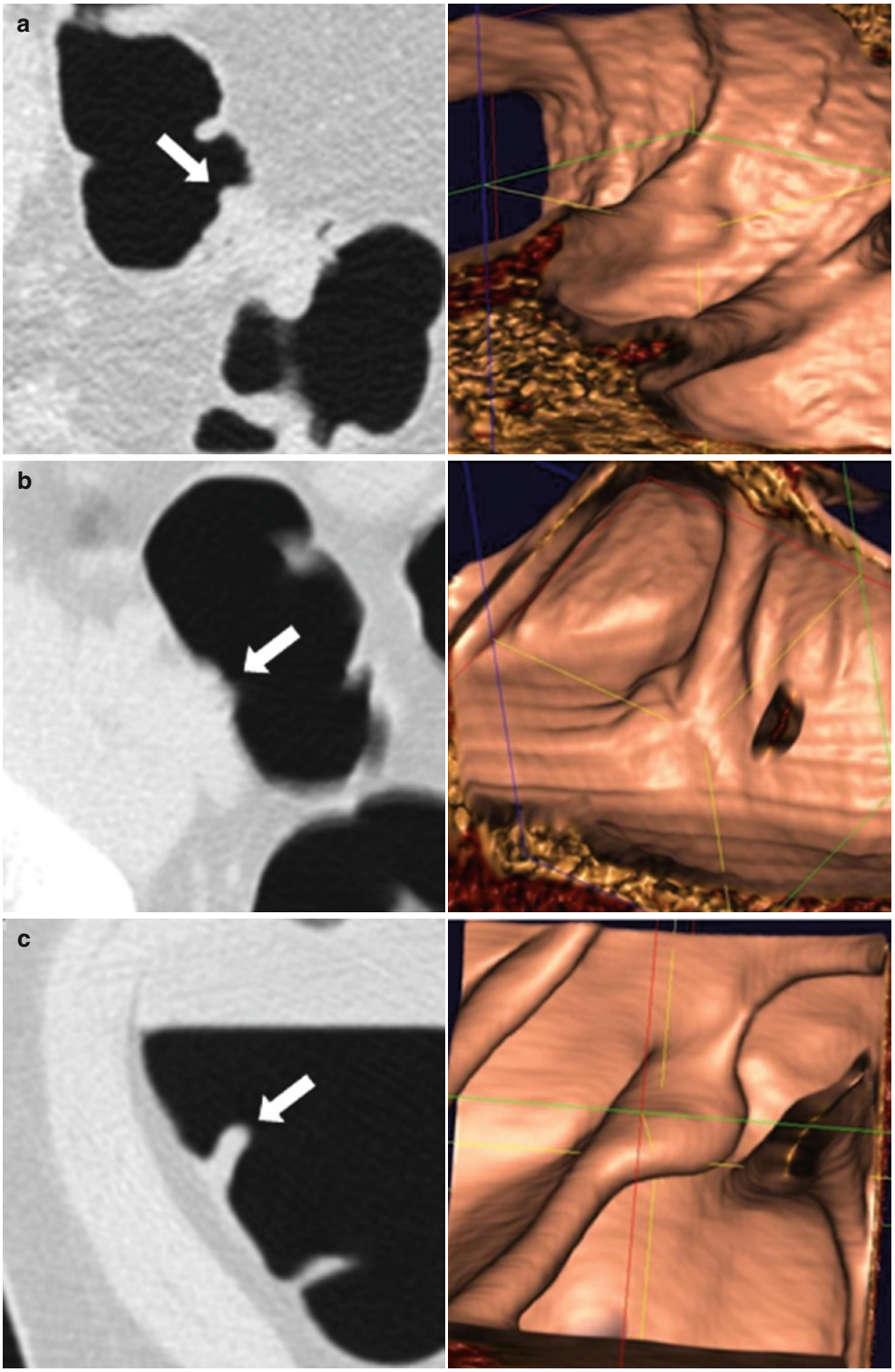

Fig. 12.7 Illustrations of polyps "missed" by reporting radiologists during initial reading in the original trial in 2D views (*upper images*) and 3D endoluminal views (*lower images*), which were detected by our MTANN CAD scheme. (**a**) A small polyp (6 mm hyperplastic) in the sigmoid colon was detected correctly by our CAD scheme (indicated by an *arrow*). This polyp was missed in both CTC and reference-standard optical colonoscopy in the original trial. (**b**) A small polyp (6 mm adenoma) in the sigmoid colon. (**c**) A sessile polyp on a fold (10 mm adenoma) in the ascending colon

[75]. Although the detection sensitivity of polyps in CTC is comparable to that in optical colonoscopy [76], flat lesions are a potentially major source of false-negative CTC interpretations in view of their uncommon morphology [77, 78]. Thus, detection of flat lesions in CTC is essential in colorectal cancer screening.

Limitations of Current CAD Schemes for Flat-Lesion Detection

Although current CAD schemes could be useful for detection of polypoid polyps, the detection of flat lesions is a

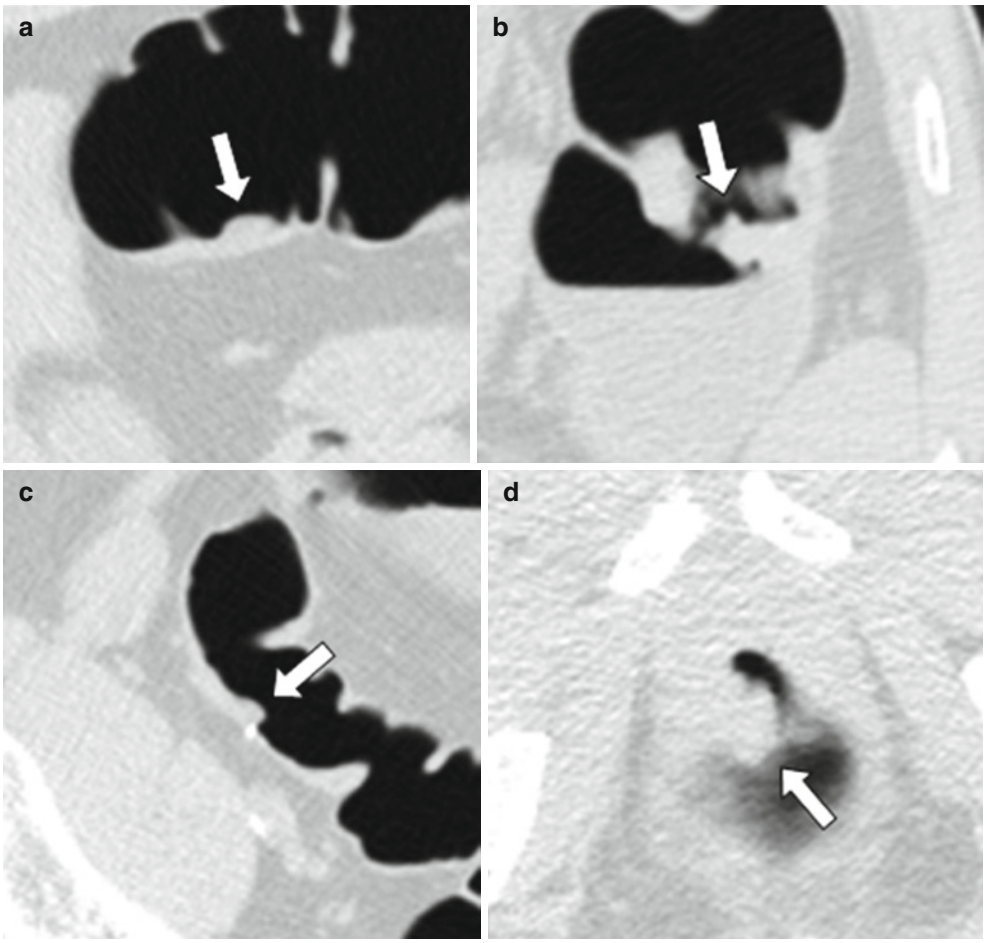

Fig. 12.8 Illustrations of FPs produced by our CAD scheme, which were categorized by subjective grading of ease. Moderate cases: (**a**) collapsed colon segment and a fold, and (**b**) stool. Difficult cases: (**c**) stool and (**d**) a hemorrhoid

major challenge [79], because existing CAD schemes have focused on the detection of pedunculated and sessile polyps; thus, they are designed for detecting the common polypoid shape. Existing CAD schemes use geometric, morphologic, and textural characteristics to distinguish polyps from normal structures in the colon (e.g., haustral folds, stool, the air/liquid boundary, the ileocecal valve, a rectal catheter). One of the most promising methods for doing this is to use the mathematical SI to characterize the shape of a polyp [32]. A polyp is characterized with the SI as a cap-like structure. Haustral folds and the colonic wall are characterized as saddle-like structures and cup-like structures, respectively. Thus, existing CAD schemes are not likely to detect flat lesions which exhibit a nonpolypoid shape.

Flat-Lesion Database

In order to create a flat-lesion database, an expert radiologist measured lesions on CTC images on a CTC viewing workstation (Vitrea 2 software, version 3.9, Vital Images, Minnetonka, MN) [80, 81]. Two-dimensional images were viewed with three tailored window/level settings: "lung," "soft tissue," and "flat." Magnified axial, coronal, and sagittal planes were reviewed in 2D for detection of the longest axis and maximal height of the lesion as seen on each data set (supine and prone). On a close-angle 3D endoluminal view, the lesion was viewed from various angles for first deciding on its borders. The longest axis and maximal height were measured on each data set. Comparison of 2D and 3D images before measurements were made were permitted for assessment of the lesion shape and borders in the same session, because this approach corresponds to the method that would be used in clinical practice when lesions are measured. Measurements of maximal thickness on the 3D volume-rendered views required the observer to make a subjective best estimate as to where to place the cursor.

Suzuki and colleagues analyzed data from the 3D endoluminal view and the 2D view in each of the three window/level settings to determine which measurements fit the definitions of "flat" lesions as determined by a "height" <3mm or a "ratio" of height <½ of the long axis. Based on the measurements of 50 CTC cases by a radiologist, they found 28 flat lesions in 25 patients (i.e., the prevalence of flat lesions we found was about 30%). Eleven flat lesions among the 28

lesions were not detected by reporting radiologists at their initial clinical reading in the original trial; i.e., these were "missed" lesions; therefore, they can be considered "very difficult" lesions to detect. Lesion sizes ranged from 6–18 mm with an average of 9 mm based on optical colonoscopy measurements.

Development of a 3D MTANN for Flat Lesions

To investigate the feasibility of a 3D MTANN in the detection of flat lesions, a 3D MTANN was applied to flat lesions in the flat-lesion database containing 28 flat lesions in 25 patients. The 3D MTANN was trained with sessile polyps (which are not flat lesions, but appear relatively flat compared with common bulbous polyps) in a different database and with various nonpolyps such as a rectal tube, haustral folds, the ileocecal valve, and stool, which are major sources of FPs. The trained 3D MTANN was applied to the 28 flat lesions in the flat-lesion database.

Evaluation of the Stand-Alone Performance of the MTANN CAD Scheme

The initial polyp-detection scheme without LDA yielded a 71% by-polyp sensitivity with 25 FPs per patient for the 28 flat lesions, including 11 lesions "missed" by the reporting radiologists in the original clinical trial. With LDA, 105 FPs were removed with loss of one TP, thus yielding 68% by-polyp sensitivity with 16.3 FPs per patient. The trained expert 3D MTANNs was applied for further reduction of the FPs. The 3D MTANNs were able to remove 39% of the FPs without removal of any TPs. Thus, this CAD scheme achieved a by-polyp sensitivity of 68% with 10 FPs per patient, including six of the 11 flat lesions "missed" by the reporting radiologists in the original trial. The MTANN CAD scheme detected 67% and 70% of flat lesions ranging from 6 to 9 mm and those ≥10 mm, respectively, including six lesions "missed" by the reporting radiologists in the original trial, with 10 FPs per patient.

Figure 12.9 shows examples of flat lesions which are very small or on a fold (these are major causes of human misses).

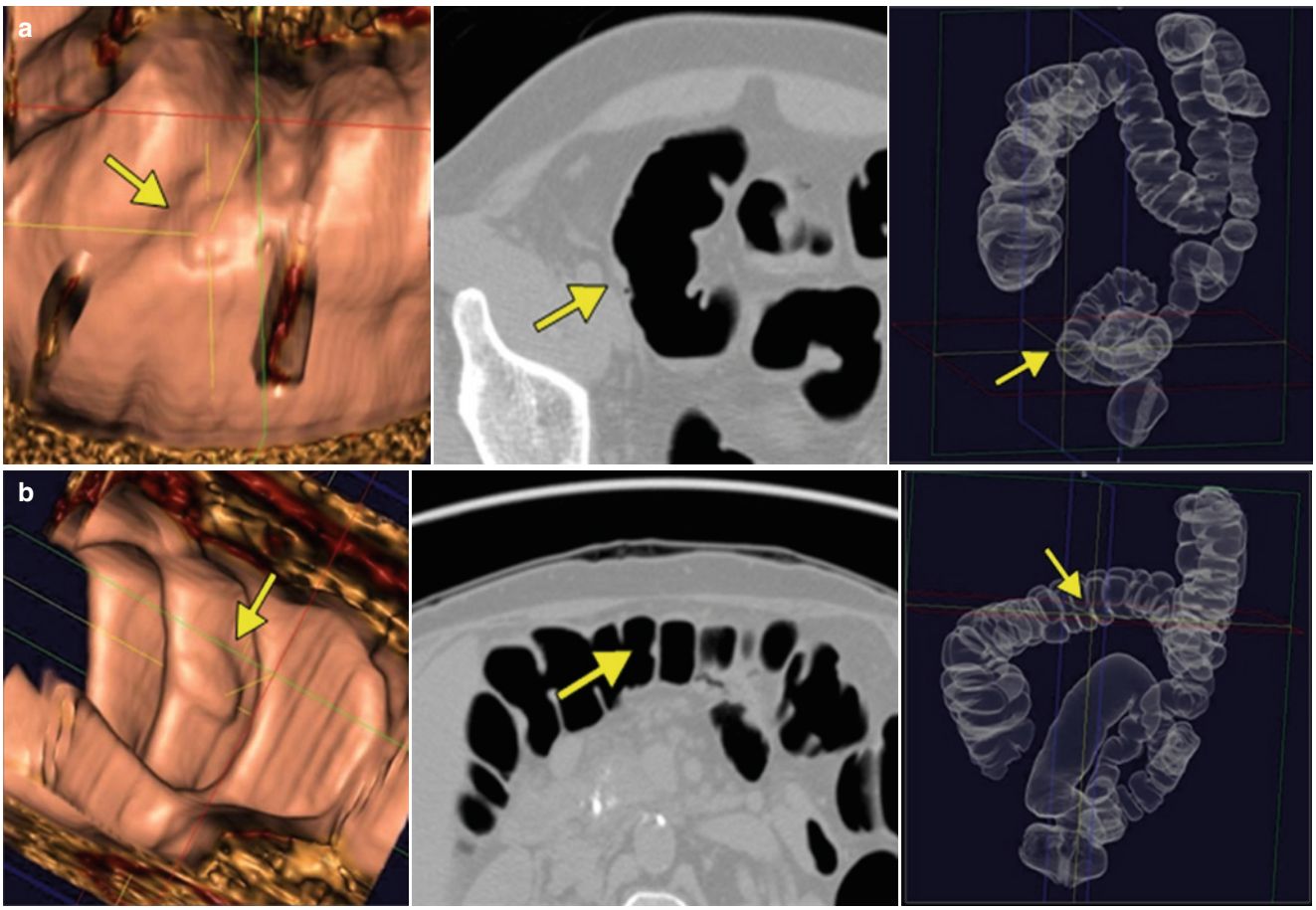

Fig. 12.9 Illustrations of flat lesions which were detected by our MTANN CAD scheme (From *left* to *right*: 3D endoluminal view, 2D axial view, and 3D transparent colon view). (**a**) A small flat lesion (6 mm adenoma) in the sigmoid colon was detected correctly by our CAD scheme (indicated by an arrow). This polyp was missed in CTC in the original trial. (**b**) A flat lesion (10 mm adenoma) on a fold in the transverse colon

Some flat lesions are known to be histologically aggressive; therefore, detection of such lesions is critical clinically, but they are difficult to detect because of their uncommon morphology. Our CAD scheme detected these "difficult" flat lesions correctly. It should be noted that these two cases were "missed" by the reporting radiologists in the original trial; thus, the detection of these lesions may be considered "very difficult."

Multi-reader/Multi-case (MRMC) Observer Performance Study

In reader studies, CAD has been shown not only to detect easy (Fig. 12.10) and difficult (Fig. 12.11) polyps, but to help detect polyps missed by readers (Fig. 12.12). Petrick et al. used a screening cohort with a subset of 60 patients for whom four readers used CAD in a second reader mode to analyze

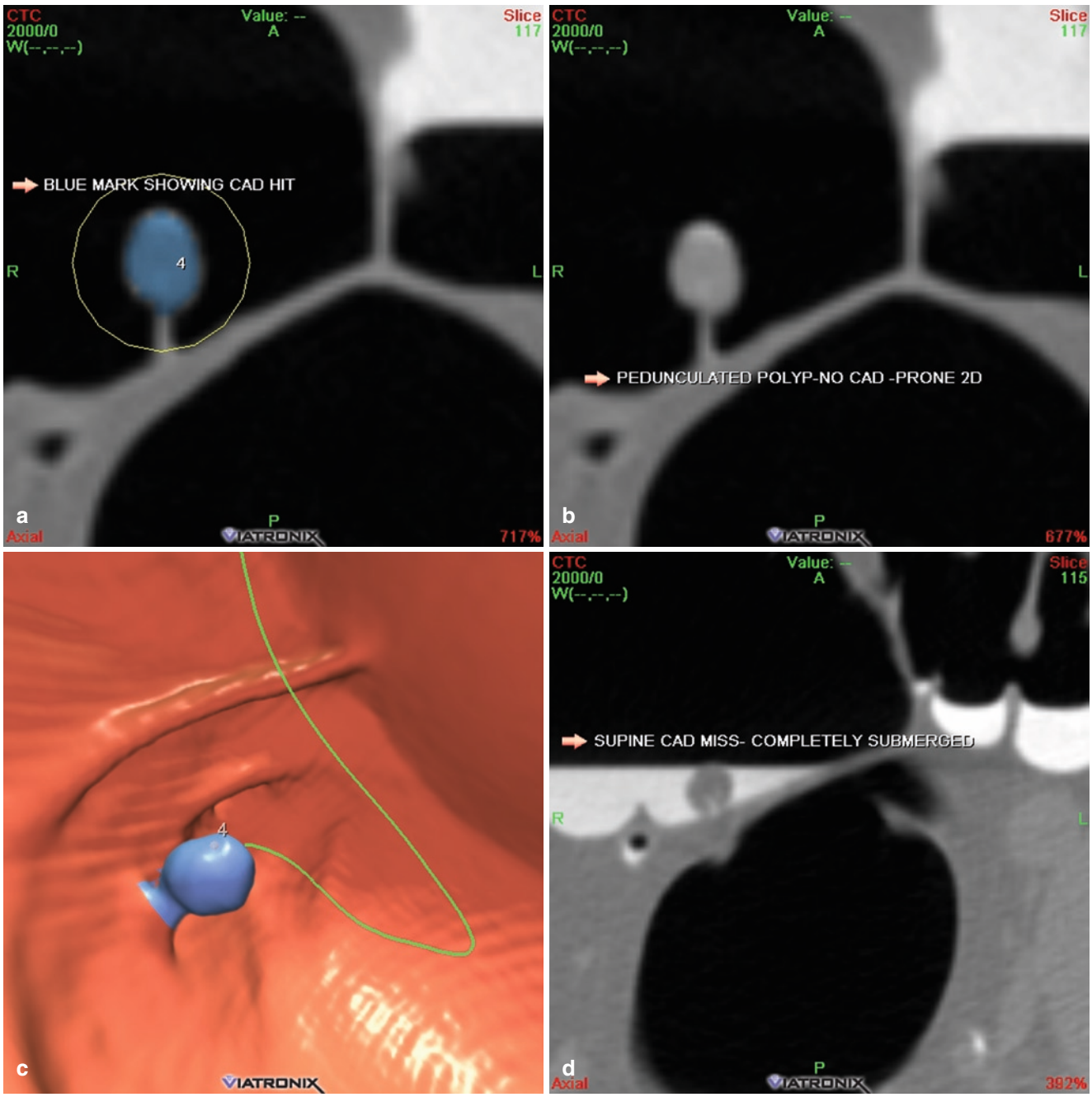

Fig. 12.10 Illustration of a polyp easily detected both by the reader and CAD. Prone, axial, magnified images in soft tissue window setting show a pedunculated polyp with (**a**) and without (**b**) CAD mark. The polyp is easily identified on 3D prone view (**c**).The polyp is seen as completely submerged in tagged fluid in supine, axial view (**d**). It was missed by CAD in supine view

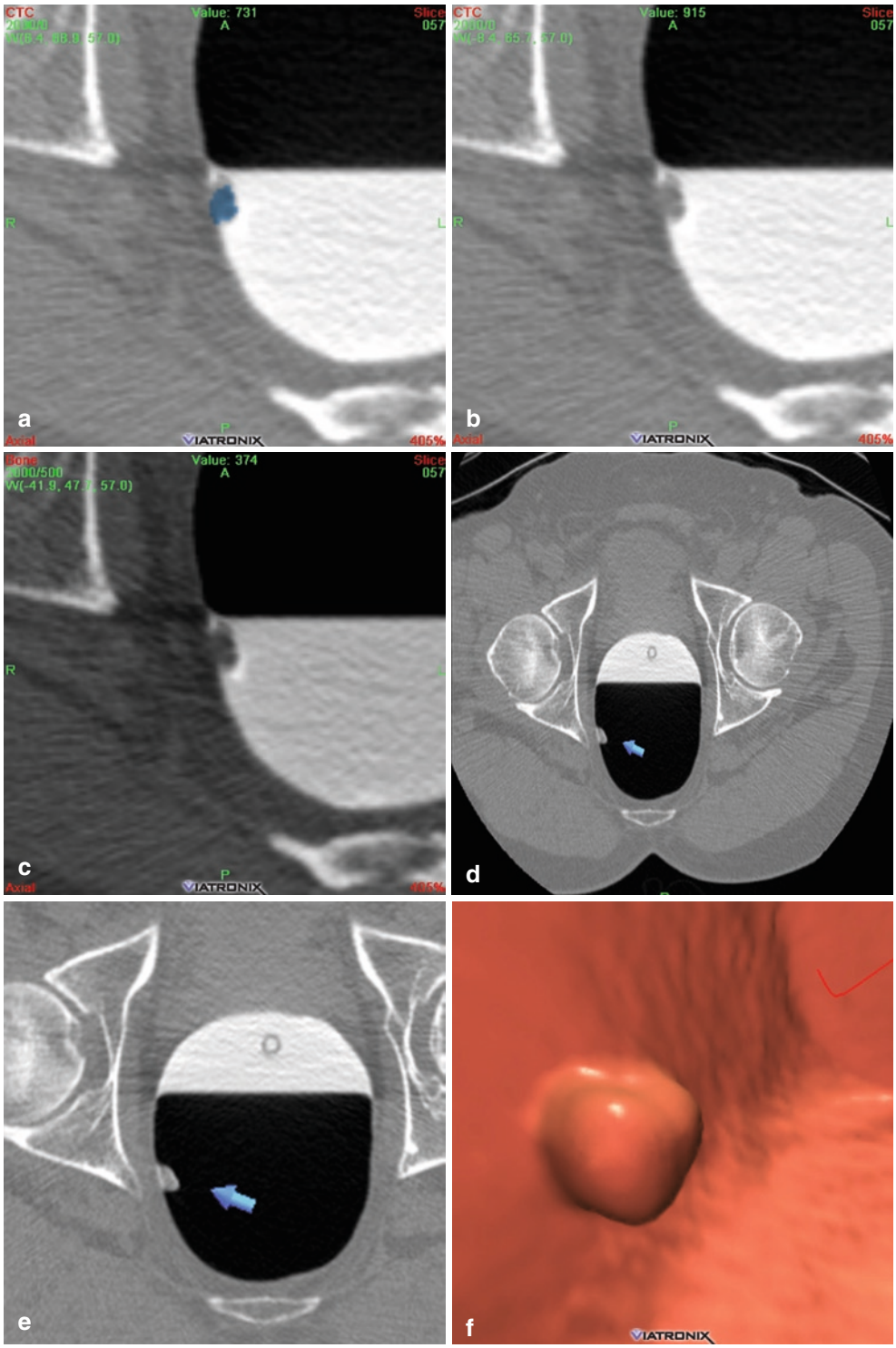

Fig. 12.11 Example of a difficult polyp detected both by the reader and CAD. Supine, axial, magnified images shown in soft tissue window setting show a completely submerged, slightly pedunculated polyp with (**a**) and without (**b**) CAD mark. The same polyp shown in bone window (**c**) could easily be confused for a lipoma. The corresponding prone, axial image (**d**) shows the polyp, not submerged, identified at 2.5 cm from the anal verge. Figure (**e**) is the magnified view of the same polyp. The polyp can be easily identified on a 3D prone view (**f**)

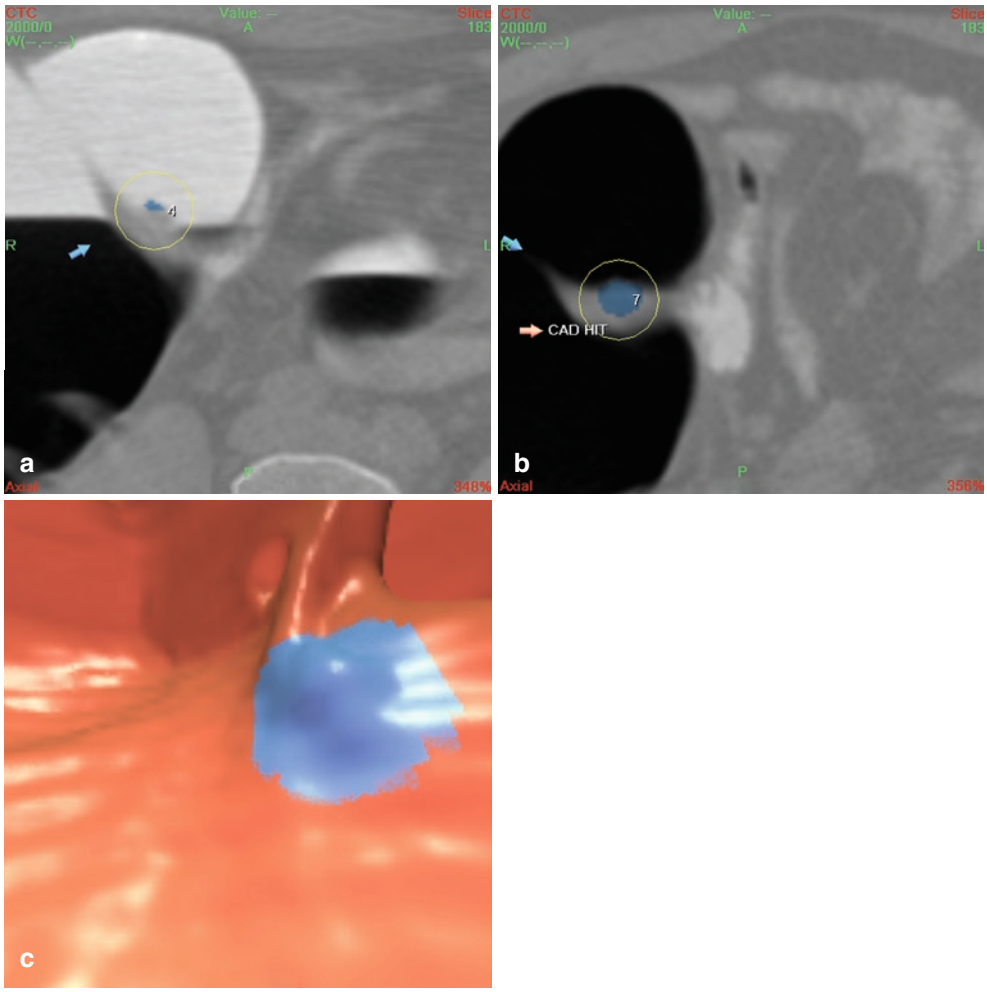

Fig. 12.12 Example of a reader false negative detected by CAD. Prone, axial 2D image (**a**) in soft tissue window setting, shows a CAD mark (*arrow*) completely submerged. On supine 2D (**b**) and 3D (**c**) a small sessile polyp can be identified (*blue mark*) on a fold. The polyp was missed by the reader in both supine and prone views probably due to its small size, presence on a fold, and location on the edge of tagged fluid

only neoplastic polyps (not all polyps) [11]. A significant improvement with CAD was found for the sensitivity of polyps in the ≥6 and 6–9 mm groups (in which CAD increased sensitivity by 0.15 and 0.16, respectively) with a corresponding decrease in specificity of 0.14. For the ≥10 mm group, the changes with CAD and area under the curve analysis did not achieve statistical significance.

Taylor et al. [26] evaluated ten radiologists who read 25 data sets containing 69 polyps in three reading modes: unassisted, CAD second read mode, and CAD concurrent read mode. They reported their key metric as an odds ratio of detecting a polyp ≥6 mm of 1.5 when using CAD in either mode and mean areas under the ROC curve for each of the three respective reading modes (at the 95% confidence interval) of 0.83, 0.86, and 0.88, respectively, and by-polyp sensitivities were 0.77, 0.83, and 0.81, respectively[26]. The five experienced readers had higher by-polyp sensitivities and higher FP rates than the five inexperienced readers, but all readers had higher sensitivities with CAD, and the by-patient sensitivities were not reported. While the baseline unassisted sensitivity was higher in that trial compared with ours, the improvement with CAD in our study is comparable or better, e.g., when comparing our average 0.84 increase in sensitivity for 6–9 mm adenomas (since no exact metrics are reported identically).

Taylor et al. [82] evaluated the effect of FPs of CAD on reader specificity and reading efficiency in a low-prevalence screening population. Four readers each read 48 data sets from a screening population, first without and then with a commercial CAD system (ColonCAD API, version 2.0; Medicsight). Data sets were divided into two groups: cases with 15 or fewer FP CAD marks (12.7 FPs per patient on average) and cases with more than 15 FP CAD marks (21.1 FPs per patient on average). Across all readers, CAD resulted in four additional FP detections. There was no correlation between an increasing number of CAD FP marks and reader confidence or correct study classification, but there was a positive correlation with CAD-assisted reading times.

Taylor et al. [83] investigated polyp characteristics correctly annotated by CAD but dismissed by readers. Among 111 polyps detected by CAD, 86 polyps that were missed by at least one of two readers without CAD were divided into those remaining unreported with CAD (no CAD gain, $n = 36$) and those reported correctly by at least one additional reader (CAD gain, $n = 50$). Their analysis showed that the odds of CAD gain decreased with increasing polyp size (odds ratio,

0.92) and irregular morphology (odds ratio, 0.28). Thus, larger irregular polyps are a common source of incorrect radiologist dismissal, despite correct CAD prompting.

In a recent large MRMC trial [66] using commercial software (VeraLook 1.0, iCAD, Inc.), a cohort of 100 colonoscopically proven cases was utilized: 52 positive cases had 74 polyps ≥6 mm in 65 colon segments; 48 negative cases had no polyps. Nineteen blinded readers interpreted each case at two different times, with and without the assistance of a commercial CAD system. The impact of CAD was assessed in segment-level and patient-level ROC curve analyses. The trial results showed the following: 13 of 19 readers (68%) demonstrated higher accuracy with CAD, as measured by the segment-level ROC area. The readers' average segment-level ROC area with CAD (0.758) was significantly greater (P = 0.015) than the average ROC area in the unassisted read (0.737). Readers' by-segment, by-patient, and by-polyp sensitivity for all polyps ≥6 mm was higher (P = 0.011, 0.007, 0.005 for readings with CAD compared with reading unassisted): 0.517 vs 0.465, 0.521 vs 0.466, and 0.477 vs 0.422). Sensitivity for patients with at least one large polyp ≥10 mm was also higher (P = 0.047) with CAD than without (0.777 vs 0.743). Average reader sensitivity also improved with CAD by >0.08 for small adenomas. Use of CAD reduced specificity of readers by 0.025(P = 0.050). These results showed significant improvement in several more parameters as compared with many prior reports such as Petrick et al. The authors concluded that the use of CAD resulted in a significant improvement in overall reader performance. CAD improves reader sensitivity when measured by segment, by-patient and by-polyp for small polyps and adenomas and also reduces specificity by a small amount. Note that important differences in the study designs when comparing this MRMC study with that of Petrick et al. include the large size of the cohort (100 cases), the large number of readers (19) including nonexperts, the inclusion of nonneoplastic polyps in the cohort and not excluding cases known to also contain polyps <6 mm in size, and the use of both primary 3D and primary 2D reading methods. When reading CTC the histology of a polyp is not known a priori and thus statistical analyses which include both all polyp histologies and a separate analysis of the target lesion of CRC screening, neoplasia (namely the adenoma and adenocarcinoma), is a reasonable study design when testing a CAD system.

University of Chicago Observer Performance Study (Prior Trial Cases Re-read)

To investigate the actual usefulness of CAD as a second reader, Suzuki and colleagues conducted a free-response (i.e., multiple responses/lesions per case are allowed) observer performance study with radiologists in the detection of "difficult" polyps from the clinical trial. For observer study cases, we selected "difficult" polyps which had been either "missed" by the reporting radiologists in the clinical trial or rated "difficult" in our retrospective review.

The database was obtained from the previous multicenter clinical trial that included an air-contrast barium enema as well as same-day CTC and optical colonoscopy[11, 67]. In the original trial, 155 patients had 234 clinically significant polyps (6 mm or larger). Among them, 69 patients had FN interpretations (i.e., the by-patient sensitivity was 55%). The 234 polyps were divided into 120 TP polyps and 114 FN polyps. An expert radiologist rated the 120 TP polyps as "easy," "moderate," and "difficult" to detect. The cohort selected consisted of 20 positive cases randomly from the cases with at least one "difficult" or FN polyp, including 13 FN patients with 14 FN polyps and seven TP patients with seven "difficult" polyps and two "easy" polyps. In addition, ten negative cases were randomly selected from 459 polyp-free patients.

The CAD system with MTANN technology [35, 36, 52, 68] was highly sensitive and specific to the "difficult" cases. The system achieved a sensitivity of 74% with 3.1 FPs per patient for the observer study database containing 20 patients with 23 polyps including 14 FN and seven "difficult" polyps and ten negative patients. The MTANN system achieved a sensitivity of 96% with 1.1 FPs per patient for TP cases[36]. The performance of our system in terms of various lesion characteristics is shown in Table 12.2. Flat lesions were identified under a "height" criterion (≤3 mm)[78, 79].

To investigate the usefulness of the advanced MTANN CAD system as a second reader, four board-certified abdominal radiologists (three CTC experts and one radiologist with >50 positive CTC cases read) participated. They read the 30 cases in the study database on a CTC workstation (Viatronix). They were asked, first without and then with CAD, to indicate the location of polyps and their confidence level regarding the presence of polyps. They were free to use 3D endoluminal or 2D multiplanar views for polyp detection and problem solving. They were blinded to the prevalence of polyps, but were told the general performance of our CAD. Figure 12.13 illustrates the interface for the integrated CTC-

Table 12.2 FP sources of our CAD scheme. Folds, flexural pseudo-tumors, and stool are major sources of FPs

FP source	No. of FPs
Folds or flexural pseudo-tumors	25 (40%)
Stool	20 (32%)
Small bowel	4 (6%)
Collapsed colon	3 (5%)
Rectal tubes	3 (5%)
Ileocecal valves	2 (3%)
Miscellaneous sources	6 (10%)

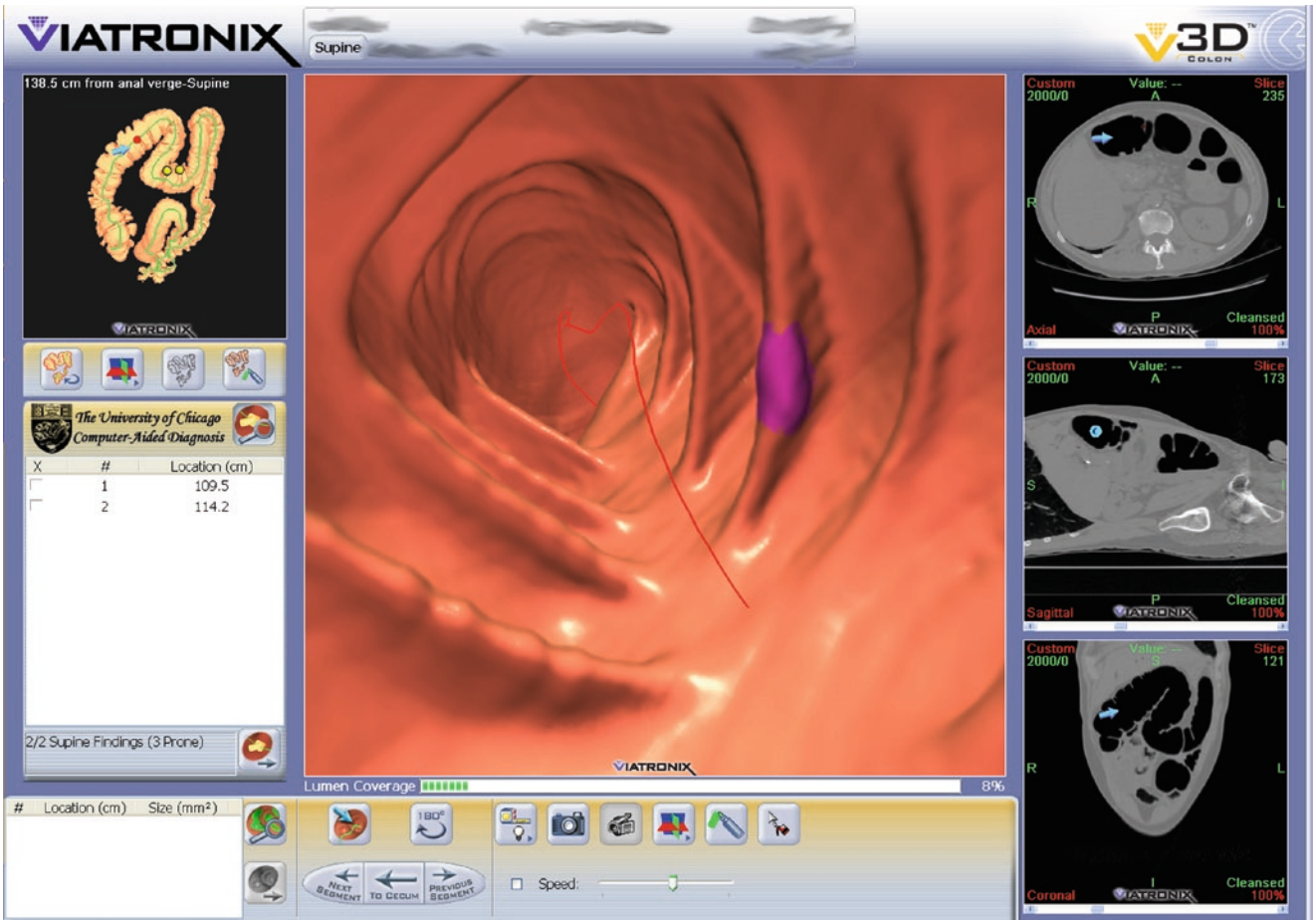

Fig. 12.13 Interface for the integrated CTC-CAD workstation. The centerline of the colon is determined automatically (*green line in the upper left panel*). Along the centerline, the workstation lets the radiologist navigate through the colon so that he/she can check the entire colon efficiently (*central panel*). CAD marks for suspicious polyps are displayed on the segmented colon view (*upper left panel*). When the radiologist clicks on the CAD detection in the *lower left panel*, the software quickly brings him/her to the CAD detection location, which is *highlighted in pink* in the endoluminal view (*central panel*), as well as three multiplanar reconstructed views (*three right panels*). Thus, the radiologist can focus on the small number of regions indicated by the CAD, so that he/she does not have to examine, or needs only quickly to survey, a large portion of the colon that is likely to be normal

CAD workstation, where our CAD scheme is incorporated into the CTC viewing workstation.

Each radiologist had a gain in the by-polyp sensitivity and in the positive predictive value (PPV) with CAD, as shown in Fig. 12.14. Table 12.3 summarizes the results of this MRMC observer study. With CAD, the average by-polyp sensitivity of radiologists was improved from 53% (47% for polyps 6–9 mm; 66% for polyps ≥10 mm) to 63% (60% for polyps 6–9 mm; 69% for polyps ≥10 mm) at a statistically significant level (P = .037). The PPV was also improved from 57% to 67% with CAD (P = .098). The average figure of merit (i.e., the area under the curve) in jackknife alternative free-response ROC analysis [84] was statistically significantly improved from 0.79 to 0.83 (P = .006). The average reading time without and with CAD was 12 and 2 min per case, respectively. Figure 12.15 illustrates polyps missed by two radiologists without CAD but detected with CAD. Small lesions and flat or sessile lesions were major sources of reader FNs. Figure 12.16 illustrates nonpolyps erroneously detected by a radiologist with CAD. These are pitfalls in the use of CAD.

Table 12.3 Summary of the results of the observer performance study

	w/o CAD	w/ CAD	Gain
Sensitivity (by polyp)	53% (±16%)	63% (±12%)	10% (±6%)*
PPV (by patient)	57% (±8%)	67% (±1%)	10% (±8%)
Figure of merit$^{(JAFROC)}$	.79 (±.05)	.83 (±.05)	.04 (±.01)*
Time (min.)	12 (±7)	2 (±2)	

*Difference was statistically significant (P<.05)

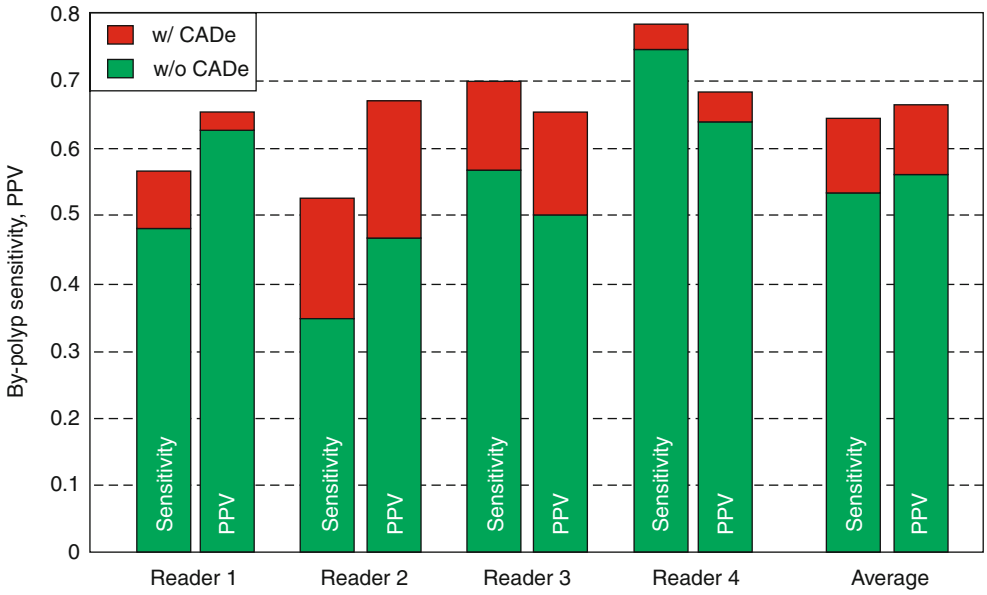

Fig. 12.14 Effect of CAD on the sensitivity and PPV of each individual radiologist and average effect for the four radiologists

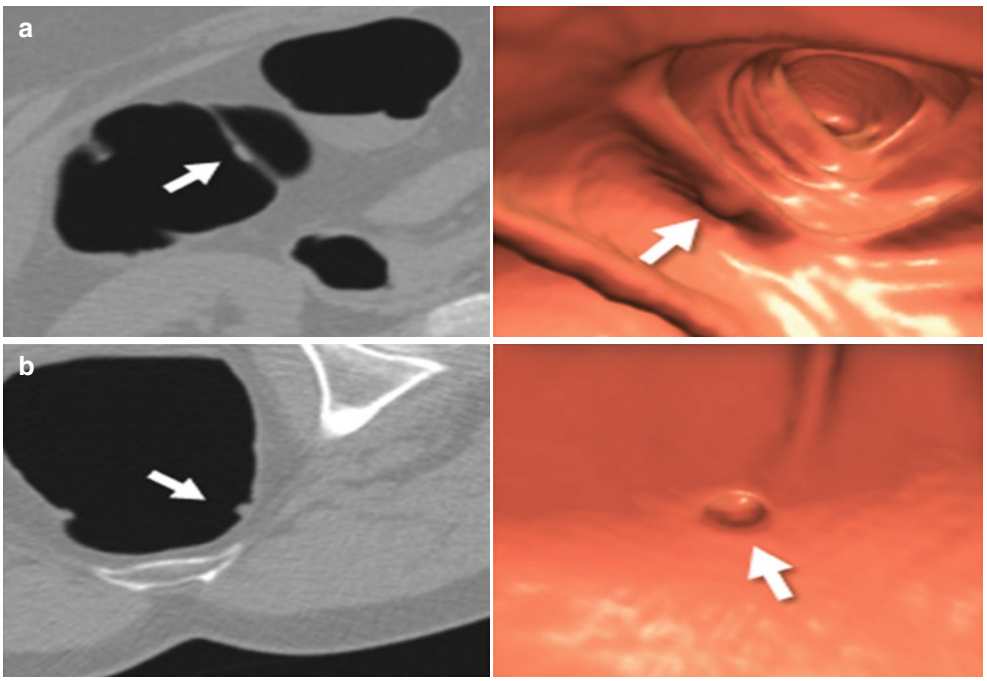

Fig. 12.15 Illustrations of polyps missed by two of four radiologists without CAD, but detected with CAD. (**a**) 6-mm flat adenoma in the ascending colon (TP in the original trial, but rated "difficult" in our retrospective review). 2D supine and prone images show a thickened haustral fold near the hepatic flexure. A small, smooth polyp is seen extending from the haustral fold. This polyp is more conspicuous on 3D endoluminal images. (**b**) 7-mm sessile adenoma in the rectum (FN in the original trial). It is difficult to match the polyp in 2D supine and prone images because the shape looks different and it is small, but it is seen in 3D fly-through images

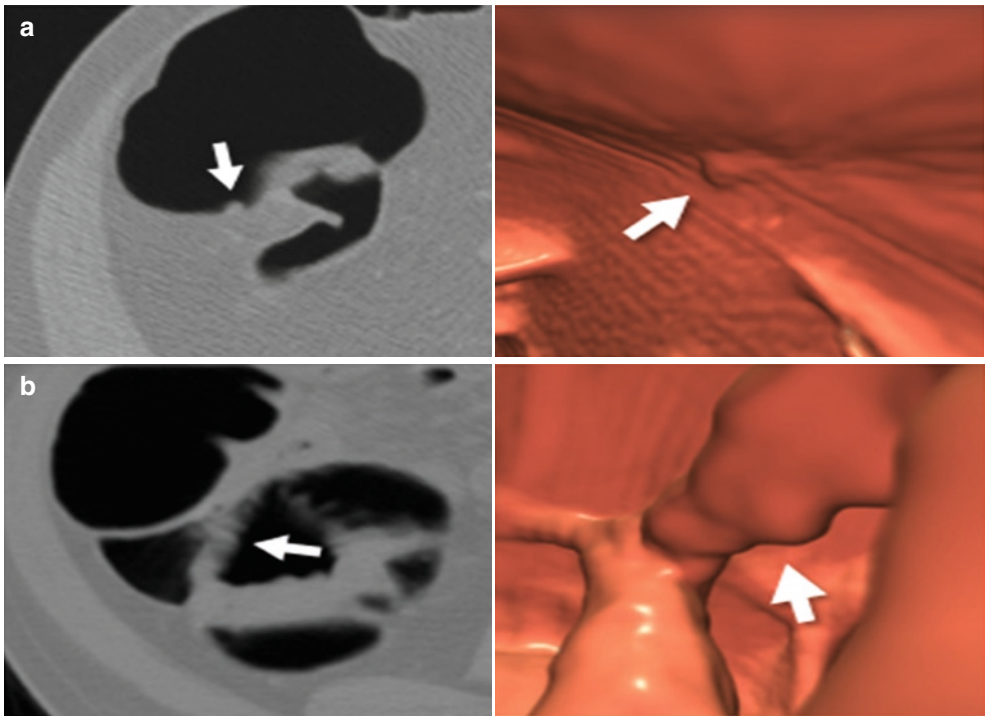

Fig. 12.16 Nonpolyps erroneously detected with CAD by a radiologist. (**a**) Small residual stool. Supine/prone comparison does not rule it out, but the irregular shape in 3D images would determine that it is stool. (**b**) Mottle of stool on a haustral fold. The small bits accumulate and look like a larger polyp on 3D images, but are more convincing of no polyp on 2D images (*an arrow*)

Conclusion and Authors' Perspective

CAD is emerging as a powerful tool to assist readers with the interpretation of CTC. Several academic and industry-sponsored software programs are emerging. Stand-alone data show excellent performance of CAD. Clinical MRMC trials are now showing clinical value to CTC CAD, but the data are software specific. CAD users should look for software that has been studied and documented in peer-reviewed publications, with reporting of sensitivity and specificity for small and large polyps for patient populations similar to that of the user's own. Reader time with CAD is expected to increase, but only by a small amount.

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Part II

Atlas

Normal Anatomy

13

Franco Iafrate and Andrea Laghi

To report CT colonography (CTC) studies, radiologists must have a working knowledge of normal colorectal anatomy and be comfortable evaluating the colon in "soft copy" format in the axial plane as well as in multiplanar and endoluminal reconstructions. This chapter focuses on normal colorectal anatomy and normal variants as seen on CTC.

Six Colorectal Segments

For the purposes of reporting CTC studies, the colon is usually divided into six segments: the rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and cecum. Each has different landmarks as detailed below. The mid to lower rectum is usually well distended at CTC [1]. Three distinct rectal folds (rectal valves of Houston) are usually visible in the mid-rectum on both axial and endoluminal images (Fig. 13.1a–d). Hemorrhoids may be identified on CTC as smooth mucosal elevation in proximity of the anal margin (Fig. 13.1e–f). The rectosigmoid junction and sigmoid colon are frequently tortuous and are best distended in the prone position [1, 2]. (Fig. 13.1g–h) Evaluation of the sigmoid colon (Fig. 13.2a–c) is particularly difficult in patients with diverticular disease due to a combination of spasm, under-distension, and fold thickening [3, 4]. The descending colon is frequently featureless segment of colon with occasional gracile folds (Fig. 13.3a–c). The splenic flexure (Fig. 13.4) is general more tortuous than the hepatic flexure (Fig. 13.5a–b). The transverse colon has triangular configuration in a cross-section and may dip deep into the pelvis (Fig. 13.6a–c). The ascending colon (Fig. 13.7a–c), like the descending colon, has thin haustral marking. The ascending and descending colon are more fixed in location as compared to the sigmoid or transverse colon, but normal variants in the mesoclon may result in redundant and mobile descending and ascending colon. The cecum (Fig. 13.8a–c) is identified as a capacious segment of colon with the appendix at its base (Fig. 13.9a–d) and the ileocecal valve generally located on its medial wall (Fig. 13.10a–l). The cecum can have variable density also be located in variant positions (Fig. 13.10) including medially, to the left of midline and when a hyper-rotation abnormality is present, even in the right upper quadrant [5]. It can have a variable density (Fig. 13.11a–d) being purely fatty, mixed fatty and soft tissue or homogeneously soft tissue [6].

Knowledge of the potential variants of ileocecal valve, the most frequent pathologic conditions as well as some pitfalls encountered during the analysis of CTC images are thus indispensable for radiologists who perform and interpret such examinations and for general practitioners who are approaching this technique [6, 7]. The ileocecal valve can have a labial, papillary or mixed pattern and can be seen in the open or closed positions. Identification of the ileocecal valve is required in reading any CTC exam because flat masses can mimic the appearance of the valve and be located close to the valve. Combined analysis of 2D axial and reformatted slices and 3D endoluminal views and 3D transparency views, provides the highest level of diagnostic accuracy.

Current 3D CT colonographic reading techniques include fly-through, and virtual dissection views. Virtual dissection is an innovative technique whereby the three-dimensional (3D) model of the colon is virtually unrolled, sliced open, and displayed as a flat 3D rendering of the mucosal surface, similar to a gross pathologic specimen [8, 9]. These and other alternate views are discussed in more detail in Chap. 8. To avoid potential pitfalls in image interpretation, the radiologist must be familiar with the unique appearance of the normal colon anatomy and of various pathologic findings when using virtual dissection with two-dimensional axial and 3D endoluminal CT colonographic image data sets (Fig. 13.12a–f).

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Rectum

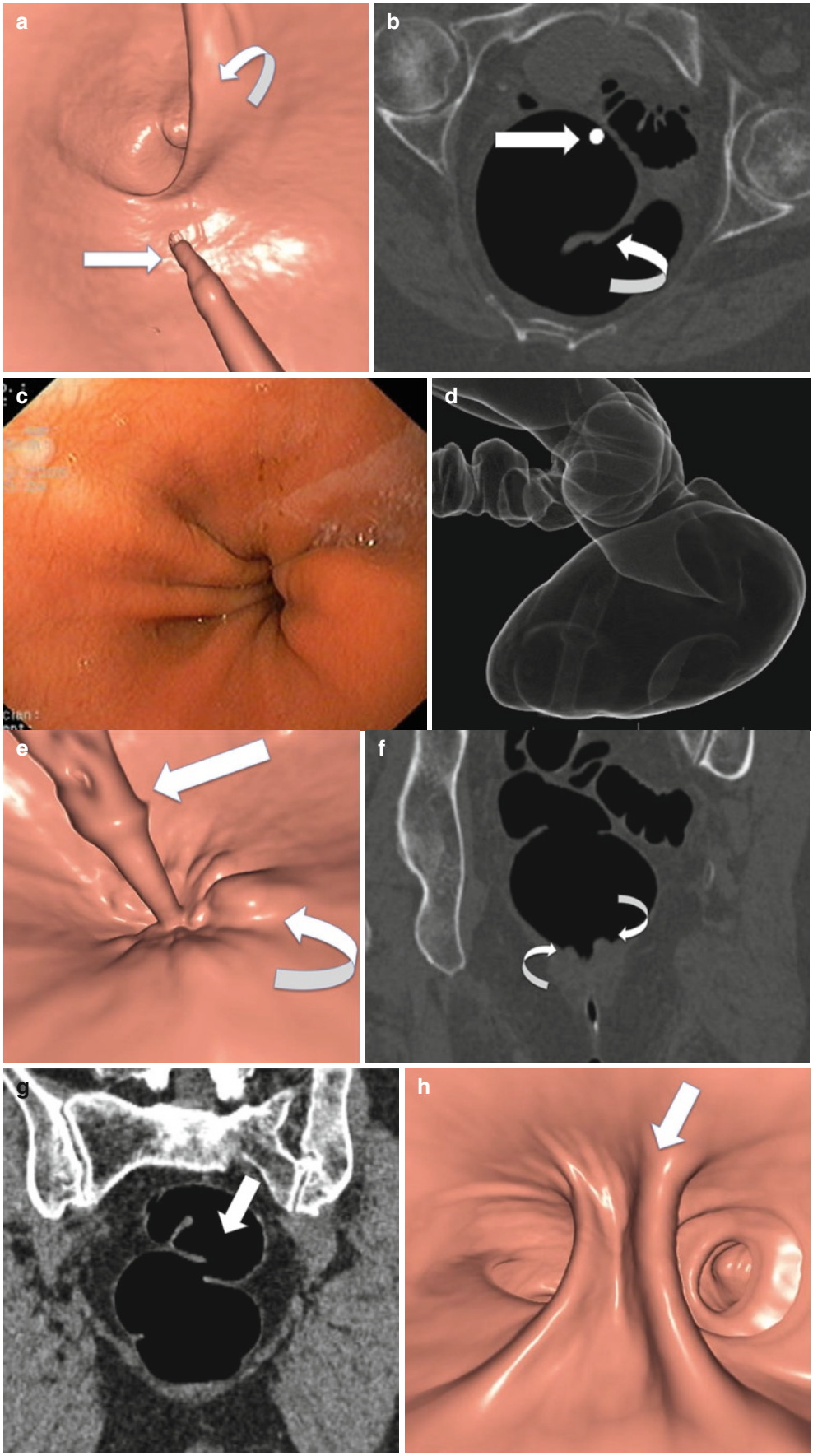


Fig. 13.1 **Rectum with Foley catheter (*straight arrow*) and Distal Valve of Houston (*curved arrow*).** (**a**) 3D endoluminal view looking from the rectum proximally toward the sigmoid, (**b**) axial 2D image view in a bone window/level setting to show the Valve of Houston and the radiopaque tip of the rectal catheter, (**c**) retroflexed endoscopic view showing normal folds converging toward the anal verge, (**d**) double contrast enema ("transparency") view with the balloon-inflated catheter in place. **Rectum with Foley catheter (*straight arrow*) and hemorrhoids (*curved arrow*)**, (**e**) 3D endoluminal view showing thin rectal foley catheter (*arrow*) and thicker, slight more irregular varices (*curved arrow*). (**f**) coronal 2D image through the hemorrhoids shown in a bone window/level setting (the balloon is present but not visible in this setting). **Rectosigmoid junction (*arrow*)**. (**g**) Coronal 2D image through the proximal Valves of Houston (*straight arrow*) and (**h**) the corresponding 3D endoluminal view

Sigmoid Colon

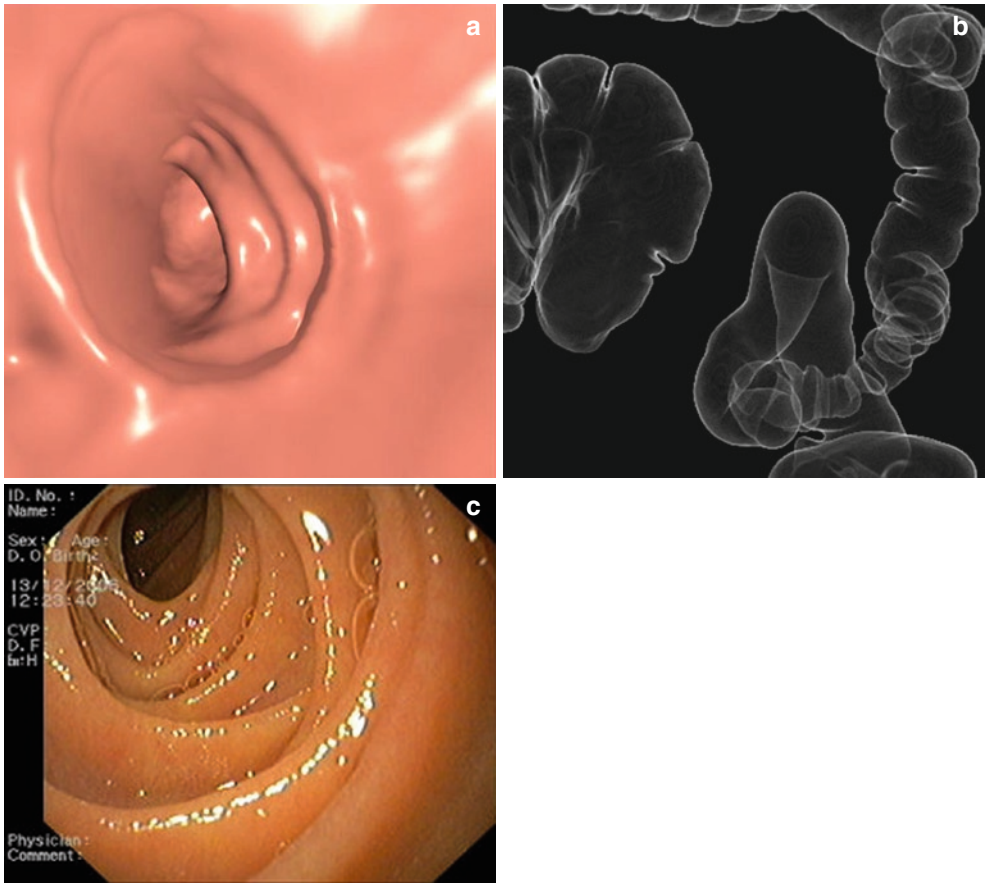


Fig. 13.2 **Sigmoid colon**. (**a**) 3D endoluminal view showing smooth folds in this patient who has no muscular hypertrophy or diverticulosis, (**b**) similar double contrast transparency view showing minimal tortuosity and (**c**) corresponding endoscopic view

Descending Colon

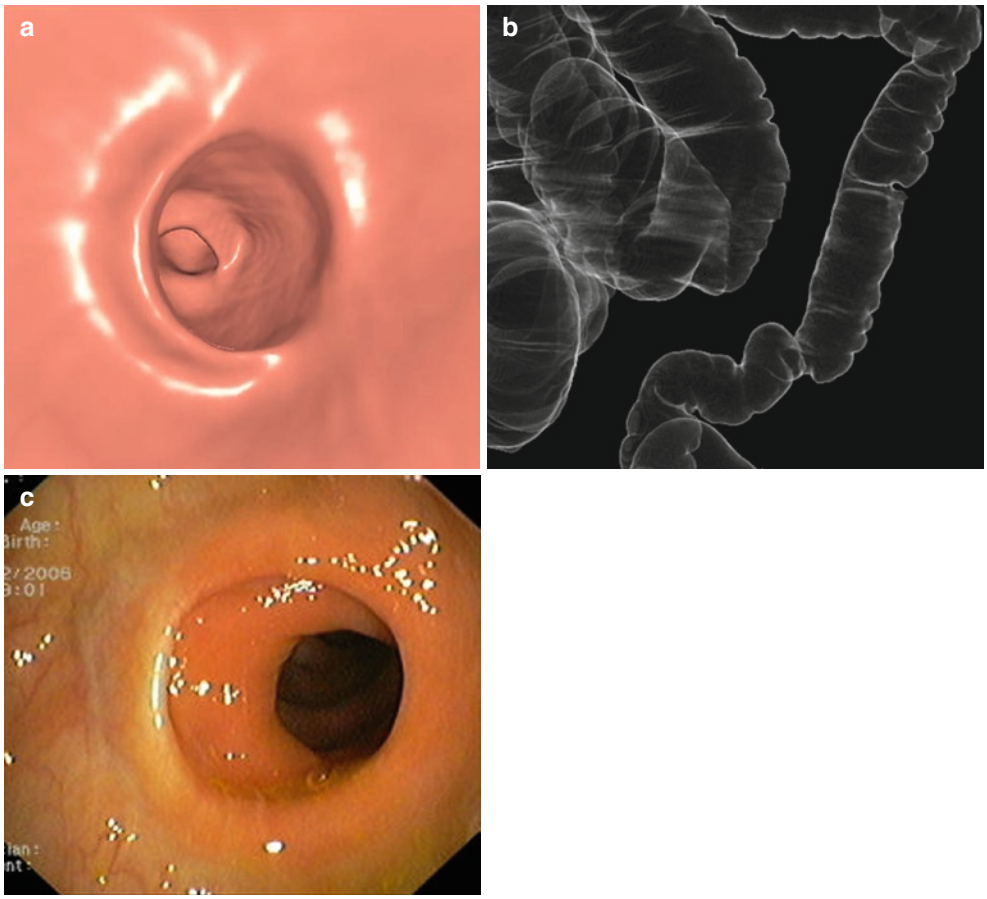


Fig. 13.3 **Descending colon**. (**a**) 3D endoluminal view, (**b**) similar double contrast enema view, and (**c**) endoscopic view show the folds are farther apart in the descending colon

Splenic Flexure

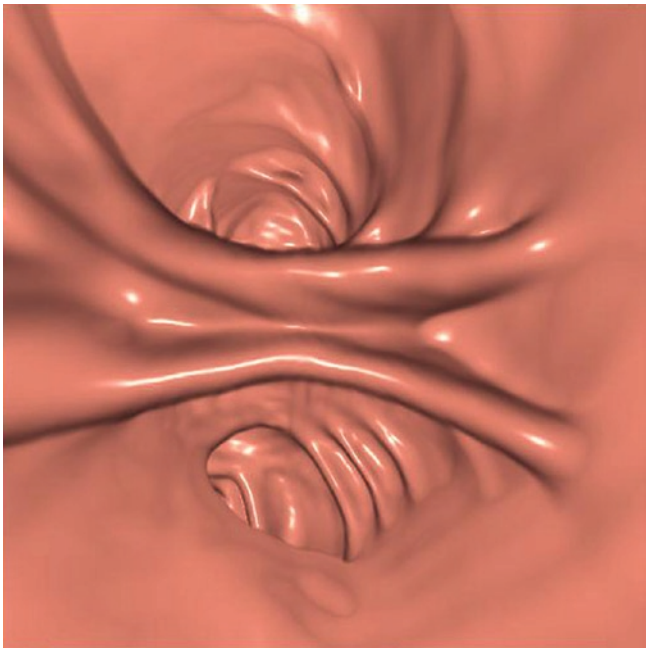


Fig. 13.4 **Splenic flexure**. (**a**) 3D endoluminal view looking "up" the flexure into both the proximal and distal limbs

Hepatic Flexure

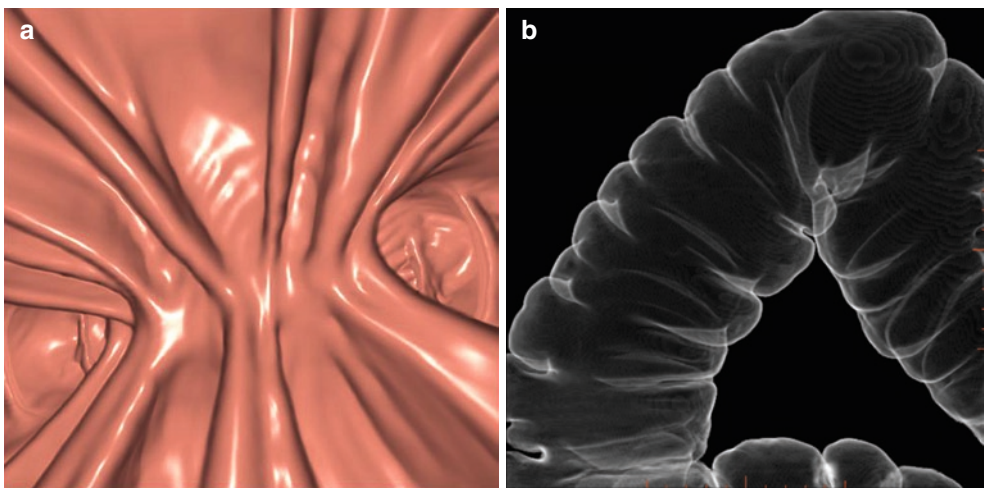


Fig. 13.5 **Hepatic flexure**. (**a**) 3D endoluminal view and (**b**) corresponding double contrast transparency view

Transverse Colon

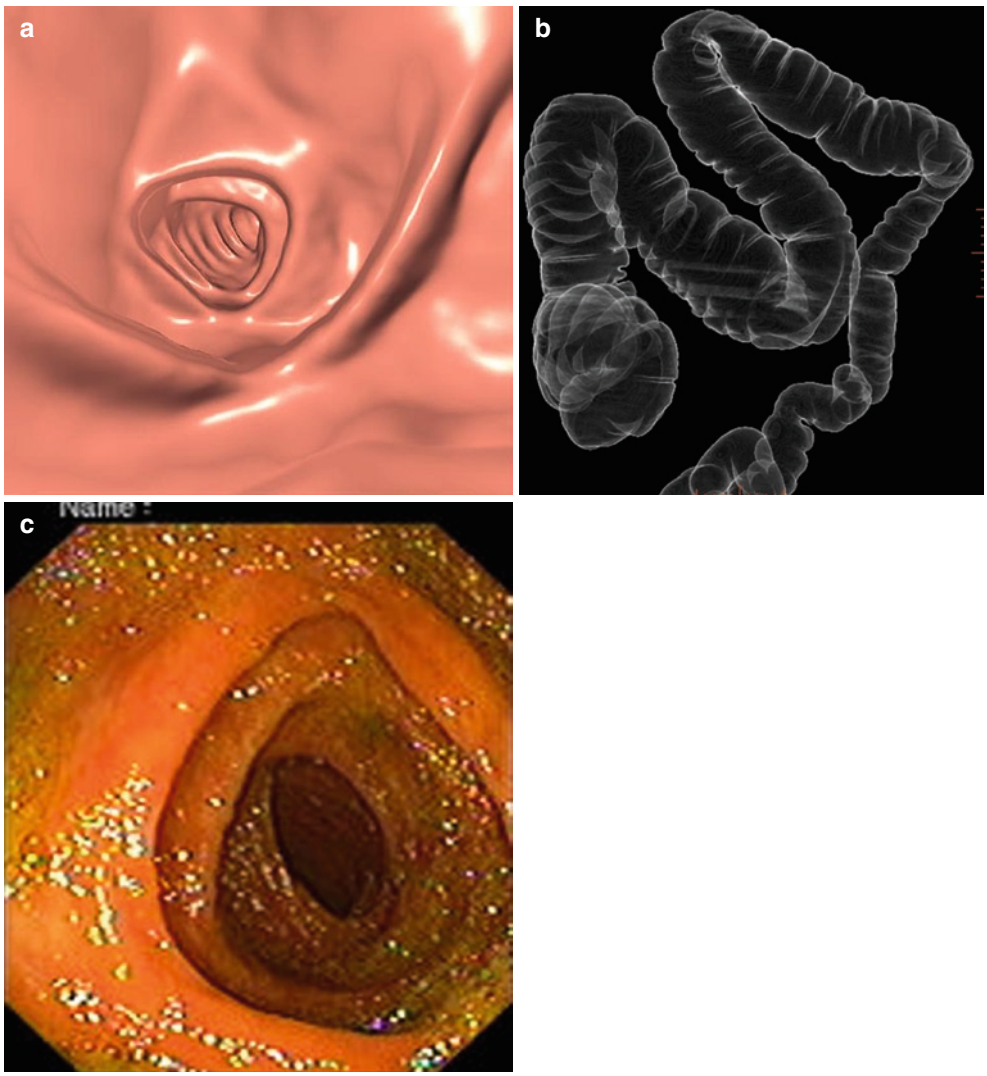


Fig. 13.6 **Transverse colon**. (**a**) 3D endoluminal view shows a more "triangular" shape to the lumen, (**b**) similar double contrast transparency view shows typical mild redundancy of the transverse colon, and (**c**) endoscopic view

Ascending Colon

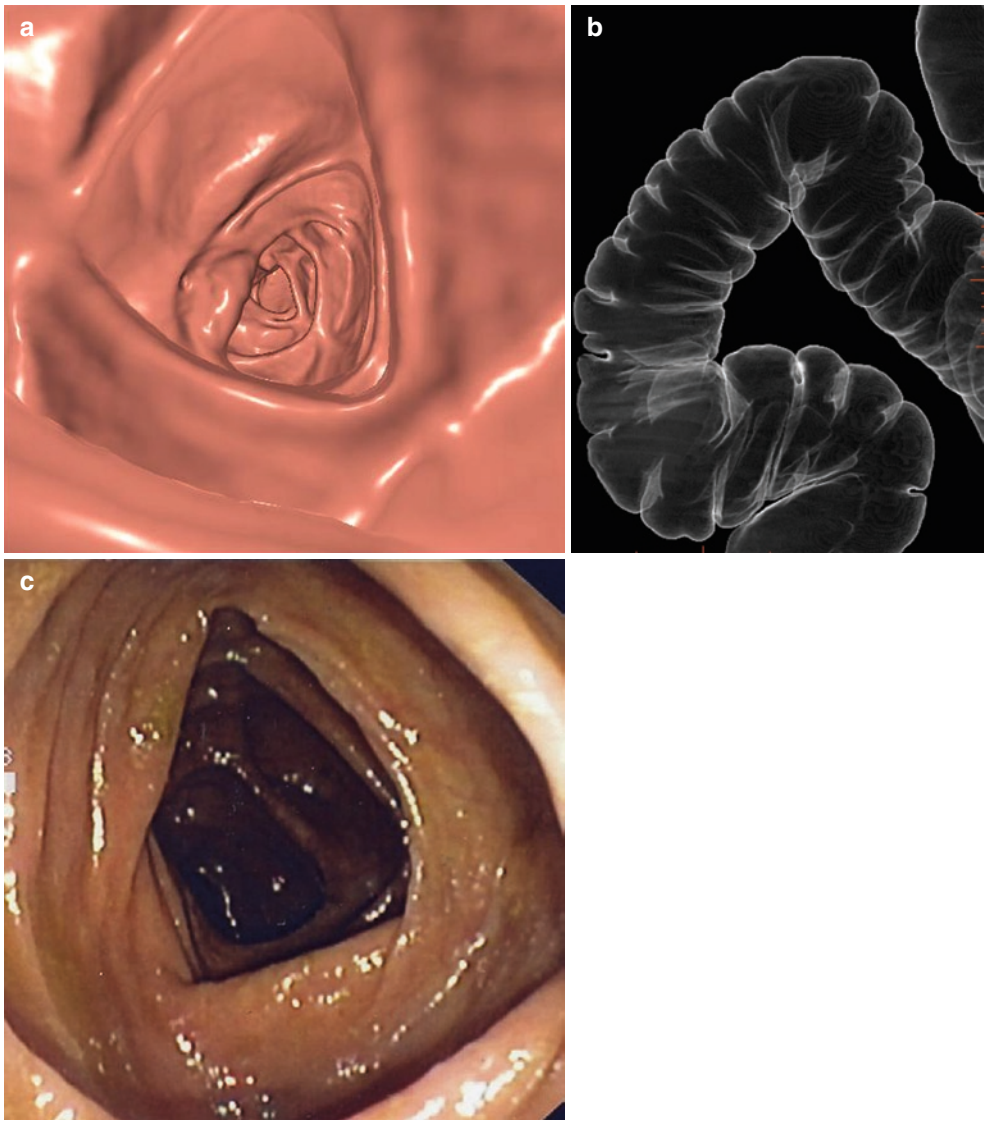


Fig. 13.7 **Ascending colon**. (**a**) 3D endoluminal view shows a somewhat triangular lumen, (**b**) similar double contrast transparency view, and (**c**) corresponding endoscopic view

Cecum

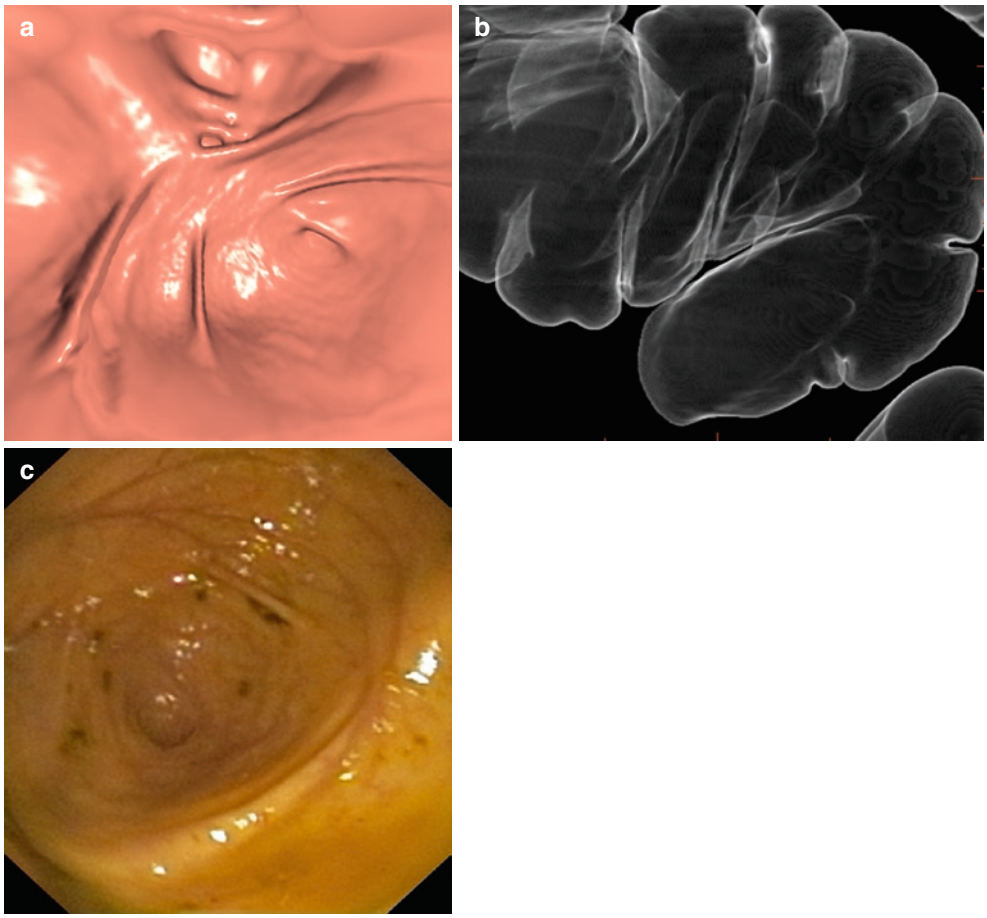


Fig. 13.8 **Cecum**. (**a**) 3D endoluminal view, (**b**) similar double contrast transparency view, and (**c**) endoscopic view

Appendiceal Orifice

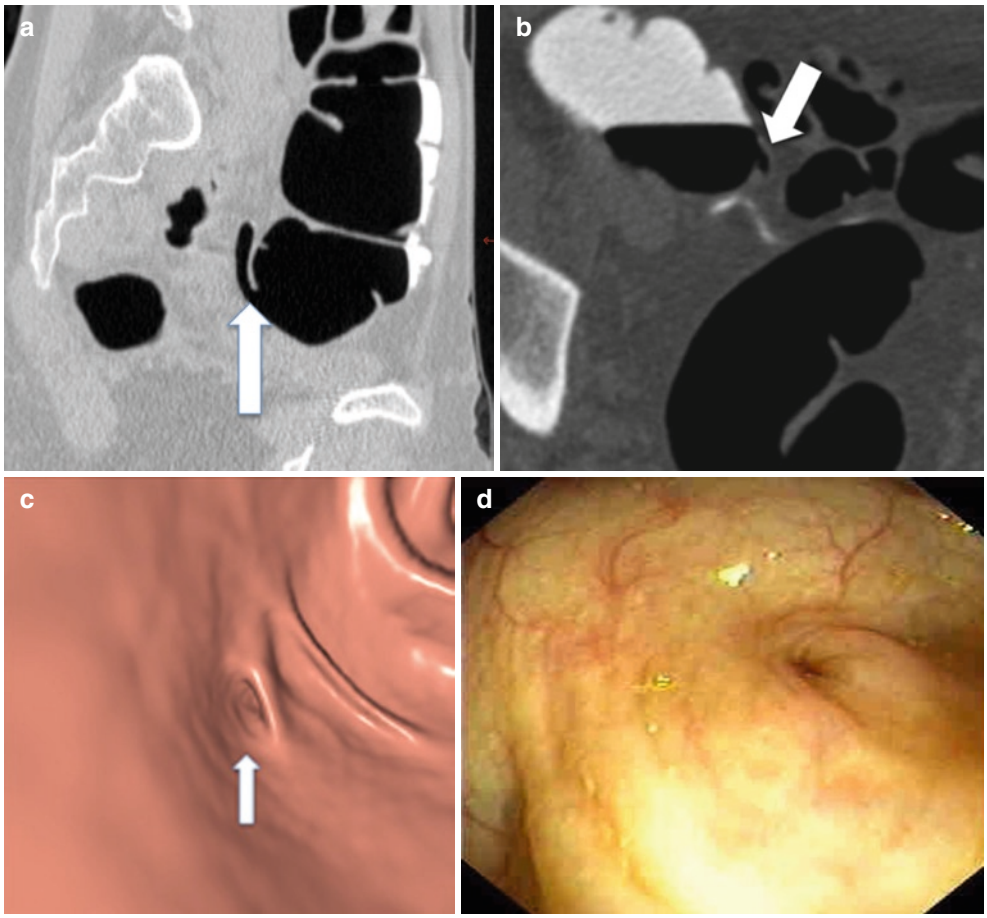


Fig. 13.9 **Appendiceal orifice (*arrow*). Note oral contrast was administered**. (**a**) Sagittal 2D view shown in a bone window/level setting, (**b**) prone, axial 2D view, (**c**) 3D endoluminal view, and (**d**) endoscopic view

Ileocecal Valve

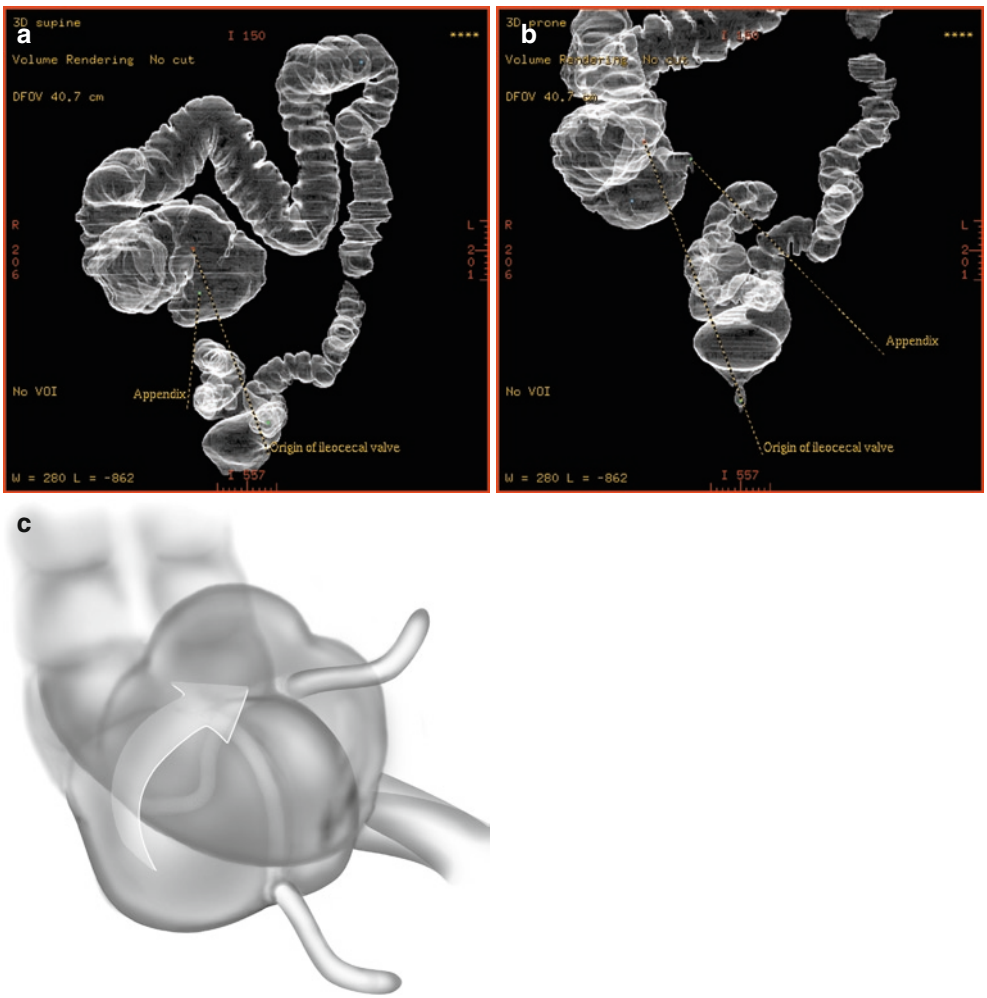


Fig. 13.10 **Mobility of the right colon**. Due to a variable length mesentery, the cecum and *right* colon can be mobile. 3D transparency views from the prone (**a**) and supine (**b**) views show the marked mobility of the *right* colon in this patient. Diagram (**c**) shows variable axis of the cecum even when fixed in the *right lower* quadrant (Part C, reprinted with permission from Chen et al. [5])

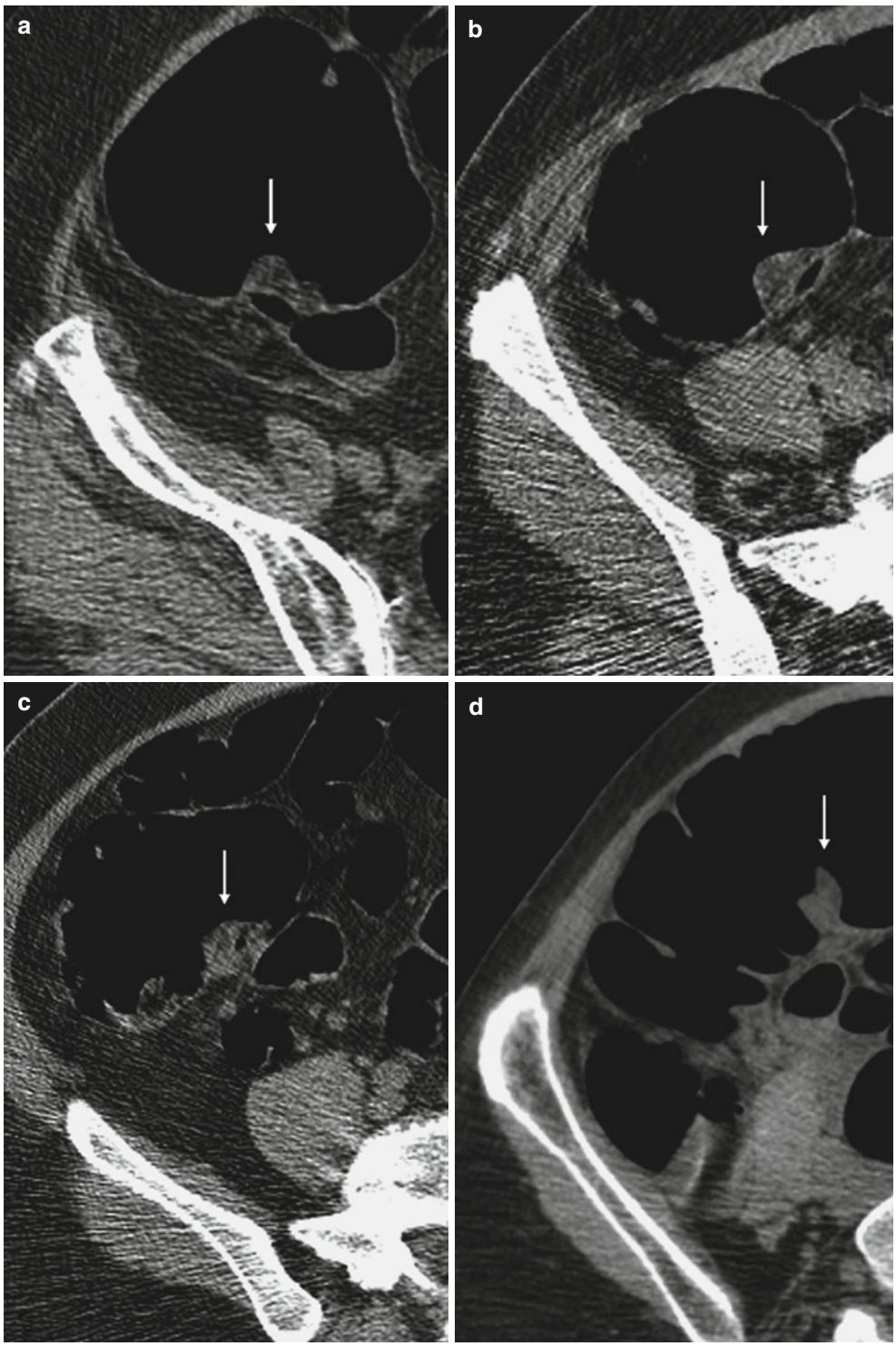


Fig. 13.11 Variable density of the ileocecal valve. Magnified axial images from supine CTC examinations to demonstrate the subjective classification system used to classify the ICV based on density and composition. (**a**) Homogeneously low-density valve, (**b**) heterogeneously low-density valve, (**c**) heterogeneously high-density valve, and (**d**) homogeneously high-density valve

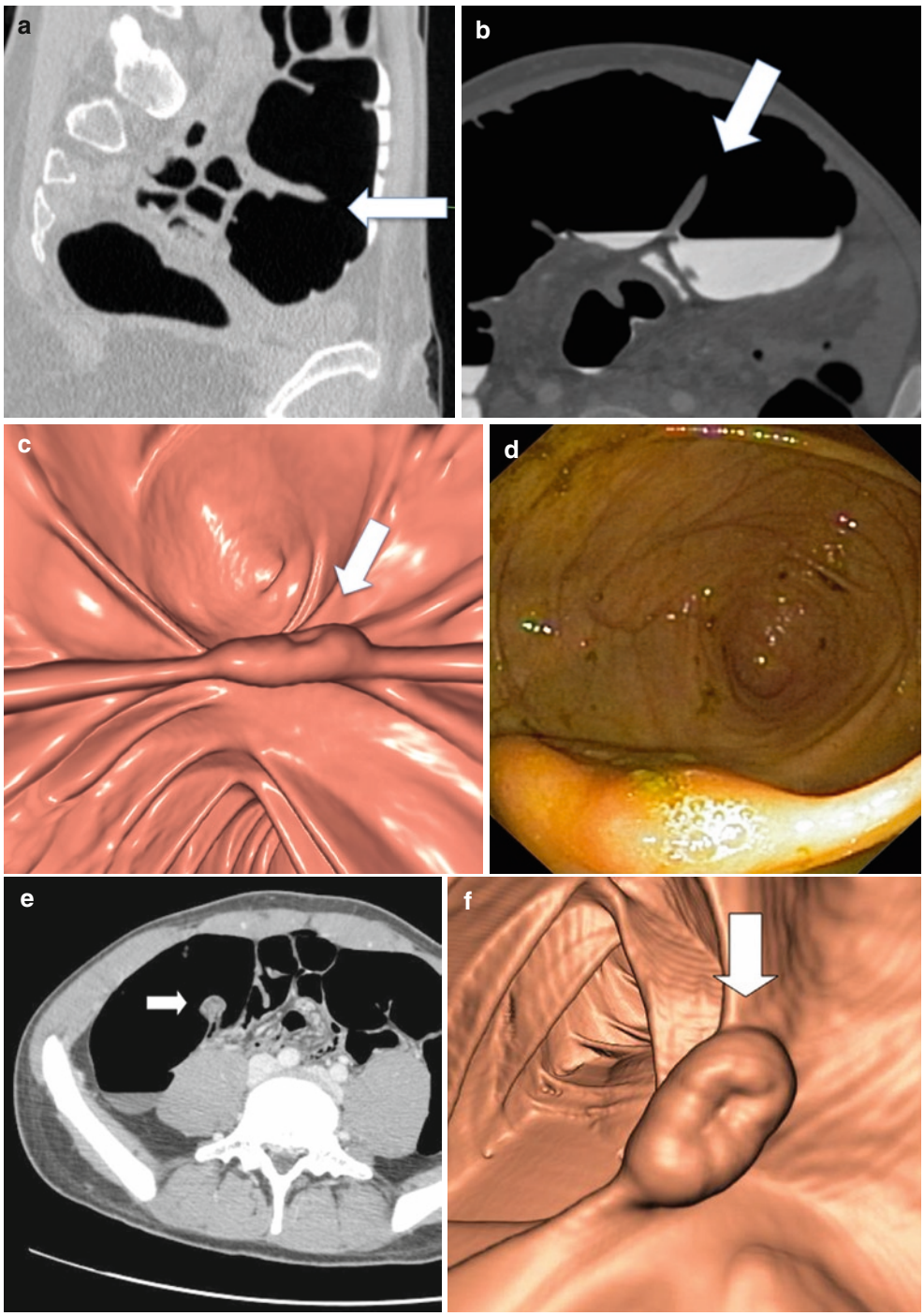


Fig. 13.12 **Ileocecal valve with "labial" morphology**. (**a**) Sagittal 2D view, (**b**) axial 2D view, (**c**) 3D endoluminal view, and (**d**) Endoscopic view. **Ileocecal valve with "papillary" morphology:** (**e**) Axial 2D view. Note this exam was done without oral contrast but with intravenous contrast thus normal fat and enhancing vessels can be seen, (**f**) 3D endoluminal view, and (**g**) endoscopic view. **Ileocecal valve with opened orifice**: (**h**) Coronal 2D view, (**i**) 3D endoluminal view, and (**j**) endoscopic view

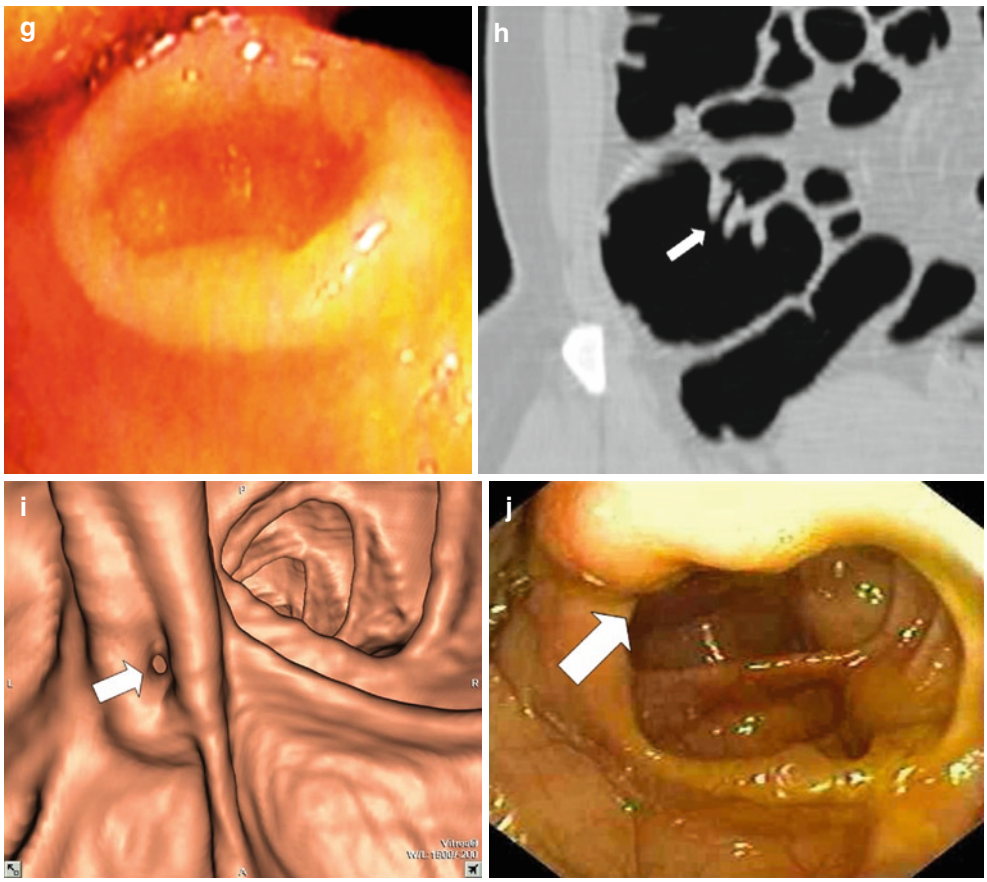


Fig. 13.12 (continued)

Virtual Dissection Normal Anatomy

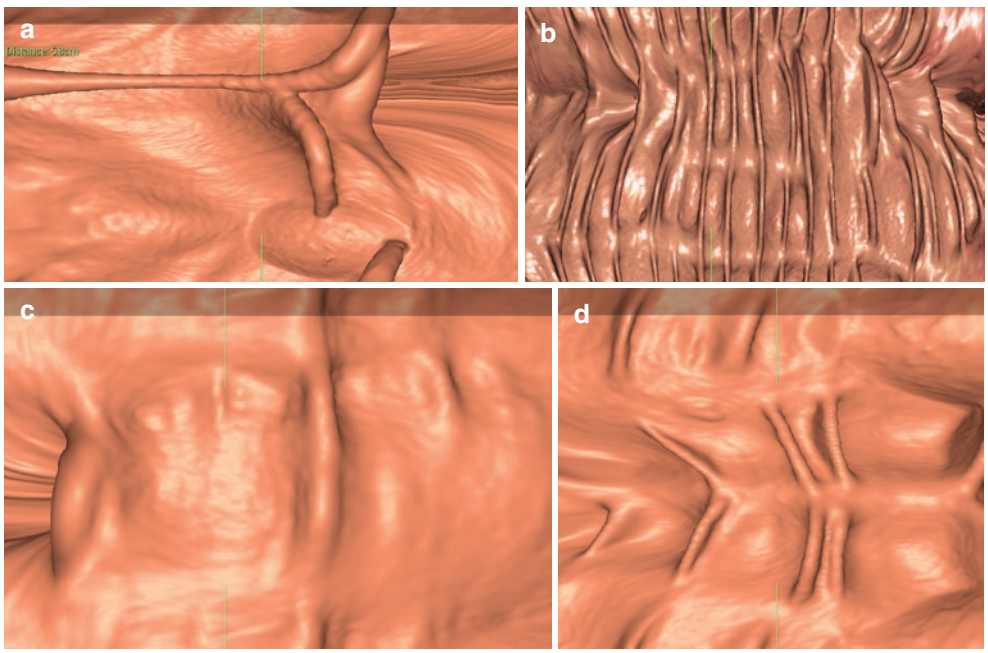
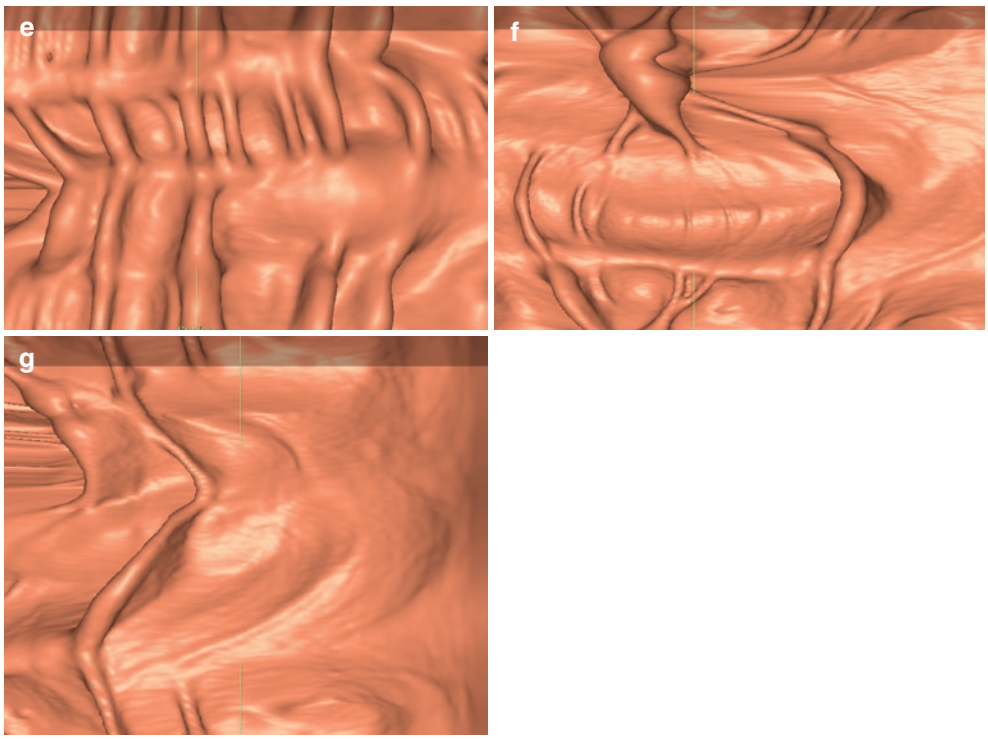


Fig. 13.13 **3D Perspective Fillet views** (Philips), of (**a**) rectum, (**b**) sigmoid, (**c**) descending colon, (**d**) transverse colon, (**e**) ascending colon, (**f**) ileocecal valve, and (**g**) cecum. These views are discussed in more detail in Chap. 8

Fig. 13.13 (continued)



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Sessile polyps

14

Franco Iafrate and Andrea Laghi

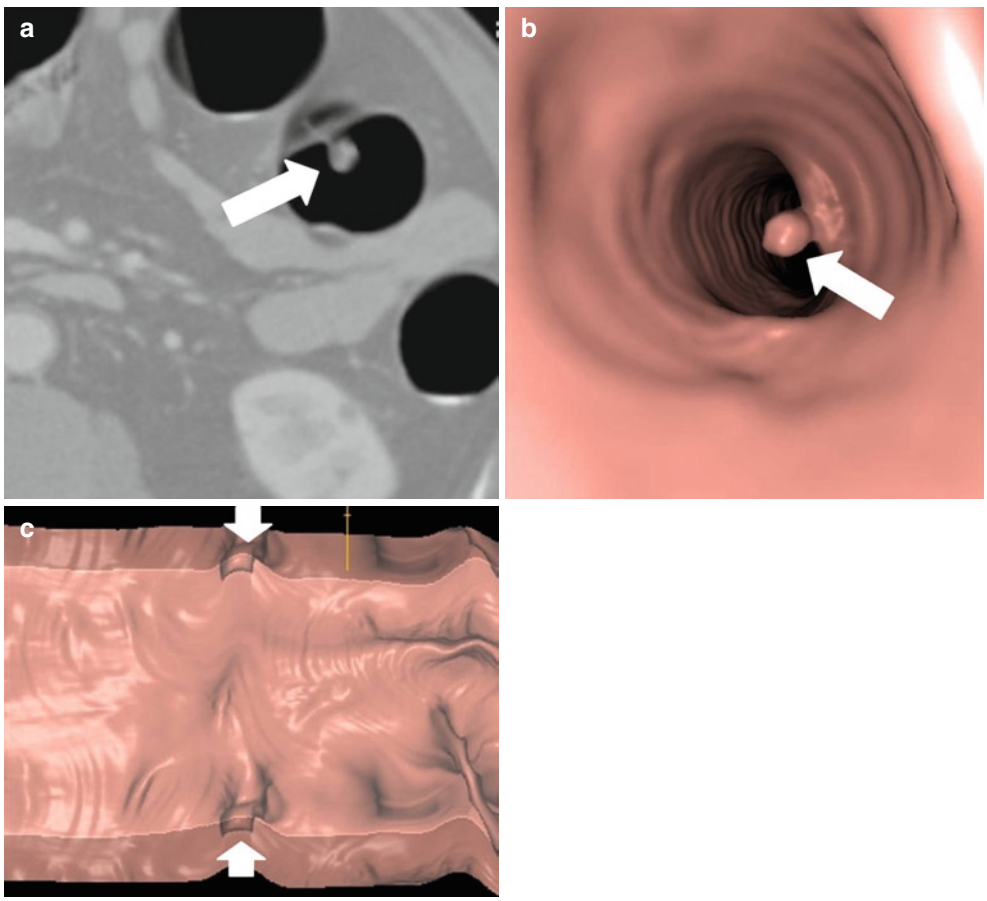

Fig. 14.1 **Smooth morphology**. (**a**) Supine axial CT image shows an 8 mm homogeneously attenuating soft tissue density polypoid lesion (*arrow*) in the descending colon. (**b**) 3D volume-rendered endoluminal image shows smooth morphology (*arrow*) of this lesion consistent with a sessile polyp growing off a fold. Note that some radiologists might consider this polyp to have a narrow neck and classify it as pedunculated, but we prefer to use the term "sessile" for all lesions without a frank stalk. This sessile polyp (*arrow*) is clearly detectable on (**c**), the virtual dissection view. Note the darker shaded *upper* and *lower* stripe are intentionally redundant overlapped portions, thus this is a single polyp appearing both on the *upper* and *lower* shaded stripe

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DOI: 10.1007/978-1-4419-5852-5_14,

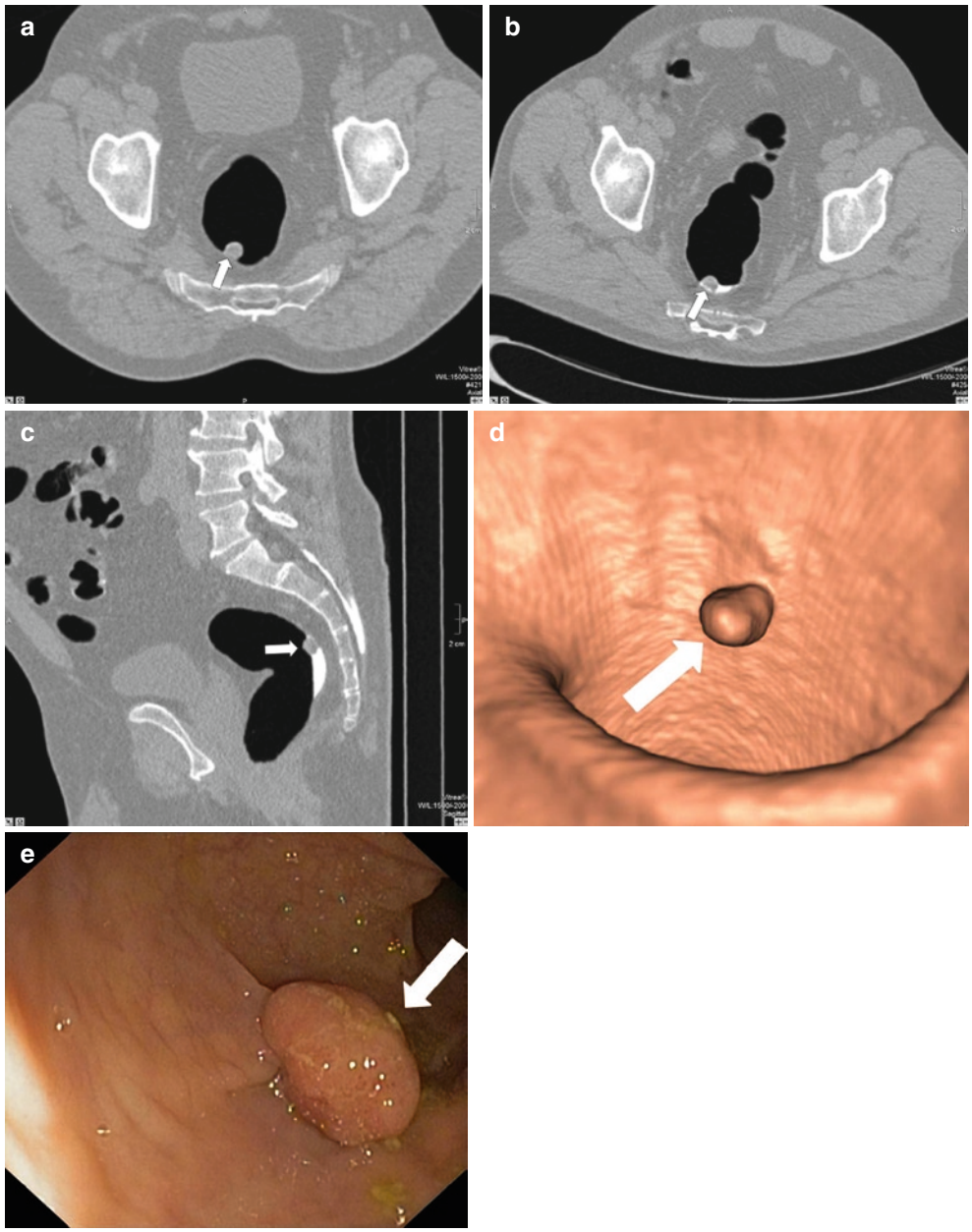


Fig. 14.2 **Need for supine and prone imaging**. (**a**) Prone axial CT image shows a sessile polyp (10 mm) of the posterior wall (the non-dependant side) of the rectum (*arrow*). Note how the oral contrast appears to "coat" the polyp. (This is a helpful sign and should not be confused for tagging of stool in which the tagging agent enters the entire substance of the polyp candidate, proving that it is in fact stool.) In the same patient, axial CT image (**b**) and sagittal CT images (**c**), both acquired in the supine position, show that the polypoid lesion (*arrow*) has not changed position, remaining adherent to the posterior rectal wall. (**d**) 3D endoluminal image of the sessile polypoid lesion (*arrow*). At endoscopy, (**e**) a 10 mm sessile adenomatous polyp was confirmed (*arrow*)

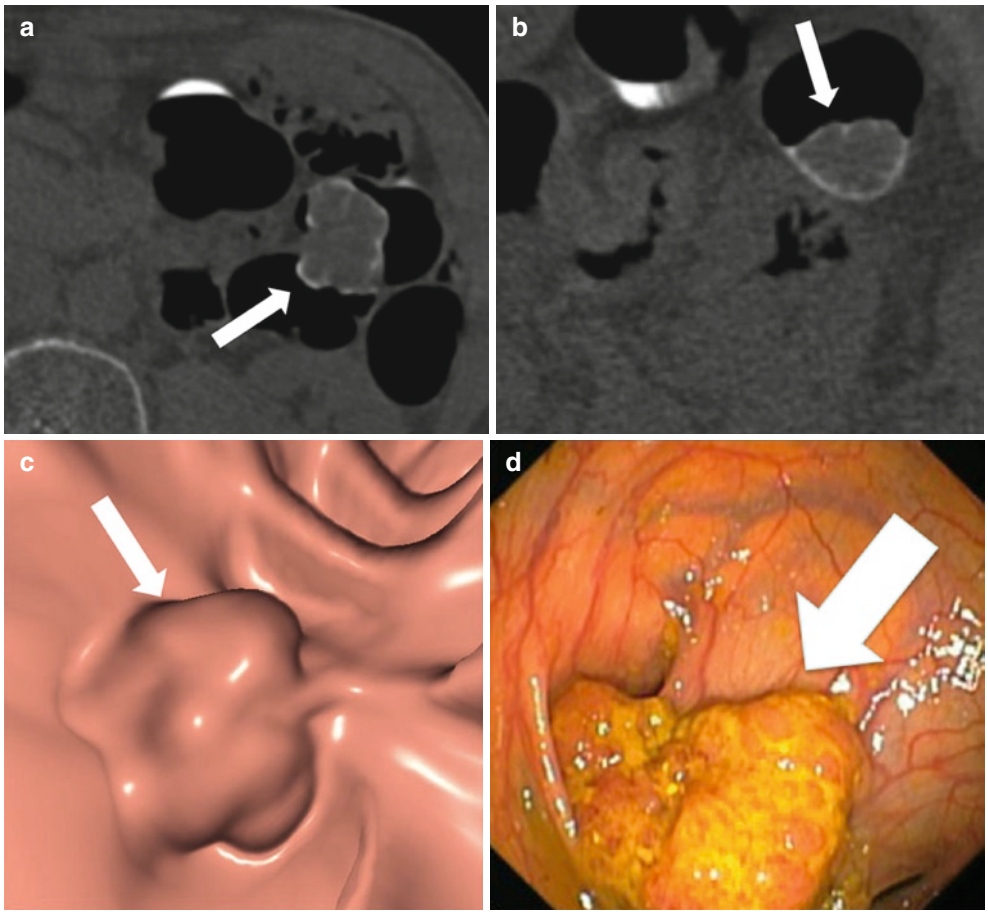


Fig. 14.3 Large sessile polyp with apparent positional change. (**a**) Prone axial CT image showing a large and lobulated polypoid filling defect (*arrow*) near the splenic flexure protruding within colonic lumen (**b**) On the axial supine CT image, the same lesion (*arrow*) seemed to move to the posterior bowel wall due to partial torsion of the flexure and due to the weight of this large lesion. Note how contrast appears to "surround" the entire lesion on both views. This should not be mistaken for stool – the image is simply not though the "footprint" or attachment of the lesion to the colonic wall. (**c**) 3D endoluminal image showing a precise correlation of the lesion (*arrow*) between CTC and the endoscopic image (**d**)

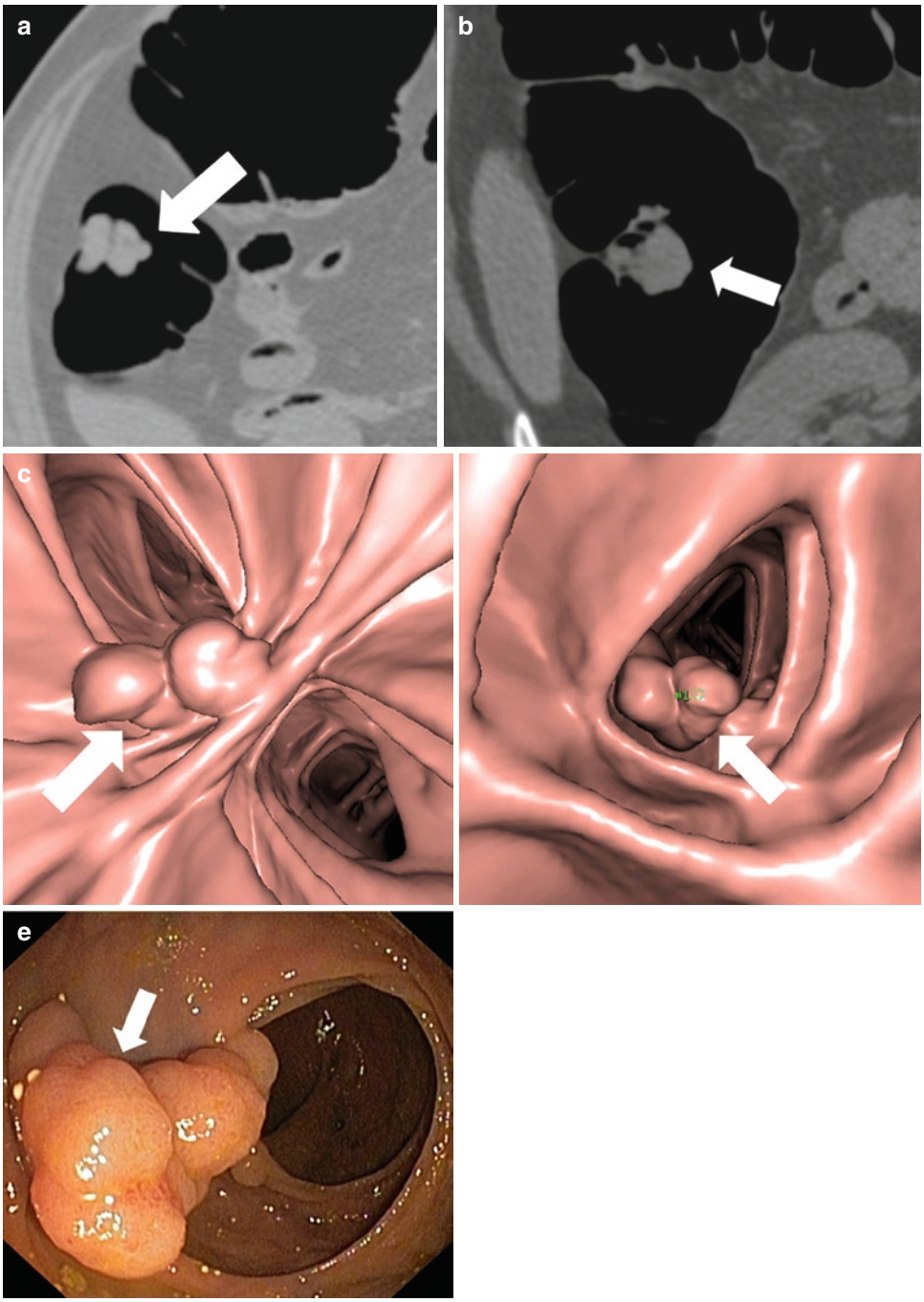


Fig. 14.4 Careful search of the "top" and "bottom" of each loop on the axial images. Axial CT images obtained in supine (**a**) and in prone position (**b**) show a large sessile and lobulated polyp (*arrow*) on the most superior wall of the hepatic flexure. Evaluating the same lesion (*arrow*) on 3D endoluminal images obtained on supine (**c**) and prone (**d**) position it's easily appreciable the lobulated morphology of the lesion (*arrow*) that origins from an haustral fold of the hepatic flexure. The 3D view however could be confused for two lesions, but paging thought the axial images shows that it is actually only a single lesion as confirmed on (**e**), the endoscopy.
Teaching point: The colonic flexures (hepatic flexure or splenic flexure) can make an acute angle with a high superior wall. Lesions – especially small lesions - are sometimes apparent on only one or two slices. When reviewing these regions, using a primary 2D approach, it is important to page completely through the colonic lumen to ensure no polyps are missed. Obviously for lesions located near the flexures, 3D fly-though facilitates detection of polyps

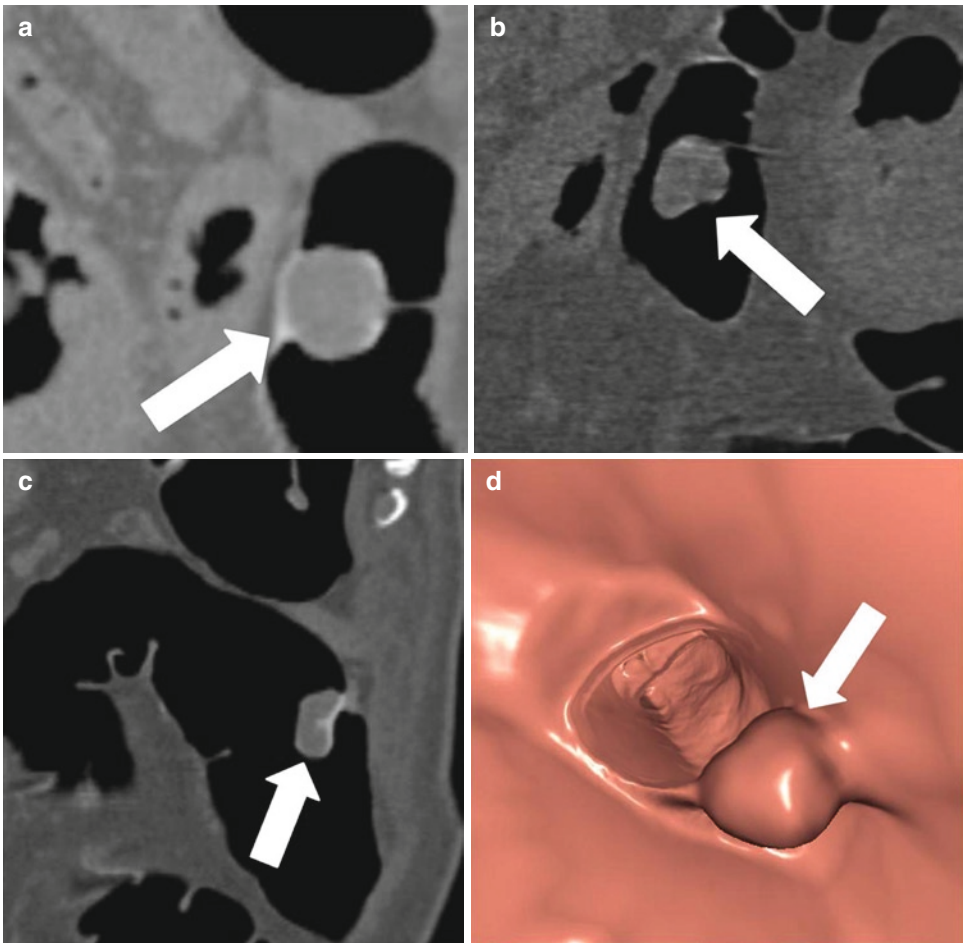


Fig. 14.5 Sessile polyp arising from a haustral fold. Axial supine CT image (**a**) demonstrates a large, 25 mm, sessile polyp (*arrow*) partially covered by tagging agent, arising from a thin haustral fold in the descending colon. Coronal (**b**) and sagittal (**c**) reformatted 2D images better depict its relationship with the fold. The corresponding 3D CT endoluminal image (**d**) shows the typical appearance of a polypoid lesion (*arrow*) growing off a fold

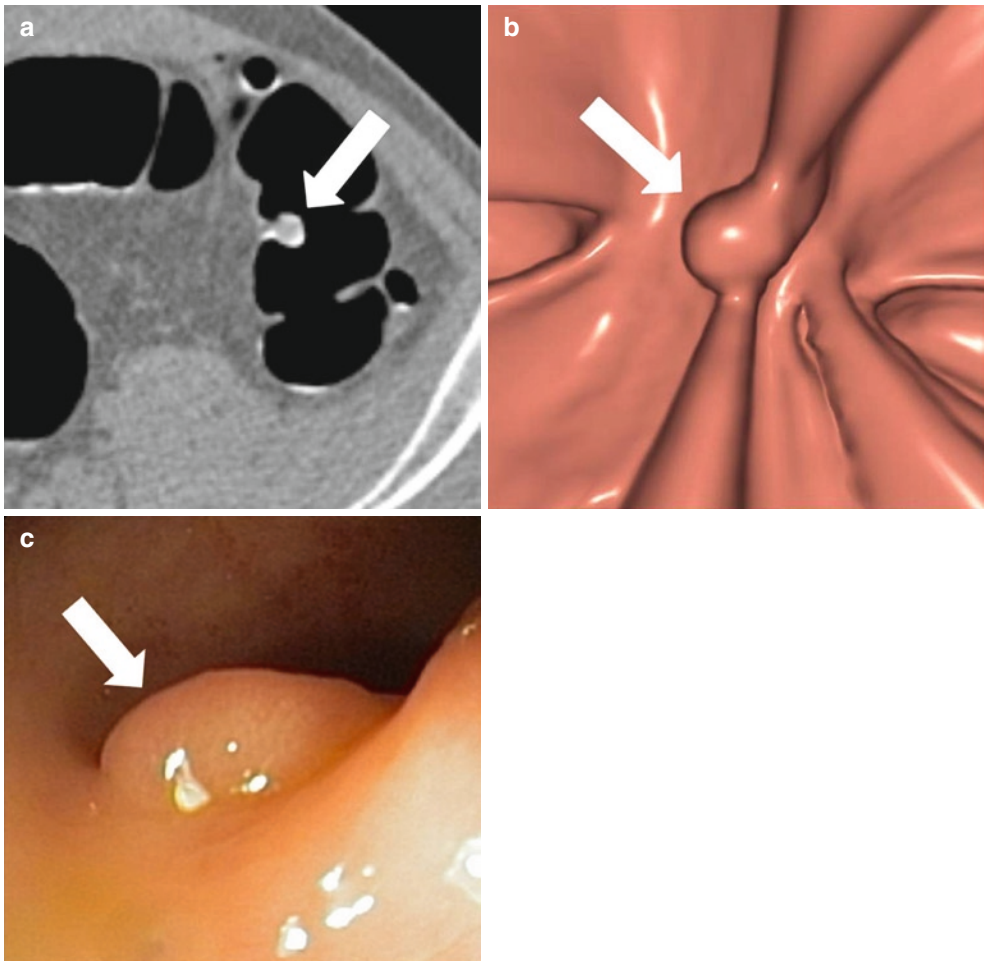


Fig. 14.6 Small polypoid lesion arising off of a fold. Axial CT supine image (**a**) shows a small, 6 mm, sessile polyp (*arrow*) located on medial aspect of the descending colon in proximity of splenic flexure. The 3D endoluminal view (**b**) is helpful in demonstrating the location of the lesion on the fold, providing an easier detection of the lesion (*arrow*) at optical colonoscopy (**c**)

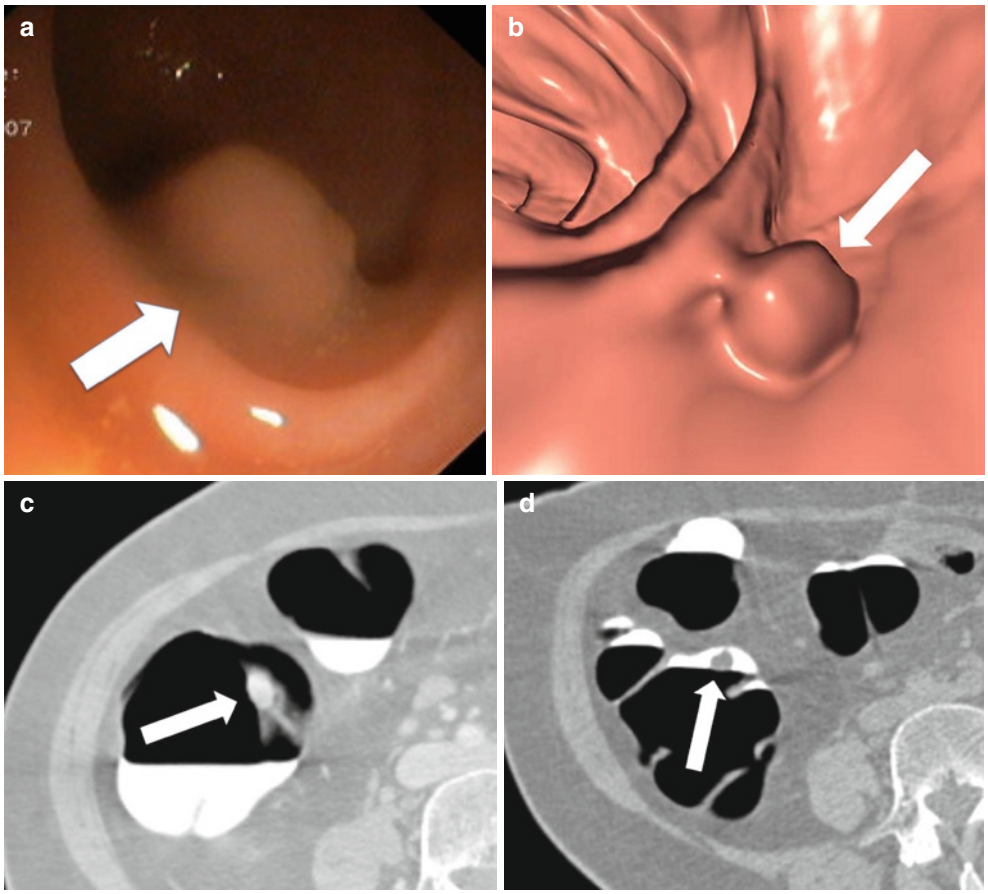


Fig. 14.7 Sessile adenomatous polyp adjacent to a haustral fold. (**a**) At optical colonoscopy. (**b**) 3D CTC. A polyp (*arrow*) in this location can be challenging to differentiate from a bulbous or incompletely distended haustral fold. 2D CTC obtained on supine and prone position (**c–d**) images oriented in cross-section to the colon midline showing more clearly the polyp (*arrow*) as hypodense filling defect fully submerged by tagging agent and its relationship to the adjacent fold

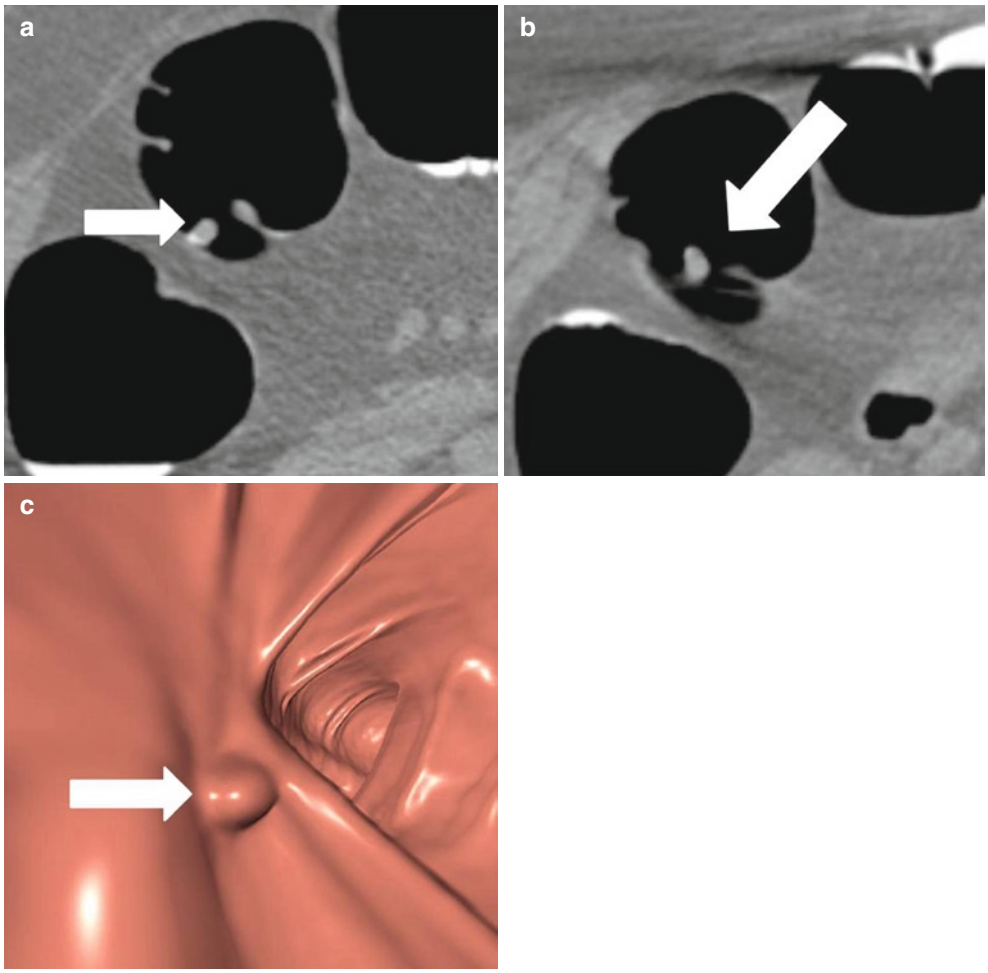


Fig. 14.8 Polyp adjacent to a haustral fold on endoluminal view. 2D CTC obtained both in supine (**a**) and prone (**b**) positions show a 7 mm sessile polypoid lesion (*arrow*) that remains on the same aspect of bowel wall after fecal tagging preparation. 3D CTC (**c**) better depicts the relationship of the lesion (*arrow*) to the near haustral fold

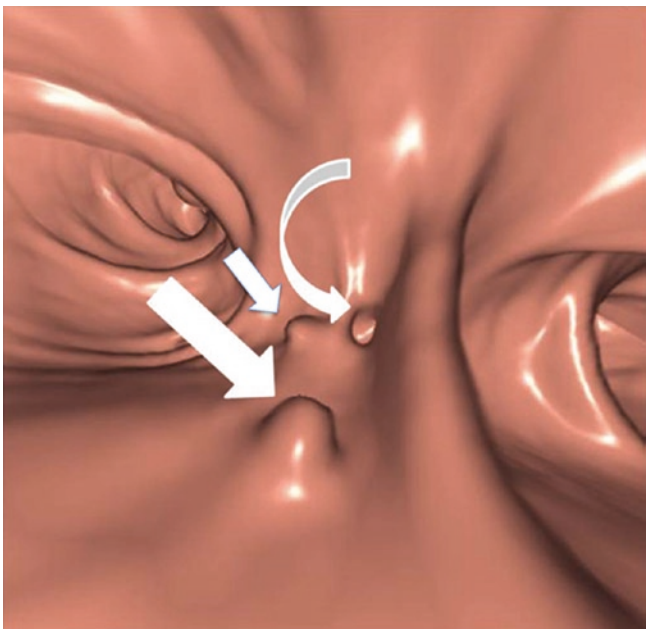


Fig. 14.9 Differentiating a polyp from a diverticulum. A 3D image shows three lesions in the sigmoid colon; a diverticulum (*curved arrow*) and two polyps (*straight arrows*). In general, a diverticulum will be seen to have complete ring around it and a polyp an incomplete ring. Correlation with 2D imaging is also helpful in differentiating the two. Note that when a polyp is viewed perfectly "head-on" it may appear to have a complete dark ring as well (compare to Fig. 2**d**)

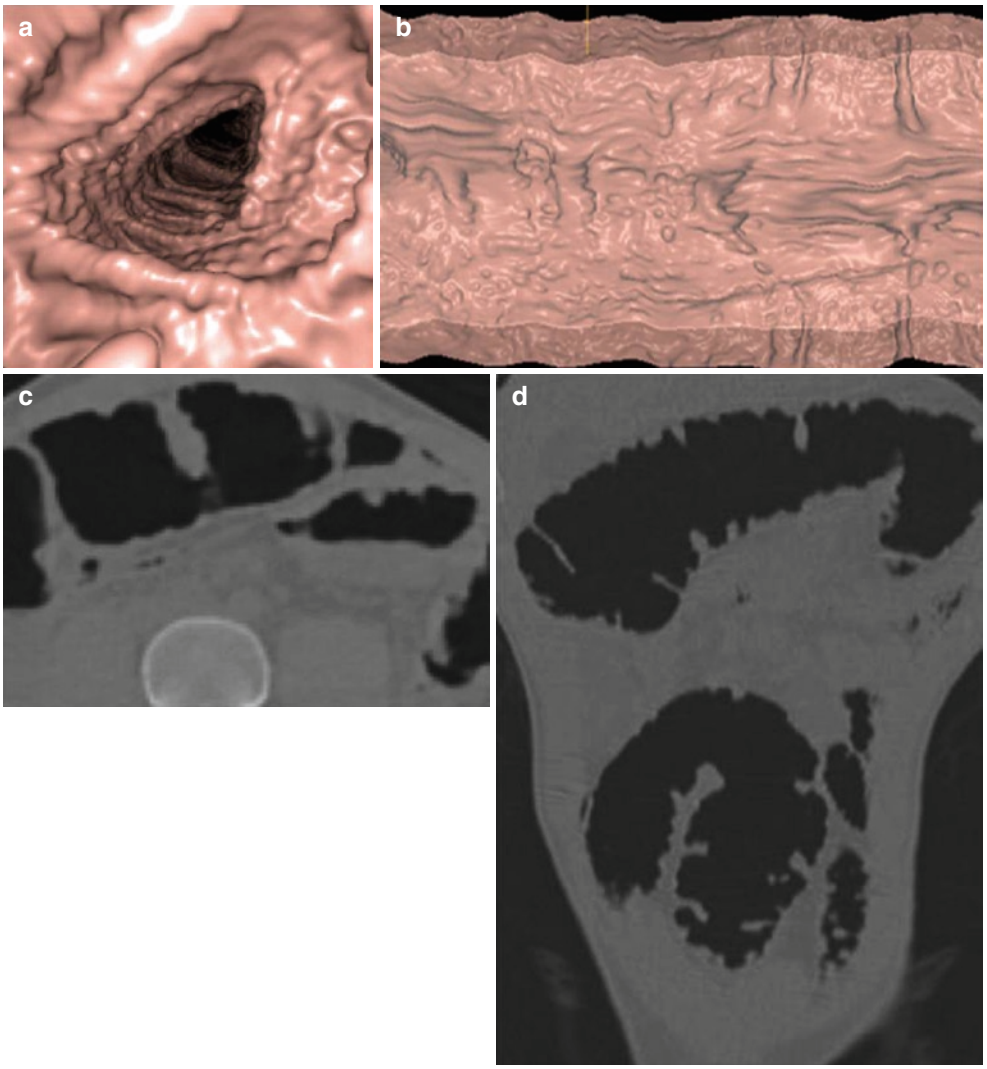
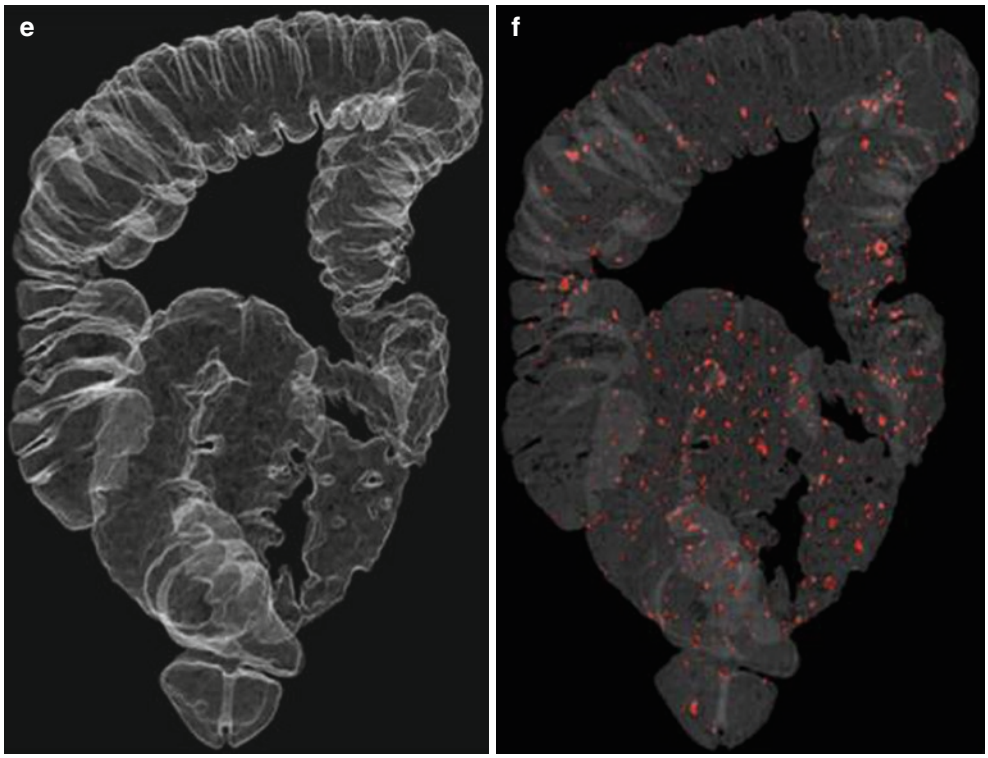


Fig. 14.10 **Multiple small polyps in familial polyposis (FAP) syndrome**. 3D CTC endoluminal (**a**) and virtual dissection view (**b**) are difficult to be interpreted even for expert readers, as the same image can be misinterpreted as a "dirty" colon, i.e., a poor preparation with retained stool. Making a correlation with 2D reformatted axial (**c**) and coronal (**d**) images can be helpful for correct interpretation as the presence of multiple soft tissue density tiny polypoid lesions; none of the lesions have any internal gas characteristic of stool. Similar double contrast barium transparency view (**e**) alone, and after applying CAD software (**f**), clearly demonstrate the presence of tiny lesions diffusely in all colorectal segments. **Teaching point**: FAP does not represent an indication to perform a CTC, however rarely this syndrome can be found unexpectedly as a spontaneous mutation and/or without a known family history of FAP. Obviously when a FAP is detected, even CAD software can't reduce the interpretation time as it recognizes multiple findings requiring much time for radiologist to evaluate

Fig. 14.10 (continued)



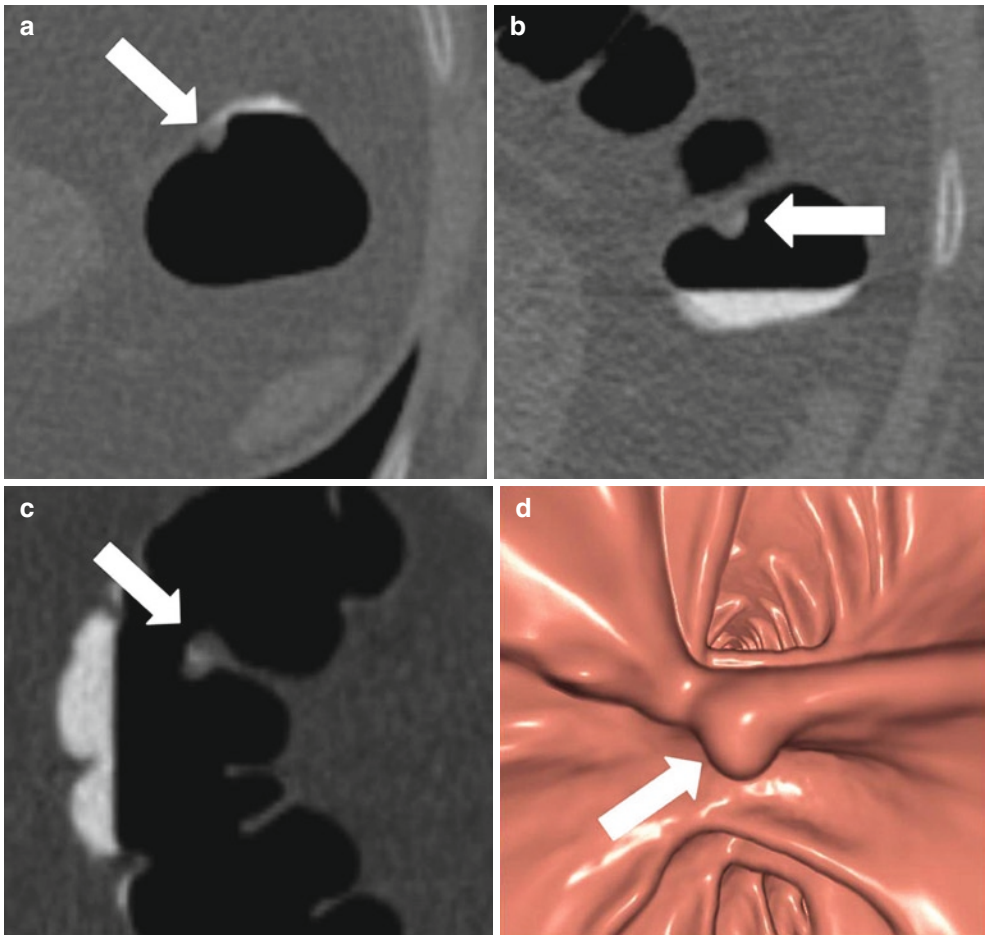


Fig. 14.11 **A 68 year old male undergoing CTC for screening. A 5 mm polyp was discovered that extends from a haustral fold at the splenic flexure**. (**a**) Prone axial CT image shows a tiny polypoid filling defect (*arrow*) on upper fold at splenic flexure, partially covered by tagging agent. Turning the patient to the supine position (**b**), shows a small polypoid lesion (*arrow*) which persistently remains on the same aspect of the fold. Sagittal reformatted 2D image (**c**) shows the relationship of the lesion (*arrow*) to the splenic flexure. (**d**) Endoluminal reconstruction from superior advantage point

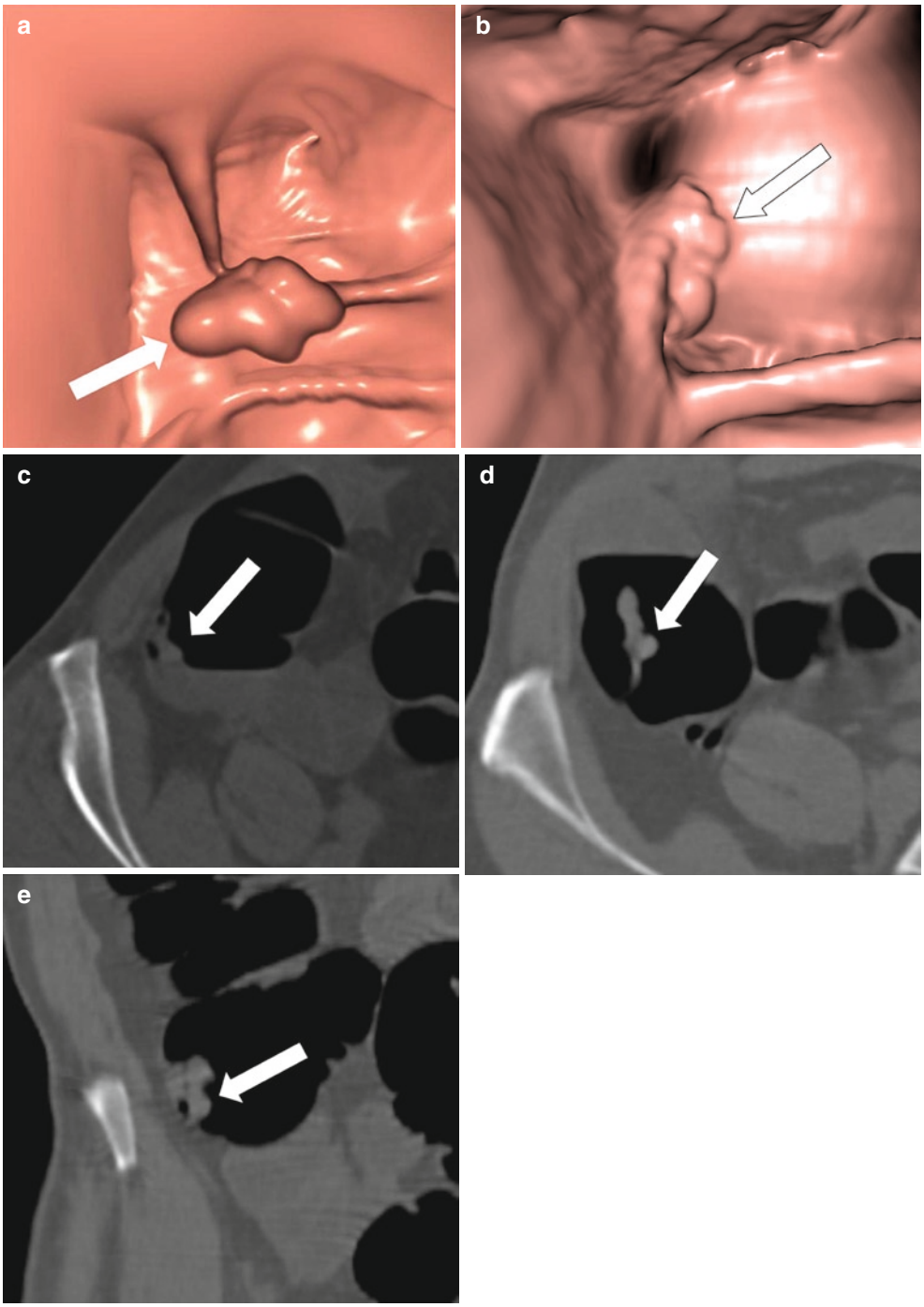


Fig. 14.12 **Polyp with lobulated contours**. Not all polyps at CTC will have smooth surface. 3D images (**a**, **b**) show an endoluminal cecal polypoid lesion (*arrow*) with lobulated contours and an irregular morphology that can be misinterpreted with stool. Axial 2D iamges obtained in both the supine (**c**) and prone (**d**) positions as well as coronal 2D image (**e**), demonstrate a homogenous soft tissue filling defect that allows the reader to exclude stool, and to correctly diagnose a sessile polyp (*arrow*). Note that no oral contrast was used in this patient, so only polyp texture or mobility can be used to indicate stool. Irregular shape, while characteristic of stool, is not a reliable sign. Polyps with irregular surface tend to be missed more often than those with smooth surface, possibly because they are confused for stool. **Teaching Point:** Some lesions located on right colon, if evaluated only on axial 2D images as in this case, can be misinterpreted as pedunculated lesions. Data suggest that pedunculated polyps are less common in the right colon. Additionally, 3D better depicts and clarify that the long structure connected to the head of the polyp that appeared to be a pedicle, is actually a normal fold. Secondly, in those case where a fecal tagging is not used, obviously the use of 2D coronal and sagittal reformatted images are crucial in helping to detect lesion that are partially submerged by untagged fluid

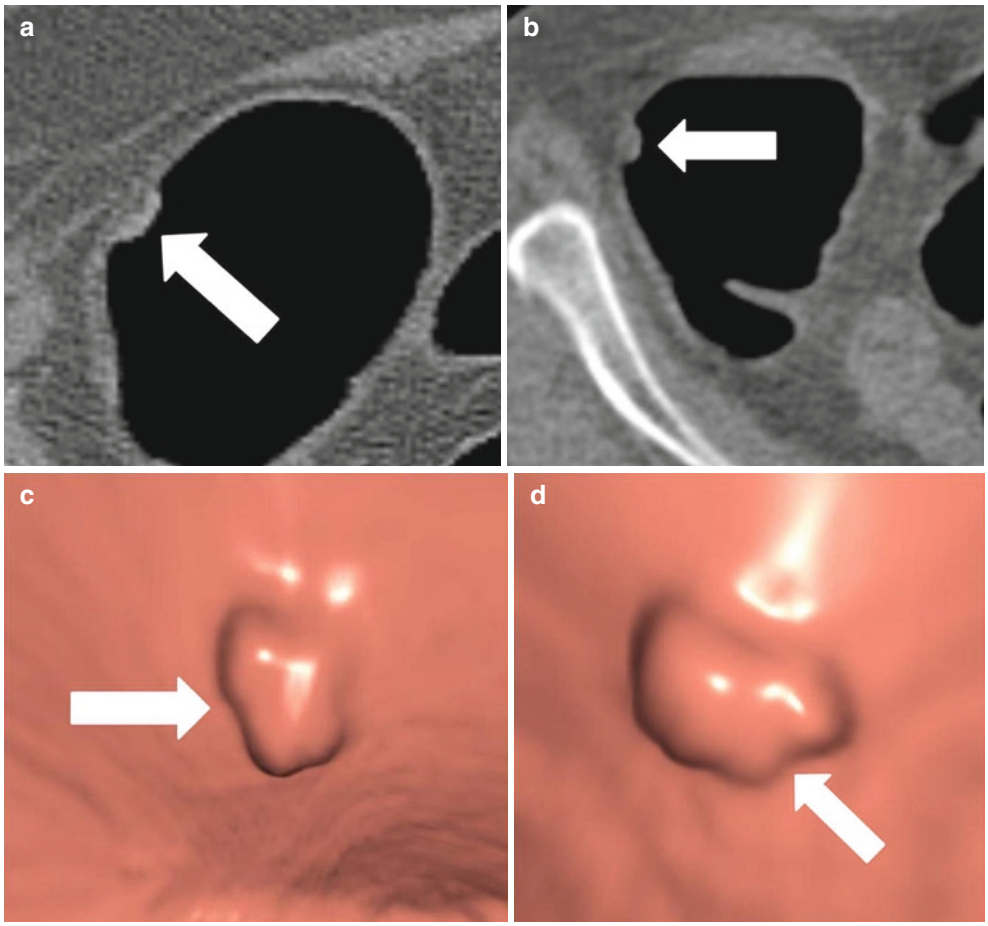


Fig. 14.13 **Flat Hyperplastic polyp**. Supine (**a**) and prone (**b**) axial, 2D and 3D endoluminal images (**c–d**) show an approximately 9 mm filling defect (*arrow*) with a large base, in the right lateral wall of the cecum, a few millimeters under ileocecal valve characterized by a height of 3 mm. After polypectomy, histologic analysis showed this to be a hyperplastic lesion. Flat hyperplastic polyps are less visible than adenomatous polyp

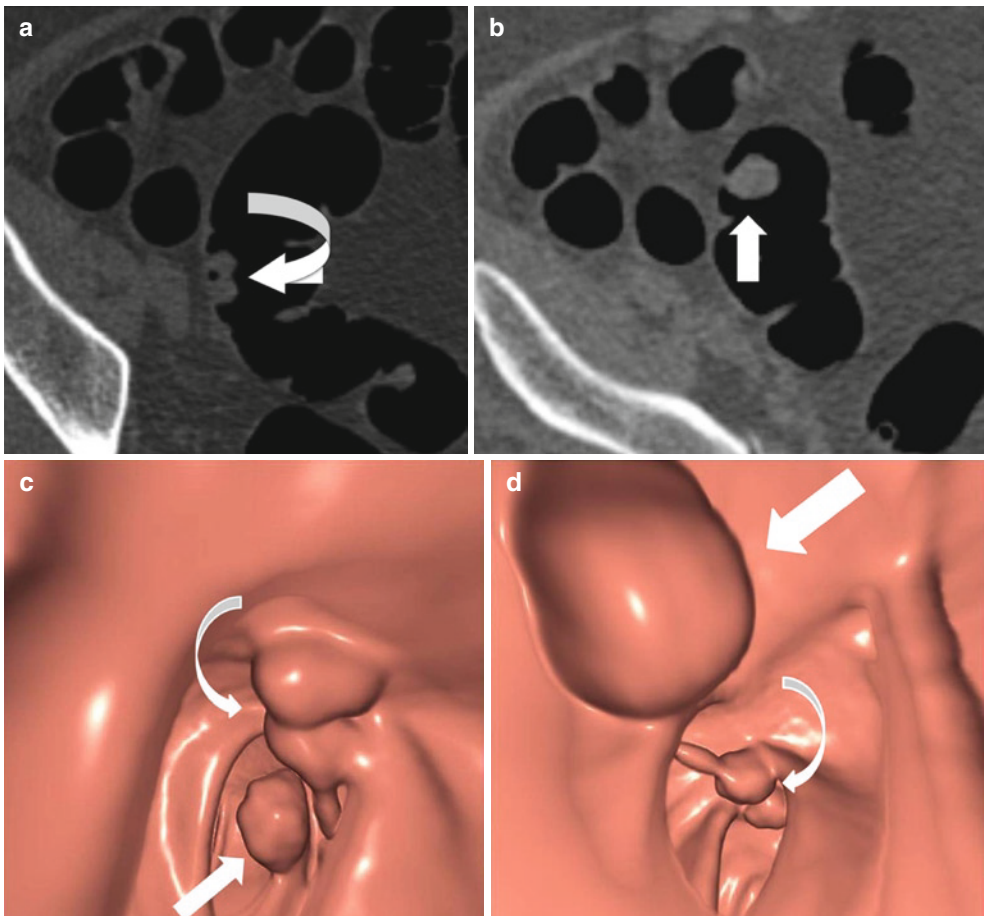


Fig. 14.14 **Multiple polyps**. (**a–b**) Axial CT images both in prone and supine position show two 10 mm sessile polyps (*curved arrows*) show a 17 mm sessile polyp (*arrow*). There were three adenomatous polyps in this patient who presented with anemia and a positive fecal occult blood test (FOBT). The three polyps are seen both on and in-between folds on these 3D images providing an "all in one" view (*arrow and curved arrow)* (**c, d**). The three sessile polyps are clearly seen also in endoscopic image (*arrow and curved arrow*) (**e**)

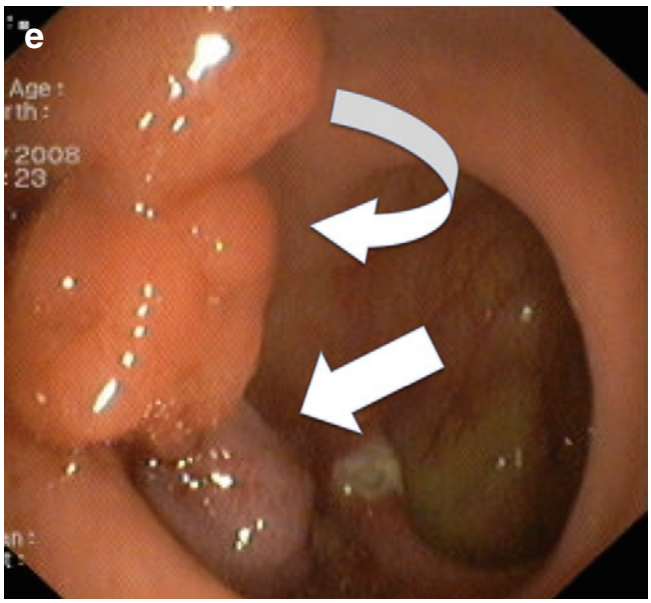


Fig. 14.14 (continued)

Pedunculated Polyps

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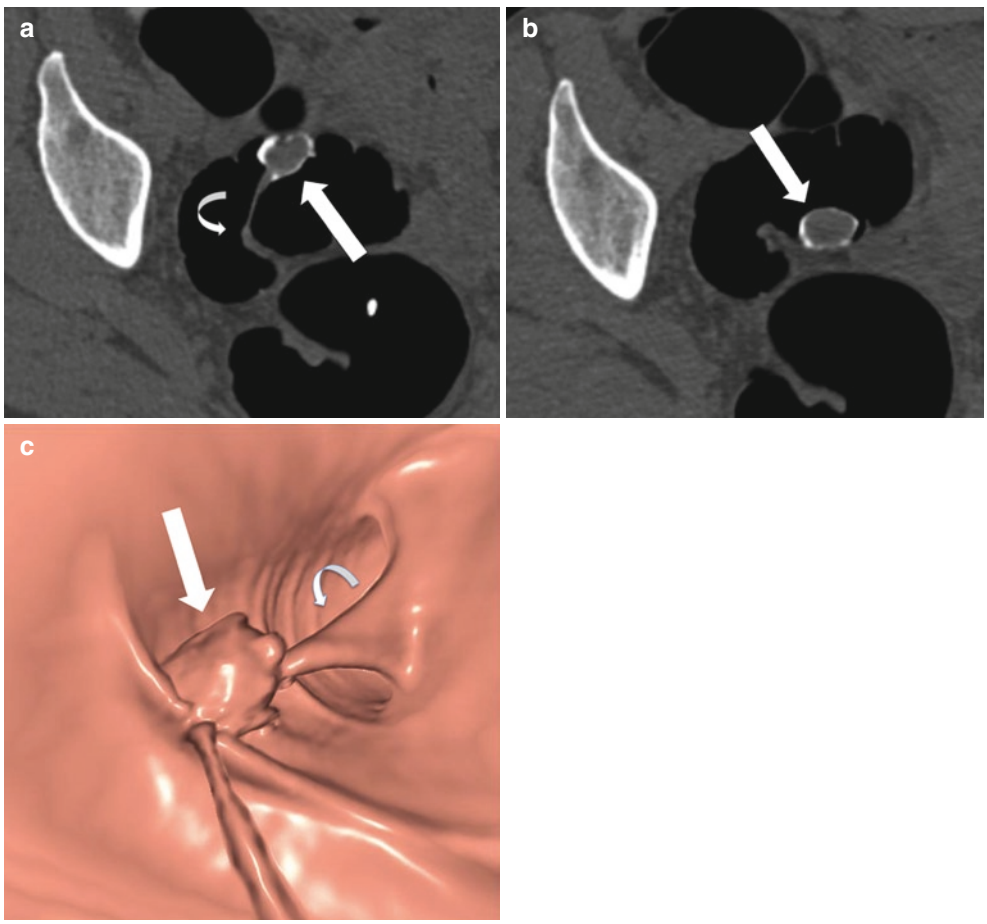

Fig. 15.1 **Pedunculated polyp with long stalk**. Axial CT prone image (**a**) shows a 20 mm polypoid lesion in the sigmoid colon with a head (*arrow*) partially covered by tagging agent, connected to colonic wall by a long and thin stalk (*curved arrow*). Axial CT supine image (**b**) shows the typical marked positional change of the polyp's head (*arrow*) that moves to the posterior wall of sigmoid colon in response to gravity. At 3D image (**c**), the pedunculated polyp with its head (*arrow*) and its stalk (*curved arrow*). **TEACHING POINT**: An important issue concerning pedunculated polypoid lesion is that they can move, sometime dramatically when the stalk is long, during changing of decubitus due to gravity and they represent so called "mobile polyps." They may move not only from the anterior to posterior surface (or vice versa), but axially along the length of the colon as well. The automatic supine to prone linking done by the workstation software will need to be "unlinked" to show the comparison properly

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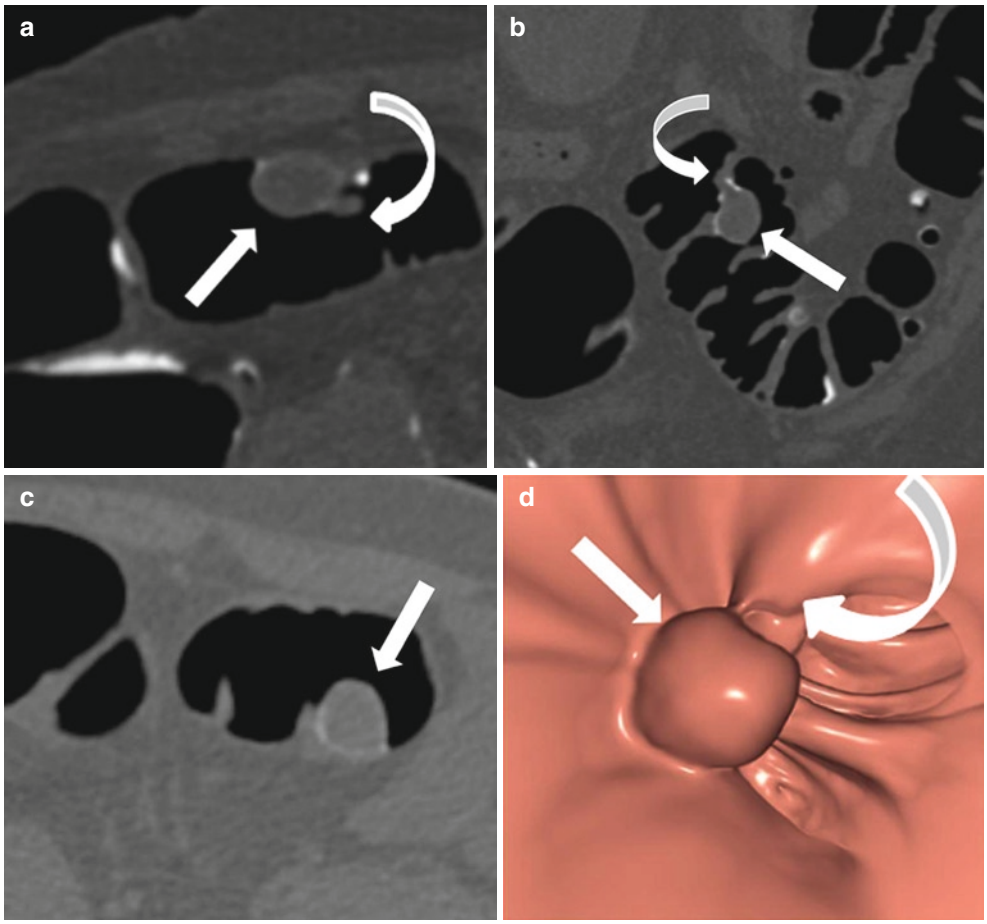


Fig. 15.2 **Pedunculated polyp, mobile**. Axial CT prone image. (**a**) shows a polypoid lesion with a head (*arrow*) and its stalk (*curved arrow*). Coronal reformatted 2D image (**b**) clearly shows the head (*arrow*) within the colonic lumen and a thin pedicle (*curved arrow*) recognizable separately from adjacent haustral folds. Axial CT supine image (**c**) confirms the positional change of the head (*arrow*). The 3D endoluminal image (**d**), shows the pedunculated polyp with its head (*arrow*) and its stalk (*curved arrow*)

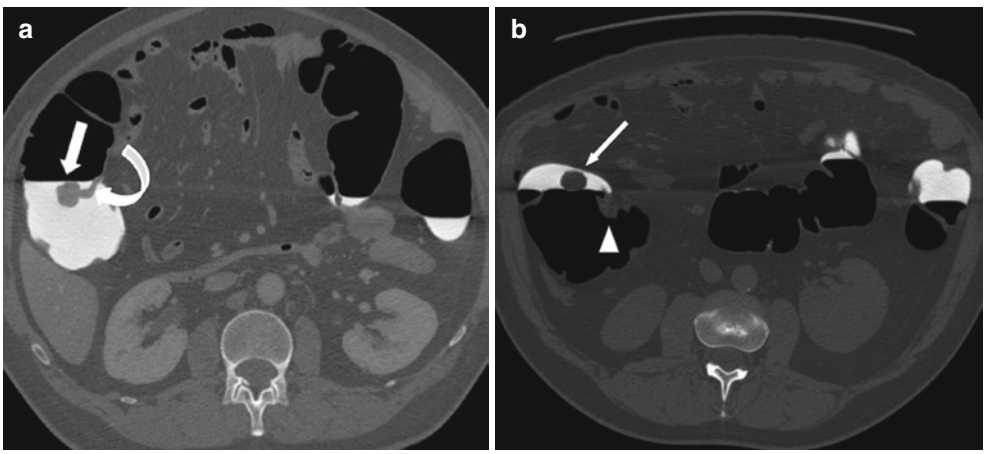
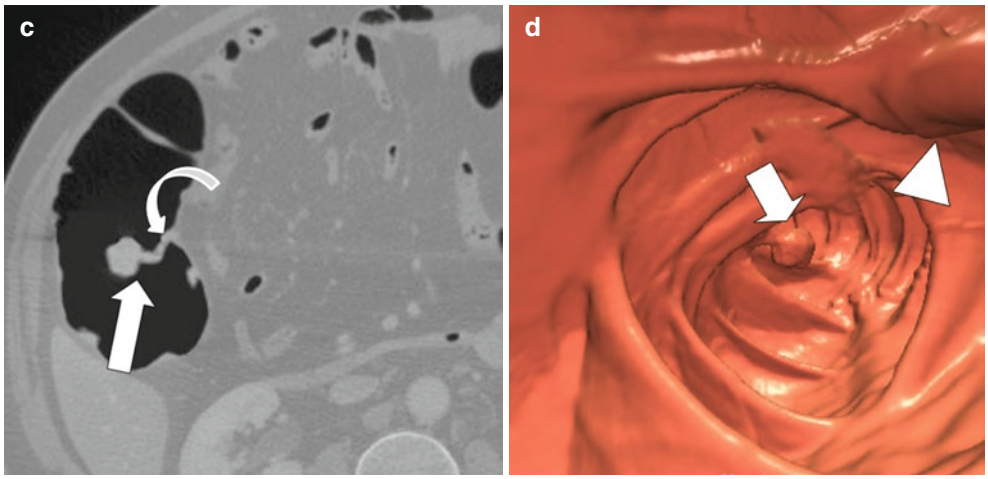


Fig. 15.3 **Pedunculated polyp, right colon, submerged in tagged fluid**. Axial supine (**a**), prone (**b**) and coronal reformatted 2D CTC images show, in the ascending colon, a 20 mm polypoid lesion with the head (*arrow*) protruding within the colonic lumen and anchored to the medial bowel wall by a long stalk (*curved arrow*) just few centimeters above the ileocecal valve (*arrowhead*) .The entire pedunculated polyp is easily detectable within the dense iodated contrast as the head moves with gravity and remains fully submerged both in prone and supine positions. Axial 2D (**c**) and endoluminal 3D CT (**d**) images show the pedunculated polyp (*arrow*) after electronic cleansing of tagged fluid and ileocecal valve (*arrowhead*)

Fig. 15.3 (continued)



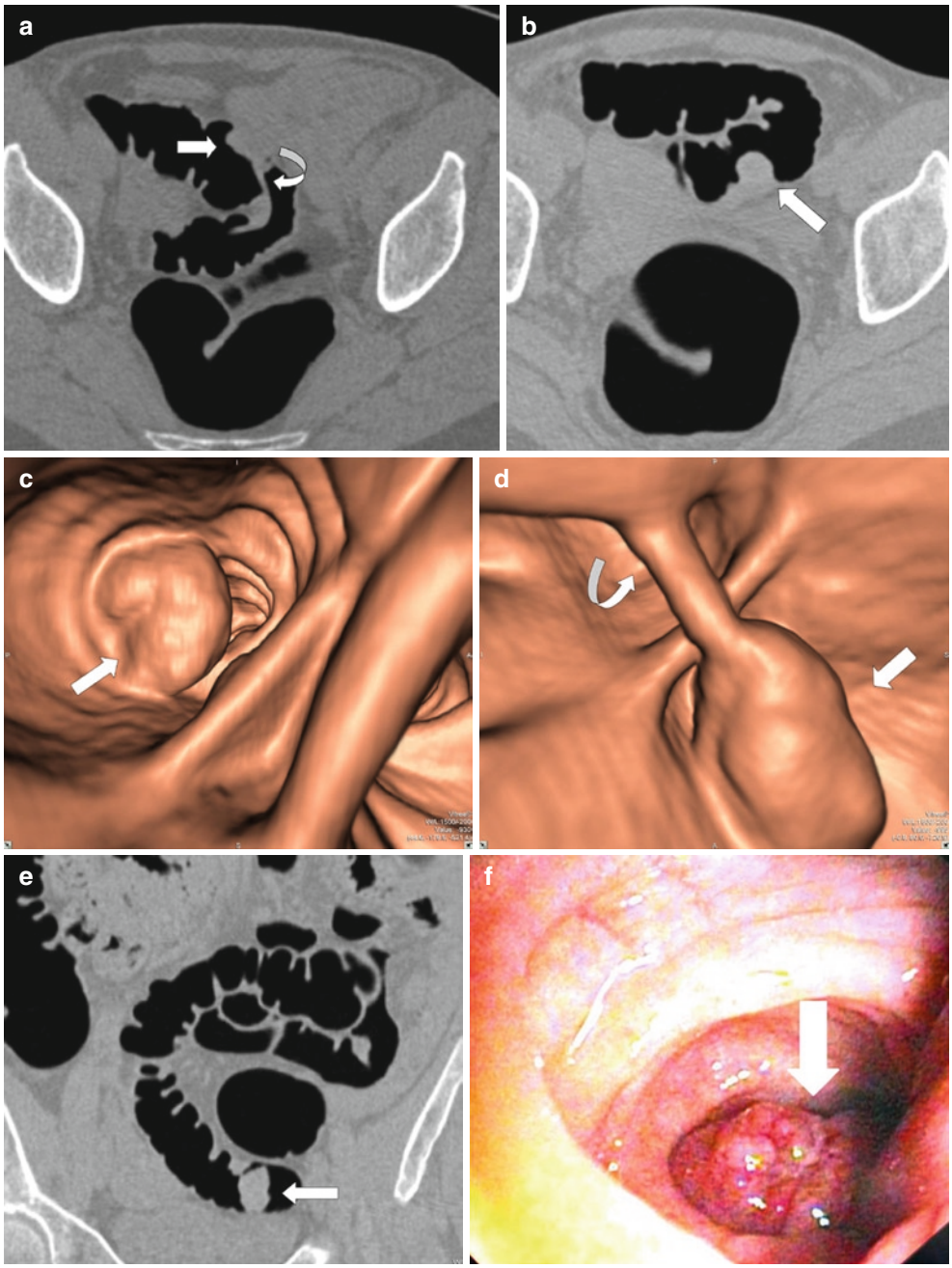


Fig. 15.4 **Pedunculated polyp stalk conspicuous on only one view**. Axial CT prone image (**a**) shows, in sigmoid colon, a polypoid lesion with a head (*arrow*) connected to colonic wall by a stalk (*curved arrow*). Axial CT supine image (**b**) shows the typical positional change of the head (*arrow*) according to gravity and the stalk is hard to see. At 3D CT images (**c, d**) the pedunculated polyp with its head (*arrow*) is seen well on both view, but the stalk (*curved arrow*) is hidden on the supine view (**c**) as the head of the polyp abuts the stalk. On coronal reformatted 2D supine image (**e**) only the polyp's head (*arrow*) is clearly visible (**f**). Endoscopic image showing the lesion (*arrow*) (**f**)

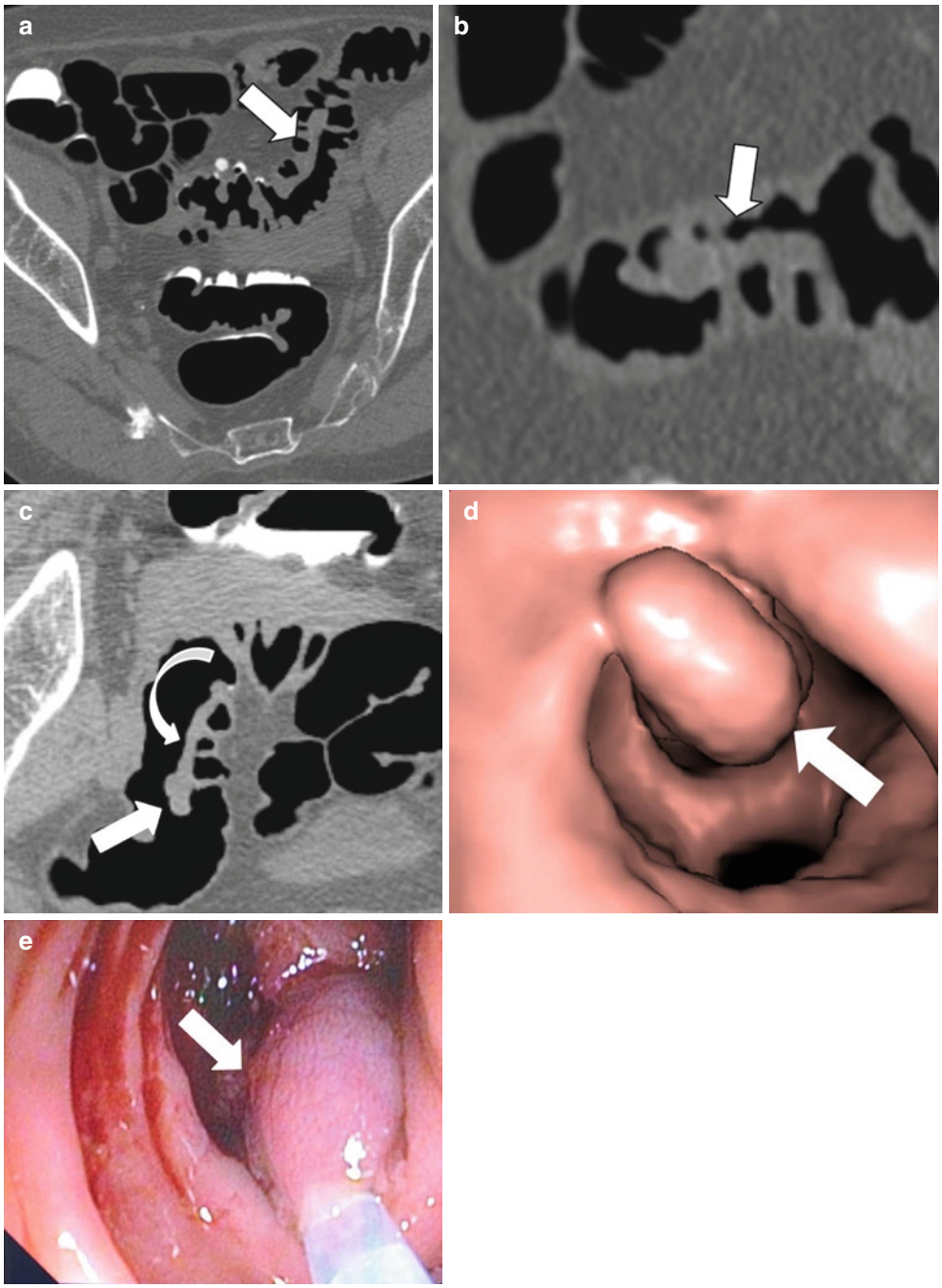


Fig. 15.5 Long stalk more conspicuous on 2D than on some 3D views. Axial, prone (**a**) and supine (**b**) 2D reformatted images show a pedunculated polyp with its head (*arrow*) and a long stalk (*curved arrow*) following the colon axis at a right angle to the sigmoid haustral folds. In this patient with hypertrophy of muscle layer and severe diverticular disease there is reduced distensibility of the sigmoid lumen. After intravenous injection of a spasmolytic agent, with the aim to have a more distension of intestinal lumen during CTC examination and reduced pain permitting administration of additional air, the stalk (*curved arrow*) is now easily distinguishable from thickened folds (**c**). 3D CT (**d**) and endoscopic (**e**) images show endoluminal view of the head (*arrow*) of the polyp

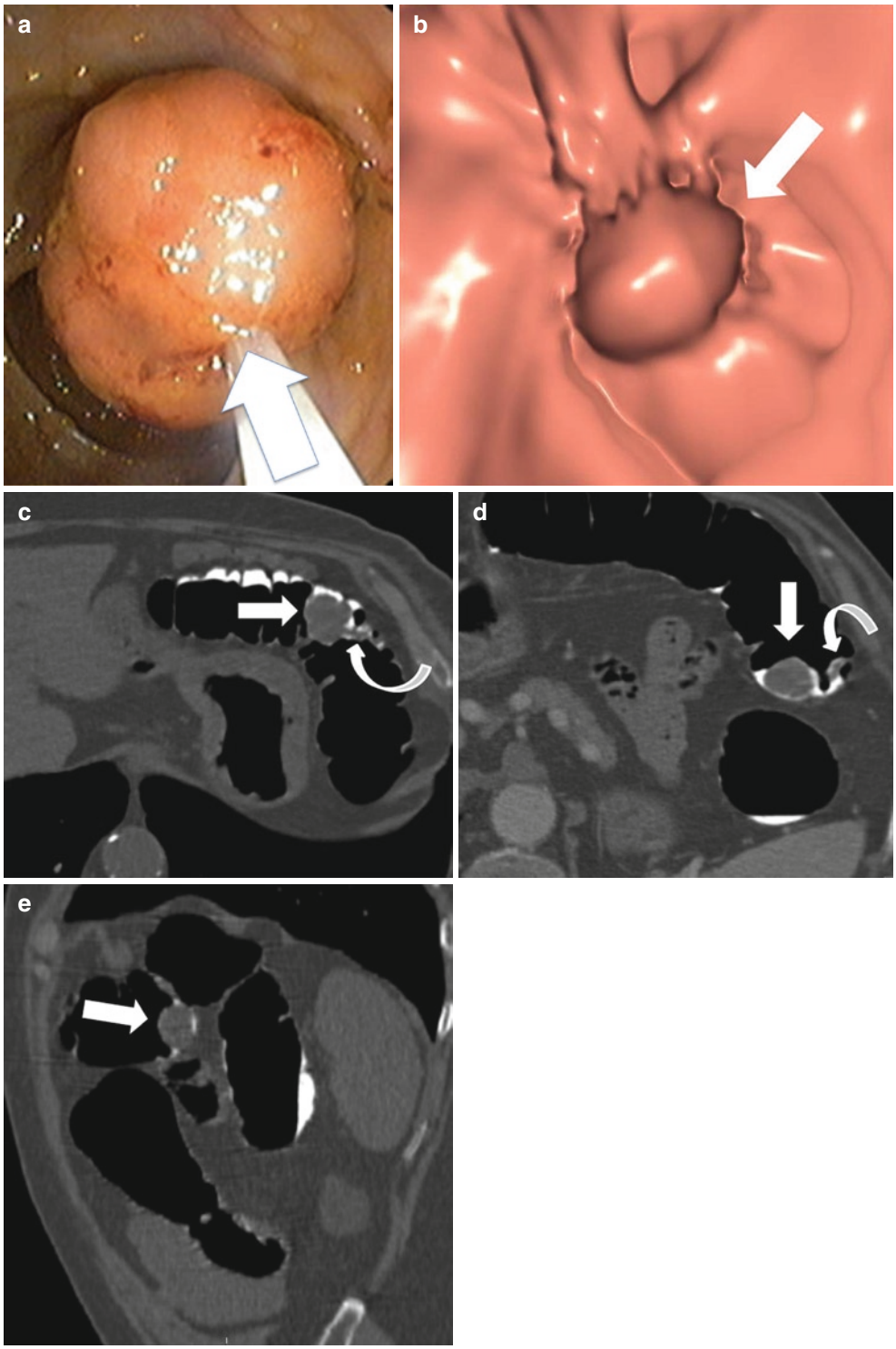


Fig. 15.6 **Large pedunculated polyp**. (**a**) At colonoscopy. (**b**) 3D CTC: the head (arrow) of this polyp can be seen lying adjacent to some haustral folds. (**c**, **d**) 2D CTC obtained on prone and supine position and 2D reformatted sagittal imaging (**e**) showing the head (*arrow*) and the stalk (*curved arrow*) of this polyp partially covered by tagging agent. Large (≥10 mm) polyps can be seen equally using either 2D or 3D images

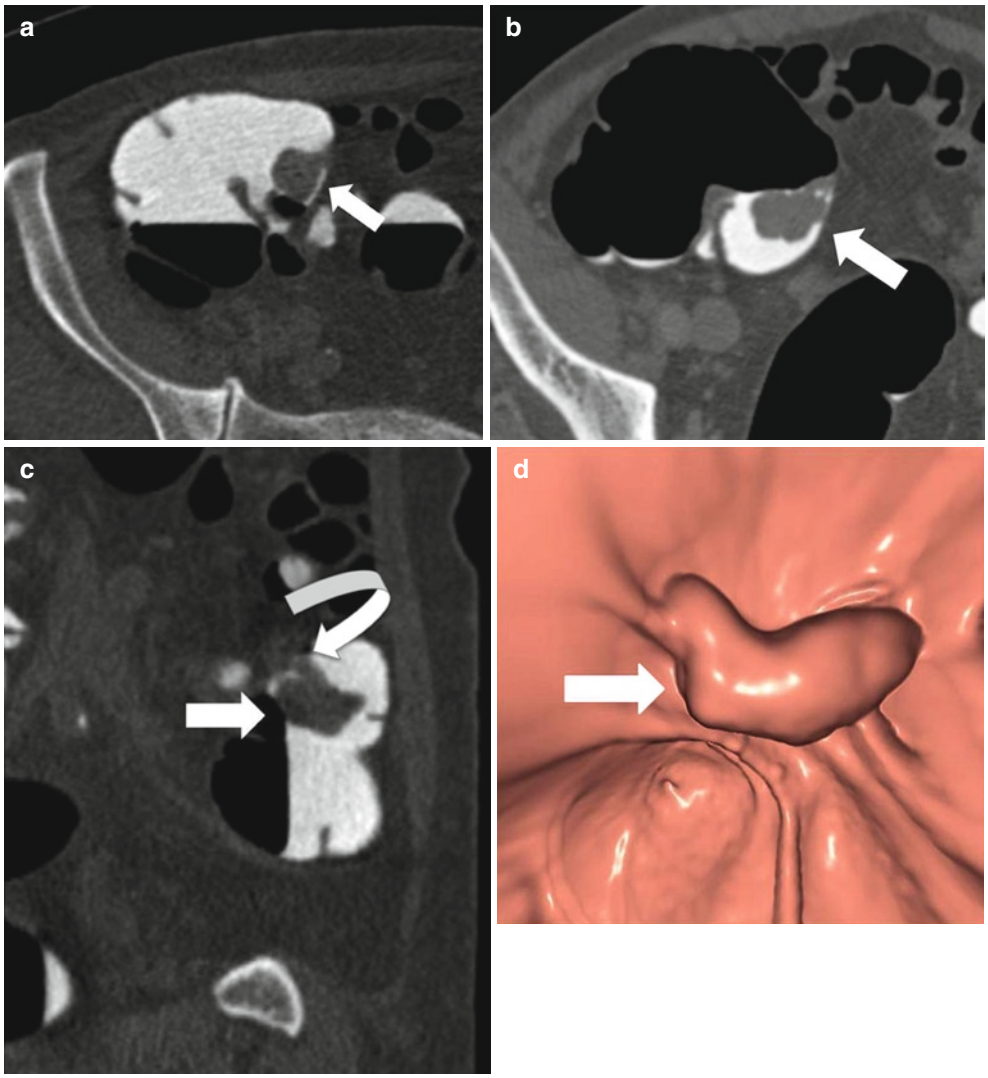


Fig. 15.7 Pedunculated polyp with a short stalk. Axial CT prone (**a**), supine (**b**) images showing within the cecum, a filling defect appearing like a polypoid soft tissue (*arrow*) easily recognizable due to the fact that is fully submerged by tagging fluid. Sagittal reformatted 2D image (**c**) showing the lesion (*arrow*) anchored by a short stalk (*curved arrow*) to the bowel wall 3D image (**d**) confirms the presence of a pedunculated lesion (*arrow*) clarifying the presence of short stalk. Note that when measuring a pedunculated polyp, only the head of the polyp should be included in the measurement, using either bi-dimensional or single longest dimension as the key metric. The length and thickness of the stalk can be described in a subjective manner

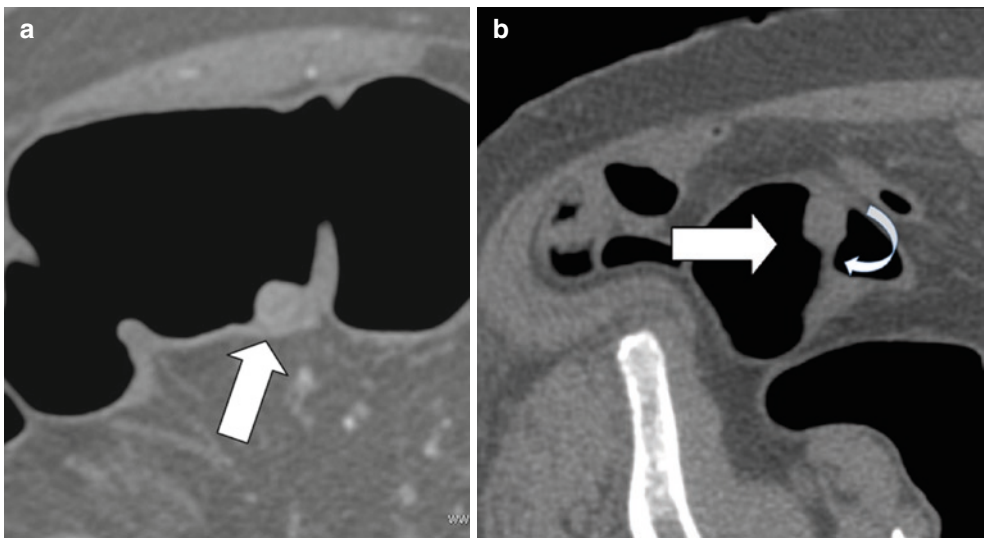
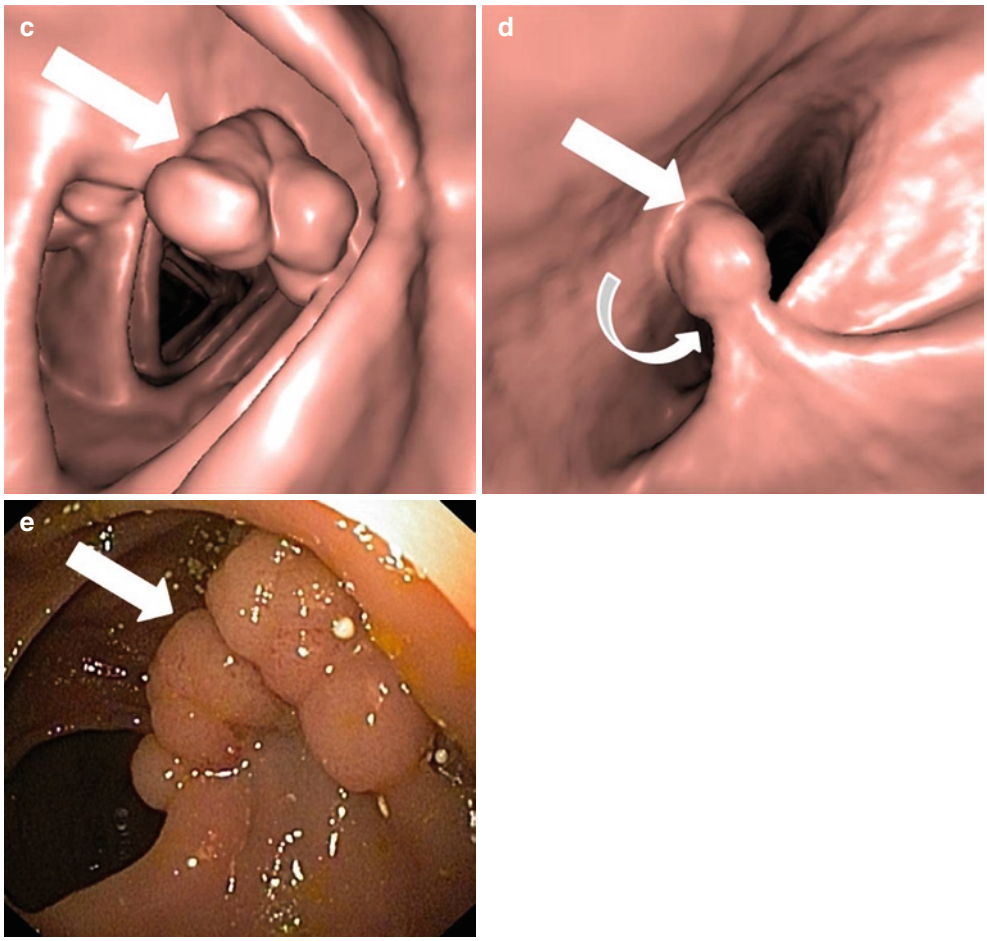


Fig. 15.8 Lobulated polyp with short thick stalk. (**a**) Supine axial image showing a polyp (*arrow*) in the sigmoid colon that seems to be a sessile lesion. On prone image (**b**) the lesion (*arrow*) moves from posterior to anterior bowel wall showing a short and thick pedicle (*curved arrow*). 3D images (**c, d**) obtained either on supine either on prone position showing two different virtual views of the lesion (*arrow*) with lobulated contours better depicted on supine and with a short and thick pedicle (*curved arrow*) visible only on prone. At colonoscopy (**e**), lobulated morphology of the pedunculated adenoma was confirmed

Fig. 15.8 (continued)



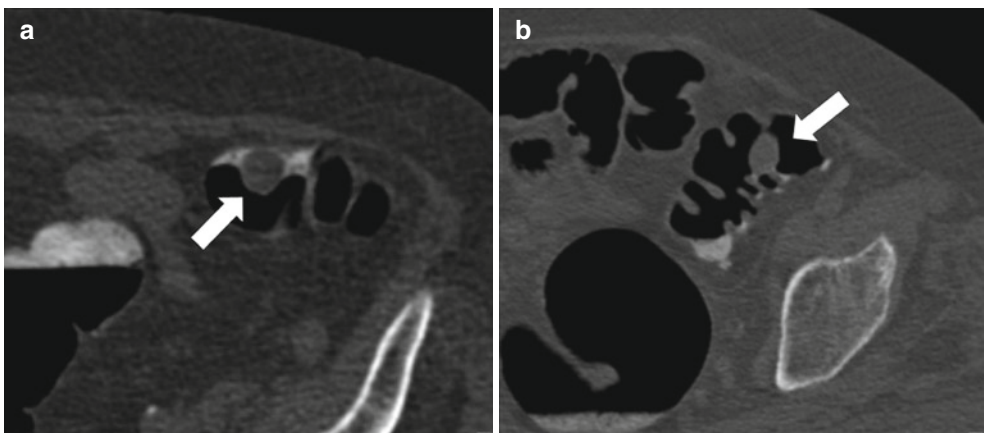


Fig. 15.9 **Pedunculated polyp with short stalk**. Axial CT prone (**a**), supine (**b**) and coronal (**c**) images show, in the sigmoid, a pedunculated polyp (*arrow*) with a short stalk. 3D image (**d**) represents the virtual view of the lesion (*arrow*)

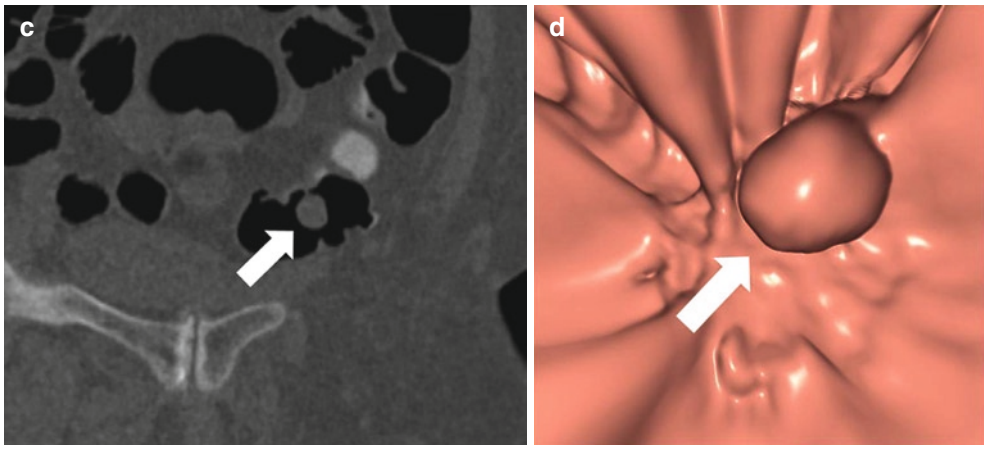


Fig. 15.9 (continued)

Diminutive Polyps

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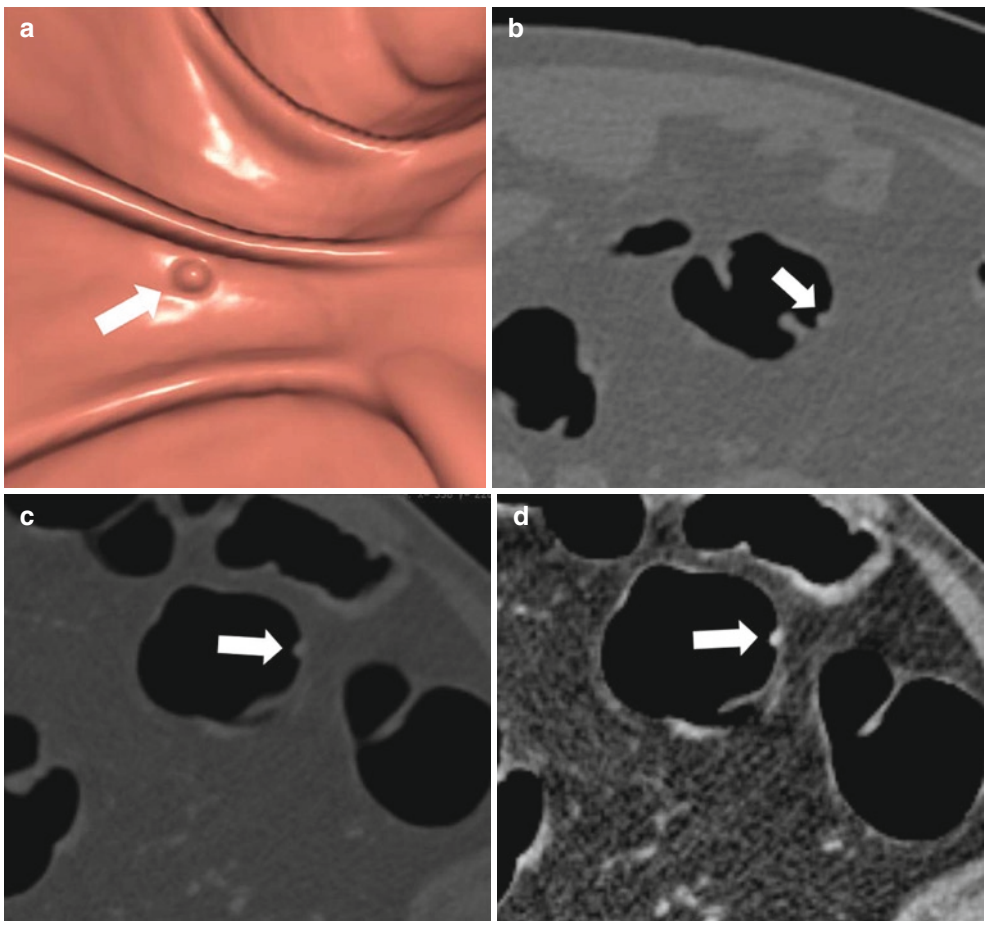

Fig. 16.1 **Sessile hyperplastic polyp** (0.4 cm) (**a**) Endoluminal 3D CTC image shows a sessile polyp (*arrow*) located between haustral folds. (**b**) Supine axial CT image shows a 4 mm homogeneously attenuating polypoid filling defect (arrow) of the sigmoid colon that remained on the same lateral aspect of bowel wall after changing to both the decubitus and the prone position (**c**). When viewing the axial 2D image with an abdominal soft tissue window-level setting (**d**), one can now appreciate the homogeneous soft-tissue density of this tiny lesion (*arrow*).
TEACHING POINT: Note how small polyps are generally more conspicuous on 3D images than on 2D images

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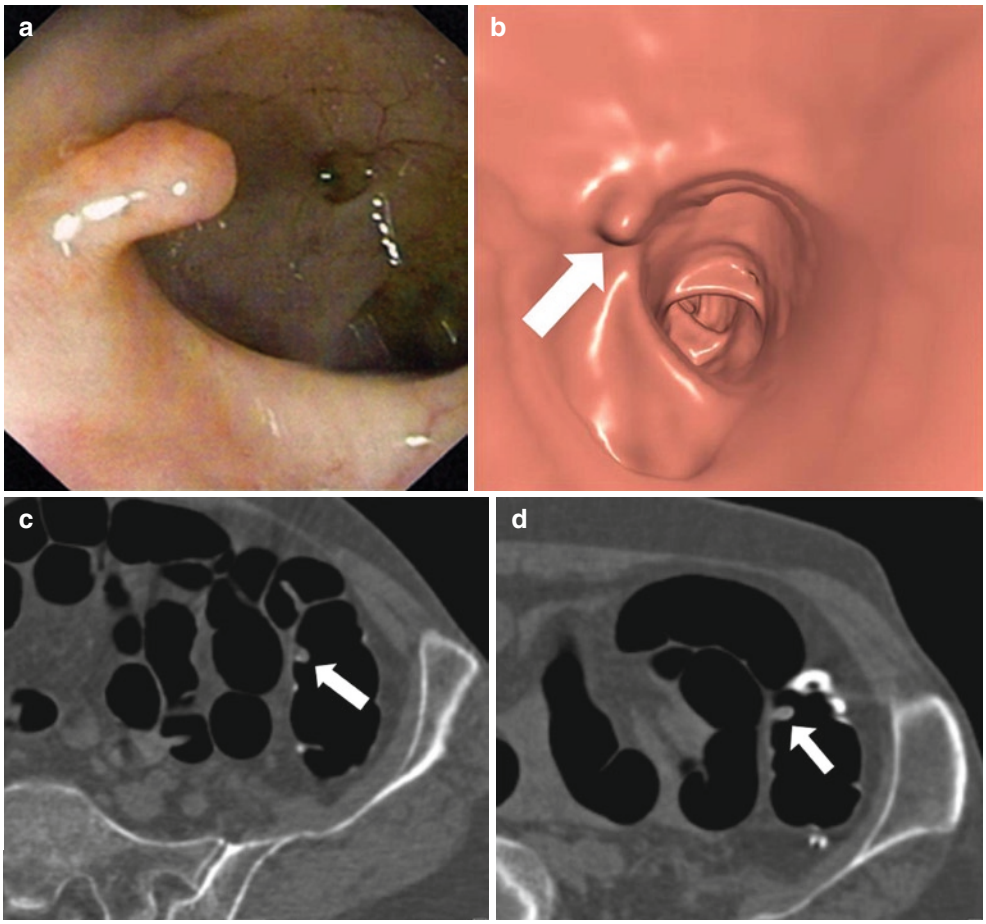

Fig. 16.2 **Sessile small-sized polyp in the descending colon**. (**a**) At endoscopy, a 5 mm sessile hyperplastic polyp (*arrow*) is visible growing off a fold. (**b**) Three-dimensional CTC endoluminal image shows the same lesion (*arrow*) and its relationship to a fold. (**c**) Axial CT image obtained both in supine (**c**) and in prone (**d**) position showing a small-sized 5 mm sessile polyp (arrow) located on medial wall of the descending colon.
TEACHING POINTS: Diagnosis of polyp is easy due to the fixed position of the lesion on both the prone and supine acquisitions and due to the fact that the lesion is hypodense and not tagged, whereas the residual fluid is well tagged. The proper measurement of the lesion is the long axis, which in this case is the height of the polyp given its elongated shape, as seen best on the endoscopic view. The radiologist should work to obtain the best single longest dimension of the lesion (per C-RADS recommendations)

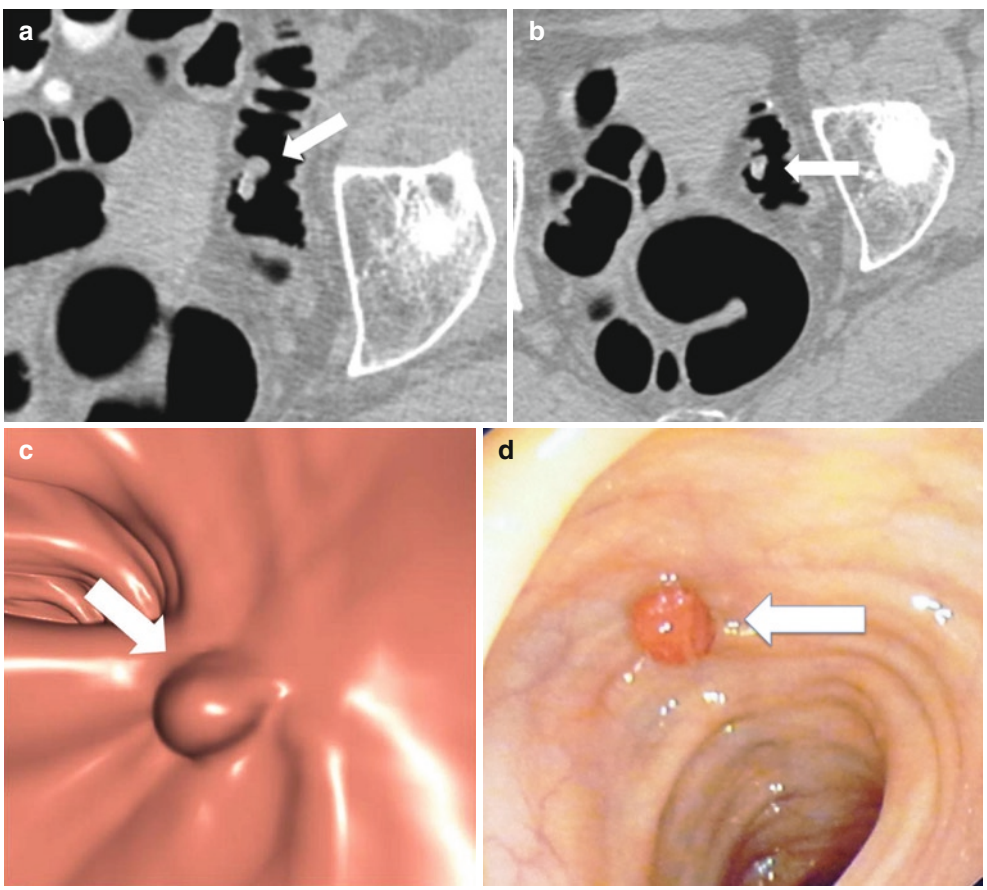

Fig. 16.3 **Sessile 7 mm hyperplastic polyp growing off a fold on the descending colon**. (**a**) Axial supine CT image showing a diminutive 7 mm polypoid filling defect (*arrow*) in proximity to the mid-descending colon protruding within colonic lumen. (**b**) On axial prone CT image, the same lesion (*arrow*) seems to be coated by the oral tagging agent, which, when recognized, helps improve lesion conspicuity. The polyp is a sessile lesion growing off the lower aspect of a fold. (**c**) 3D endoluminal image showing a precise correlation of the lesion (*arrow*) between CTC and endoscopic image (**d**). Also note that precise measurement of polyps in the 7–9 mm range is important, since overmeasurement to 10 mm will convert the C-RADS classification to a C2 (immediate colonoscopy), whereas 6–9 mm lesions are classified as C3 (option for 1- to 3-year follow-up)

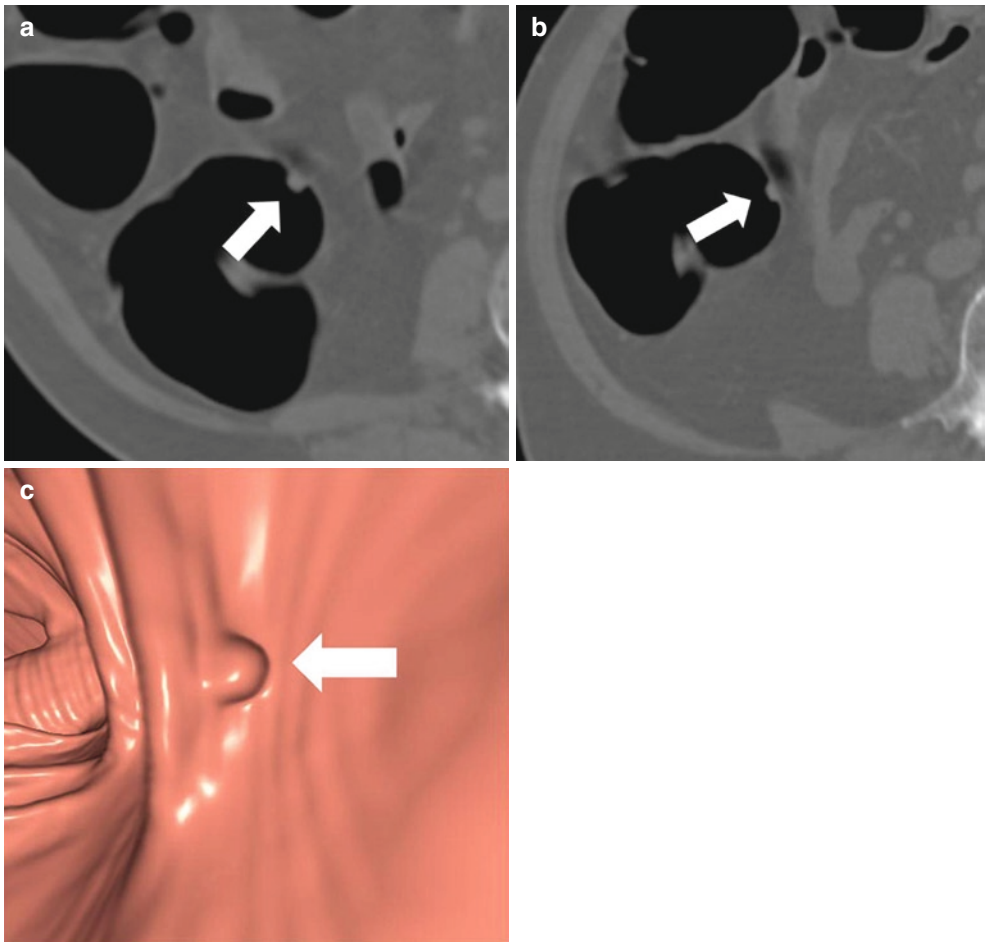

Fig. 16.4 Sessile medium-sized polyp in the ascending colon. Prone CTC axial 2D image (**a**) showing a small polypoid filling defect (*arrow*) located on medial aspect of ascending colon. On axial 2D supine image (**b**) the lesion remains on the same medial aspect of the ascending colon, thus providing the right diagnosis of small polyp. (**c**) Three-dimensional CTC endoluminal image showing polyp (*arrow*). Small polyps are often more conspicuous on the 3D endoluminal fly-through

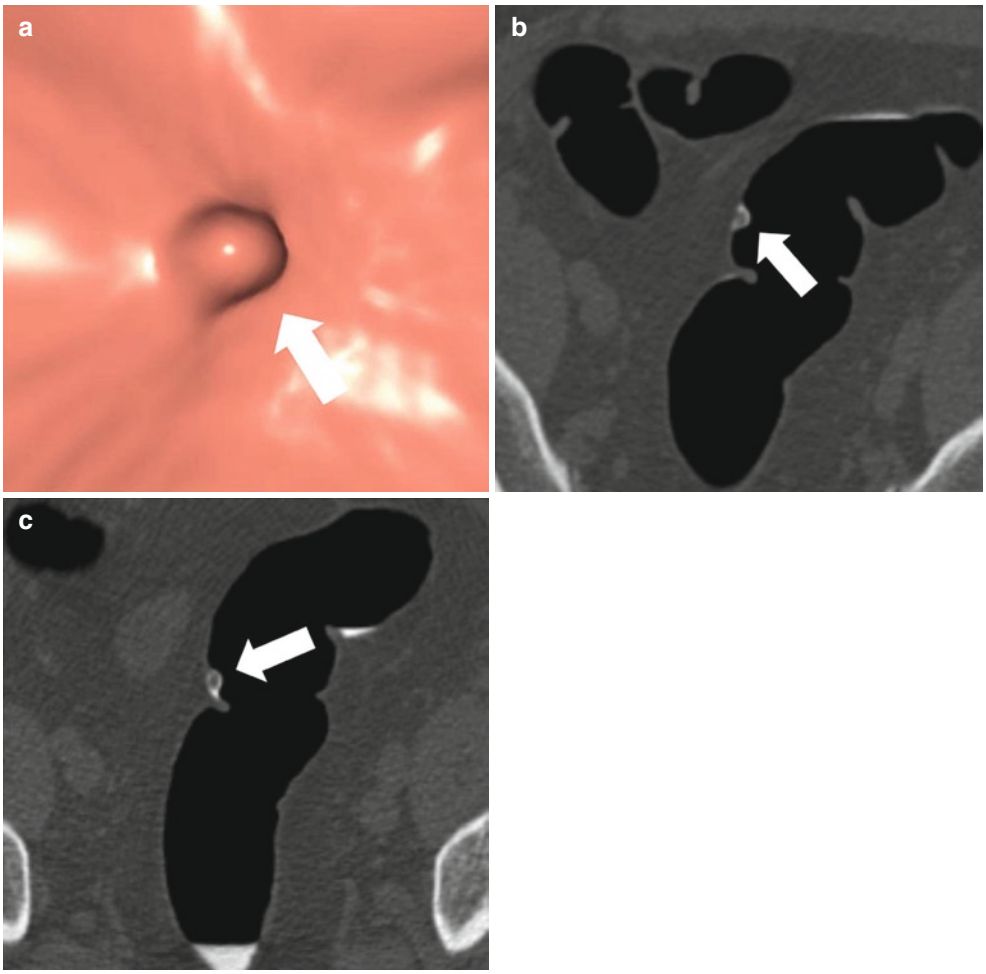

Fig. 16.5 **Sessile 3 mm hyperplastic polyp in the sigmoid**. (**a**) Three-dimensional CTC image shows a 3 mm sessile polyp (*arrow*) in the sigmoid colon. (**b**) Axial CT 2D image obtained on prone position showing a polypoid hypodense filling defect (*arrow*) partially submerged by tagging agent. After changing of decubitus on axial CT 2D image obtained on supine position, (**c**) the small lesion remains anchored to medial bowel wall partially covered by tagging agent, thus providing a diagnosis of small polyp.
TEACHING POINTS: When a polyp is on the proximal side of a fold, be sure to include this information in the report and alert the endoscopist, since polyps on proximal sides of folds are more likely to be missed on conventional endoscopy because the endoscope is an end-viewing instrument. Some newer instruments have better visualization with very wide angle lenses. Also note that the use of fecal tagging is crucial in increasing conspicuity and detection of small polyps as well as specificity of the technique. Although normally polyps under 5 or 6 mm are not reported per C-RADS guidelines, when patients have large polyps, the incidence of synchronous polyps is about 25%, and under these circumstances, other diminutive polyps can (optionally) be reported

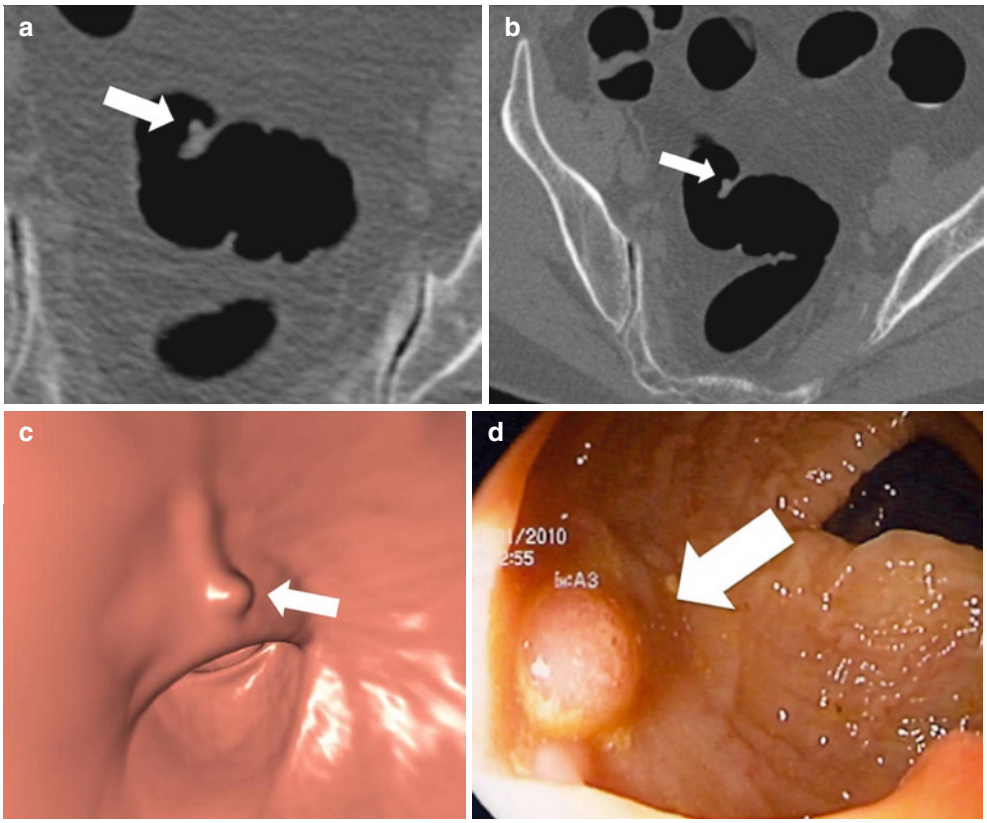

Fig. 16.6 Sessile 6 mm adenomatous polyp of sigmoid arising from haustral fold. Axial prone CT image (**a**) demonstrates a diminutive sessile polyp (6 mm) (*arrow*) arising from a slightly haustral fold in sigmoid colon. (**b**) Axial 2D CT image obtained on supine position depicts its relationship with the fold. On 3D CT endoluminal image (**c**) is seen the typical appearance of polypoid lesion (*arrow*) emerging off a fold. (**d**) Endoscopic view. As in Fig. 16.5, this polyp is on the proximal side of a fold, and this observation should be mentioned in the report

Flat Lesions

17

Franco Iafrate and Andrea Laghi

Flat lesions are discussed in detail in Chap. 9. Numerous additional examples of flat lesions demonstrating a spectrum of teaching points are shown here.

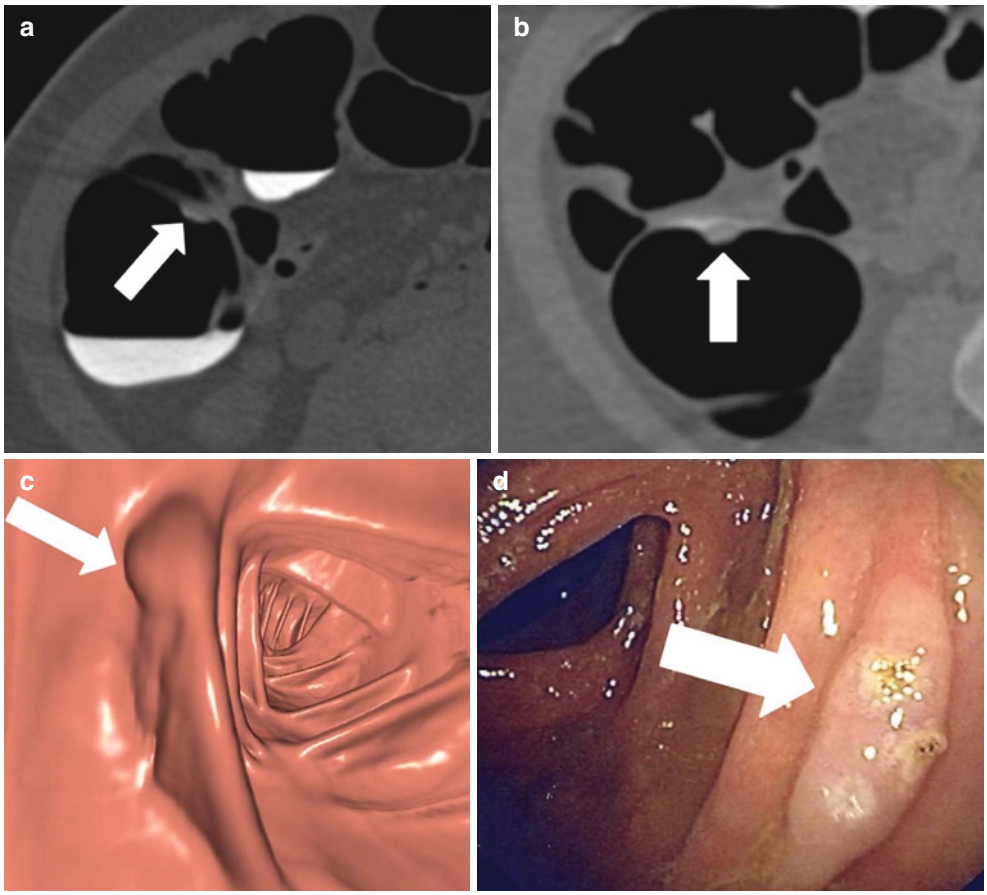

Fig. 17.1 Flat lesion in ascending colon. Flat lesion is defined as superficially elevated lesion lower than 3 mm in height or lesion with a largest diameter at least three times higher than the height. Two-dimensional CTC axial supine image (**a**) of a 15 mm "nonpolypoid" flat superficially elevated lesion (*arrow*) in the ascending colon, partially submerged by iodine-tagged fluid on prone acquisition (**b**), thus providing its easier detection. Endoluminal 3D reconstruction (**c**) showing the lesion (*arrow*) and its relationships with the fold. Endoscopic appearance (**d**) of the same lesion (*arrow*). Patient removed endoscopically the lesion and histopathological analysis revealed an adenoma with low degree of dysplasia

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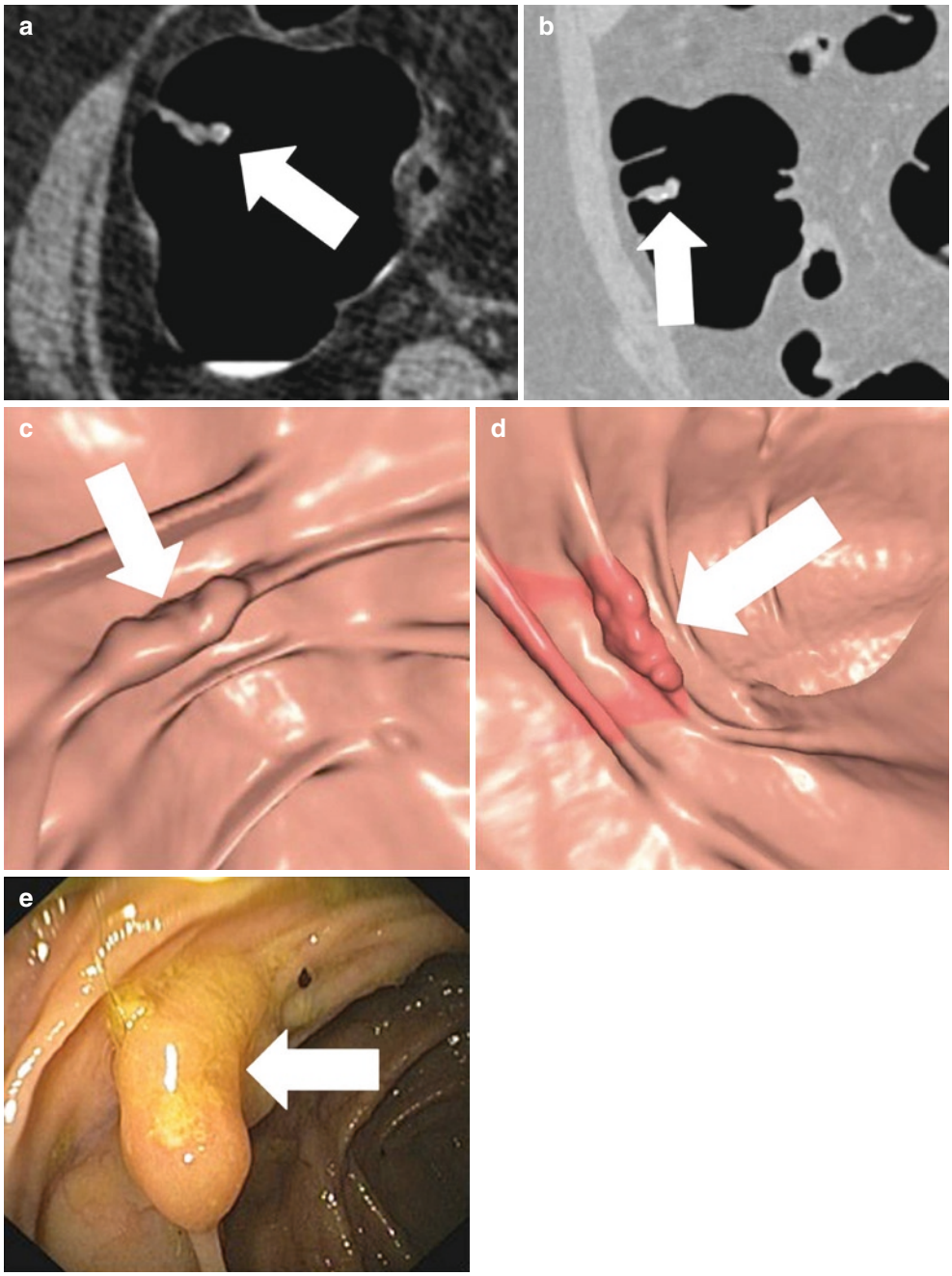


Fig. 17.2 Flat lesion presenting as a thickened haustral fold. Two-dimensional CTC axial (**a**) and coronal (**b**) images using a CTC window level setting, showing a flat lesion arising from a haustral fold (*arrow*). Two-dimensional endoluminal CTC image (**c**) into Three-dimensional endoluminal CTC image (**c**) shows lesion presenting as thickening of haustral fold (*arrows*) in ascending colon. Three-dimensional endoluminal image, after applying CAD software (**d**) helps in identifying this lesion (*arrow*) coloring in red. Optical colonoscopy (**e**) shows thickened fold with surface lobulations (*arrow*), which is in contrast to sharp and smooth appearance of normal haustral folds in adjacent area of ascending colon

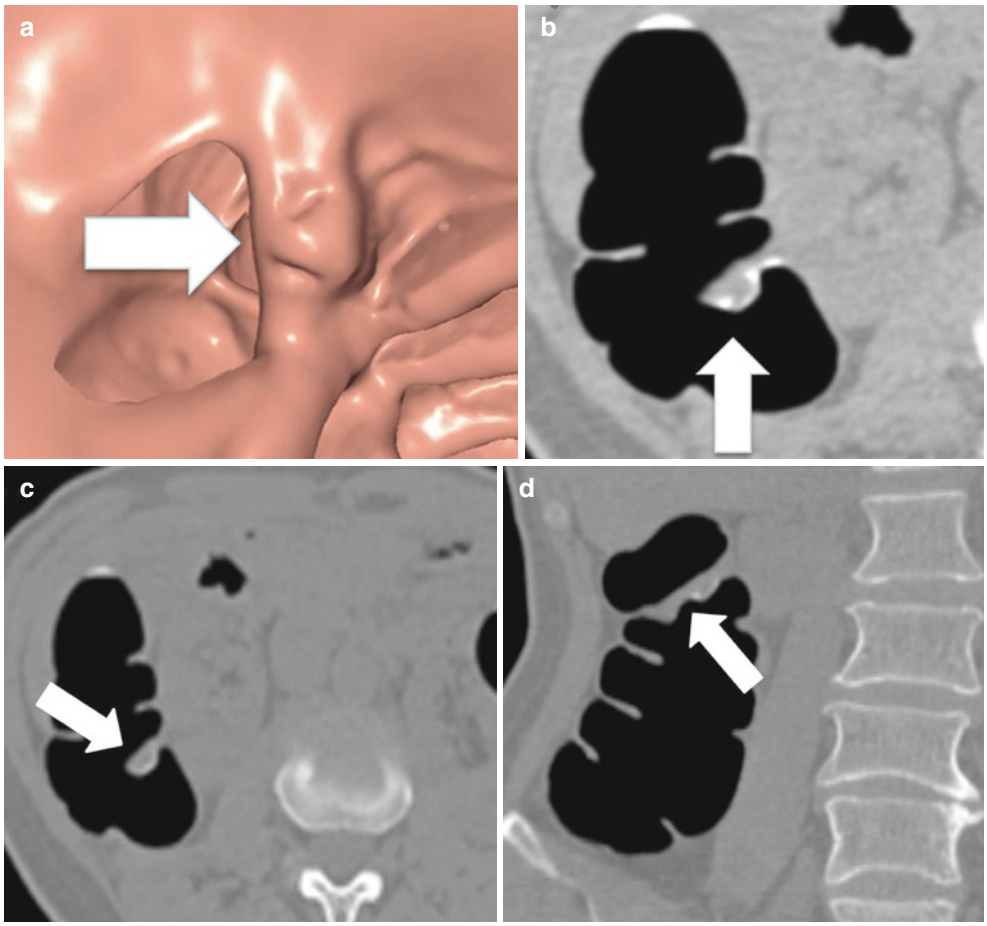


Fig. 17.3 Flat lesion on a fold. Three-dimensional endoluminal CTC image (**a**) shows focal thickening of a fold (*arrow*) within the ascending colon. This appears to be just adherent tagged stool, but 2D correlation, with axial (**b, c**), coronal (**d**), and sagittal images (**e**) show that this is a true soft-tissue lesion (*arrow*) with contrast coating of its surface. Note how the contrast clings only to the polyp and not the normal mucosa. Endoluminal 3D reconstruction after applying CAD software (**f**) that automatically detected the lesion (*arrow*) and marked in red (*arrow*). At colonoscopy (**g**) (*arrow*)

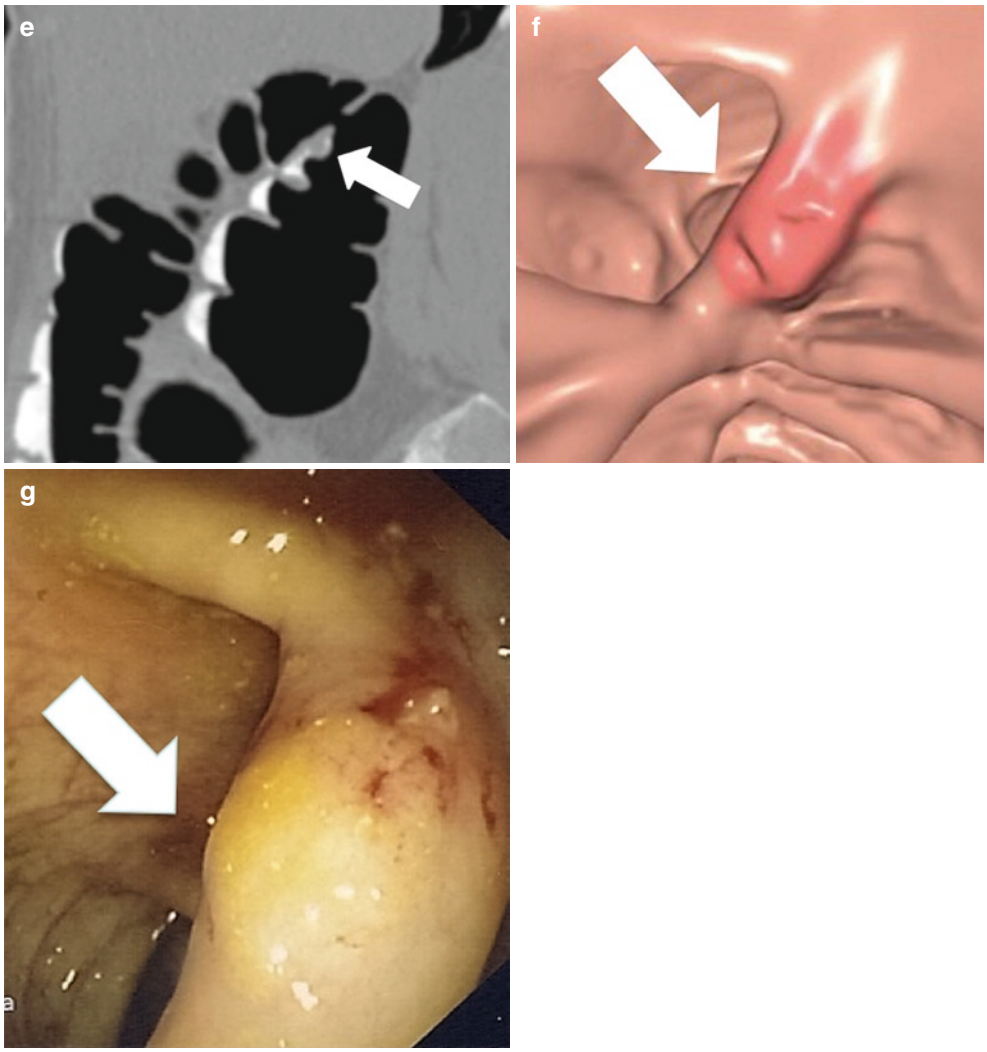


Fig. 17.3 (continued)

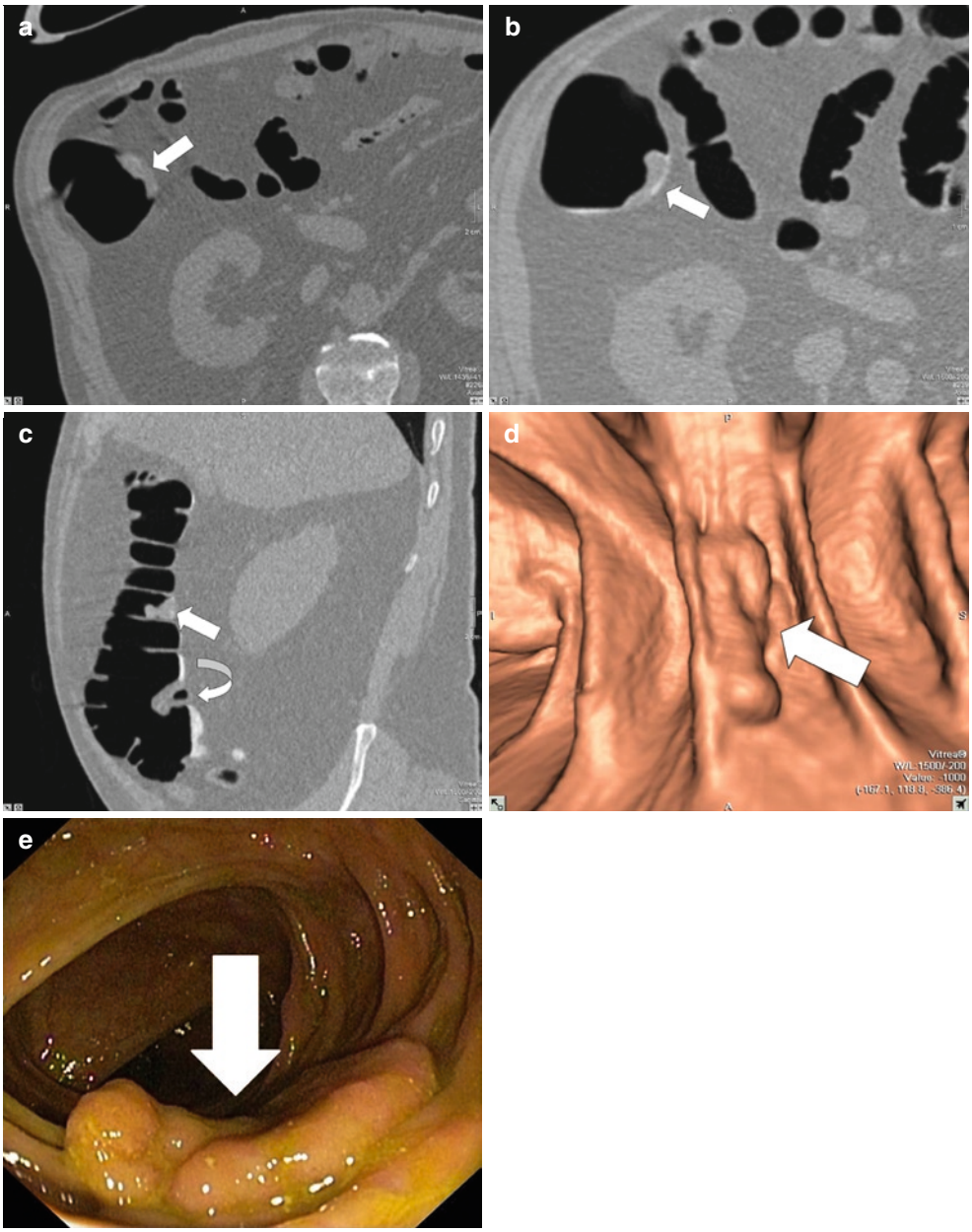


Fig. 17.4 Flat lesion with a central depression. Two-dimensional CTC transverse image obtained on prone position (**a**) and supine position (**b**) showing a lobulated flat lesion (*arrow*) on a fold. The use of multiplanar sagittal (**c**) reformatted image better clarifies the distance of the flat lesion (*arrow*) from ileocecal valve (*curved arrow*). Three-dimensional endoluminal CTC image (**d**) and endoscopic view (**e**) show a slightly elevated lesion (*arrow*) with central depression

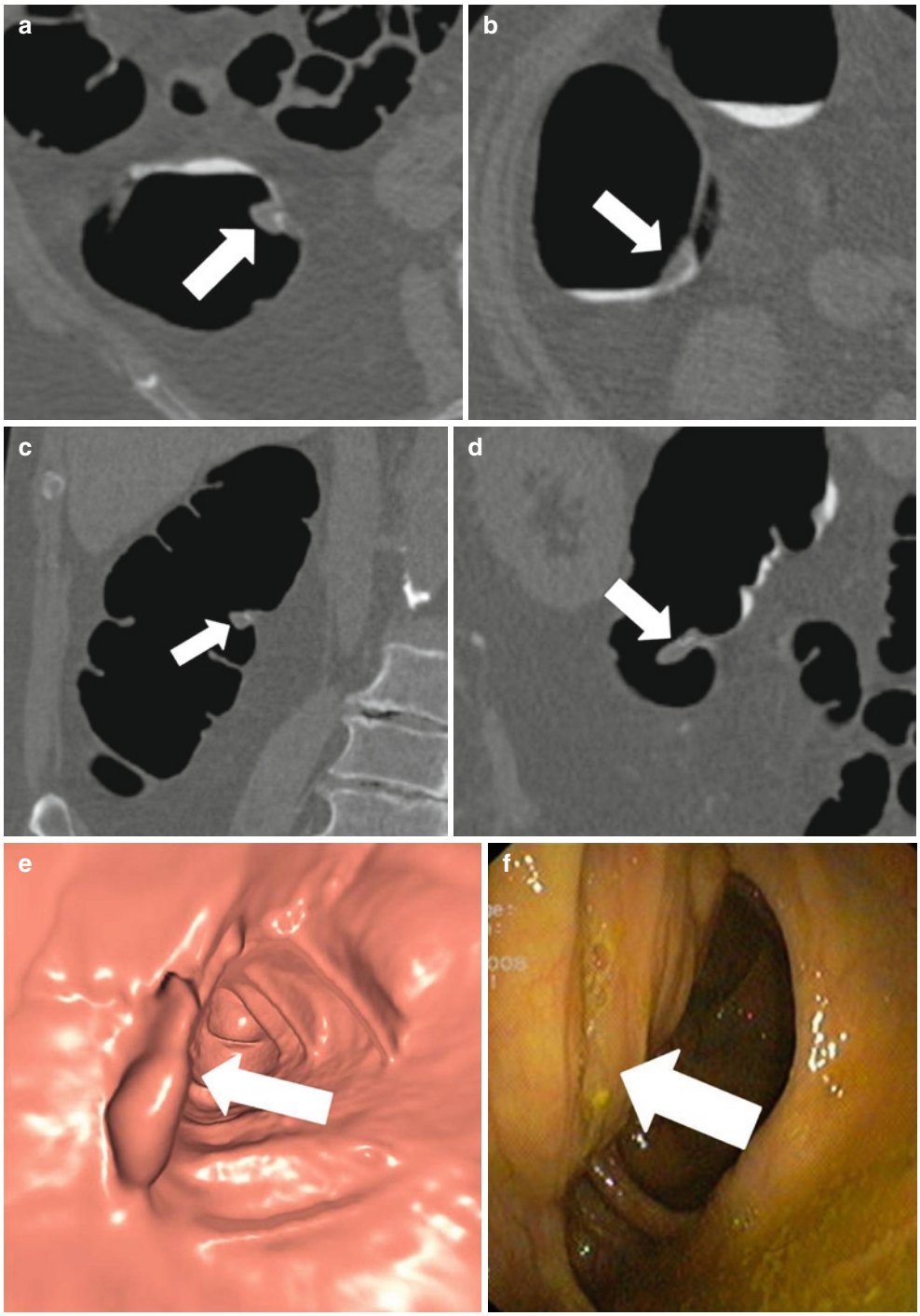


Fig. 17.5 Flat lesion with cigar-like appearance. Occasionally, flat lesion has a small focal attachment to the colonic fold, with the majority of the lesion protruding within bowel lumen. When this occurs, flat lesion acquires a cigar-shaped appearance. Note this appearance of flat lesion (*arrow*) in the right colon at CTC axial prone (**a**), axial supine (**b**), coronal (**c**), and sagittal (**d**) images and 3D endoluminal view (**e**). At colonoscopy (**f**)

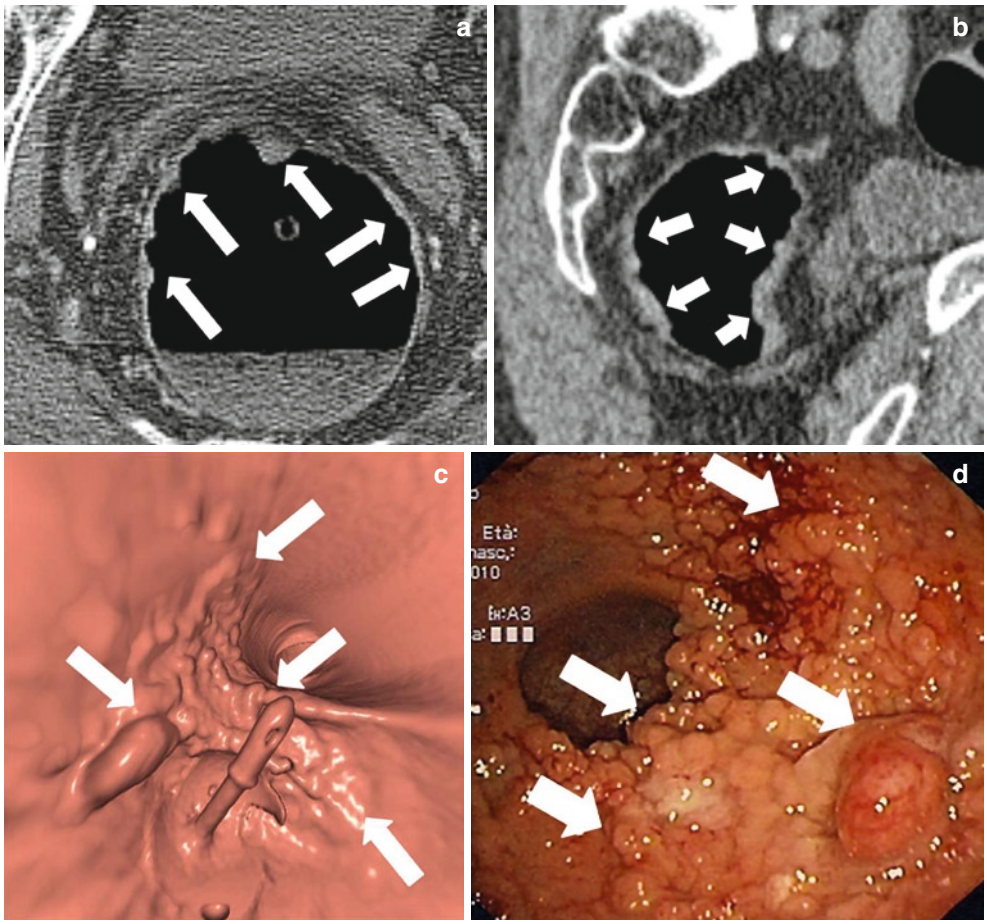


Fig. 17.6 Flat lesion with carpet-like appearance. Two-dimensional axial supine (**a**) and sagittal (**b**) images show flat elevation with nodular surfaces (*arrows*) involving the entire rectal circumference. Three-dimensional endoluminal CTC image (**c**) shows diffuse and irregular mucosal nodularities (*arrows*) surrounding Foley catheter. Colonoscopy (**d**) shows typical carpet-like appearance of the flat lesion (*arrows*)

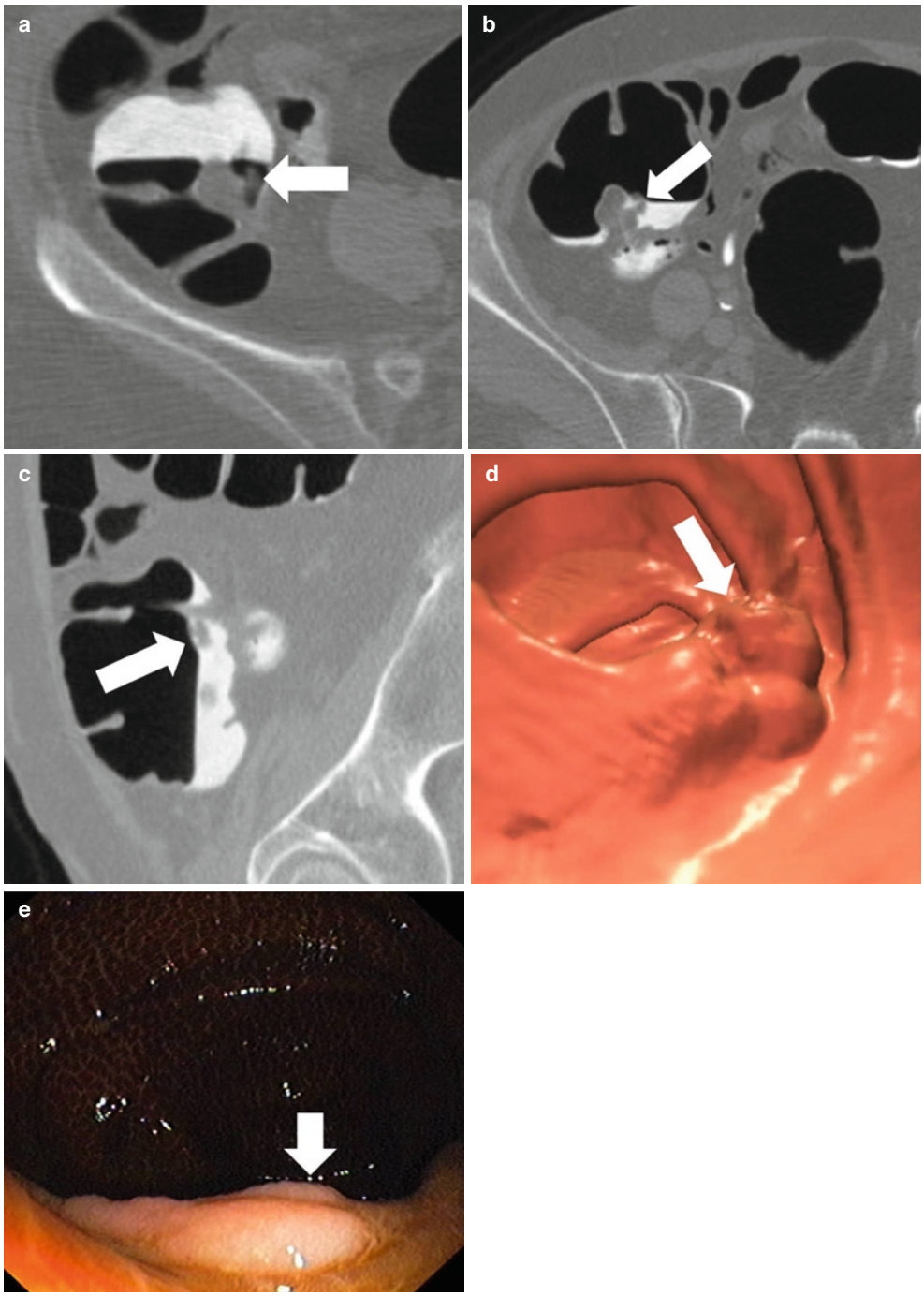


Fig. 17.7 Ileocecal valve presenting a flat lesion. Two-dimensional CTC images on axial prone (**a**), axial supine (**b**), and sagittal (**c**) show a slightly elevated lesion (*arrow*) located on ileocecal valve. Three-dimensional CTC image (**d**) shows a mild irregularity of the surface of the ileocecal valve due to the presence of flat lesion (*arrow*). Colonoscopy (**e**) shows flat lesion (*arrow*) originating from the ileocecal valve and an alteration of colonic mucosa, so-called melanosis coli. Melanosis coli is a condition usually associated with chronic laxative use in which dark pigment (lipofuscin) is deposited in the lamina propria (one of the lining layers) of the large intestine. The pigment deposition results in a characteristic dark brown to black discoloration of the lining of the large intestine. Note how the valve with the flat lesion is the only area free of the melanosis coli

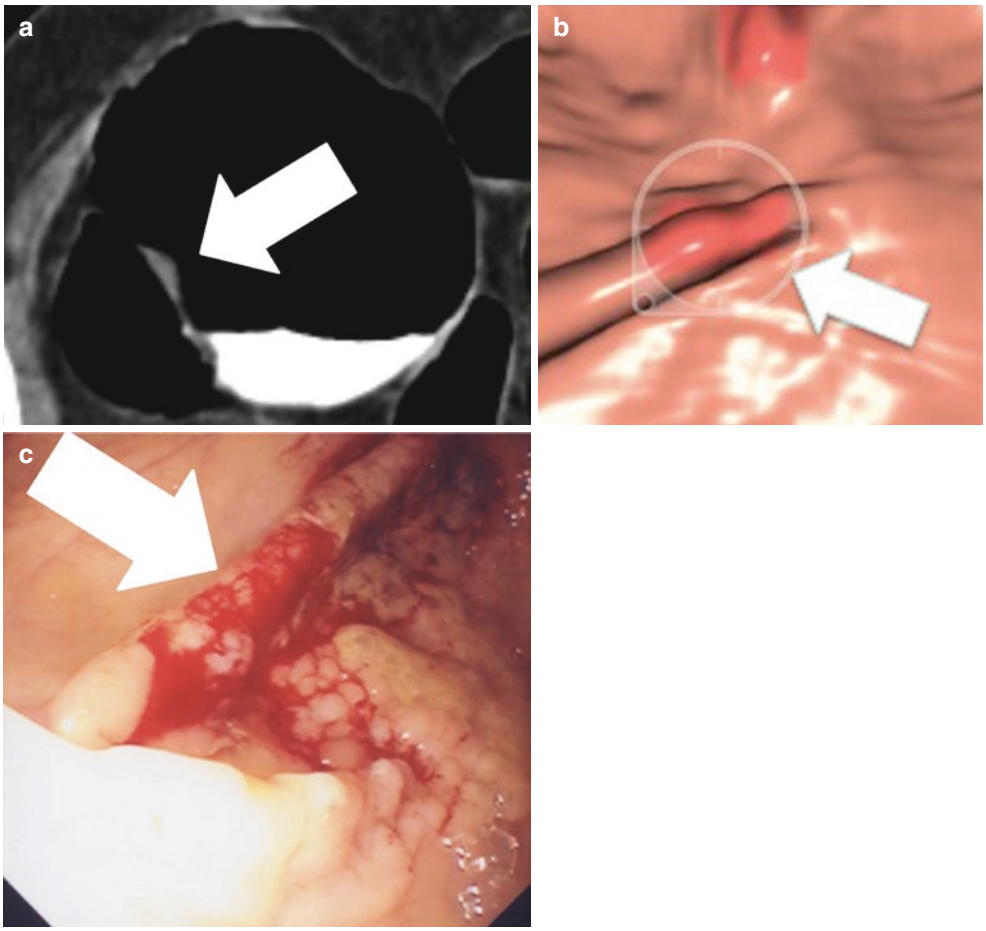


Fig. 17.8 Flat lesion with cigar-like appearance on a fold. Flat lesion may appear only as a subtle area of soft tissue thickening. Two-dimensional CTC axial image (**a**) shows how minimal soft-tissue thickening (*arrow*) is better seen using a soft-tissue window setting. Three-dimensional CTC endoluminal image (**b**) and colonoscopy (**c**) show a thin elevated lesion (*arrow*) rising from a fold

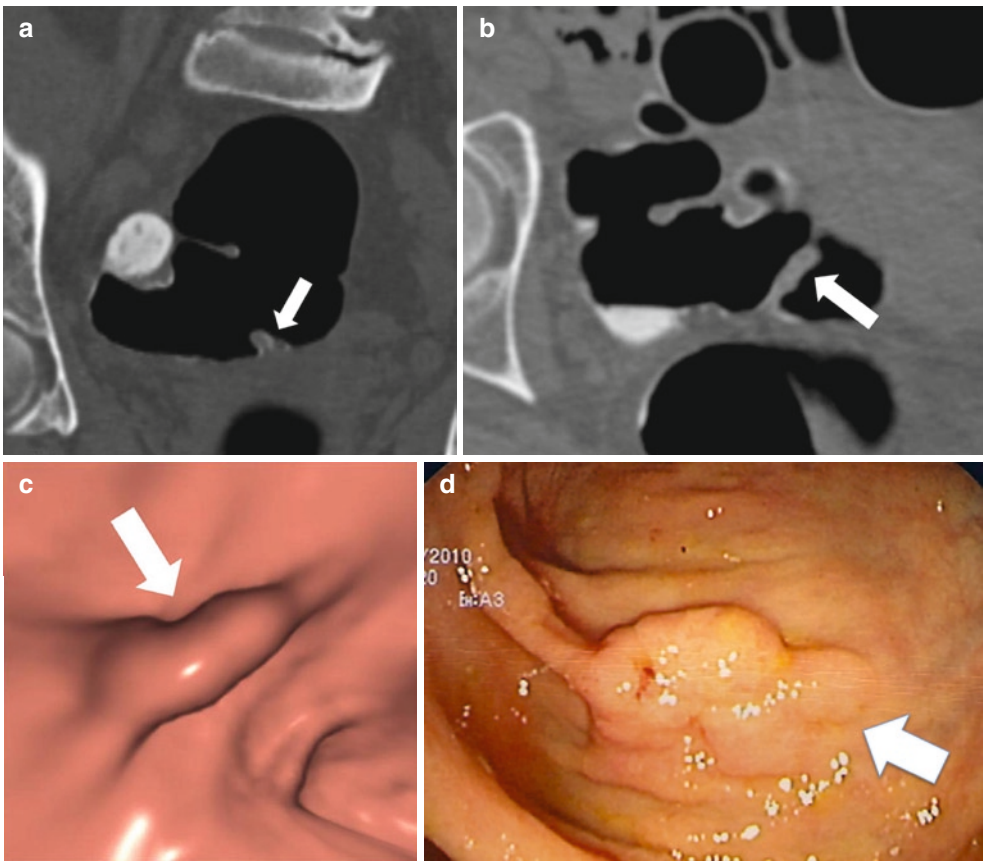


Fig. 17.9 Flat lesion on sigmoid colon. Two-dimensional CTC axial images obtained both in prone (**a**) and supine (**b**) position showing a nonpolypoid flat lesion (*arrow*) of colonic mucosa. On 3D, CTC (**c**) flat lesion (*arrow*) is much more evident, located on a fold. At colonoscopy (**d**), flat lesion (*arrow*) is evident

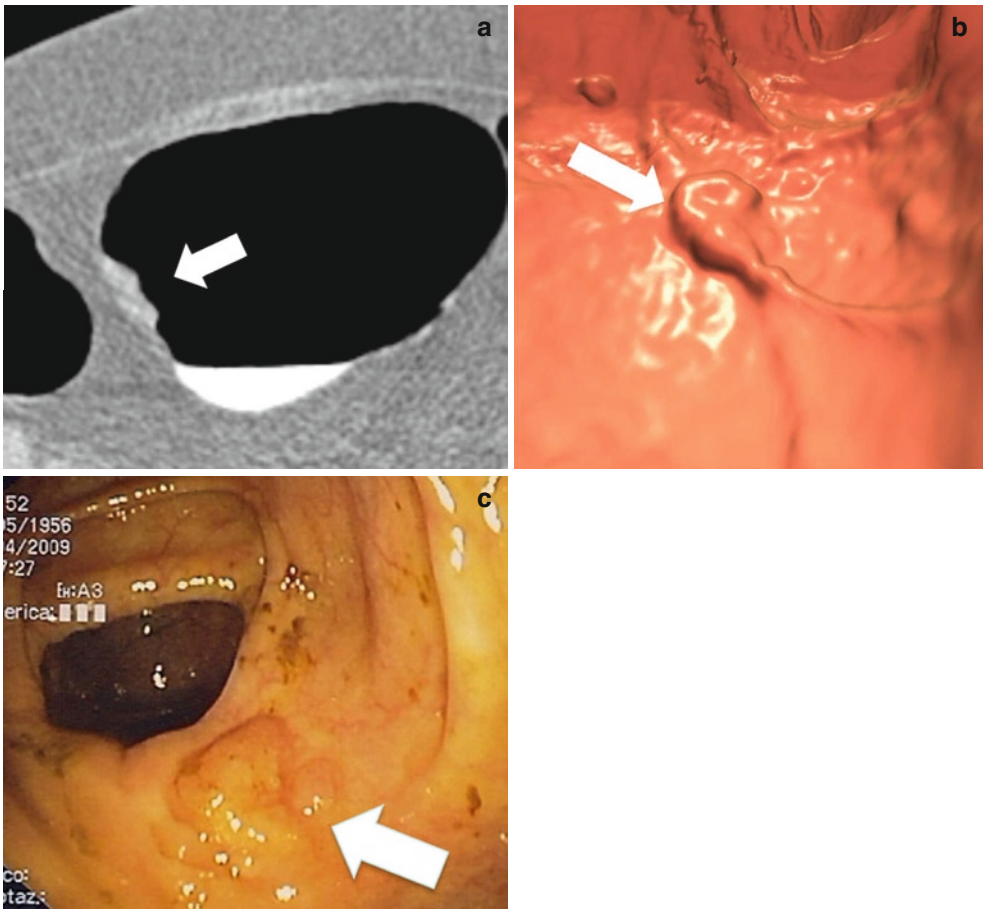


Fig. 17.10 **Flat lesion of the cecum**. Axial 2D CTC (**a**) image showing a slight elevated flat lesion of the apex of the cecum, easily appreciable using abdominal window level setting. Three-dimensional CTC endoluminal (**b**) shows the typical flat morphology of the lesion (*arrow*) confirmed by colonoscopy (**c**)

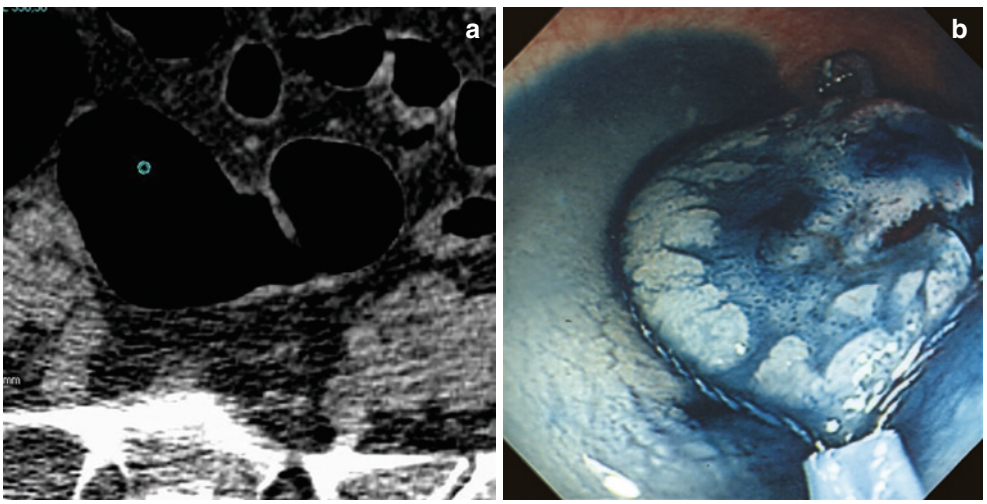


Fig. 17.11 **Flat villous adenoma**. (**a**) Two-dimensional supine image shows variable-height, focal wall thickening (*arrows*) along the dorsal wall of the sigmoid colon. (**b**) Corresponding endoscopic view shows the flat lesion made more conspicuous by indigocarmine dye. A snare is shown around the lesion (Courtesy Stuart Taylor, MD)

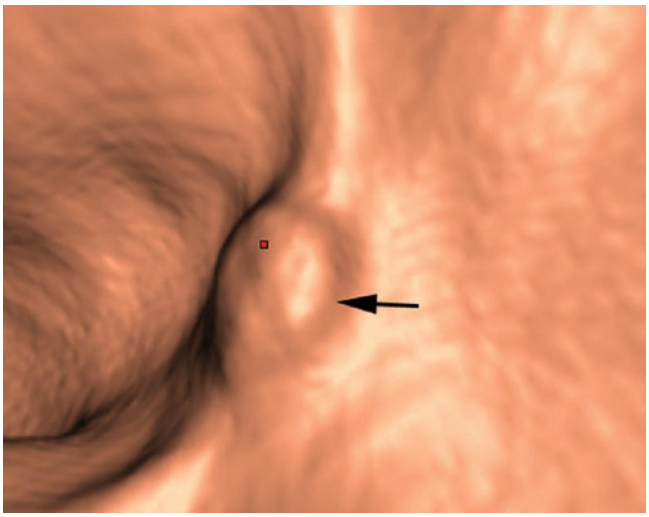


Fig. 17.12 Three-dimensional endoluminal CTC image demonstrating a CAD mark (*red dot*) on an 11-mm transverse colonic T1 cancer (*arrow*) (Reprinted with permission from Taylor SA, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol.* 2008;18:1666–1673)

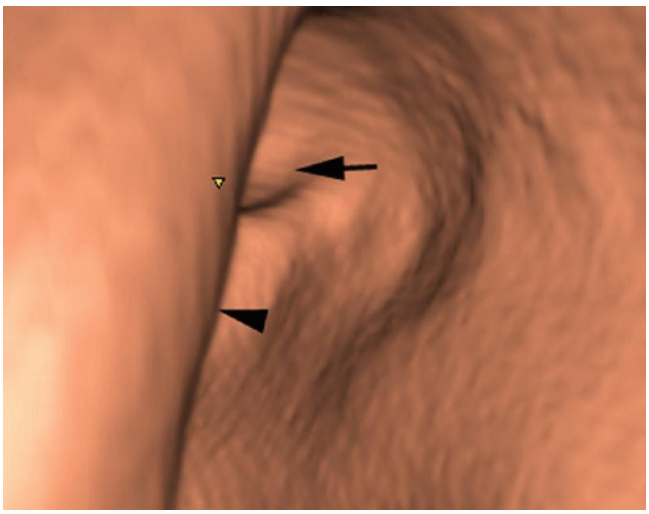


Fig. 17.13 Three-dimensional endoluminal CTC image demonstrating the same lesion (*arrow*) as Fig. 17.2 barely visible behind a haustral fold (*arrowhead*). CAD alerts the reader to the hidden lesion via a yellow triangle (Reprinted with permission from Taylor SA, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol.* 2008;18:1666–1673)

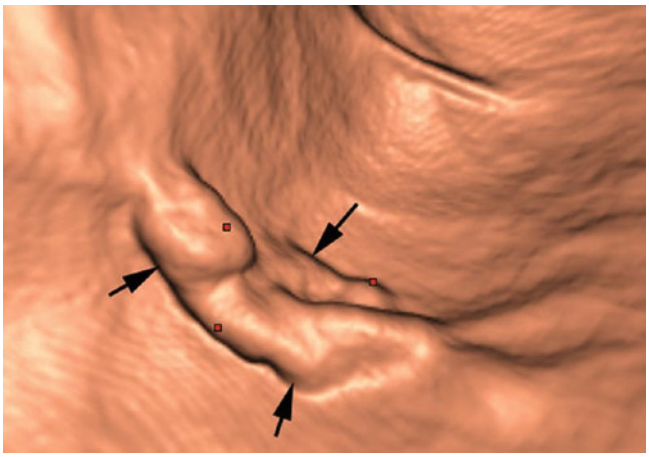


Fig. 17.14 Three-dimensional endoluminal images show a transverse colon type 0-IIa cancer with three correct CAD marks (*red dots*) (Reprinted with permission form Taylor SA, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol*. 2008;18:1666–1673)

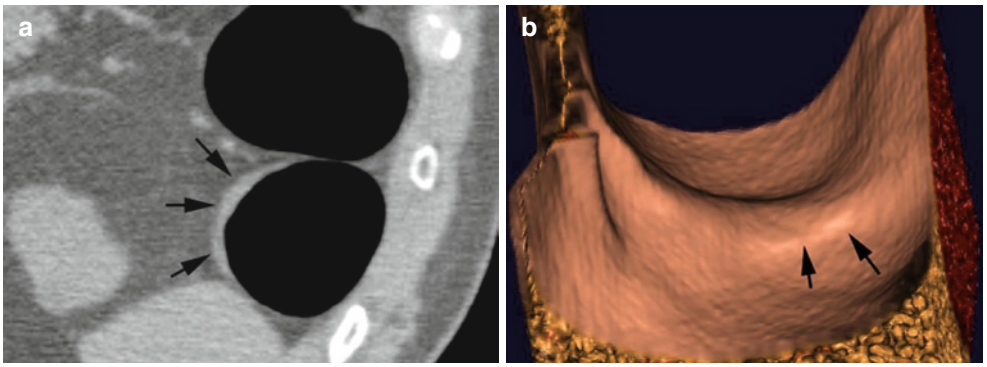


Fig. 17.15 Two-dimensional axial CTC image (**a**) shows a type 0-IIa cancer (*arrows*) as an area of subtle mural thickening. The lesion was not detected by CAD. (**b**) Three-dimensional endoluminal CTC image showing the same lesion as 5A. The lesion (*arrows*) is barely visible (Reprinted with permission from Taylor SA, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol.* 2008;18:1666–1673)

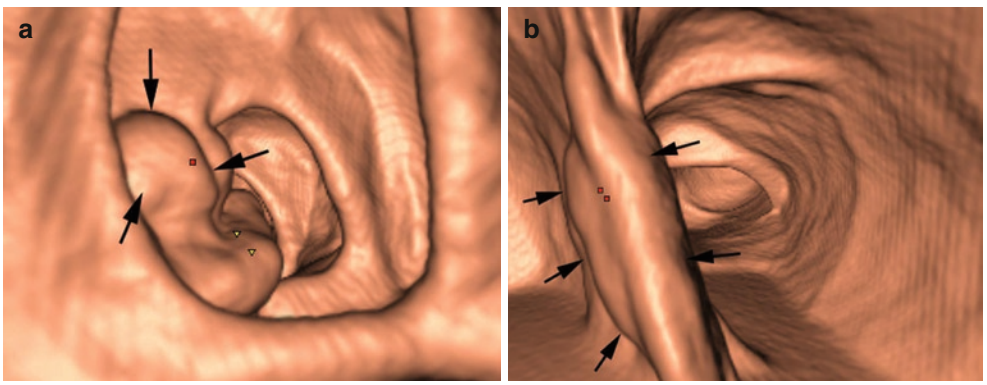


Fig. 17.16 (**a**) Three-dimensional endoluminal CTC image showing a CAD detected type 0-IIa + IIc T1 ascending colonic carcinoma (*arrows*). The CAD detection (*red dot*) was classified as "focal," i.e., located on a recognizable focal elevation. Yellow triangles represent further correct CAD marks on the hidden side of the lesion. (**b**) Three-dimensional endoluminal CTC image shows a CAD-detected type II transverse colonic carcinoma (*arrows*). The two correct CAD marks were classified as nonfocal (Reprinted with permission from Taylor SA, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol.* 2008;18:1666–1673)

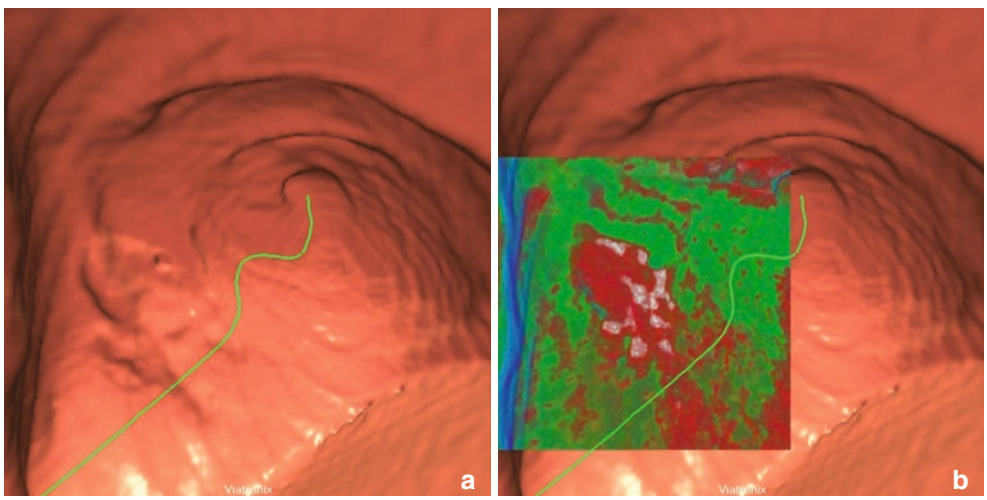
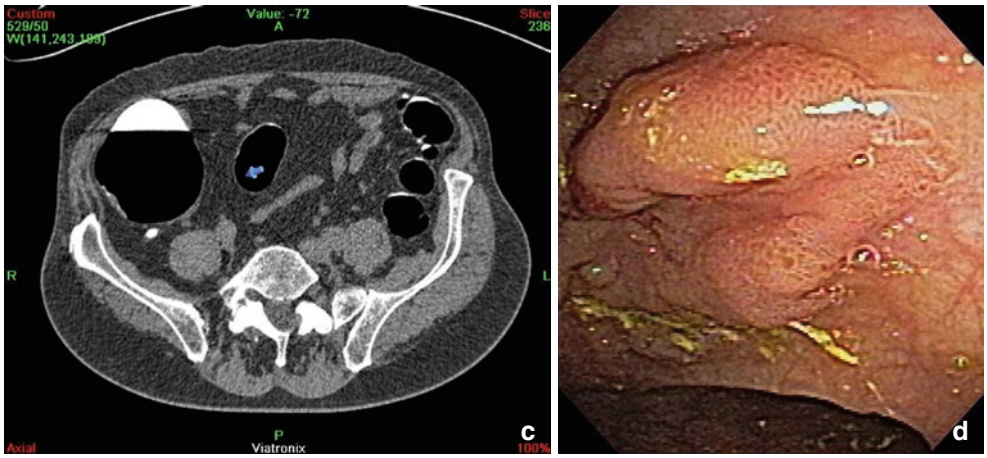


Fig. 17.17 (**a**) The 2 cm (long axis) flat lesion on this 3D endoluminal CTC image is extremely hard to see, but (**b**) the color map ("translucency tool") helps to show the lesion and its soft-tissue composition. In (**c**), the prone 2D axial image (in a soft-tissue window setting), the lesion (*arrow*) with slight tagging on the surface is extremely easy to appreciate. (**d**) Corresponding conventional endoscopic image (Courtesy Amy Hara, MD, Mayo Clinic Arizona)

Fig. 17.17 (continued)



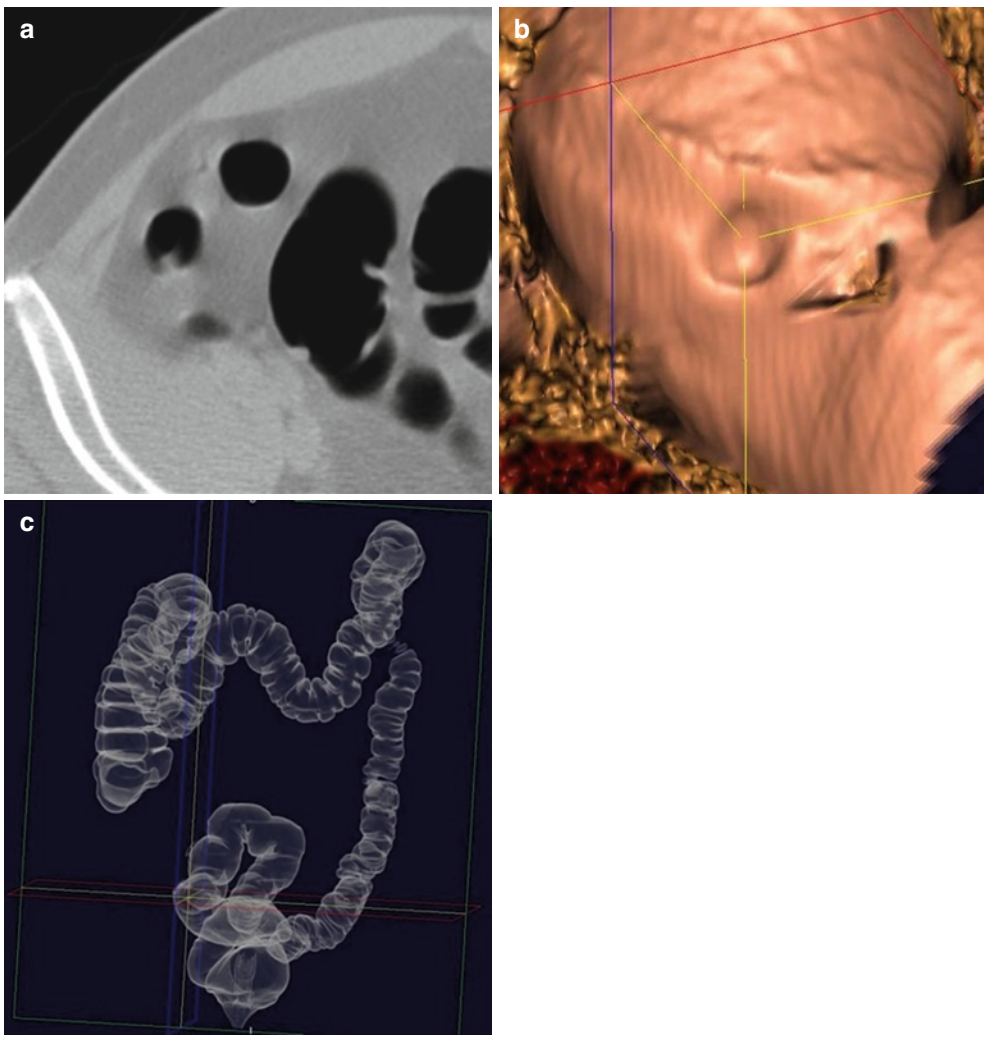


Fig. 17.18 **Diminutive lesion, also "flat."** Small flat (≤3 mm height) lesion (6 mm hyperplastic polyp) in the sigmoid colon ("missed" initially in a CTC clinical trial; Rockey et al.), well visible on 2D axial image (**a**) and 3D endoluminal image (**b**)

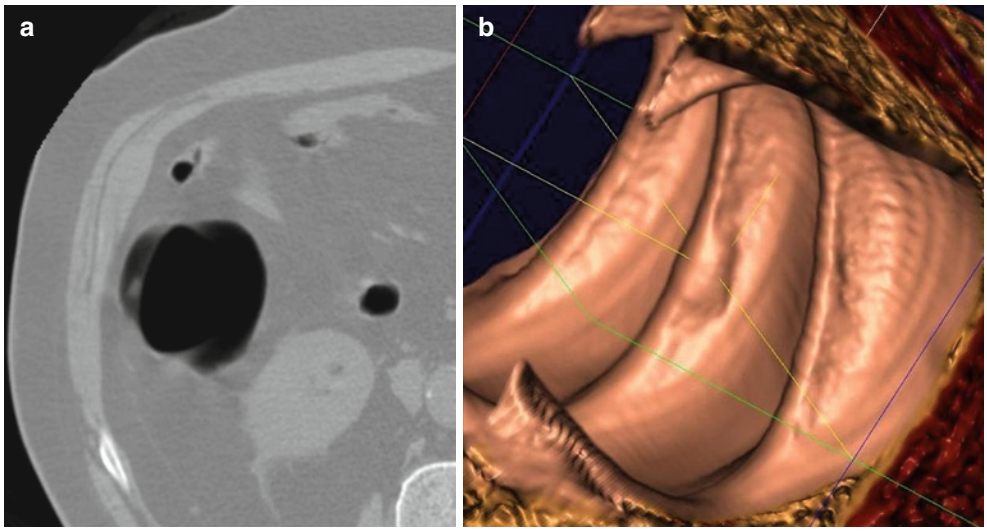


Fig. 17.19 Diminutive flat lesion on a fold. Flat lesion on a fold (10 mm hyperplastic polyp) in the ascending colon ("missed" initially in a CTC clinical trial; Rockey et al.) well visible on 2D axial image (**a**) and 3D endoluminal image (**b**)

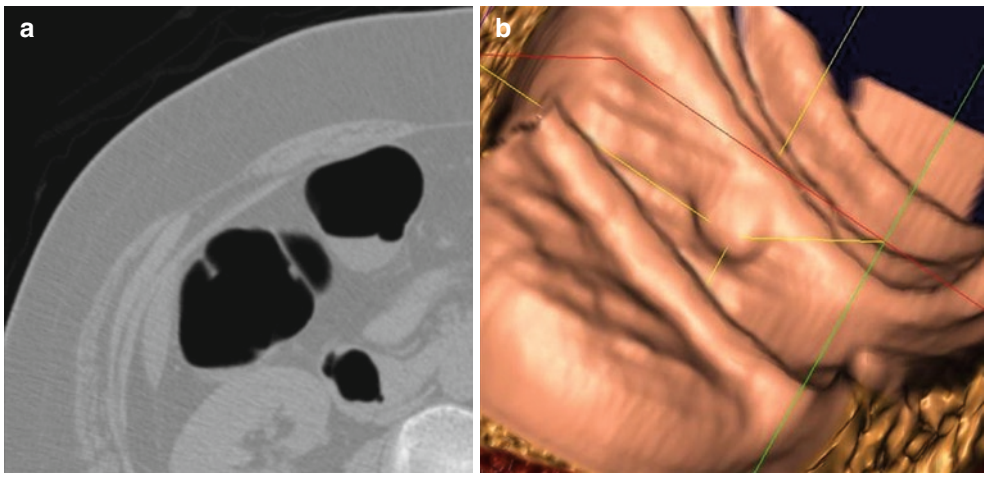


Fig. 17.20 Diminutive flat lesion of a fold. Flat lesion on a fold (6 mm adenoma) in the ascending colon on 2D axial image (**a**) and 3D endoluminal image (**b**)

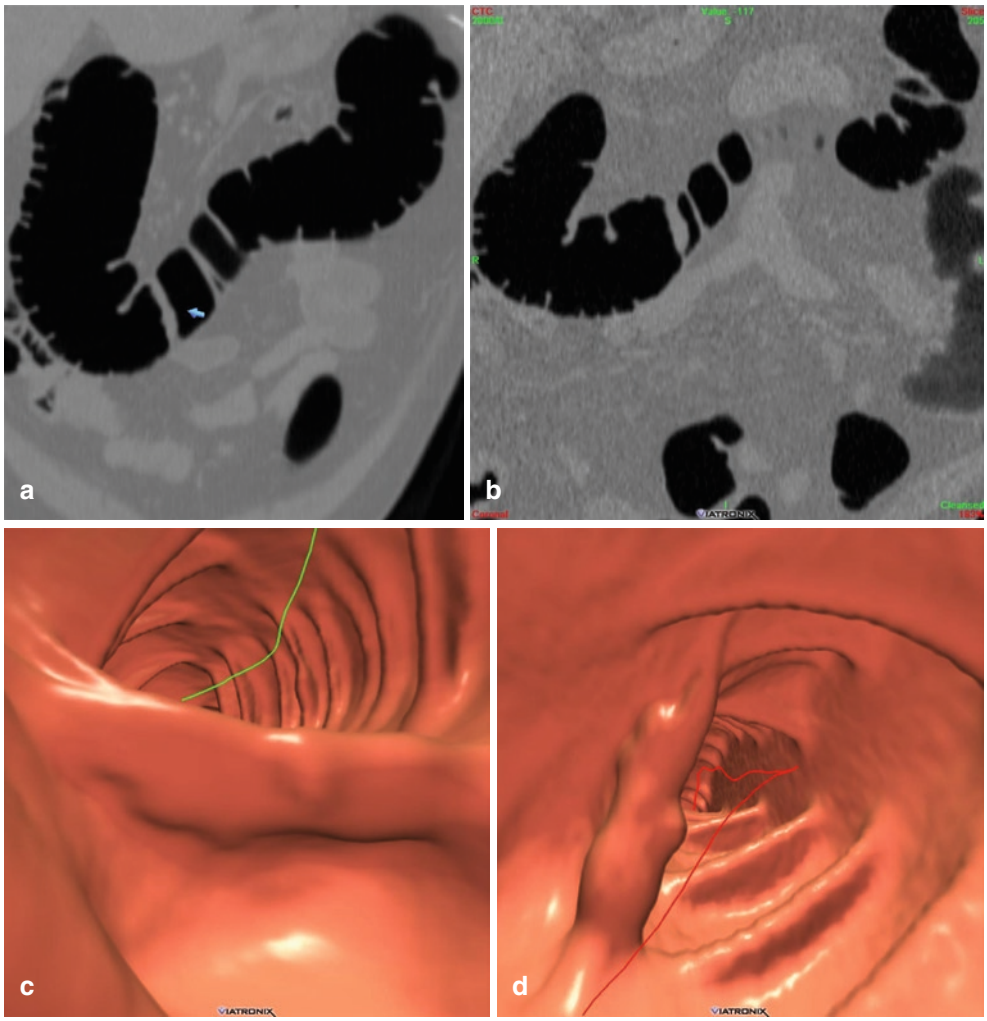


Fig. 17.21 Flat adenoma in the transverse colon. There is a focally thickened fold, markedly different than all the adjacent thin folds in the transverse colon. Prone (**a**) and supine (**b**) coronal 2D images and endoluminal 3D views (**c, d**). Flat lesions often have a sharp delineation with the adjacent normal mucosa and a variable height. This case was conspicuous both at primary 3D and primary 2D interpretation. At pathology a sessile tubular adenoma without local invasion was found (Courtesy Tanya Chawla)

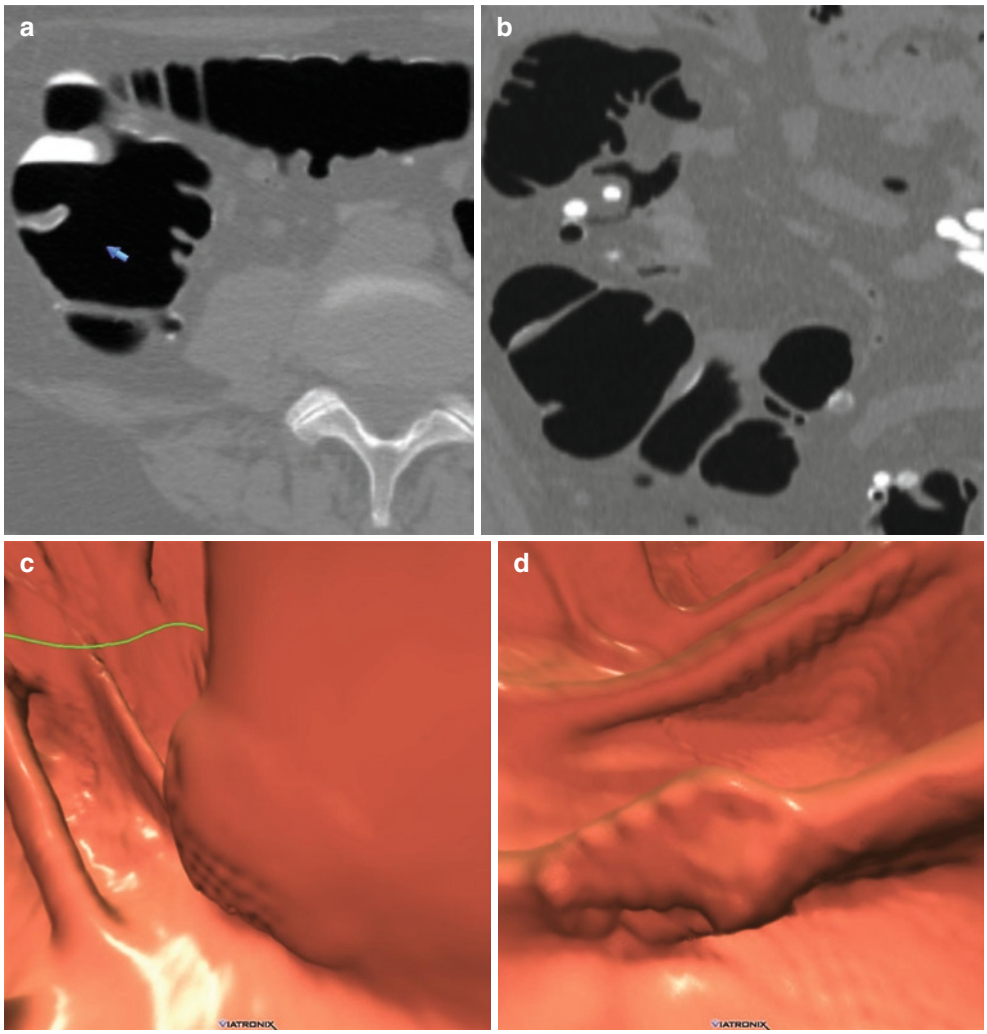


Fig. 17.22 Coated flat lesion on a fold in the ascending colon. (**a, b**) Axial prone and coronal views and (**c, d**) corresponding endoluminal 3D views show a flat lesion, slightly coated with oral contrast. The oral contrast helps improve the conspicuity of the lesions. At histopathological analysis a sessile serrated adenoma was diagnosed (Courtesy Tanya Chawla)

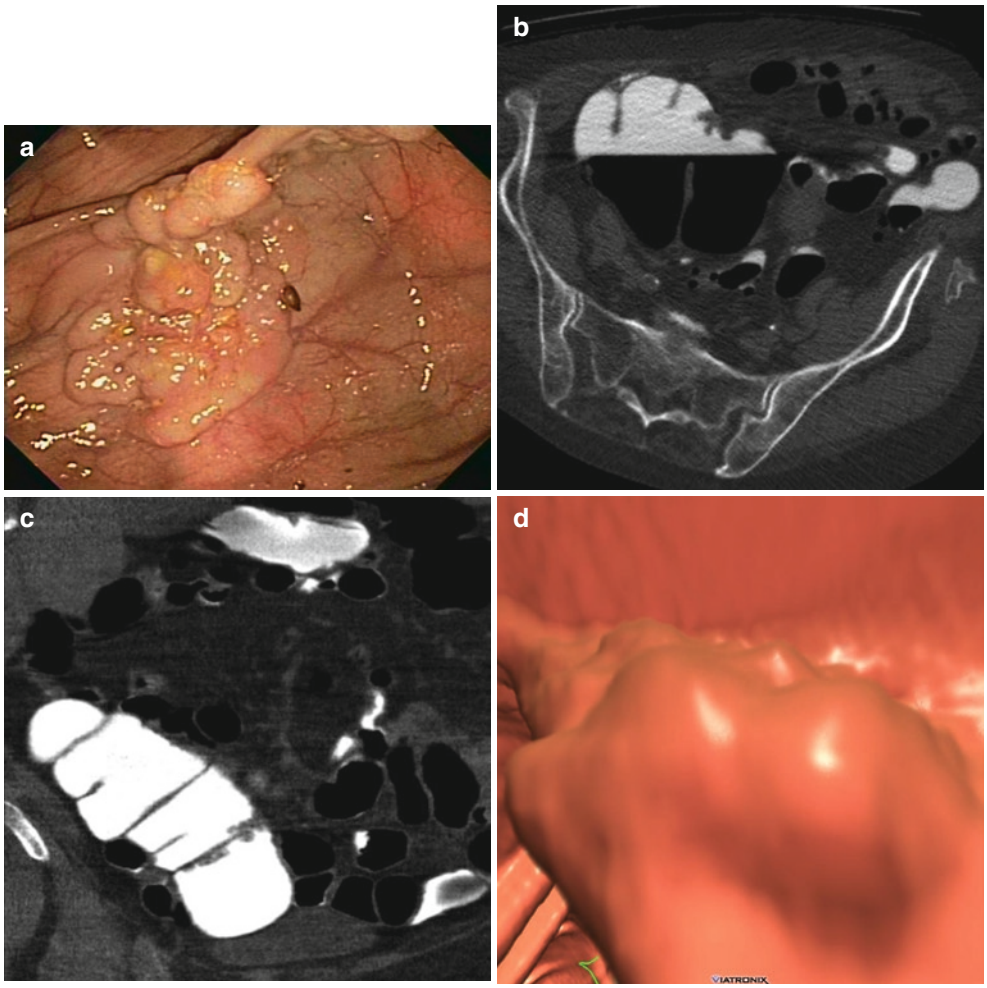


Fig. 17.23 Flat tubulovillous adenoma. (**a**) Optical endoscopic photograph shows the typical "frond-like" surface pattern of villous tumors. Note the inseparable lobular lesion on the fold. (**b**) Prone axial and (**c**) coronal images show the lesion in the proximal ascending colon along the anteromedial wall, outlined by fluid and densely tagged with oral contrast. (**d**) Corresponding endoluminal 3D view. (**e**, **f**, **g**) The supine axial, coronal, and endoluminal views where the lesion is outlined by luminal gas and the lobular component on the fold is shown on the endoluminal view. At histopathology, a sessile tubulovillous adenoma was diagnosed (Courtesy Tanya Chawla)

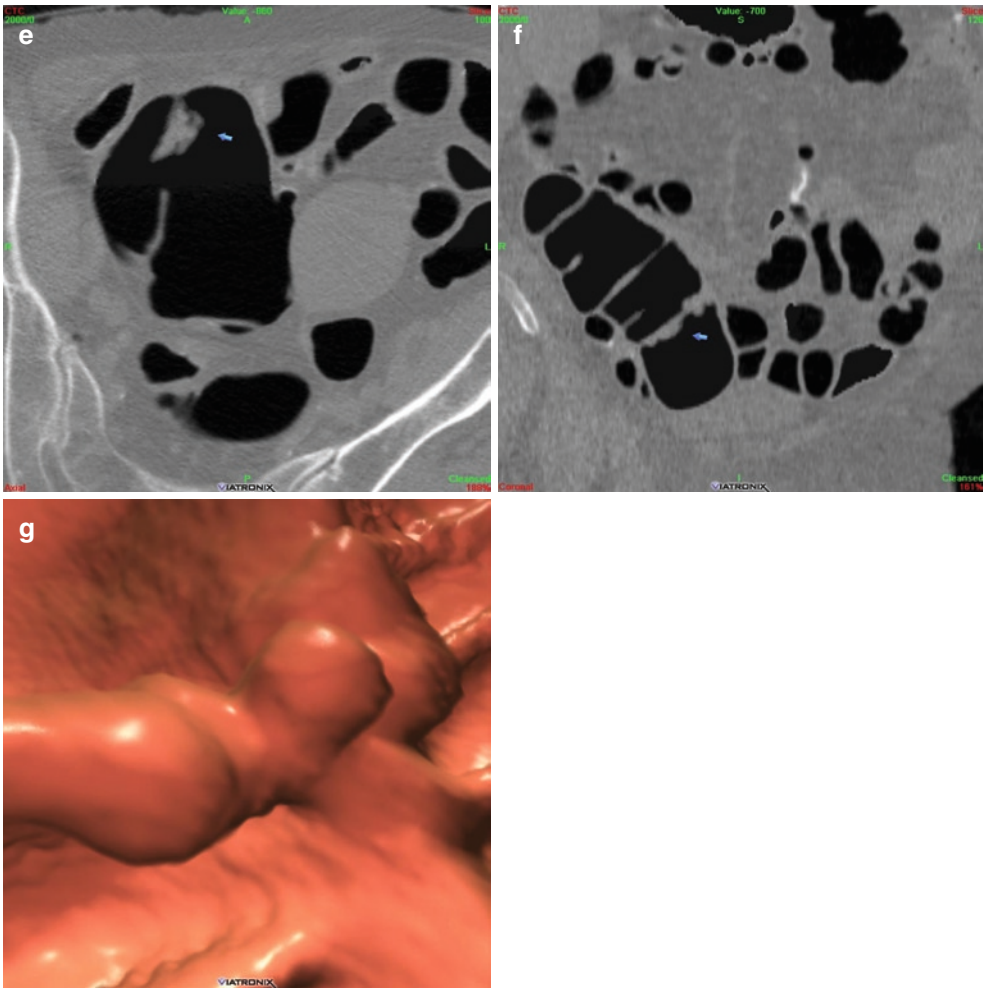


Fig. 17.23 (continued)

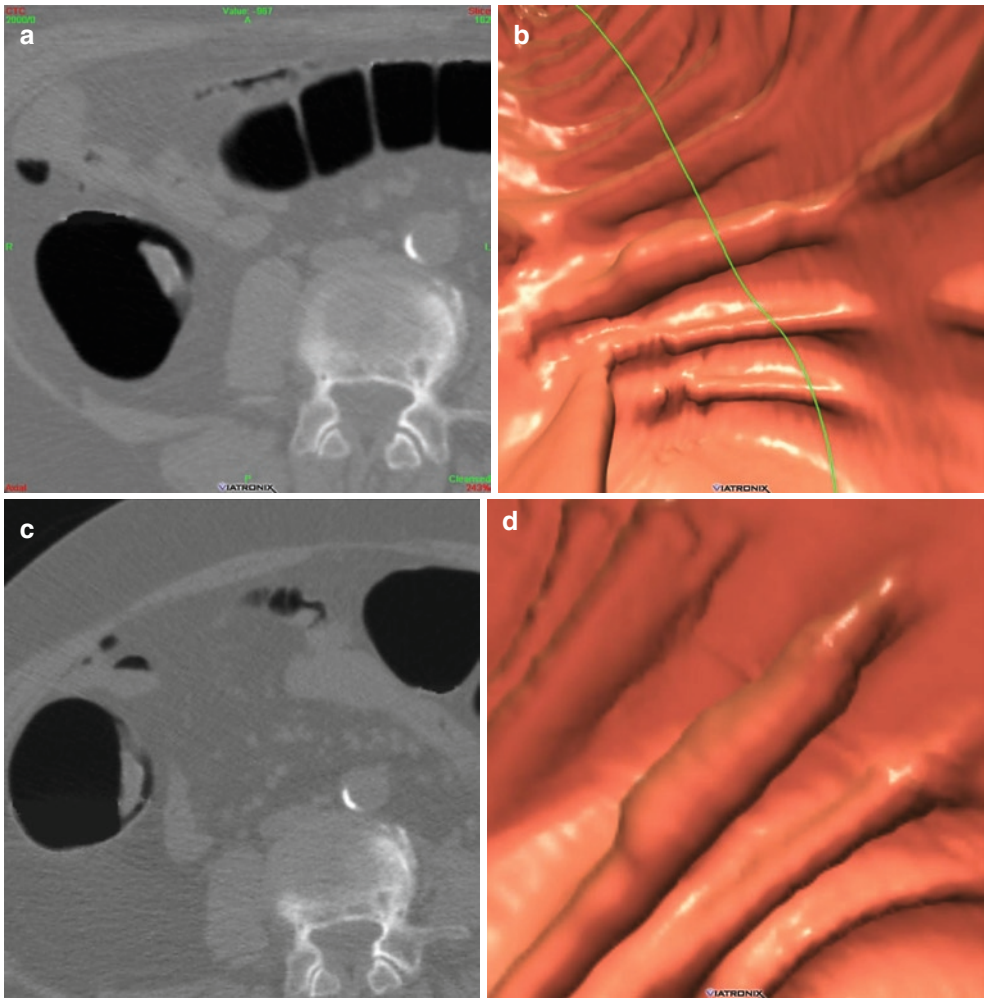


Fig. 17.24 Flat adenoma in the proximal ascending colon. On the prone 2D (**a**) and endoluminal 3D (**b**) views, the fold with the flat lesion appears to "hang" ventrally toward the dependent surface and similarly shift on the supine views (**c**, **d**) toward the dorsal surface. There is subtle incomplete coating of the lesion with oral contrast (Courtesy Tanya Chawla)

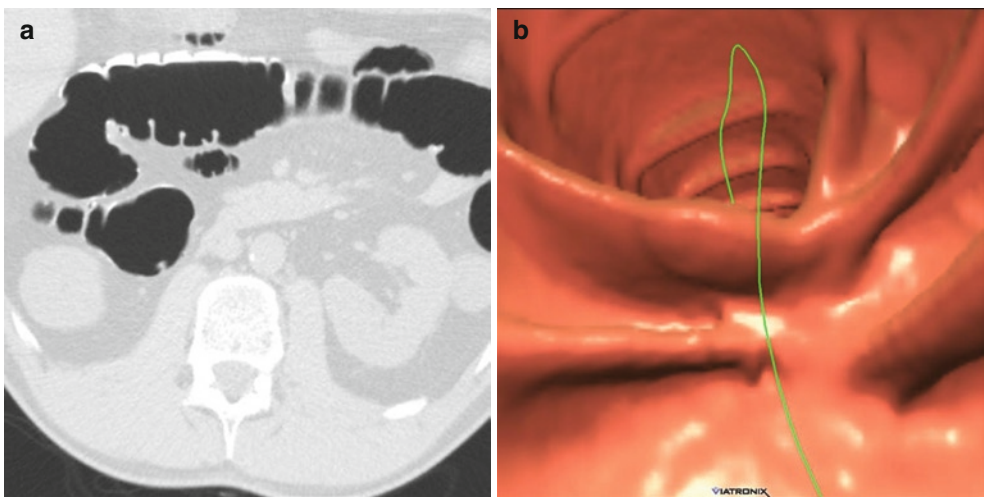


Fig. 17.25 Flat adenoma on a fold, mid-transverse colon. (**a**) Prone axial image shows a focally thick fold on only a few slices. There is minimal oral contrast coating the lesion. (**b**) Corresponding endoluminal 3D view. At pathology, flat adenoma with no evidence of high grade dysplasia was diagnosed (Courtesy Tanya Chawla)

Stool, Diverticulosis

18

Franco Iafrate and Andrea Laghi

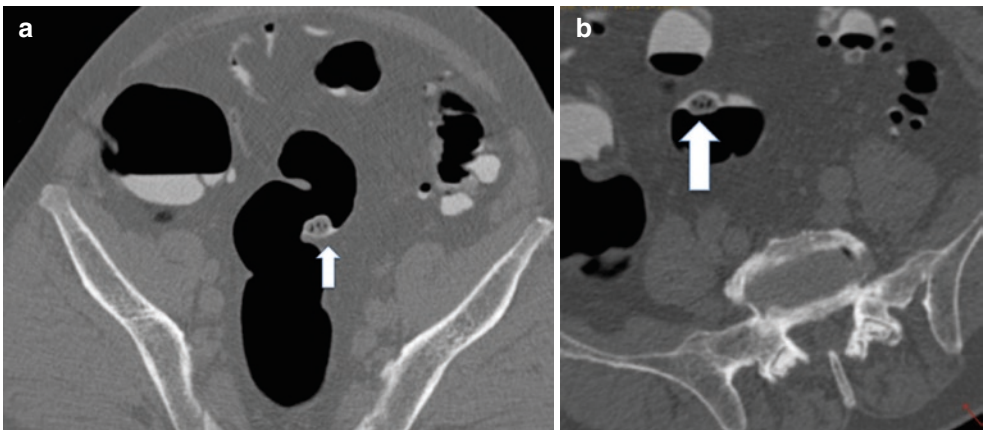


Fig. 18.1 **Nontagged stool contained air bubbles**. (**a**) Supine and (**b**) prone axial CT images showing the presence of a polyp candidate not tagged by surrounding oral contrast, but the diagnosis of fecal residue is easily made both by the presence of air bubbles within the polyp candidate and by recognizing the fact that it moves with change in patient position to remain on the dependent surface (and no "stalk" is seen, since a long stalk will allow a polyp to move; see chap. 15). Note on the supine view (**a**), the stool is resting on a distal sigmoid fold (*arrow*)

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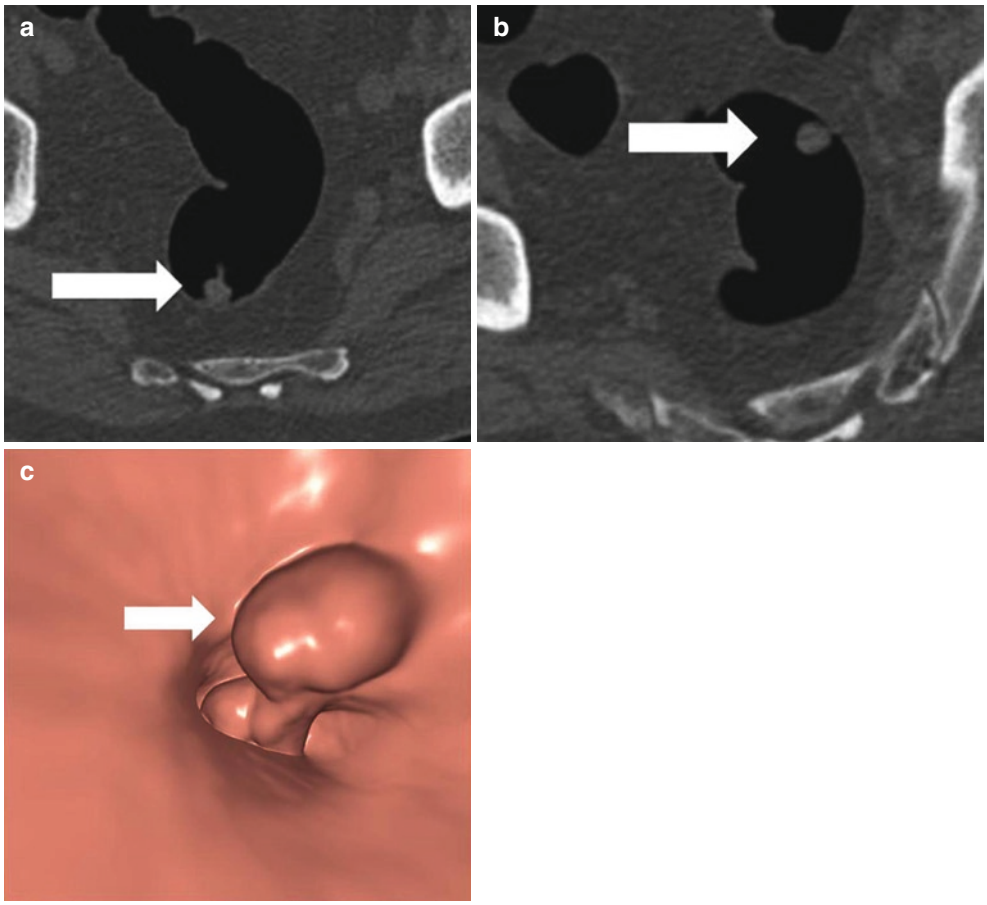


Fig. 18.2 **Solid, nontagged stool showing positional change**. (**a**) Supine and (**b**) prone axial CT shows a 20 mm sessile filling defect (*arrow*) in the rectum. On the supine view, it is on the posterior wall, and on the prone view it is on the anterior wall. This is the typical positional change seen with stool. The 2D views do not show gas or tagging agent within the polyp candidate. Thus only the mobility of the lesion suggests that this may be stool. The 3D view (**c**) shows definitively that no stalk is present (see chap. 15 for pedunculated polyps, which can also move with change in patient position.)

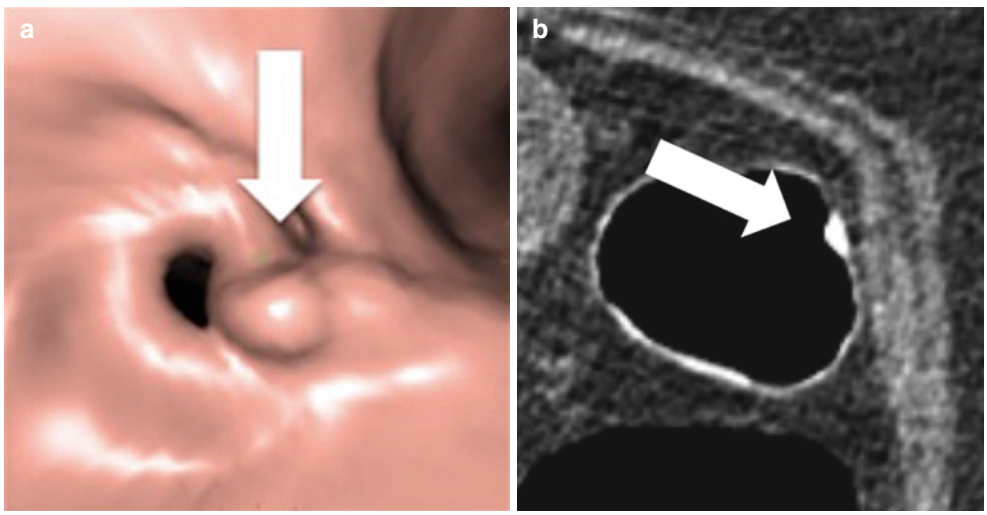


Fig. 18.3 **Tiny particulate stool completely tagged**. (**a**) Three-dimensional volume rendered endoluminal image shows geometric morphology (angled edges) (*arrow*) of a filling defect suggestive of adherent residual stool. (**b**) Axial CT image shows a corresponding 5 mm focus (*arrow*) in the descending colon that is homogeneously extremely densely tagged throughout all pixels, proving that it represents fecal residue

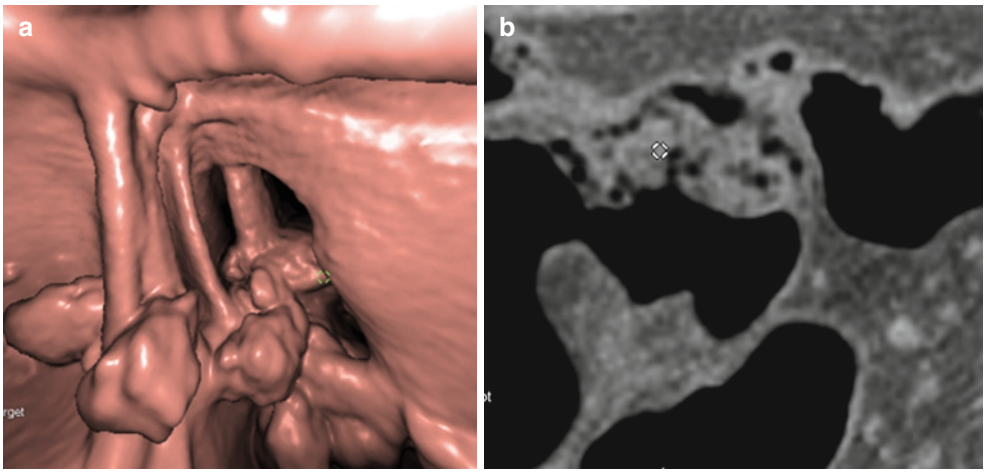


Fig. 18.4 **Poor colonic cleansing resulting in a large amount of residual stool**. When performing a primary 3D read (**a**), excessive stool can mimic a large lobular carcinoma or a polyposis. The use of 2D (**b**) can be helpful in making diagnosis of fecal residue due to the presence of inhomogeneity and bubble gas within all the "lesions." When very extensive, this will make the exam too tedious to interpret and the patient should be re-prepped. Technologists should confirm that the patient ingested the cathartic agent and is not having any substantial formed stool before proceeding with the insufflation

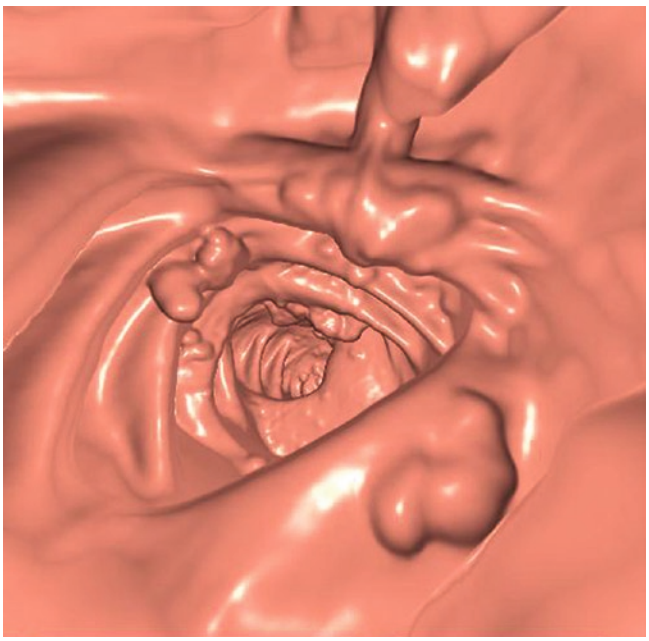


Fig. 18.5 **Poor colonic cleansing resulting in a large amount of residual solid stool**. Similar to Figure 18.4, this patient has too much retained stool to interpret the exam. If a patient insists that he/she is "clean," check that the lesions are not all soft tissue foci in a patient with familial polyposis

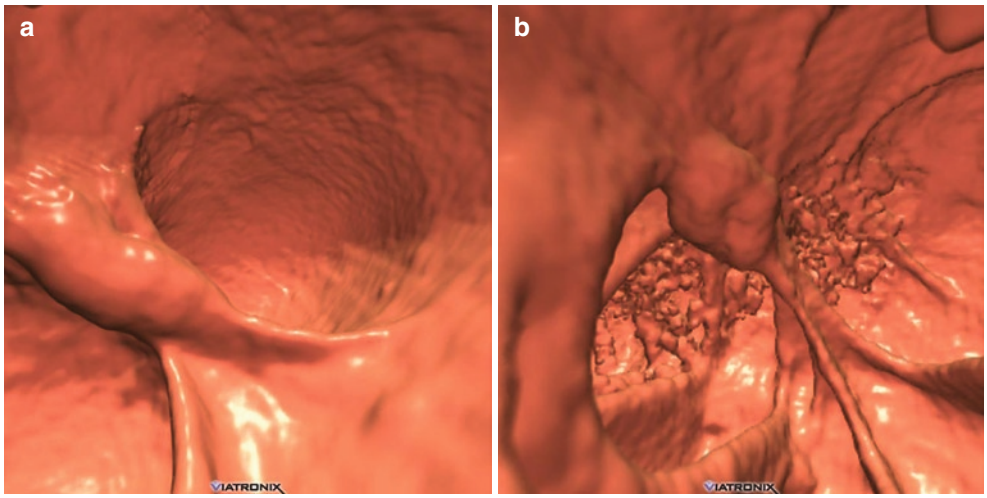


Fig. 18.6 Comparison of an excellent and poor bowel preparation on the endoluminal views. (**a**) Excellently prepped patient showing a 3D volume rendered endoluminal image of the ascending colon with no residual fecal material. The colonic wall is smooth. (**b**) Three-dimensional volume rendered endoluminal image in a different patient with a poor preparation shows residual fecal material, limiting evaluation of the colonic wall

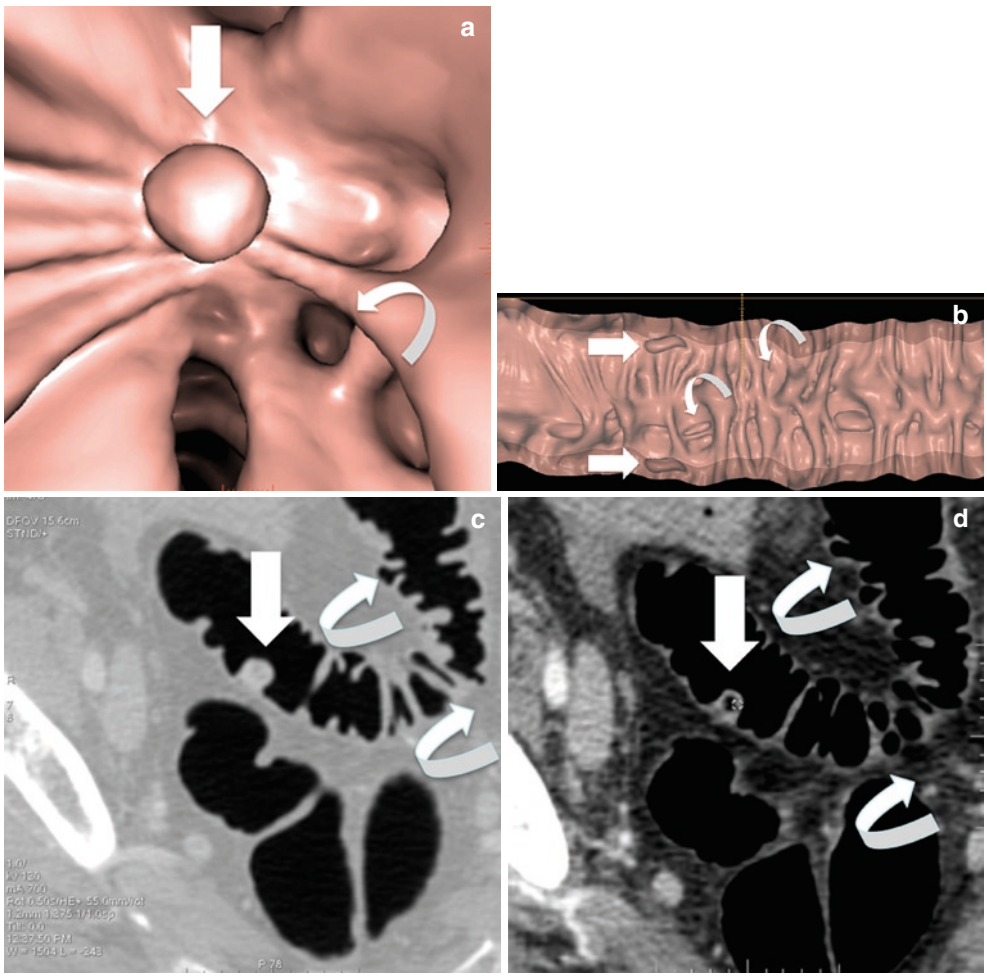


Fig. 18.7 Fecal residue mimicking a polyp. (**a**) Three-dimensional CTC endoluminal imaging shows a polypoid filling defect (*arrow*) within sigmoid colon affected by severe diverticular disease (*curved arrow*). (**b**) Virtual dissection 3D image shows typical distortion of the polypoid lesion (*arrow*) and clearly depicts the length of sigmoid where multiple large diverticular orifices (*curved arrows*) are evident. (**c**) Axial supine image displayed in a CTC window-level setting shows a polypoid lesion (*arrow*) on the posterior wall of the sigmoid colon, as well as multiple diverticulae (*curved arrows*). After changing window level setting to a narrower "soft tissue" window (**d**), the presence of gas within the polypoid filling defect (*arrow*) proves the diagnosis of fecal residue

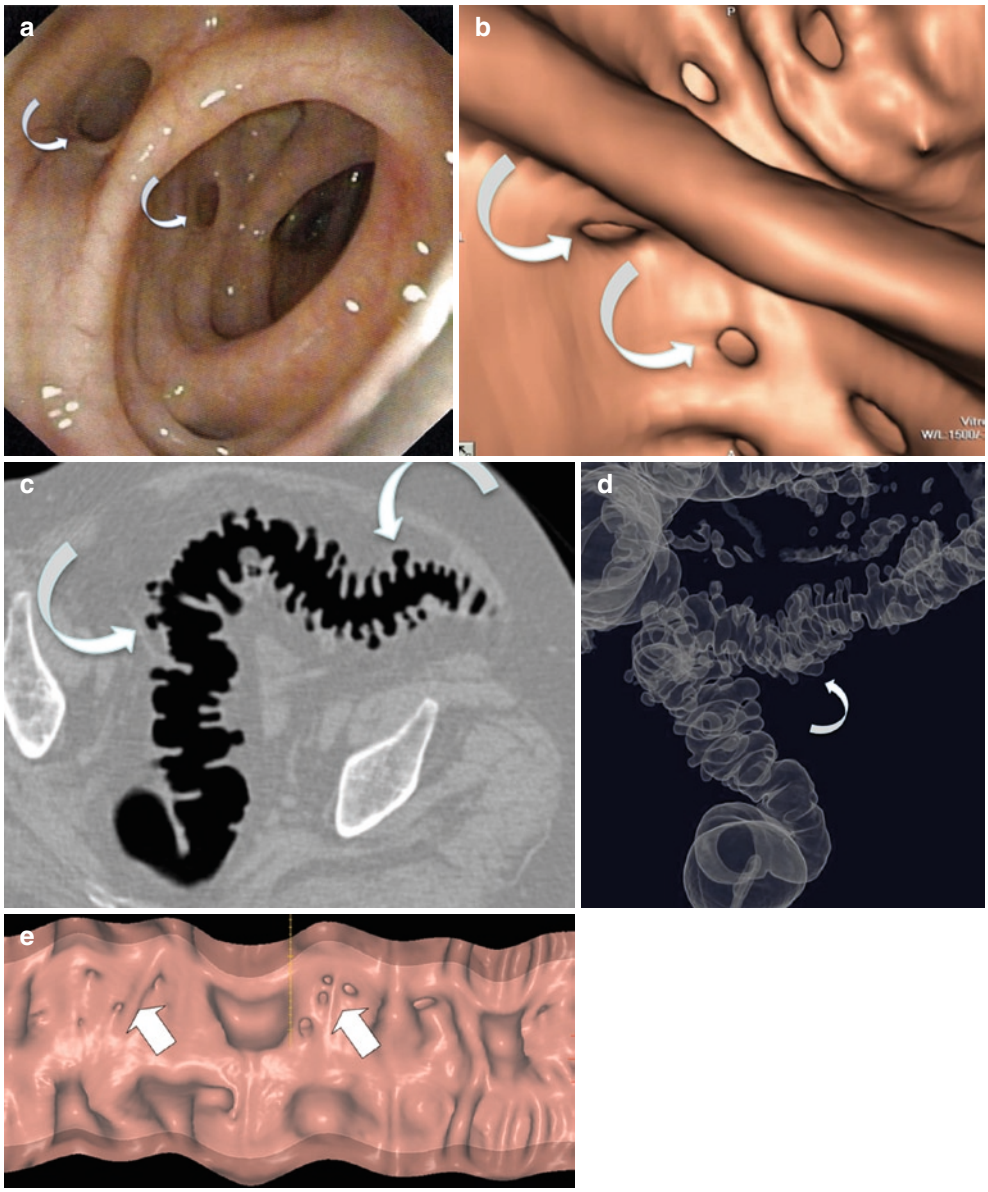


Fig. 18.8 **Diverticulosis**. (**a**) At optical colonoscopy, multiple diverticular orifices (*curved arrows*) can be seen. (**b**) Corresponding 3D endoluminal view of the sigmoid colon showing multiple diverticular openings (*curved arrows*). Note that the diverticular openings form a complete dark ring whereas polyps when viewed at any angle other than straight en-face, appear as an incomplete ring. (**c**) Corresponding supine axial image shows multiple diverticula (*curved arrows*) with no sign of diverticulitis. (**d**) Double contrast enema ("transparency") view with the balloon-inflated catheter in place and (**e**) virtual dissection view, likewise clearly depict the extensive diverticulosis

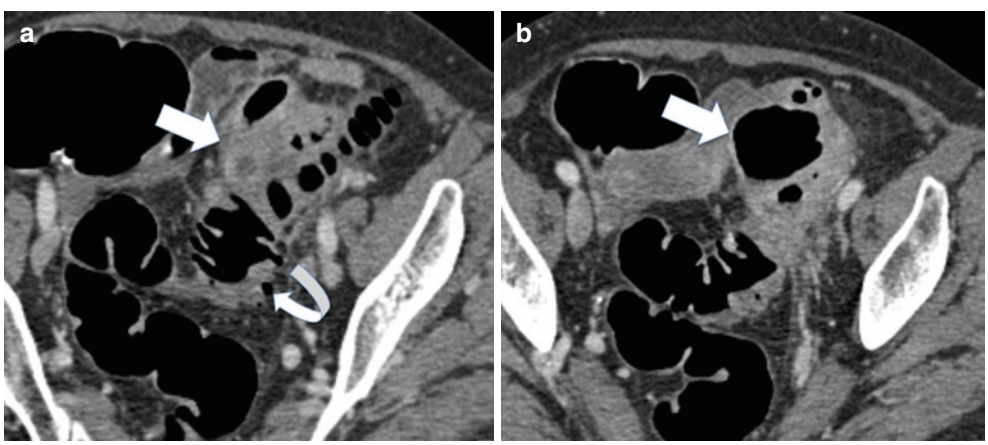


Fig. 18.9 **Diverticulitis with gas containing abscess**. Supine axial images (**a** and **b** at slightly different levels) show multiple diverticular orifices and marked asymmetric sigmoid colon wall thickening of concern for neoplasm and associated with a large loculated extraluminal gas collection (*arrow* in **b**) due to acute diverticulitis with a walled-off perforation and abscess formation

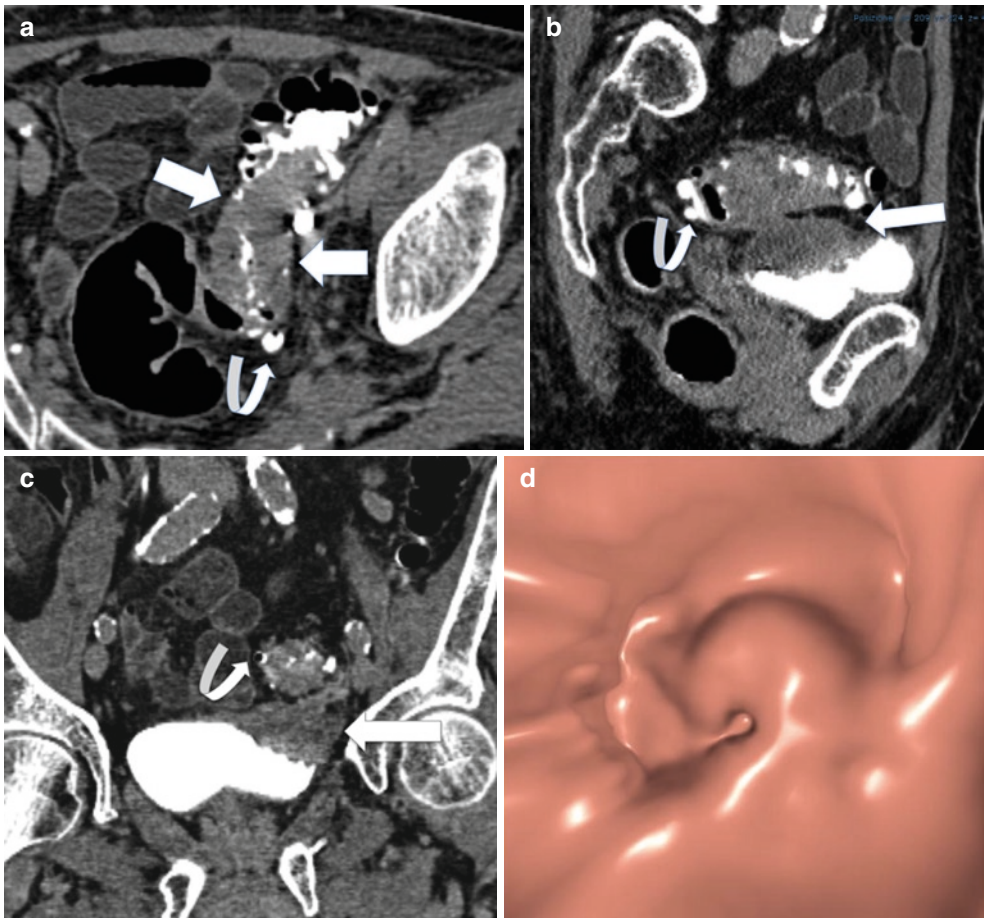


Fig. 18.10 **Diverticulitis with extraluminal phlegmon**. (**a**) Supine axial image from a CTC done with oral contrast administration for fecal tagging shows a severe circumferential thickening (*arrow*) of the sigmoid colon over a 10 cm long segment. Multiple diverticular orifices (*curved arrows*) are evident. (**b**) Sagittal and coronal (**c**) multiplanar reformatted images show the presence of an extraluminal soft tissue inflammatory abscess (*arrow*) between sigmoid colon, where diverticular orifices (*curved arrows*) are evident, and the bladder wall. (**d**) Three-dimensional endoluminal image shows the presence of endoluminal narrowing (*arrow*)

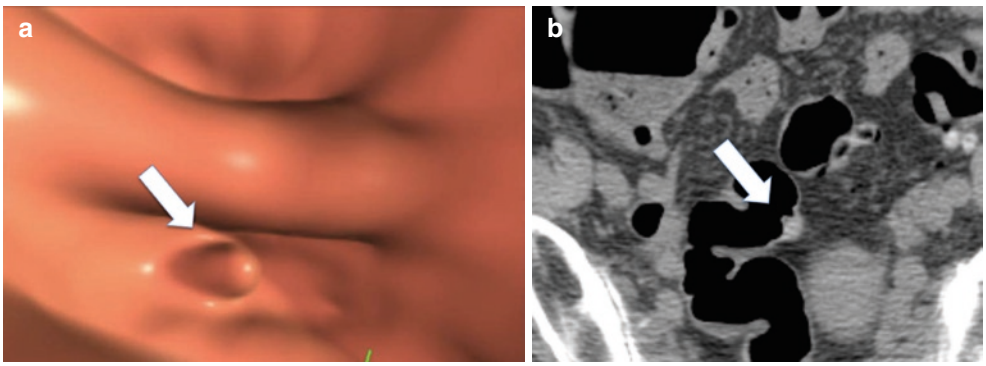
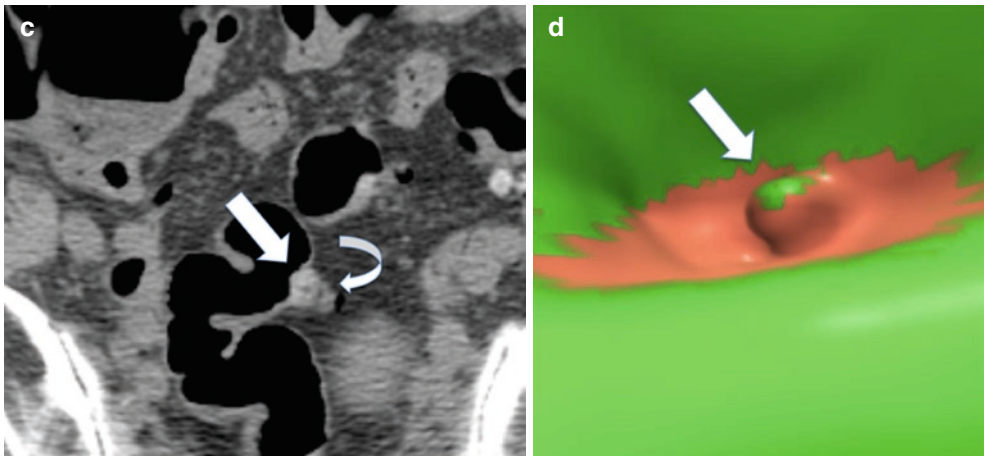


Fig. 18.11 **Impacted diverticulum** (**a**) A 3D threshold-rendered image shows sessile filling defect in the sigmoid colon (*arrow*) between two folds; differential diagnosis includes small polyp or fecal material. (**b**) Axial CT image of the lesion shows its endoluminal aspect with a triangular configuration and also shows gas attenuation within the lesion, consistent with stool. (**c**) Axial CT image at a slightly more caudal level showing that the lesion (*arrow*) projects outside the lumen (*curved arrow*), demonstrating that it is an impacted diverticulum. (**d**) Three-dimensional endoluminal image after applying a 3D "missed region" tool which colorizes the viewed mucosal surface in green. Note that on the routine initial fly-though, much of this polyp candidate and its surrounding mucosa were missed, representing so-called "blind areas" that are not colored in green. Thus, this is an example of a polyp candidate (*arrow*) between two folds which was not seen during 3D interpretation

Fig. 18.11 (continued)



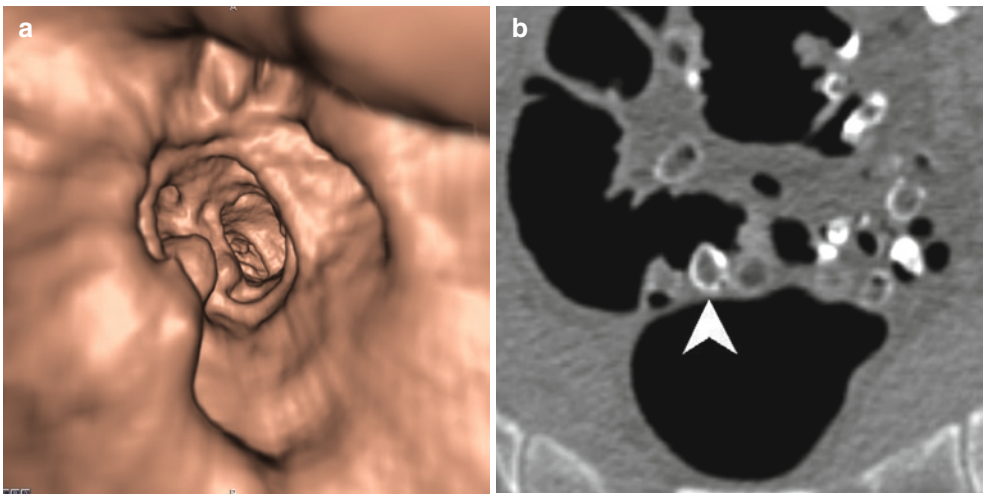


Fig. 18.12 **High-density stool impacted in a diverticulum**. (**a**) Three-dimensional endoluminal view shows multiple polyp candidates and no diverticular orifices. However, the 2D view (**b**) is easily recognized as showing innumerable diverticula impacted with solid stool, some of which is not tagged, some of which is tagged only along its surface seen as a hyperdense peripheral ring with hypodense center (*white arrowhead*). A few other foci show the tagging agent penetrating into the volume of the stool completely. Note that although this patient did have oral contrast, occasionally impacted stool will be high density due to water resorption, even without the use of oral contrast

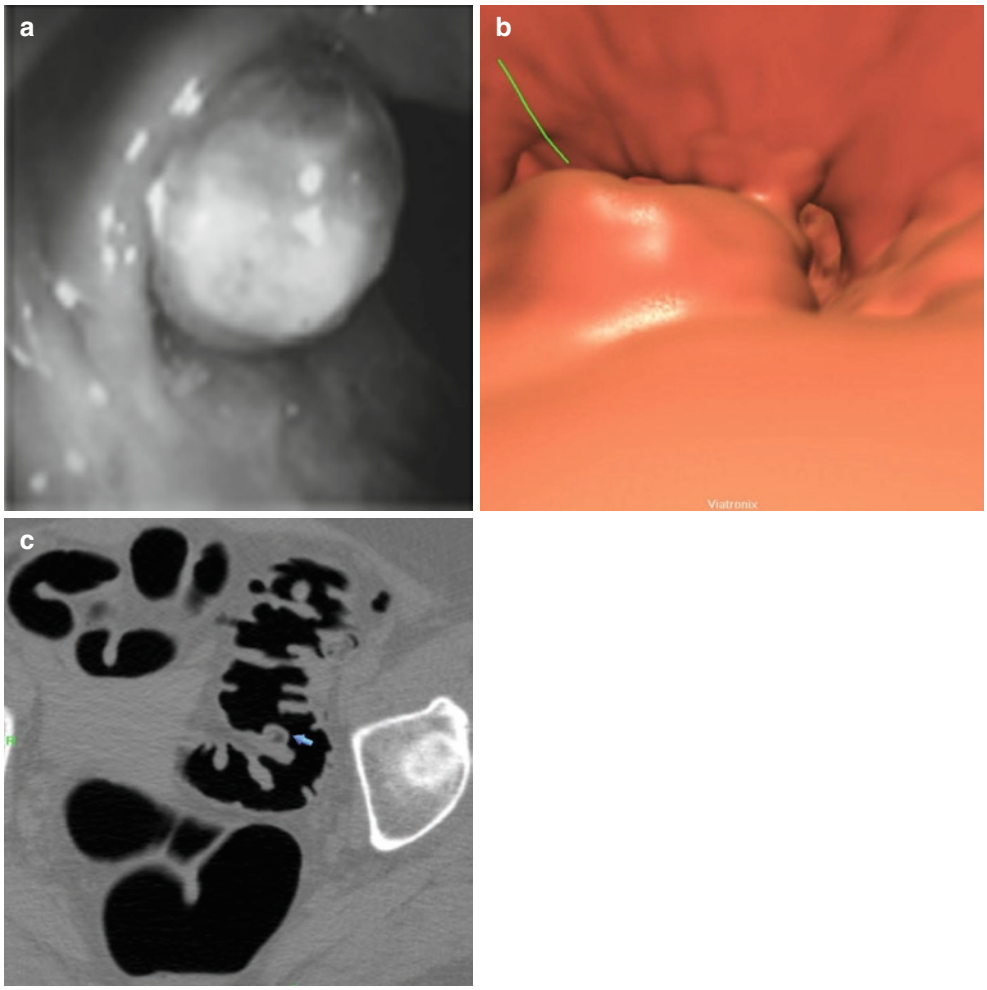


Fig. 18.13 Inverted diverticulum. When a diverticulum inverts, both the optical endoscopic view (**a**) and the CTC endoluminal 3D view (**b**) are indistinguishable from a polyp. Sometimes, with increased intraluminal pressure (e.g., more insulation at endoscopy or CTC), the diverticulum will revert to its usual position as an outpouching and be recognized. If it remains inverted, only a careful inspection of the 2D view (**c**) shows internal fat tracking to the serosa and sometimes a central "dot" representing a blood vessel. (Courtesy Tanya Chawla)

Masses

19

Franco Iafrate and Andrea Laghi

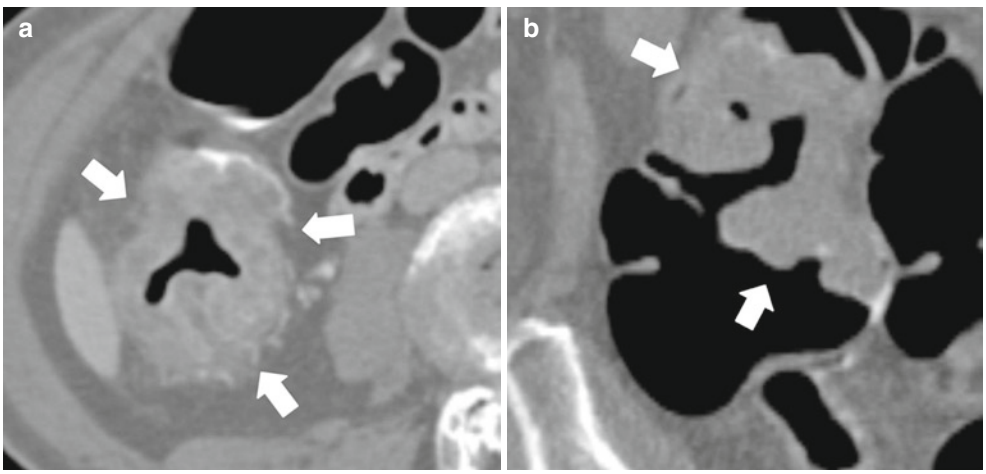


Fig. 19.1 Annular mass of the ascending colon in a 94-year-old woman. Two-dimensional CTC axial (**a**) and coronal (**b**) images show a circumferential and irregular thickening of the ascending colon associated with severe stenosis of the colonic lumen (*arrows*). The lesion (*arrows*) has a 6 cm cranio-caudal extension (**c**) and infiltration of the pericolic fat as well. Enhancement of the neoplastic mucosa (*arrows*) is evident using abdominal window level setting after intravenous injection of iodinated contrast agent (**d**). Three-dimensional endoluminal view (**e**) of the stenotic lesion shows an extremely lobular surface (*arrow*). An adenocarcinoma was histologically confirmed

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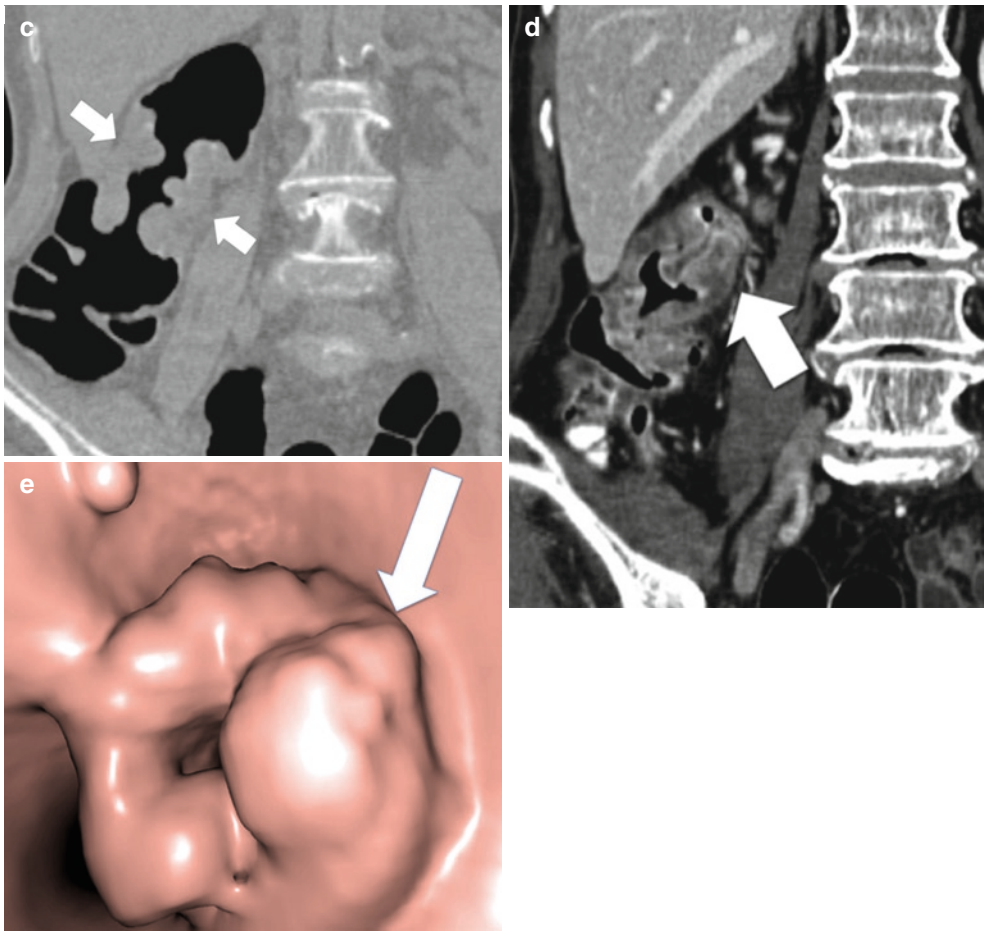
Fig. 19.1 (continued)



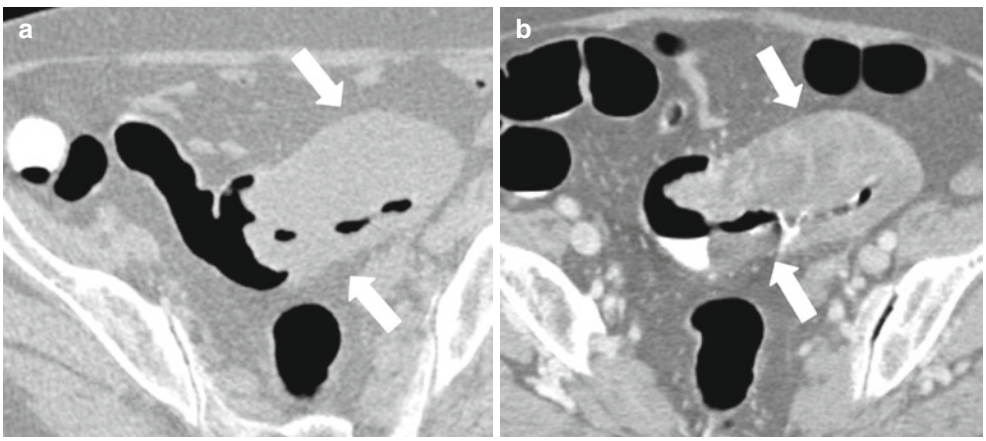
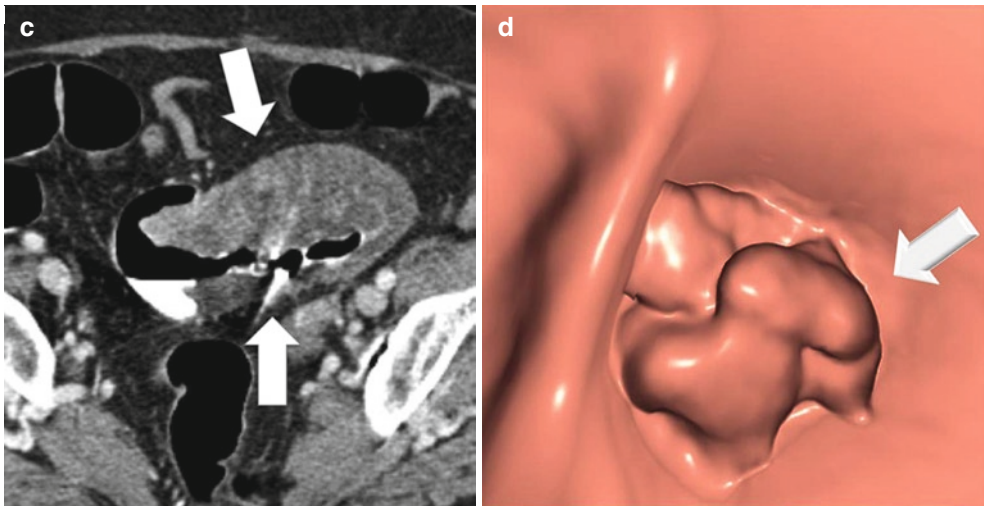


Fig. 19.2 **Large annular sigmoid tumor in a 66-year-old woman with obstructive symptoms**. Prone (**a**) and supine (**b**) axial images show an asymmetrical annular thickening (*arrows*) of the colonic wall (11 cm long) with greater involvement of the anterior sigmoid wall, but near complete obliteration of the luminal gas. When viewed in an abdominal window level setting (**c**) after intravenous injection of iodinated contrast agent, the supine axial images show enhancement of the neoplastic mucosa (*arrows*). The endoluminal 3D image (**d**) of the lesion shows an irregular surface (*arrow*) and complete obstruction of the colonic lumen. An adenocarcinoma was histologically confirmed

Fig. 19.2 (continued)



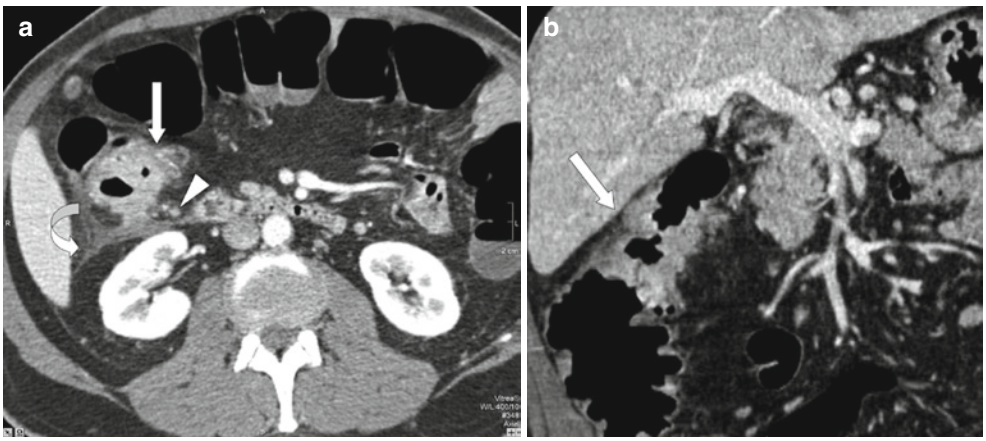
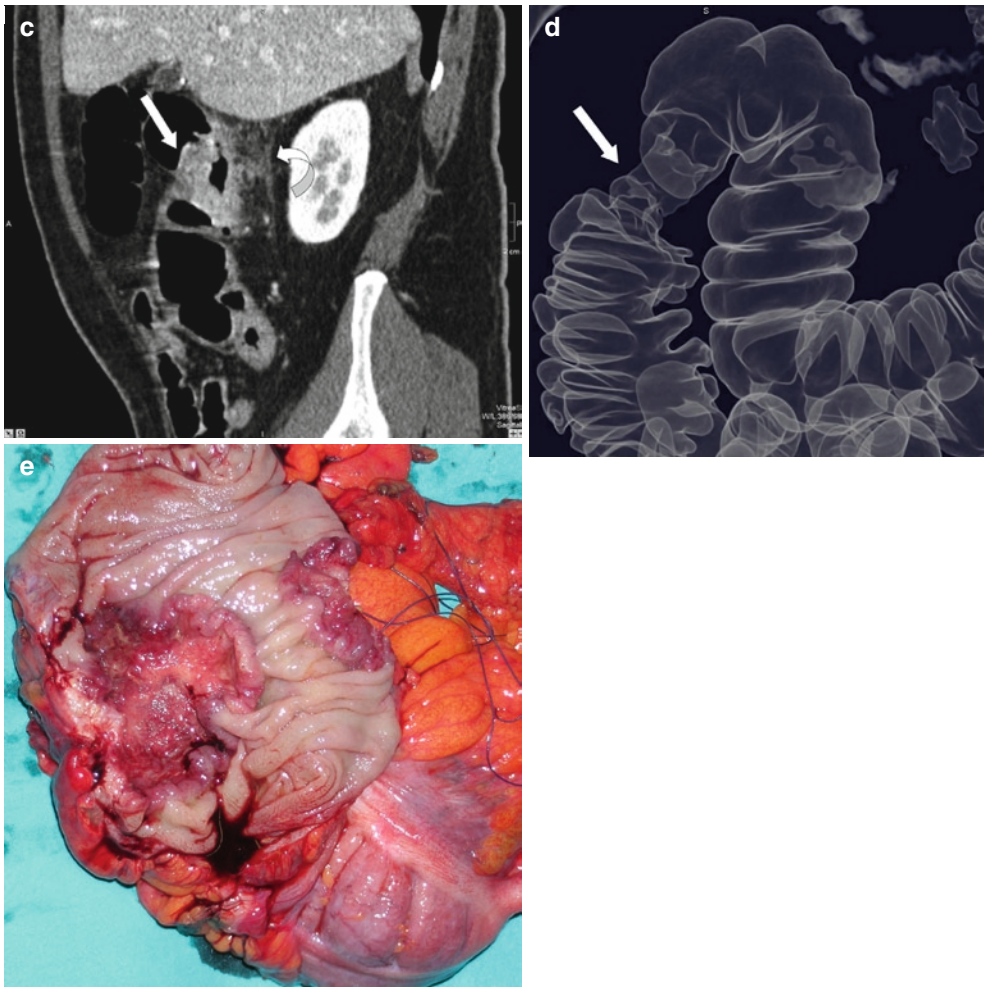


Fig. 19.3 **Annular mass in the ascending colon with pericolonic fat stranding**. Contrast-enhanced 2D CTC images (**a**–**c**) show circular and irregular thickening (*arrow*) of the ascending colon. Pericolic fat stranding and fluid (*curved arrow*) are clearly visible behind the lesion and over the anterior renal fascia. Lymphadenopathy is present (*arrowhead*). Double contrast enema ("transparency") view (**d**) shows an "apple core" sign, which suggests stenotic lesion (*arrow*) corresponding to the mass as seen in the gross surgical specimen (**e**). A right hemicolectomy was performed and adenocarcinoma was histologically confirmed

Fig. 19.3 (continued)



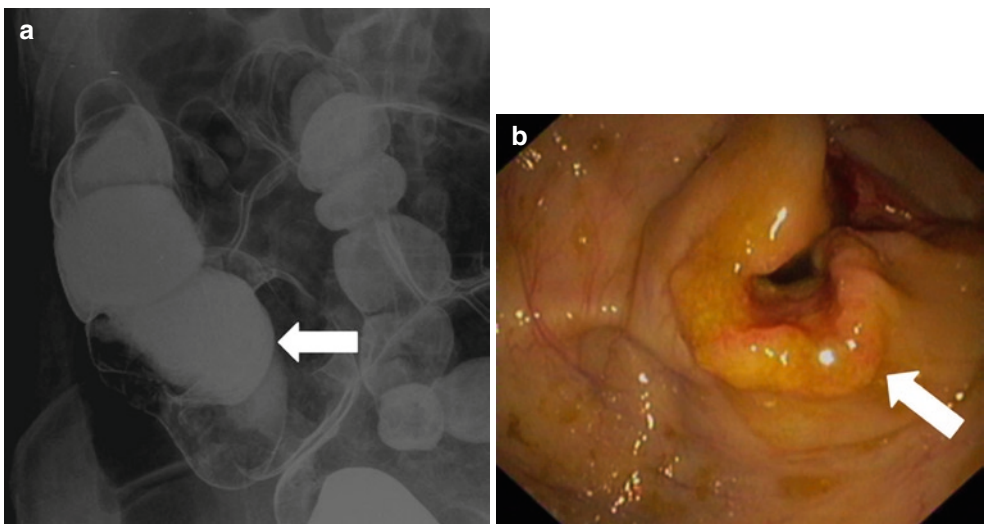
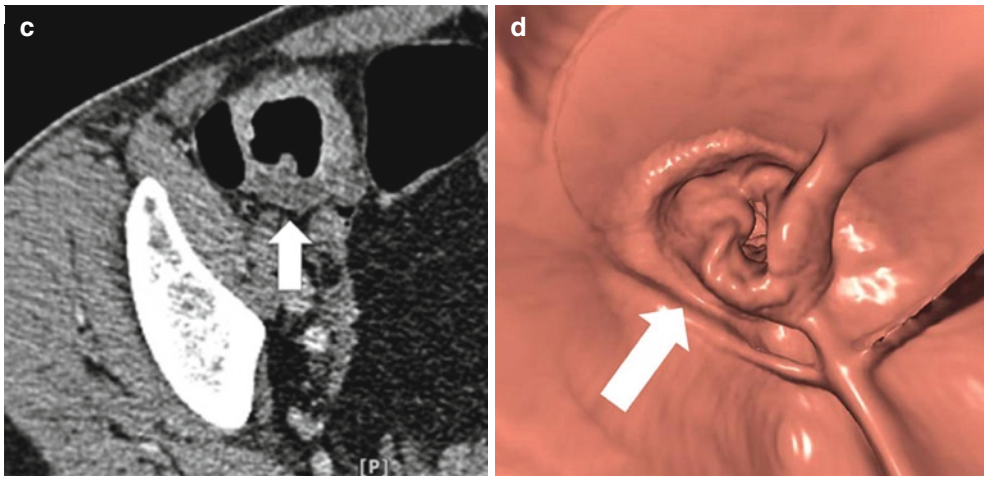
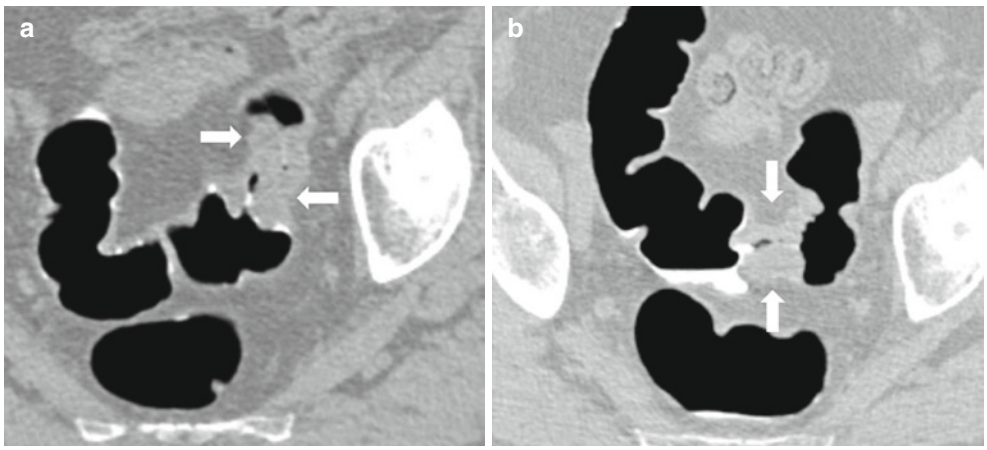
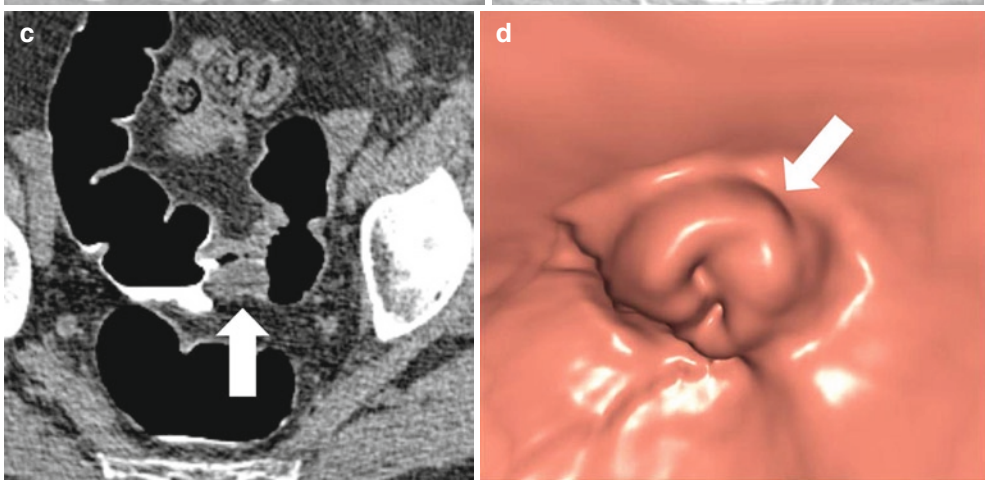


Fig. 19.4 Annular mass of the cecum misdiagnosed at barium enema examination. Barium enema (**a**) image does not show any abnormalities of the medial aspect of cecal profile (*arrow*). At colonoscopy (**b**), a stenotic lesion of the cecum is clearly visible (*arrow*). CTC (**c**) provides a complete preoperative evaluation of the lesion (*arrow*) using 2D images after intravenous injection of iodinated contrast agent, and 3D endoluminal CTC image (**d**) shows a perspective of the lesion (*arrow*) which is extremely similar to the endoscopic view obtained with conventional colonoscopy

Fig. 19.4 (continued)







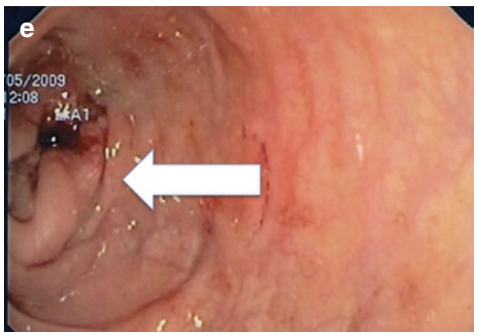


Fig. 19.5 **Annular cancer of the sigmoid colon in a 73-year-old woman with abdominal pain and a family history of colorectal cancer**. Axial CT prone (**a**) and supine (**b**) images show an asymmetrical annular thickening (lesion) of the colonic wall (3 cm in cranio-caudal extension). An abdominal window level setting (**c**) shows homogeneous density of the neoplastic mucosa (*arrow*). Three-dimensional endoluminal image (**d**) shows an irregular surface of the mass (*arrow*) and complete obstruction of the colonic lumen. Optical endoscopy (**e**) confirms the presence of neoplastic lesion (*arrow*)

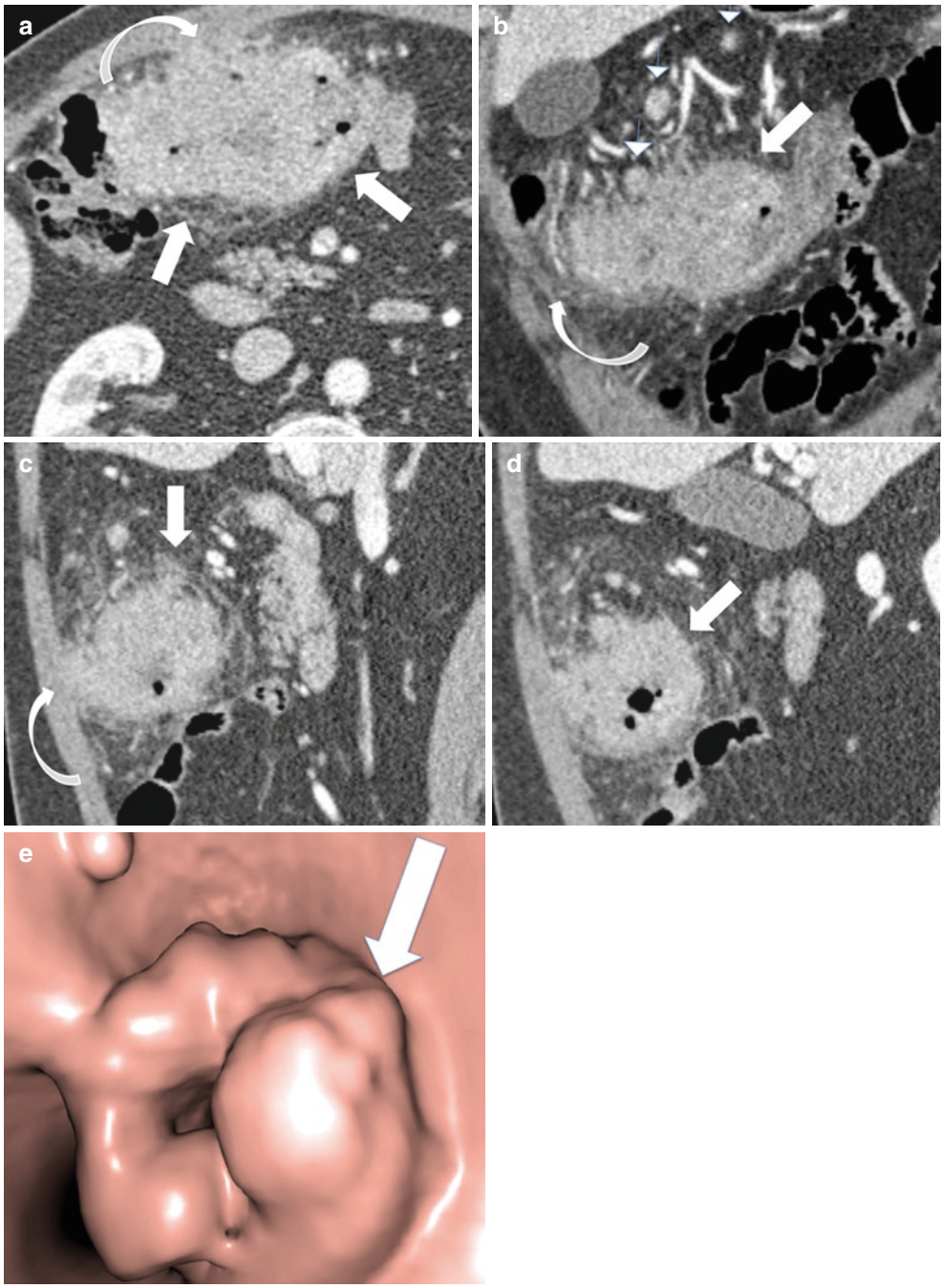


Fig. 19.6 Large annular mass of the ascending colon with diffuse pericolic infiltration and lymphadenopathy. Contrast-enhanced 2D supine axial (**a**), coronal (**b**), and sagittal (**c**, **d**) CTC images show a circumferential thickening (*arrow*) of the colonic wall with diffuse fat stranding, pericolic lymphadenopathy (*arrowhead*), and infiltration of the abdominal wall (*curved arrow*). Three-dimensional CTC image (**e**) shows a lobular mass (*arrow*) in the lumen without causing obstruction

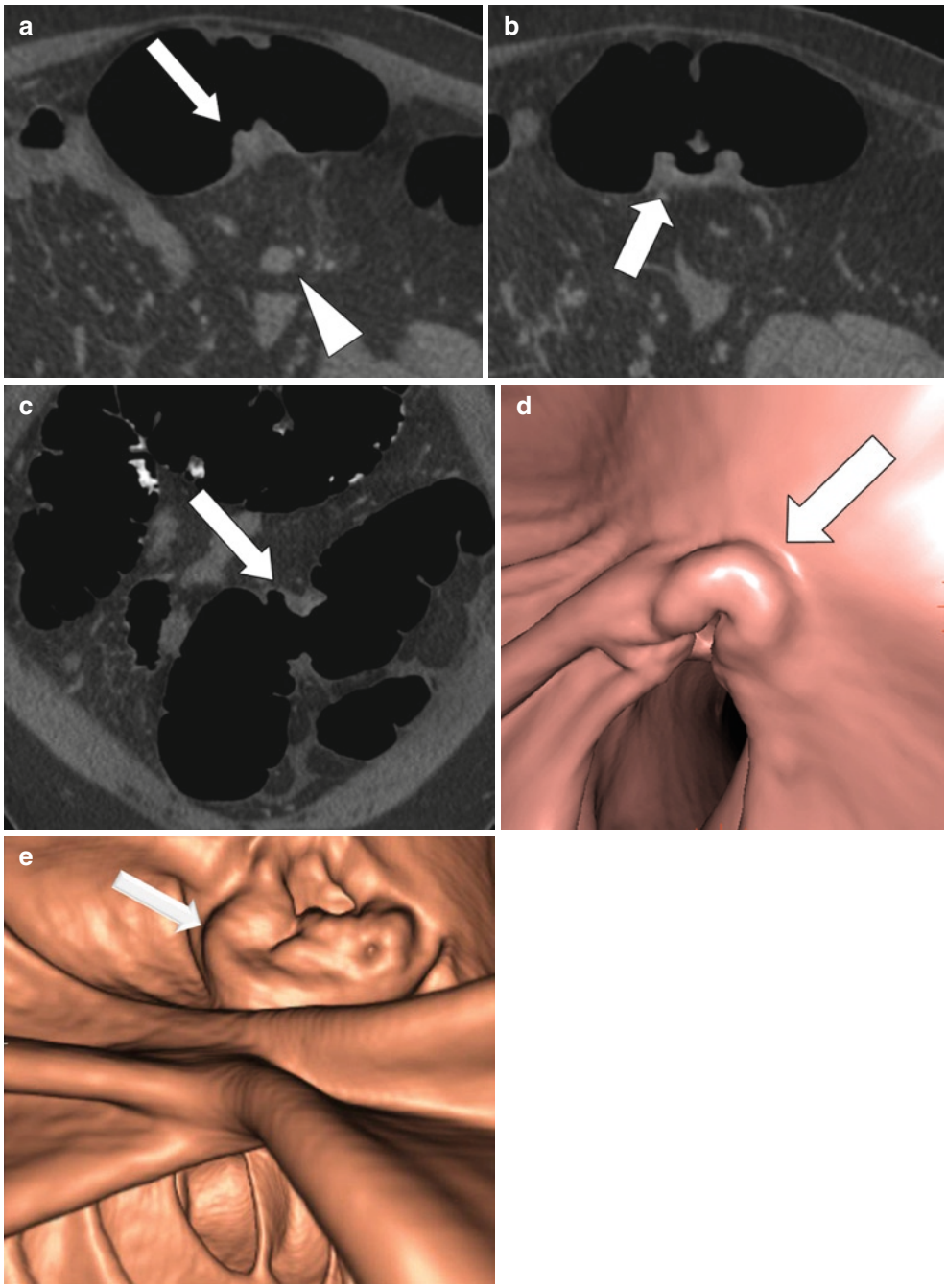


Fig. 19.7 Slight colonic wall thickening with pathological lymph nodes. Two-dimensional axial prone (**a**), axial supine (**b**), and coronal (**c**) CTC images show focal and asymmetrical thickening (*arrow*) of the colonic wall with central ulceration, associated with local lymphadenopathy (*arrowhead*). Three-dimensional CTC images (**d**) allow visualization of the lesion and its endoluminal features. It is important not to mistake focal thickening on the inside of a curvature for a "flexural pseudo-tumor" (**e**). This was an infiltrative adenocarcinoma

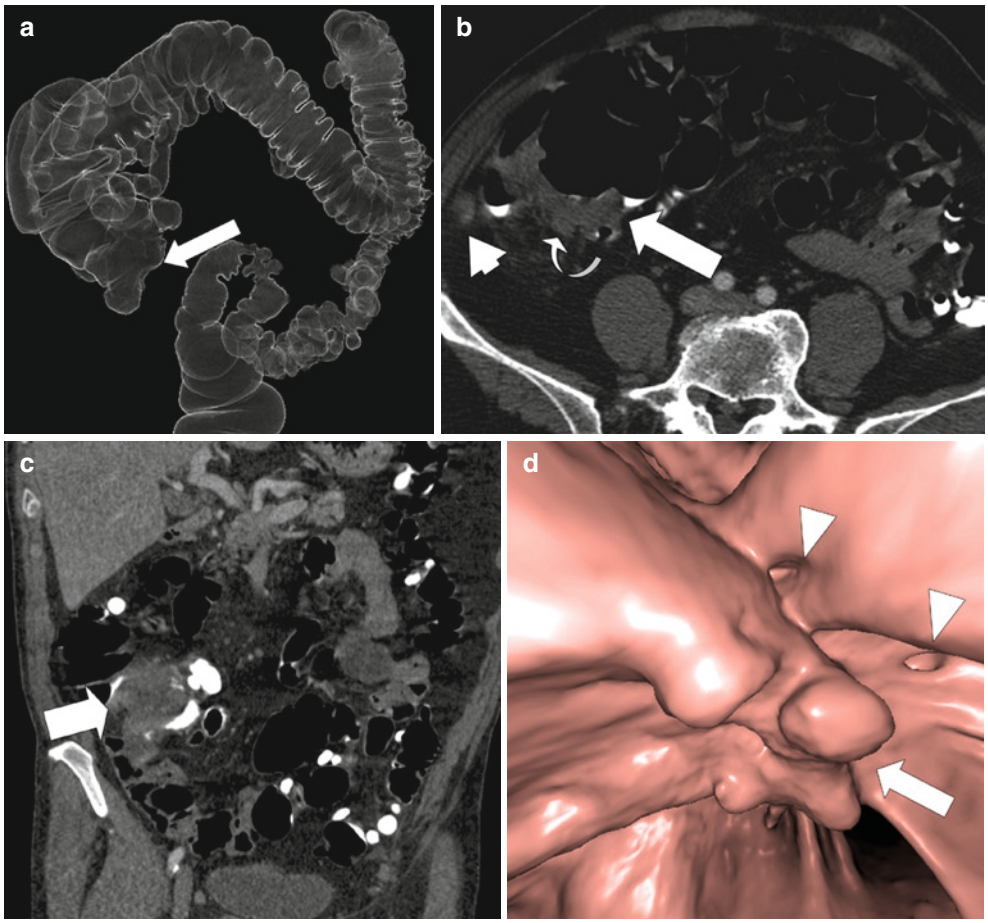


Fig. 19.8 Tumor mass involving the ileocecal valve. Double contrast enema ("transparency") view (**a**) shows a filling defect of medial bowel wall of the cecum (*arrow*). Two-dimensional supine (**b**) and coronal (**c**) images show a filling defect due to an irregular mass (*arrow*) which is contrast enhanced and involves an ileocecal valve that is not recognizable. The tumor has infiltrated the small bowel loops and pericolic fat (*curved arrow*). Pericolic lymphadenopathy (*arrowhead*) is also evident. The 3D endoluminal image (**d**) shows the tumor (*arrow*), and diverticular orifices (*arrowheads*) are clearly visible. Note that masses that fill the cecum may make the remaining air filled ascending colon "cecum-like" in shape, as suggested on (**a**). As with barium enema or optical colonoscopy, the exam is not "complete" unless the cecum is seen as proven by anatomic landmarks (i.e., appendiceal orifice, ileocecal valve, and terminal ileum), *not* by shape of the lumen

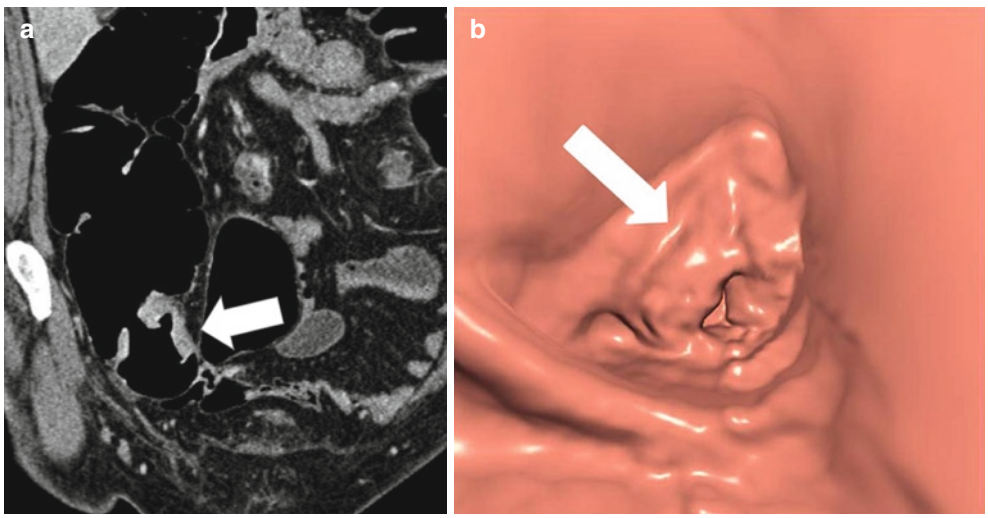


Fig. 19.9 Tumor mass arising from the ileocecal valve. CTC 2D coronal image (**a**) showing an irregular thickening (*arrow*) of ileocecal valve. Three-dimensional CTC endoluminal image (**b**) shows a stenosis of cecal lumen (*arrow*)

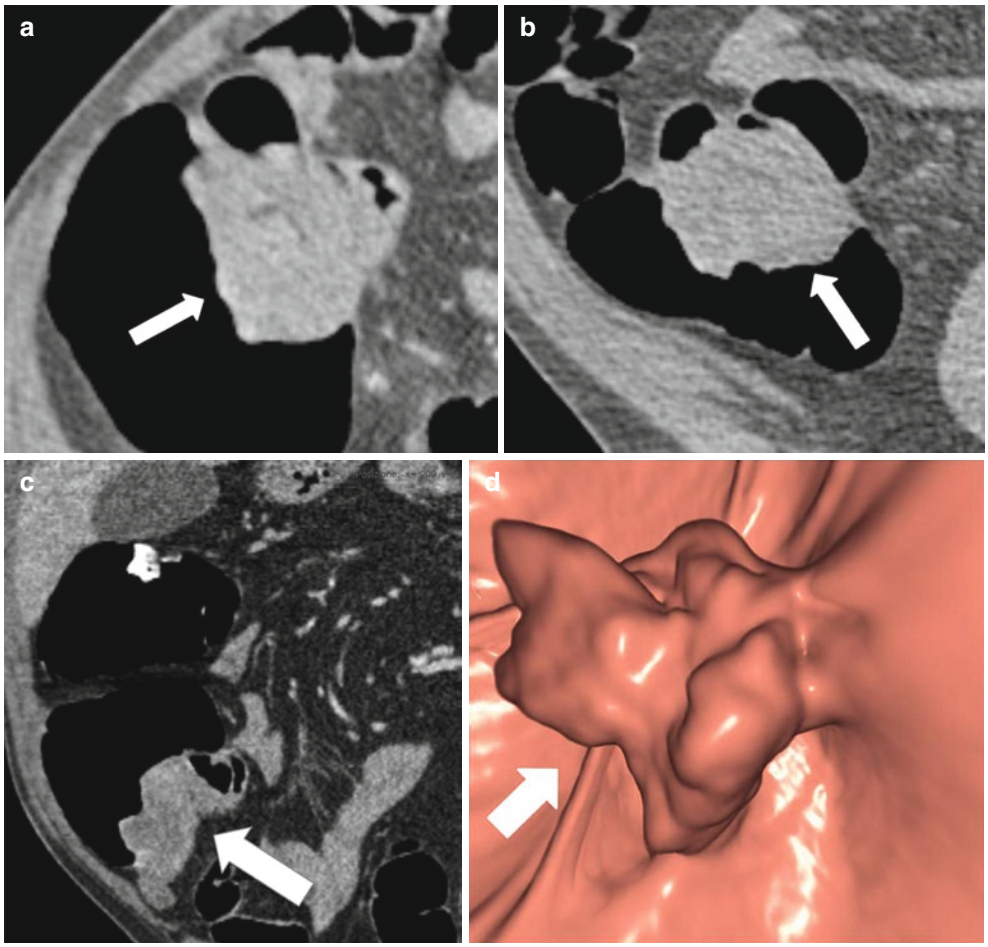


Fig. 19.10 **Colorectal cancer arising from the ileocecal valve in a 77-year-old man with anemia and blood in the stool**. Supine axial (**a**), prone axial (**b**), and coronal (**c**) images show an endoluminal irregular tissue mass (*arrow*) arising from the ileocecal valve. The lesion demonstrated contrast enhancement and measures 5 cm. In the 3D endoluminal image (**d**), the ileocecal valve is unrecognizable and completely deformed by the tumor (*arrow*)

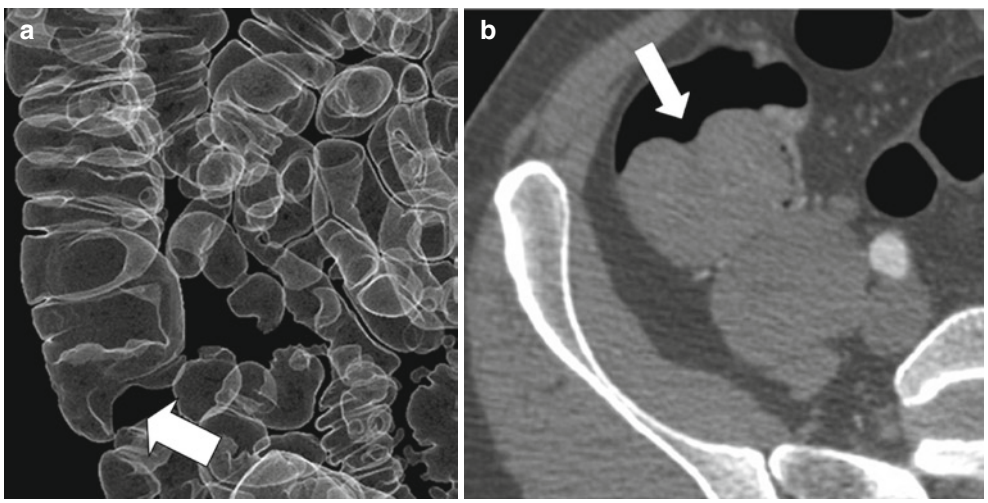
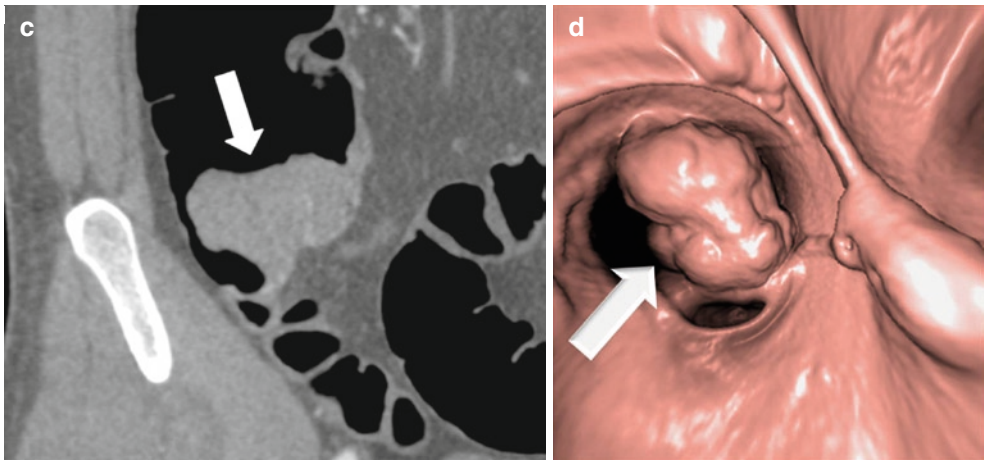


Fig. 19.11 **Large cecal mass just caudal to ileocecal valve**. The CTC double contrast enema ("transparency") view (**a**) shows a filling defect in the cecum (*arrow*) 20 mm under ileocecal valve. Axial supine (**b**) and coronal (**c**) images after the administration of intravenous contrast show a large, irregular cecal mass (*arrow*). (**d**) The 3D endoluminal view clearly depicts both the tumor (*arrow*) and ileocecal valve

Fig. 19.11 (continued)



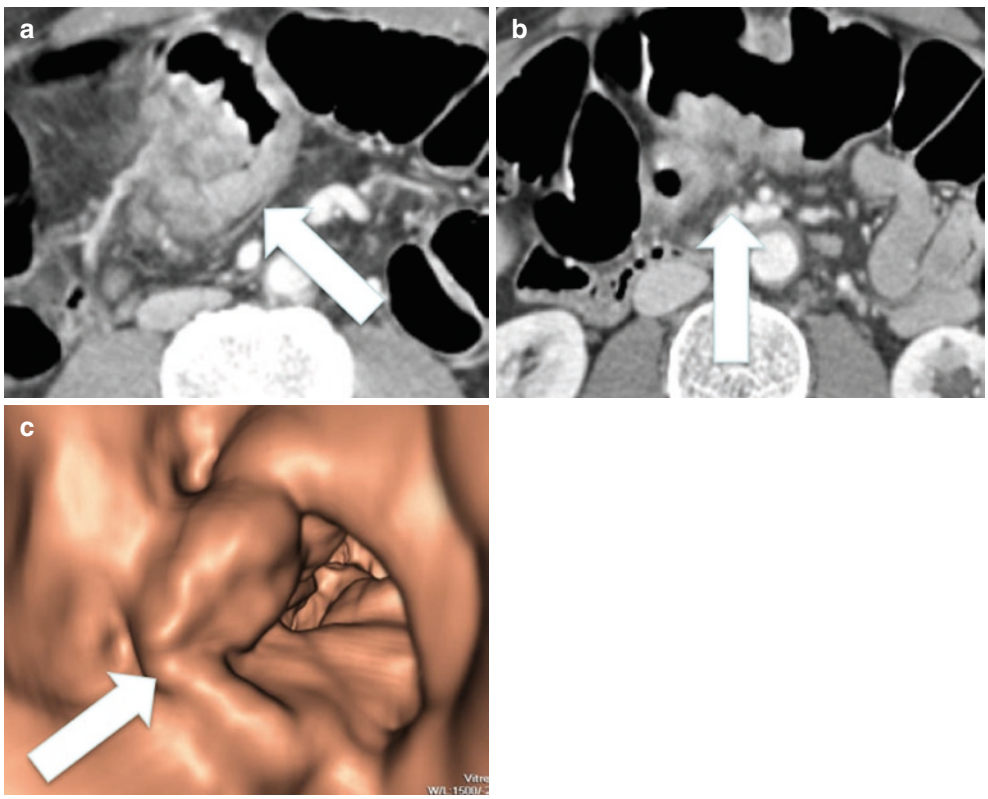


Fig. 19.12 **Postoperative colon in a patient who underwent hemicolectomy for colorectal cancer**. Two-dimensional CTC (**a**, **b**) shows asymmetrical thickening of the colonic wall and diffuse pericolic infiltration (*arrow*) due to recurrence of colorectal cancer. The 3D endoluminal image (**c**) shows a lobular mass (*arrow*)

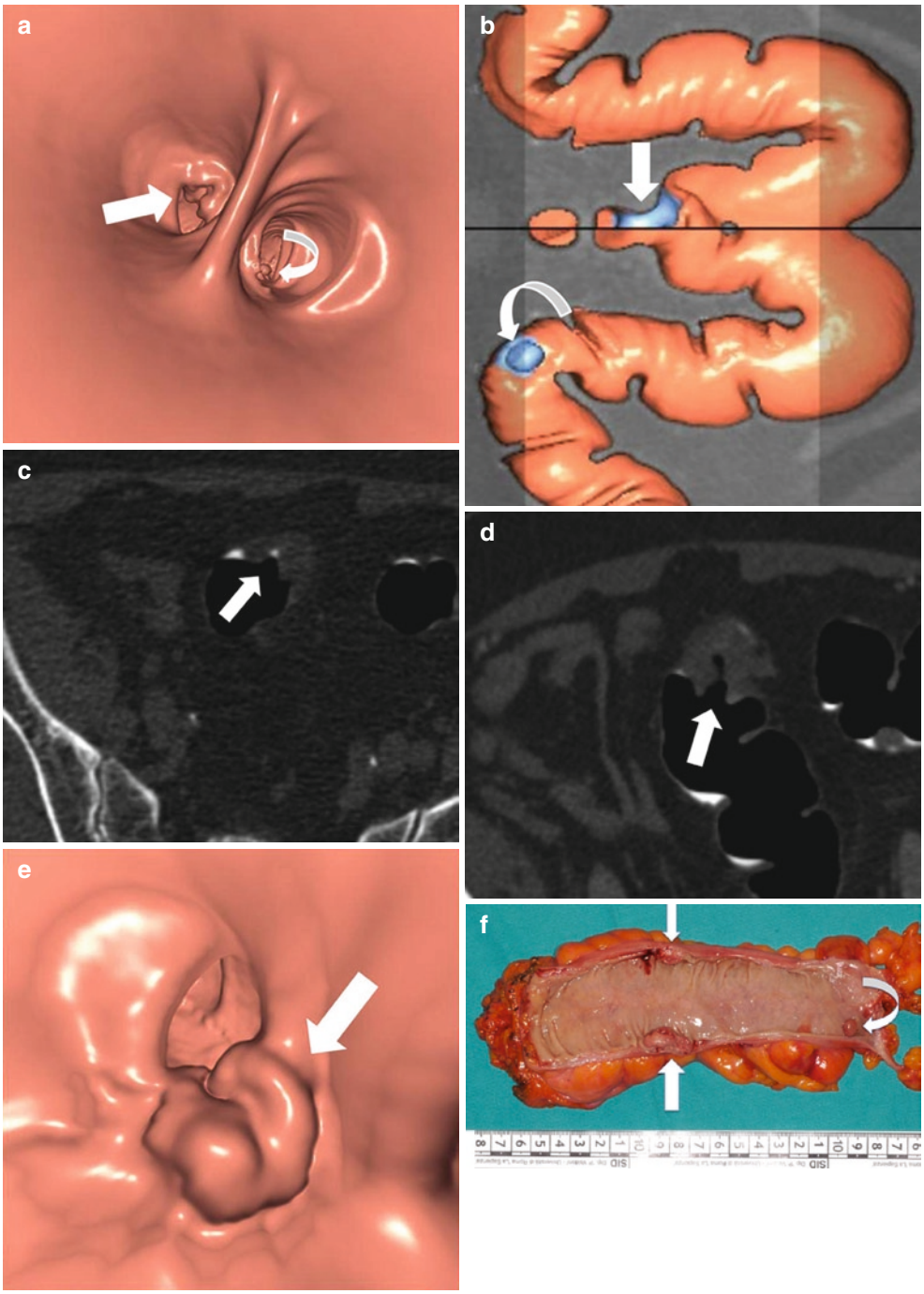


Fig. 19.13 Tumor of sigmoid with a synchronous polyp. The 3D endoluminal view (**a, b**) and corresponding bisected 3D view shows both a semi-circumferential mass (*straight arrow*) and, more proximally, a small polyp (*curved arrow*). Axial prone (**c**) and supine (**d**) images in an abdominal window level setting show a sigmoid mass (*arrow*), and on the supine view (**d**) a polyp in the sigmoid colon more distally with a surrounding shallow layer of densely tagged fluid. The 3D endoluminal view (**e**) shows the slightly lobular mass (*arrow*). (**f**) Fileted-open gross surgical specimen showing the lobular mass (*straight arrows*), and about 10 cm away from the mass is a synchronous polyp

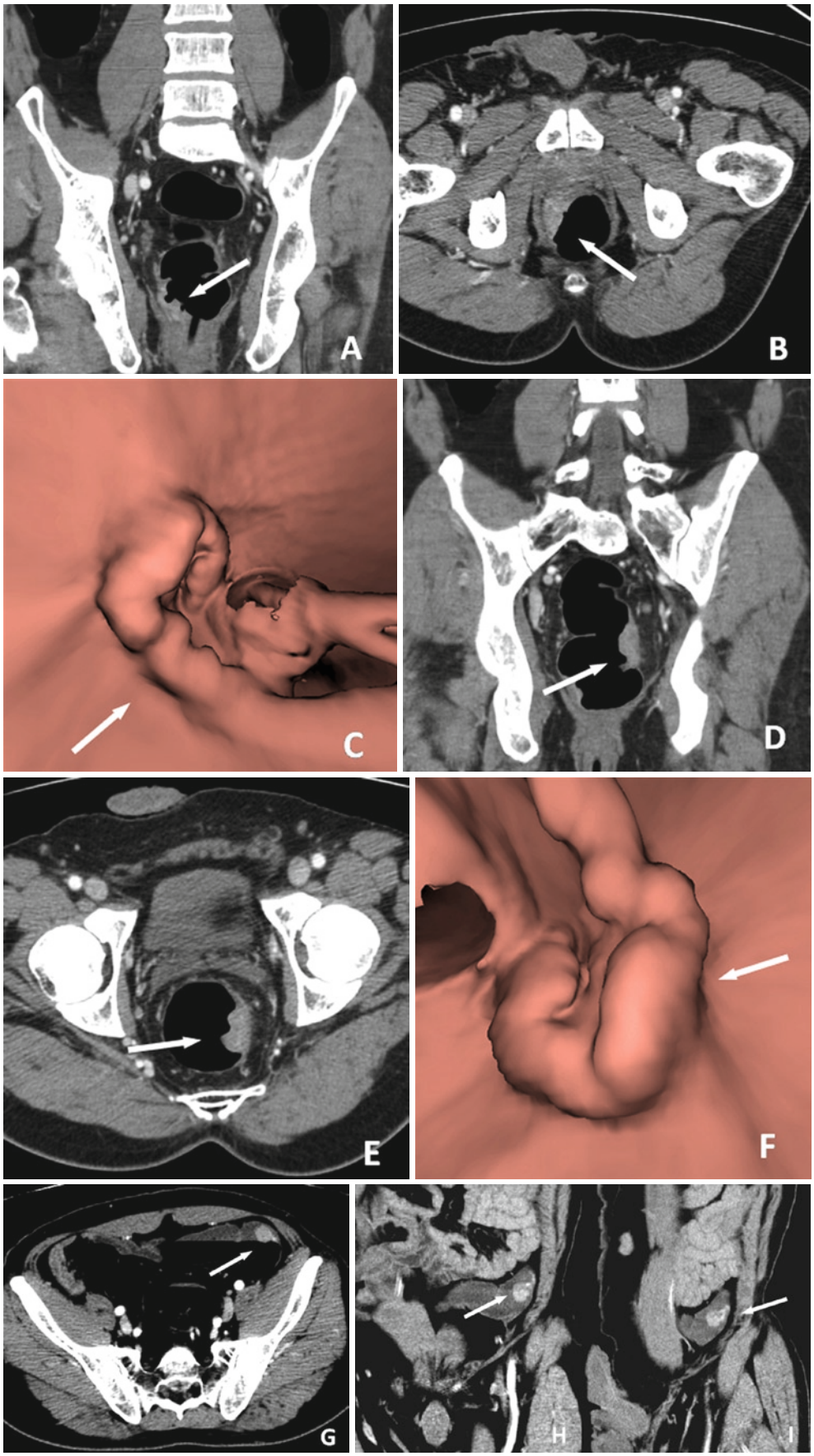


Fig. 19.14 **Adenocarcinoma of the distal third of the rectum** with infiltration of the right side of the anal sphincter: (**a**) coronal, (**b**) axial, and (**c**) virtual endoscopy images. A synchronous lesion on the left lateral wall of the rectal ampulla: (**d**) coronal, (**e**) axial, and (**f**) virtual endoscopy images. An associated synchronous pedunculated polyp of the distal third of the descending colon: (**g**) axial (**h**) coronal and (**i**) sagittal images

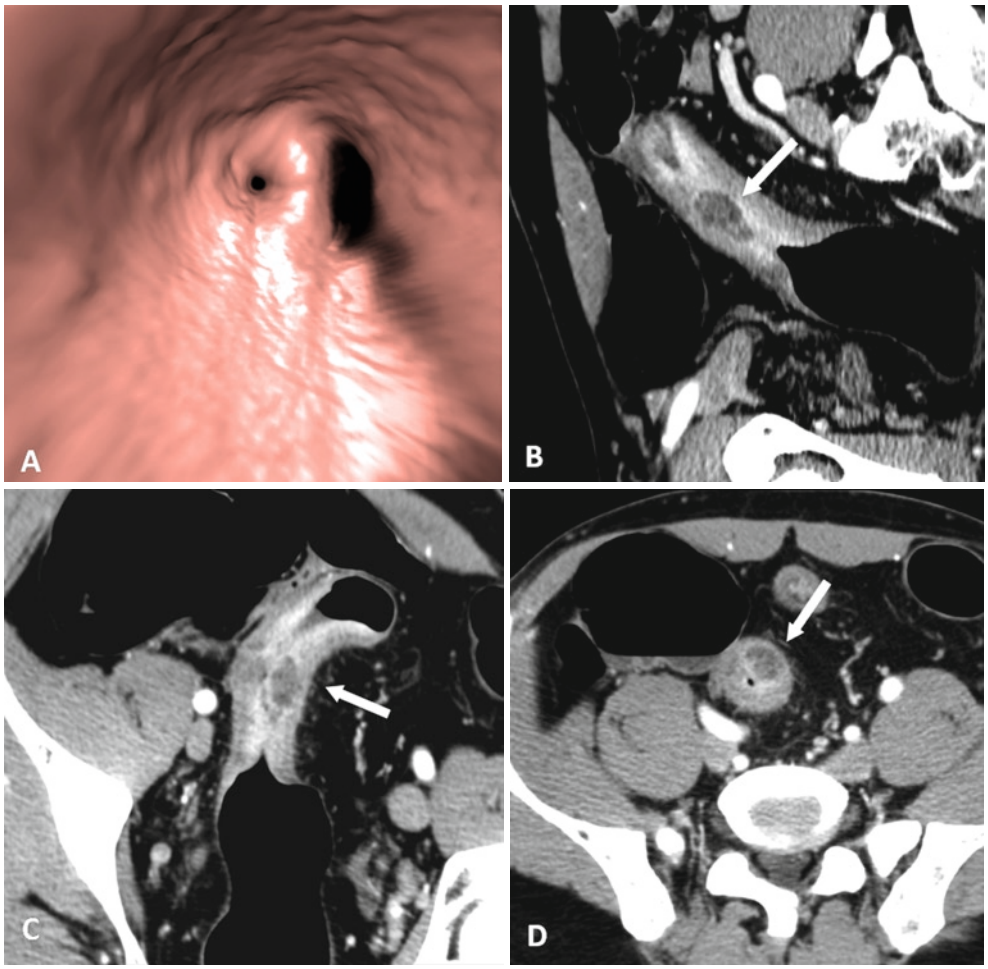


Fig. 19.15 Ulcerative colitis on CTC. Although CTC is not indicated for inflammatory bowel disease, it could be an unexpected finding, or there could be rare reasons to insufflate the colon and use CTC technique. (**a**) Endoluminal 3D view, (**b**) 2D sagittal, and (**c**) coronal reformations, and (**d**) axial view showing a circumferential thickening at the distal third of the sigmoid colon in a patient with ulcerative colitis presenting with an intramural lesion (*arrows*)

Pitfalls and Miscellaneous

20

Franco Iafrate and Andrea Laghi

The recognition of pitfalls is of great interest to both the novice and the expert. Every experienced reader has seen some unusual pitfall, and in this chapter we share some examples. Certain categories of pitfalls are covered in prior chapters as well, e.g., mobile pedunculated polyps in Chap. 15, diminutive polyps in Chap. 16, flat lesions in Chaps. 9 and 17, and stool or diverticula-related pitfalls in Chap. 18.

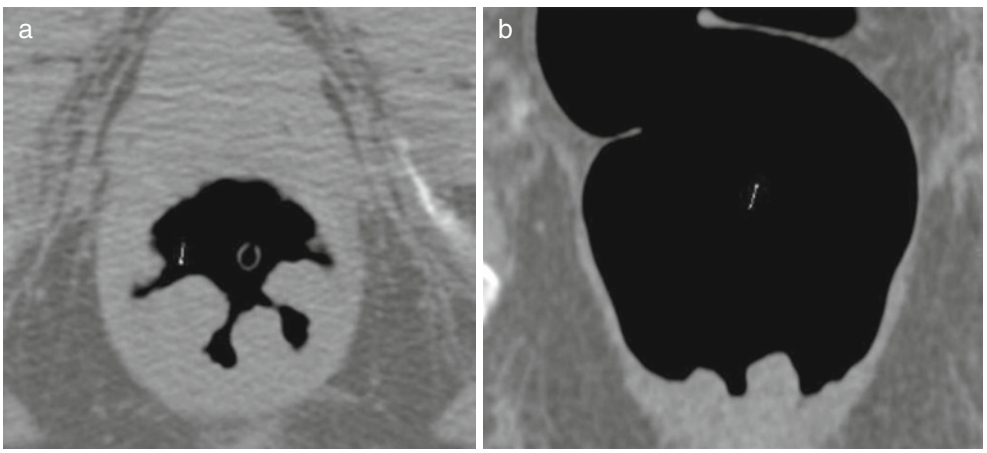


Fig. 20.1 **Internal hemorrhoids**. Axial (**a**), coronal (**b**), 2D, and endoluminal 3D (**c**, **d**) CTC images show prominent internal hemorrhoids appearing like some soft-tissue rounded bulges around the rectal catheter. At colonoscopy, which is performed for other colonic positive findings, internal hemorrhoids are confirmed (**e**)

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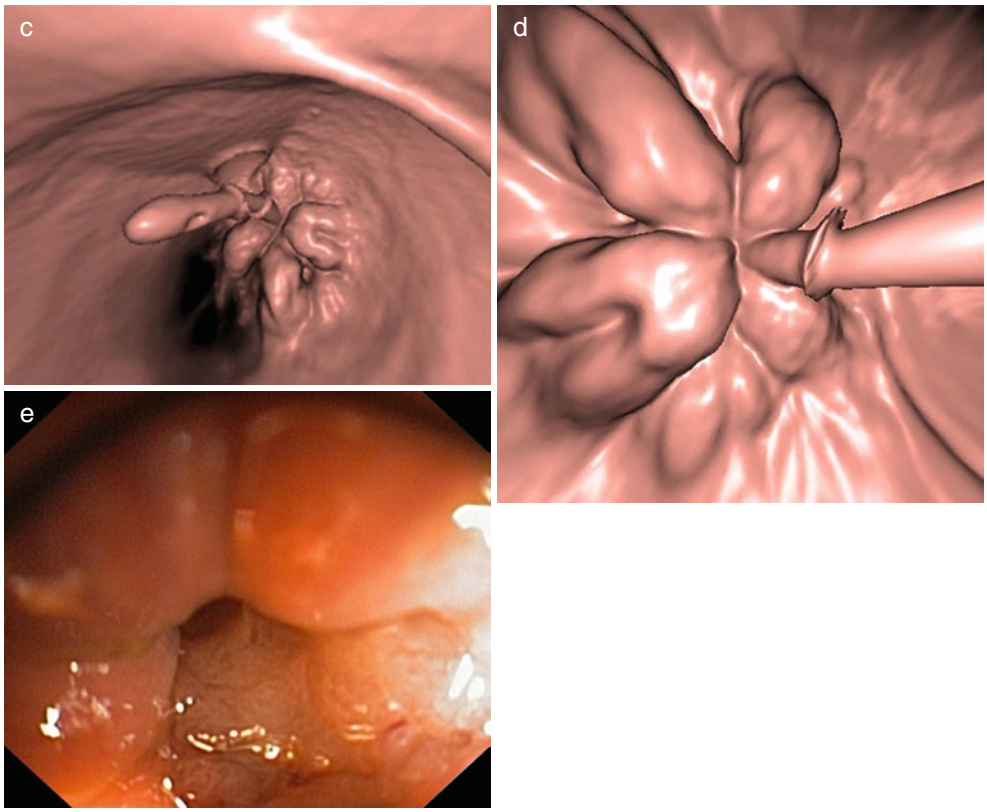
Fig. 20.1 (continued)



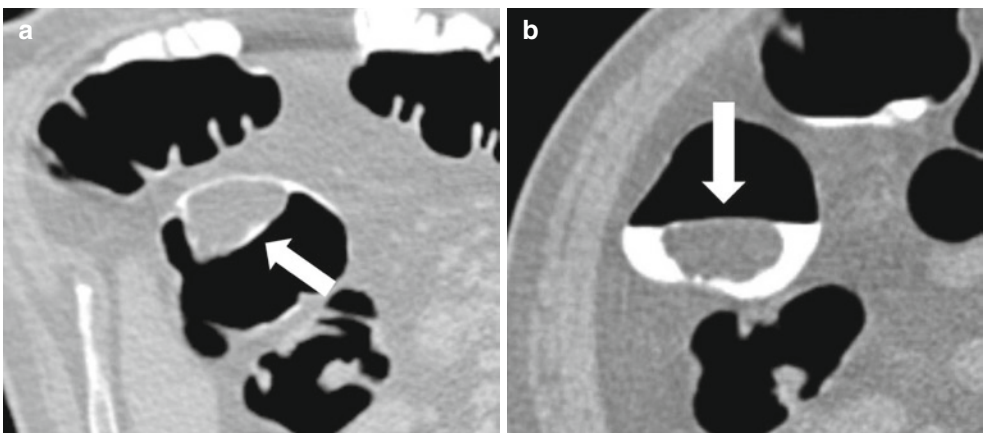
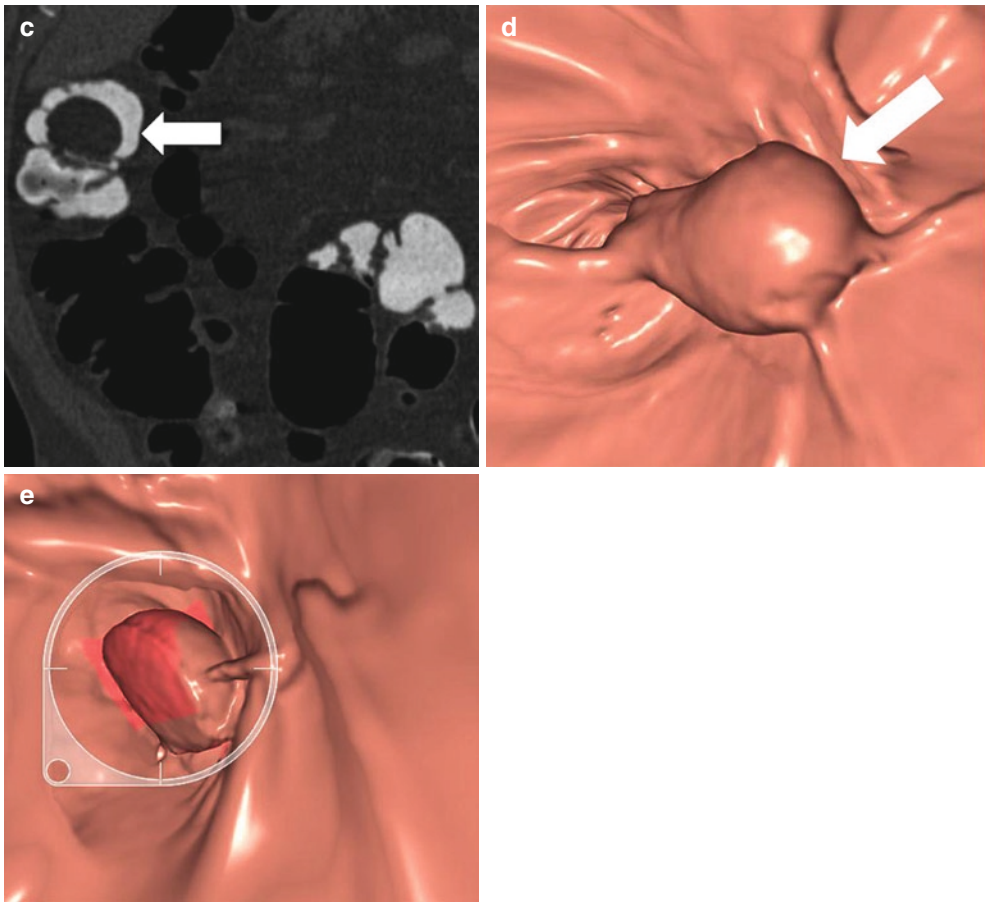


Fig. 20.2 **Submucosal colonic lipoma**. The key issue in the detection and evaluation of submucosal lipoma on CTC is based on the evaluation of axial prone (**a**) and axial supine (**b**) 2D MPR images that show some typical features like oval-shaped, smooth demarcation and, upon changing the window level setting, (**c**) the presence of homogeneous fat density within the lesion that is crucial for diagnosis. The use of 3D endoluminal images (**d**) could be helpful, as lipomas usually appear as pedunculated oval lesion. The lesion is also detected by CAD (**e**)

Fig. 20.2 (continued)



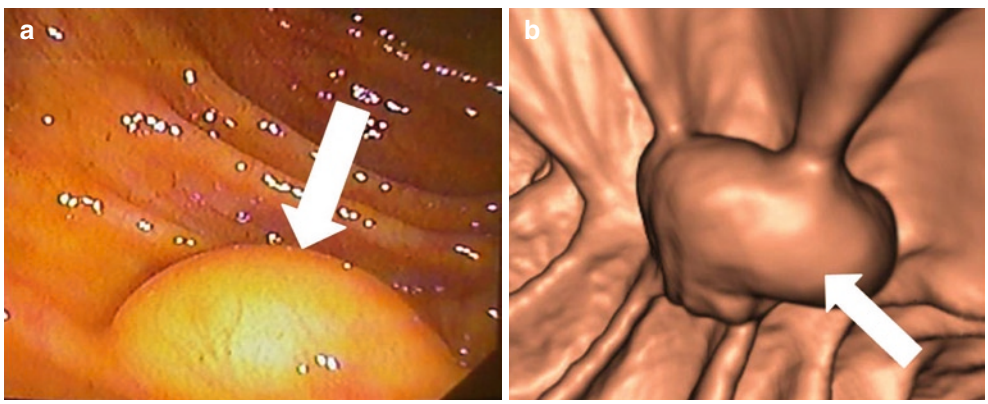


Fig. 20.3 **Pedunculated lipoma**. Colonoscopy (**a**) and 3D endoluminal (**b**) CTC image show a smooth polypoid lesion (*arrow*). Using 2D CTC images (**c**–**e**), the lesion shows a uniform fat tissue attenuation (*arrow*), which is diagnostic of lipoma

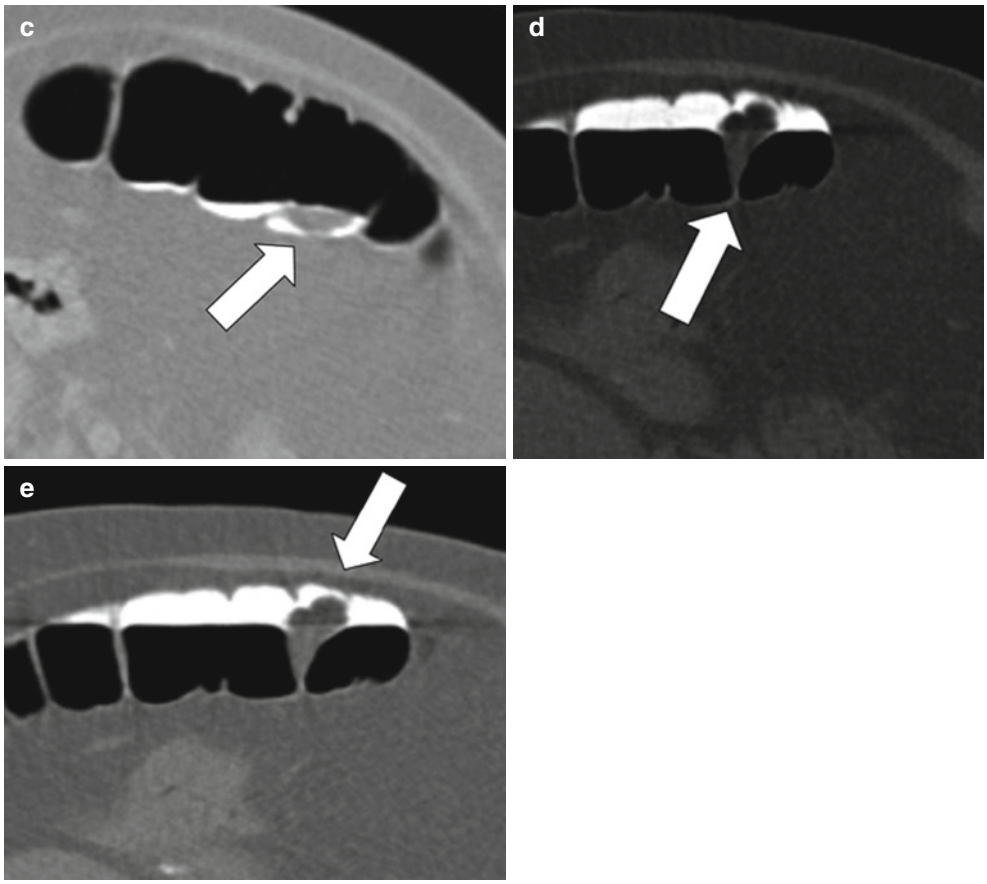


Fig. 20.3 (continued)

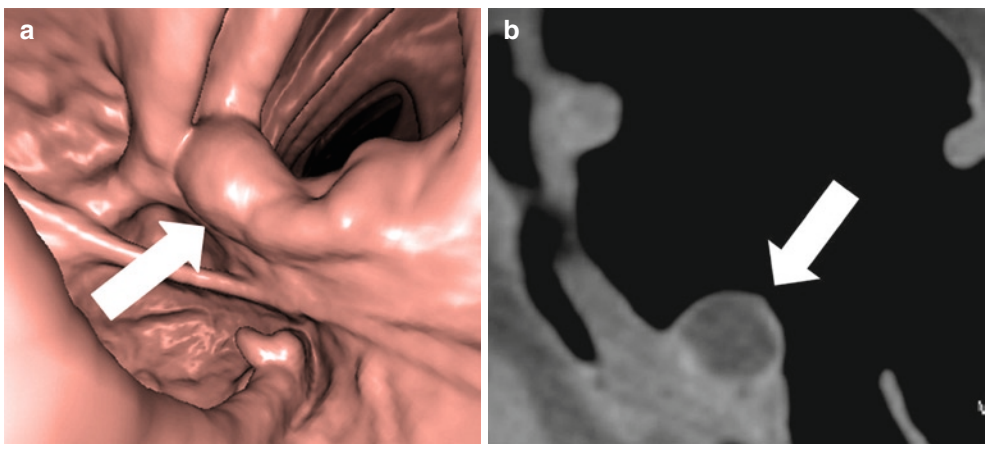


Fig. 20.4 **Lipoma of ileocecal valve**. Three-dimensional CTC image (**a**) shows an ileocecal valve with a quite irregular profile due to a smooth rounded protuberance (*arrow*). Axial 2D CTC image (**b**) shows a submucosal uniform fat attenuation core of ileocecal valve

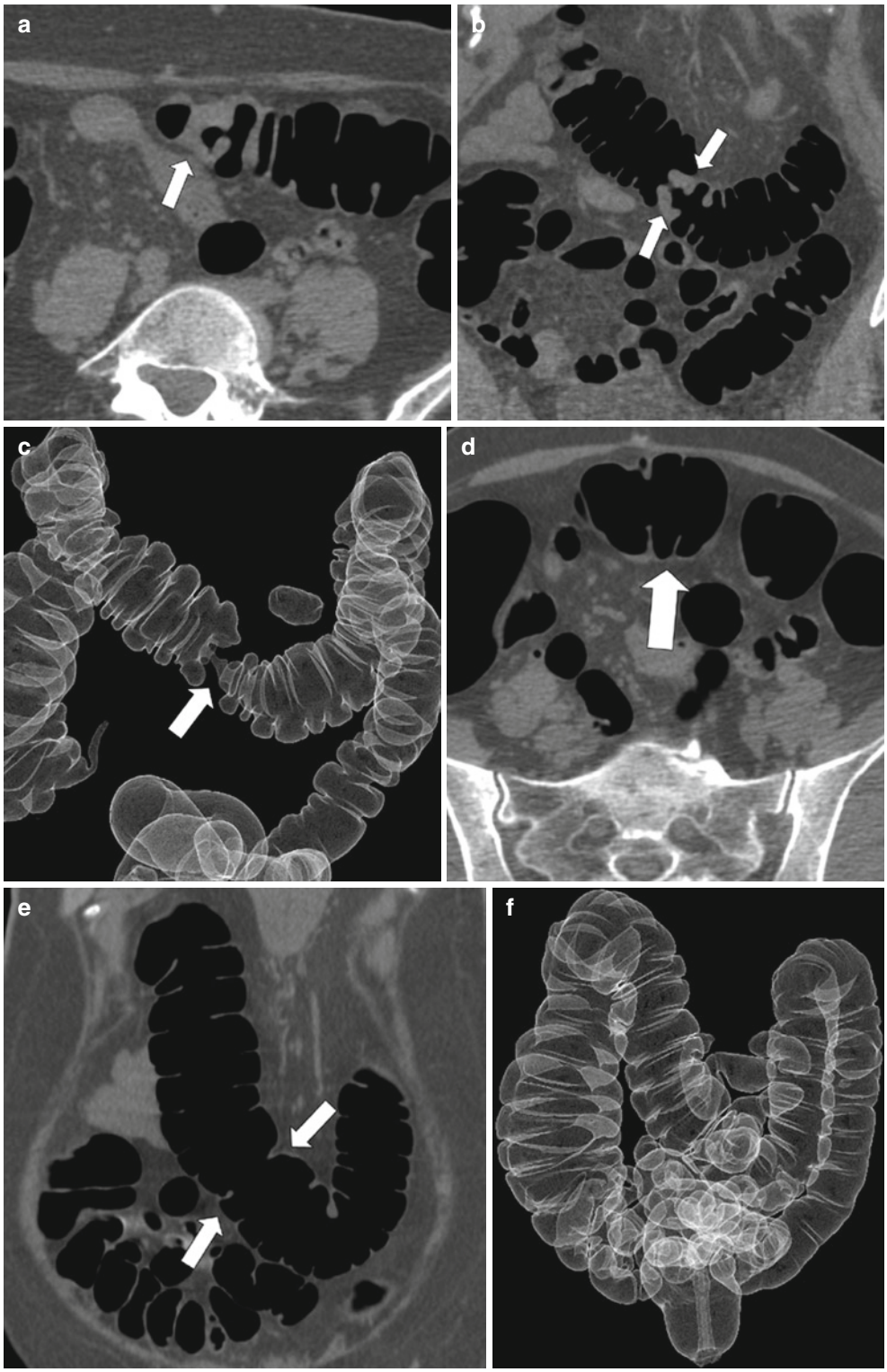


Fig. 20.5 Colonic spasm simulating "apple core" neoplastic lesion. Axial prone (**a**) and coronal prone (**b**) 2D CTC images show a circumferential wall thickening (*arrow*) associating with an "apple core" sign (*arrow*) on a double contrast enema "transparency" view (**c**). At axial supine (**d**), coronal supine (**e**), 2D CTC image, and double contrast enema "transparency" view (**f**) acquired in supine position, the colonic wall thickening seems completely resolved (*arrow*) as a transient colonic spasm

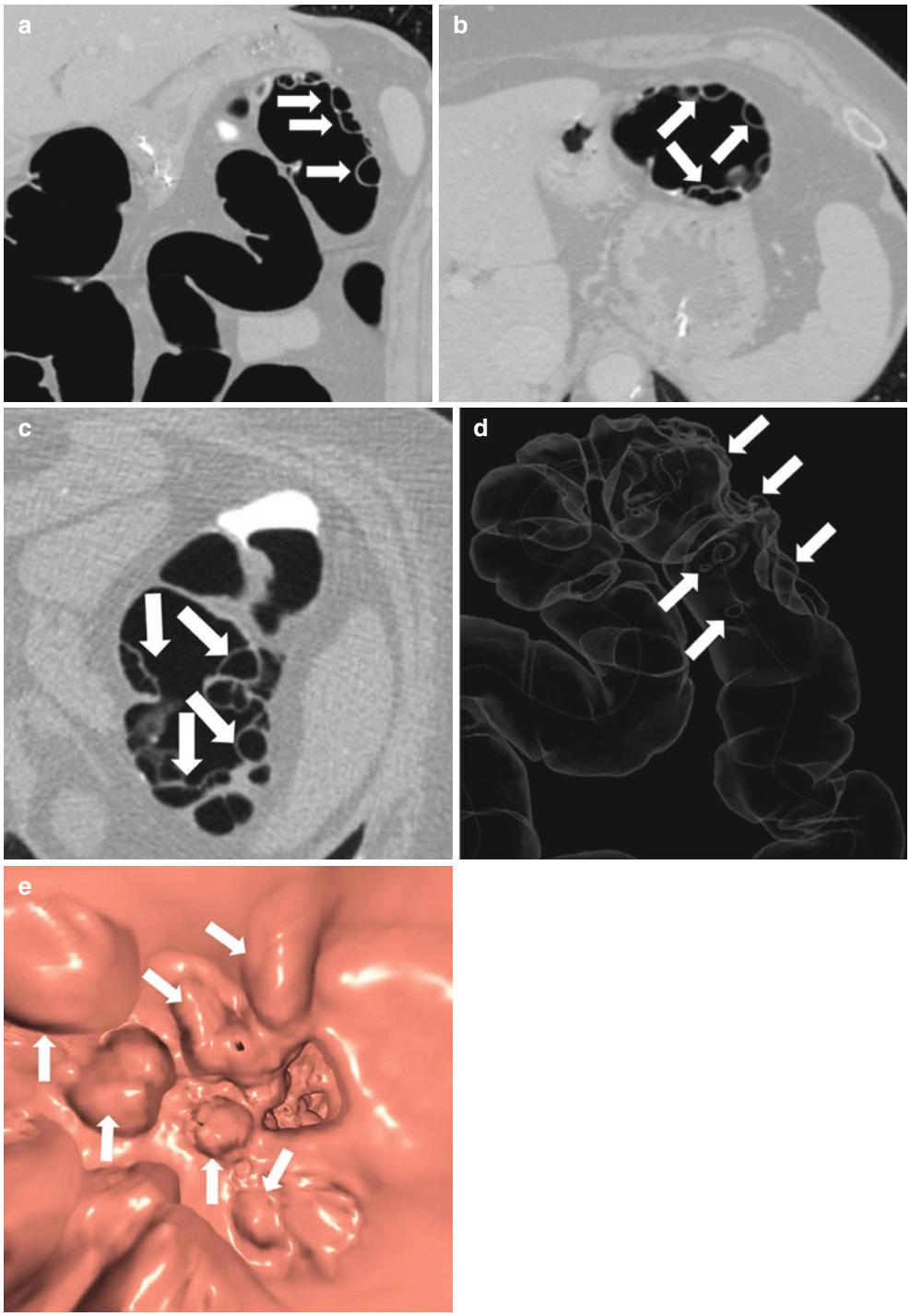


Fig. 20.6 Pneumatosis intestinalis. Pneumatosis intestinalis (PI) is defined as an abnormal location of gas within the bowel wall. It may be idiopathic and accidentally discovered or may be related to a large variety of diseases like ischemia or infection of the bowel; in these cases air from the lumen may enter the bowel wall because of mucosal necrosis. The key issue in the detection and evaluation of PI is the tight combination between 2D MPR images. (**a**) coronal, (**b**) supine axial, (**c**) prone axial, and (**d**) double contrast barium enema "transparency" and 3D endoluminal images (**e**) that will better clarify the presence of cystic endoluminal lesions protruding within colonic lumen (also see Fig. 7.17.)

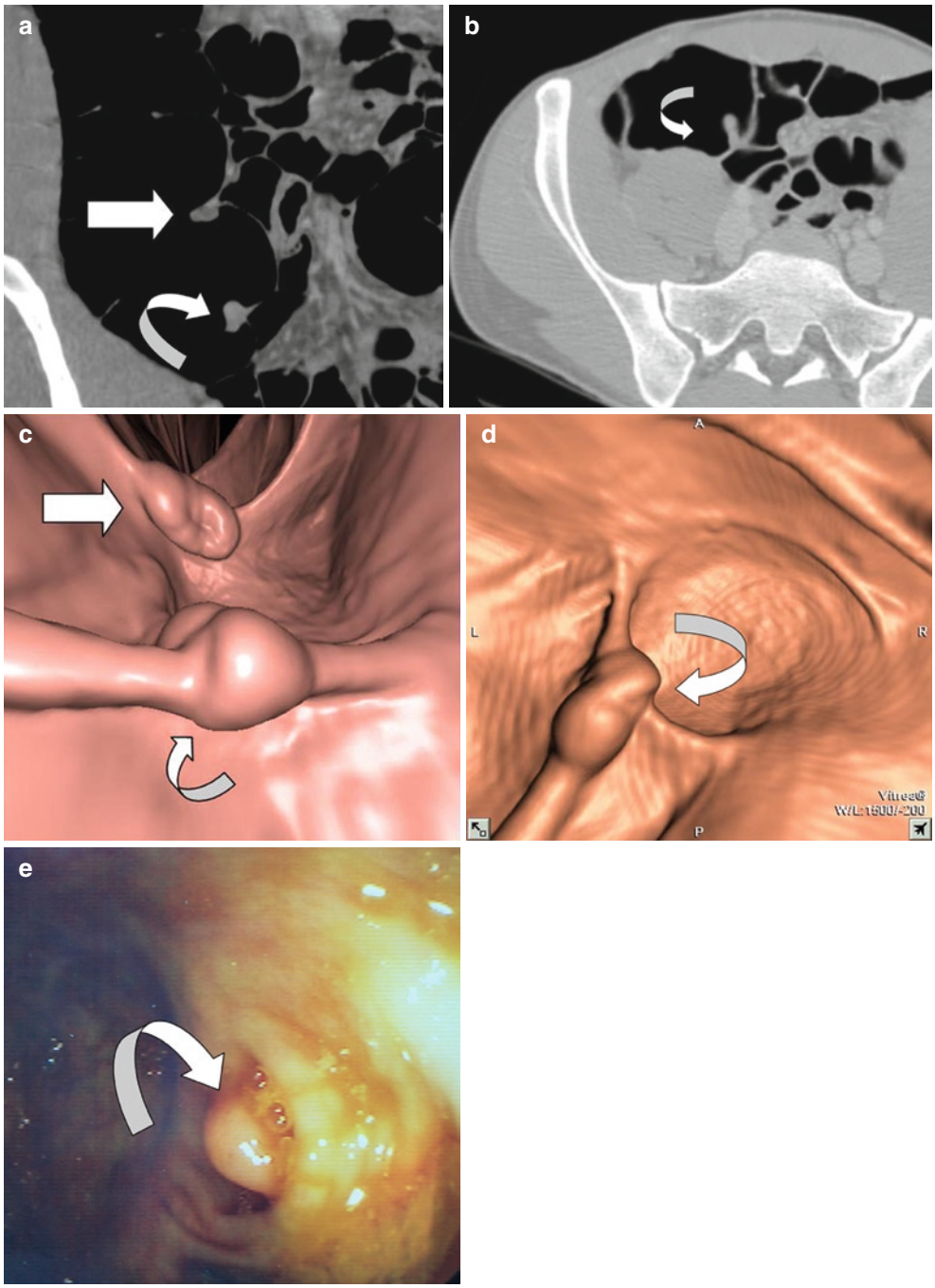


Fig. 20.7 **Inverted appendiceal stump**. CT colonography shows in 2D axial (**a**) and coronal (**b**) images and 3D images (**c**, **d**) the stump as a round, smooth polypoid filling defect (*curved arrow*) near the ileocecal valve (*arrow*) and usually arising from the cecal wall at the expected orifice of the appendix. The main differential diagnosis is with a polyp. Both lesions have homogeneous soft-tissue attenuation and are not mobile. In this case, endoscopy is required (**e**)

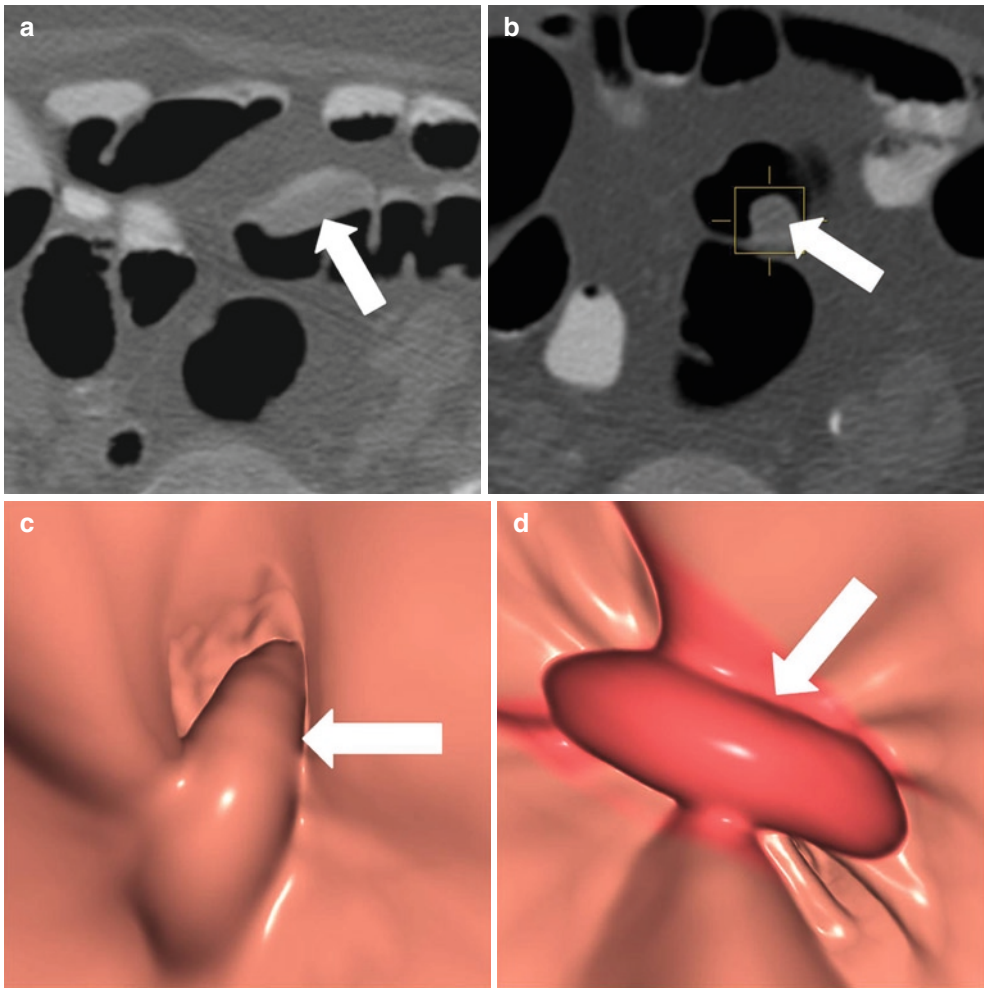


Fig. 20.8 A luminal foreign body: a suppository drug. Two-dimensional CTC images show an ovoid filling defect with smooth surface (*arrow*) and mobility from prone (**a**) to supine (**b**) position to gravity. Endoluminal 3D CTC (**c**, **d**) images show an ovoid uniform body (*arrow*) consistent with a retained suppository (Courtesy of Gabriella Iussich and Daniele Regge)

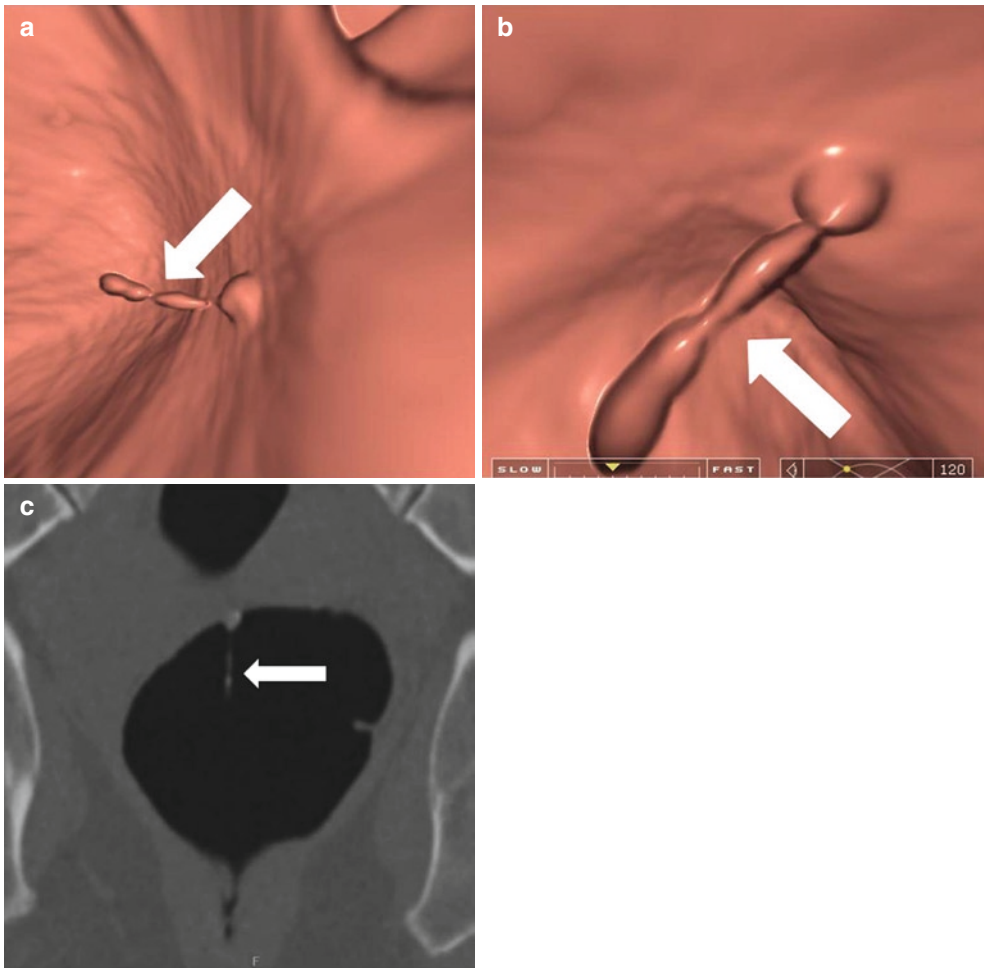


Fig. 20.9 Mucous filament. Three-dimensional endoluminal CTC images (**a**, **b**) show a long and thin filling defect (*arrow*) suspected to be a pedunculated polyp. Two-dimensional CTC image (**c**) shows that the lesion has a peripheral high attenuation (*arrow*), which suggests an incompletely tagged mucous filament or "strand"

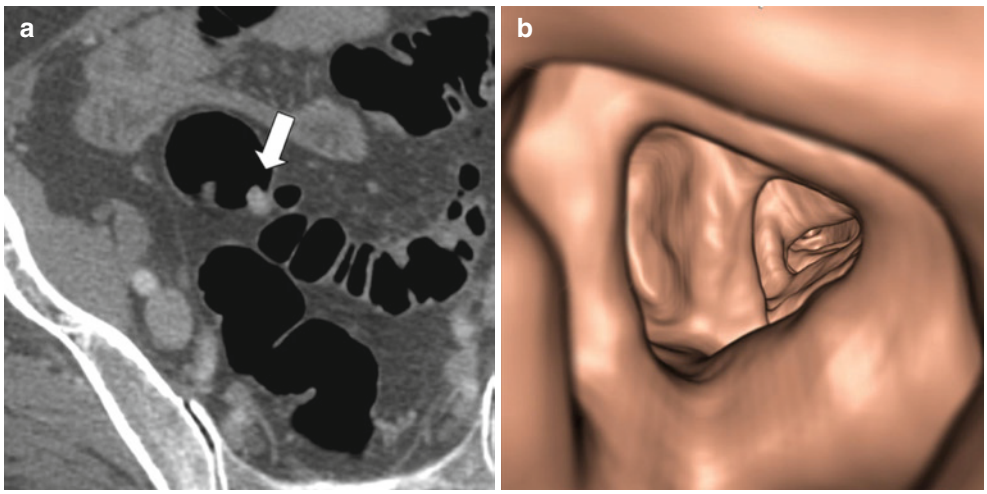
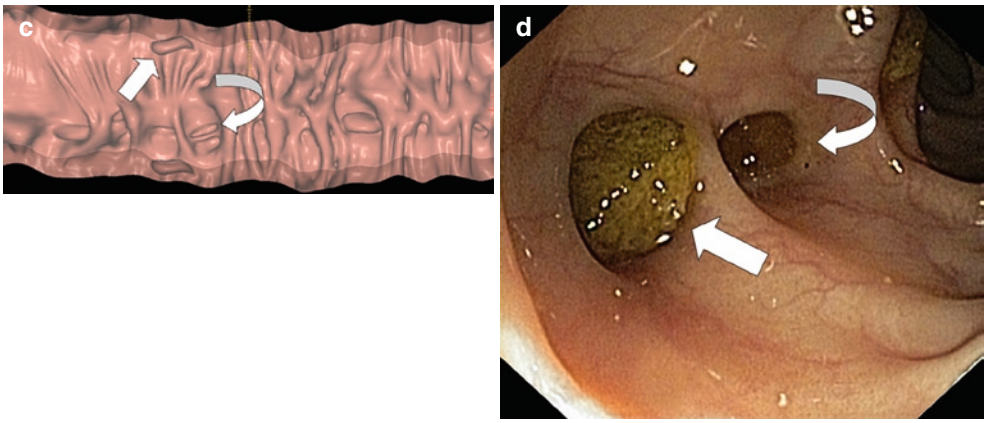


Fig. 20.10 Fecal residue impacted in a diverticulum. Two-dimensional CTC image (**a**) shows a soft-tissue polypoid filling defect (*arrow*), which seems not to take origin from colonic wall. Three-dimensional endoluminal (**b**) and virtual dissection (**c**) views, show the polypoid filling defect (*arrow*) near a diverticular orifice (*curved arrows*). Optical colonoscopy (**d**) confirms the presence of diverticular orifice (*curved arrow*) and shows a fecal residue impacted on diverticulum mimicking a polyp on CTC

Fig. 20.10 (continued)



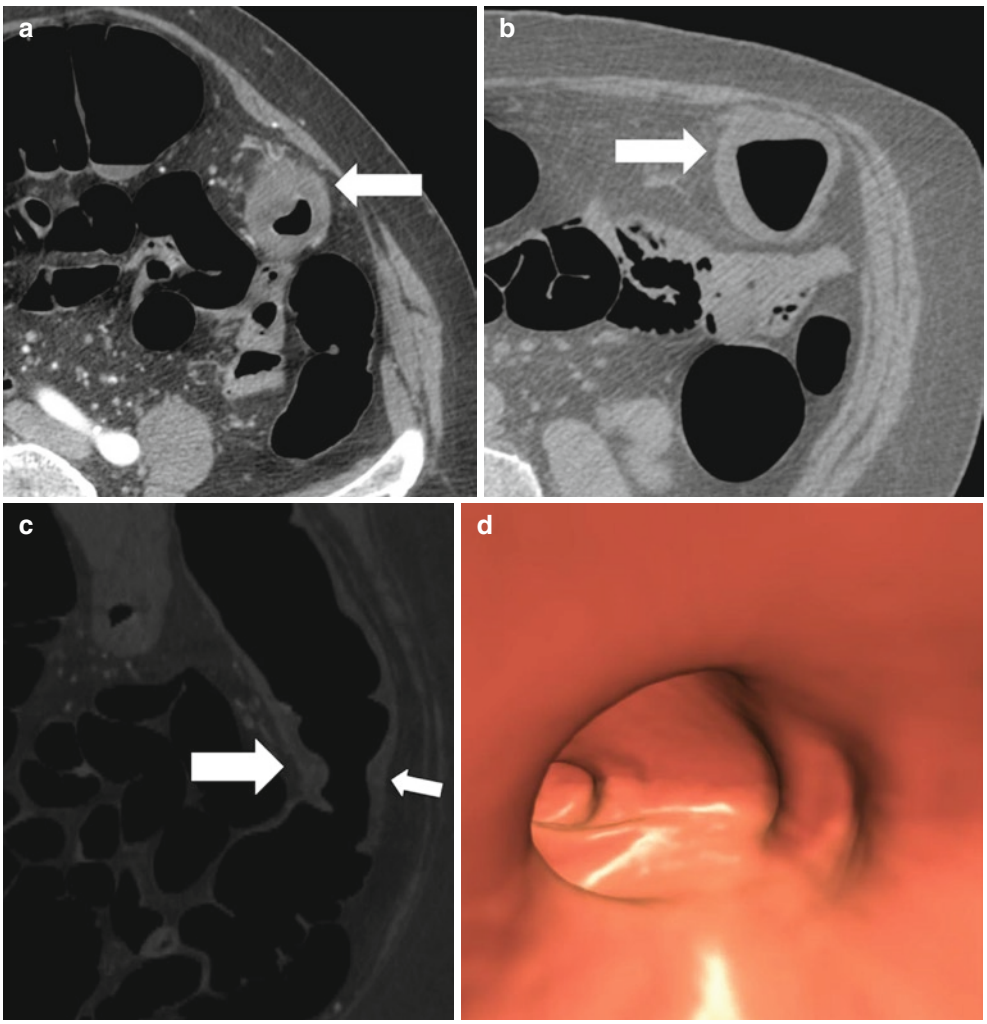


Fig. 20.11 **Colonic ischemia**. Axial 2D CTC obtained on supine (**a**) and prone (**b**) position showing a diffuse triangular shake thickening of colonic bowel wall. Note how the colon is better distended on prone position. Two-dimensional coronal (**c**) reformatted image after intravenous administration of contrast agent shows a mild enhancement of wall thickening due to presence of segmental ischemia. Three-dimensional CTC endoluminal image (**d**) shows a mild diffuse reduction of bowel lumen with no evidence of a stenosing lesion

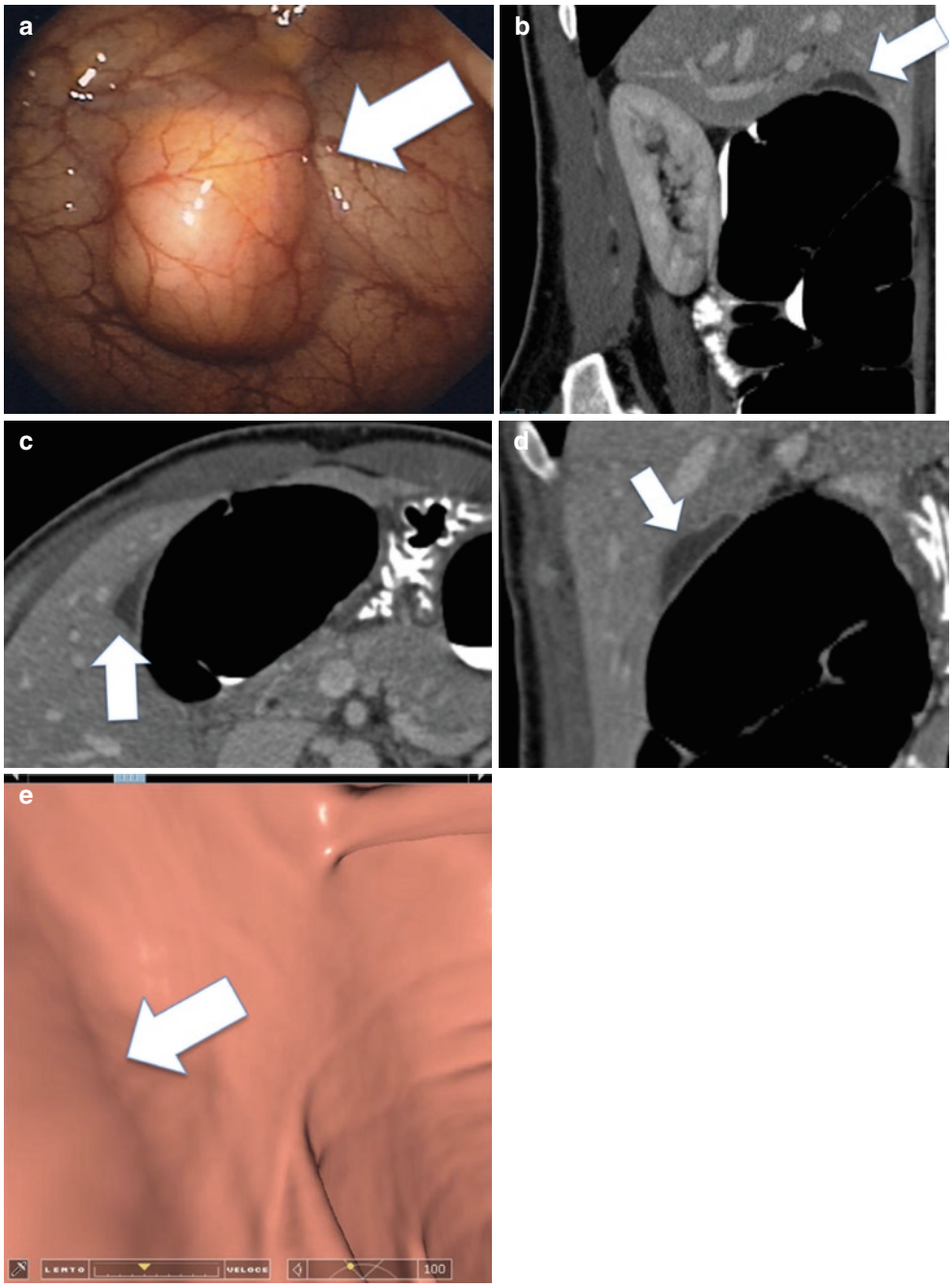


Fig. 20.12 Pitfall on conventional colonoscopy. At colonoscopy (**a**), a polypoid filling defect (*arrow*) is evident and related to extrinsic compression from outside bowel wall. Two-dimensional CTC on sagittal, axial, and coronal views (**b**–**d**) demonstrate that there are no filling defect protruding within colonic lumen and gallbladder (arrow) that is strongly compressed between colonic wall and liver surface. Three-dimensional CTC endoluminal image (**e**) shows the normal distension of colonic lumen with no filling defect

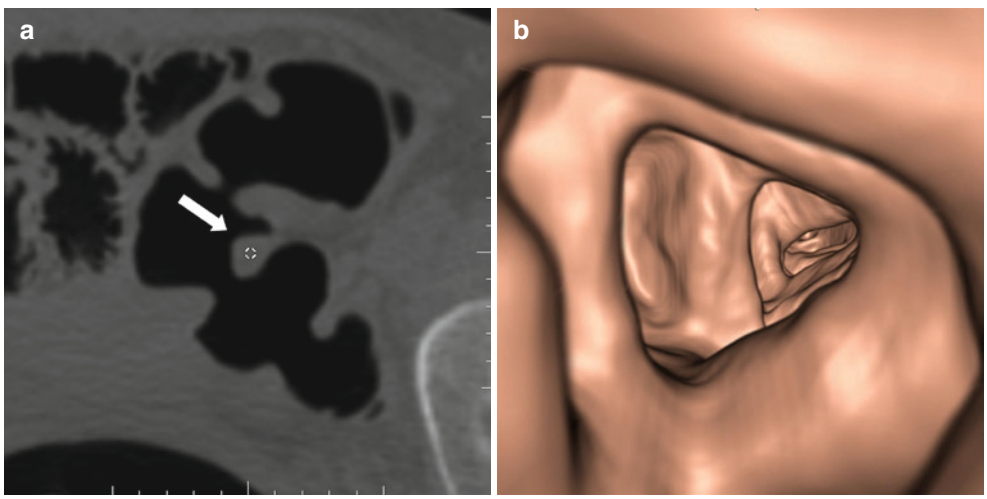


Fig. 20.13 Converging thick folds or "branching folds" aka "doubling folds." Two-dimensional CTC image (**a**) showing a polypoid filling defect (*arrow*) at the level of sigmoid colon. Three-dimensional CTC endoluminal image (**b**) showing that the filling defect is easily related to a "doubling of folds"

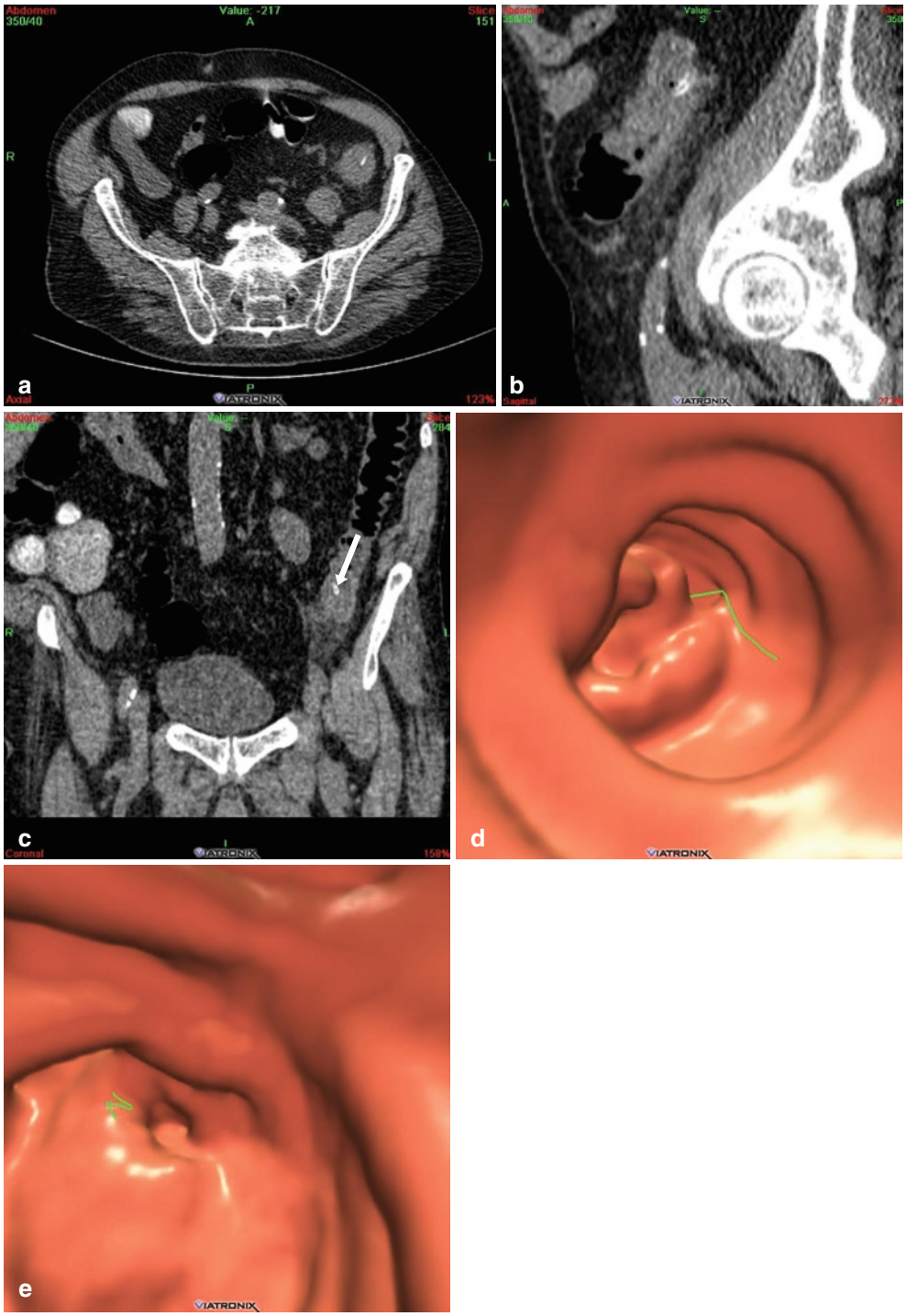


Fig. 20.14 Foreign body with associated inflammation. A 65-year-old male with constipation. Optical colonoscopy showed a mass in the sigmoid colon. For completion the patient was referred for CTC. Axial supine image (**a**), sagittal reconstruction (**b**), and coronal reconstruction (**c**) demonstrated a high-density linear structure (*arrow*) in the "mass." The inflammatory change caused a distortion of the mucosal contour, as seen on 3D endoluminal views (**d**–**e**). At surgery a fish bone was found (Courtesy Jacob Sosna, MD, Hadassah Hebrew University Medical Center, Jerusalem, Israel)

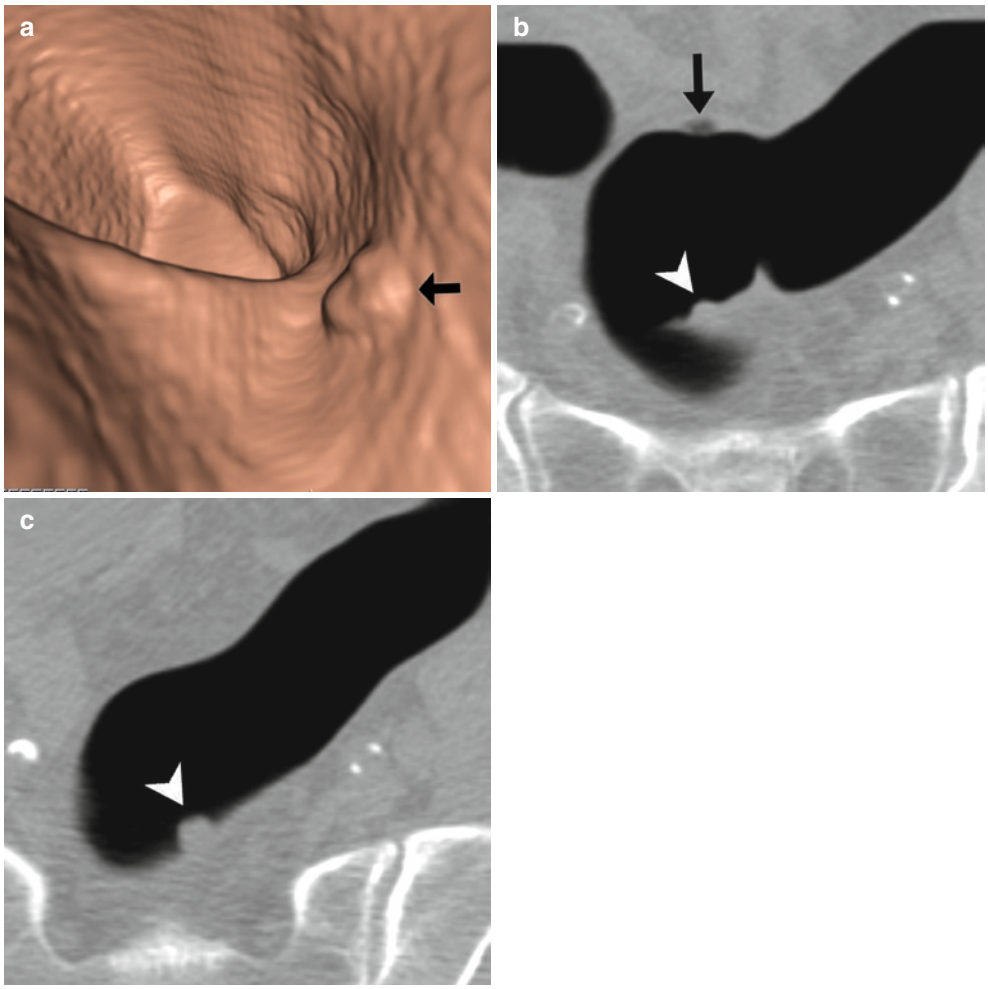


Fig. 20.15 Untagged, sticky stool. Images from a CTC done without fecal tagging. In a primary 3D read, the 3D view would be interpreted first. The 3D endoluminal view (**a**) shows a sessile polypoid lesion in the sigmoid on 3D (*black arrow*). The (**b**) supine and (**c**) prone axial images show a nonmobile soft-tissue lesion without gas bubbles, indistinguishable from a polyp (*white arrowhead*). The patient was referred to optical colonoscopy (appropriately, since such a lesion must be assumed to be a polyp), but none was found. This emphasizes the importance of using an oral tagging agent (Courtesy Philippe Lefere)

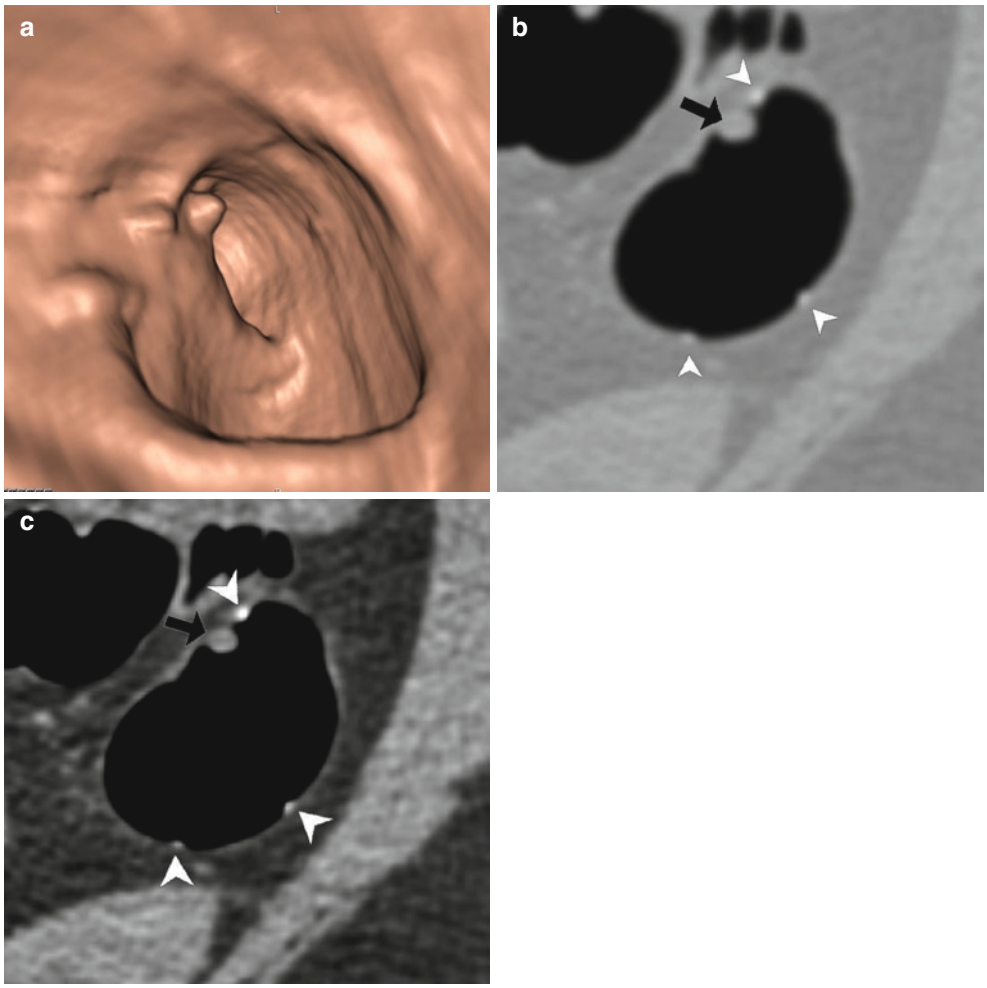


Fig. 20.16 **Distraction by tagged stool**. (**a**) The 3D endoluminal view shows several small polyp candidates in the descending colon. Fecal tagging was used. The supine axial images shown in (**b**) CTC window level setting and (**c**) a soft-tissue window level setting show a sessile polyp (*black arrow*) among several foci of tagged fecal residue (*white arrowheads*). It is important to use the abdominal windows to assess the tagged nature of the stool and not to be distracted by multiple foci, all except one being stool (Courtesy Philippe Lefere)

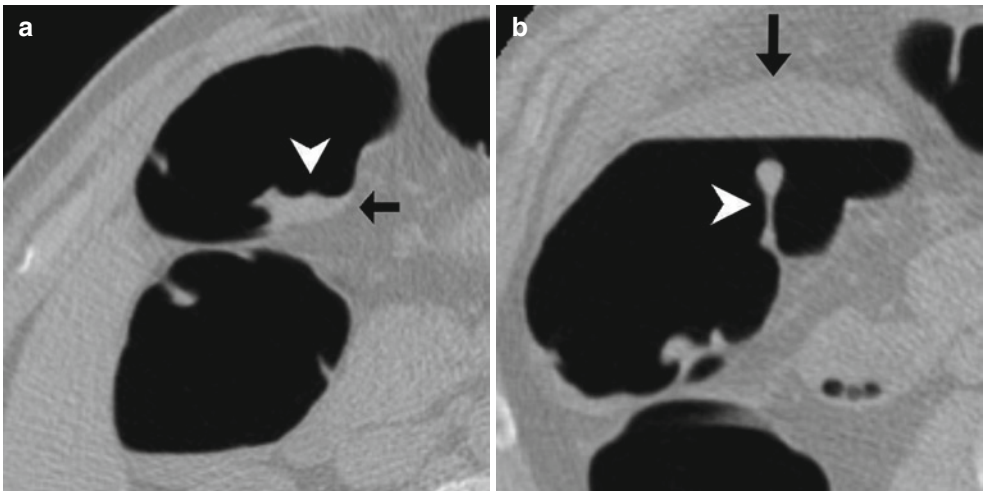


Fig. 20.17 **Untagged fluid hides a polyp**. (**a**) Supine and (**b**) prone axial images show residual untagged fluid (*black arrows*) on both views. The fluid moves and reveals a polyp on a fold in the prone view (**b**). Note that even on the supine view (**a**) a small "bump" is seen (*arrowhead*) on the fluid level indicating a possible polyp. The two key teaching points are that untagged fluid will hide polyps and that a fluid level must be perfectly straight. Any "bump" on the surface of a fluid level could be a fold, stool, or polyp, and it must be assumed to be a polyp unless other views prove that it moved (Courtesy Philippe Lefere)

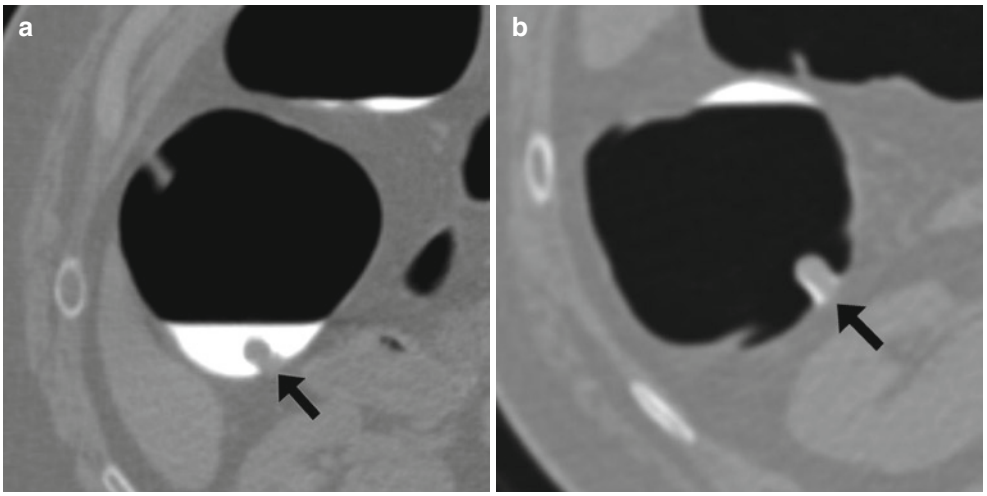


Fig. 20.18 **Polyp submerged in tagged fluid**. On the supine view (**a**) there is densely tagged residual fluid. Even on CTC window level settings, a soft-tissue filling defect consistent with a polyp is seen on the dependent surface. On (**b**) the prone view, the fluid moves to the dependent anterior wall, and some oral contrast agent remains on the surface of the polyp (*black arrow*). The surface tagging is an important clue to help find a polyp. Surface tagging is quite different from tagging inside the lesion, which would indicate stool. (However, partial volume effect can make surface tagging look slightly "internal" due to partial volume effect.) A polyp with a short pedicle was found on colonoscopy (Courtesy Philippe Lefere)

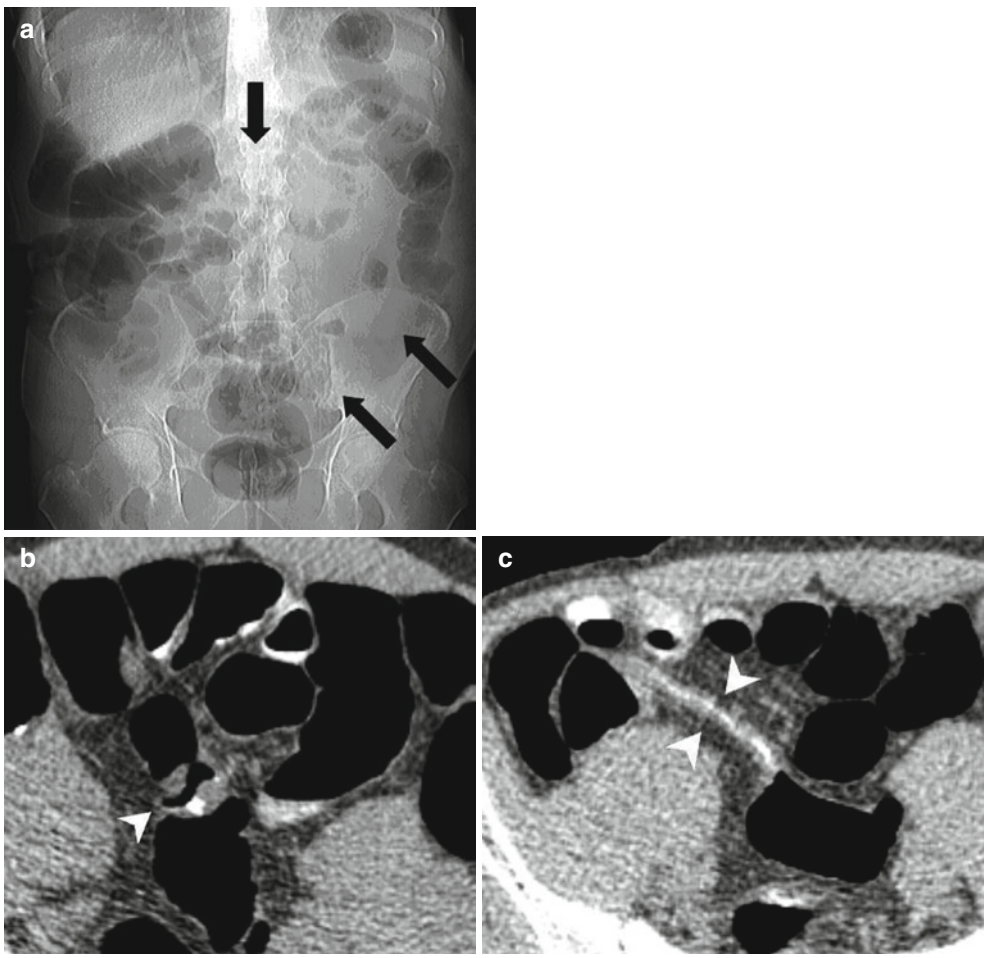


Fig. 20.19 **Inadequate colonic distension**. The scout view (**a**) is used by the technologist to initially assess colonic distension. Poor colonic distension is seen in the transverse and sigmoid colon (*arrows*). The supine axial images (**b**, **c**) of the redundant sigmoid show a focal distal short segment of collapse in (**b**) and a long segment of collapse in (**c**). It is impossible to reliably differentiate among spasm, stricture, and tumor. This emphasizes the importance of optical distension (see Chap. 7) (Courtesy Philippe Lefere)

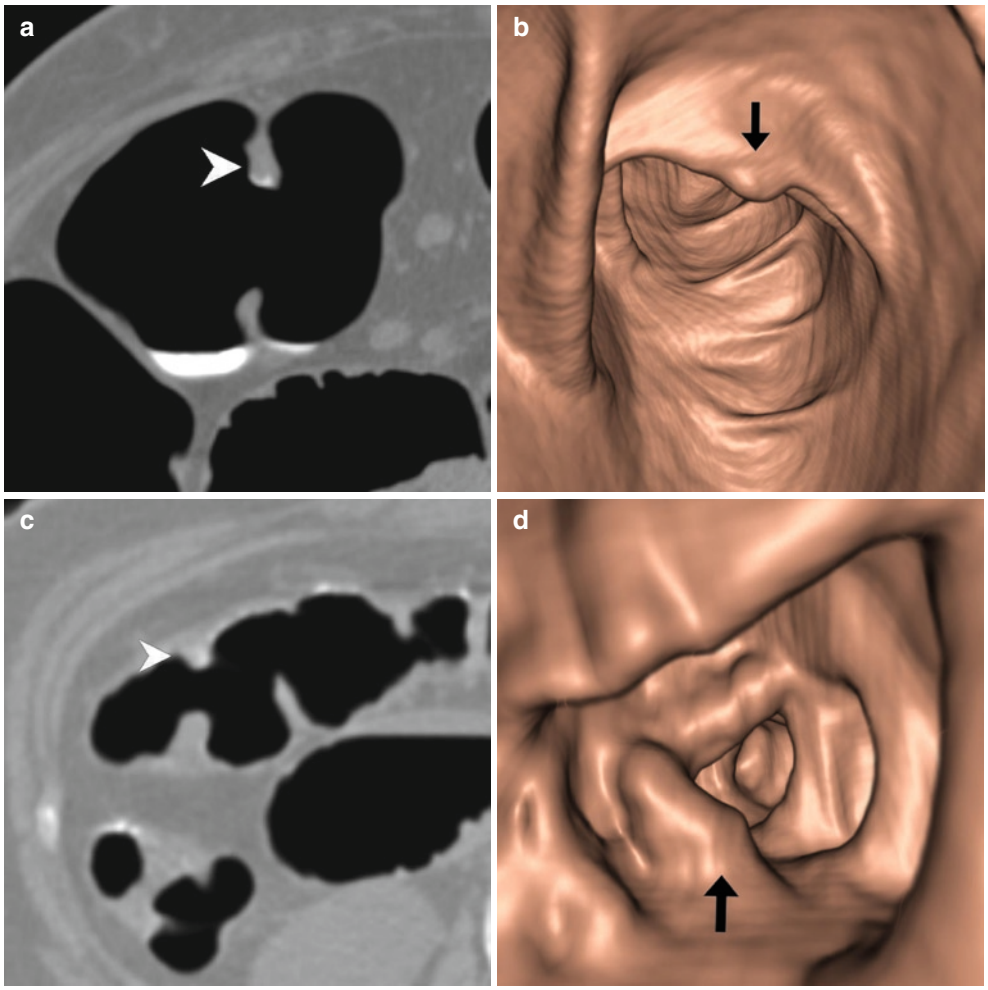


Fig. 20.20 Suboptimal distension limits "confidence of interpretation." Patient with an 8 mm sessile polyp in the transverse colon. The axial supine view (**a**) has good distension and shows a polyp with partial surface coating with oral contrast (*white arrowhead*). Although subtle, the polyp is thicker than the fold on the opposite wall – a clue to help find a polyp. The corresponding 3D view (**b**) clearly depicts the polyp on a fold (black arrow). Suboptimal distension in prone position (**c**, **d**) makes the polyp (*white arrowhead in* **c** *and black arrow in* **d**) almost impossible to reliably distinguish from a thick fold. Nevertheless, the logic of interpretation demands that this be considered a polyp (Courtesy Philippe Lefere)

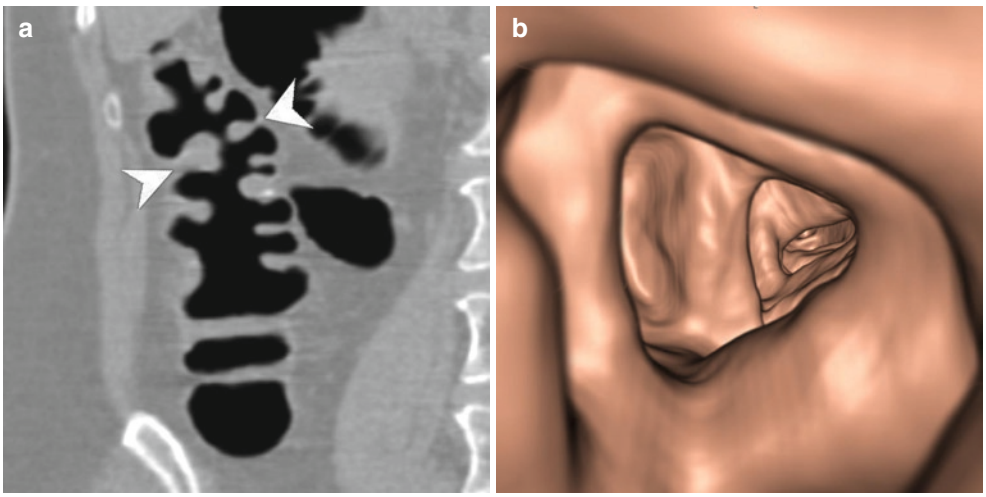


Fig. 20.21 Suboptimal distension hides a polyp. In the ascending colon, there is sufficient distension to prevent the walls of the colon from deforming, yet it results in "pseudo-thickening" of the haustral folds. On coronal image (**a**), where folds just barely touch, they are termed "kissing folds" (*level of the white arrowheads*). While such an exam is still considered diagnostic, it may limit the sensitivity of the exam for small polyps. (**b**) Endoluminal 3D view shows a triangular configuration to the colonic lumen and mild nodularity of the folds caused by the contraction of the tenia coli (Courtesy Philippe Lefere)

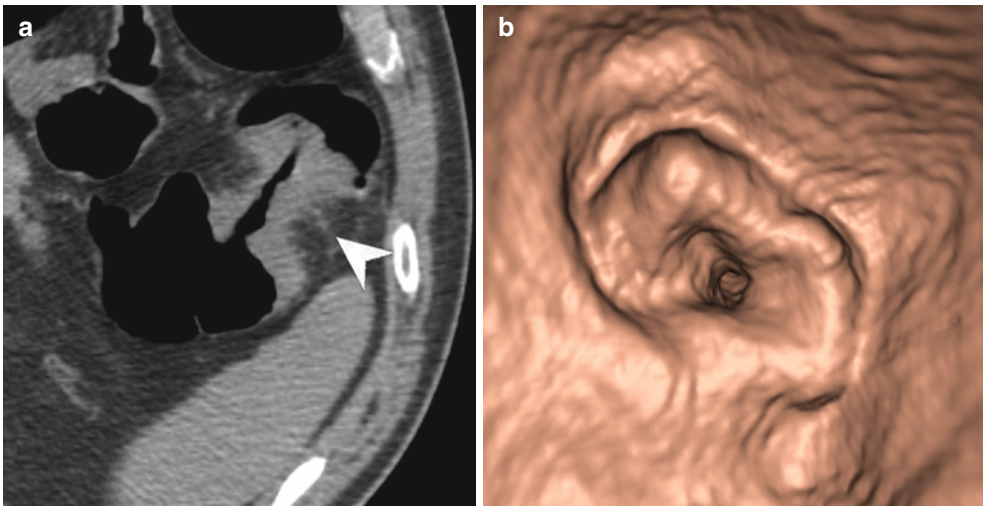


Fig. 20.22 Differentiating spasm from annular mass. The supine axial image (**a**) is shown in a soft-tissue window. The narrowing is not due to spasm but to large stenosing tumor (*white arrowhead*) with shouldering, overhanging edges and mild stranding of the pericolonic fat. (**b**) The corresponding 3D view shows luminal distortion with overhanging edges. Annular masses are easier to recognize on the 2D images. The 3D images cannot readily differentiate a benign stricture from an annular mass (see Chap. 19 for additional examples) (Courtesy Philippe Lefere)

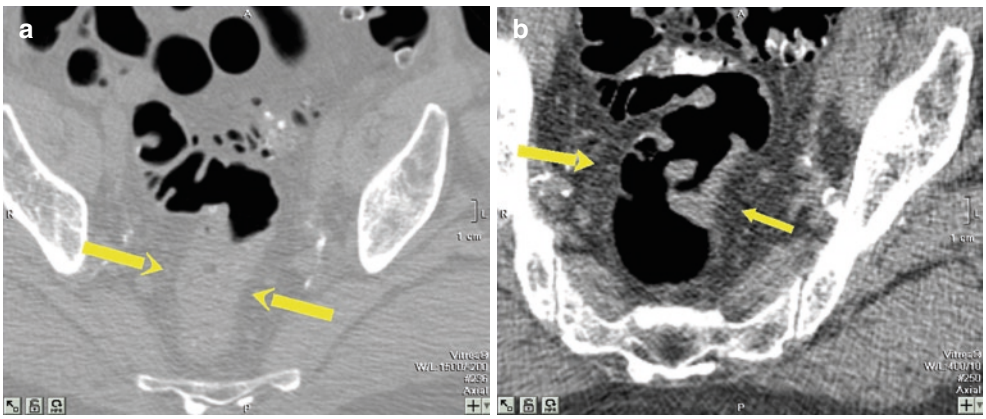


Fig. 20.23 Annular mass hidden by collapse. The supine view (**a**) shows complete collapse of the rectum and rectosigmoid junction obscuring a mass. Typically, distension of the rectum and rectosigmoid colon is better on the prone views. The prone view (**b**) shown in soft tissue window settings shows the slightly asymmetric semi-annular malignant mass (*arrows*) (Courtesy Philippe Lefere)

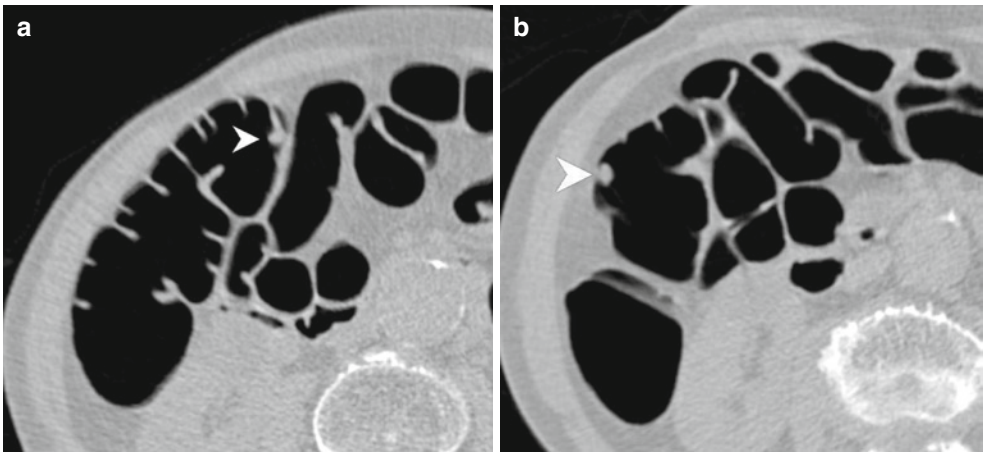


Fig. 20.24 **Colonic mobility causes a polyp to resemble mobile stool**. In the proximal transverse colon, the axial supine image (**a**) shows a 7 mm polyp in the transverse colon at the hepatic flexure (*white arrowhead*). The corresponding prone view (**b**) shows a distinct change in position of this polyp candidate (*white arrowhead*). This could lead the reader to assume that this is untagged mobile stool. It is important to look at the 3D overview and the sagittal and coronal images to notice whether the colon segment twisted and changed configuration with the change in patient position. After viewing the axial views, when the reader is prepared to dismiss a polyp candidate solely on the basis of mobility, this pitfall – colonic mobility – should be searched for (Courtesy Philippe Lefere)

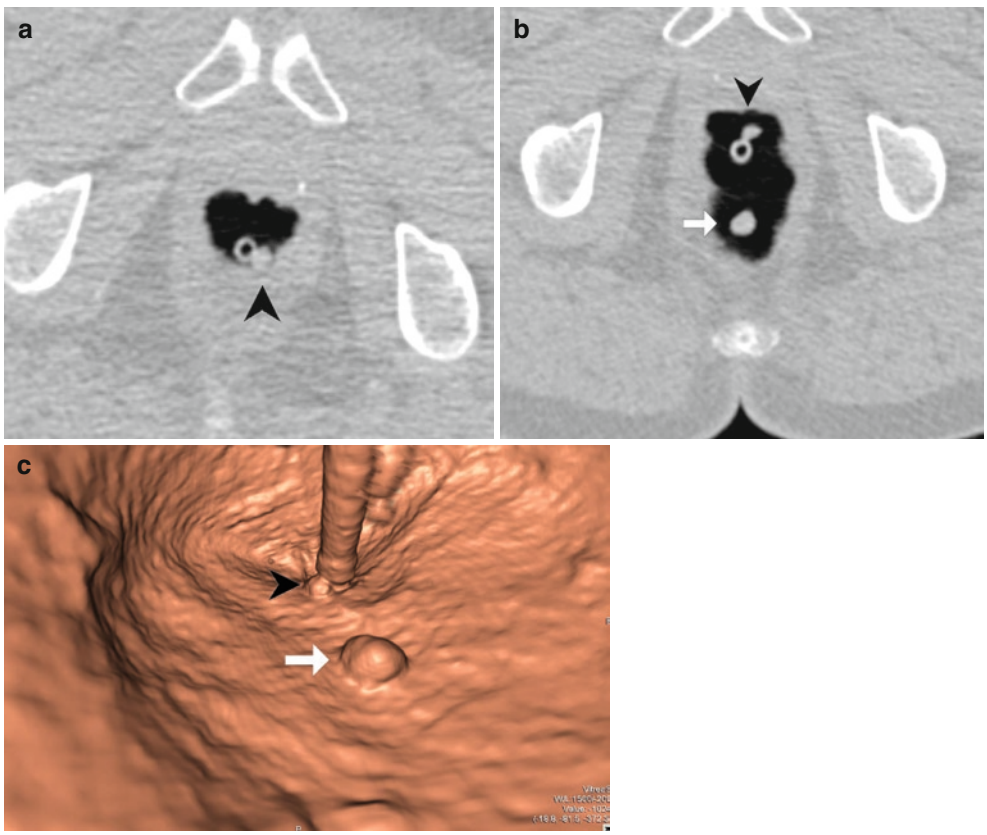


Fig. 20.25 **Polyps near the anal verge or rectal catheter**. (**a**) Supine view of the rectum showing polypoid defect (*black arrowhead*) abutting the rectal catheter. Corresponding prone view (**b**) shows two lesions (*black arrowhead and white arrow*), both confirmed on (**c**), the endoluminal 3D view (compare this with Fig. 20.1, hemorrhoids) (Courtesy Philippe Lefere)

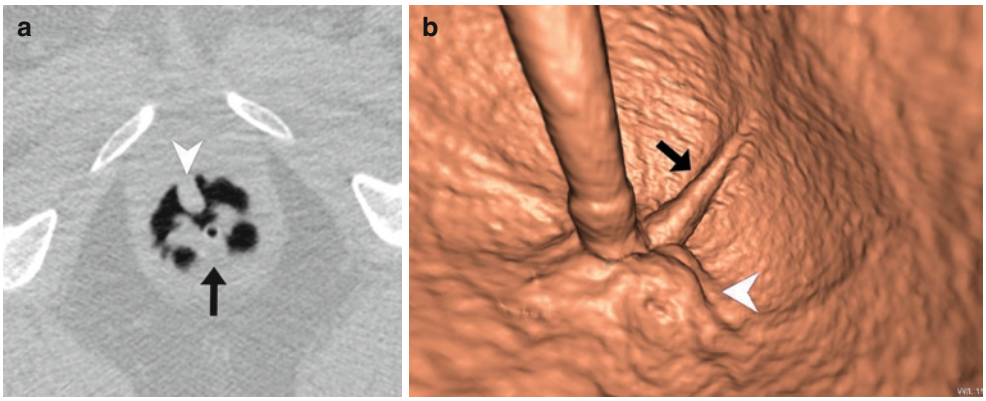


Fig. 20.26 **Internal hemorrhoids at the anal verge surrounding the rectal catheter. Rectal "bar."** (**a**) Several lobular, luminal defects around the rectal catheter are caused by internal hemorrhoids (*white arrowhead*) on supine axial view and on (**b**) corresponding 3D endoluminal view. A normal structure, a longitudinal fold or rectal bar (*black arrow*) is also seen (Courtesy Philippe Lefere)

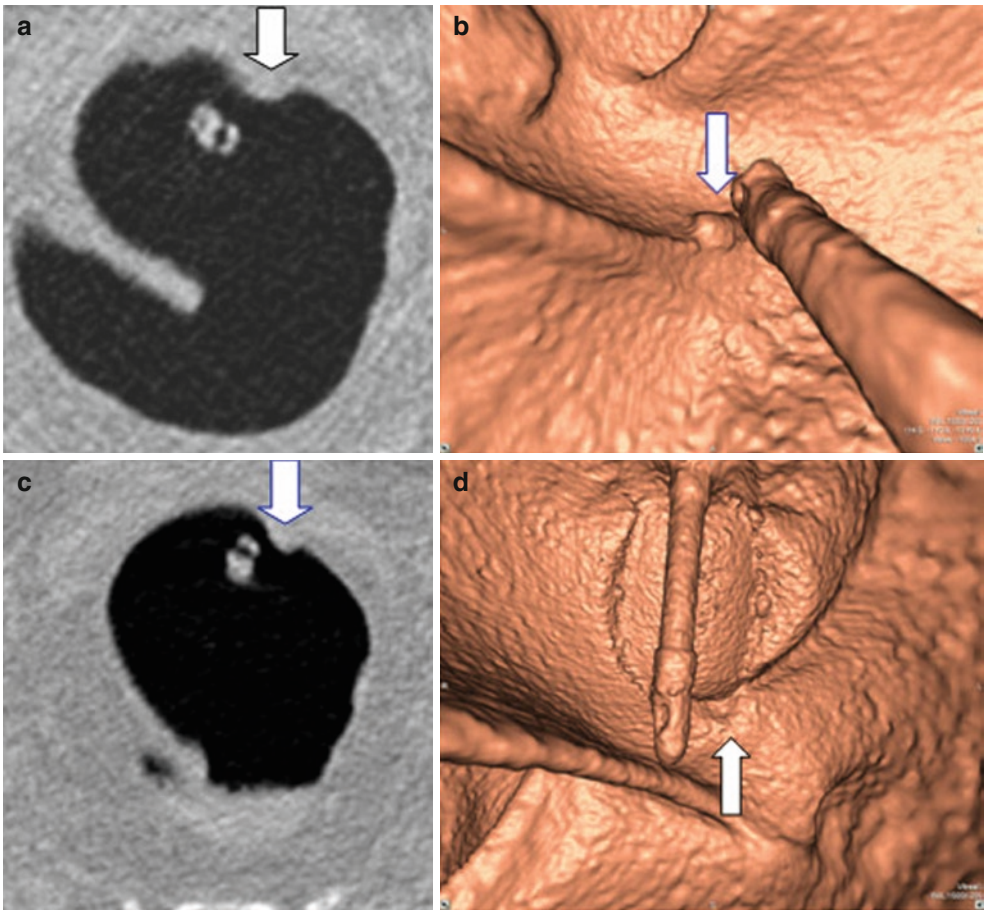


Fig. 20.27 **Inflated rectal balloon partially obscures a polyp**. An inflated rectal balloon has been implicated in obscuring low-lying polyps. Some experts recommend using a small balloon, inflating it only minimally, and even completely deflating the balloon for the prone view. In this patient, a small polyp is seen in (**a**) the axial supine view and is barely conspicuous on (**b**) the corresponding endoluminal 3D view. The polyp is better seen with the balloon deflated in the prone position, axial view (**c**) and endoluminal 3D view (**d**) (Courtesy Philippe Lefere)

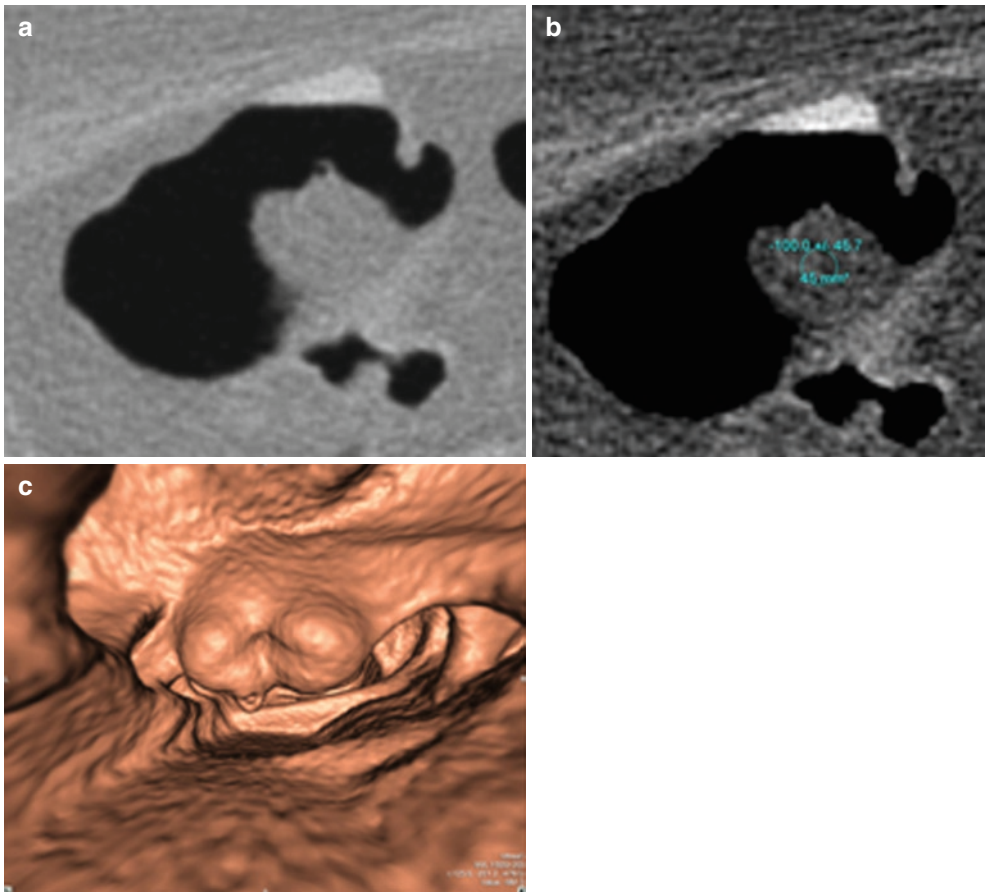


Fig. 20.28 **Lipomatous infiltration of the ileocecal valve**. Axial prone 2D views in (**a**) CTC and (**b**) soft-tissue window level settings show a prominent but fatty ileocecal valve. (**c**) Corresponding 3D endoluminal view shows a closed "doughnut"-shaped valve.The ileocecal valve should be inspected on every case, since it is covered with colonic mucosa, and polyps can occur on or near the valve (see Chap. 13 for additional view of the ileocecal valve) (Courtesy Philippe Lefere)

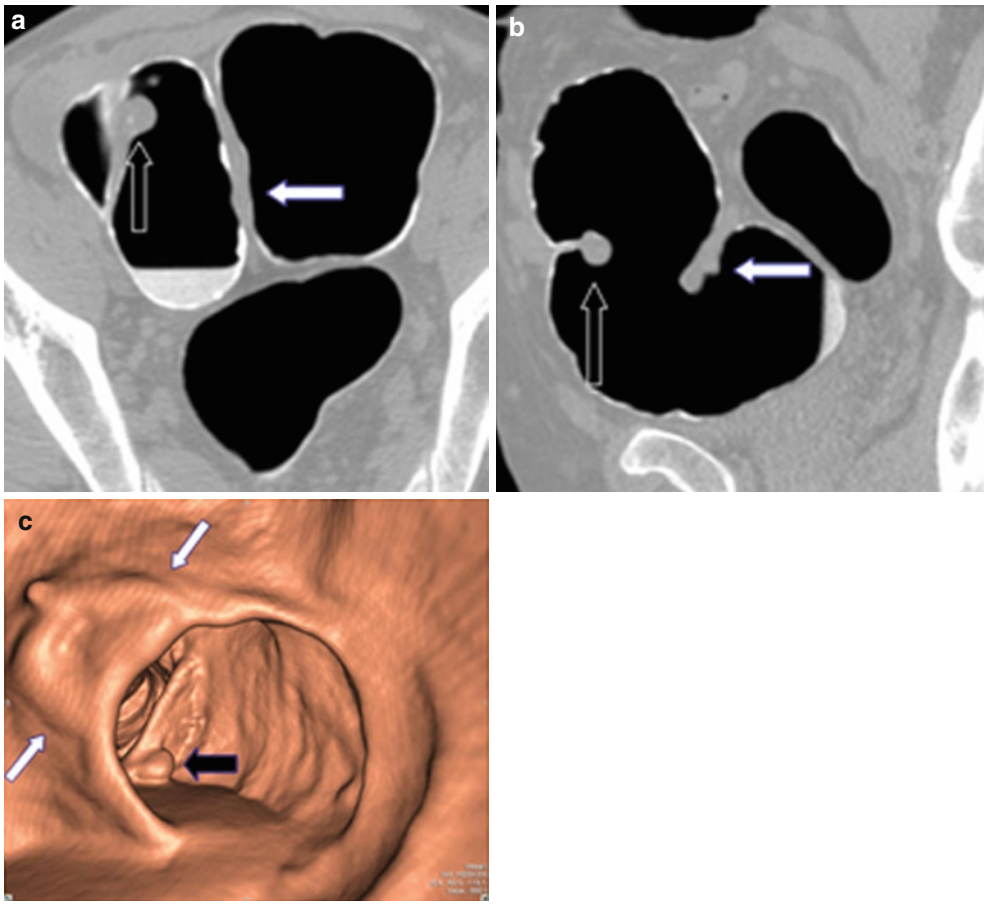


Fig. 20.29 **Ileocecal valve and adjacent polyp**. (**a**) Supine axial, (**b**) coronal, and (**c**) endoluminal 3D views show the ileocecal valve (*white arrows*) and on the opposite wall a polyp (*black arrow*) (a tiny focus of tagged stool is seen on the ileocecal valve) (Courtesy Philippe Lefere)

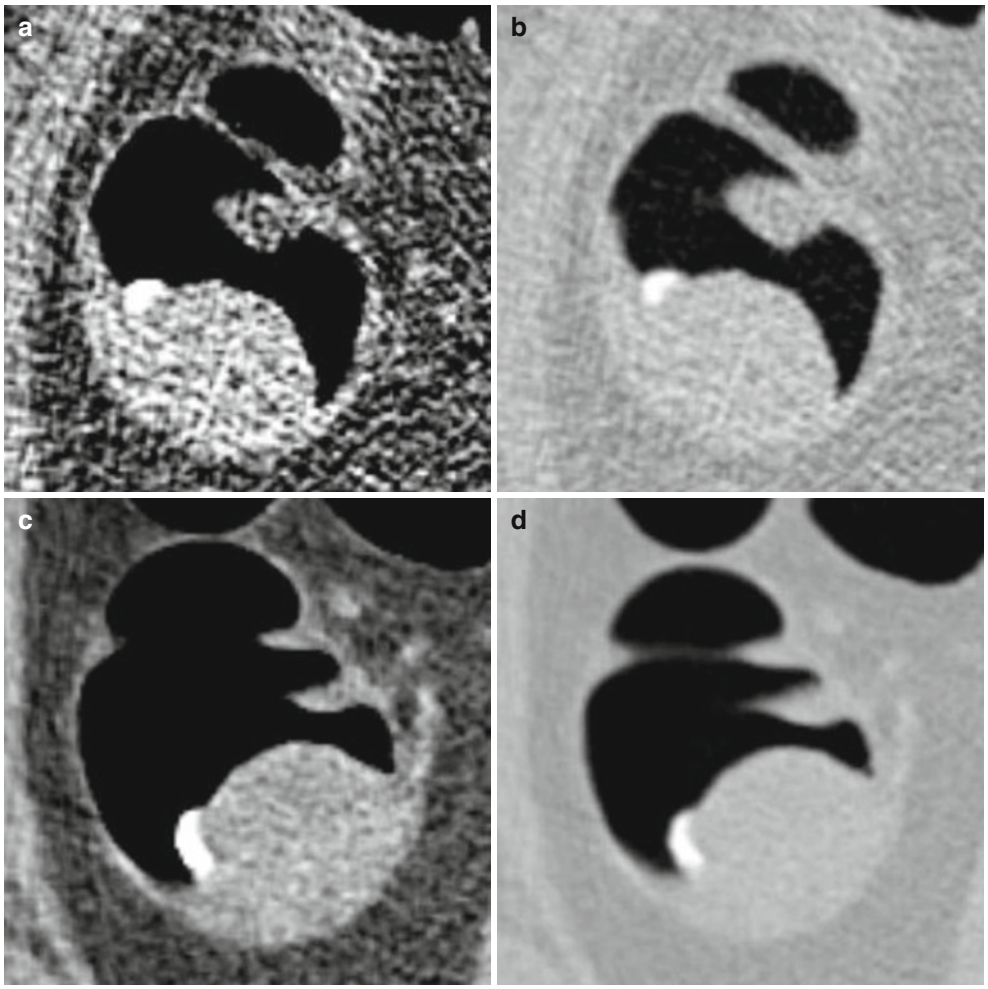


Fig. 20.30 Image noise due to low radiation dose CTC technique. Left images (**a, c**): ultra-low-dose 140 kV, 10 mAs shown in (**a**) soft tissue and (**c**) CTC window setting. Right images (**b, d**): 120 kV, 100 mAs, shown in same window setting. Note the increased noise on the ultra-low dose acquisition is seen mainly on the stoft tissue window setting ("pseudo-enhancement") (400/10). Depending on the vendor software, some 3D endoluminal views might have a very grainy appearance, with many "floaters" in the lumen. Some vendors' software will permit adjustment of the lower limit volume rendering threshold. Raising the threshold (e.g., from a default setting of –800 HU to and higher setting such as –600 HU) will help remove the floaters. However, such threshold adjustment may hide flat lesions (Courtesy Philippe Lefere)

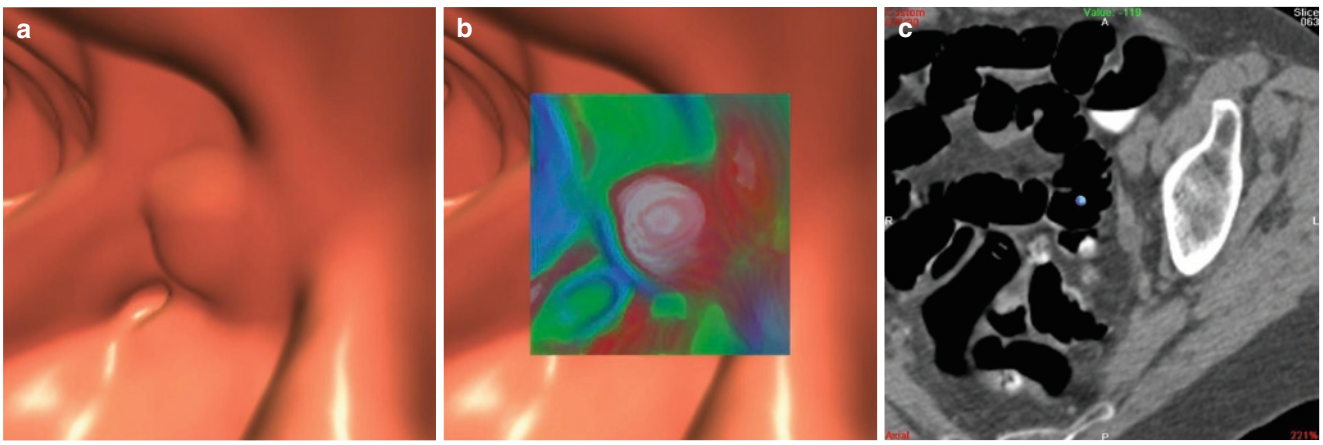


Fig. 20.31 Translucency Tool: An enhancing polyp simulates barium. Two different patients are shown here. In the first exam performed without intravenous (IV) contrast, the translucency tool shows tagged stool: (**a**) endoluminal view showing a polyp candidate, (**b**) translucency tool turned on showing the tagging agent as white, corresponding to the barium; (**c**) the axial 2D image (*6 o'clock position relative to the blue arrow*). In a different patient in whom a pedunculated polyp is seen, the pre-IV contrast CTC shows the endoluminal view (**d**) with the translucency tool colorizing the polyp as red, indicating soft tissue (consistent with a polyp). After IV contrast administration for the prone series, the endoluminal view with the translucency tool off is shown in (**e**). With the translucency tool on (**f**), the polyp head and stalk are white, thus simulating tagging agent (if the reader was unaware that IV contrast was given). The tool should not be used when IV contrast was given (Cases courtesy Amy Hara MD, Mayo Clinic Arizona). *Cases 20.32–20.38 are examples with the use of intravenous contrast CT in conjunction with CTC*

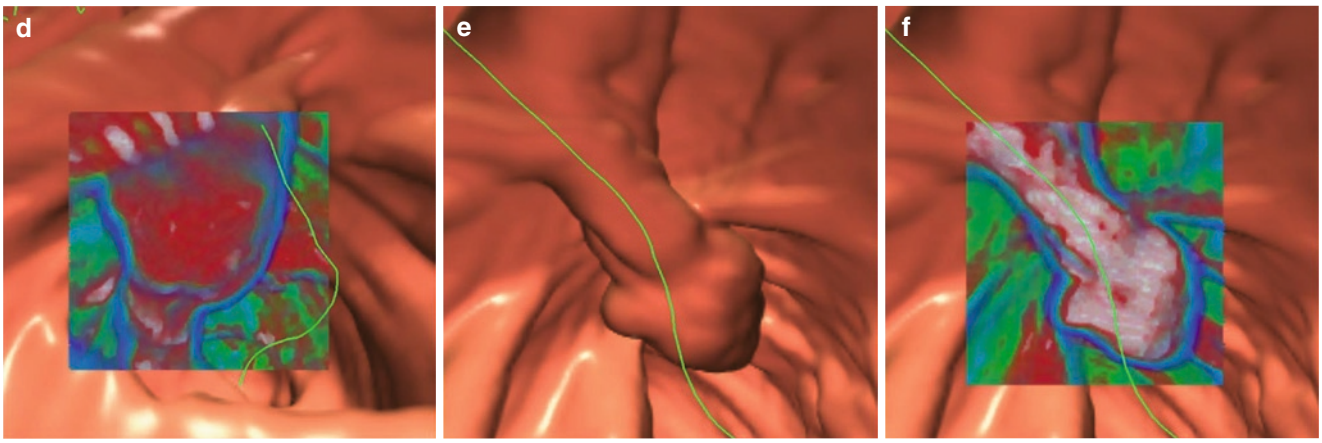


Fig. 20.31 (continued)

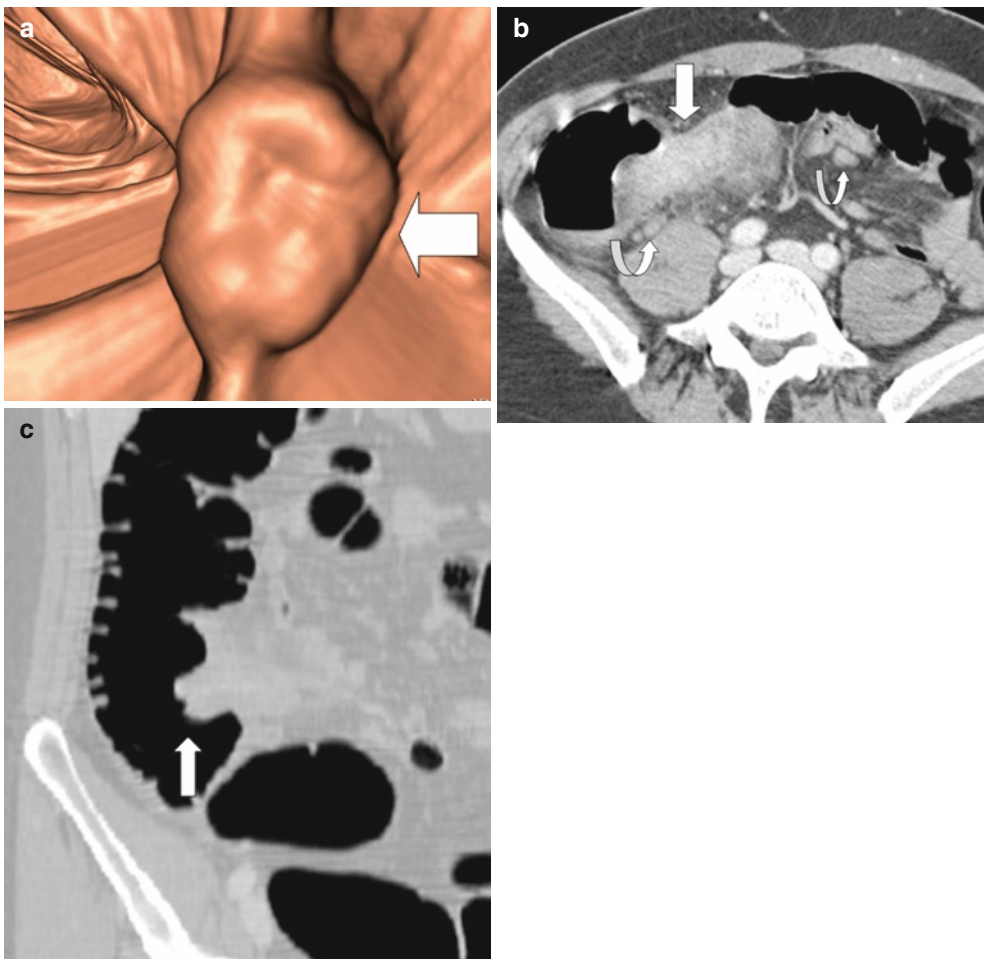


Fig. 20.32 **Distal ileitis from Shigella**. Three-dimensional threshold-rendered endoluminal CTC view (**a**) of the ascending colon shows an enlarged and bulbous iloececal valve (*arrow*). On axial (**b**) and coronal (**c**) CT image obtained after intravenous administration of contrast agent, a long thickening (*arrow*) of distal small bowel loop as well as lymphadenopathy (*curved arrows*) are evident, providing a diagnosis of ileitis

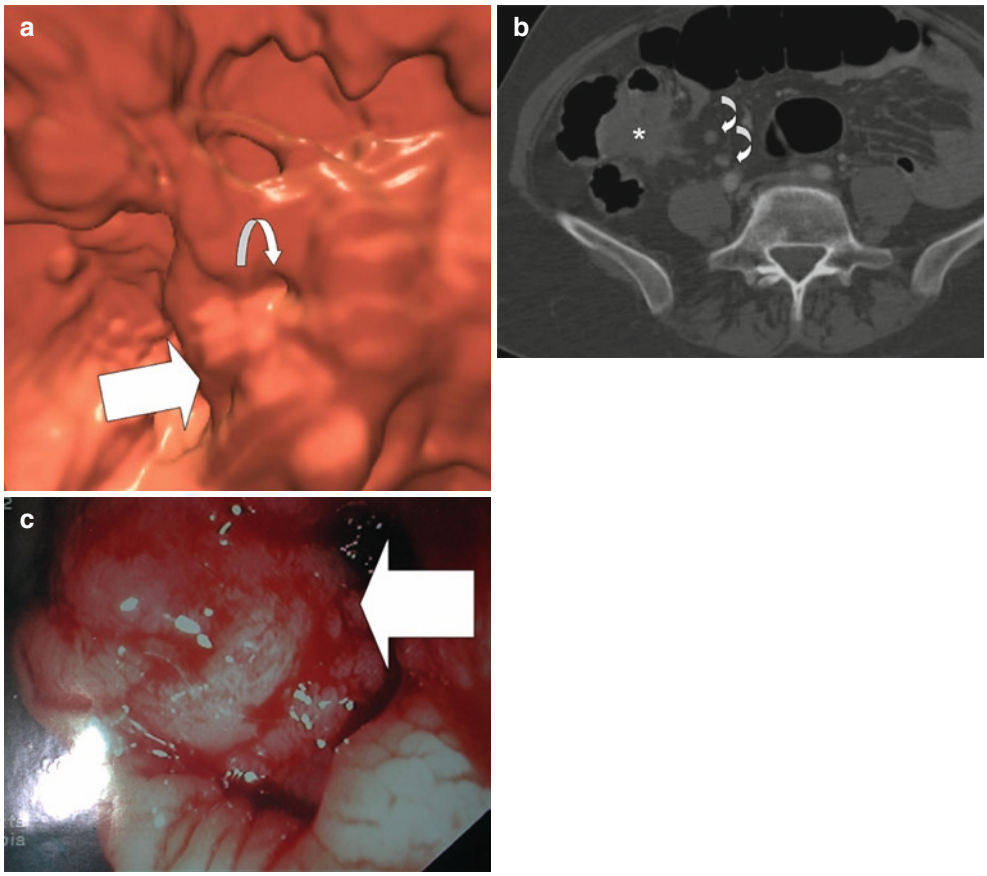


Fig. 20.33 **Lymphosarcoma of ileocecal valve**. Three-dimensional endoluminal view from CTC (**a**) of ascending colon shows an irregular and enlarged iloececal valve (*arrow*), whereas the orifice is clearly visible (*curved arrow*). Axial CT (**b**) scan shows a huge mass (*) involving either the ileocecal valve or the terminal ileum, representing a lymphosarcoma. Note lymphosarcoma arising from the valve usually involves terminal ileum, while adenocarcinoma is usually confined to the cecum. Multiple loco-regional lymphadenopathy is visible (*curved arrows*). Endoscopic (**c**) examination shows a huge mass (arrow) in the expected region of ileocecal valve, protruding into the lumen and narrowing it

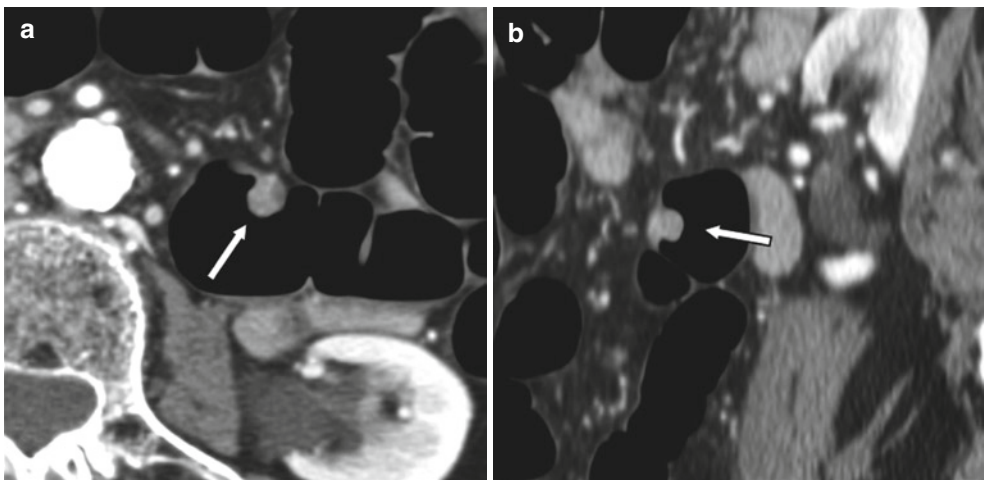
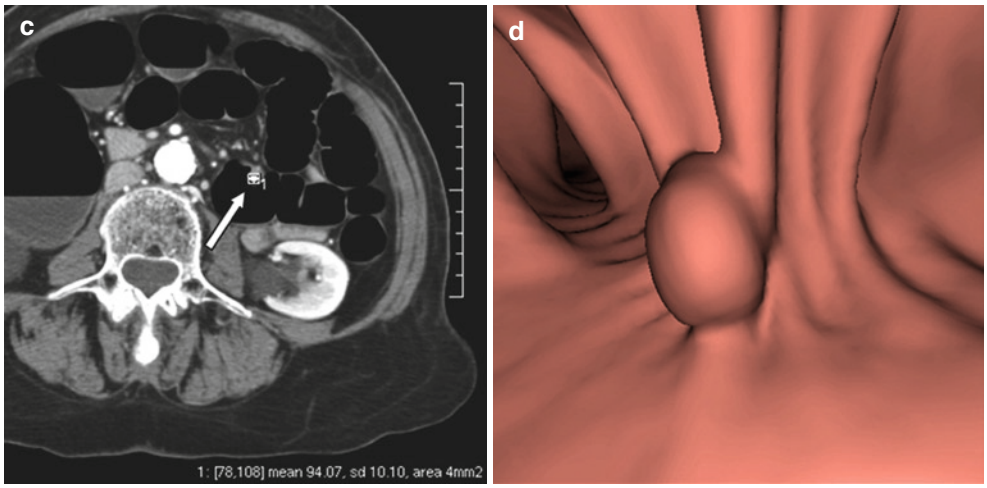


Fig. 20.34 Sessile polypoid lesion rising from a fold; (**a**) axial image showing (**b**) a significant contrast enhancement after the intravenous injection of contrast medium. (**c**) axial image with region of interest on the enhancing polyp showing a measurement of 78 HU. (**d**) endoluminal 3D image

Fig. 20.34 (continued)



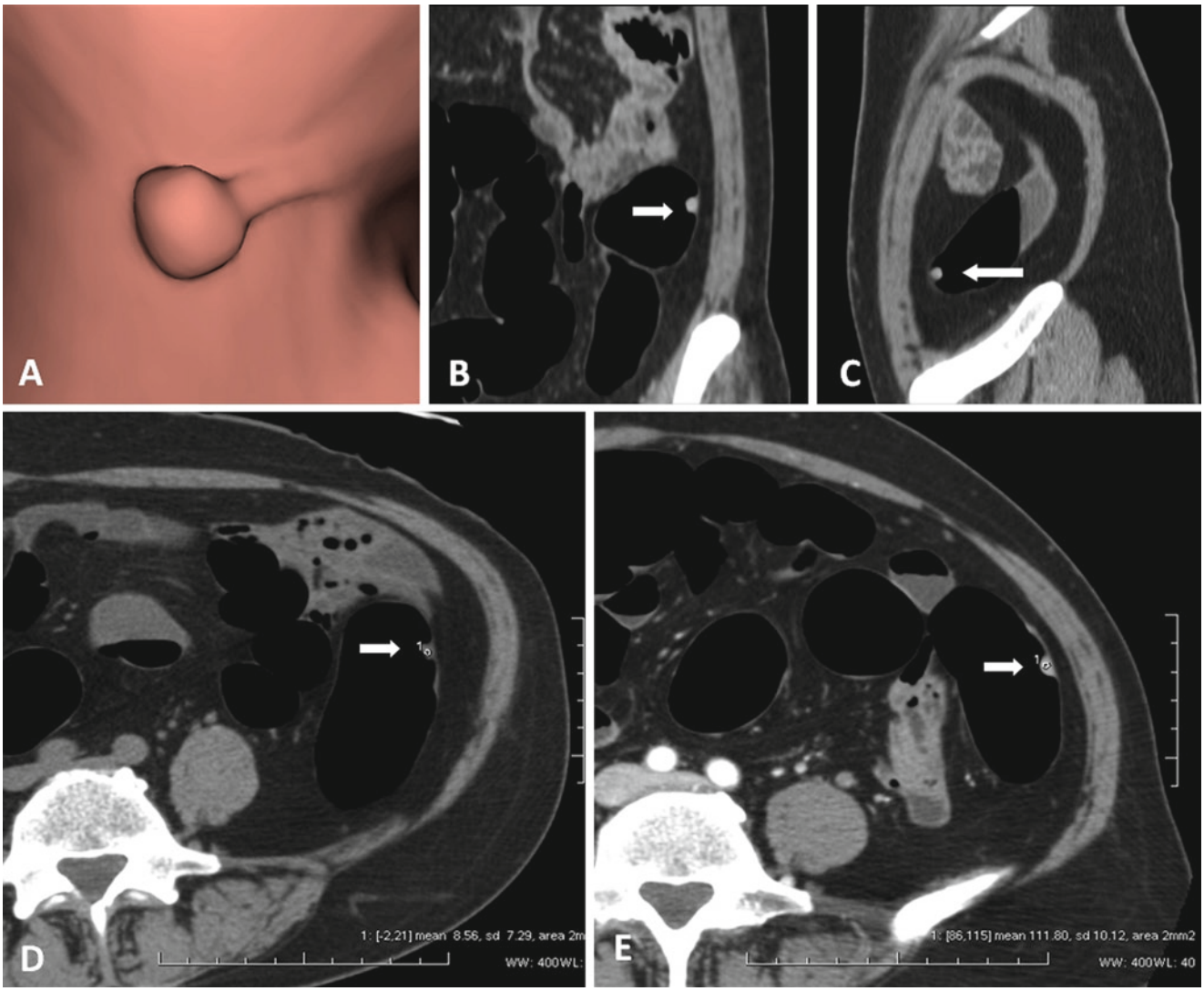


Fig. 20.35 Pedunculated polyp of the distal third of the descending colon: (**a**) "virtual endoscopy" image and (**b**) coronal and (**c**) sagittal reformations. (**d**) Axial unenhanced image with region of interest compared to (**e**) contrast enhanced image shows a significant contrast enhancement after the intravenous injection of contrast medium (changing from –2 to 86 HU)

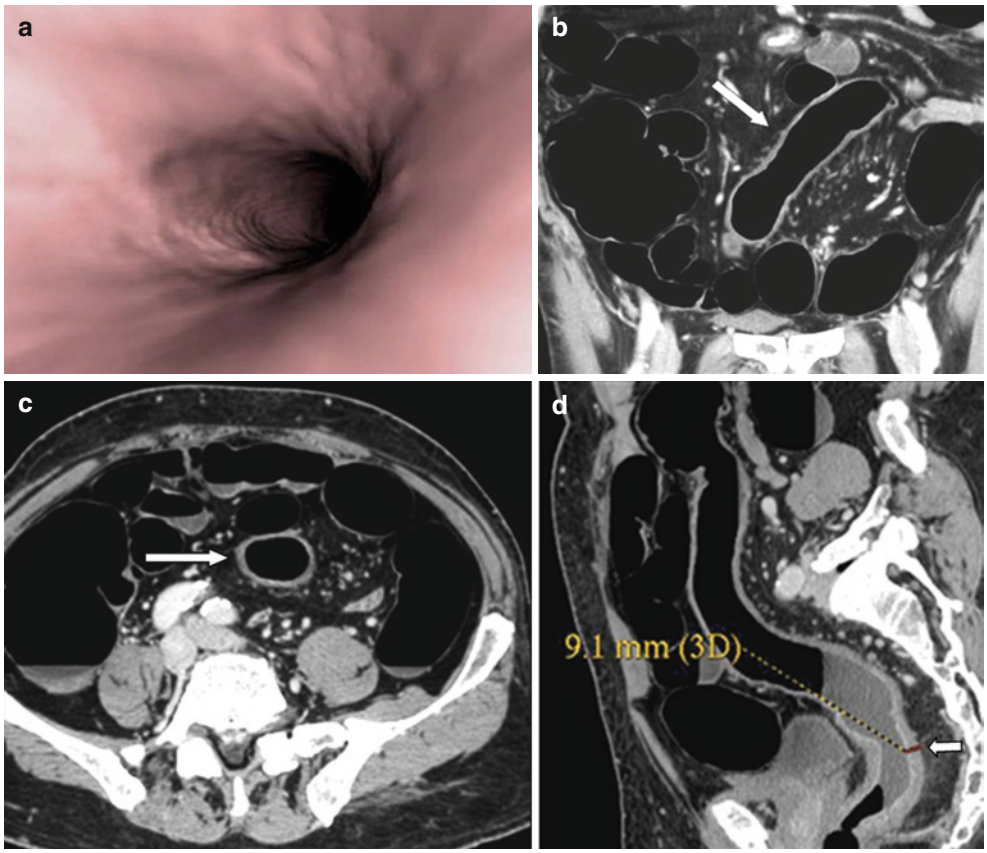


Fig. 20.36 (**a**) "Virtual endoscopy" navigation showing the loss of haustral coli: (**b**) coronal, (**c**) axial, and (**d**) sagittal reformations in which a concentric parietal thickening (*arrow*) and a inhomogeneity of the surrounding soft tissues may be observed in a patient affected by ulcerative colitis

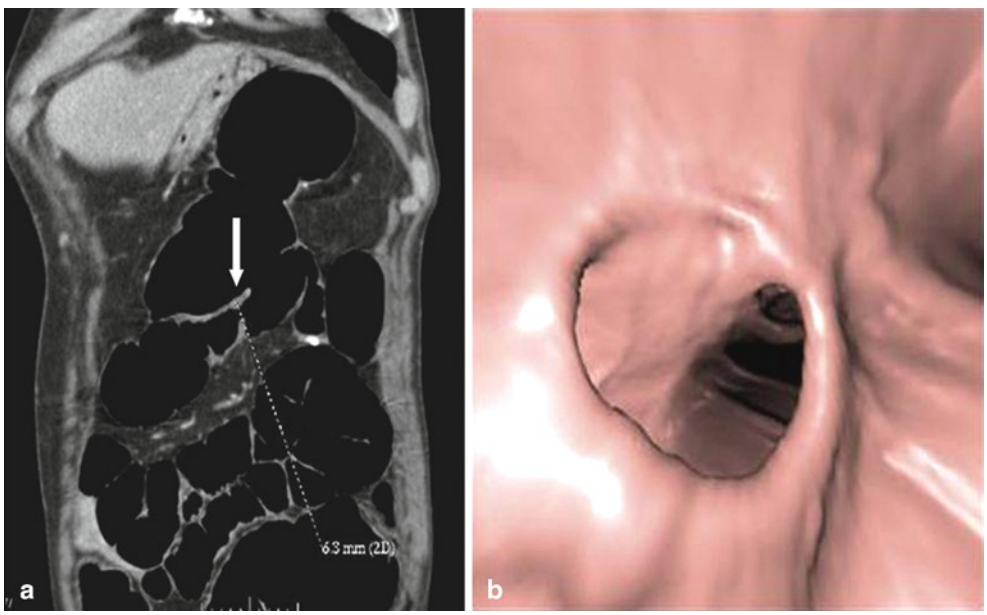


Fig. 20.37 (**a**) Coronal reformation and (**b**) "virtual endoscopy" navigation. Concentric parietal thickening of the pre-anastomotic ileal tract documenting a relapse in a patient affected by Crohn's disease

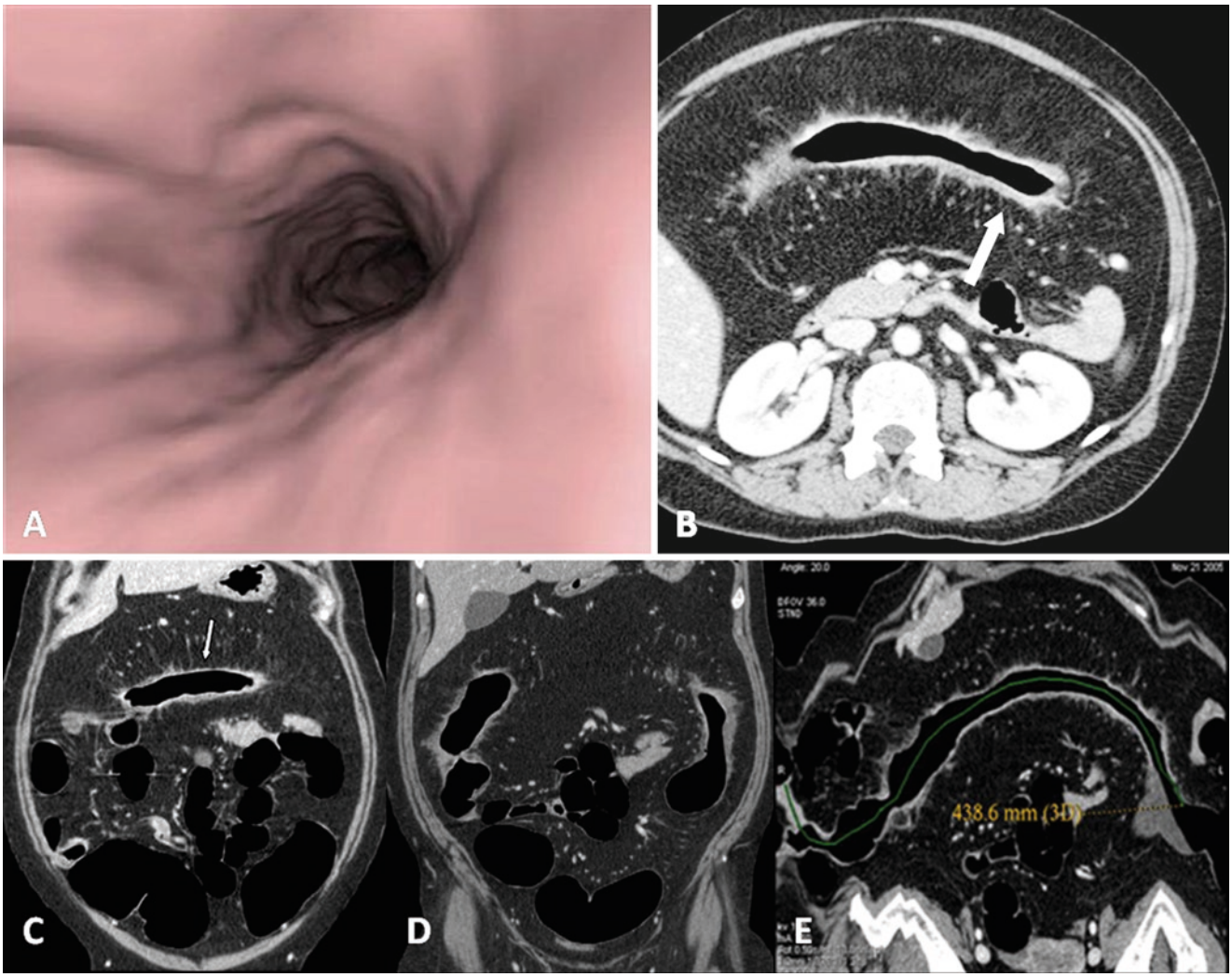


Fig. 20.38 "Virtual endoscopy" navigation showing the loss of haustral coli and a cobblestone appearance of the mucosa with (**a**) an associated irregular concentric wall thickening from the cecum to the distal third of the descending colon with (**b**–**d**) alterations in caliber and a dilatation of the preceding tract in a patient affected by Crohn's disease. (**e**) Curved reformations show the length of the interested tract

Appendix

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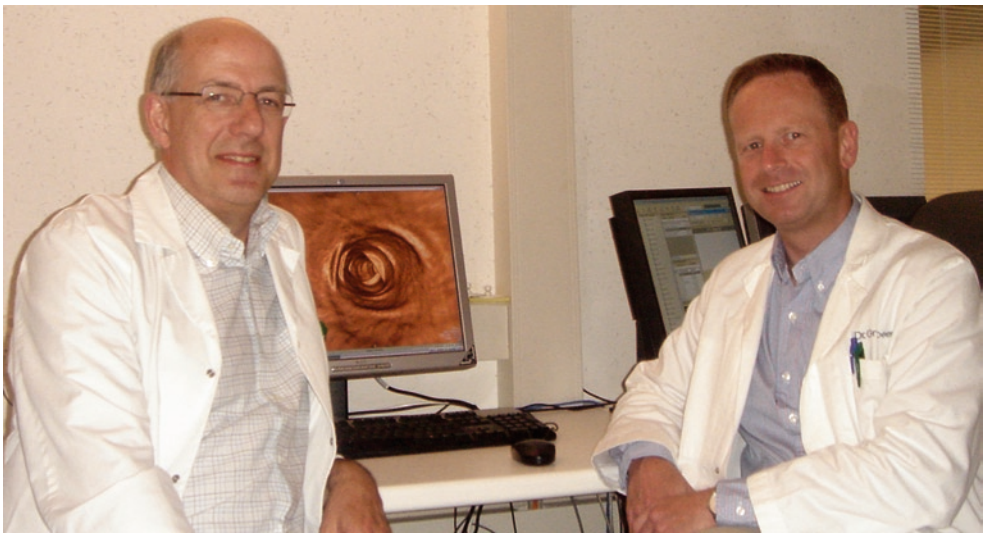


Belgium: From left to right: Philippe Lefere M.D., Stefaan Gryspeerdt M.D.

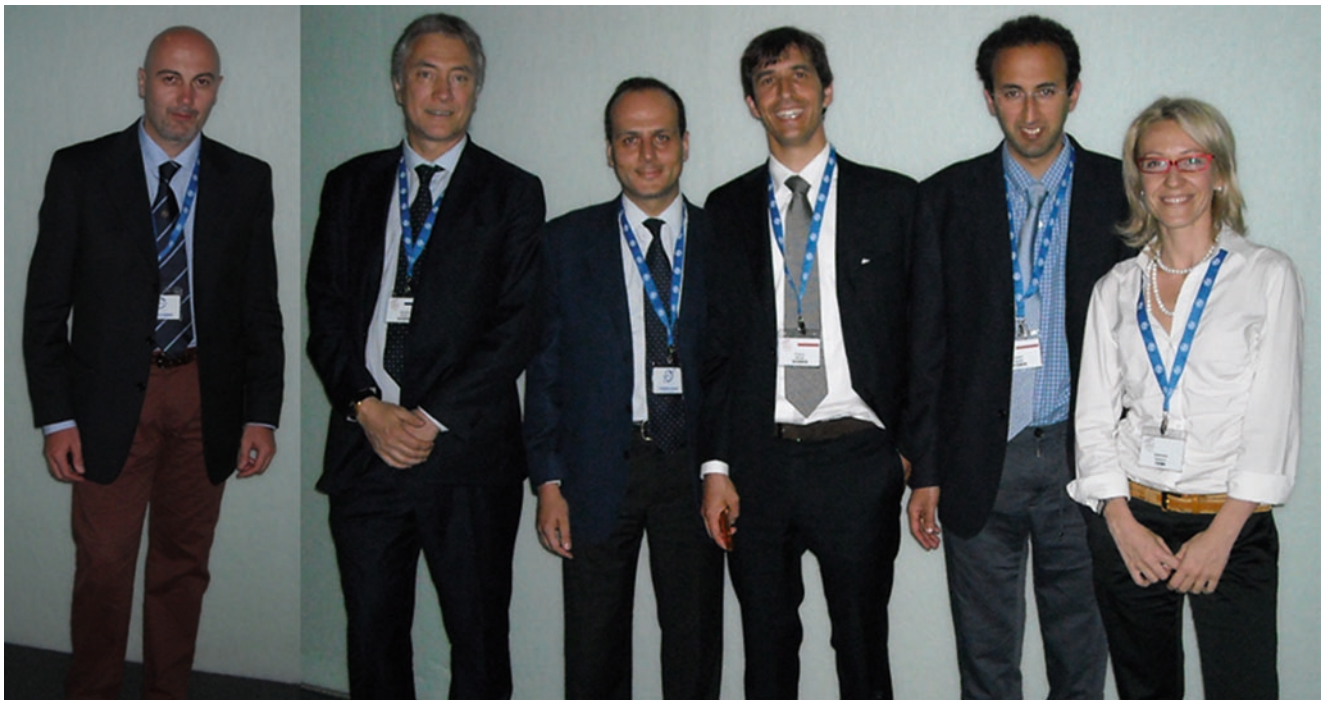
Canada: Tanya Chawla, MD

France: Mehdi Cadi, MD

Germany: Patrick Rogalla

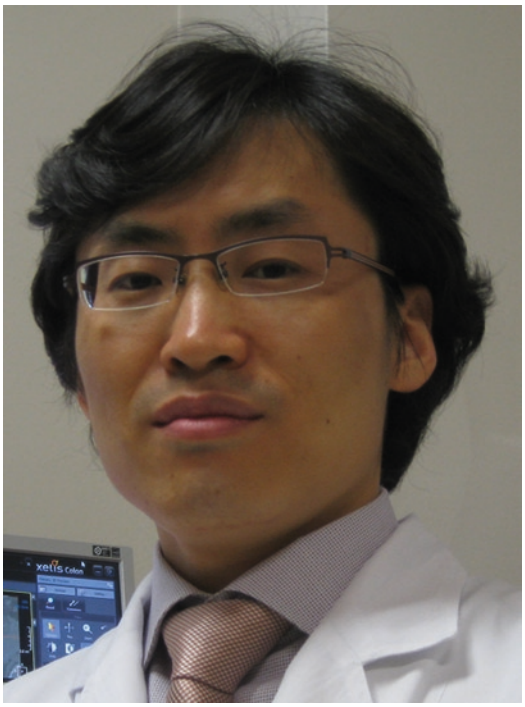
Israel: Jacob Sosna, MD

Ireland: Matina Morrin, MD



Italy: From left to right: Emanuele Neri (University of Pisa), Daniele Regge (Institute for cancer research and treatment, Candiolo), Andrea Laghi ("Sapienza" University of Rome), Franco Iafrate ("Sapienza" University of Rome), Cesare Hassan (Gastroenterology Unit, Nuovo Regina Margherita Hospital, Rome), Gabriella Iussich (Institute for cancer research and treatment, Candiolo).

Japan: Japanese CTC members of the CTC training course in JRC 2010, from right side: Technician Mr. Yushi Hirano, Dr. Hideto Tomimatsu, Prof. Yutaka Imai of Tokai University, Dr. Mototaka Miyake, Dr. Gen Iinuma, Dr. Satoshi Nozu, Dr. Kenichi Utano, Dr. Tamaki Ichikawa, Technician Mr. Michihiro Yamazaki, Technician Mr. Masahiro Suzuki, Dr. Tsuyoshi Morimoto.



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