C. Nimsky and R. Fahlbusch (eds.)

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Preface

This supplement of Acta Neurochirurgica contains the proceedings of the Joint Convention of the Academia Eurasiana Neurochirurgica (13th convention) and the German Academy of Neurosurgery (9th convention) held in Bamberg, Germany, September 1–3, 2005.

The major focus was "Medical Technologies for Neurosurgery". Internationally well-known experts discussed recent developments, among them aspects of imaging, image processing, robotics, workflow analysis, and ethics.

The tremendous, evolving progress in medical technologies of the recent years has increasingly influenced our daily neurosurgical practice. Ethical principles in the application of such technologies have become more and more important. As a consequence, the first four contributions focus on ethical aspects in the light of different religious viewpoints, just to name the contributions by J. Zycinski (the Roman Catholic viewpoint), Z. Rappaport (Jewish ethical perspectives), C. Özgen (the Islamic viewpoint), and T. Ohta (the Buddhist/Shintoist viewpoint).

Then F. Nüsslin provides an overview on the current status of medical technology, followed by an example of the increasingly important topic of image processing, focusing on aspects of uncertainty in diffusion tensor fibre tracking by H. Hahn *et al.*

The next section deals with the application of robotics, i.e. the use of mechatronic assistance systems in the neurosurgical operating rooms. A. Benabid defines the tools for neurosurgery, H. Wörn reviews the projects within the German Research Foundation Cluster SFB 414, and K. Hongo introduces telecontrolled micromanipulators for neurosurgery.

In the last section a comprehensive overview on the progress of intraoperative imaging with special respect to intraoperative magnetic resonance imaging is given. Four different setups with different magnet designs and magnetic field strengths are discussed. Y. Muragaki *et al.* report on their 0.3 T experience in regard to glioma resection, while S. Mittal and P. Black summarize the Boston experience with a 0.5 T system. This is followed by our own experience with intraoperative anatomical and functional imaging applying a 1.5 T scanner, while the report by N. Pamir gives an outlook on the application of ultra-high field strength imaging for intraoperative use utilizing a 3 T magnet.

We are convinced that progress in medical technology will result in an actual benefit for our patients, however, all neurosurgeons and cooperating partners in the neighbouring medical disciplines as well as engineers, computer scientists, physicists in the universities and the manufacturers of medical technology should well be aware of the different ethical implications connected with the growing applications of modern technology in medicine.

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Bioethics, technology and human dignity: the Roman Catholic viewpoint

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Summary

Many important questions dealing with human dignity in medical research are raised by new medical technologies. The paper presents the Roman Catholic approach to the use of new technologies, the research on human embryos, the ethical aspects of studies on human genome. The concept of "human ecology", as proposed by John Paul II, is to reconcile human dignity, the academic freedom of research, the sacredness of life understood as its quality so important for the cultural growth of *Homo sapiens*. To protect human ecology it is our moral duty to defend human dignity and to recognize the importance of those values that are fundamental in the process of development of human species.

Keywords: Anthropology; ANT-OAR; biotechnology; genethics; human dignity; human embryos; personalism.

Introduction

Contemporary scientific-cultural transformations bring important challenges, in which the very concept of humanism is called into question. On the one hand, Francis Fukuyama declares that the perspective of reproductive cloning and genetic engineering could result in a "posthuman society", if unrestricted biotechnological manipulations would introduce essential changes in human nature [10]. On the other hand, in post-modern nihilism one finds radical declarations of the death of God, the death of man, the end of history, and the total deconstruction of those values that constitute the domain called "human ecology" by John Paul II [15]. Between new scientific achievements and profound cultural transformations one has to define both the general anthropological perspective and fundamental ethical principles necessary to defend human dignity as a basic value in contemporary medical praxis.

The cosmic odyssey of the species *Homo sapiens*

The scientific discoveries of the 20th century radically changed our way of seeing the human place in space and time. In the middle of the 19th century, Charles Darwin's contemporaries were convinced that the universe was not more than six thousand years old. Darwin himself did not differentiate between the content of the Old Testament and the naïve calculations of the Anglican archbishop James Usher contained in "Annales Veteris et Novi Testamenti", according to which the cosmos was supposed to be created on 28 October 4004 BC at 9:00 AM. Today we realise that the universe in its present form is 13.7 billion years old. In the course of time since Darwin's death, it was necessary to multiply the age of the universe by a factor of 2.5 million. The palaeontologists who were contemporaries of Darwin realised that Usher's estimates were false; they believed that it was enough to multiply them by a factor of about a hundred. At that time, the discovery that cosmic evolution has been taking place for billions of years would have been unthinkable. Today an immense universe evolving for billions of years has been regarded as "our cosmic habitat" [22]. It brings important philosophical and moral issues which should be discussed in the context of new scientific discoveries concerning the biological evolution of the human species.

Africa is the continental homeland of our species. About seven million years ago our humanlike ancestors accepted a bipedal style of walking, which gave them the opportunity to use their upper limbs to manipulate tools. As a result of the biological process called "adaptive radiation", groups of hominids called *Australopithecus africanus* and *Australopithecus* *robustus* emerged. A little bit more than two million years ago, the increase in their brain size brought the first representative of the genus *Homo*, classified as *Homo habilis*. Whereas representatives of the species *Australopithecine* died out a million years ago, the representatives of the species *Homo* survived. Over a million years ago in what is now Kenya, there emerged *Homo erectus* – the first hominid who used fire, practiced systematic hunting and made stone tools. His descendants later reached Java, Europe and the area of present-day Beijing. It is significant that no genetic traces of the descendants of this first *Homo erectus* have so far been found. Some authors suggest that a primeval holocaust took place, described in a dramatic way in the biblical account of the death of Cain.

A number of studies in the field of the genetics of mitochondrial DNA have allowed us to state that the human species emerged in Africa some 200,000 years ago. These genetic estimates have not yet been backed up by the necessary evidence from archaeological digs. Archaeological discoveries so far provide us with evidence of considerably later stages of the development of our species. The scientific research confirms the hypothesis of the second human exodus out of Africa. A second wave of migration out of Africa took place about 100,000 years later. After moving to Asia our ancestors spread eastward, reaching New Guinea and Australia about 50,000 years ago. Thus, in our biological lineage we all come from Africa, even though from the cultural point of view we find more interesting elements of our heritage in ancient Greece.

What is amazing is this radical disproportion between billions of years of cosmic evolution and thousands of years of human existence. It means that there was no human observer when the universe evolved from the initial singularity to the mitochondrial Eve. Some sceptics argue that our present situation is untypical since the universe that began its evolution without human observers will quickly enter into a post-human era to continue its physical development again without the observing presence of the representatives of *Homo sapiens*. This form of sceptical futurology cannot be rationally justified.

It is interesting that in the cultural evolution of our species many phenomena emerged that cannot be submitted to the biological principle of the struggle for survival. In our intellectual development there are many elements which are not in any way related to the attainment of a biological advantage. Among these elements one could mention ethics, mathematics, metaphysics, religion, and aesthetics. In their intellectual concerns, our ancestors moved far from the question of pragmatic interests. They stressed the role of spiritual self-awareness inspired by the principle of *gnothi seauthon*. They developed the role of the Socratic ethical evaluations so important in moral dilemmas. Only man, endowed by God with the breath of immortality, has created contemporary science and has stressed the role of altruism in our culture. While remaining an element of the evolving nature and remaining subject to the laws of biology and physics, man has been able to create a rich world of spiritual values, art, poetry and beauty.

At the same time, however, human beings have been able to create concentration camps, threaten people with the charge of being an enemy of the working class, and to seek the final solution of the Jewish problem by extermination. The process of evolution continues. In our time, evolution is happening to a large extent on the level of the human psyche, spirituality and values which make up our natural environment. It will depend on us whether the search for success and pleasure will dominate our world or whether respect for human dignity, sympathy and solidarity with other people will become our principal values. When discovering this reality, the human person was oriented towards a transcendent world which does not bring any immediate tangible gains, but which constitutes the very core of the being that we call *animal rationale* or *homo meditans*. I am grateful that we continue this tradition by undertaking bioethical issues at this meeting of the Academia Eurasiana Neurochirurgica.

Human ecology and the medical hierarchy of values

The awareness of the role of the human person as seen in the framework of cosmic evolution helps us to look with a certain distance at the new biotechnological challenges. Genetic technology, as any scientific discipline, can be used to reduce human suffering and thereby protect human dignity. It can also use a human person instrumentally. Both in Jewish and Christian theology, humankind has been understood as a special creation of God, made in His image and likeness (*Gn 1:26ff*). Created in God's image we should appreciate reason and scientific research to express our cooperation with God who made us. Specifically in the domain of molecular biology one has to remember that the pioneer of genetics, Gregory Mendel, was a Christian monk. Ethically responsible use of genetics implies, however, that we use the power of better understanding of the human genome in a way that protects us and our neighbors from being harmed or manipulated for the sake of risky visions of a posthuman future. Consequently, human dignity must be recognized as a basic value in biomedical research.

This positive vision of scientific progress was expressed by John Paul II when he said in his address to the Pontifical Academy of Life: "I therefore hope that the conquest of this new continent of knowledge, the human genome, will mean the discovery of new possibilities for victory over disease and will never encourage a selective attitude towards human beings", [14, p9]. The same positive and optimistic accents dominate in motu proprio *Vitae mysterium* in which in 1994 the Pontifical Academy of Life was founded. John Paul II wrote then: "this new situation opens up fascinating horizons for interventions at the sources of life itself, it also gives rise to a variety of new moral questions that man cannot ignore without the risk of taking steps that could prove irreversible".

In the Catholic concept of human dignity three basic factors are recognised:

1. respect for life,
2. the integral union of bodily and spiritual element in human person,
3. human liberty.

Respect for life is expressed in excluding most research on human embryos and zygotes. It also excludes manipulations tending to create groups of different people and/or provoking new marginalisations in society. Finally it rules out any intervention that reduces life to an object, and forgets that it has to do with a human subject, capable of intelligence and liberty.

In this personalistic perspective, John Paul II declared to the participants of the fourth assembly of the Pontifical Academy for Life on February 23, 1998: "it is unlawful to carry out any intervention on the human genome unless it is aimed at the good of the person, understood as a unity of body and spirit; nor is it lawful to discriminate between human subjects on the basis of possible genetic defects". "It is necessary to denounce the rise and spread of new selective eugenics which leads to the suppression of embryos and fetuses suffering from any disease", [14, p8f].

In 1987, during his visit to the Catholic University of Lublin, John Paul II emphasised that very often in research practice the human person is treated as an object, as an experimental animal, to which everything can be done and which can be subjected to all kinds of exploratory manipulations. To defend human values in contemporary civilization, it is our duty to divert this world trend. The creation of a new responsibility for the future of our species has become a major task which unites both scientists and theologians. We must not lose that set of values which include truth and freedom, altruism and dedication, solidarity, friendship and compassion, all of which constitute the axiological homeland of our species. These values constitute the domain which John Paul II calls "human ecology" [15, no 39]. Taking into consideration the exceptional place of *Homo sapiens* in our cosmic homeland, we must undertake new challenges concerning our intellectual responsibility for human dignity.

In medical praxis the recognition of human dignity should be reconciled with a hierarchy of values in which scientific success and social needs play the basic role. An important axiological proposal is provided in the Convention on Human Rights and Biomedicine, (Oviedo, April 4, 1997). Its article 2 declares: "The interests and welfare of the human being shall prevail over the sole interests of society and science". This article, entitled as "Primacy of the Human Being", is expressed usually in the words: Human dignity and human life are more important than any advance in science, medicine including, or any financial achievements [3, p7]. On January 1998, the European Parliament confirmed the Convention, invited to its ratification and prohibited human cloning. Two years later this prohibition was extended in a resolution of the European Parliament. It declares that "'therapeutic cloning', which involves the creation of human embryos solely for research purposes, poses a profound ethical dilemma". Consequently, the European Parliament calls on the United Kingdom government to review its position on human embryo cloning and postulates a United Nations ban on the cloning of human beings at all stages of development [8].

In the same spirit the World Medical Association's Declaration of Helsinki (October 2000) affirms that "in medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society" (principle 5). Principle 10 of the Declaration recognizes "the duty of the physician in medical research to protect the life, health, privacy and dignity of the human subject". In the adopted hierarchy of values, the medical care of human health still remains an expression of this basic openness to human dignity which cannot be replaced by financial profits or exploratory success.

How could one extrapolate these principles of philosophy of personalism on the domain of embryo research? In 2002 a committee of the American National Academy of Sciences acknowledged that from the moment of fertilization human embryo should be regarded as "a developing human" (18, pE-5). This terminology had semantic equivalents in many scientific publications of that period. Also in 2002 we find in *Nature* a strong statement: "developmental biologists will no longer dismiss early mammalian embryos as a featureless bundle of cells" [19]. Does it imply that human embryos should be regarded as a human person in the framework of Christian anthropology?

First of all, let us refer not to Christian principles but to the common human experience shared by all of us. Each one of us was once an embryo in the same way as any of us was once a newborn, though we do not have any recollection of specifically human experiences of that stage of life. This does not imply necessarily that the embryo has the moral status of a person. One must not, however, make claims about personhood in order to understand a moral obligation to respect and protect human life. In this anthropological framework, the instruction *Donum vitae* issued by the Congregation for the Doctrine of the Faith emphasises that in medical research human embryos should be respected "as a human person"; such research would be ethically unacceptable it they threaten either life or the integral growth of the human embryo [7].

When defending the humanity of an embryo many Christian authors argue that intentional destruction of the embryo cannot be reconciled with the well-known facts of human embryology and developmental biology. One's identity as a human being does not vary with or depend upon one's age, size, stage of development, environment, or condition of dependency. Human dignity cannot be subordinate to utilitarian principles specifically when one tries to justify wrongdoing for the "greater good".

According to Christian ethics, we are called upon to treat each and every living member of the human species, including the embryo, as a human person with fundamental rights, the first of which is the right to life. This approach is sometimes assessed as naive. In social practice its humanistic dimension was already confirmed by the so-called adoption of the embryos in the USA. The adoption was originated by "Pro Life" groups that decided to create natural biological conditions for the development of embryos that were frozen as byproducts of earlier IVF procedures. Children that were born as a result of this action confirm the common conviction that the difference between the embryo and the adult human person is nothing but the question of the degree of development of the developing human.

In this context one can consistently refer to the classical principle: The end does not justify the means. Human persons can be never treated instrumentally as a means to research success or financial profits. In recognition of similar principles, an important role is played by historical factors and cultural milieu. Gerald P. McKenny [17, p288] and Kurt Bayertz [1, pp167–180] indicate that in contemporary discussions on eugenics there are many German participants who reject arguments accepted by their Anglo-Saxon colleagues. McKenny claims that this specific sensitivity found at this time in Germany depends on both the dramatic Nazi abuses in eugenics and the illusions of human development underlying Friedrich Nietzsche's conception of *Übermensch*.

Leaving aside the intellectual heritage of Friedrich Nietzsche and of Josef Mengele, one has to notice that many participants in contemporary discussions on new biotechnologies positively refer to the tradition of Nazi eugenics. In particular Peter Singer's concept of the quality of life is comparable to the Nazi classification of the worth of life according to which the mentally handicapped were classified as unworthy of life. In this context it is our intellectual and moral duty to protect human dignity and to recognize the importance of those values that were and are fundamental in the process of development of human species.

Stem cells and the ANT-OAR project

To obtain embryonic stem cells without destroying living human embryos, Dr. William Hurlbut, biochemist of Stanford University, developed a procedure called Altered Nuclear Transfer-Oocyte Assisted Reprogramming (ANT-OAR), in which an adult nucleus is reprogrammed to a pluripotent stem cell. The cells produced in the ANT-OAR procedure never demonstrate any property characteristic of a totipotent single-cell embryo. They have all positive properties of a pluripotent stem cell. Consequently, generating the pluripotent human stem cells via ANT-OAR creates a chance of avoiding the moral dilemmas born by earlier research practice where killing the human embryos was involved.

The essence of the ANT alteration of the human genome is expressed in removing one of the 30,000 genome in the donor's cell genome. The removal of the gene CDX2 necessary for the development of the trophoblasts yields the situation in which the human zygote cannot develop past the blastocyst. This new possibility interested especially those scientists who consistently assert that no scientific progress could justify the intentional creation and destruction of human embryos. The critics of the ANT alteration argue, however, that the procedure proposed "should be considered ethically wrong" because even the mere possibility of the involvement of human embryo in this procedure would suffice to reject it [4].

The basic philosophical issue involved in this project deals with the question whether the result of genetic reprogramming should be regarded rather as a disabled embryo in which turning off a gene seems insufficient to render the entity non-human or rather as an artificial teratoma to which no human categories should be applied. Hurlbut himself is a strong pro-life advocate who consistently claims that life begins at conception; he developed thus the analogy with teratoma. His critics argue that the result of ANT is a human organism with full human genome in which some genes are silenced [13]. They define human organism in categories of its morpho-functional unity (*indivisum in se*), not by its ability to reach a more advanced stage of development. In this perspective, early cleaving embryos are living organisms that grow in accordance with an exact plan of development.

The defenders of Hurlbut's approach argue that an ANT produced entity is a sub-organism, even when it is still at a stage of organization, because the lack of the ability to maintain that organization is present. In their arguments, the deficiency of the needed genetic structure to maintain that organization, seems the basic factor. This discussion implies basic philosophical presuppositions in which the concepts of human being, sub-organism, and crippled embryo play the basic role.

The objections faced by defenders of the ANT procedures are avoided by supporters of the OAR technique who proposed OAR as an ethically acceptable extension of ANT. They argue that the OAR technique is morally acceptable because in it all cells of the human body contain the entire genetic code for a human being. The supporters of this procedure refer to protein transcription factors (TRF) which are absent in the zygote but present in the morula and in the inner cell mass of the blastocyst. In this approach, one can distinguish the human organism, i.e. the totipotent single cell zygote, from the inner cell mass by reference to an epigenetic factor, a protein called "nanog" [11]. So far nanog is found in pluripotent cells and not in the totipotent zygote. Accordingly in the ANT-OAR procedure the gene producing nanog is activated before its transfer into the enucleated oocyte. It seems justified to argue that a totipotent zygote is never present when using this technique; consequently certain moral issues basic to ANT are avoided in ANT-OAR. The suggestions that "crippled embryos" are produced by ANT-OAR are criticised as "both misleading and scientifically unsupported" [6, p8].

Some radical critics of moral aspects of ANT-OAR emphasise that biological research dealing with the detection of nanog cannot go beyond methodological limits characteristic of natural sciences where one can reach only statistical certainty, not the moral certainty basic to the discussed bioethical issues. Similar objections could have been formulated, nonetheless, against many medical procedures in the entire field of biomedical techniques. It would be grotesque to call in question the techniques used in modern medicine because a risk is involved in using them and most of them imply only the statistical certainty. In medical practice, very often "statistical" means also "moral" certainty. In their initial stage many medical means seem risky and controversial at least for psychological reasons till the moment when they become popular and are commonly accepted without moral objections.

The present embryo controversies indicate how important a role has been played in biotechnology not only by moral issues but also by anthropological concepts. To avoid purely pragmatic approaches in which human dignity is denied we need a clear anthropological vision where the concept of the human person plays the decisive role. In his defence of such basic concepts as "human", "personal", "subject" Card. Josef Ratzinger wrote in 1998 when he referred to the dignity of human embryo: "personality can also remain hidden as in the human embryo, but it is given from the very beginning and has its rights. It is this personality which gives men their dignity. It distinguishes them from *things* and makes them subjects". The distinction between the object and the subject is important also when we try to define the human dignity of ourselves. Thus Card. Ratzinger continues: "it is also clear that the looking by which I freely accept to turn toward the other determines my own dignity. When I am able to reduce the other to a 'thing' to be used and destroyed, I must also accept the consequences of this manner of looking, consequences which will affect me" [21, p20].

The critics of the ANT-OAR project also disapprove of this project for instrumental treatment of human values. They emphasise that to modify genetic programme by RNA interference in laboratory praxis many human embryos must be destroyed which brings well-known moral problems. The supporters of ANT-OAR reply that hitherto all their research has been done on mice, thus human embryos are not treated instrumentally. The same reply is given to the authors who suggest instrumental treatment of women and their eggs in the OAR procedure. This objection is groundless because the programme could be developed with immature eggs left over from IVF procedures as well as obtained from laboratory stimulation of ovarian tissues obtained during surgical removal of the ovaries for therapeutic reasons. For moral reasons Dr. Hurlbut rejects the idea of intentional superovulation to obtain eggs for experiments. A recognition of moral aspects of his project was expressed by a group of respected "pro life" scholars who published a Joint Statement to endorse Hurlbut's respect for humanistic values [16]. Adrian J. Walker, who personally rejects the ANT-OAR procedure, acknowledges their care for human dignity when he writes: "many, if not most, of the scholars who have endorsed the Joint Statement proposing OAR are publicly identified with the Catholic Church's magisterium on the whole range of contemporary issues affecting marriage, sex, and procreation. I have nothing but praise for the work that they have hitherto done in these areas." [25].

Dignity *versus* quality of life

The anthropological standpoint which stresses the special dignity of the human person is contemporarily called into question in many currents where pragmatic and utilitarian factors are respected while the quality of life is much more appreciated than human dignity. The classical form of such an approach is proposed by Peter Singer, a Princeton professor in bioethics, who argues that infanticide is permissible within a person's first two years of life [24, p182]. In his utilitarian approach Singer tries to justify the decision of killing a newly born baby if the infant suffers from Down's syndrome, autism or slight perturbations in regular development. In his pragmatic arguments the author of *Practical Ethics* concludes that there is no point in keeping disabled old people alive when the elderly are no longer productive or useful for the society.

Singer's radical proposal illustrates that we cannot defend human dignity when we refer merely to pragmatic-utilitarian factors. One cannot convincingly argue that there is an unsurmountable abyss between man and the lower animals when one merely takes into consideration the behavioural and empirical elements of human existence. Such a difference can be acknowledged only when we refer either to the theological aspects of our existence or to the philosophical principles of (Christian) personalism. In the utilitarian framework adopted by Peter Singer, all actions approved by the majority of society can be ethically justified. In this approach, the statistical concept of social acceptance replaces the classical understanding of human dignity. In the framework of Christian anthropology, the quality of life cannot be appreciated more than the life of a human person. The so-called quality of life cannot be reduced to the comfort of life because the sacredness of the existence of those who are handicapped and ill has also been an important quality of human life.

Peter Singer is not isolated in the utalitarian denying of human dignity. The same attitude is represented by Gregory E. Pence, professor of bioethics at the University of Alabama. He claims that there is "a continuum from the primates to man. In some ultimate sense, humans are both nothing more than, and just as wonderful as compassionate monkeys. We know that baboons, gorillas, and dolphins possess the ability to communicate through signs and other sounds.... Making genetic transfers of human genes to such mammals ... might also improve such mammals to the point where they could communicate better and tell us whether they were thinking" [20, p170]. Consequently, the author postulates "the weakening of the ethical boundary between non-human and human animals ... so as to allow doing to humans some of the things we think quite normal to do to animals."

Thomas H. Regan, professor of ethics at the University of North Carolina, tries to justify a similar proposal by ascribing a fundamental role to the concept of subject. He argues that all mammals over a year of age are subjects but children below that age are not. In his anthropology, to be a subject it is necessary to be capable of such mental activities as memory, anticipation of the future, intentional actions in the pursuit of conscious goals [23, p243]. Regan admits that some other animals, not necessarily mammals, may also be subjects. Consequently, killing chimpanzees can be as immoral as killing children but one cannot regard as human subjects newborn infants, people with Alzheimer's or people diagnosed to be in a permanent coma; consequently one could ethically justify killing them. This form of moral permissiveness is called "high-tech cannibalism" [5, p16] by those authors who defend the unique place of the human person in nature. At the same time it illustrates that we should not expect unanimous decisions concerning the question of moral principles in research on human embryos when some authors regard killing infants as an acceptable human action. Similar radical proposals are very often presented as products of a new ethic for medicine and society free of Western prejudices. It is important to notice that they are not completely new because one could find them in various versions of eugenics.

It was André Glucksman, who as a basic rule of postmodern society, proposed the principle: "Nothing inhuman is alien to me". In a society which accepts similar commandments, the traditional model of humanism would be easily called in question. As an alternative to this attitude novel intellectual patterns of the so called genethics [2, 12] are developed in which both genetic and ethical issues are discussed. In this time of profound cultural transformations it is our intellectual duty to follow the classical principle: "Nothing human is alien to me" to defend human dignity and to reject the immature version of "anything goes" anthropology.

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Robotics and artificial intelligence: Jewish ethical perspectives

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Summary

In 16th Century Prague, Rabbi Loew created a Golem, a humanoid made of clay, to protect his community. When the Golem became too dangerous to his surroundings, he was dismantled. This Jewish theme illustrates some of the guiding principles in its approach to the moral dilemmas inherent in future technologies, such as artificial intelligence and robotics. Man is viewed as having received the power to improve upon creation and develop technologies to achieve them, with the proviso that appropriate safeguards are taken. Ethically, not-harming is viewed as taking precedence over promoting good. Jewish ethical thinking approaches these novel technological possibilities with a cautious optimism that mankind will derive their benefits without coming to harm.

Keywords: Robotics; artificial intelligence; Judaism; ethics.

Introduction

Technological advances have become the hallmark of modern medicine and especially of neurosurgery. Advances in computerized imaging of the central nervous system (CNS) have allowed us to integrate semi-automatic aiming devices into our surgical armamentarium paving the way for robotics within the operating room. Present work concentrates on surgical enhancement technologies, surgery at a distance, and devices that can replace manual skills in procedures that are suitable for automation. A second field of advanced technology deals with neurocybernetics. The recording of neurophysiologic signals from the brain can be linked to electrical stimulation devices leading to the abortion of incipient epileptic seizures and the activation of neural prostheses. The implantation of electrodes for brain stimulation can be utilized for a variety of neurological and behavioral human disorders.

The general public views these advances with ambiguity. On the one hand, technological advances in medicine are not only welcomed, but also expected. On the other hand, there is a fear of tinkering with our basic concepts of the human, undermining long-established notions of mind-brain duality and concepts of personal autonomy. Nowhere do these qualms become more apparent than in the brain sciences.

In the present article I wish to briefly summarize the scientific efforts that are in progress, raise the ethical concerns as reflected in the popular media, and outline Judaism's approach to these apprehensions.

Present status

The present work on robotics in the neurosurgical field may be divided into 3 categories: 1) A supervisory system in which computerized imaging is downloaded to an industrial style robot that aligns itself according to the operator's instructions and performs the procedure under his supervision within the guidelines of the imaging coordinates [3]; 2) a telesurgical system in which the surgeon controls a remote robot. The procedure is dependent on the surgeon's real-time input via a haptic interface with visual and manual feedback. A master-slave relationship exists in which the remote robot faithfully follows the surgeon's input [6; 23]; 3) a shared control system in which the surgeon's movements are modulated by the robot for greater accuracy and dexterity [17].

These devices, as yet in the experimental stage, do not in themselves harbor major ethical questions. The main concerns deal with patient safety and with assignment of responsibility for the success of the procedure [10]. Although we include these procedures under the category of robotics, we are simply using advanced surgical tools for the benefit of the patient.

The second category of surgical procedures deals with the modification of human function by implanting computerized electrical stimulating devices that modify the CNS. Examples of such devices range from the now FDA approved electrical stimulation of the subthalamic nuclei in Parkinsonism [4] to deep brain stimulation for obsessive-compulsive disorders [1], obesity [5], and motor cortex stimulation for chronic pain [18]. While cochlear implants to enhance hearing have been on the map for many years, visual prostheses utilizing stimulation of the occipital cortex are still under development [9]. A device that detects incipient epileptic seizures by monitoring the electrical activity of the brain and aborting the seizure by giving a counter-current has recently been described [19]. This technology had been predicted in Michael Crichton's popular best-seller, The Terminal Man [7], where the potentially dire consequences of autonomous stimulation of the brain were outlined. Neurocybernetic systems under brain control are being developed for the development of neuroprostheses, raising the prospects of a bionic man or woman [25]. While neuroaugmentative surgery has been generally accepted, questions are raised concerning the ethics of behavior modification and personality alterations, especially when dealing with psychiatric abnormalities. In this debate, the advantage of modern stimulatory technology over the old psychosurgical destructive procedures [20], is that it is potentially reversible by stopping the stimulation.

Ethical concerns in popular media

Science fiction both written and in movies have mirrored societies' love-hate relationship with technology throughout the 20th century. Before the Second World War the main themes dealt with the potential for technological misuse. The dropping of the atom bomb led to a heightened concern that technology itself may be dangerous to humanity. Major elements in technophobia relate to a fear of being supplanted, fear of losing control, and fear of losing one's humanity [2].

In Samuel Butler's novel *Erewohn* (1872) machines are seen to perform all tasks better than man, replacing his skills and leading to the atrophy of his capabilities. In Fritz Lang's movie *Metropolis* (1927) workers are mere cogs in the industrial machinery of the underground city, eventually following a robot towards rebellion. Computers can beat grand masters at chess and produce poetry and music that can affect their listener's emotionally. The concern that technological innovation would lead to the loss of traditional human skills is actually ancient and is reflected by Plato's aspersions concerning writing as being detrimental to face-to-face discourse.

A major theme in science fiction has been the fear of losing control over technology that has developed autonomy of its own. In Stanley Kubrick's film *2001* (1968), the supercomputer HAL that runs a spaceship mission, actually harms the crew when it's artificial intelligence decides that they no longer have the mission's success at heart. Unintended detrimental consequences of technology are evident in the proliferation of nuclear weapons and in global warming. Dystopias see a world dominated by machines with humans subservient to their needs as in the recent movie *The Matrix* (Andy & Larry Wachowski, 1999).

A third concern reflects the blurring of the distinction between man and machine. The Sony AIBO ERS-7M3 Entertainment Robot [22] plays soccer, lies down and rights itself, expresses a wide variety of emotions with its tail, eyes, and ears, and recognizes three owners with vocal/visual recognition ability. Could a child be asked to distinguish between cruelty to this toy and to a live pet? This theme is expanded upon in the movies *AI* (Steven Spielberg, 2001) and *Blade Runner* (Ridley Scott, 1982), where humanoids are virtually indistinguishable from humans. This raises the question of what makes a human being a human being, and a robot a robot. As the artificial intelligence researcher Marvin Minsky pointed out: ". . . . only one thing's sure right now: there's something wrong with any claim to know, today, of any basic differences between the minds of men and those of possible machines" [16]. Norbert Wiener, the founder of cybernetics, predicted that the quest to construct computer-modeled AI would come to impinge directly upon some of our most widely and deeply held religious and ethical values [24].

Jewish ethical approach

A key feature in the Jewish ethical approach to medical therapy is the emphasis on the value of life [21]. In contrast to current secular ethical themes the Jewish attitude towards patient autonomy is more paternalistic. The patient does not have an absolute right to do whatever he desires, but must follow the societal norms and regulations. Ethical decisions concerning medical therapy are based on a case-by-case analysis, trying to achieve the best result for the patient within the confines of the broader religious precepts. Therefore the

Fig. 1. The Golem from the film of the same name (Paul Wegener, 1920)

attitude towards technological innovations is in general welcoming, provided appropriate safeguards are present that do not endanger the individual's life.

Jewish folklore tells of the creation of a Golem already in the third century. It is described as a giant humanoid fashioned from clay and animated by a fragment of cabbalistic text. The most famous version of the legend relates to the creation of a Golem by Rabbi Loew, the leader of the Jewish community in 16th century Prague. It was created to defend the local community, but the creature escapes from its designer's control and runs amok until he manages to disable it. The legend became widely known through Gustav Meyrink's 1917 novel [15] and Paul Wegener's expressionistic film (*The Golem*, 1920) (Fig. 1).

The attitude in Judaism towards the Golem may be contrasted to Frankenstein's monster, also a man-made creature, which could function autonomously. In Mary Shelley's 1831 novel of the same name, the creation of the creature is viewed as an abomination against the natural order of the world. The novel criticizes the hubris of the scientist and his lack of responsibility for what he does. Judaism, on the other hand, views the creation of the Golem, with equanimity. No moral judgment is expressed about having designed a Golem, which was to aid the community. If it malfunctioned, the creator could simply switch it off.

There is a body of Jewish religious jurisprudence dealing with the legal standing of a potential Golem [13]. Can one add a Golem to a religious quorum? Should someone who destroys a Golem be held guilty of murder? Is cruelty to a Golem to be distinguished form cruelty to animals? The tenor of these issues reflects a non-judgemental acceptance of the creation and a desire to delineate its implications for human moral contact.

The premise on which this attitude is built lies in the view that man is in a partnership with God. Adam and Eve were "put in the Garden of Eden to dress it and tend to it" [11]. This may be interpreted that man is obligated to care for what God has created and to improve creation so as to meet human needs. The creation is summed up in the following words: "*and God blessed the seventh day, and sanctified it, because on it he had rested from all his work which He created and made.*" The actual Hebrew words read, "*which God created to make.*" [12]. A rabbinic interpretation of this is "*which God created for man to make and improve upon.*" The implication is that man was given his intelligence to improve himself and the world he lives in. Of course he must, however take precautions that no harm is caused by his innovations.

This principle is derived from the biblical context: "*When you build a new house, you shall make a battlement for your roof, so that you should not bring blood upon your house, if any men fall from there*" [8]. The act of building a new house itself is not forbidden; we are only commanded that reasonable safety measures be taken. The wall must be sufficiently high to prevent people from accidentally walking off the roof. Furthermore it has to be strong enough for the average man to lean on it without falling down [14]. The example of building a house serves as a paradigm for all novel technology. The creation of technology is part of man's nature. He must however make sure that the dangers that are inherent in any technology are minimized. New technology would only be unethical if its potential for harm would detract from its benefit.

Conclusion

Robotics, artificial intelligence, and neurocybernetics are at the forefront of scientific technology and have aroused fears in the public as reflected in the popular media. While present technology is as yet far from the realms of science fiction, the public attitude towards possible scientific innovations is tainted by these qualms. Jewish ethics allows for a permissive attitude to scientific innovations, recognizing that these endeavors are at the heart of humanity. While acknowledging that every innovation has its potential dangers, these risks are accepted as long as appropriate safeguards exist to prevent undue harm being done. The essence of man is to create, and the essence of ethics is to harness this creativity for the good of mankind.

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Ethics in the use of new medical technologies for neurosurgery: "Islamic viewpoint"

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Summary

It is very clear from developments in technology and its global expansion that we cannot survive the 21st century with 20th century ethics. The developments in technology, especially those in the field of medicine have a direct and fast effect on human life expectation and survival. Thus, this issue has to be seen and studied in the context of ethics. In this paper, ethical principles in the application of new medical technologies in neurosurgery from an Islamic viewpoint will be given.

Keywords: Ethics; Islamic viewpoint; nanotechnology; neurosurgery.

Introduction

In the 21st century, the application rate of new inventions in different areas has become very fast and thus it is not always possible to adjust the pace of technological development to the pace of social and moral considerations connected with them. This is especially true for medicine. It is worth considering the new challenges in the field of neuroscience and neurosurgery within this context.

Some of the new technologies and developments that will be applied in the near future in neurosurgery and neuroscience can be listed as follows:

– Virtual-reality Surgery Training Systems [13]
– Intraoperative Stereoscopic Quicktime Virtual Reality [2].
  Robotic microscope and digital cameras
  Robotics to improve the precision of surgical action [6].
– Robotic long-distance telementoring in neurosurgery [7]
– Microelectromechanical systems, MEMS, already in use in sensors and in drug delivery. Future application of this technology will be the measurement of mechanical properties of microscopic structures, in *nanoscale* for noninvasive micromanipulation.
– Convection-Enhanced Delivery (targeted therapies in neuro-oncology).
– High frequency cerebral stimulation,
– Neural Precursor Cells
– Restorative Neurosurgery such as Deep Brain Stimulation (DBS). Electrodes or a growth factor implementation through a catheter or placing a engineered cell (dystonia, cervical dystonia and medically intractable epilepsy, disorders such as Parkinson's disease, essential multiple sclerosis tremor, obesity, obsessive-compulsive disorder and substance abuse)
– Stem cell implantation (calm/stimulate, depression/epilepsy)
– Vagal nerve stimulation
– Ventricular assistance devices, subretinal implantable chips, implantation of electrodes into visual cortex of the brain to facilitate the use of a prosthesis that can improve sight; cochlear implants (ear implants, cortical implants for a prosthesis to improve hearing loss), hypodermically injected muscle stimulators.

Among the many new and future applications of new technologies as listed above, application of nanotechnology in the brain is possible for imaging, sensing, visualization, localization and navigation via robots.

It is well known that, starting from the 19th century, industrial revolution took first place in textiles, railroads and then in automobiles, up to 20th century. It was followed by the information revolution with the help of computers till the end of the 20th century. The new era in the 21st century belongs to nanotechnology.

Richard Moore [10] defines "Nanotechnology" as "the science and technology of manipulating things at the atomic or molecular level: ... our ability to work at nano-level to produce useful machines, materials or products in a multidisciplinary way." This means study of the "super small". Nano language is seen in many fields, with nano nomenclature such as; nano-devices, nanoelectronics, nanostructures, nanomaterials, nanosensors, nanobiotechnology, molecular/nano-mechanics, nanosatellites, nanomedicine. Nanomedicine has been defined by Albert Tsai as "the use of engineered nanodevices and nanostructures to monitor, repair, construct, and control the human biological system on a molecular level" [1]. Freitas [5], a research fellow at the Institute of Molecular Manufacturing said in an interview, "I immediately realized that medicine would be the single most important application area of nanotechnology." Later he wrote a book called "Nanomedicine" on advanced molecular nanotechnology with examples. An enormous impact of the book on the perception and development of micro-nanotechnology is expected.

The use of nanomedical devices in neuroscience and its impact, its social challenge, the ethical viewpoints of the applications from a world perspective and from the Islamic perspective will be described below.

Use of nanomedical devices in neuroscience

Eric Drexler [4] states that "If we are made of atoms and molecules, nanotechnology allows us to put our atoms anywhere we want, and attach or detach them from any other atoms as we may please, thus we will be able to control our health almost totally." Thus, in the 21st century, as inventions in the field of nanotechnology expand, many areas will be subject of interest for the application of nanomedicine, i.e. diagnosis of diseases, monitoring of the internal chemistry of the body, implanted devices to dispense drugs or hormones, heart defibrillators and pacemakers, artificial antibodies (white and red blood cells), antiviral nanorobots. Also, fixed nanomachines may be implanted in the nervous system to monitor pulse, brain-wave activity, and other functions. Nanomachines might replicate themselves, or correct genetic deficiencies by altering or replacing DNA molecules. Neural implants may be used to tap the brain's electronic communication system. A single artificial neuron could be able to store the entire library and brains may have the ability to link directly via nanoengineered devices with computers, with other brains, or with the Internet. Thus, brain enhancement by means of artificial, improved neurons will mean unlimited memory and intelligence.

This technology can eliminate disease, can be used to prevent aging and expand the human lifespan. Starting from 1997, it can be seen that in many countries government investments have increased five fold in nanotechnology. However, can we proceed endlessly in this field without any constraints or should we consider the social impacts that we might have to face in the near future relating to these new developments?

Social challenge

It is not always easy to differentiate between treatment of a disease or disability and self-improvement. If some improvements are ethical, what distinguishes legitimate improvements from manipulative alterations of people?

Humanist Percy Lavon Julian, African-American chemist, stated in one of his speeches that "The scientist ... recognizes the magnitude of responsibility resting upon his/her shoulders, when the nations entrust so much of its wealth in his/her hands. The goal of both science and humanity is to enrich and enable the good life of humans. Science is more than methodologies, symbolism and technological devices ... The mission of scientists is to spend their energies on creative imagination in the world of ideas concerning mankind and human destiny."

John Slauther [12] in his Keynote Address given in the Opening Ceremony of the 13th IFAC World Congress in 1996 opened a new discussion by stating that "... the scientist who cannot make value judgements, who cannot see beyond the facts, is of limited use and may even be a threat to society. We must not let the emerging scientific developments and technologies in our laboratories and testing facilities hypnotize us to the point where we fail to consider the moral and social consequences of our advances."

Ethical viewpoints

I. Ali Raja and M. R. Chaudhry [8] in their article wrote: "Medical science continues to make unparalleled advances in technology and skill; the balance between materialism and morality continues to shift towards the attainment of material gains". This argument is also later considered by B. Ramamurthi [9] in his article on "Islam and Medical Ethics". He stated that "Medical profession finds itself faced with many ethical dilemmas. Society, philosophy, culture and theology are not advancing at the same pace in science and technology. The future lies entirely in our own hands. Respect of human life is accepted universally. Doctors can advise but the society in its wisdom has to take the responsibility for the final decision."

On the other hand, G. Teasdale [14] during an International Conference on "Ethical Values in Health Care" said: "The attempt to solve ethical dilemmas on the basis of traditional religious beliefs implied an excessive reliance on authority and could be unethical to a modern, scientific approach to ethics. Traditional wisdom and modern concepts can be attained through *cross-cultural dialogues*."

Islamic viewpoints

A. Van Bommel, Imam [3], stated in his article that, "The Muslim perspective demands every effort to preserving life. In order to have an *inter-cultural and inter-religious* understanding, we should try to come to a common vocabulary. Consensus on issues may not always be feasible. Bioethics can benefit from the richness that characterises *cultural diversity* if opportunities are created to experience the challenge of trans-cultural dialogue."

In the following, interviews done with some theologists in different administrative positions in Turkey will be described without any interpretations from the author.

1st interview

Assoc. Prof. Dr. Ömer Turan, Vice Chair, Department of History, METU, Ankara. A Graduate of Faculty of Divinity, Ankara University; PhD from Catholic University of Leuven in History.

He said "in Islam everything is for human beings (animals and nature), human beings are the most valuable. Balance of nature must not be destroyed. FATAVA can be used in medicine (Islamic criteria) which has no fixed rules. Do not interfere with God. It is our responsibility to decide on our future. Doctors provide the scientific knowledge and the decision must be for the benefit of mankind. If a human proceeds to normality, there is no problem. Why it is done is important. However if the treatment is inhibiting the *free will*, this cannot be allowed".

2nd interview

Mr. İbrahim Paçacı Member of the Higher Council of Religious Affairs in the Presidency of Religious Affairs.

He said "in the religion of Islam, there is no forcing."

"If God would want, everybody on earth would be a believer. When this is the situation; are you the one who will force others to be a believer?" (Q:II Baqara 256 and Yunus 10/99)

He said that, "Religious responsibility prevents you from doing anything that will limit free will."

"In order to examine him, we made him hear and see. We showed him the way: whether he be grateful or ungrateful (rests on his will)." (Q:76, İnsan, 2–3)

He described FIVE important basics in Islam (Q:4, Nisa 92, Q:90–91, Mahide) and said that some can be chosen as codes for medicine. These are "protect Islam (belief, faith), protect human life, protect intelligence (mind), protect generation (family) and protect property (nature, environment)."

He said "healing is what the religion of Islam advises. Even when there is no other choice or any other way to heal a disease, something which is forbidden (like alcohol or substance, or an extract of pig) can be used for healing purposes".

Finally he said that "there must be no threat for the future of mankind and for the life of a human." (Q:173 Bakara, Mahide 3).

3rd interview

Prof. Dr. Hasan Onat, Head of Muslim Sects History, Faculty of Divinity, Ankara University.

He said "Creativity of human brain must be developed by positive thinking. Everything must be known in detail in order to decide. This can be attained by creativity and experimentation. Knowledge through Science and Technology is POWER and when applied, the control of it can only be maintained by Religion and Culture. What is the value which makes a human human? It is morality, high cultural confidence. Humans are valuable. Therefore we must struggle for human welfare and protect life as a human and being a human. To establish codes, human beings must use both vahi (communication between God and Prophet Muhammad) and intelligence. "Vahi is sent to help the human mind. There must be no attempt, no action to threaten or to damage mankind."

4th interview

Prof. Dr. Halis Bayraktar, Interpretor of Qur'an, Faculty of Divinity, Ankara University.

He asked the question: "What says religion? The answer is: What says the human? We are going to decide. The ultimate goal is stability and good order. When applied no deviation from normality can be tolerated. Religion is the experience of the human. It is whatever man has culturally. It is a very important factor which gives reasoning to the communication codes of a culture. He said instead of "Can we?", the question must be "Should we?" There is a balance of justice on earth, he said, any change of the brain or transformation must not produce inequality. Imbalance will produce unfair competition."

5th interview

Prof. Dr. Mualla Selçuk, Dean, Faculty of Divinity, Ankara University.

She said that, "target of Islam is Individual Consciousness:" Islam addresses human beings on the basis of reason and freedom. Qur'anic language and perspective offer the right to free choice based on free will. Qur'an says "there is no compulsion in religion" (Q:11 Baqara, 256) [11].

She also said that "personal responsibility is important and therefore the final decision must be given by the individual." "Islam Religion's mission is to raise up people with free will and not to make a human way of living difficult. Therefore, she said, when new developments are applied, mental and body health must not be destroyed, harmony with society must be maintained, creativity must be enhanced. Hence, applications that – without destroying the nature of human beings-will make men more creative, more productive and better can be accepted."

6th interview

Prof. Dr. Ali Bardakoğlu, The President of The Presidency of Religious Affairs of the Republic of Turkey.

He said that "all sayings that can be found in Islam literature, and the sayings of Prophet Muhammad are examples for the application of social responsibilities in history. They are not fixed models or models closed to interpretation. They are practical examples of those days in order to protect humanity. Today, we have to produce new examples due to new developments in science and technology. These examples must protect humanity and must protect common social responsibilities." He continued by saying that,

"There can be no conflict between science, intellect and religion. They both have the same mission: To provide good welfare of mankind and to let man live in happiness, friendship and in peace.

- Science is developed with experience, with intellect, with wisdom and creativity.
- The subject of religion is the source of knowledge and the source of the creation of human beings.
- Science and religion are two aspects of a whole. They complete each other. Intellect and knowledge gained by science is POWER. How are we going to control that power?
- Human beings can talk (not the animals) and can use symbols. But we never say everything we can. We stop ourselves on purpose. Ethics and our cultural values serve us and stop us from saying everything. Thus, scientists in their research must not feel too independent and free. But they should learn ethics and their cultures. They must care for ethics to protect human dignity and to protect common social responsibility. Any treatment for the curement of illness is accepted. But we must not forget our social responsibility."

He has also given some important Islamic Codes that can help some decisions with regard to applications in the field of medicine:

- "Mankind was created by God. Any input that prevents a human being from being human, cannot be accepted."
- "In all religions, the family concept and the raising of children in a family atmosphere are important (to have a healty character/soul). This must not be disturbed."
- "The dignity of mankind must be protected. Man must be respected in all possible ways."

He gave his answer to the question:

- "What are the constraints in research to protect the dignity of a human being?" as
- "International Codes in medicine must not be determined in consideration of any specific religion.
- Instead, a committee must be formed from theologians, sociologists, scientists, science historians, philosophers and representatives of liberal arts. A concensus must be reached."

Conclusions

Remembering the words of Martin Luther King, Jr.: ''Science deals mainly with facts; religion deals mainly with values'', and that of Einstein: ''Religion without science is lame; science without religion is blind'', and considering the interviews given above, it is understood that we must search for the truth by using our creative thinking endlessly. But in application we must respect human life, free will, human dignity, social responsibility, family and cultures.

The ultimate goal should be the health and welfare of mankind. For achieving this goal, strategies are trans-cultural dialogue, inter-cultural and inter-religious understanding.

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Shadow of Buddhism and Shintoism in neurosurgical practice in Japan

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Summary

Background. In Japan, almost all culture and civilization were introduced from abroad; in the past from China and now from U.S. and European countries, owing to her geographical features circumscribed by oceans and separated from the continents. Neurosurgical science and practice have been received in the same way as other activities. However, there are some exceptions such as organ transplantation from the brain dead and brain–dock, which means a brain check-up system of asymptomatic brain diseases. Reasons why these are practised or not in Japan are considered from the viewpoint of Buddhism and Shintoism. If our special practises could appeal to people in other countries, our neurosurgical philosophy might become widespread and welcome worldwide.

Findings. Organ transplantations from brain dead have routinely been performed in many countries, while only 37 cases have been executed in Japan, after the Japanese government accepted its application in 1997. In contrast, brain–dock is widely practised without any national insurance systems, while this is rarely practised in other countries. It seems to me that Buddhism and Shintoism have influenced on these special situations, due to extreme fear and impurity of the dead body and a way of comprehending the oneness of body and mind, and also deep concern for the impact of their diseases to their families rather than for themselves.

Summary. We neurosurgeons should realize that our profession is directly related to ultimate human sufferings such as aging, disease, and death, as pointed out by Gautama Buddha. We are in fact in a position to study the real way for resolution of the human sufferings, mentally and physically. Based on our experiences, the foundation of a new academic discipline like "cultural medical science" should urgently be considered in all parts of the world and in light of individual cultural, economical, geographical, and population problems.

Keywords: Buddhism; Shintoism; organ transplantation; brain dead; brain dock; impurity of the dead; oneness of body and mind.

Introduction

It is now 50 years ago that I became a medical doctor. Throughout my career, I have quite naturally thought of myself as an ordinary clinical neurosurgeon as well as a research worker in this field, but I never thought seriously of myself either as a Buddhist or a Shintoist. However, during that time I found a few unique and strange neurosurgical practices in our country.

One is the super-acute clipping of ruptured intracranial aneurysms. In the 1970s, it was the elective surgery in the Western countries to operate after the patient recovered to a good condition. However, we challenged to clip them in the super-acute stage, and this policy is now accepted all over the world. At that time, medicine in our country consisted of typical paternalism, and we were really urged to save the patients from recurrences. Since recently, if in good condition, ruptured intracranial aneurysms have routinely been performed in the super-acute stage worldwide.

Next comes organ transplantation from the brain dead. This kind of surgery is routine procedure abroad, while only 37 cases have been done in Japan after the government accepted these procedures in 1997 (Table 1, 2). Last is the detection of asymptomatic brain diseases in special clinics, which in Japa-

Table 1. *Reality of organ transplantations from brain dead in Japan (2005/03/22)*

A: Case numbers per year	
1999	4 cases
2000	6
2001	8
2002	6
2003	4
2004	4
2005	5
Total	37 cases
B: Donor's age	
10 years	1 case
20	6
30	6
40	9
50	8
60	3
Unknown	4 cases

Table 2. *Donor's original diseases (2005/03/22)*

1) Cerebrovascular Diseases	24 cases (65%)
– Subarachnoid Haemorrhage	13
– Intracerebral Haemorrhage	5
– Cerebral Infarction	6
2) Head Injury	6 (16%)
3) Cardiopulmonary Arrest	1
4) Unknown (information proposal rejected)	6 (17%)
Total	37 cases

nese English is called brain dock. Such brain dock clinics are very popular in Japan, while they have rarely been reported from abroad.

These phenomena are quite strange to me, because all medical sciences and practices were introduced from abroad and were performed in Japan almost without exception in the same way as in the original country. There might be two reasons; one is the medical education system and the other is the different mentality due to individual cultures on both sides. As regards our education system in medicine, it is almost equal to that of the Western countries. A key question is the differences in Japanese mentalities, probably due to different religious backgrounds in Japan and other countries. I decided to analyze these causes and conditions from the viewpoint of Buddhism and Shintoism. One of the most prominent difference between their and our religions is that the majority of people in the Western countries belong to Christianity, while the majority of Japanese are either Buddhists or Shintoists; the former being monotheistic and the latter polytheistic.

History of Buddhism in Japan

Buddhism was introduced from China in the 6th century, and was soon accepted as state religion in Japan. We can imagine that many, far advanced arts and knowledge were introduced simultaneously with Buddhism. However, Buddhism from China was already mixed and fused with Confucianism and Taoism. Therefore, its main faith and philosophy are (1) worship of the ancestor, (2) universal compassion, and harmony with nature in order to be of the greatest benefit to other sentient beings, (3) to end the suffering of cyclic existence by reaching true reality, that is spiritual enlightenment, (4) such an indefinite view of life as something transient and empty, that is, a view of an absolutely relative thinking in the cosmological orientation. In one of the most famous sutra called Hannya Shingyo, we can find a self-contradictory, but very famous phrase as follows; Form – it is, in fact, emptiness. Emptiness – it is, in fact, form. According to my understanding, it is a kind of dialectic of being and nothingness. For instance, I am here in my office, but my existence equals nothingness in the cosmological orientation. You can remember archbishop Zycinski's comments on the temporal orientation between the Big Bang of the universe and appearance of the human being in African Savanna. From a statistical point of view, the ratio of duration of human existence compared to the universe is 0.00072%, which is nearly nothing. However, we are here, in reality. This is a kind of a general theory on the relativity in human existence.

Also Buddhism strongly advises and teaches the ways of achieving spiritual enlightenment. There are two ways; one is salvation by faith alone or tantric practice mainly in the aged, and the other is salvation by oneself with ascetic practices including Zen meditation mainly in the youth. Another aspect of Buddhism which is completely different from Christianity is that the founder of Buddhism, Gautama Buddha, is not a god but an ordinary man like us, and therefore there are no gods but several enlightened famous priests in Buddhism.

During the early stage of introduction of Buddhism, Shintoism was easily fused into Buddhism but a few initial conflicts. However, the two religions were soon able to co-exist harmoniously and even complement each other. Within Buddhism, Shinto's gods ("Kami") were regarded as being manifestations of various Buddhas (the enlightened one) and Bodhisattvas (the one striving for enlightenment). Meanwhile within Shintoism, the Buddha was viewed as another "*Kami*". This syncretistic fusion of Buddhism and Shintoism is called as "*Shinbutu-shugo*" in Japanese. At the time of introduction of Buddhism, all major temples were built in the center of cities, but soon they were built in the mountains when fusion of the two religions had penetrated all areas of Japan; the mountains were major ascetic places in Shintoism.

History of Shintoism in Japan

Shintoism ("the way of the gods") is the indigenous faith of the Japanese people and as old as Japan herself. It is clear that the introduction of Buddhism had a profound impact on the development of a unified system of Shinto beliefs. It remains Japan's major religion besides Buddhism. It must be clarified from the beginning that the concept of plural gods in Shintoism called "kami" is completely different from God in Christianity. It is a polytheistic religion, venerating almost any natural objects and phenomena important to life.

According to Shintoism, the divine spirit dwells in all of nature, and brings joy and bounty to our lives. Through intimate contact with nature, we can continue to imbibe its breath of life. Mountains with heroic peaks, deep valleys, a huge waterfall, and the wide ocean were viewed as dwellings of the divine; other natural objects such as huge trees and a pair of rocks in between the sun rises at New Year were considered as media or symbols of divine spirits. Among the natural phenomena, it is the sun that is most appealing to the Japanese, and the Sun Goddess is regarded as the principal deity of Shintoism, particularly by the Imperial Family. In that sense, it might be called as primal animism, which means spiritual being.

One of the most characteristic features in Shintoism is that there are no absolutes, that is, there is no absolute right and wrong, and nobody is perfect. It is an optimistic faith, as humans are thought to be fundamentally good, and evil is believed to be caused by evil spirits. Consequently, the purpose of most Shinto rituals is to keep away evil spirits by purification, prayers and offerings to the kami. In that sense, it might be useful to shift the question of the Kami concept to the question of the Japanese value system, so that we could avoid unnecessary misunderstandings. Polytheism which is based on pluralism does not consider the existence of the absolute truth. If there are two things which contradict each other or cause a conflict between the two, both of them are wrong and right at the same time. Also people who stand on pluralism consider that coexistence is possible, even among those who have different opinions or ideas because each individual has a truth in its individuality. It is coexistence by harmony. The Japanese accepted foreign religions such as Buddhism, Confucianism and Taoism, as the Japanese always have lived according to this plural-value orientation. In fact, in Shinto mythology no mention is made of omniscient and omnipotent Kami. According to Shintoism, there is no Kami who has no defect.

Another feature in Shintoism is that it does not consider life after death like Buddhism, and there are no sutras, like the Bible, at all. Main faith is to keep one's life clean and cleanse both physical and mental impurities with Shinto ritual. Also the dead body in Shintoism is thought to be impure, which should be a main reason why the Japanese hates to accept the brain dead as donor.

One might be surprised to realize that everyone can join local kami automatically at death and be revered by their families as the ancestral gods. The extraordinary people, such as great warriors, leaders and scholars are often enshrined as kami at some shrine. It is a fundamental way of thinking of the Japanese that any sin can be purified by death [4]. For instance, a Samurai (soldier) in the past would commit suicide by perforating his abdomen in order to purify his sin. Yasukuni Shrine (Tokyo), controversial shrine dedicated to the 'peace of the nation', all soldiers fought to death have been enshrined as gods, even first order war criminals were enshrined as usual. Japanese think that death is the most strenuous thing to happen in one's life, and therefore dead persons can be permitted to have been purified by themselves.

In general shrines are not built in a solemn manner but are extremely simple and usually are surrounded by wide natural forest on a hill or in the mountain, and therefore have a mysterious atmosphere.

Temporarily it was once a state religion to unify and strengthen the Japanese and to avoid colonial rule of far advanced countries at the time of the Meiji restoration, but it completely lost its status after World War II.

Recent Buddhism in Japan

Today, Buddhism in daily life usually plays a major role at funeral ceremonies; there is a memorial service in favour of the ancestors once every few years after death. However, a family Buddhist altar is usually located in the main room of our house, and we offer incense sticks, light a candle, and pray for the health and safety of the family members every morning. Usually once a month, we visit the ancestor's grave in the field of the temple.

A few big festivals are hosted by Buddhist temples, such as a welcome festival of the ancestors at home once every year in August. It is one of the national events. At that time, there is a big Japanese migration toward the native community, and trains, airplanes, and also all of the main roads are completely crowded like in a traffic jam in downtown.

In some of Zen Buddhism, meditation training to citizens is periodically held for their psychological peace. Zen Buddhism also had great influence on creating our own philosophy at the time of opening our country to the West. Recently, Buddhism, of which one discipline is nothingness or emptiness of our existence, has become more a subject of oriental philosophy rather than a pure religion [2, 5, 6].

Recent Shintoism in Japan

One of the big features in Shintoism today is that almost all festivals in Japan have been promoted by Shinto shrines according to their rituals, but the citizens gathered do not realize it as ritual, but take it simply for part of our own culture. Also, when a child is born, the family visits the local shrine to celebrate child birth, and almost all wedding ceremonies are performed in front of a portable shrine situated in a room of a hotel.

Shintoism can also be described as the religion of rituals or ceremonies, mostly for purifications or exorcism. At least, we feel a solemn atmosphere during rituals. At the ground-breaking ceremony or the start-up of new facilities, a Shinto priest is always invited to perform the purification and exorcism rituals. Regarding Toyota Motor, it is reported, and this is just one example out of many, that top executives perform the corporate ritual every autumn at the Ise Grand Shrine, the spiritual home of the Sun Goddess, with their latest models, undertaking a 3-hour drive from their headquarters near Nagoya. Shintoism is thus firmly embedded in today's corporate society. Their daily functions are to be focused on helping ordinary people gain better fortunes for themselves through maintaining good relations with their ancestors. People seek support from Shintoism by praying at a home altar or by visiting shrines. A whole range of talismans are available at shrines for traffic safety, good health, business success, safe deliveries, good exam performance and more.

Many famous Japanese cultural and social activities have their origins either directly or indirectly rooted in Shintoism. For example, it is clear that the Shinto ideal of harmony with nature underlies such typically Japanese arts as flower-arranging and traditional Japanese architecture and garden design. A more explicit link to Shintoism is seen in Sumo wrestling where, even in the modern version of the sport, many Shinto-inspired ceremonies must be performed before a bout, such as purifying the wrestling arena by sprinkling it with salt. It is still very common for Japanese to say "I humbly partake" ("*Itadakimasu*" in Japanese) before eating, and the Japanese emphasis on proper greetings can be seen as a continuation of the ancient Shinto belief. Many Japanese cultural customs, like using wooden chopsticks and removing shoes before entering a room at home, have their origin in Shinto beliefs and practices.

Anyhow, Shinto way of thinking takes an important part in the Japanese mindset. Therefore, we need more explanation about "Kami" in Shintoism.

"Kami" in Shintoism

The Kami are the Shinto deities. In order to understand the concept of Kami of the Japanese, it is important to wipe off a preconception caused by the word "God" in English. The word "Kami" is generally translated as "gods", but the Kami bears little resemblance with the God of monotheistic religions. In Shintoism people feel awe to some natural elements that have especially great influence on human life, and worship their spirituality and pray for their blessing. In the case of animals, these have their own spirits. Because they were considered to be sometimes mischievous to human beings, people performed rites in order to console the animal spirits. This faith is still observed nowadays. In medical faculties of almost all universities, for instance, Shinto or Buddhism rites are performed once a year, in order to console the spirits of animals which were killed for experimental purposes. There are other examples of performing a rite: to console the spirits of dolls, and also some tools which were familiarly utilized and became old in everyday life such as needles, combs, Japanese type of pens, or to purify buildings before inaugurating them including even nuclear power stations or computer factories, wishing that all the labor and productions involved would be done properly and safely. According to Shintoism, Kami in general also gets angry and brings some misfortunes to people, although Kami usually guards and blesses people. Accordingly, it is very important to practise faith by performing rites for Kami.

Although there are no gods in Buddhism, we have many gods, for instance 8 million gods, in Shintoism. Every part in nature that lets us feel sacred is believed to be gods. In Shintoism, there is no faith in the concept of the absolute, one god. The ancient Japanese had not divided material and spiritual existence but considered that both were inseparable, regarding everything to be spiritual. According to the myth of Shintoism, there was one thing at the beginning of this universe. Its faith starts with a belief in this mythology. Therefore, it does not acknowledge the existence of the substantial difference or discontinuation between Kami and man, nature and human beings. Well-known Japanese eclecticism experienced in religion, politics, and government policy was already seen in ancient times.

Mental influences of Shintoism and Buddhism on neurosurgical practice

As already mentioned above, in the past we introduced Chinese culture and knowledge, but we had enough time to select and rearrange them to harmonize our culture. After having opened the country to the West, we introduced everything directly, as far as science is concerned. We did not have enough time to rearrange new achievements with our own culture, and now they are being received straight away via every type of information processes.

According to the Shinto faith, a human spirit is believed to remain forever like the spirit of Kami does. The spirit, however, is not conceived as a substantial existence, but is believed to dwell at the other world. According to folk's faith, there is a belief of 'the other world in the mountains'. This faith is connected with the fact that the chief temples have been opened deep in the mountains, and that priests exercise their ascetic trainings by walking around the mountains. The other world, however, is neither described as utopia nor as hell. There is no difference at all from this world. It reflects a faith in the spirit of the dead who can visit this world if people make a ritual to revere the spirit, like the divine spirits visit this world whenever people show their reverence holding festivals. There is also the belief that Kami and ancestral spirits protect their descendants as long as the descendants continue to hold festivals. It can be said that Shintoism is not a religion that centralizes its interests in life after death, but rather in this world. Actually, Japanese seem to be supposed that the dead is still living in another world.

Finally, our unique and strange neurosurgical practices should be reviewed through the mental influences of Buddhism and Shintoism. As mentioned above, everything coming from abroad was believed to be far advanced. In spite of that, there are three exceptions. One is the negative attitude toward organ transplantation from the brain dead. As mentioned already, we have performed only 37 cases since the Japanese government allowed organ transplantation from the brain dead in 1997. The main reason I suppose is that our philosophy consists of the oneness of body and mind, and therefore the body of the brain dead is not a body, but an important memento in his life. And we need to have the last and grief time to send him to the other world as an extension of the present world. Therefore it is impossible for us to regard the brain dead with his heart still beating as a dead person. Also, the dead body is believed to be impure in Shintoism. Furthermore the Buddha prohibited to consume meat if a monk knows that an animal was killed specifically for him.

Next is the brain-dock clinic, which has been prevailing throughout the country without any national insurance support. It costs about 400 Euro-, or 500 American dollars. Elder Japanese are quite worried about suffering from mental or physical diseases, which means their health would very much influence their family's happiness and harmony, more than their own suffering. It is shame for them [1]. That is why they visit brain dock clinics for a health check-up even if they have to renounce at several big dinners or traveling for sight-seeing.

Finally, super-acute clipping of ruptured intracranial aneurysms was not a standard procedure in the 1970s, although it is now thought a standard operation throughout the world. This challenging attitude seemed to be based on the compassionate attitude of Buddhism and self-sacrifice of Japanese neurosurgeons toward the poor patients. At that time our attitude was derived mainly from paternalism, and we did not need to ask for informed consent. We really wished to rescue the poor patients in front of us. In the past in Japan, the patients and their families expected a doctor to be a Bodhisattva, and at the same time, we, the doctors, wanted to be a Bodhisattva [3].

Resumé

1. Buddhism and Shintoism seem to have been almost effaced in our own native culture, but still they have a profound influence throughout the Japanese society, especially Buddhism contributed to create an oriental philosophy, and Shintoism is a basis of Japanese ethics in our daily life.
2. As regards the negative attitude towards organ transplantation from the brain dead, ideas of Shintoism, such as impurity of the dead body and continued being of the dead in another world, have great influence.
3. As for the positive attitude towards the brain dock clinics, deep compassion for the family members

lets elder people check their health, not for their own happiness but to avoid trouble for the family to care for the patient.

4. A quarter century before, there was a medicine of paternalism in Japan; therefore we could establish the super-acute clipping of ruptured intracranial aneurysms. In this medical practice, patients and their families expected us to be a Bodhisattva, and the doctors wanted to be Bodhisattva.

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Current status of medical technology

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Summary

Background. Medical Technology (MT) provides innovative instrumentation and methods designed for the purpose of improving prevention, diagnostics, therapy and rehabilitation. MT rooting in science, engineering and the biosciences is characterized by its inter- and transdisciplinarity.

Method. The current status of MT is described emphasizing the five aspects: (1) review of milestones, (2) the impact of MT on the health care system, (3) the economic significance of MT, (4) the financial resources dedicated to research and development in MT, and (5) the challenges for education and training in MT. The material used is a government issued survey on the situation of MT in Germany, data of health care authorities and congress reports from World Conference on Medical Physics and Biomedical Engineering 2005.

Results. The following fields of MT have emerged in recent years and will dominate future development: BioMEMOS, imaging technology, minimally invasive surgery, computer assisted diagnosis, therapy and treatment monitoring, e-health/telemedicine/networking, and medical engineering for regenerative medicine. Development of MT is driven by the following facts, (1) early and individualized diagnosis enables better treatment, (2) MT enhances cost effectiveness in health care, (3) MT is an economic factor based on fast innovation cycles, a roughly 50% export share and a 6% growth rate in turnover during the last 10 years. A downward tendency of the domestic MT market is a challenge for appropriate measures in improving both the economic and the academic infrastructure, in particular by targeted actions to support research and education.

Conclusion. The impact of MT on prevention, diagnostics, therapy and rehabilitation is significant and still increasing. Due to a wide spreading in all medical areas, the high innovation rate, and the potential to improve health care, MT is considered one of the key technologies even in the future.

Keywords: Medical technology; health care system; research & development in medical technology.

Introduction

To the benefit of the patient Medical Technology (MT) serves the physician by enabling earlier, more reliable diagnosis and better treatment. Today, there is no branch of medicine that does not benefit from the ever more widespread and fast progressing application of technical equipment and related methods. Particularly in neurosurgery, the track of technical evolution is most impressive beginning with the prehistoric Incan trepanation towards MR-image guided navigation and high precision interventional technologies such as laser or radiation surgery to detect and destroy the even tiniest structure in the brain. Medical technology has widely revolutionized medicine and created a number of new subspecialities such as medical image technology, computer aided surgery, minimal invasive interventions etc., and even beyond the limits of medical territory, at least in the highly industrialized countries progress in medical technology has a considerable impact on economy, the entire society and not least moves deeply the common sense of our traditional ethical system.

Medical Technology as an inter- and transdisciplinary field, dealing with the development of instrumentation, is specifically designed for clinical application in prevention, diagnostics, therapy and rehabilitation. Medical Technology is linked to the various areas of biosciences, especially biomedical physics, biomedical engineering, biomedical computing and medicine. Medical technology has its roots in science like physics, engineering, informatics, mathematics and chemistry (Fig. 1).

This paper aims to review the current status of medical technology by addressing five aspects, a summary of milestones of MT, the impact on the health care system, the economic significance, the financial resources of research and development, and the challenges for education and training.

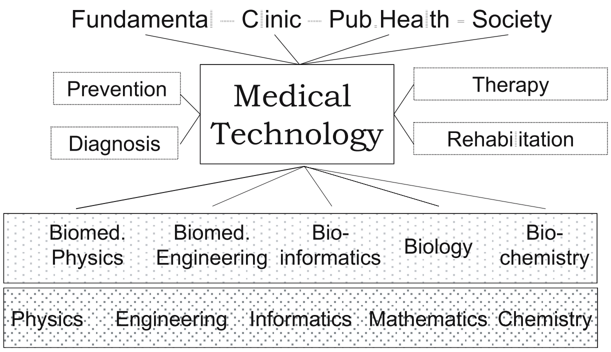

Fig. 1. Inter- and Transdisciplinarity of Medical Technology

Milestones of MT

Looking back at history, there is a nearly endless chain of MT inventions to mention only eye glasses, hearing apparatus, stethoscope, surgical instruments, X-ray tube, iron lung which revolutionized medicine and improved the patient's life. Just in the last few decades we have been witnessing the enormous progress in science and technology, which obviously advances MT even faster. Fundamentally new approaches in diagnostics and therapy, and beyond that in prevention of diseases and rehabilitation after treatment seem to speed up the permanent cycle of innovation, clinical implementation and evaluation up to industrial commercialization. The notoriously high innovation rate of MT makes it difficult to assess the future route of development; however, at least short-term trends may be extrapolated from current highlights in MT research [7].

According to a recent questionnaire-based survey on the situation of MT in Germany six areas of current MT research have been identified [1]:

Bio-microelectromechanical, biomedical fluidics and optical systems (BioMEMS)

Progress in micro-miniaturisation stimulates the development of different types of MEMS, including various physical and biomedical sensors, sample handling platforms of varying complexity, specifically implantable microsystems such as passive, active, sensoric, telemetric ones. These devices serve the purpose to manipulate smallest amounts of substances either for diagnostic or for therapeutic purposes. Microfluidics provide the technological basis for sample uptake, handling and delivery and comprise primarily micropumps and -valves. Another field is the development of implantable microsystems designed for in-vitro diagnostics at cellular and molecular level (lab-on-chip, DNA- and protein-chips etc.) which closely interacts with research on biocompatibility of materials. Furthermore, micro- and nanosystems for neural protheses or as interfaces to the peripheral nervous system are explored. Most challenging are active subretinal implants which are now close to clinical evaluation. Optical techniques such as NIR spectroscopy, for instance applied for non-invasive monitoring of muscle oxygenation during exercises, is currently gaining increasing interest.

Functional, cell- and molecular imaging

In many diseases early diagnosis is a key issue for improvement of curability rates. New methods allow for combining morphological, physiological and molecular imaging. Promising innovative systems have emerged in CT-, MR-, ultrasound and optical imaging. The new class of hybrid scanners like SPECT/CT, PET/CT, and most recently early studies on MR/PET may revolutionize imaging in the clinical environment. Ultra-fast PET detector systems and high-field MR machines for functional, diffusion-tensor and spectroscopy imaging are coming up and are subject to current clinical evaluation. Most rapidly progressing is optical imaging including 3D-optical coherence tomography. Particularly promising is near-infrared fluorescence imaging which has evolved to a powerful and cost-effective tool for non-invasive imaging of target-specific interactions in animals. Molecular imaging is particularly driven by the rapid developments of tracers and biomarkers as well as by investigation of new molecular targets. With this regard, creation of small animal imagers is of growing importance.

Minimally invasive surgery and interventions

Advancement in this area is expected from combining micro-instrumentation with high-precision navigation and robotic technologies, in particular based on imaging and endoscopic methods. For example, a class of new lightweight electronic microscopes for endoscopically assisted neurosurgery linked to compact, semi-robotic platforms for spatial manipulation of a stereoscopic camera is now on the market. Other fields of research relate to interventional techniques and development of special stents.

Computer assisted diagnosis, therapy and treatment monitoring

The significant progress in computer power and capacity of storage media provides new approaches, most strikingly in medical imaging technology when being combined with knowledge based modelling and simu-

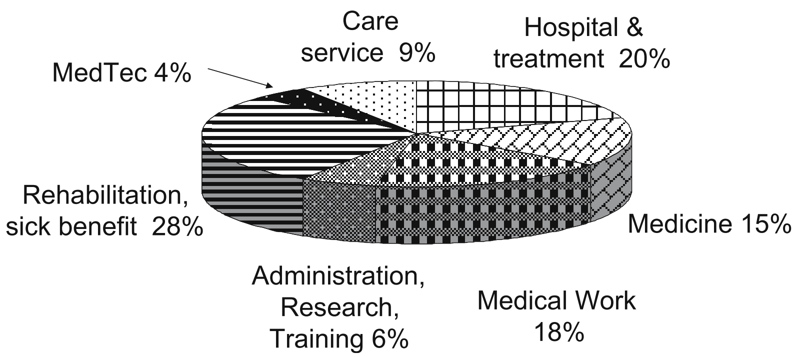

Fig. 2. Cost of Health Care System in Germany. Status 1994 (Ref. 4)

lation. In particular, biosignal-processing linked to models describing signalling pathways or metabolism processes will provide a deeper insight in the disease itself and allow for more individualized treatments. Even smarter and more specific control of respiratory devices or dialysis equipment will be possible by computer assisted systems. Access to computer-based knowledge systems and libraries will improve disease management and optimise the individual treatment.

e-health, telemedicine, networking

The fast progressing communication technology offers a broad range of applications in medicine and health care. Some of the current issues are electronic patient record which in a few countries is starting to become routine (2006 in UK), the patient data card (PDC), health professional card (HPC), e-prescription, e-reporting. Networking and tele-consulting supports patient care in regions with larger distances to hospitals. Multi-purpose wireless network infrastructure designed for hospital applications are to be developed. In general, e-health technology is expected to contribute to improved work-flow management and cost-effectiveness.

Medical engineering for regenerative medicine

The fundamental research field envisaged here is tissue engineering which combines several medical disciplines with cell and molecular biology, material sciences, physics and engineering aiming at developing methods for regenerating, repairing or replacing human tissue. Currently most important in regenerative medicine are skin, cartilage and bone tissue, particularly as a novel treatment option in injuries. Tissue engineering approaches based on stem cell biotechnology methods may have a significant potential for tissue regeneration. Another more recent route in tissue engineering is the use of genes, proteins and small molecules for in situ stem cell control and manipulation focusing particularly on stem cells of the central nervous system for neurogeneration. However, independent of limitations due to the on-going stem cell debate more than expected difficulties emerged in the transition process from research to certified products which are ready for clinical application. The corresponding disenchantment is reflected by the economic development: the capital value of publicly traded tissue-engineering corporations has decreased by almost 90% from US dollars 2.5 billion at the end of 2000 to US dollars 300 million at the end of 2002 [4].

The relevance of the above six main areas of research and development in MT is considered in the framework of the impact on the most important diseases. From that assessment multimodal imaging, minimally invasive surgery and interventions, and medical engineering for regenerative medicine are ranked highest (Fig. 2). Interestingly, that ranking does not correlate with the funding spent for the top research fields. Interpreting this positively, research activities are typically envisaging far horizons aiming to explore the potential of yet non-mature technology. For instance, almost double the resources invested into tissue engineering today compared to surgery related MT may somebody advocate to be a good decision considering the wide spectrum of future applications.

Impact on the health care system

In general, MT improves or aims to improve the patient's quality of life, but today it hardly does extend expectation of life. Compared to the 19th century, modern intensive care and medical technology have decreased mortality by about 0.3% only. Given the advantage of MT from the individual patient's viewpoint the economic impact of MT on the health care system is ambivalent. In general, early diagnosis of a disease ensures reduced hospitalisation, shorter time and less effort of nursing per patient and thus has a cost decreasing effect. On the other hand introducing new cellular and molecular diagnostic methods, launching expensive screening programs to shift diagnosis to early stages of a given disease and enabling better quality of life by technical aids, particularly for non-curable diseases, may partly balance out the net gain of MT. However, it is not the individual patient but just the economic perspective which primarily challenges the health care system itself and to some extent the development of new diagnostic methods. The key problem of any health care system in industrialized countries today is the pyramid of age of the population and the cost explosion.

The age group over 55 years in the population of the Western World is expected to increase within the next 5 years by about 25%. Simultaneously, expectation of life and age related multimorbidity will increase. The cost explosion challenges the health care system more and more to focus on cost effectiveness rather than on technical feasibility. MT contributes significantly to cost effectiveness which is illustrated in the following example from German health care authorities: in 1996 we had 17.2 Mio in-patients (incl. rehabilitation) staying on average for 13.5 days in the hospital; in 2005 the corresponding figures were 22 Mio patients hospitalized for 8–10 days. Promoted by recent technical developments minimal invasive surgery allows for reducing hospitalization time by more than 50%, which means a potential cost saving in the order of about 500 Mio € by means of MT. In Germany the growth national product (GNP) in 2003 was about 2121 Billion €, the health care expenses share is about 11.3%, i.e. 239.7 Billion € or 2900 € per inhabitant [6]. In contrast to the public meaning, MT contributes not more than 4% to the GNP (Fig. 3).

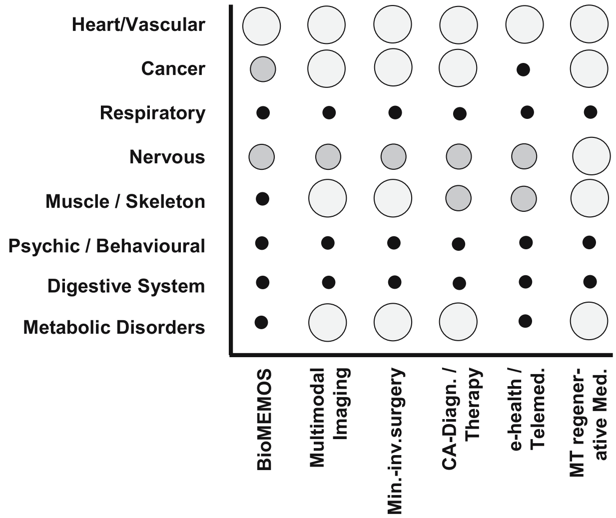

Fig. 3. Relevance of current MT research areas for most important diseases. The currently most promising MT research areas (*abscissa*) projected on the spectrum of disease classes (*ordinate*). The assessment of the relative importance of the various MT areas according to the survey of the BMBF MT-study (Ref. 2) is divided into 3 classes, high (*large circles*), medium (*small circles*) and low (*dots*). Data from Ref. 2

The economic factor MT

In recent decades MT has become a rapidly growing market with increasing relevance for the national economies in all industrialized countries. The most important factors influencing the development of MT is the aging population, the pattern of diseases and the financing system. The aging population with a shift to multimorbidity and chronic diseases like M. Parkinson or M. Alzheimer challenges MT increasingly to provide products which improve the quality of life. Technical aids, disease specific devices and telemedicine will allow the elder patient to live a self-determined life at home for a longer period than years ago. However, according to a recent study, as from 2013 population in Germany will decrease – in 2050 population is expected to be comparable to that of 1963 – which counteracts to some extent the age related request for medical products. Another factor enhancing the request for products of MT is the progress in surgery which allows offering surgical interventions more and more also to the elder patients. Artificial hip replacement is not longer unusual today even at ages beyond eighty. Other expanding fields are ophthalmology with lens extraction for cataracts and coronary surgery (bypass, stent etc.). So, widening the age spectrum for surgical interventions and the request for technical aids in nursing are the two major driving forces to make MT an economic factor with increasing relevance for the GNP. As for Germany, this may be illustrated by the following data (Table 1).

Accordingly, MT is one of the industrial branches with the highest innovation rate. The MT-industry makes 25% of its turnover with products not older than 2 years and invests ca. 10% of its turn-over into

Table 1. *Data on the economic role of MT in Germany (press release MEDICA 2005)*

World Market Medical Technology 2001	170 Bill €
Turnover of German Medical Technology Industries (1200 companies) in 2004	13.6 Bill € (home 45%, abroad 55%)
Growth rate 1995–2001	5.8%/year
Growth rate 2003–2004	Home: −1%, Abroad: 15.8%
Employees MT-industry 2004	87 900
Employees whole health care system	4.2 Mio (10% of all employees)

research and development, and by this it is an outrider of innovation.

From the viewpoint of global economy it is interesting to note that the main customers of German MT-products are the EU (38%) and the USA (20%). The world market leader of MT-industry are USA (40%), Japan (15%) and Germany (8%).

Resources for research and development

Despite the significant increase in global commerce of MT products during the last years, Germany is now much more challenged to take the appropriate measures in order not to fall back in the ranking scale of the leading countries in the MT market. Besides the economic constraints – downward tendency of the domestic MT market and rapid growth of foreign economies – there are two factors which are decisive for the future development of MT: The resources available for R&D and the infrastructure, particularly the academic environment and the education and training system. Comparing the various industrial branches, MT counts among the most research dependent ones. MT industry spends more than a double share (ca. 8–10%) of the overall-turnover in R&D compared to processing industries (ca. 3–4%). In particular, the greater companies with more than 250 employees have a more significant share (43–63%) in R&D whereas the processing industries are much behind (26–49%).

R&D in the MT-industry is primarily based on their own resources; only 3% of all R&D expenses are spent for contracting universities and scientific institutions. Yet the knowledge transfer from science to industry is essential for the innovation process, and therefore the quality and the public financing of the academic environment has a significant impact on the MT industry.

According to an EU survey from 2003 [5], the per capita expenditures for research in Germany is 98 € which is half of the amount spent in Sweden. The share of GNP spent for research in Sweden, Japan, USA and Germany are 3.6%, 3%, 2.8% and 2.5%, respectively.

To catch up the leading countries, a number of initiatives and public-financed programmes have been launched, most importantly the recent excellence initiative of the Federal Government. That 1.9 Billion € five-year program aims to promote at a large scale universities and research institutions by establishing 40 graduate schools, 30 excellence clusters and plans for advancing top-level university research. Independent of this initiative there are a number of already existing actions and programmes, sponsored by public institutions:

– German Research Foundation (DFG)
– Federal Ministry of Education & Research (BMBF)
– Industry Donation for German Science
– University in-house Funding Programs
– EU-Frame Work Program line (currently in force 6th Framework Programme)
– Various foundations, Associations, Universities, Charities

The German Research Foundation (DFG) is the central, self-governing research organisation that promotes research at universities and other publicly financed research institutions in Germany. The DFG serves all branches of science and humanities by funding research projects and facilitating cooperation among researchers. In order to promote MT a specific project group has been created by DFG [2]. The goals and responsibilities of this project group are to define important research fields for basic research by holding regular strategy workshops, support interdisciplinary collaboration in these fields by initiating the joint and coordinated review and cross-group funding of projects, promote young researchers by launching a "Medical Technology Action Plan" and coordinate programmes and projects with other research funding organisations. The latest initiative launched by DFG to encourage early postdocs is the *Excellence Academy* program where a small group of postdocs selected by a competitive process are trained for one week under a thematic frame. That program includes also specific training in publishing and in submitting a successful grant application.

Whilst DFG is focusing more on fundamental research, BMBF supports primarily applied research and development. The BMBF has integrated its different funding measures into a medical technology framework concept which aims to strengthen and expand the growth market of medical technology. The major goals of the BMBF MT research support are:

- Improved cooperation between industrial companies
- Intensified and early coordination between industry & users
- Increased cooperation between science & economy

Besides the annual Innovation Competition to Promote Medical Technology, the BMBF created two funding instruments, the "Centres of Competence in MT" (CCMT), and "Individual Innovative Approaches in Medical Technology" which are designed to meet these goals.

The aim of a CCMT is networking competencies in a special field of Medical Technology in order to exploit synergies and to surmount obstacles of innovation. Therefore, a CCMT is characterized by its trans- and interdisciplinary approach and is structured to cover the entire "*chain of value addition from the idea over research up to development, production, and marketing*" [3]. Each CCMT comprises university institutes, non-academic research institutions and industrial companies. The total funding over the 6-year grant period is 30 Mio € (1999–2005).

After the first announcement in 1999, it was in 2003 that – based on an international evaluation process – the following eight applications for a CCMT were approved:

- **Aachen**, AKM: *Miniature technology for faster healing*
- **Bochum**: KMR: *Gentle waves instead of harsh X-rays KMR – Kompetenzzentrum Medizintechnik Ruhr*
- **Hannover**, MEDIMPLANT: *High-tech for the heart Centre of Competence Cardiovascular Implants*
- **Jena**, OIT: *Modern Medical Technology improves visual acuity – The Competence Centre Ophthalmoinnovation Thüringen*
- **St.Ingbert**, MOTIV: *Protection and aid with modern technology – Miniaturised Monitoring and Intervention Systems*
- **Karlsruhe**, TELTRA: *Telemedicine for Accident Victims Competence and Service Centre for Traumatology*
- **Oldenburg**, Competence Centre HörTech: *The intelligent hifi hearing aid of the future*
- **Tübingen/Tuttlingen**, MITT: *Large Operations with Small Cuts – Minimally Invasive Medicine & Technology Tübingen – Tuttlingen*

Education & training

The declining trend of studying science or engineering observed during the last decade has a negative impact on the development of MT although that trend seems to level out slowly. Education in MT is a domain of Technical Schools and Universities for Applied Sciences UAS). Nineteen UAS offer courses of study in MT. At five universities full study of MT is possible and at seven universities focused programs in MT have been established. The German Research Foundation (DFG) promotes scientific advancements of young researchers in the pre- and postdoctoral phase. For instance, DFG is operating a *Fellowships in the Research Training Group Programme*. With regard to MT topics eight universities (Berlin, Bielefeld, Darmstadt, Dresden, Erlangen, Göttingen, München and Regensburg) applied successfully for that programme. In the framework of the recent excellence initiative of the Federal Government, a new Graduate School Programme may be awarded to doctoral students for completing doctorates within a coordinated research and study programme directed by a number of university teachers. Applications for that rather broad programme are expected from institutions involved in MT.

In general, a good quality of the study of MT in Germany is confirmed. However, similar to other professions in health care like Medical Physics there are no state regulations guaranteeing comparable quality levels for Medical Engineers. Another problem arises from the fact that training of the physicians in fundamentals of MT is not demanded legally. However, in clinical routine the European Medical Device Directive with its specific requirements on regular training of medical staff in the use of all equipment may be considered as an appropriate measure to limit the risks potentially caused by applying any medical instrumentation.

Conclusion

MT is a rapidly growing multidisciplinary area which links science, engineering, biology, informatics, biochemistry with medicine. It is characterized as one of the most innovative disciplines with promising new perspectives for innovative instrumentation and methods in all fields of medicine. The impact of MT on prevention, diagnostics, therapy and rehabilitation is significant and still increasing. In alliance with other areas of the biosciences MT contributes tracing back diseases to its genetic origins and helps explore the mechanisms of progression at the molecular level up to the organ specific manifestation and malfunction.

That broad scope of future development of MT challenges for an appropriate infrastructure of the research and education system, and not least for adequate financial resources.

Compared to other leading industrial countries MT in Germany is well positioned, particularly with respect to imaging technologies. In that particular field the economic role of MT has become most obvious. The increasing significance of MT as an economic factor is reflected in a more than 50% export rate and a more than 6% growth in turnover in the recent years. Research and development is concentrated in the industry itself whereas public support needs to be enhanced. Accordingly, specific programs recently launched by the government and other research organisations like DFG, will hopefully strengthen the promising perspective of future development of MT in Germany.

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Uncertainty in diffusion tensor based fibre tracking

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Summary

Background. Diffusion tensor imaging and related fibre tracking techniques have the potential to identify major white matter tracts afflicted by an individual pathology or tracts at risk for a given surgical approach. However, the reliability of these techniques is known to be limited by image distortions, image noise, low spatial resolution, and the problem of identifying crossing fibres. This paper intends to bridge the gap between the requirements of neurosurgical applications and basic research on fibre tracking uncertainty.

Method. We acquired echo planar diffusion tensor data from both 1.5 T and 3.0 T scanners. For fibre tracking, an extended deflection-based algorithm is employed with enhanced robustness to impaired fibre integrity such as caused by diffuse or infiltrating pathological processes. Moreover, we present a method to assess and visualize the uncertainty of fibre reconstructions based on variational complex Gaussian noise, which provides an alternative to the bootstrap method. We compare fibre tracking results with and without variational noise as well as with artificially decreased image resolution and signal-to-noise.

Findings. Using our fibre tracking technique, we found a high robustness to decreased image resolution and signal-to-noise. Still, the effects of image quality on the tracking result will depend on the employed fibre tracking algorithm and must be handled with care, especially when being used for neurosurgical planning or resection guidance. An advantage of the variational noise approach over the bootstrap technique is that it is applicable to any given set of diffusion tensor images.

Conclusions. We conclude that the presented approach allows for investigating the uncertainty of diffusion tensor imaging based fibre tracking and might offer a perspective to overcome the problem of size underestimation observed by existing techniques.

Keywords: Neurosurgical planning; risk analysis; white matter tracts; fibre tracking; diffusion tensor imaging; bootstrap methods.

Introduction

Magnetic resonance imaging (MRI) plays a major role in neurosurgical planning and decision support by depicting lesions within their anatomical context, information that can be used in a neuronavigation system. Moreover, intraoperative MRI allows for objective determination of the extent of resection during surgery [25]. Over the last five years, diffusion tensor imaging (DTI) received increasing attention in the neurosurgical community with the motivation to identify major white matter tracts afflicted by an individual pathology or tracts at risk for a given surgical approach [11, 24, 30]. Colour-encoded maps of fractional anisotropy (FA) computed from intraoperative DTI were also successfully employed to depict the shifting of major white matter tracts during surgery [19].

An explicit geometrical reconstruction of major white matter tracts has become available by fibre tracking (FT) based on DTI data [18]. The feasibility on intraoperative DTI data has been shown by Nimsky *et al.* [20]. Rather than requiring manual segmentation on every image slice, FT uses the directional information of the DTI data to three-dimensionally (3D) trace major diffusion paths starting from seed points or a seed region [2, 18]. The reliability of current DTI-based FT, however, is known to be limited by image distortions, image noise, low spatial resolution, and the problem of identifying crossing fibres [11, 16]. Therefore, additional functional and electrophysiological image guidance is mandatory in many cases [11].

The problem of image distortions is most often related to the use of Echo Planar Imaging (EPI) for DTI, which offers fast imaging with acceptable signal-to-noise ratio (SNR). While the possibility of distortion compensation by post-processing the images, such as intra-subject spatial alignment to a high-resolution anatomical image, is limited by the loss of image information caused by strong distortions, novel acquisition techniques promise to deliver mostly undistorted images at the cost of longer acquisition times [21].

The dependency of DTI-FT on image noise has been studied by various researchers based on theoretical consideration and numerical simulations [1, 12, 16, 27]. The main finding reported in literature is the mean tract deviation to increase approximately linearly with the distance from the seed point and to decrease with increasing SNR and diffusion anisotropy within the fibre bundle [1, 12]. Still, Yamada *et al.* [30] reported that on a standard 1.5 T whole-body scanner with parallel imaging a scan time of less than five minutes already suffices for clinically useful FT.

The dependency of the FT result on the image resolution has not been widely described so far. In most publications, a close to isotropic image resolution of approximately 1.8–2.0 mm is used to acquire the DTI data. Tournier *et al.* found within simulated experiments that partial volume effects have a detrimental effect for tracking narrow fibres surrounded by anisotropic background [27]. Still, the question remains if and how image resolution and the corresponding partial volume effects might also afflict the tracking of larger fibre bundles. A specific effect of currently employed FT techniques is that the actual size of fibre bundles is underestimated while the direction of fibres often can be well assessed. This has been reported to be problematic when related to neurosurgical applications [11]. It has to be questioned whether this underestimation is due to the limited resolution of DTI images or due to inadequacies in existing image analysis methods.

Recently, a so-called bootstrap approach [4] has been used to visualise statistical properties of a given FT method and a given image quality [9]. Therein, a non-isotropic distribution of FT uncertainty has been found, such as expressed by the local orientation uncertainty, in accordance with the regions of low anisotropy or branching fibre tracts [8, 10].

The goal of this paper is to bridge the gap between basic research on FT uncertainty and neurosurgical applications and requirements. To this end, we propose an alternative method that follows the same idea as the bootstrap approach. This alternative allows in any DTI data set to assess the geometrical variability of fibre tract reconstructions corresponding to a given FT algorithm and parameterisation in dependence of image quality. Furthermore, we present an FT algorithm as an extension of the deflection-based approach by Weinstein *et al.* [28] with enhanced robustness to impaired fibre integrity such as caused by diffuse or infiltrating pathological processes. We apply these methods to reconstruct the pyramidal tracts in a glioma patient and parts of the posterior corpus callosum in a healthy volunteer. The data stem from a 1.5 T and a 3.0 T magnet, respectively. Finally, we examine in a realistic but controlled environment the effects of resolution and SNR on the FT results in order to assess the feasibility of FT on low-quality scans that might be routinely acquired by current clinical scanners in an acceptable timeframe.

Methods and materials

Image acquisition

One patient suffering from a right hemispheric glioma (F, 73 y) and a healthy volunteer (M, 31 y) are considered. For the tumour patient, echo-planar DTI data is acquired on a 1.5 T Siemens Sonata (image resolution $1.875 \times 1.875 \times 1.9$ mm^3, 60 slices, 6 gradient directions, single channel standard head coil, scanning time ~6 min., cf. Fig. 1). For the healthy volunteer, DTI data is acquired on a 3 T Siemens Allegra (image resolution $1.846 \times 1.846 \times 1.6$ mm^3, 80 slices, and 30 gradient directions each, single-channel head coil, averaged over 5 repetitions, scanning time ~13 min.). The image noise of these images can easily be determined as described by Sijbers *et al.* [26] and serves as basis for comparison with the images including artificially added complex Gaussian noise.

Image filtering

In many cases, DTI data is acquired using an anisotropic image resolution, i.e. the slice thickness, commonly without inter-slice gap, is larger than the in-plane pixel spacing. Thus, the highest encoded spatial frequency is larger along the x and y axis (constituting the image plane) than along the z axis (the patient's y axis, running perpendicularly to the imaging plane). In such case, if no spatial normalization is applied to the image data, FT results would depend on the fibre orientation with respect to the imaging plane. For example, a highly curved tract would be reconstructed more accurately within in the x-y plane than within the x-z or y-z planes.

Before FT, we consequently propose to discard the highest frequency content in x and y direction in order to obtain the isotropic image content from the primary image data with an isotropic voxel size equal to the original slice thickness (e.g. $0.8 \times 0.8 \times 2.5$ mm^3 is mapped to $2.5 \times 2.5 \times 2.5$ mm^3). To this end, the resolution reduction in x and y direction would ideally be performed by k-space cropping in order to maintain MR image characteristics. A good approximation to this k-space operation is resampling with a Sinc or Lanczos filter in the spatial domain. In this study, we use a three-lobed Lanczos filter separately along all three principal coordinate axes.

The isotropic MR data is then interpolated in order to provide DTI information at any spatial position. We propose to perform a supersampling of the data before FT to an isotropic target voxel size of approximately 1.0–1.5 mm using a higher-order filter in order to enhance the quality of FT results. This supersampling does not add information to the image, but allows for using a simple tri-linear interpolation at the later tracking stage. In correspondence to the primary resampling step, supersampling would ideally be performed by zero-filling in k-space. Again, we propose to use a Lanczos-3 filter in the spatial domain that represents a good trade-off between computational speed and filtering accuracy.

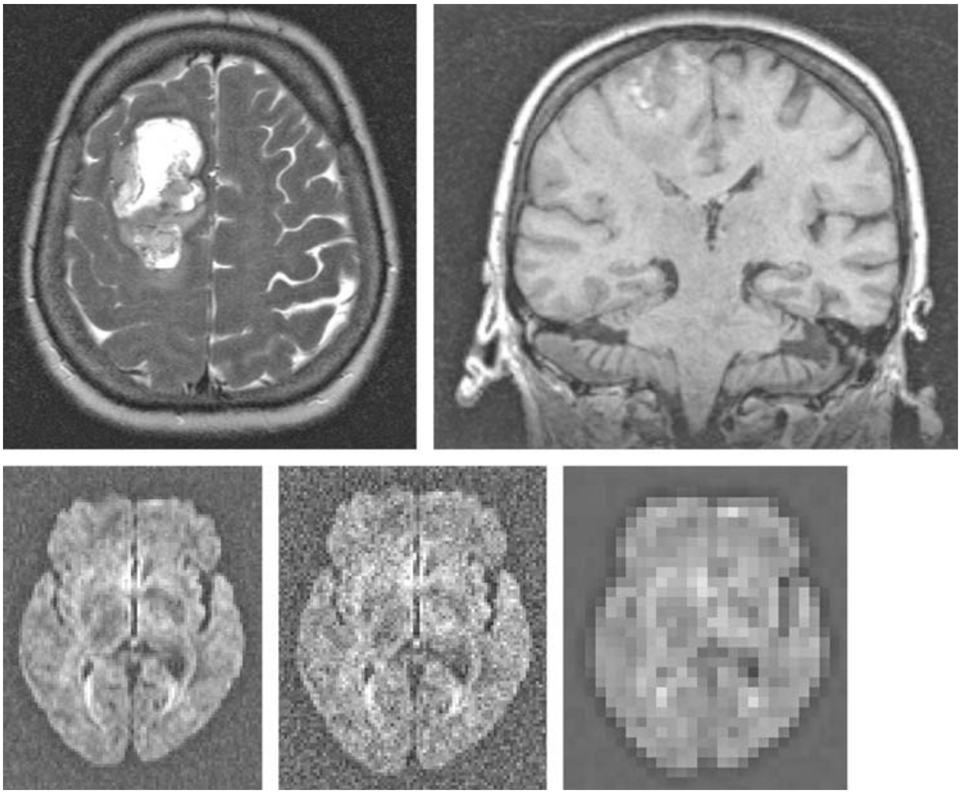


Fig. 1. MRI data of glioma patient; top left: axial T2 weighted image, top right: coronal T1 weighted image; bottom left: original DTI data (first of six gradient directions, $b = 1000$); bottom center: same as before but additive complex Gaussian noise ($\sigma = 20$, compare to Figs. 3 and 4 bottom right); bottom right: same as bottom left but downsampled to an isotropic resolution of $6 \times 6 \times 6$ mm^3 (compare to Figs. 3 and 4 middle row, right image)

In addition to spatial resampling, denoising of the original MRI data might be beneficial in case of high image noise, but also induces assumptions, which cannot be warranted in general, on the underlying signal [17]. Instead of denoising, it is also common to simply smooth the data using a Gaussian filter, while the filter width is chosen empirically according to the respective SNR; larger filters for low SNR, and vice versa. We did not consider Gaussian smoothing within this study.

Extended fibre tracking method

The FT algorithm we employed is based on the deflection-based approach by Weinstein *et al.* [28] and makes use of the full diffusion tensor information during tracking. In contrast, streamline-based algorithms that are commonly employed, such as the FACT (Fibre Assignment by Continuous Tracking) method [18], take into consideration only the largest eigenvector representing the main diffusion direction. In comparison to the method described by Weinstein *et al.* [28], we added a novel moving average estimation of the fibre curvature and anisotropy to the tracking algorithm, which leads to more accurate tracking dynamics and more robust termination criteria [23].

In most cases, FT is applied to discrete images, but the tracking algorithm leads to sub-voxel positions r^t. Therefore, we calculate the new direction for the diffusion tensor at each corner of the cube including r^{t-1} and use tri-linear interpolation for the calculation of the new direction at position r^t.

Usually, the diffusion anisotropy (DA) and the curvature at the current tracking position determine whether the tracking terminates. Tracking is stopped as soon as the DA falls below or the curvature exceeds some threshold value. These local termination criteria are highly sensitive to noise, because the FT could be trapped in a local minimum or maximum of the DA or the curvature, respectively. Furthermore, whether the FT is trapped or not at some local extremum depends unpredictably on the step size. Tournier *et al.* showed that the accuracy of FT sensitively depends on the step size [27]. In order to avoid this problem, we calculate moving averages of both the DA and the curvature with respect to a window on the tracked fibre.

Since on the one hand fibre bundles with high curvature are reconstructed with streamline more accurate than with deflection-based tracking and on the other hand deflection-based tracking is more robust to orientation uncertainty (OU), we set the main vector weighting equal to the curvature normalized by the maximal expected curvature.

Furthermore, we scale the weighting factors for the trilinear interpolation of the new directions at each corner of the cube including r^{t-1} with $(p/2 - \theta)$, where θ is the angle of uncertainty. This curvature and OU weighting was found to significantly improve fibre reconstruction especially at the border of simulated fibre bundles or given white matter tracts, respectively [23].

All image analysis methods used in this paper have been built upon the research and development platform MeVisLab [31].

Assessment of fibre tracking uncertainty

Although an assessment of the FT with respect to its uncertainty is essential in clinical applications, only little work has been done in this area. In a recent paper by Jones *et al.*, the bootstrap method [4, 22] was used for visualizing the uncertainty of fibre orientation in conjunction with the trajectory data [10]. However, their method needs several repetitions of each image that are not available in the standard setting.

To overcome this problem, we present a new method that allows for an efficient computation of diffusion weighted images with user-defined noise while retaining the MRI noise characteristics. The resulting images are used to analyse the tracking uncertainty resulting from image noise. The main idea is to add complex Gaussian noise to the magnitude images. In contrast to the bootstrap method, our technique needs only a single data set so that the amount of required original data and the time for computing the artificial data can be reduced dramatically.

Complex Gaussian noise

The noise distribution of acquired MR images, even after 2D inverse Fourier transformation, is commonly assumed to be Gaussian [26]. However, after magnitude calculation the data is no more complex and the noise is Rician distributed [6]. We now propose to add complex Gaussian noise to the magnitude images, so that the noise distribution is equivalent to those of standard MR images.

Given a pixel value $|\tilde{I}_{x,y}|$ of the magnitude image, we define a corresponding complex number $\tilde{C}_{x,y} = |\tilde{I}_{x,y}| + 0i$ because we can choose an arbitrary point on the circle of the magnitude, the magnitude determination of the complex MR signal $\tilde{I}$ being rotation-invariant. For the moment, let us assume we would like to add noise with a complex Gaussian distribution of width σ to $\tilde{C}_{x,y}$. The resulting complex number is $\tilde{C}'_{x,y} = \tilde{C}_{x,y} + \tilde{N}(0,\Sigma)$, where $\tilde{N}(0,\Sigma)$ denotes a normal distributed complex number with mean 0 and covariance matrix $\Sigma = \sigma^2 E$. Thereafter, the corresponding new magnitude value can be determined as $|\tilde{C}'_{x,y}|$ (cf. Fig. 2). Now, let us assume that the MR signal $\tilde{I}$ is corrupted by Gaussian noise with variance σ_1^2. Further, let σ_2^2 denote the desired variance of the resulting image. It is well known that, if $X_1 \sim N(\mu_1, \Sigma_1)$ and $X_2 \sim N(\mu_2, \Sigma_2 - \Sigma_1)$ are independent variates, then $X_1 + X_2 \sim N(\mu_1 + \mu_2, \Sigma_2)$. As a consequence, σ^2 can simply be determined as $\sigma^2 = \sigma_2^2 - \sigma_1^2$, so that the standard deviation of the noise to be added is $\sigma = \sqrt{\sigma_2^2 - \sigma_1^2}$. The complexity of our new approach is only in $O(s)$, with s being the number of voxels, because all new images can be derived from the single set of existing images.

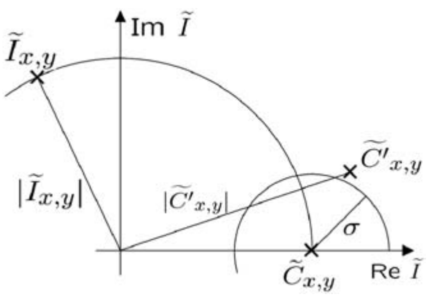


Fig. 2. Schematic drawing of adding complex Gaussian noise of width s to a pixel value $|\tilde{I}_{x,y}|$ of the magnitude image with corresponding complex number $\tilde{C}_{x,y}$. The new magnitude value is denoted as $|\tilde{C}'_{x,y}|$

Visualizing the uncertainty

Let σ_2 denote the desired noise of the images from which we would like to visualise the uncertainty. Then, the difference noise σ can be added to the original images as described above.

For the resulting new data set, FT is performed for a (small) set consisting of n seed points and the streamlines are stored and accumulated within a set of streamlines S. This process is repeated m times for the same seed points resulting in a set S consisting of $n \cdot m$ streamlines.

Now, the uncertainty can be regarded as the difference between the so-called superset trajectories – the streamlines that result when we add no noise to the original images (cf. Figs. 3 and 4 top left) – and the set S, while the probability density of the FT uncertainty is reflected in the geometrical path distribution within S.

Results

In this section we describe the experimental setup and give a short summary of corresponding fibre tracking results. An extensive discussion of the results is given in the next section.

For the glioma patient we defined two seed regions, each consisting of $n = 100$ seed points at the level of the cerebral peduncle as well as two destination regions in the precentral gyrus for tracking the fibres of the pyramidal tract. For the healthy volunteer we defined a single small seed region with $n = 20$ midsagittally within the posterior part of the corpus callosum. For the pyramidal tract, $m = 5$ was chosen, where m denotes the number of how often the FT algorithm is started each with independently generated *variational noise* and for each seed point. For the corpus callosum, m was set to 10.

Original FT results vs. variational noise

Figure 3 and Figure 4 (upper row) compare the original (superset) FT result with that achieved by adding complex Gaussian noise ($\sigma = 5$ or 10, respectively) to the images. As one can see, this so-called *variational noise* causes a widening and an aggregation of the fibres.

Resolution effects

We examined the FT result depending on the resolution of the DW images. Before supersampling the images to an isotropic resolution, we downsample them to $4 \times 4 \times 4$ mm^3 or to $6 \times 6 \times 6$ mm^3, respectively, also using a three-lobed Lanczos filter. The results can be found in Figure 3 and 4 (middle row), which show that the reconstructed paths are smoothed with decreasing resolution. Moreover, new branchings appear within the reconstruction and others are missed (cf. Fig. 4 middle row).

SNR effects

We also examined the effect of adding noise to the images. Before supersampling, we added noise of $\sigma = 10$ and $\sigma = 20$ to the images. The corresponding FT results can be found in Figure 3 and 4 (bottom row). Note that the noise leads to a thinning of the reconstructed fibre bundles and only some new false paths are reconstructed. It is remarkable that all important paths are still reconstructed despite the bad image quality (cf. Fig. 1 bottom center).

Discussion

Our results must be discussed with respect to the anatomical accuracy of diffusion tensor based fibre tracking. Current DTI protocols used for FT yield an effective image resolution of approximately two millimetres, while the acquired SNR represents a trade-off between scanning time and image quality. Due to the limited resolution, only larger white matter tracts can be reconstructed in principle. The anatomical accuracy of a given FT algorithm is related to its sensitivity, i.e. its ability to delineate white matter tracts of a given size and diffusion anisotropy, to its behaviour at branching or crossing fibre bundles, and to its ability to accurately represent the size or width of a given fibre tract. From a neurosurgical perspective, the sensitivity and the size representation are critical as soon as the FT results are used in combination with neuronavigation as a basis for resection guidance [11].

For most figures presented in this paper, we used variational noise with repeated FT under identical starting and boundary conditions in order to demonstrate the uncertainty of FT. When comparing the results with and without variational noise, a systematic widening of the reconstructed fibre tracts can be observed with variational noise. This can be interpreted such that conventional FT tends to avoid the boundary of the white matter tract to be reconstructed and to run towards the centre of the tract. This can be explained by the fact that due to partial volume averaging the diffusion anisotropy is decreased and the main diffusion direction is disturbed at the tract borders. In contrast, after adding variational noise the reconstructed paths are slightly disturbed such that the probability of reaching the tract border increases. After accumulating multiple repetitions with independently generated noise, the overall set of reconstructed paths yield a better representation of the true tract size than without variational noise, even though the seed and target regions as well as the FT parameters are kept constant. As a further effect of accumulating multiple FT repetitions with variational noise, the detection probability of a given fibre branching increases, since more diffusion paths on slightly variable data are reconstructed. Also, we expect that this approach has a higher chance to reconstruct thin and highly curved white matter tracts.

It is instructive to compare the FT results for two types of artificially impaired image quality, first the decrease of image resolution (Figs. 3 and 4 middle row) and second the decrease of SNR (Figs. 3 and 4 bottom row). Decreasing the image resolution yields smoother FT results as can be easily explained due to omitting the spatial high-frequency content of the image data. The increased path smoothness seems a benefit at first sight, but also means that in areas of high tract curvature the tracking accuracy is impaired. For instance, the structures of the cortical tips of the reconstructed pyramidal tract are blurred with decreasing image resolution (Fig. 3 middle row). As secondary effects, some paths become much longer while other paths are missed (Fig. 4 middle row). Conversely, decreased SNR yields more wiggly tracked fibre bundles. Still, the boundary of major tracts is more or less constant when compared to the results on the original data set (Fig. 4 bottom row). As secondary effects, some paths are terminated earlier and some false minor branches are reconstructed (Figs. 3 and 4 bottom row).

Other than discussed in literature, we find that tract reconstruction is only mildly impaired by increased image noise up to a certain level. While simulations suggest that the path deviation approximately increases linearly with the distance to the seed point [1, 12, 16], we find that the reconstructed tracts do not exceed a given boundary. We argue that this is due to the fact that the anisotropic diffusion pattern contained in the image data does not allow for arbitrary path deviations even though considerable noise was added.

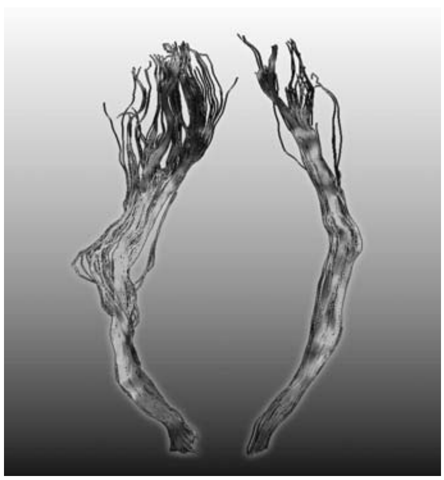
no variational noise

variational noise ($\sigma = 5$)

downsampling (4×4×4 mm³) and
variational noise ($\sigma = 5$)

downsampling (6×6×6 mm³) and
variational noise ($\sigma = 5$)

additional basic noise ($\sigma = 10$) and
variational noise ($\sigma = 5$)



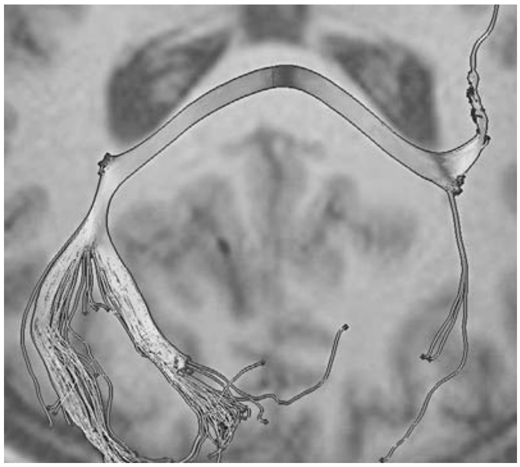
additional basic noise ($\sigma = 20$) and
variational noise ($\sigma = 5$)

Fig. 3. Visualization of FT uncertainty for different resolutions and levels of noise for the pyramidal tract. Before tracing, all data sets were supersampled to $1.5 \times 1.5 \times 1.5$ mm^3 using a three-lobed Lanczos filter

no variational noise

variational noise ($\sigma = 10$)

downsampling (4×4×4 mm³) and
variational noise ($\sigma = 10$)



downsampling (6×6×6 mm³) and
variational noise ($\sigma = 10$)

additional basic noise ($\sigma = 10$) and
variational noise ($\sigma = 10$)

additional basic noise ($\sigma = 20$) and
variational noise ($\sigma = 10$)

Fig. 4. Visualization of FT uncertainty for different resolutions and levels of noise for a seed region within the corpus callosum. Before tracing, all data sets were supersampled to $1.5 \times 1.5 \times 1.5$ mm^3 using a three-lobed Lanczos filter

Otherwise stated, under average imaging conditions we do not see the danger that the reconstructed tract size is overestimated. Rather, as discussed above, most current approaches are likely to underestimate the tract size.

We did not assess the effects of dedicated noise removal schemes such as proposed by Chen and Hsu [3] and McGraw *et al.* [17]. In an optimal case, however, one could hope that white matter tracts are reconstructed more completely but without removing details of the individual paths as an effect of smoothing.

Moreover, it is surprising how well the pyramidal tracts in the glioma patient were reconstructed even though downsampling the image data to an isotropic resolution of as coarse as $6.0 \times 6.0 \times 6.0\ \text{mm}^3$ before FT. We see this as effect both of using a higher-order filter for interpolation of the data before FT and of the properties of the employed extended deflection-based FT algorithm.

We conclude that the presented approach might offer a perspective to overcome the problem of size underestimation observed by current FT approaches. Moreover, the effects of image quality on the tracking result will depend on the employed FT algorithm and must be handled with care. An advantage of the variational noise approach is that it is applicable to any acquired set of diffusion tensor images other than the bootstrap approach that requires individually stored repeated acquisitions. Even though the computation efforts are greatly reduced compared to bootstrapping, future work is required in order to further reduce the required computation time to the order of a few seconds.

Kinoshita *et al.* state that "further validation of fibre tracking images and the improvement and optimisation of the fibre tracking technique are required" [11]. Based on our preliminary findings, we propose to deepen the systematic evaluation of FT applied to major white matter tracts under controlled but realistic imaging conditions in dependency of image resolution, SNR, and pathology. Therein, also newer FT algorithms should be taken into account (e.g. [5, 7, 29]). The evaluation on in-vivo images should be complemented by a variety of phantom studies, both physical phantoms that are suitable as a basis for DTI scanning and software phantoms [14, 23], which should be designed to model typical white matter tract configurations under specific imaging conditions with an exactly known ground truth on the modelled anatomy and tissue anisotropy.

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Robotics in neurosurgery: which tools for what?

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Summary

Robots are the tools for taking advantage of the skills of computers in achieving complicated tasks. This has been made possible owing to the "numerical image explosion" which allowed us to easily obtain spatial coordinates, three dimensional reconstruction, multimodality imaging including digital subtraction angiography (DSA), computed tomography (CT), magnetic resonance imaging (MRI) and magneto encephalography (MEG), with high resolution in space, time, and tissue density. Neurosurgical robots currently available at the operating level are being described. Future evolutions, indications and ethical aspects are examined.

Keywords: Robotics; neurosurgery; spatial coordinates; robotic microscope; stereotactic robot.

Introduction

Why do we need robots in Neurosurgery [1–5]? Robots are the tools for taking advantage of the skills of computers in achieving complicated tasks. This has been made possible owing to "numerical image explosion" which allowed us to easily obtain spatial coordinates, three dimensional reconstruction, multimodality imaging including digital subtraction angiography (DSA), computed tomography (CT), magnetic resonance imaging (MRI) and magneto encephalography (MEG), with high resolution in space, time, and tissue density.

The concept of "Spatially Defined Neurosurgery" is based on this availability of a large amount of data, providing comprehensive information concerning the patients. These data are loaded onto a workstation, where they are processed, and then can be used for archiving, display, or sent to the control units of effectors which are what we call robots: robotized microscope, stereotactic robot or robotized radiosurgery.

Materials and methods

Neurosurgical robots currently available at the operating level

The robotized microscope: surgiscope®

The Surgiscope has been designed in Grenoble in conjunction between the University of Grenoble, INSERM, and the industrial company AID.

The first Surgiscope was installed in the operating rooms of the neurosurgical department in 1996 and currently two operating rooms are equipped, allowing us to perform about 6 procedures per week in a routine manner. This is used for most of the intracranial operations, particularly when the approach needs navigation between sensitive neural elements visible through a very restricted surgical approach. A good example of this is given by micro vascular decompression: although the anatomical structures are easy to recognize and do not need by themselves to be identified through neuronavigation, however, the minimisation of the skull opening in the retrosigmoidal area and the avoidance of the sigmoid sinus as well as the best location of the skin incision are facilitated under surgiscope or whatever kind of neuronavigation. The pre-planning of the trajectory will also help placing the patient in the most convenient position for surgery (Fig. 1).

This is also very well demonstrated in the case of cavernomas which might be deeply situated and dimensions of which are usually small. Even when they are superficially situated they might not be visible even through a very thin layer of cortex (Fig. 2). This allows therefore optimizing targeting of the lesion in order to reduce the skin incision as well as the diameter of the opening. We quite often use trephines of less than 5 cm for cortical cavernomas.

Stereotactic radiotherapy: the CyberKnife®

The concept of radio surgery relies strongly on the acute definition of the lesion and its position in space as well as its dimensions. Calculation of the isodoses, depending on the number of beams to be used as well as on the diameter of the collimators, requires usage of sophisticated computer programs. However, this approach, which is well demonstrated by the GammaKnife or by the systems called Linac, usually allows a limited number of incidences or beams, which all of them are given in a static manner.

Since several years now, a new concept has been in use transforming radiosurgery in a stereotactic and robotized manner through a

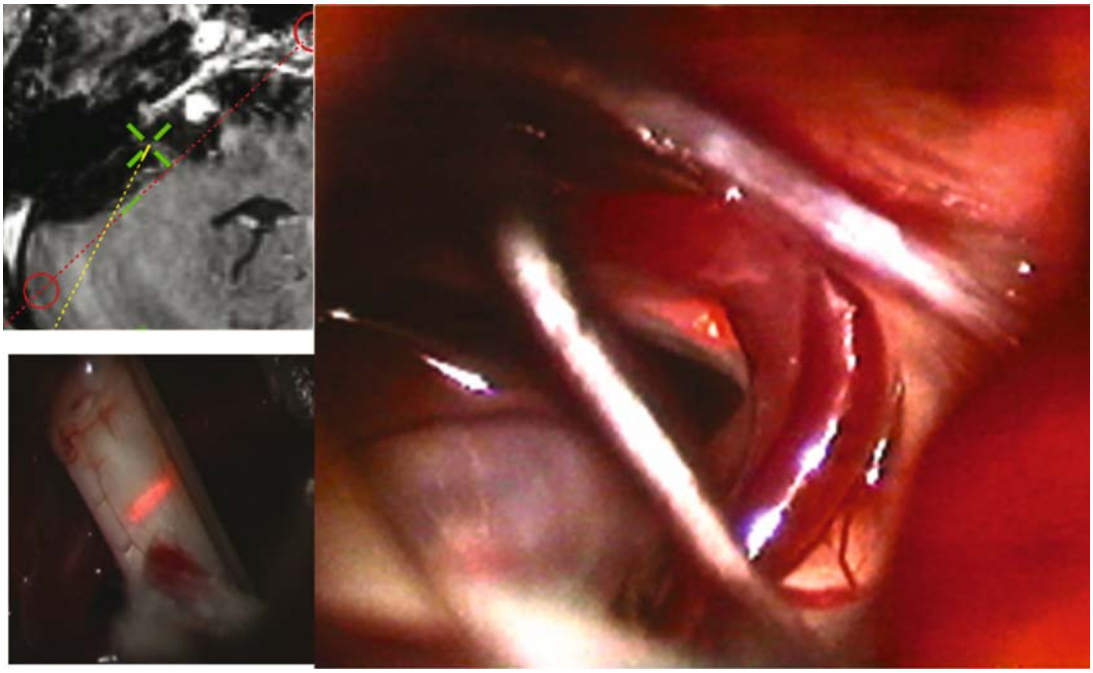

Fig. 1. Microvascular decompression under Surgiscope guidance: (*Right*) Microsurgical view of the nerve-vessel conflict. (*Upper left corner*) Planning of the approach and track with the entry point avoiding the sigmoid lateral sinus, and the target point close to the trigeminal nerve. (*Lower left corner*) Laser spot on the acoustico-facial group

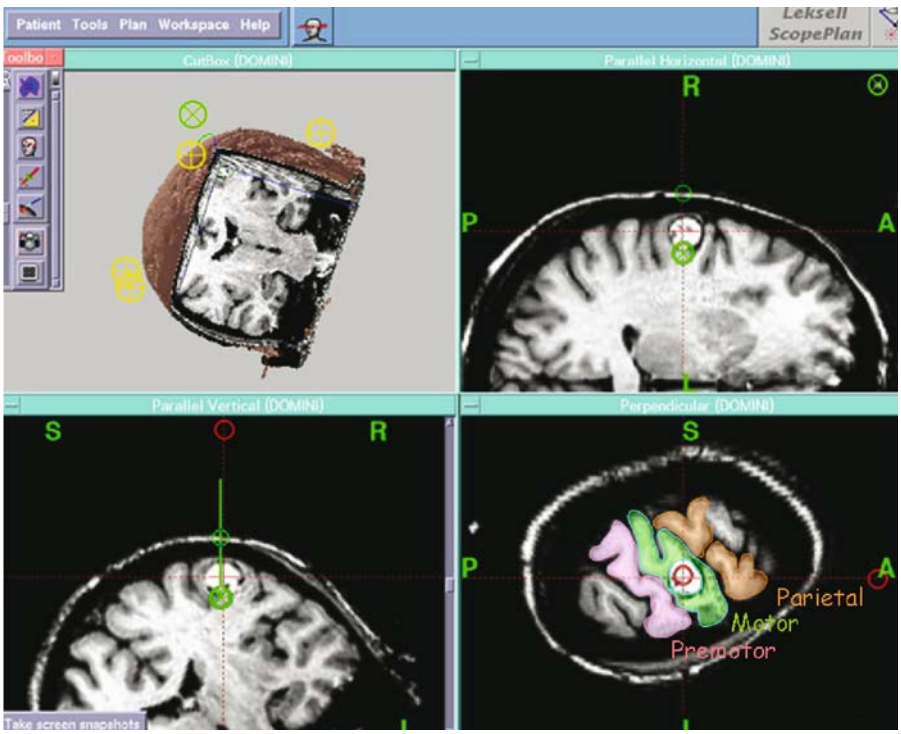

Fig. 2. Cavernomas under Surgiscope guidance: Screen copy of the Surgiscope surgical planning. (*Upper left corner*) 3-D rendering. (*Lower left corner, and upper right corner*) Orthogonally reconstructed images along the planned track. (*Lower right corner*) "Surgeon's Eye view", perpendicular image to the planned track with the recognition of the functional cortices highlighted in colours (Premotor, motor, parietal)

Fig. 3. Cyberknife: the robotized solution for radiosurgery (Courtesy of Accuray)

system called Cyberknife (Fig. 3). This is probably one of the new avenues for radiosurgery as it allows a very precise delimitation of the lesion, and the calculation of sophisticated combinations of radiation beams based on the inverse deconvolution of the envelope of the tumour to be irradiated. This is also facilitated by the possibility to deliver this radiation using a continuous motion of the accelerator, allowing an even better distribution of the surface doses which as a consequence reduces the side effects of an unwanted irradiation outside the envelope of the target. Because of the mobility of the system and its digital determination, it has been possible to develop a "slave" methodology, allowing for instance to irradiate mobile tumours, such as small lung lesions during the session where the patient is breathing normally.

Stereotactic robot: the Schaerer-Mayfield Neuromate®

Since 1989, through the same cooperation between Grenoble University, INSERM, and industrial companies, we have been able to use in the stereotactic room a robotized arm which is linked to the stereotactic frame through solid bonds, the combination of the robotized arm and the frame being screwed on the floor and therefore in a permanent situation at the intersection of 2 long distance (3.5 meters) of the 2 X-Ray tubes mounted on the ceiling and on the wall of this dedicated stereotactic room (Fig. 4). The system is completed by 2 flat X-Ray detectors allowing the acquisition of digital images, either for plain skull X-Rays or for angiograms or for ventriculography.

Ventriculography is still used to determine the target coordinates for deep brain stimulation: X-Rays are taken in a continuous manner as a digital segment recording the equivalent of 24 frames within 12 seconds, during the iodine injection of contrast (Fig. 5). A previous injection of one to 2 millilitres of air is performed to make sure that the catheter is properly inserted into the ventricle. 6.5 ml of Iopamiron Schering are injected within 5 seconds. This recorded video segment visualizes the different features of the ventricles, which provide precisely the location of the main landmarks which are used for stereotactic determination of coordinates such as the posterior commissure (PC), the anterior commissure (AC), the top of the thalamus which is represented by the bottom of the floor of the lateral ventricle as well as the midline of the third ventricle which will be used to calculate the laterality of the target. The determination is made using drawing tools, which have been implemented into the software which is associated to the flat detector acquisition system. The inclusion of those digital tools is made possible by the digital nature of the images which are acquired. It is easy to develop tools which automatically will report on those ventriculographic stereotactic images the coordinates of the target (for instance, for the subthalamic target, the anteroposterior distance is 5.22/12th of the AC-PC length, the verticality is – 1.21/8th of the height of the thalamus and the laterality is 11.6 millimetres from the midline for the target and 35 millimetres for the entry point on the skull).

The second step is the acquisition of MRI in a stereotactic manner using a stereotactic localizer (Fig. 6) where the patient can be repositioned without anaesthesia as this is not invasive, using the bone screws which have been inserted during the ventriculography session. The MRI acquisition gives us 100 T1 weighted axial images and 50 T2 weighted coronal images which will be loaded onto the software of the stereotactic robot allowing to program the robot to reach the position corresponding to the desired trajectory of implantation. The MRI images by themselves cannot be of sufficient precision but may help the decision making of the trajectories, particularly at the level of the cortical surface where the vessels might be more easily avoided. Currently, the most frequently targeted structure is the subthalamic nucleus which is a small structure with dimensions of about $8 * 6 * 6$ millimetres situated above the substantia nigra, lateral to the red nucleus, medial to the internal capsule and below the thalamic complex and the zona incerta. Most of the time, on the axial and coronal section in T2 the subthalamic nucleus is visible as a strongly hypointense signal which is not easily discernable from the substantia nigra pars reticulata on the axial slices. Despite the unequal quality of the MRI images and also to the strongly variable visibility of the STN nucleus, these images may help correcting the indirect targeting obtained from the coordinates.

The software of the robot (Voxim 5.5 version from IVS) integrates the various modalities including ventriculograms, and MRI in T1 and T2 weighted sequences which can be reconstructed according to the axial, sagittal or coronal images. This can also be connected to an inbuilt digital version of the Schaltenbrandt and Wharen atlas. The software of the robot integrates also a flight simulator which allows choosing among the various solutions which are proposed by the robot internal controller the one which is the most comfortable for the surgeons during the procedure. Once the electrodes are inserted (in our practice, we use 5 parallel cannulas separated by 2 millimetres

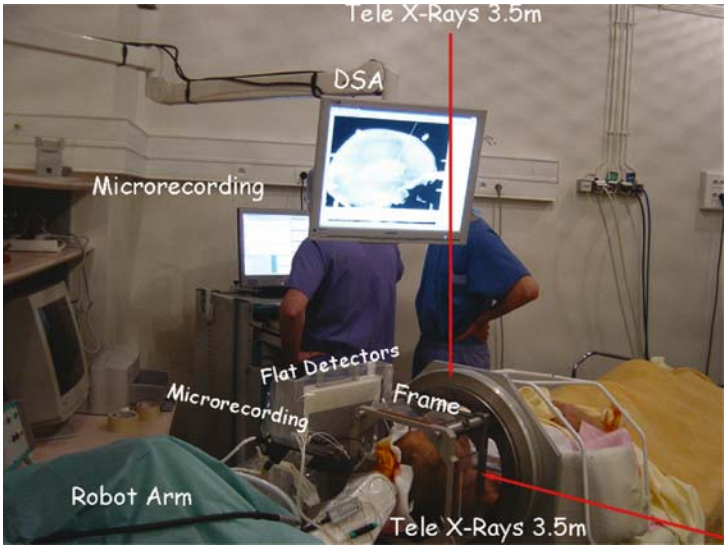

Fig. 4. Neuromate: the robotized solution for stereotaxy. Grenoble setting in the dedicated stereotactic robotized room. The frame holding the patient is at the Crossroads of the two teleradiological orthogonal x-ray beams, and images are captured by an orthogonal set of digitized flat detectors. The x-rays are visualized on a flat screen display for the operator team. The robot arm is holding the microdrive propelling the microelectrode into the brain and allowing microrecording, which is analyzed on the Alpha Omega console by the electrophysiology team, visible in the back of the room

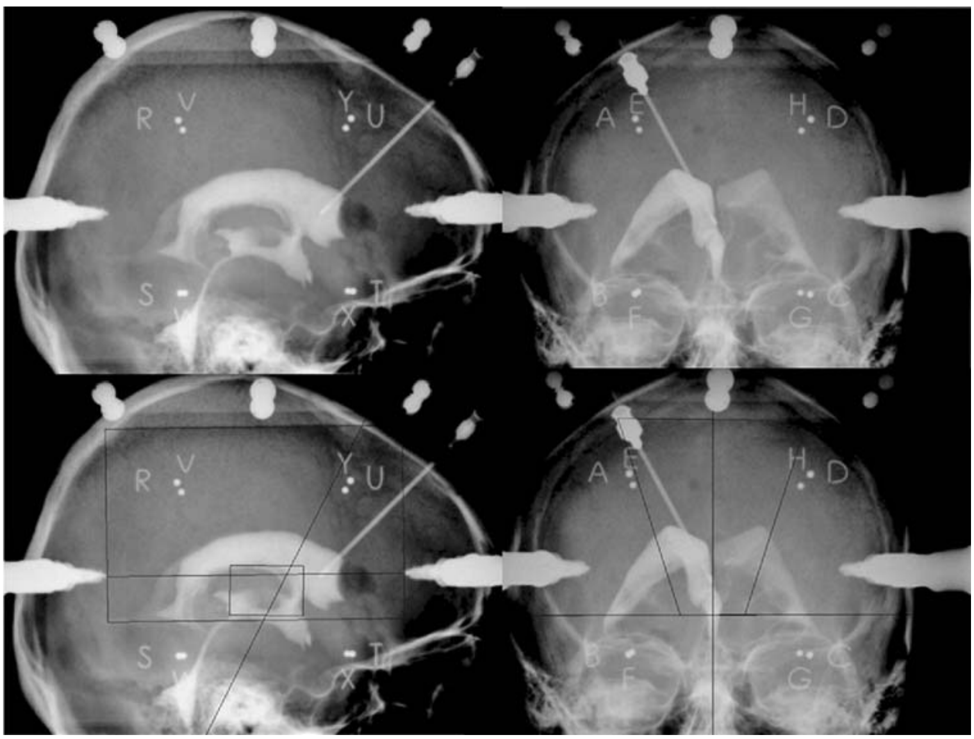

Fig. 5. Digitized ventriculography and target coordinates determination: (*Upper Lane*) Lateral and anteroposterior to ventriculographic images. (*Lower Lane*) Automatic drawing of the coordinates of the target and of the trajectory with determination of the entry point at the level of the skull

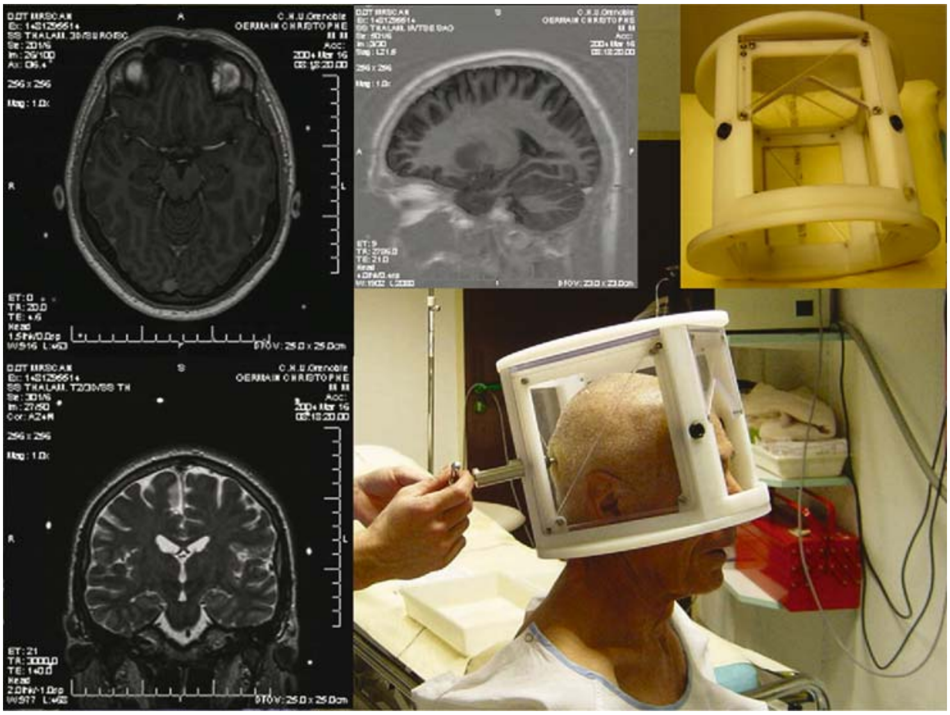

Fig. 6. Stereotactic MRI localizer: (*On the left*) Triplanar MRI images in stereotactic conditions. (*Upper right corner*) Stereotactic MRI localizer. (*Lower right corner*) Installation of the MRI localizer on the head of the patient, using the implanted bone screws

allowing the exploration of an about 6 millimetre in diameter tube, but also allowing us to perform never more than 1 pass of this 5 electrode set. The microdrive (Neuromap by Alpha Omega) is used to propagate the electrode down the trajectory and to perform recording as well as micro stimulation all along the track, down to the target and beyond the target. At the end of this procedure, combination of the data coming from the MRI, from the recording as well as from the results of the stimulation observed by the clinical team (including the neurosurgeons and the neurologists) allows us to choose which of the five tracks is the best one and to replace in this track the microelectrodes by the chronic stimulating electrodes (Medtronic reference 3389). This allows also, based on data gathered from several hundred patients, constructing the statistical distribution of the best contact which is clinically validated and chosen for stimulation of the patient. This defines clinically validated ''functional STN'' for which probabilistic maps are provided [8].

These integrated data are used to define the track, aiming at the target point, and starting at the entry point, on the cortex. The structure to be traversed by the penetrating tools can be visualized, and the track might be changed on the basis of the potential risks encountered in the brain depth, before reaching the target: for instance, it has been observed that after bilateral stimulation of the STN nucleus, a certain degree of confusion which may last 2 hours to 2 weeks has been observed in several patients. This happens mostly during the second track, much higher than the level of the target itself. The analysis of our data has shown that this is more than likely related to the mechanical injury of the 2 caudate nucleus at the level of the border of the lateral ventricles where the 5 electrodes are passing very closely (Fig. 7). In view of this observation, the robotized navigation avoids as much as possible not only the ventricle but also the border of these ventricles where the caudate nucleus is situated.

The ''hand'' of the robot is the tool holder and may hold biopsy cannulas, guide tubes, for microrecording and implantation of electrodes, and a microdrive, linked to an electrophysiology multi channel system allowing performing stereotactic neurophysiology during

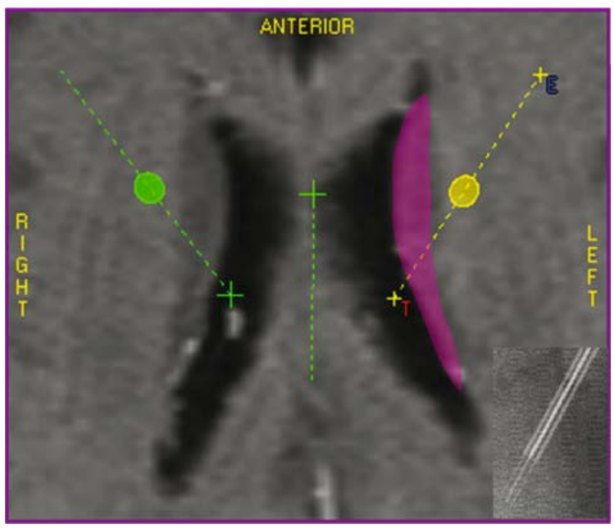

Fig. 7. Possible role of the caudate nucleus in post bilateral DBS confusion. The planning of the two trajectories allows positioning the entry point, such as the electrode track avoids crossing the area of the caudate nucleus, clearly visible at the lateral border of the ventricles

the procedure. Since the completion of the first prototype in 1989, two more sophisticated systems have been developed to lead to the current version. Using this robotized arm, we have been able to operate more than 500 DBS implants, performing 1,500 tumour biopsies and implanting 2,000 SEEG electrodes. Currently this installation is used in routine for an average of 5 procedures a week.

Discussion

What are the future evolutions?

They can be foreseen as integration of MRI, MRI spectroscopy, functional MRI, MRI tractography using diffusion tensor imaging, as well as magneto encephalography (MEG) and SPECT and PET. The more comprehensive the picture of the target and of the lesion will be, the more accurate the placement of the surgical tools will be leading in theory to the best treatment possible.

Why do we need in reality robots in neurosurgery and particularly for what indications?

This is currently used for movement disorders, epilepsy, cluster headaches, and we are on the process of applying deep brain stimulation for malignant cases of obesity. A new field which is now open is the field of psychosurgery which had been obliterated about 30 years ago for several reasons. These reasons were the fact that, at that time, the pathological concepts were still fuzzy, the methods for locating the targets were extremely reduced to the air ventriculography and some electrophysiology. Also very little was known about the electrophysiology of targets for psychosurgery. The most determining reason why psychosurgery was abandoned is mostly due to the malpractice and the reckless extension of the indications for reasons which were not always medically based.

However, this period has been useful in demonstrating that this type of functional neurosurgery could be strongly efficient on indications such as obsessive compulsive disorders (OCD) and major depression. These are severe pathological conditions impairing strongly the patients' lives and it is more than needed and warranted to try to reconsider those indications. The introduction of deep brain stimulation of high frequency which can mimic lesioning methods which were previously used but has the important advantages of introducing variability, adaptability and mostly reversibility, which induces also very secure practice as allowed by ethical committees around the world to reconsider favourably the reintroduction of these methods.

One current indication concerns obsessive compulsive disorders (OCD) that constitute very severe pathological situations affecting a rather large number of patients and particularly young patients in a very active period of their lives. Based on the knowledge that lesions in various parts of the brain, but particularly in the anterior limb of the internal capsule, were providing satisfactory clinical results, the application of the equivalence of high frequency stimulation to lesion has been made by the group of Bart Nuttin in 1999 as published in Lancet [9]. Their data were encouraging but very quickly showed that the target was probably situated much deeper and more posteriorly, close if not within the nucleus accumbens. This makes sense with the fact that high frequency stimulation, although the mechanism is not really understood, is not able to inhibit the activity of fibres which are excited at low as well as at high frequencies. The inhibiting effect of HFS is mostly observed in cellular structures and it makes sense that the final target would be in the nucleus accumbens. This has been considered efficiently by the group of Professor Sturm in Köln [10], who has gathered some experience in this field. In parallel, it was incidentally observed in Parkinsonian patients, who had traits of obsessive compulsive disorder, that stimulation of the STN given to alleviate their parkinsonian symptoms had effect also on their obsessive compulsive disorder [6]. Hence this has been the rationale of a multicenter study in France, currently going on, using the limbic part of the STN nucleus (2 millimetres more anterior and one millimetre more medial than the "classical" Parkinson's target). The preliminary results of this study so far are extremely encouraging and allow, due to the specific advantages of deep brain stimulation (adaptability and if needed reversibility), to be efficient with much less ethical concerns than if we were using irreversible lesioning methods.

Similarly, data just recently retrieved from the extensive work of functional imaging in psychiatric disorders, led by Helen Mayberg [7], have shown that in severe pharmacoresistant depression the subgenual medial limbic cortex of the cingulum (CG 25 area) is hyperactive using PET scan monitoring the cerebral blood flow using water labelled with the oxygen 15, while on the contrary the prefrontal area F9 is hypoperfused. They have on these bases targeted CG 25 where 2 deep brain stimulation electrodes have been chronically implanted. The preliminary results re-

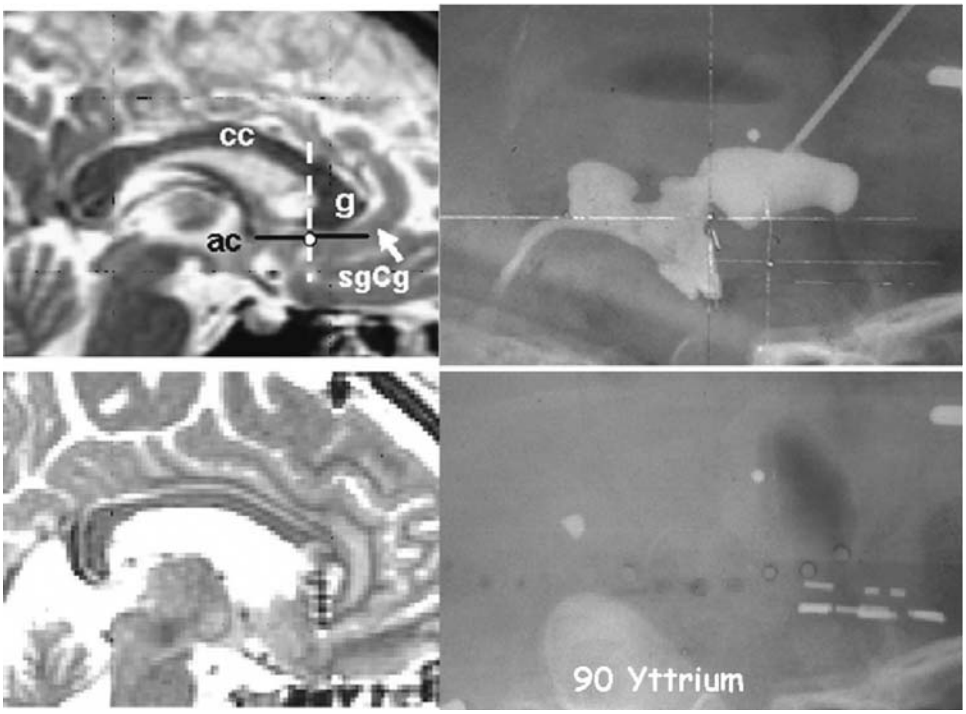

Fig. 8. CG25 and 90Yttrium. Comparisons of the target used by Mayberg and Lozano for deep brain stimulation of the subgenual cortex in depression (*left side of the Fig.*), with the target used for subcaudate tractotomy with ^{90}Yttrium seeds according to Knight, as we used to perform it in the seventies

ported in their Neuron paper show that activation of those electrodes at high frequency induces a very strong decrease in the activity, concomitant with very significant improvement of patient's mood condition.

It is interesting to compare the target which is used for electrode implantation to targets which were used about 30 years ago for subcaudate leucotomy (Knight method) using implantation of Yttrium 90 seeds (Fig. 8).

Conclusion

Is it ethically legitimate to follow this procedure? A tool might induce dysfunction and malpractice, overuse and the procedure itself might induce side effects. Particularly in Parkinson's disease, HFS of STN has been associated with depression, apathy, hypomania, gambling due to the disruption by high frequency stimulation of dysfunction affecting a network. This is multifactorial and the strong decrease in dopaminergic medication has to be taken into account. But even if these side effects were related to stimulation, once again the advantage is that high frequency stimulation is reversible. Psychosurgery in this field deserves a special mention. Yes, we do change behaviour and personality but this is legitimate if reversible and when behaviour and personality are out of range for pathological reasons. The behaviour and personality are abnormal but the abnormality is above threshold. What means abnormal? Functional symptoms are the inappropriate expression of normality and the standard deviations of each item of the personality profile are actually defining the individual personality. According to this concept, one might consider that the patients are in a pathological state when these deviations are out of the range defined by standard deviation.

All these approaches, including robots in stereotactic and functional neurosurgery, are strongly submitted to financial constraints: the field of application is defined by the market and companies go where the money is, which is not always where medical interest is. Costs of these technologies are not always in relation to the cost of production. The health budgets, in our Western countries, are strongly dominated by political and societal considerations and are not always placed in the best budget priorities.

Is the benefit worth the cost? We have to hope so and to work to make it worthy. Neurosurgery has the responsibility to develop methods and to make them available for the benefit of the patients. Robotization may be one of the means to achieve this goal. We are currently experiencing the development of new methodologies which are expensive but are aiming at increased precision and increased availability for various indications. Those indications are enlarging strongly, going out of the classical field of functional neurosurgery, which were the tumours, pain and movement disorders, to spread to epilepsy, other symptoms such as vascular diseases including cluster headaches, complex situations leading to obesity and the important and very sensitive field of psychosurgery which responds to real needs from the patients but has to be accepted by the society. This warrants from the neurosurgical side the best efforts to be as free from side effects as possible, which goes through very dedicated and precise surgical practice, which obviously might benefit from the development of new methods, including robotized functional neurosurgery.

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Computer- and robot-aided head surgery

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Summary

In this paper new methods and devices for computer and robot based head surgery are presented. A computer based planning system for CMF-surgery allows the surgeon to plan complex trajectories on the head of the patient for operations where bone segments were cut out and shifted. Different registration methods have been developed and tested. A surgical robot system for bone cutting on the head has been developed and evaluated at the patient in the operating theatre. In future, laser cutting of bones with a robot will be seen as a new powerful method for robot based surgery. A 3D augmented reality system will assist the surgeon in the future by augmenting virtual anatomical structure into the situs.

Keywords: Workflow; head surgery; computer based planning system; localisation; navigation; marker based registration; non-invasive markerless registration; surface matching; assistive surgical robot system; human machine interface; laser cutting; 3D-augmented reality system.

Introduction

In the collaborative research centre "Information Technology in Medicine – Computer- and Sensor-Aided Surgery" of the German Research Foundation (SFB 414) a surgical workflow was established [1]. This is shown on Fig. 1 for computer- and robot-aided head surgery. It starts with image acquisition where tomography slices of the head are acquired. Based on these data a 3D-model of the head is generated. The surgeon can now define trajectories on this virtual head. Thereafter simulation on a workstation can be performed with graphical models. After such verification of the operation plan, real operation with the robot can be started at a later point of time.

Planning

A precondition for robot aided head surgery is a computer based planning system. In the SFB 414 a computer based planning system for CMF surgery (cranio maxillofacial surgery) was developed at the IPR (Institute for Process Control and Robotics). Figure 2 shows the planning procedure of a fronto orbital advancement. First, basepoints of a complex trajectory are defined. These basepoints consist of tuples of a point on the outer side and a corresponding point on the inner side of the skull. The basepoints are connected to a continuous trajectory e.g. to allow a surgical robot to precisely drill the given trajectory. After defining the trajectory the bone segment can be cut out of the skull model. Finally, the cut out bone segment can be moved. While doing this, the planning system gives an estimation of the volume, gained by movement of the bone segment. If the surgeon is satisfied with the simulated result of the planned intervention, he can pass the operation plan via XML to the executing unit e.g. a surgical robot. With this procedure it can be assured that an operation plan with an accuracy of 1 mm is realised.

Another application of the planning system is shown in Fig. 3. With the use of reference data it is possible to transfer an operation plan onto another patient. The skull model of the patient can be compared with a normalized reference skull. The deviation will be visualized color coded. The normalized data is stored in a database generated from several patients in several form classes. With this approach the surgeon can plan an intervention on the normalized data and transfer the operation plan to the skull model of the patient. Also the opposite way is possible. Thus different operation plans can be compared.

Registration

A further precondition for robot-aided head surgery is a registration system which localizes intraoperatively

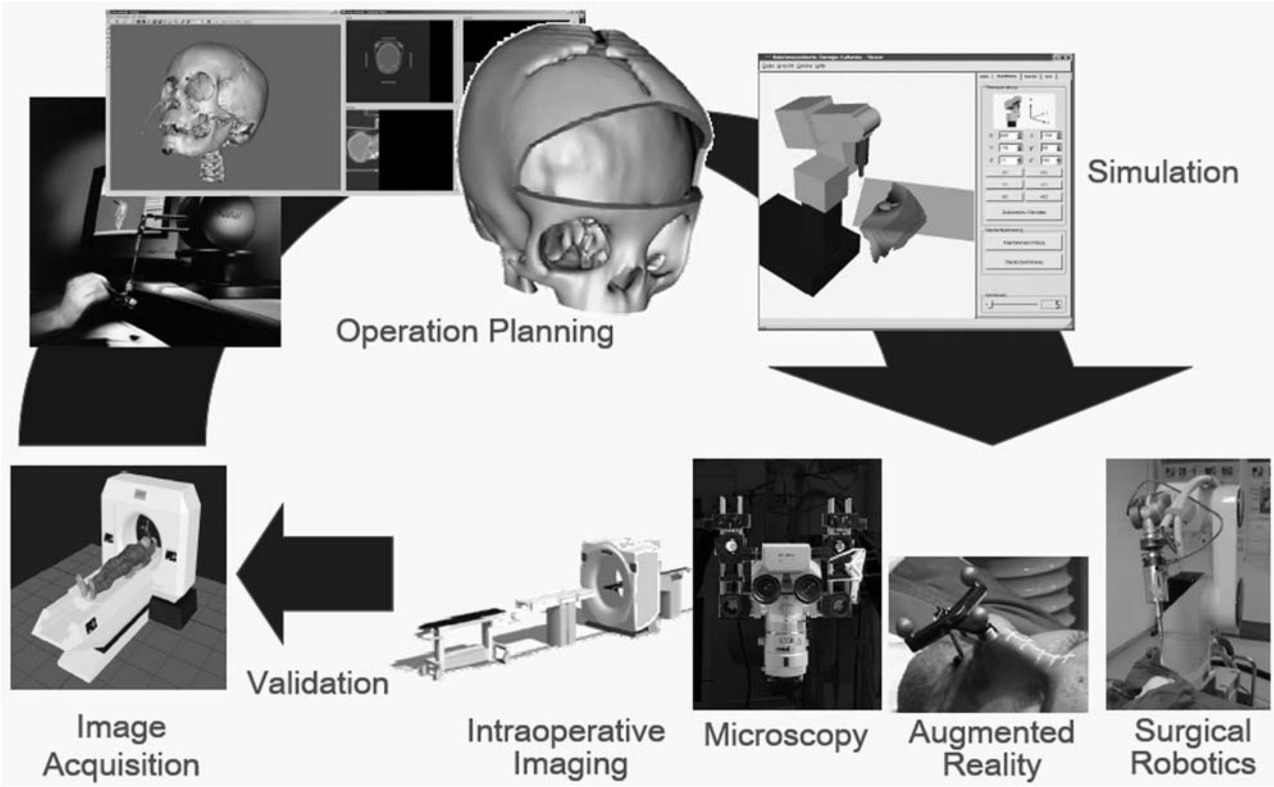

Fig. 1. Computer and robot-aided head surgery workflow

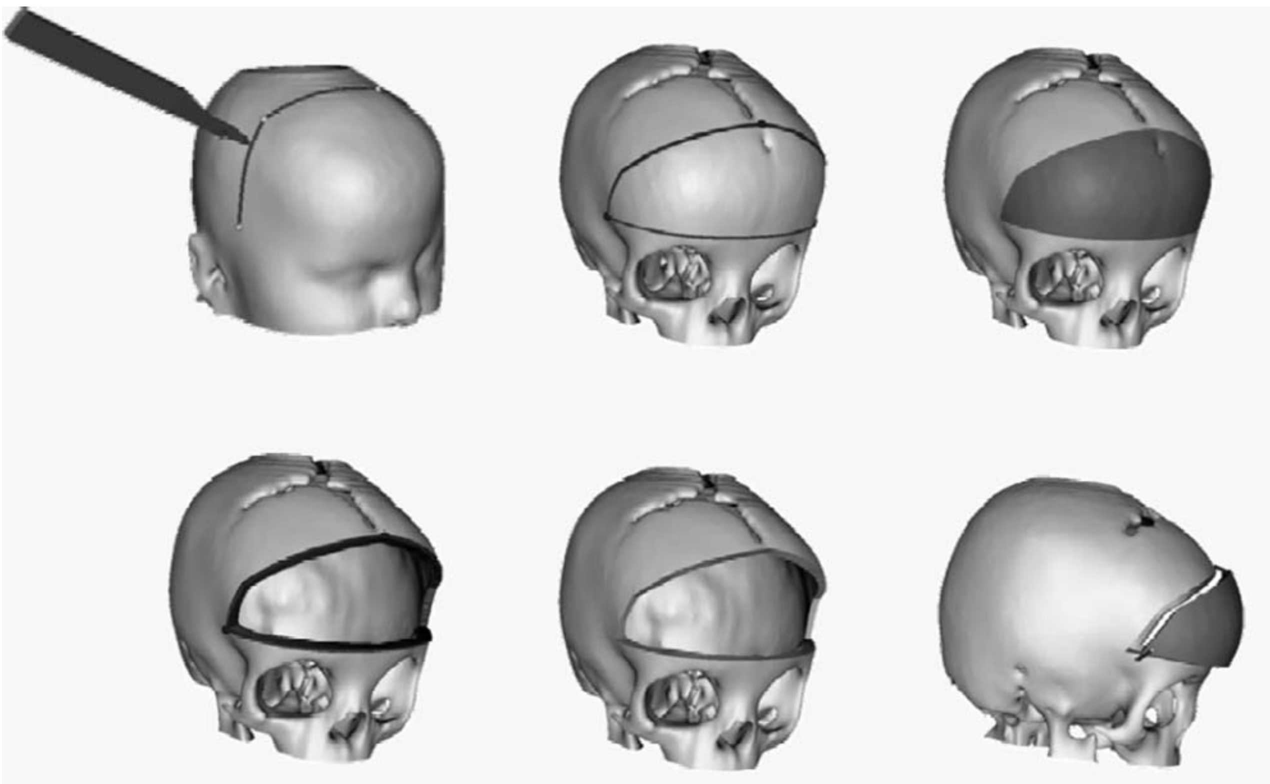

Fig. 2. KasOp/planning of trajectories

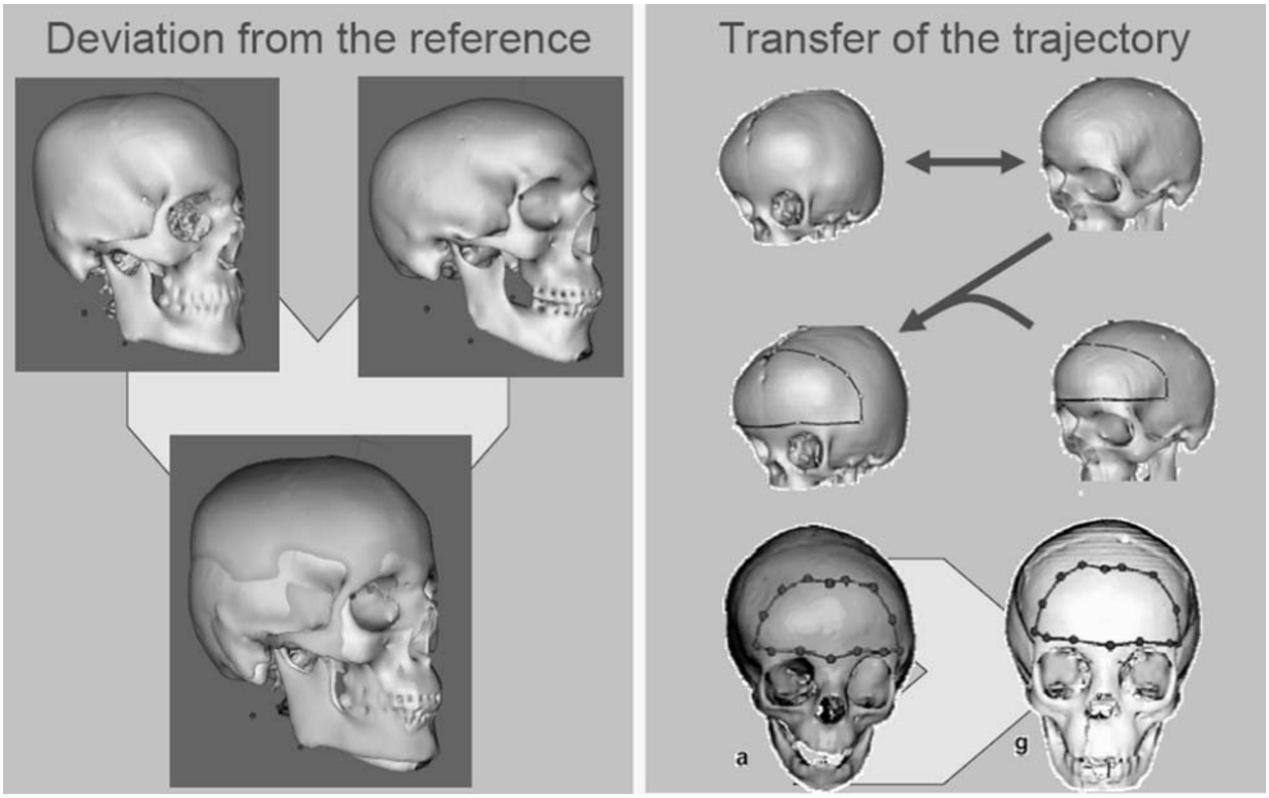

Fig. 3. KasOp/application of reference-data

the head of the real patient and calculates the transformation of the coordinates between the virtual model of the patient and the real patient. In the SFB 414 three registration possibilities were evaluated [2]. First, a marker based registration system is used (see Fig. 4). Preoperatively, at least three to four titan mini screws are inserted in the skull of the patient. Afterwards, images of the patient are acquired in order to segment the screws. Intraoperatively, these screws are localized with an optical 3D-navigation system or the interactively moved robot in order to calculate the transformation between the virtual patient (DICOM data or planning system coordinate system) and the real patient (coordinate system in the OR). With this marker based registration method a high accuracy of 0.5 mm is achieved.

Second, there was the wish to have a non-invasive registration method. For this, in the SFB 414, a non-invasive markerless registration method with surface matching has been developed at the IPR. The system of the surface scanner contains a common video projector and two cameras which all have a photogrammetric calibration. To generate a 3D point cloud of the patient's skin a sequence of stripe patterns (coded light) is projected. The resulting scan point cloud can be matched to the preoperatively segmented surface of the diagnostic image data (CT, MRI) on which the surgical plan was defined (see Fig. 5). A global matching algorithm assures that two surfaces which are touching each other have at least three contact points. This fact reduces the search space to three dimensions and accelerates the matching time. After the global search an Iterative Closest Point algorithm calculates the transformation between the planning data and real patient. In laboratory environments the maximum deviation is less than 1 mm. Quality of the scanning and matching results are depending strongly on the surface.

Third, a new registration concept for intraoperative imaging in head surgery was developed by the IPR and MAQUET company [3]. It uses the MAQUET AWIGS (Advanced Workplace for Image Guided Surgery) system, which is a synthesis of an operating table, a radiolucent patient transfer board and an intraoper-

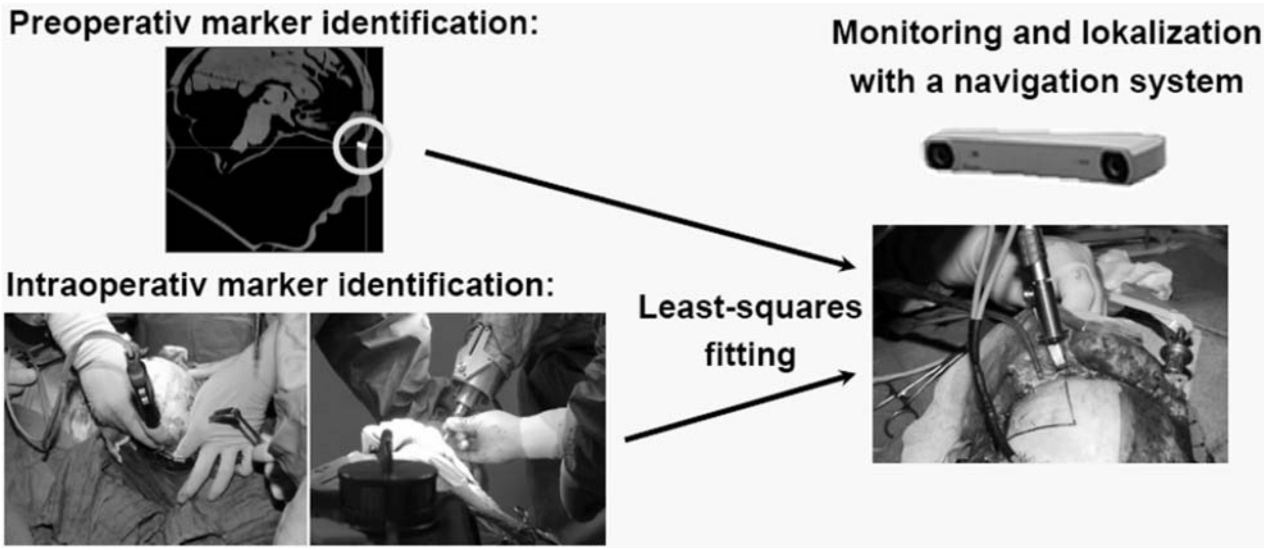

Fig. 4. Marker based registration of the skull

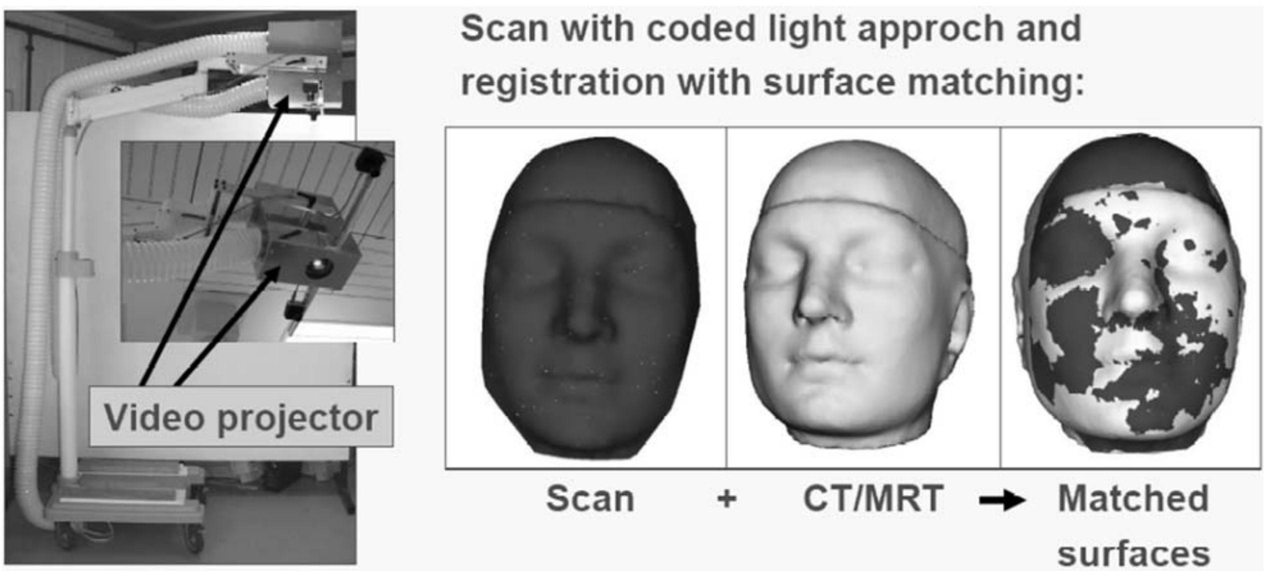

Fig. 5. Non-invasive markerless registration with surface matching

ative Computer Tomograph (CT). Automatic registration works with the DICOM data from the CT and the image based detection of a scan reference frame (SRF). An automatic algorithm searches fiducials in the tresholded and binarized image data and calculates a transformation. This transformation can be used by navigation systems e.g. a mechanical 3D pointing device, which is shown in Fig. 6. Fiducial Registration Errors below 0.35 mm are possible for different pixel-spacings up to 0.8 mm.

Surgical robot

The system RobaCKa (Fig. 7) has been developed in cooperation between the University of Karlsruhe (Institute for Process Control and Robotics) and the Ruprecht-Karls-University Heidelberg (Department for Oral- and Cranio-Maxillofacial Surgery) [4]. It is based on the platform of a former CASPAR robot that was adapted for use in CMF surgery and enhanced by a redundant control architecture to improve

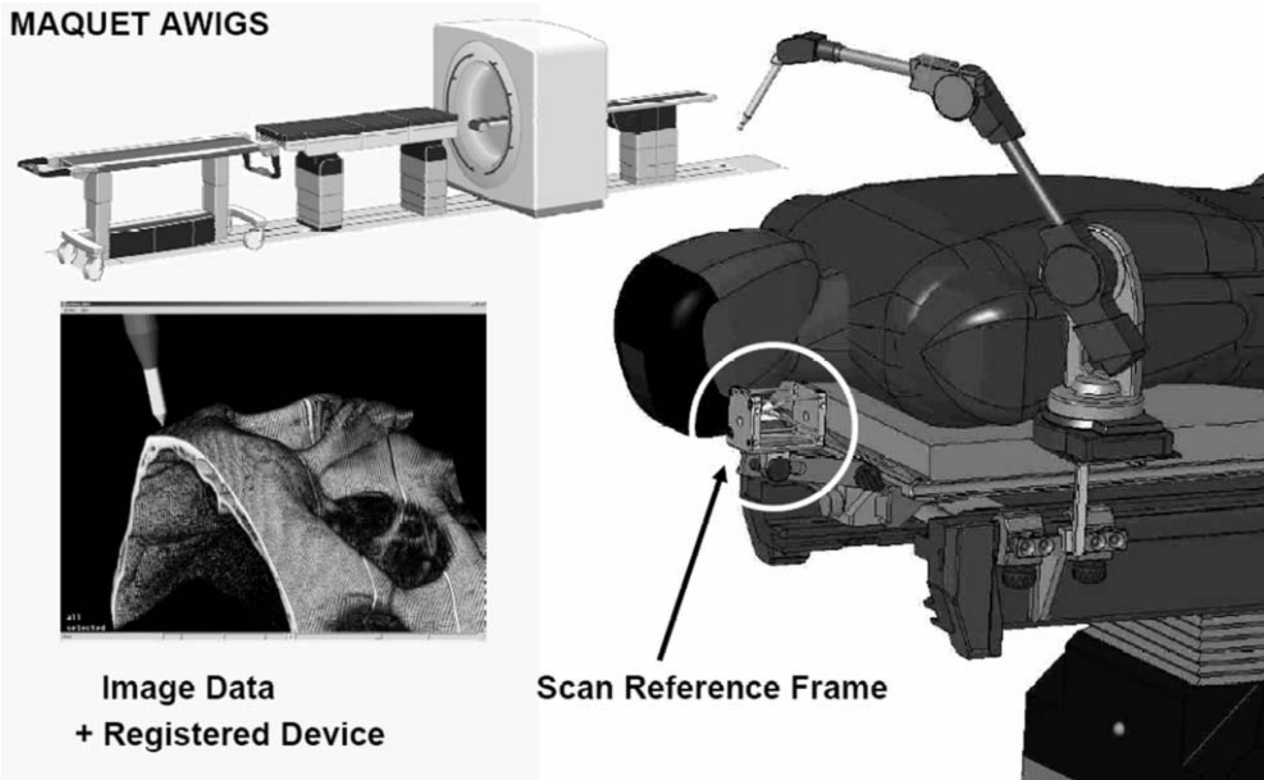

Fig. 6. Automatic registration with intraoperative image data

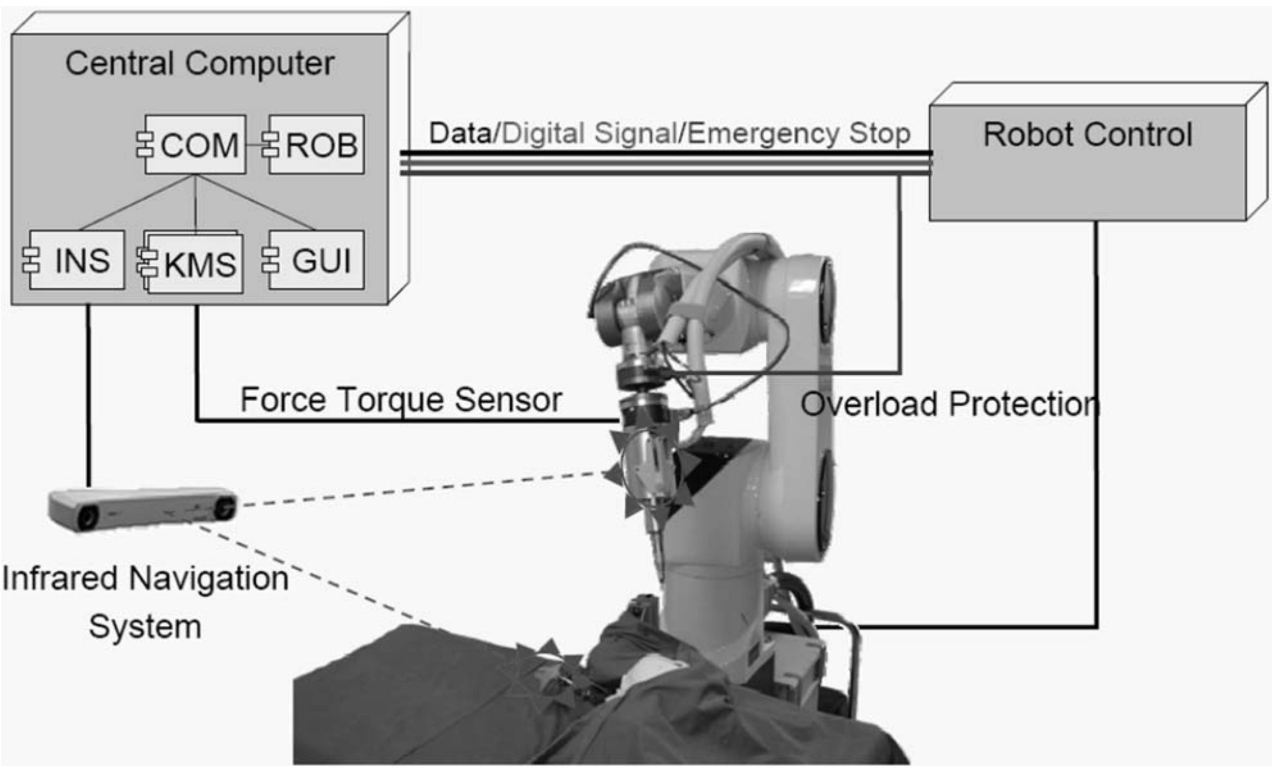

Fig. 7. Architecture of the assistive robot system RobaCKa

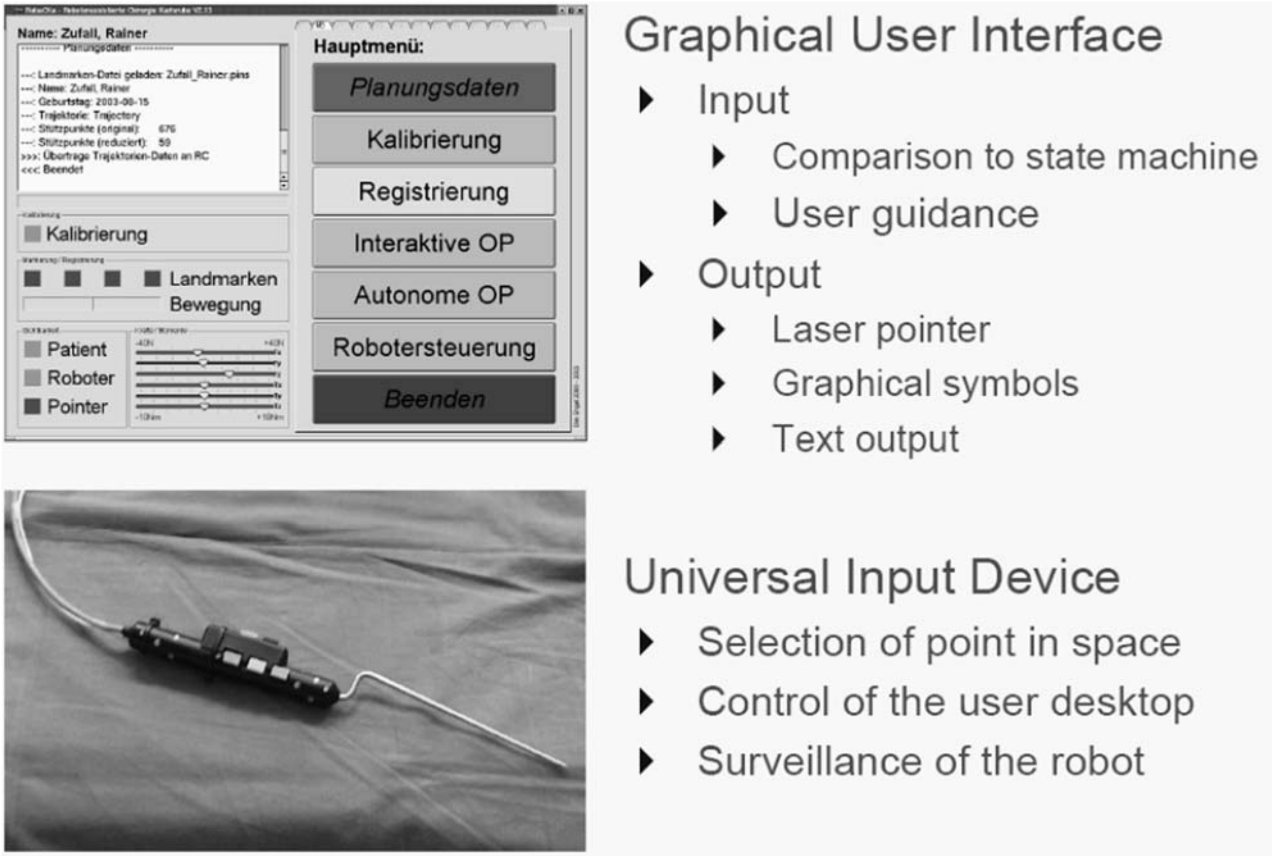

Fig. 8. Human machine interface of the robot system RobaCKa

safety. The control system includes the proprietary robot control, an infrared navigation system, a force-torque-sensor and an overload-protection. The supervision and sensor-fusion is managed by a central computer running a realtime operating system. The positions and orientations of the milling cutter are controlled by the robot controller and monitored for safety reasons by the infrared-navigation system redundantly during the whole intervention. The robot only performs slow movements and adjusts the speed during the milling process according to the measured forces (feed control). The surgeon has to confirm the movement by pressing two confirmation buttons. One button is directly connected to the robot's emergency circuit. If the button is released, the robot's power supply is completely cut within milliseconds and no movement is possible. The control of the robot system during surgery is supported by a graphical user interface (GUI). It is very simple and has only a minimum of menus and buttons (see Fig. 8).

When RobaCKa is used, the surgical workflow includes the following steps:

Data acquisition
First four titanium screws (fiducial landmarks) are implanted into the patient's head for later intraoperative registration. Then computer tomography images are taken.
Segmentation and model generation
For intuitive trajectory planning, the generation of 3D-models is required. These models are segmented from the CT slices.
Planning and simulation
The model is used for the surgical operation planning with "KasOp". The final path is transmitted to RobaCKa's control computer. Even for people who are experienced with robot's kinematics, it is difficult to find a valid position without constraints in moving around the milling trajectory. Therefore an algorithm was developed supporting the planning of the robot's

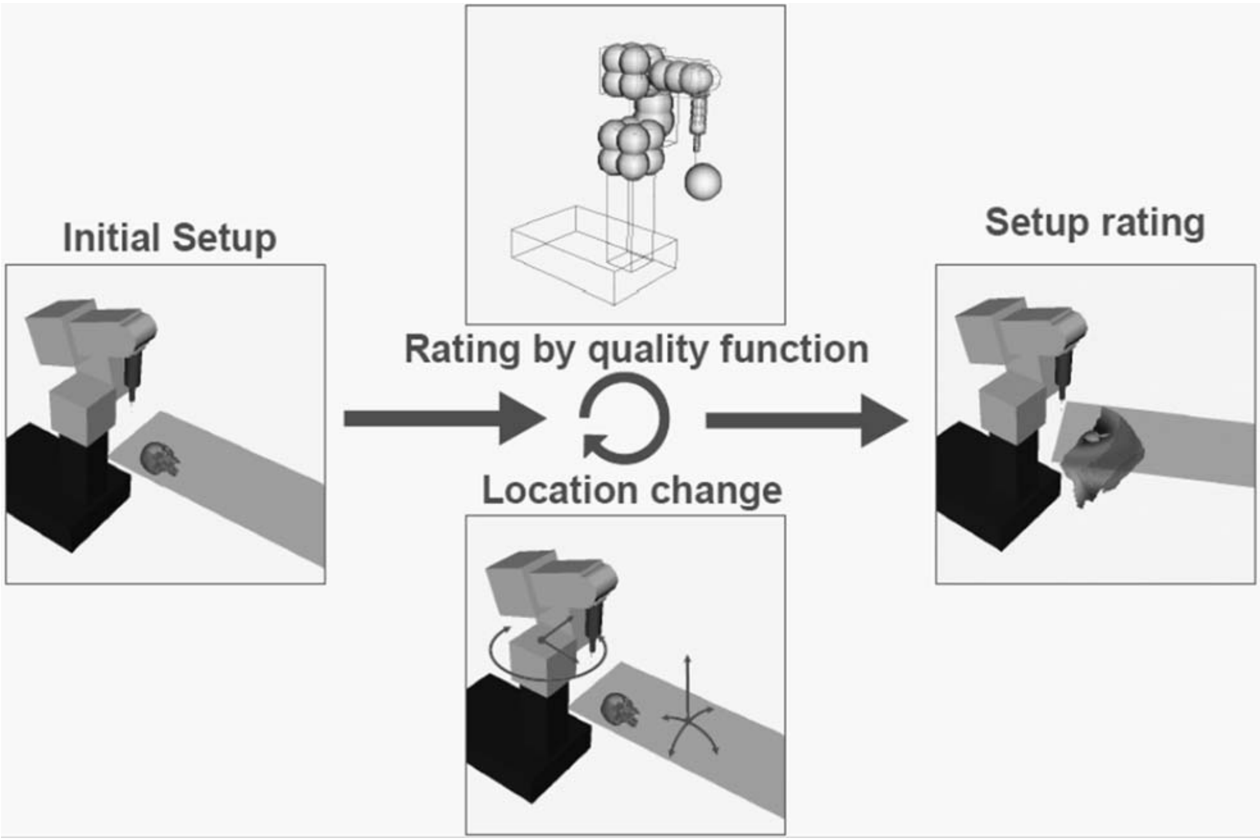

Fig. 9. Simulation system for localisation decision of the robot

location in relation relative to the patient and therefore to the operating table. This algorithm takes into account: (1) Reachability of the trajectories interpolation points (2) not close to singularities (3) collision of robot with patient (4) consideration on the operative approach and patient's position on the operating Table (see Fig. 9).

Patient fixation

It is necessary to fix the patient's head during milling by the robot. The proper fixation of the patient is supervised by the navigation system. If a movement is detected, the robot will be stopped immediately.

Registration

In robotic surgery it is necessary to register the image coordinate system, the patient coordinate system and the robot coordinate system. In RobaCKa this is performed by a two-step registration method (see Fig. 10). First the four fiducials are detected by a navigated pointer within the infrared-navigation system's coordinate frame. These coordinates are transformed to the image frame by determination of a transformation matrix with a least squares algorithm. Then the system checks out whether the robot can reach the fiducials and the trajectory on each interpolation point. In the second step the robot moves automatically close to the pin (the approximate position is already known from the first registration step), then the surgeon guides interactively the instrument's tip into the fiducial's cone. For this the force-torque sensor is used. Determination of transformation is again performed by the least-squares method.

Milling

Is supervised by the infrared navigation system, the force-torque sensor, and the surgeon, who has to push the dead man buttons (see Fig. 11). In our experiments 50% maximum of the skull's thickness is removed by the robot, the rest is milled by the surgeon conventionally. This is done for safety reasons because image processing is not accurate enough.

Validation

The infrared-navigation system's and force-torque sensor's data are recorded during the complete milling

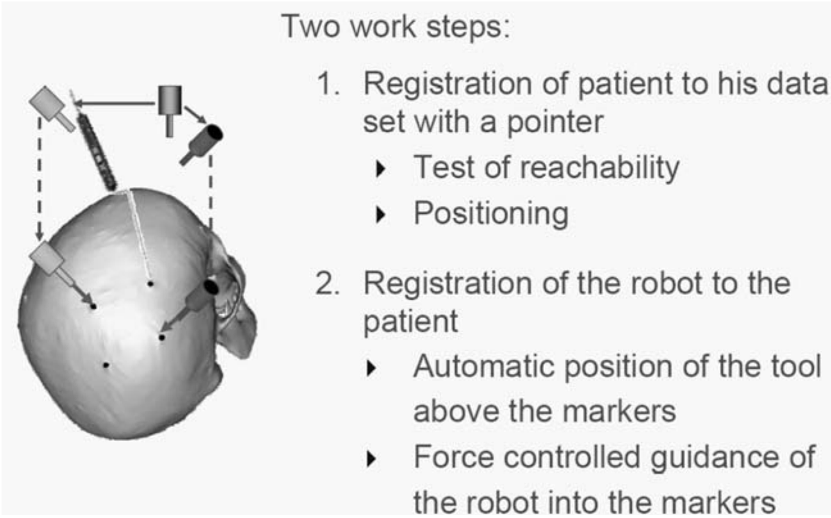

Fig. 10. Registration of patient and robot to patient's data set

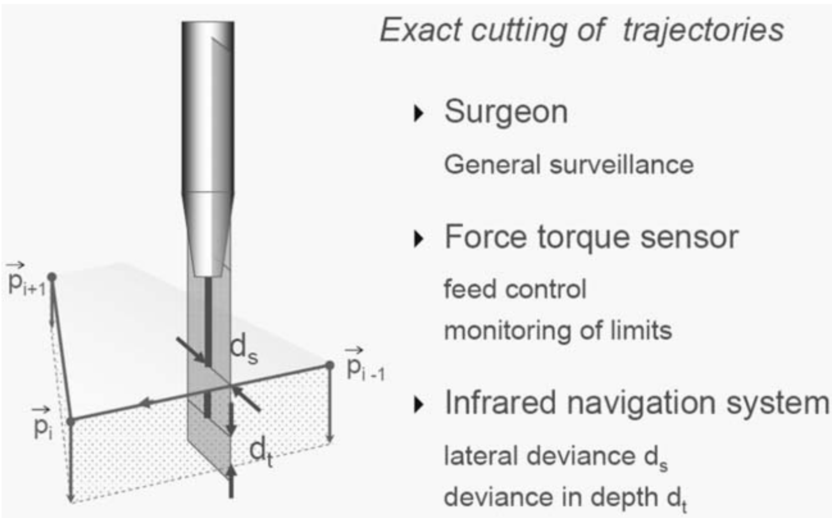

Fig. 11. Monitoring in autonomous operating mode of the robot

process as are the intervention steps that are called from the GUI. All of this data can be evaluated and analysed later on.

In April 2003 a patient with a lesion of unknown origin in the petrous bone was treated with the RobaCKa system. A transfrontal approach was chosen to remove the lesion. Therefore first a bicoronal incision and preparation of the periost was done. Then the robot was used to perform the craniotomy of the bony skull.

The RobaCKa system has proven the feasibility of robots in the operating room, although for milling the use of one of today's robots is yet too cumbersome. New technologies like laser ablation offer completely new opportunities in robot-based surgery. Here, the guidance by a robot is a precondition, because the laser beam has to be positioned far more steadily than it is possible for a human (see Fig. 12). The IPR is performing research in this field.

3D-augmented reality for an operating microscope

In order to assist the surgeon, a 3D-augmented reality system for an operating microscope is being devel-

Fig. 12. Oulook/laser cutting with robots

oped at the IPR in cooperation with the head surgery department of the University of Heidelberg [1]. Figure 13 shows the principal concept of the augmentation of virtual anatomic structures into the situs. Two display units are attached to the operating microscope. Their images are injected into the microscope via beam splitters. The operating microscope is being observed by a navigation system. As can be seen on the right side of Fig. 13, two microoptical benches are attached to the operating microscope. At the top of each microoptical bench a microdisplay is integrated. The images being shown by the microdisplays are taken from two virtual cameras, which are positioned by the calibration procedure. The virtual cameras generate the 3D view of artificial objects which shall be superimposed to the view of the surgical field.

Figure 14 shows the process model for an intervention using an operating microscope and augmented reality. The process model is divided into two parts, a preoperative and an intraoperative phase. In the preoperative phase we regard general processes that have to be executed before the surgical intervention can take place. The calibration has to be accomplished every time the microoptical bench is mounted onto the operating microscope. This process will determine all camera parameters including the correction of optical errors which are generated by 'non perfect' lenses.

In the preoperative phase, patients' image data e.g. from magnetic resonance imaging (MRI) or additional functional magnetic resonance imaging (fMRI) are required. In the process of segmentation a reference surface model is segmented manually. The reference model as well as the MRI data has to be matched onto the patient's anatomy. This is done by the registration process using the navigation system.

In the intraoperative phase it is intended to acquire new patient's image data for example intraoperative MRI or ultrasound to readjust the planning data.

The current reference model is used for collimation into the microscope's optics. Finally the Model is visualized using the Visualization Toolkit and overlaid onto the operating situs.

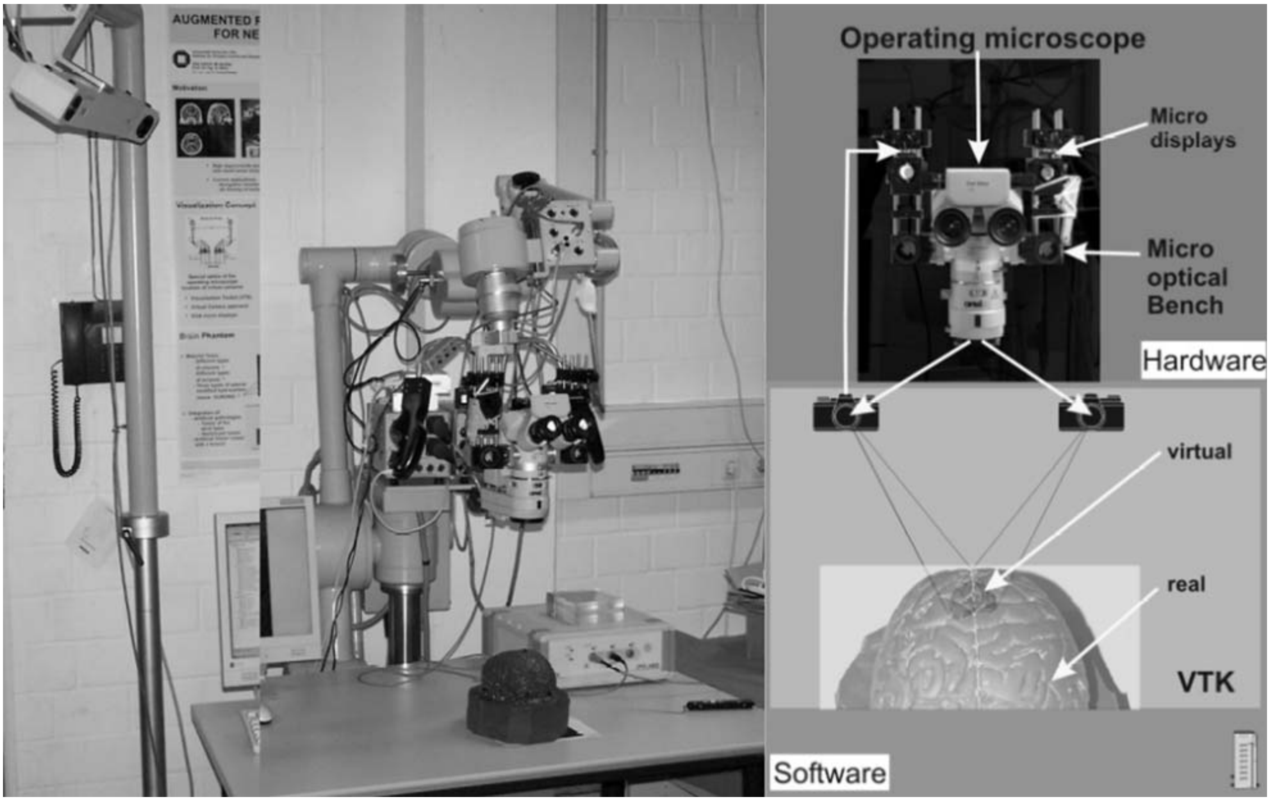

Fig. 13. Concept of the 3D-augmentd reality system for an operating microscope

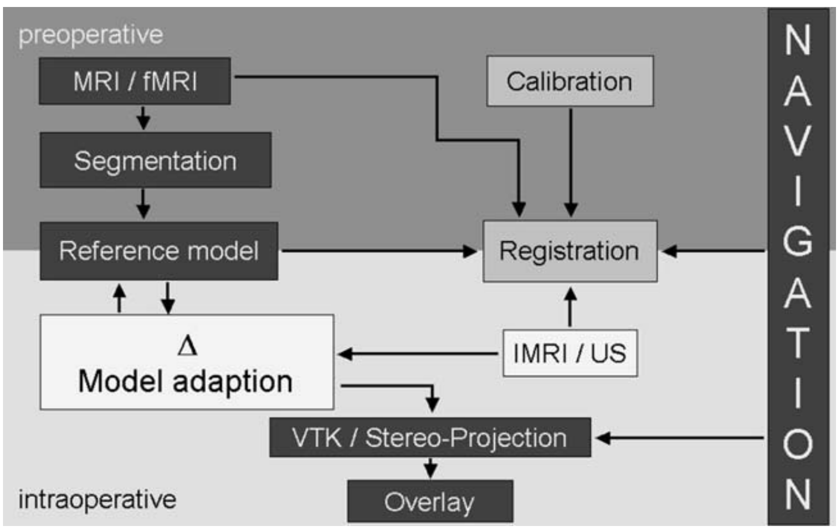

Fig. 14. Process model for an augmented reality microscope based intervention

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The current reference model is used for collimation into the microscope's optics. Finally the Model is visualized using the Visualization Toolkit and overlaid onto the operating situs.

Conclusion

New methods and devices for computer and robot based head surgery are presented. A computer based planning system for CMF-surgery allows the surgeon to plan complex trajectories on the head of the patient for operations where bone segments were cut out and shifted. Different registration methods have been developed and tested. A surgical robot system for bone cutting on the head has been developed and evaluated at the patient in the operating theatre. In future, laser cutting of bones with a robot will be seen as a new powerful method for robot based surgery. A least, a 3D augmented reality system will assist the surgeon in the future by augmenting virtual anatomical structure into the situs.

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Telecontrolled micromanipulator system (NeuRobot) for minimally invasive neurosurgery

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Summary

Background. To perform less invasive neurosurgery, a telecontrolled micromanipulator system has been developed and applied to clinical situations. Basic experiments for telesurgery have also been conducted.

Method. A cadaver head was used to carry out surgical simulation of the opening of the sylvian fissure and third ventriculostomy. After obtaining permission from the Ethical Committee of Shinshu University School of Medicine, part of the recurrent meningioma in a 45-year-old man was removed. As basic experiment for telesurgery, surgical simulation was also conducted in a rat brain with the operating console transported to a hospital 40 km distant from the University.

Findings. Opening of the sylvian fissure and third ventriculostomy were accurately performed. Tumour removal in a patient with recurrent meningioma was safely achieved. Surgical simulation in the rat brain was accurately and correctly carried out, operated on from a hospital 40 km distant.

Conclusions. The NeuRobot, telecontrolled micromanipulator system, can be used as a tool for less invasive neurosurgery.

Keywords: Microsurgery; minimal invasiveness; micromanipulator; surgical robotics.

Introduction

With the recent advancements in neuroendoscopy, less invasive neurosurgery has been conducted for deep-seated lesions. The neuroendoscope is the "surgeon's eye" to see deep into the operating field, but it does not have "surgeon's hands" which can perform sophisticated operative procedures; it can only do simple tasks such as grabbing, fenestrating with occasionally one working channel. We have developed a surgical robotics system, a telecontrolled micromanipulator system, which we coined "NeuRobot" to conduct sophisticated surgical procedures for deep-seated lesions [4–6, 8]. In this paper, we describe basic functions of the system, surgical simulations using a cadaver head, clinical application, and also discuss on telesurgery.

Materials and methods

This is a master-slave manipulator system, and it was designed so that a surgeon operates the slave manipulator by controlling three levers on the operation-input device, master manipulator, while watching a three-dimensional (3D) monitor (Fig. 1). The micromanipulator, part of which is inserted into the operating field, has a thin tubular cylinder of 10-mm diameter, and three microinstruments of 1-mm tip were installed therein (Figs. 2, 3). Each microinstrument has three degrees of freedom: rotation, neck swinging, and forward/backward motion. The range of movement of the swing of the neck is 0 to 90 degrees, and the minimal movement is less than 20 micrometers/driving motor pulse. There are five small holes in the tubular cylinder available for irrigation and suction. Various types of microinstruments can be used as surgical tools including microforceps, micro-hook, micro-needle, laser tip. They can be exchanged during surgery. Two of the three microinstruments can be used as a pair of bipolar coagulator, which were connected to the amplifier of the commercially available bipolar coagulator system [7].

A cadaver head was used to conduct surgical simulation. Opening of the sylvian fissure and third ventriculostomy were carried out.

After obtaining permission from the Ethical Committee of the Shinshu University School of Medicine, the NeuRobot was applied in a patient with a recurrent tentorial meningioma. Part of the tumour was resected with this system.

Preliminary experiment of telesurgery was carried out with the operating console transported to an affiliated hospital 40 km away from the University, and the operating console and the slave manipulator were connected with a light fiber. The surgical simulation was performed on a rat brain.

Results

Cadaver experiment

The right frontotemporal craniotomy was made and the dura mater was opened with standard surgical procedures in the cadaver head, the slave manipulator was

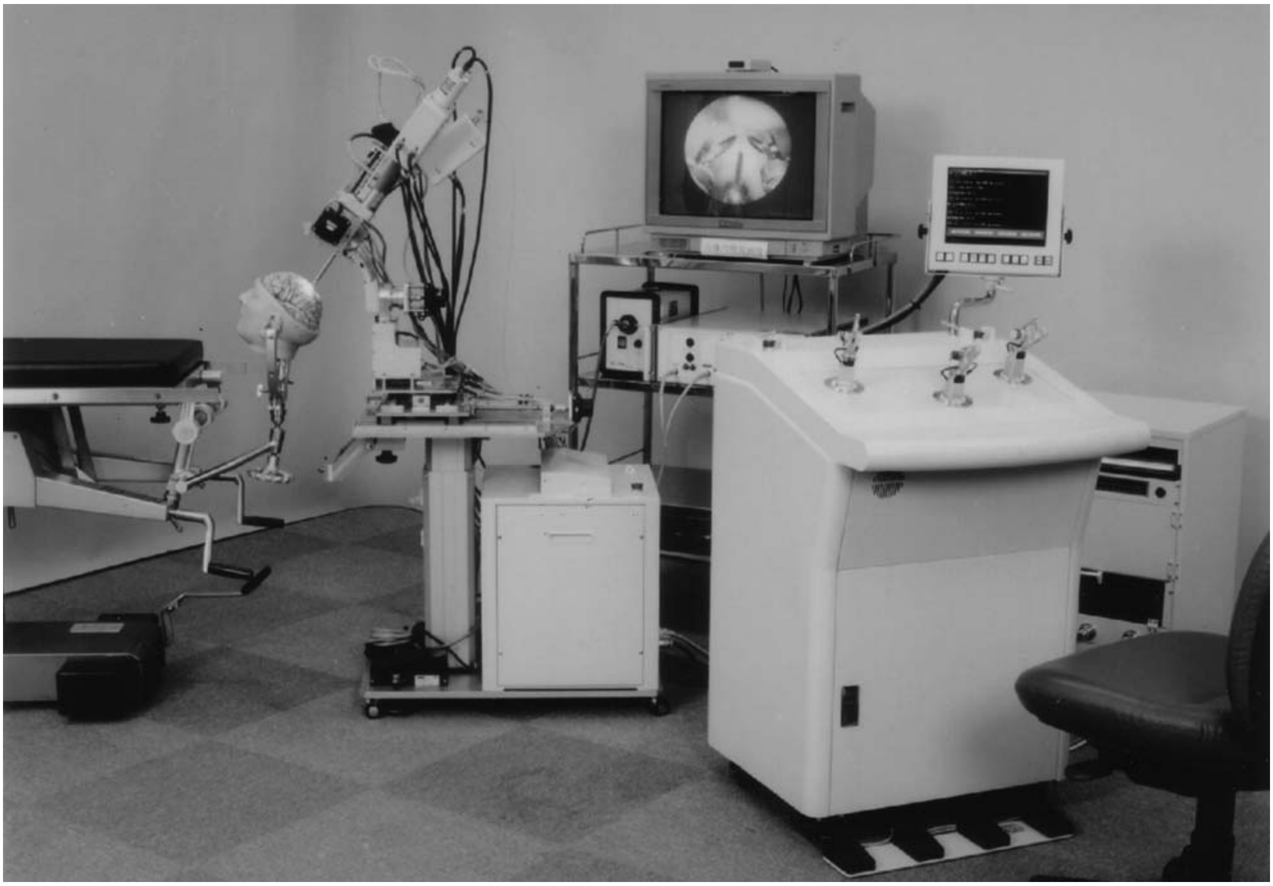

Fig. 1. Photograph of the NeuRobot system consisting of operating console, monitor and slave manipulator fixed in the supporting device

introduced to the surface of the brain over the sylvian fissure. The arachnoid membrane of the sylvian fissure was incised with a micro-needle and the cut edges of the arachnoid membrane were held with two micro-forceps. The slave manipulator was slightly shifted anteriorly and deeply, and the arachnoid membrane was further dissected with using two micro-forceps. The sylvian fissure was thus opened widely in a stepwise fashion, the right optic nerve and internal carotid artery were then adequately exposed.

Through a burr hole in the right frontal bone and a small cortical incision, the slave manipulator was introduced into the right lateral ventricle. The micro-forceps were advanced to the third ventricle, the floor of the third ventricle was incised and opened with two micro-forceps. The opening in the third ventricular floor was widened by pulling-apart the opened floor with two micro-forceps. The prepontine cistern was visible beneath the opening, the third ventriculostomy was completed.

Clinical application

In a 45-year-old man who had a recurrent meningioma of the cerebellar tentorium, the superficially located part of the tumour was partly resected with the use of NeuRobot. Under general anaesthesia, parietal craniotomy was carried out and the dura mater was opened. The slave manipulator was set over the surface of the brain, the border of the tumour was dissected from the surrounding normal cerebral cortex with using two micro-forceps. A small portion of the tumour was then resected using a laser. The remaining larger part of the tumour was removed with conventional microsurgery. There were no complications related to the use of NeuRobot.

Telesurgery

The surface of the rat brain was exposed. The slave manipulator was controlled with an operation input

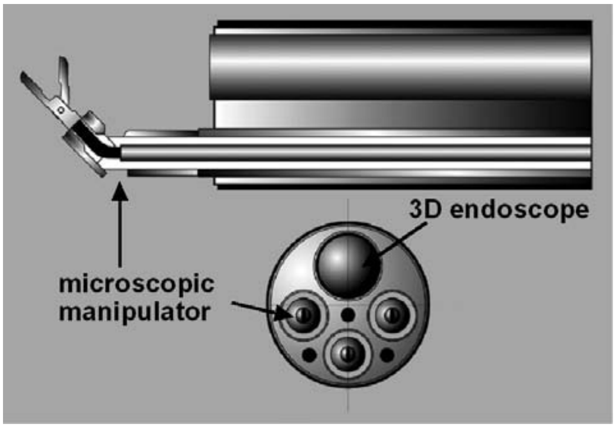

Fig. 2. Schematic drawing of the slave manipulator. The diameter of the tube is 10 mm, the tip of the microinstrument is 1 mm, and the diameter of the endoscope is 4 mm

Fig. 3. Photograph of the tip of the slave manipulator. Three micro-forceps are installed, which are exchangeable during surgery

device placed in a hospital 40 km away from the University. The surgeon using the NeuRobot cut the pial vessels of the cortical surface with controlling the levers, and haemostasis was achieved by shifting two micro-forceps close to the bleeding point. The bleeding point was coagulated and haemostasis was completed.

Discussion

In the present study, the NeuRobot was confirmed suitable as a surgical tool that can safely and accurately be used to conduct sophisticated surgical procedures such as holding, cutting, dissection from normal structures, and so on. Not only for superficially located lesions, but also for deep-seated lesions such as intraventricular lesions, the system was confirmed appropriate. Third ventriculostomy is currently a standard technique for obstructive hydrocephalus, and the neuroendoscope has been used for this purpose [2, 3, 11]. Fenestration of the floor of the third ventricle, however, can be achieved with the NeuRobot micromanipulator more safely and more accurately than with the neuroendoscope, which has only one working channel and opening of the floor is performed with a balloon catheter pushed in and balloon inflated. With our system, the floor of the third ventricle was safely fenestrated without injury to the basilar artery and its perforating arteries located beneath the fenestrated portion, the prepontine cistern.

Telesurgery has previously been reported in fields other than neurosurgery [1, 9, 10]. Relevant issues for telesurgery are security of signal transmission and delay of surgical procedures. In the present study, we used a light-fiber line that had been installed between the University and the remote hospital exclusively for this purpose. There were no signal interferences. Regarding a possible delay in performing surgical procedures, surgical simulation can be done without any difficulty. It must be clarified with how much delay surgical procedures can be carried out without difficulty.

The NeuRobot, telecontrolled micromanipulator system, can be utilized for carrying out sophisticated surgical procedures in a less invasive way. Further developments are needed for achieving more maneuverability.

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Usefulness of intraoperative magnetic resonance imaging for glioma surgery

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Summary

Background. Radical resection of gliomas can increase patient's survival. There is known concern, however, that aggressive tumour removal can result in neurological morbidity. The objective of the present study was to evaluate the usefulness of low magnetic field strength (0.3 Tesla) open intraoperative magnetic resonance imaging (iMRI) for complete resection of glioma with emphasis on functional outcome.

Methods. From 2000 to 2004, 96 patients with intracranial gliomas underwent tumour resection with the use of iMRI in Tokyo Women's Medical University. There were 50 men and 46 women; mean age was 39 years. Tumour volume varied from 1.2 ml to 198 ml (median: 36.5 mL). Resection rate and postoperative neurological status were compared between control group (46 cases, operated on during the initial period after installation of iMRI), and study group (50 most recent cases, in whom surgery was done using established treatment algorithm and improved image quality).

Findings. Overall, mean resection rate was 93%, and medial residual tumour volume was 0.17 ml. Total tumour removal was achieved in 44 cases (46%). Compared to control group, resection rate in the study group was significantly higher (91% vs. 95%; $P < 0.05$), whereas residual tumour volume was significantly smaller (1.7 mL vs. 0.025 mL; $P < 0.001$). Nine patients in the control group (20%) and 24 in the study group (48%) experienced temporary postoperative neurological deterioration ($P < 0.01$), however, the rate of permanent morbidity evaluated 3 months after surgery did not differ significantly between the groups investigated (13% vs. 14%).

Conclusions. Use of iMRI during surgery for intracranial gliomas permits to attain aggressive tumour resection with good functional outcome. Nevertheless, surgical experience with the iMRI system, establishment of treatment algorithm, and improvement of image quality are of paramount importance for optimal results.

Keywords: Glioma; surgery; outcome; intraoperative MRI; intraoperative neuronavigation; intraoperative brain mapping.

Introduction

Gliomas are the most frequent primary brain tumours, management of which is extremely challenging. Despite advances in modern treatment modalities, including resective surgery, radiotherapy, chemotherapy, and immunotherapy, outcomes of patients with malignant gliomas remain poor. Furthermore, there is still significant controversy with regard to the goals of surgical resection [12, 25]. Some believe that since the relationship between resection rate and patient prognosis has not yet been established [7, 23], the possible benefit of radical removal of tumour is overshadowed by the relatively high risk of postoperative neurological morbidity. At the same time others argue that correlation between resection rate and prognosis has sufficiently been defined [1, 8, 14, 15] and that total tumour removal is the most effective treatment for malignant glioma.

Regardless of this controversy, most investigators agree that better demarcation of the tumour border in the eloquent areas of the brain would result in an increased resection rate with reduced risk of postoperative neurological deterioration. The objective of the present study was to evaluate the usefulness of low magnetic field strength (0.3 Tesla) open intraoperative magnetic resonance imaging (iMRI) for complete resection of glioma with emphasis on functional outcome.

Methods and materials

From 2000 to 2004, 244 neurosurgical procedures with the use of iMRI were performed in Tokyo Women's Medical University. Ninety-six patients had resection of intracranial glioma and these cases were selected for the present retrospective analysis. The vast majority of procedures were performed by the same neurosurgeon with subspecialization in surgical neuro-oncology (Y.M.). Informed consent was obtained before surgery from each patient and his/her nearest family member. Resection rate and postoperative neuro-

Table 1. *General clinical characteristics of 96 patients with intracranial gliomas operated on with the adjunct of the iMRI system*

Case characteristics	Total cohort (N = 96)	Comparative subgroups		P-value
		Control group (N = 46)	Study group (N = 50)	
Mean age ± SD (years)	39 ± 16	39 ± 18	40 ± 15	P = 0.78*
Gender (men/women)	50/46	22/24	28/22	P = 0.43**
Tumour (initially diagnosed/recurrent)	66/30	26/20	40/10	**P = 0.04****
Tumour WHO histological grade				P = 0.25**
– I	3 (3%)	2 (4%)	1 (5%)	
– II	27 (28%)	10 (22%)	17 (34%)	
– III	33 (34%)	15 (33%)	18 (36%)	
– IV	30 (31%)	16 (35%)	14 (28%)	
Tumour functional grade§				P = 0.39**
– I	16 (17%)	7 (15%)	9 (18%)	
– II	29 (30%)	17 (37%)	12 (24%)	
– III	51 (53%)	22 (48%)	29 (58%)	
Median tumour volume in mL (95% CI)	36.5 (28.7–43.9)	35.5 (19.8–46.1)	41.3 (26.7–52.4)	P = 0.52*

* According to Student's t test; ** according to chi-square test; bold: statistically significant difference ($P < 0.05$), § Sawaya functional grade; grade I (non eloquent), grade II (near eloquent), grade III (eloquent) [26].

logical status were compared between control group (46 cases, operated on during initial period after installation of iMRI), and study group (50 most recent cases, in which surgery was done using established treatment algorithm and improved image quality).

General clinical characteristics

General clinical characteristics of patients are presented in Table 1. There were 50 men and 46 women; mean age was 39.0 years (range: from 6 to 78 years). Initially-diagnosed neoplasms were found in 66 cases, whereas recurrent neoplasms were seen in 30. Sixteen tumours (17%) were located in the non-eloquent areas of the brain (Sawaya functional grade I) [26], 29 (30%) in near eloquent areas of the brain (Sawaya functional grade II), and 51 (53%) in eloquent areas of the brain (Sawaya functional grade III) [26]. The tumour volume varied from 1.2 ml to 198 ml (median: 36.5 ml).

Typing and grading of gliomas were done according to criteria of the World Health Organization (WHO) classification. There were 29 glioblastomas multiforme, 19 anaplastic astrocytomas, 15 diffuse astrocytomas, 7 anaplastic oligoastrocytomas, 6 oligodendrogliomas, 5 oligoastrocytomas, 4 pilocytic astrocytomas, 3 pleomorphic xanthoastrocytomas, 2 anaplastic ependymomas, 2 ependymomas, and one subependymoma. Three tumours (3%) corresponded to WHO grade I, 27 (28%) to grade II, 33 (34%) to grade III, and 30 (31%) to grade IV. In 3 recurrent cases histological typing and grading of tumour were not possible due to presence of extensive radiation necrosis.

Intraoperative MRI and MR compatible operating devices

The internal organization of our "intelligent operating theatre" is presented on Fig. 1A. MRI was selected as an intraoperative imaging method, because it provides excellent spatial resolution without radiation exposure [13]. Intraoperative MRI scanner (AIRIS II, Hitachi Medical, Tokyo, Japan, Fig. 1B), as available at Tokyo Women's Medical University, has a disc-shaped permanent magnet with a magnetic field strength of 0.3 Tesla and a gantry gap of 43 cm in width. Low magnetic field strength creates narrow 5-gauss line, and the patient can easily be moved outside of the field but still remaining in the operative theatre, which permits to use some conventional surgical devices (for example, high-speed drill). Nevertheless, all surgical devices and instruments that are used within the 5-gauss line, such as operating table (MOT2000-MRI, Mizuho Ikakohgyo, Tokyo, Japan, Fig. 1C) and operating microscope (MRI-30, Mitaka Kohki, Tokyo, Japan, Fig. 1D), are constructed from non-ferromagnetic material to prevent accidents and avoid image artifacts.

Body coils for the scanning of the abdominal region were used as receiver coil in the control group, while original coils for the scanning of open brain surgery with higher signal-to-noise ratio were developed later on (Head Holder Coil, Hitachi Medical, Tokyo, Japan, Fig. 1E) and used in the study group. Although the field strength of this scanner is low, it can provide images of sufficient quality for identification of residual tumours, and allows generation of 3-D reconstruction images, magnetic resonance angiography (MRA), and cine-MRI.

During surgery MR images were obtained at 3-mm slice thickness (1.5-mm slice intervals, 100 slices) under the following conditions: field of view (FOV), 230 × 230 mm; TR, 27 msec; TE, 10 msec (for T_1-weighted spin echo), and FOV, 230 × 230 mm; TR, 3000 msec; TE, 120 msec (for T_2-weighted turbo). An MRI contrast agent (gadolinium diethylenetriamine pentaacetic acid) was administered intravenously at 0.2 ml/kg in the control group and at 0.4 ml/kg in the study group. Scanning duration was 3 min and 36 sec for T_1-weighted images and 5 min for T_2-weighted images. All MRI data were displayed on the in-room display screen.

Intraoperative "real-time" update neuronavigation

A surgical navigation system (PRS navigator, Toshiba, Tokyo, Japan, Fig. 1F) was used in 35 recent cases to facilitate tumour removal and detection of its remnants. The navigator was based on a conventional infrared location-identification device, which shows the location of the suction tip and position of the suction tube in 3 sectional planes. Navigation DICOM format files of MR images were transferred to a computer through a local area network. Images were available for use in less than 5 minutes after MR scanning.

Surgical procedure

In 84 cases surgery was performed with patients in the supine position, whereas 12 patients were in prone position. After induction of

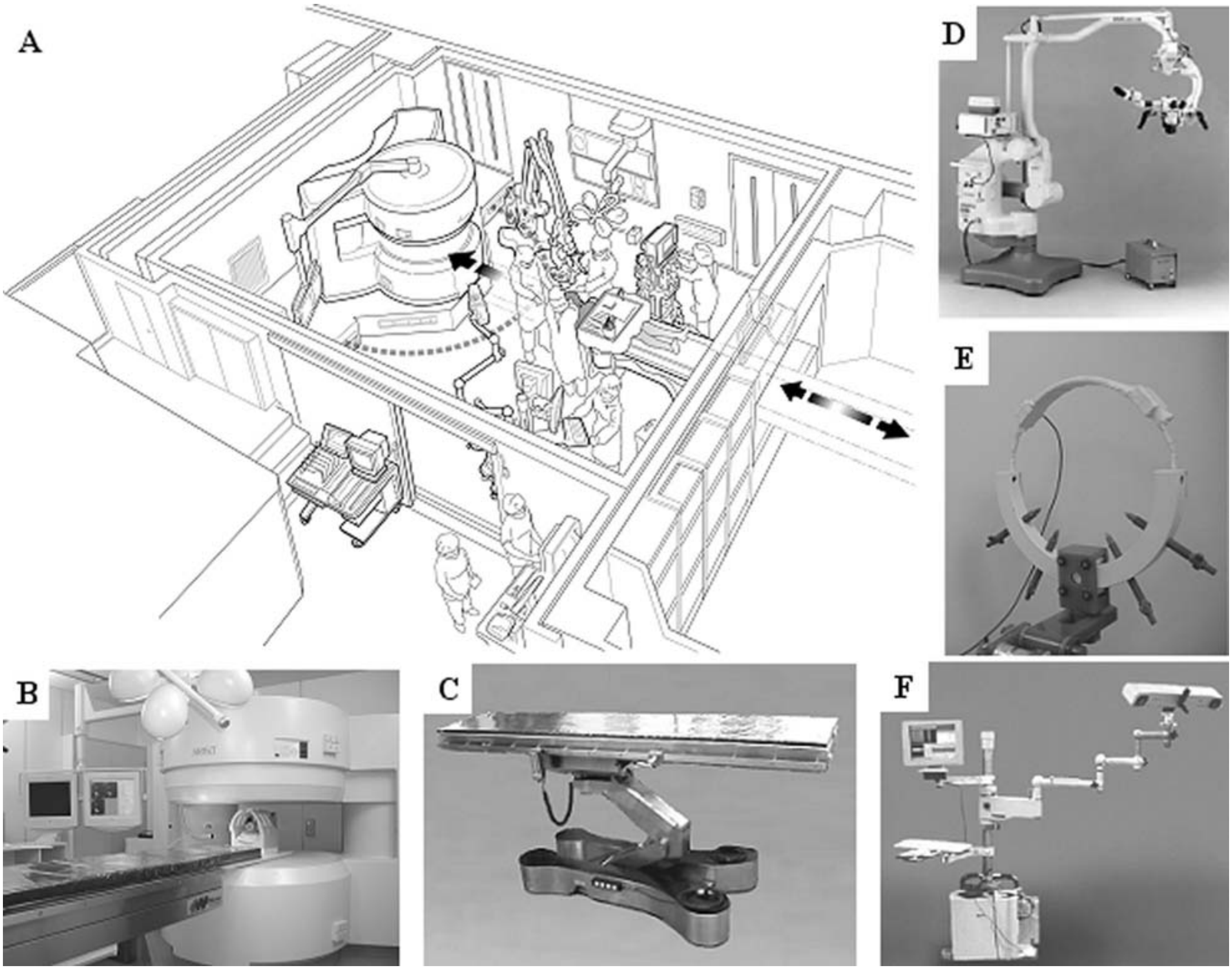

Fig. 1. The internal organization of the "intelligent operating theatre" at the Tokyo Women's Medical University: general view (A) with marked 5-gauss line (*dotted line*), 0.3 Tesla open iMRI (B), MR-compatible operating table (C), MR-compatible operating microscope (D), original receiving coil for scanning of open brain surgery (E), surgical neuronavigation system (F)

anesthesia, the patient head was fixed in a four-point head holder coil. Craniotomy was performed in a usual manner, followed by opening of the dura mater and arachnoid. Thereafter, fiducial markers were fixed to the skull, the covering coil was connected to the four-point head holder coil, and the operating table was covered with the second transparent drape. Patient's head was moved in the center of the MRI gantry by sliding the upper portion of the operating table. MR imaging was performed, and data were transferred onto a computer for further neuronavigation. The fiducial markers were registered in the computer, which permitted use of "real-time" update neuronavigation during tumour removal.

If the tumour was located near or in eloquent brain areas, cortical mapping, neurophysiological monitoring, and/or stimulation of the cranial nerves were performed – as appropriate before resection of neoplasm – for identification of the motor area, speech area, cranial nerves and its nuclei. Somatosensory evoked potentials (SEP) and motor evoked potentials (MEP) were routinely monitored during surgery.

After removal of the neoplasm, iMRI was performed again to assess the completeness of tumour resection, identification of the residual neoplasm or possible adverse effects such as haemorrhage. If residual tumour was identified and considered suitable for additional resection, the newly obtained MRI data were transferred to the navigation computer and further resection of the neoplasm was performed using this updated information. When resection of the tumour was completed, final iMRI was done to evaluate the resection rate.

Such treatment algorithm permitted us a more precise orientation in the operative field compared to conventional neuronavigation systems, which are based on MR images obtained before surgery and constitute a risk for possible mislocalization errors due to brain shift after removal of CSF and the tumour itself [18, 19].

Outcome evaluation

Comparative evaluation of neurological signs and symptoms was done before surgery, within 2 weeks after tumour resection, and 3 months thereafter.

Comparison of pre- and post-operative MRI was performed to assess resection rate and residual tumour volume. The latter was defined as an area of increased signal intensity on contrast-enhanced T_1-weighted images [28], or, if the tumour did not show contrast enhancement, as an area of increased signal intensity on T_2-weighted images corresponding to the defined mass lesion. An area of abnormal signal intensity was computed for each slice and multiplied by the slice width (1.5 mm), and a cumulative value was obtained by adding the values for the individual slices.

Statistics

Statistical analysis was performed using Statview 5.0 (SAS Institute, Cary, NC). The level of significance was determined at $P < 0.05$.

Results

In all cases second iMRI permitted to identify the residual tumour, and additional resection was performed whenever possible (Figs. 2 and 3). If according to intraoperative brain mapping or neurophysiological monitoring the residual tumor infiltrated eloquent brain structures, it was left *in situ*. Overall, total tumour removal was achieved in 44 cases (46%), mean resection rate was 93 ± 10%, and median residual tumour volume was 0.17 ml (95% CI: 0–0.93 mL) (Table 2). Residual tumour volume was greater in neoplasms of higher histological and functional grade, but such trends did not reach statistical significance (Wilcoxon signed-ranks test or ANOVA).

Early surgical complications included 2 cases of wound infection (2%) (Table 3). No case of postoperative haemorrhage occurred. Immediately after surgery 16 patients (17%) showed improvement in pre-existing signs and symptoms, 63 (66%) remained unchanged, whereas 33 (34%) exhibited more or less prominent neurological deterioration. Therefore, total short-term morbidity was 36%.

At 3 months the neurological status of 13 patients (14%) still remained worse than before surgery. In long-term follow-up one patient died due to infection, while another one exhibited deep pulmonary embolism. Therefore, total long-term morbidity was 14% and mortality 2%.

A comparison of the two groups of patients revealed their compatibility in clinical characteristics. At the same time, resection rate in the study group compared to control group was significantly higher (91% vs. 95%; $P < 0.05$), whereas residual tumour volume was significantly smaller (1.7 mL vs. 0.025 mL; $P < 0.01$) (Table 2). The number of cases with total removal was also higher in the study group as compared to the control group (52% vs. 39%), but this difference did

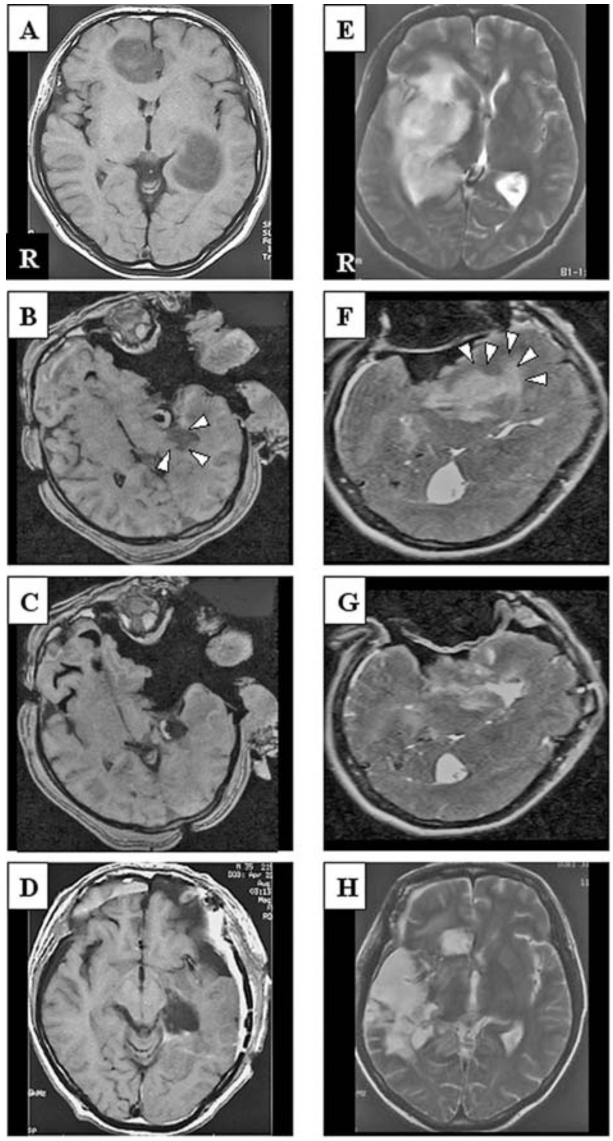

Fig. 2. Identification of residual tumor by iMRI and its further aggressive resection. In Case 1 (*left column*) primary multiple cerebral astrocytomas in the right frontal lobe and left (dominant) hippocampus (A) were removed during surgery, but residual tumour in the left hippocampal tail (*arrowhead*) was disclosed by control iMRI (B), and was removed thereafter (C) with total removal confirmated on postoperative MRI (D); the patient had transient aphasia but no permanent neurological deficit. In Case 2 (*right column*) a giant glioblastoma in the right fronto-temporal lobe, insular cortex and basal ganglia (E) was removed during surgery, but residual tumour (*arrowhead*) in the insular cortex and deep frontal lobe was identified (F) and subtotally (97%) removed (G), which was confirmed by postoperative MRI (H); the patient did not have motor deficit after surgery

not reach statistical significance. Further subgroup analysis showed that residual volume of WHO grade IV tumours (4.6 ml vs. 0.05 ml; $P < 0.05$) and neoplasms of Sawaya functional grade III, located in

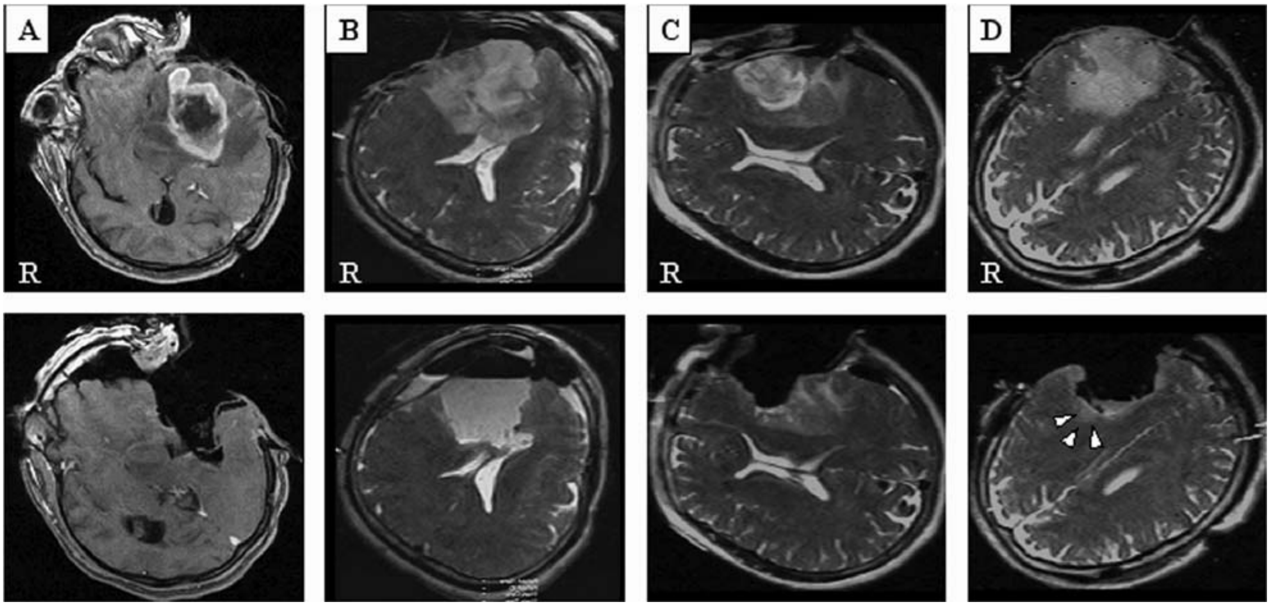

Fig. 3. iMRI before (*upper row*) and after (*lower row*) aggressive resection of gliomas located in or near eloquent brain areas: 99% removal of malignant (WHO grade IV) tumour from the left temporal lobe and insular cortex (A); 100% removal of the tumour (WHO grade II) with contralateral extension through the corpus callosum (B); 97% removal of the tumour (WHO grade III) located in the Broadmann area 44 (classical Broca zone) (C); 98% removal of the tumour (WHO grade III) located in the right parietal lobe in the vicinity of the pyramidal tract (D) with preservation of functionally important brain tissue (*arrowhead*)

the eloquent areas of the brain (3.8 ml vs. 0.23 ml, $P < 0.05$), as well as resection rate of the latter (88% vs. 95%, $P < 0.05$) were significantly improved in the study group compared to the control group (Table 2).

Nine patients in the control group (20%) and 24 in the study group (48%) experienced temporary postoperative neurological deterioration ($P < 0.05$) (Table 3). However, the rate of permanent morbidity, which was evaluated 3 months after surgery, did not differ significantly between the groups investigated (13% vs. 14%) (Table 3).

Discussion

Using intraoperative MRI

First iMRI systems were introduced in 1997 by Black *et al.* [3] and Tronnier *et al.* [32, 36]. Since then, such devices have been used for real-time observation of surgical manipulations, for assessment of the extent of tumour resection, and evaluation of the intraoperative complications. Different modifications include a twin theatrer system developed by Tronnier and Steinmeier *et al.* [29, 32], a rotatable patient table system introduced by Rubino *et al.* [24], a ceiling-mounted movable MR gantry system presented by Sutherland *et al.* [30], and high-field (1.5-Tesla) hamburger-type MR gantry system used by Nimsky *et al.* [21]. While intraoperative observation and guidance of surgery by iMRI are theoretically presumed to produce the most favorable outcomes, the available devices usually provide relatively narrow working space and necessitate all surgical devices and instruments to be composed of non-ferromagnetic materials. By contrast, systems that employ MR imaging at some temporary break points during surgical procedure, while labor and time increase for patient transfer to the MRI venue, can provide a higher degree of freedom to the surgeon and permit to use standard (not MR-compatible) surgical instruments. It should be noted that any type of iMRI system increases the operation time, because MR imaging by itself is a time-consuming process.

Hadani *et al.* [11] previously reported experience with compact mobile 0.15 Tesla MRI. Such system has definite advantages in terms of cost-performance, but needs a special magnetic shield to prevent artifacts and limits space for surgical manipulations due to narrow MR gantry gap. On the other hand, high magnetic field strength iMRI scanners can provide higher image

Table 2. *Surgical outcome in 96 cases of intracranial gliomas operated on with the adjunct of the iMRI system*

Surgical outcome parameters	Total cohort (N = 96)	Comparative subgroups		P-value
		Control group (N = 46)	Study group (N = 50)	
Median residual tumour volume in ml (95% CI)	0.17 (0–0.96)	1.6 (0–4.2)	0.025 (0–0.67)	**P = 0.006***
Median residual tumour volume in ml in regard to WHO histological grade:				
– II	0	0	0	P = 0.10*
– III	0.91	1.6	0.88	P = 0.37*
– IV	0.13	4.6	0.05	**P = 0.02***
Median residual tumour volume in mL in regard to Sawaya functional grade:				
– I	0	0	0	P = 0.07*
– II	0	0.2	0	P = 0.32*
– III	0.93	3.8	0.23	**P = 0.02***
Mean resection rate ± SD (%%)	93 ± 10	91 ± 11	95 ± 10	**P = 0.04***
Mean resection rate (%%) in regard to WHO histological grade:				
– II	94	93	96	P = 0.41*
– III	96	94	97	P = 0.11*
– IV	90	88	92	P = 0.43*
Mean resection rate (%%) in regard to Sawaya functional grade:				
– I	97	93	100	P = 0.06*
– II	94	95	94	P = 0.84*
– III	92	88	95	**P = 0.03***
Number of cases of total removal	44 (46%)	18 (39%)	26 (52%)	P = 0.21**

* According to Student's t test; ** according to chi-square test; bold: statistically significant difference ($P < 0.05$).

Table 3. *Functional outcome after removal of intracranial gliomas with the adjunct of the iMRI system*

	Total cohort (N = 96)	Comparative subgroups		P-value
		Control group (N = 46)	Study group (N = 50)	
Neurological status				
– improved	16 (17%)	11 (24%)	5 (10%)	P = 0.68**
– unchanged	63 (66%)	26 (57%)	37 (74%)	P = 0.07**
– temporary deteriorated	33 (34%)	9 (20%)	24 (48%)	**P = 0.01****
– permanently deteriorated	13 (14%)	6 (13%)	7 (14%)	P = 0.04**
Surgical complications				
– infection	2 (2%)	2 (4%)	0 (0%)	P = 0.14**
– postoperative haemorrhage	0 (0%)	0 (0%)	0 (0%)	–
– venous embolism	1 (1%)	0 (0%)	1 (2%)	P = 0.99**
– pulmonary embolism	1 (1%)	0 (0%)	1 (2%)	P = 0.99**
Total short-term morbidity	35 (36%)	11 (24%)	24 (48%)	**P = 0.01****
Total long-term morbidity	13 (14%)	6 (13%)	7 (14%)	P = 0.89**
Total mortality	2 (2%)	1 (2%)	1 (2%)	P = 0.95**

* According to Student's t test; ** according to chi-square test; bold: statistically significant difference ($P < 0.05$).

quality, shorter scanning time, and variability of imaging options, such as diffusion tensor imaging [20], functional MRI [10], and proton MRS. Image distortion during scanning, however, can cause geometric errors, which can result in suboptimal conditions for neuronavigation during tumour removal. Risk of image distortion is 5 times greater in 1.5 Tesla MR scanner compared to 0.2 Tesla one [9]. It should be also taken into consideration, that maintenance of special conditions for superconductive magnet requires high additional expenses.

Currently in Tokyo Women's Medical University low magnetic field strength (0.3 Tesla) open intraoperative magnetic resonance imaging (iMRI) is used. As it was shown in the present study such system is useful for the resection of intracranial glioma. Moreover, our latest experience shows, that such MR scanner permits to obtain intraoperative diffusion-weighted images for the visualization of pyramidal tracts [22], as well as functional MR images for identification of the motor cortex. Using specially developed coils for the scanning of open brain surgery that provide higher signal-to-noise ratio, represents significant improvement of image quality, especially of contrast-enhanced tumours, which was reflected in a higher resection rate of such neoplasms as reported in the "study group". Novel organization of the neurosurgical operating theatre with low magnetic field strength iMRI permits to perform sophisticated procedures, using conventional surgical devices and instruments. Spatial separation of the operative table and MR gantry and removable head-holder coil provides freedom for any surgical manipulations, which can be done in both supine and prone position of the patient. Therefore, it seems that compared to other available systems our device can have the best cost-to-benefit ratio, if under "benefit" one will accept image quality and system effectiveness.

Extensive removal of glioma

The benefits of resective surgery in cases of glioma include relief of compression of the tumor bulk on the surrounding brain (important for neurological improvement), reduction of the volume of neoplasm (can render adjuvant therapy more effective), and precise histological diagnosis, which is important for the choice of optimal treatment strategy and prediction of prognosis. Many investigators have demonstrated the benefits of complete resection for low-grade gliomas [2, 5, 27], which is in complete agreement with our own experience. Moreover, while not sufficiently proved [12, 25], extensive removal of malignant glioma can improve patient prognosis. According to a retrospective analysis of the brain tumor registry of Japan [31], which included 6398 cases of malignant glioma from 281 different hospitals, survival was longer if total removal of tumor was achieved, compared to subtotal resection or biopsy alone. Similar results were reported by two recent, large, multi-center cooperative trials, in which identical treatment protocols were used. Overall, 6 prospective studies published from 1990 found significant correlation between resection rate of malignant glial tumors and patient survival [1, 7, 8, 14–16, 23]. Therefore, while further well-designed prospective studies on this topic will be needed in future, currently available data suggest that complete resection of glial neoplasms can be considered as a reasonable surgical goal.

Evaluation of residual tumor volume is not a simple task. Albert *et al.* [1] reported that the use of different methods for assessment of the resection rate could significantly influence results. Particularly, the resection rate estimated by the operating surgeon was significantly higher compared to postoperative CT or MRI. Still, there is no standard definition of "complete removal of glioma", which is reflected in the wide variation of reported total resection rates (from 6.2 to 71%) [6, 33]. It may be suspected that some of such cases represent nothing more than biopsy. Our method of postoperative evaluation of residual tumor volume based on the enhanced area of T_1-weighted MR images might be criticized, because autopsy specimens showed that glioblastoma cells can be identified even beyond hyperintense signal on T_2-weighted MR images. However, Wirtz *et al.* [35] and Lacroix *et al.* [17] in their clinical studies assessed the residual tumor in the same way as we did and showed its importance for the prediction of patient survival. For glioblastoma, a resection rate of 98% or greater can be considered as prognostically significant break-point.

Complications after resective surgery for gliomas

Neurological morbidity after resective surgery for gliomas varies from 6 to 28% [4, 34], and may be even higher in cases of recurrent tumors, especially if previous radiotherapy was effected [4]. Overall, 33 patients (34%) of the present series exhibited more or less prominent worsening of their pre-existing symptoms after removal of the brain tumor. Moreover, more aggressive tumor resection, as performed in the "study group", was associated with astatistically significant increase of temporary post-operative neurological deterioration.

Removal of tumors adjacent to the corona radiata and posterior limb of the internal capsule was associated with a higher incidence of neurological morbidity.

Our treatment algorithm, based on "update" neuronavigation, permitted precise orientation in the operative field with a minimal risk of mislocalization errors. Therefore, in our opinion, neurological deterioration encountered in some patients of the present series was mainly caused not by direct injury of the specific anatomical structures, which usually are clearly identified by neuronavigation and subcortical brain mapping, but due to compromise of their vascular supply. Anyway, removal of tumor located in the vicinity of the pyramidal tracts has to be considered high-risk surgery for post-operative neurological deterioration, even if the whole spectrum of the most sophisticated modern neurosurgical armamentarium, including iMRI, is available in the operating theatre.

It has to be noted that not one case of postoperative hemorrhage was found in the present series. Previous reports suggest that such complications occur at a rate of 2–3% after surgery for parenchymal brain tumors [4, 26]. It seems that aggressive tumor resection that can be achieved with the help of iMRI, permits to avoid a condition known as "hemorrhage in the residual tumor" or "wounded glioma syndrome". Additionally, despite relatively longer operative time, the rate of infectious complications in the present series (2%) did not differ from those in other reports.

Conclusions

The use of iMRI during surgery for intracranial gliomas allows identification of residual tumor and performing aggressive resection with good functional outcome. In 49% of cases of the present series total removal of the neoplasm was attained, with a mean resection rate of 93%. Surgical experience with the iMRI system, establishment of treatment algorithm, and improvement of image quality are of paramount importance for attainment of optimal results.

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Intraoperative magnetic resonance imaging in neurosurgery: the Brigham concept

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Summary

The resection of brain tumors is limited by the surgeon's ability to precisely define margins. To overcome this problem, various neuronavigational tools have been used. The development of image-guided navigation systems represents a substantial improvement in the microsurgical treatment of various intracranial lesions. However, a major drawback of this technology is that they use images acquired preoperatively, on which the surgical planning and intraoperative performance is based. As the intracranial anatomy dynamically changes during a neurosurgical procedure, only intraoperatively acquired images can provide the neurosurgeon with the information needed to perform real-time, image-guided surgery. Because magnetic resonance imaging best delineates the soft-tissue extent of most tumors, it currently remains the superior method for intraoperative image guidance. In this review, we outline the development as well as current and possible future applications of the intraoperative MRI (iMRI) unit at the Brigham and Women's Hospital, Boston, MA.

Keywords: Intraoperative MRI; image-guided surgery; real-time imaging; neuronavigation; brain shift.

Introduction

The goal of many intracranial neurosurgical interventions is the accurate localization, targeting, diagnosis, and treatment of an intracranial lesion while minimizing injury to the surrounding neural structures. Frame-based and more recently developed frameless stereotactic localization techniques, which make the use of computed tomography (CT) or magnetic resonance imaging (MRI), are routinely used to guide surgeons to previously imaged and diagnosed brain lesions [3, 4, 18, 28]. Although these computer-assisted surgical navigation techniques have enabled neurosurgeons to access, obtain biopsy specimens, and resect intracranial lesions with great efficiency and added safety, they have several constraints. First, the accuracy of conventional stereotactic surgery requires that preoperative landmarks conform to intraoperative anatomy, but the act of opening the skull and removing tissue invariably results in distortions, shifts, and deformations of the exposed surgical site and surrounding structures [19]. Second, with conventional preoperative imaging techniques, it is not possible to track the advancing biopsy needle (or other surgical instruments) as it passes through brain tissue, nor is it possible to correct the path once the trajectory is defined. Third, during open surgery, the boundaries of some lesions, in particular low-grade gliomas, may be extremely difficult to determine by means of gross visual inspection or manipulation alone. Fourth, after conventional surgery, surgical complications may not be evident for several hours, until the effects of anesthesia are reversed or until the late consequences of a developing hematoma or edema become clinically evident.

The need for an image-guidance technique to address these important issues led to the development of an intraoperative magnetic imaging system [14]. Through an academic-industry collaboration, a vertically oriented, open-configuration, 0.5-T MR unit was developed to allow surgeons to perform intraoperative procedures with direct MR imaging guidance. This system provides near real-time imaging, as well as navigational assistance, during surgical procedures performed in a sterile environment [24].

The continuous visual feedback provided by the system allows neurosurgeons to monitor the accuracy of lesion targeting, determine the extent of resection and changes in anatomic relationships during the procedure, and identify any immediate intraoperative complications. In this article, we review our experience with the open-bore intraoperative MR imaging guidance unit at the Brigham and Women's Hospital, Boston, MA.

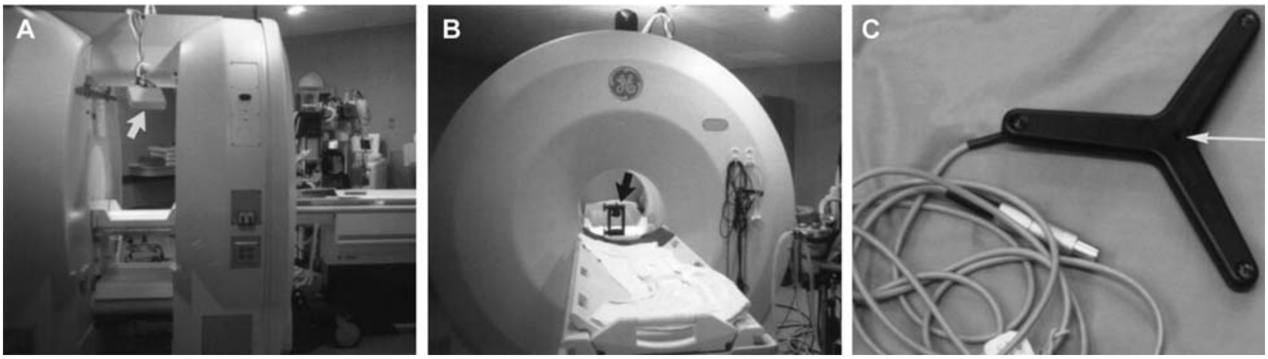

Fig. 1. Open-bore MR imaging system in the operating suite. The 56-cm-wide gap in the magnet allows surgeons access to the patient (A). Two liquid crystal display screens (*arrow*) are positioned overhead. View through the bore of the open-configuration MR imaging system shows the fixed portion of the Mayfield head frame (*arrow*) attached to the table (B). Hand-held optical tracking device (C). Note the three light-emitting diodes located at the ends of the arms of the device; these are used to establish both the plane of imaging and the proposed trajectory of a needle placed through the center (*arrow*) of the device

MR imaging system

The collaboration of surgeons and radiologists from the Brigham and Women's Hospital in Boston, MA with engineers from General Electric Medical Systems led to the development of an open-configuration MRI scanner that allows surgery to be performed with concurrent intraoperative image guidance. The initial research and development phase came to fruition in 1994 with the installation of a prototype 0.5-T MR Imager (Signa SP; GE Medical Systems, Milwaukee, WI). The first neurosurgical procedure was performed in this MRI suite in June 1995. This iMRI unit is commonly referred to as the General Electric "double-doughnut" with two vertically oriented superconducting magnets with radiofrequency coils in two separate but communicating cryostats, resulting in a 56-cm-wide vertical gap at the center of the magnet (Fig. 1A, B). The isocenter of the magnetic field is located midway between the two doughnuts of the open MR system. The modified magnet's field is homogeneous to within 10 ppm in a sphere with a 15-cm radius surrounding the isocenter. A light emitting diode (LED)-based flashpoint navigational system (Flashpoint, integrated technologies, Boulder, CO) is an integrated component of the MRI unit, and provides tracking capabilities within the 3D space at the center of the magnet. This unit differs from all other available intraoperative systems in its capacity for real-time navigation it essentially brings the operating room into the MR machine.

The development of MR-compatible surgical instruments, monitors and ventilators for anesthesia was a prerequisite for this double-doughnut MRI suite. Also, a special microscope was constructed, which is introduced into the vertical gap over the shoulder of the surgeon. Scanning takes places without moving the patient in and out of the magnet. Unlike all other systems, this iMRI suite allows craniotomy within direct intra-operative navigation. This is the most crucial and unique aspect of the double doughnut design. It combines imaging and surgery not only into one room, but also into the same space. The console, the workstation for the real-time scanning and for the software applications are situated outside the shielded MR-suite. A set of images in one plane can be obtained in 60–120 seconds. A two-way audio system and a video camera mounted overhead in the procedure room allow communication between the operators within the MR procedure room and the personnel at the console.

Another important feature of this system was the development of flexible transmit-receive surface coils. These coils are specifically manufactured for use with the iMRI system, so that they can be incorporated into the sterile surgical draping and contoured over the patient's head to allow access to the intracranial lesion through a burr hole or craniotomy [21]. Flexible double-loop surface coils provide radio-frequency excitation from both sides of the patient's head. Access to the patient is gained through a window in the loop or the space between the two loops. This flexibility allows the positioning of patients in the supine, prone, or decubitus position to optimize the approach to the lesion. Coils of two sizes are used: a larger coil (each loop: 22.5 × 23.5-cm inner diameter, 24.0 × 28.0-cm outer diameter) and a smaller coil (each loop: 15.0 × 11.0-cm inner diameter, 20.5 × 17.0-cm outer diameter). The larger coil provides deeper signal penetration and a larger area of coverage but has a decreased signal-to-noise ratio relative to that of the smaller coil. The smaller flexible surface coil is used for smaller, more superficial lesions and provides a higher signal-to-noise ratio. A single-loop coil of similar size is used over the face for imaging during transsphenoidal resection. Intraoperatively acquired MR images are displayed at external consoles and on two 5-inch liquid crystal display (LCD) monitors mounted in the gap of the magnet.

Patients selection

Patients are referred to the iMRI suite for further evaluation of intracranial lesions visualized on previous imaging studies obtained with conventional diagnostic imaging systems at our institution or elsewhere. In all cases, informed consent is obtained after the nature of the proposed neurosurgical procedure and the role in surgery of the iMRI system are fully explained to the patient.

There are several contraindications to surgery in the MRI. Patients are considered to be ineligible for surgery in the iMRI unit if they have an indwelling device that can be affected by the intense magnetic fields of the MR device such as a pacemaker or if they had metallic clips in the brain not known to be nonferromagnetic. Patients with a history of severe coronary disease are also excluded because the magnet can induce distortions in the electrocardiogram, which may obscure any ischemia-related abnormalities [26]. Also excluded are patients who are too large to fit into the bore of the magnet. Any patient with previously demonstrated sensitivity to gadopentetate dimeglumine (Magnevist; Berles, Wayne, NJ) is considered to be ineligible unless the intracranial lesion is known, from prior imaging studies, not to show contrast agent enhancement.

The feasibility of the GE Signa SP system has been established at our institution for use in a variety of procedures [6, 24]. Over 1200 neurosurgical procedures have been performed under iMRI guidance at the Brigham and Women's Hospital in Boston from June 1995 to December 2005 [1, 6]. The intracranial procedures are outlined in Table 1.

Table 1. *Neurosurgical iMRI cases at the Brigham and Women's Hospital (From June 1995 to December 2005)*

	N (total = 1200)
Craniotomy	923
Biopsy	236
Transsphenoidal resection	32
Intracranial cyst	9

Instruments, imaging protocols and procedures

Nonmagnetic materials were used for development and manufacturing of neurosurgical tools: these materials include 300-American Standard for Instrumentation (ASI)-grade stainless steel, titanium, brass, ceramic, and aluminum. Whereas titanium and ASI-200 stainless steel produce substantial artifact, the brass, ceramics, and carbon-fiber tools cause minimal artifact and, therefore, imaging can be performed while these materials are in the surgical field. The head holder (Ohio Medical, Cincinnati, OH) is composed of carbon fiber and therefore is not associated with any distortion in the images. Ultrasonic scalpels (Ethicon, Cincinnati, OH) or selector aspirators (Elekta, Atlanta, GA) are used in the magnet for separating abnormal tissue from normal tissue on the basis of differences in consistency and cohesive forces. High-speed pneumatic drills (Midax Rex, Fort Worth, TX) are similar to those used in conventional operating suites except that the ball bearings are composed of ceramic instead of stainless steel. The MR-compatible bipolar electrocautery system (Codman and Shurtleff, Randolph, MA) is also similar to that used in the conventional setting. Other devices such as intraoperative microscopes (Möller Microsurgical, Waldwick, NJ and Studer Medical Engineering, Rhenfaal, Switzerland); headsets and other light sources (Cogent Light Technologies, Santa Clarita, CA); transsphenoidal resection instruments (Aesculap, San Francisco, CA); electrocardiographic, oxygen saturation, capnographic, and blood pressure monitors (MR Equipment, Bay Shore, NY and Bruker Instruments, Wissembourg, France); the anesthesia machine (Ohmeda, Madison, WI); the ventilator (Omnivent, Topeka, KS); and the peripheral nerve stimulators (Greatbach Scientific, Clarence, NY) were modified for use in the magnet [15, 16, 26, 29].

All instruments were tested according to guidelines established by the manufacturer of the MR unit (MR safety and MR compatibility: test guidelines for Signa

SP; GE Medical Systems) to ensure that the instruments would not be affected by the static magnetic field, magnetic field gradients, or radio-frequency pulses and to ensure that they would not cause noise or artifact on the MR images [13, 17]. Instruments termed "MR safe" exhibit no torque or attraction to the magnet. The microscope and the anesthesia machine and monitors are constructed entirely from nonferromagnetic material. If the instrument was to be left in situ during scanning, it had to be constructed of a material that yielded no or little image artifact. Instrumentation and cables have to be properly shielded so that radio-frequency noise would not be received by the coil and manifested on the images.

The adapted bipolar and aspirator units are placed in a radio-frequency–tight enclosure (GE Medical Systems), which is bolted to the floor inside the magnet room. Custom-made long cables allow the cabinet to be placed outside the 200-G (20-mT) line, beyond which most instruments functioned normally outside the field. The transformers for the anesthesia monitors are placed in an electrical room adjacent to the imager room; to remove radio-frequency noise, the direct-current power cables are filtered through connectors in the penetration panel before they are connected to the monitors. Fiberoptic or carbon-fiber electrocardiographic leads are used to eliminate the risk of burns to the patient [25]. Pulse oximeter monitors are also equipped with fiberoptic leads. Components of the anesthesia machine and ventilator are powered by means of batteries designed for use in the MR environment, as are flashlights, laryngoscope handles, and the peripheral nerve stimulator. Nonconductive lines, such as the fiberoptic cables for the light sources, which are housed in the room adjacent to the imager room, are channeled through wave guides in the penetration panel without increasing the radio-frequency noise level in the imager room. The microscope is housed on a pneumatically powered articulating frame. Although the camera on the microscope functions in the magnetic field, the camera controller unit is placed beyond the 20-mT line.

Interactive image update is accomplished by using a hand-held optical tracking device (Flashpoint; Image Guided Technologies, Boulder CO) mounted with three light-emitting diodes (Fig. 1C); three high resolution infrared-sensitive video cameras located above the isocenter of the magnet are used to detect the emissions of the light-emitting diodes. We use specialized image-guidance software (Realtime Control; GE Medical Systems) implemented at an interactive workstation (model 4/670; Sun Microsystems, Mountain View, CA) [21, 27].

Images are obtained at specified distances from the edge of the localization device to determine an appropriate trajectory in three planes with a resolution of 1 mm. The optical tracking device can also be used as a virtual pointer to outline the extent of lesions or to interactively examine the brain by using multiplanar imaging. After correct localization and virtual targeting, an appropriate burr hole or craniotomy site is chosen.

Stereotactic biopsy

The approach to each lesion is determined by using near real-time imaging. A titianium, 15-cm long, 18- or 20-gauge needle (E-Z EM, Westbudy, NY) that produces minimal artifact and the tracking device are fixed to a flexible Bookwalter arm (J & J Professional and Codman, Raynham, MA), which permit precise control of the needle as it is advanced. Continuous MR imaging with the hand-held optical tracking system allows the operator to maintain a position on an intracranial lesion as a biopsy needle is advanced toward it, and three-dimensional imaging allows the surgeon to avoid important vascular structures and critical intracranial regions. If preprocedural imaging showed the brain lesion to be enhancing, imaging in the open-configuration magnet is performed after injection of gadolinium. T1-weighted fast spin-echo MR images are acquired every 14 seconds. Biopsies of nonenhancing lesions are performed under guidance with a T2-weighted fast spin-echo technique. The accuracy of approach can be gauged in three planes, which thus obviates multiple needle passes. Also, it may not be necessary to await results from frozen biopsy specimens to verify whether the lesion has been sampled (Fig. 2). Our experience is similar to that of Bernays and colleagues [5] who described 114 consecutive frameless stereotactic biopsy procedures aided by open intraoperative magnetic resonance imaging using the GE system. They reported low morbidity and complication rates and a high histological yield, with a mean procedure time of 60 minutes per patient. Our extensive experience with 236 biopsies of lesions located in the brainstem, deep white matter, thalamus, basal ganglia, cerebellum, and cortex indicates that MR imaging provides the accuracy necessary for localization

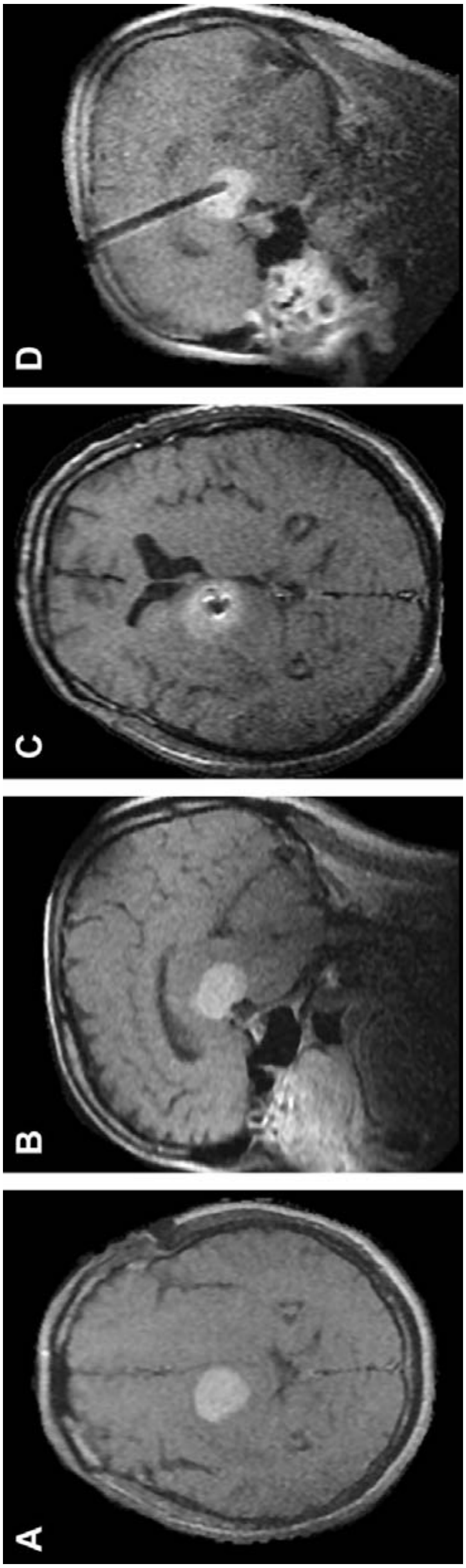

Fig. 2. T1-weighted axial MR images obtained during biopsy of an intracranial mass in a 74-year-old man with left-sided weakness show a homogeneously enhancing right thalamic lesion. The lesion was localized by using the interactive hand-held navigational system (A and B). Axial and sagital images show the tip of the biopsy needle in the target (C and D)

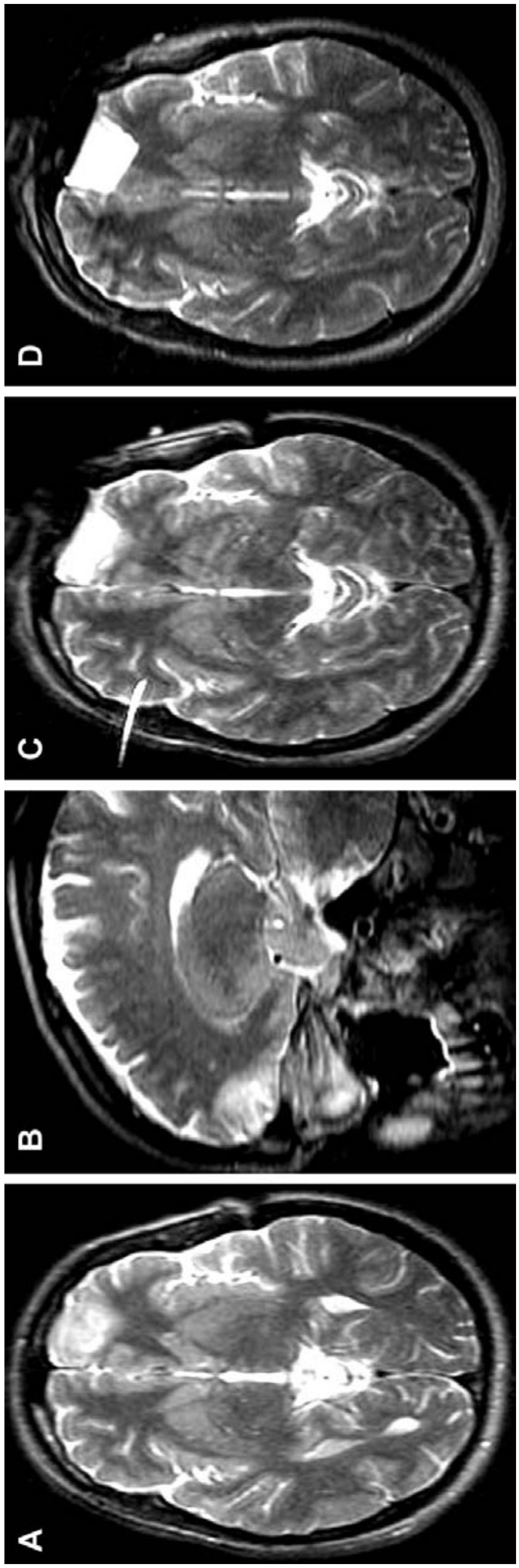

Fig. 3. T2-weighted MR imaging guided resection of a low-grade astrocytoma in a 45-year-old man with recent onset seizures. Axial (A) and coronal (B) MR image shows a well-defined high-signal intensity abnormality in the left frontal lobe. Axial MR image shows the site of craniotomy, which was performed under MR guidance (C). This image shows that after the bulk of the lesion was removed, a small focus of residual tumor, not readily visible to the surgeon, was demarcated in the posterior aspect of the resection margin. Final image obtained after the residual lesion was removed (D)

and safe targeting. Even more important, MR imaging can be used to alter the trajectory as needed during a procedure.

Craniotomy

The implementation of iMRI for craniotomy was a challenge, primarily because of the requirement of a MRI-compatible high-speed drill and an operating microscope. The first craniotomy for resection of a vascular lesion was performed in June 1996 for the excision of a cavernous malformation. The first craniotomy for resection of a brain tumor was performed in a patient with a medial temporal ganglioglioma in August 1996. Subsequently, over 921 additional craniotomies have been performed using the GE Signa SP iMRI unit to treat lesions including intrinsic neoplasms, meningiomas, cavernous malformations, and arteriovenous malformations. The greatest use has been for low-grade gliomas.

A similar protocol is followed in all cases. After informed consent is obtained, the patient is transferred to an MR-compatible operating table, which is then brought into the MR suite. General anesthesia or intravenous sedation is administered in the MR suite. Subsequently, the preprocedural setup is undertaken, which includes positioning of the coil on the basis of preoperative MR images, placement of the pins and head clamp, and preparation of the surgical site. The patient is then moved into the bore of the magnet. Initial imaging at the onset of the procedure allows localization of the lesion in relation to the position of the patient's head. It also provides for the optimal planning of the skin incision, craniotomy flap, and trajectory to the lesion. The skull and dura are opened using standard neurosurgical techniques. Verification of the intracranial location and extent of the lesion is accomplished with MR images obtained in conjunction with the navigational device. The lesion is removed, and serial imaging is acquired as necessary to guide the resection. The margins of resection can similarly be assessed. The intravenous administration of paramagnetic medium can help to determine the extent of resection (Fig. 3). A neuroradiologist is present for the duration of the resection to aid in the interpretation of the acquired images. If intravenous sedation is used, the fixation head rest is applied with a combination of short and long-acting local anesthetic and care is taken to maintain an open view to the patient's face.

Nonenhancing or poorly enhancing lesions, such as low-grade gliomas, are localized by using T2-weighted images; it is assumed that the borders of the area of abnormal signal intensity represent the edges of tumor growth. The surgeon is directed to the margins of high-signal-intensity areas on T2-weighted images in an effort to remove as much abnormal tissue as possible without disturbing eloquent cortical or subcortical regions. For lesions that are enhancing on preoperative MR images, the surgeon is directed to sites of enhancement; in cases in which high-dose radiation therapy had been administered, dynamic imaging is performed to localize sites of early enhancement that might indicate active viable tumor. Regions of increased signal intensity surrounding the enhancing tissue on T2-weighted images, which could represent a combination of infiltrating tumor and reactive edematous changes, generally are not pursued. The radiologist often relies on comparisons with preoperative images to help determine the boundaries of a lesion that remains after partial resection. The extent of resection is continuously evaluated with serial volume updates. It is noted that usually the act of tissue resection does not notably alter either the signal intensity or the contrast-enhancement characteristics of the brain, such the completeness of the resection can be assessed with accuracy. In many cases, foci of tumor inaccessible to the surgeon's restricted view can easily be seen on MR images and then removed under MR imaging guidance.

Transsphenoidal resection

Intraoperative MR imaging also was used for guidance at transsphenoidal resection of pituitary adenoma in 32 patients. Frequent image updates allows the neuroradiologist to depict the progress of surgery and helps the surgeon avoid essential structures such as the cavernous sinuses and optic chiasm.

The extent of resection was continuously monitored. In several patients, residual tumor beyond the view of the surgical microscope was detected on MR images and then completely resected. Dynamic MR imaging is used to distinguish residual tumor from normal gland and postoperative changes. The pituitary stalk and normal gland enhance early after injection, but residual pituitary adenoma tends to enhance only after the first pass of the contrast agent. It should be remembered that on conventional T1-weighted contrast-enhanced MR images, residual adenoma may be indistinguishable from hemorrhage [7]. For this reason, we routinely use gradient-recalled-echo sequences with a long echo time to indicate the presence of hemorrhagic debris.

Intracranial cysts

We also used the open-configuration MR imaging system to investigate intracranial fluid collections. Sixteen patients with intracranial cysts were evaluated after a diluted solution of gadopentetate dimeglumine was injected into the cyst or surrounding CSF spaces [23]. In twelve patients, no communication between the cyst and the subarachnoid space was demonstrated. Nine cysts were drained while the patient was positioned in the magnet, which resulted in resolution of the preoperative symptoms.

Imaging of surgical materials

Imaging during surgery requires adequate recognition of the appearance of various materials used during surgery. Sterile compressed sponges appear as curvilinear signal voids on T1-weighted images, whereas cotton balls are of intermediate intensity (if a gadolinium-based agent is injected, they increase in signal intensity on T1-weighted images as these materials tend to absorb blood. Surgical cellulose fabric, which often is placed in a surgical cavity to absorb blood, is left in place and resorbed; this tends to become stained with blood and, therefore, to appear similar to free blood on gradient-echo images obtained with a long echo time, but the absence of a fluid level or mass effect should help distinguish such fabric from hemorrhage.

Hyperacute hemorrhage

Heme-susceptibility gradient-recalled-echo imaging is used to determine the presence of acute hemorrhage. To assess for the presence of acute hemorrhage during and after the procedure, images through the surgical cavity are obtained through the resection bed by using short echo time (9 msec) and long echo time (60 msec) gradient-recalled-echo images. T2-weighted images are obtained as well. Foci of hypointense signal, which "bloom" on the long echo time image but are not apparent on the T2-weighted image, are considered to represent deoxyhemoglobin in an area of acute hemorrhage. If such a collection is noted to exert mass effect on surrounding brain or to be rapidly increasing in size, it is removed under MR imaging guidance.

Discussion

Improved resection with intraoperative neuroimaging

The advantages of iMRI guidance in achieving more complete and more accurate resection of neoplasms by craniotomy have been demonstrated in many cases. Perhaps the most important aspect of intraoperative MR imaging is the ability to visualize the MR image–delineated boundaries of a tumor during surgery. At conventional surgery, the surgeon's view of the brain surface through the craniotomy is restricted, and deeper structures can be visualized only after the more superficial tissue has been removed. Intraoperative MR imaging provides an accurate depiction of the entire surgical volume during the procedure and, even more importantly, allows updating of the changing anatomic relationships as the procedure progresses. This near real-time guidance can limit the damage to functionally intact, normal brain tissue. The open-bore magnet developed at the Brigham and Women's Hospital provides immediate imaging feedback to the surgeon, in contrast to MR systems that require the patient to be withdrawn from the magnet for surgery and advanced back into the magnet for imaging. Some of the other iMRI systems, however, are high-field (1.5-T and 3.0-T) imagers that can provide images with better resolution and can be used with more rapid imaging sequences than those that are possible with an open-bore 0.5-T magnet [1, 9].

Surgical outcome

The margins of brain lesions usually can be delineated more accurately with MR imaging than with direct visual inspection. Low-grade astrocytomas are nonenhancing lesions that generally have well-defined margins on T1- and T2-weighted images. Nevertheless, these tumors are difficult to distinguish intraoperatively from normal brain; thus, there is a tendency for surgeons to be conservative and to perform incomplete tumor resections, especially in the vicinity of eloquent cortex. We recently reviewed our experience with 156 patients who underwent surgical resection of a unifocal, supratentorial, histologically-confirmed low-grade glioma (WHO grade I or II) in the MRI suite

[8]. The 1-year, 2-year, and 5-year age-adjusted and histologic-adjusted survival rates for patients who underwent resection using iMRI were significantly higher than the rates reported using national data bases. This study suggested a possible association between surgical resection and survival for patients with low-grade glioma resected under intraoperative MRI guidance.

Radical resection

High-grade gliomas (anaplastic astrocytomas and glioblastomas) tend to enhance heterogeneously, indicating a breakdown of the blood-brain barrier. This is a useful characteristic that generally indicates the presence of tumor in untreated cases. However, these lesions tend to infiltrate brain tissue without evident enhancement, and the margins of such a tumor may be difficult to assess visually or with imaging methods. Peritumoral edema may be extensive, but it generally is not possible to determine whether the edema is reactive or the edematous tissue contains malignant tumor cells. Although there have been conflicting reports about the value of extensive cytoreductive surgery in high-grade gliomas, Albert and coworkers [2] indicated that in patients who have undergone resection of a high-grade glioma, the presence of residual enhancing tissue was correlated with decreased patient survival. We therefore generally attempt to delimit the enhancing perimeter of a high-grade intracranial tumor and to direct the surgeon to these margins while avoiding eloquent cortical regions. In many of our cases, MR imaging demonstrated the presence of residual tumor that was invisible to the surgeon. Our experience with surgery of high-grade gliomas is in keeping with the findings of Nimsky and colleagues [20] who reported that the use of iMRI increased radicality in glioma surgery without additional morbidity. However, whether this can translate into a survival advantage over conventional surgical methods still remains to be proven [12].

Radiation-induced changes

In patients in whom high-dose radiation therapy was administered to control cellular growth, marked gliosis may result, with enhancement and edema. Under these conditions, the MR image characteristics of radiation change can be indistinguishable from those of recurrent tumor [11]. In this situation, we have used intraoperative dynamic contrast-enhanced MR imaging to help with the intraoperative determination of sites of early enhancement [22]. This technique involves the use of a spoiled gradient-echo sequence performed sequentially while the gadolinium-based contrast agent is injected intravenously.

Brain shift

As the brain is not a firm organ, shifts of brain tissue often occur during craniotomy as a result of passive forces (e.g., dependent settling of tissue after the dura has been opened or after resection of tissue) or active forces (e.g., herniation of brain tumor through the dura, due to edema or shifts of brain tissue, due to hemorrhage in the surgical site). In fact, recent studies have shown that the surface of the brain is deformed by up to 20 mm after the skull is opened [10]. In the conventional setting, in which preoperative imaging data are used to direct the surgeon to intracranial lesions, such unpredictable shifts of brain tissue may invariably result in inaccuracies in navigation rendering preoperative MR images invalid. This ever changing spatial organization of the brain structures during surgery necessitated the use of intraoperative near-real time imaging modalities which could easily compensate for these changes with the continuous updating of information. This need represented one of the primary thrusts for the development of an intraoperative magnetic imaging system at the Brigham and Women's Hospital in the early 1990s.

Future applications

The recent focus in technology development is on improving our ability to understand and apply medical images and imaging systems. In the future, multimodality-based images will be merged into a single model, in which anatomy and pathologic changes are at once distinguished and integrated into the same intuitive framework. Current clinical applications are successfully incorporating real-time and/or continuously updated information for direct intraoperative visualization. In addition to using traditional imaging systems during surgery, we foresee optimized use of molecular marker technology, MR spectroscopy, diffusion-weighted imaging, and MR angiography for the diagnosis and treatment planning in patients with brain tumors. Intraoperative functional MRI will become a valuable addition for the non-invasive identification of eloquent brain areas. The role of image-guided focal thermal ablative methods (e.g., laser, RF, cryoablation, high-intensity focused ultrasound) will also become better defined in the future. Ultimately, the integration of the next generation of surgical and therapy devices (including image-guided robotic systems) will certainly contribute to more successful surgical outcomes.

Conclusion

The advent of frameless neuronavigational systems combined with iMRI have augmented the surgical accuracy. These new technologies have provided a unique opportunity to delineate normal anatomy from the brain lesion much more precisely. In addition, they allowed operators to monitor the progress of surgical procedures in a near real-time fashion. Nevertheless, the theoretically proposed and proven beneficial effects of iMRI on various neurosurgical procedures remain to be validated by larger series and randomized controlled trial.

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Intraoperative high-field MRI: anatomical and functional imaging

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Summary

Intraoperative high-field magnetic resonance (MR) imaging with integrated microscope-based navigation is at present one of the most sophisticated technical methods providing a reliable immediate intraoperative quality control. It enables intraoperative imaging at high quality that is up to the standard of up to date pre- and postoperative neuroradiological routine diagnostics. The major indications are pituitary tumor surgery and glioma surgery. In pituitary tumor surgery intraoperative MRI helps to localize hidden tumor remnants that would be otherwise overlooked. The same is true for glioma surgery, where the optimal extent of resection by simultaneous preservation of functional integrity can be achieved. This is possible since high-field MR imaging offers various modalities beyond standard anatomical imaging, such as MR spectroscopy, diffusion tensor imaging, and functional MR imaging which may also be applied intraoperatively, providing not only data on the extent of resection and localization of tumor remnants but also on metabolic changes, tumor invasion, and localization of functional eloquent cortical and deep-seated brain areas.

Keywords: Diffusion tensor imaging; functional imaging; functional navigation; glioma surgery; intraoperative imaging; intraoperative magnetic resonance imaging; navigation.

Introduction

The concept of intraoperative imaging provides an objective evaluation of surgical effects instead of the surgeon's subjective estimation about the extent of a resection, thus acting as quality control during surgery [6]. Ultrasound and computed tomography were the first imaging modalities applied for an intraoperative investigation of the extent of a resection, however, they were not accepted by the broad neurosurgical community. Magnetic resonance imaging (MRI) is the standard imaging modality for the pre- and postoperative evaluation of brain tumors. It provides techniques for sophisticated preoperative differential diagnosis, precise anatomical and functional localization for preoperative planning, as well as postoperative detection of response to treatment and tumor recurrence or progression [19].

10 years ago, in a few neurosurgical centers, the first MR scanner installations were introduced in neurosurgical operating rooms allowing intraoperative MRI [1]. There are different systems and setups ranging from ultra-low-field installations (0.12 T) up to the first installations with 3 T magnets. Basically there are two concepts to implement intraoperative MRI: to design a scanner for the need of an operating room (dedicated MR scanners, like the 0.12/0.15 T Odin system, the 0.5 T GE system, the 1.5 T IMRIS system) or alternatively to adapt a standard MR scanner to a neurosurgical operating theatre (like: 0.2 T Siemens, 0.3 T Hitachi, 1.5 T Siemens, 1.5 T Philips) [1].

After having gained experience with intraoperative low-field MRI for 5 and a half years [45], we adapted a 1.5 T MR scanner to our operating room. Intraoperative high-field MRI was realized by implementing a rotating operating table attached to the 1.5 T MR scanner, so that for surgery the patients' head is placed at the 5 G line, where normal non-MR-compatible instruments can be used. For scanning the table is then turned 160° into the scanner in less than 2 minutes; the technical details of the implementation are published [41, 42]. Combined with intraoperative imaging integrated microscope-based neuronavigation is applied which allows superimposing the tumor contour, as well as further objects identifying eloquent brain areas on the surgical field. This so-called functional neuronavigation was based initially on functional data from magnetoencephalography (MEG) and functional MRI (fMRI) [14, 25, 43]. This concept of functional navigation was extended to multi-modality navigation with integration of data from positron emission tomography (PET), metabolic maps from MR spectroscopy (MRS) [15, 50, 51], and fiber tract data from diffusion tensor imaging (DTI) [39, 40, 44, 46].

The Erlangen experience

From March 1996 until the end of 2005, we examined 1000 patients with intraoperative MRI summarizing our low-field ($n = 330$) and high-field ($n = 670$) experience. Intraoperative MRI is a safe and reliable procedure, whatever system is used [3, 4, 17, 22, 42, 45]. Neither in the low-field nor in the high-field setup had we encountered any adverse events due to the magnetic field in the operating room suite. There were no ferromagnetic accidents despite the use of standard operating instruments in the fringe field, at the 5 G zone. In the low-field system there was a distinct difference in image quality between pre- and intraoperative imaging. Intraoperative high-field MRI results in images with the same quality as in standard preoperative neuroradiological routine diagnostics [38].

Pituitary tumor surgery [12, 48] and glioma surgery [3, 4] are the most commonly agreed indications for intraoperative MRI. Focusing on our experience in these two major indications in the high-field setup, it is without doubt that intraoperative MRI results in extended resections with decreased morbidity.

Among a series of 106 patients with hormonally inactive pituitary macroadenoma in 85 patients complete tumor removal was considered preoperatively. Among them intraoperative imaging revealed definite tumor remnants or at least suspicious findings in 36 patients (42%). Imaging led to an extended resection in 29 (34%; 29 of 85) patients of this group. In 21 of them resection could be completed. This increased the rate of complete tumor removal from 58% (49 of 85) to 82% (70 of 85). In the group of patients with intended partial removal, resection was extended in 38% due to intraoperative imaging. A comparison with scans 3 months after surgery did not reveal any false negative findings of intraoperative MRI; in 6 cases intraoperative MRI was suspicious for some minor remnant which could not be reproduced in the postoperative control.

Furthermore, a series of 23 patients with acromegaly were investigated. Regarding the patients with a tumor configuration in which complete removal was considered ($n = 18$), intraoperative MRI increased the rate of endocrine normalization from 33% to 44% applying the consensus criteria for acromegaly remission and improved endocrine outcome to ‘nearly normalization’ in another 17%. Regarding preoperative growth hormone levels and tumor size, intraoperative MRI could help achieve endocrine remission in patients normally considered not being curable. However, taking growth hormone as tumor marker, even intraoperative high-field MRI was not able to detect tumor remnants in every case [13].

In a series of 137 glioma patients investigated with intraoperative high-field MRI [35] undergoing resection with the goal of at least partial resection, imaging revealed complete tumor removal initially in 27% (37 of 137 patients) (Figs. 1–3). Extension of the resection due to intraoperative imaging resulted in a final gross total removal of 40% (55 of 137) of all patients. Out of the 55 patients with a finally completed resection 18 (33%) were attributable to further tumor removal due to intraoperative MRI. In 32% (44 of 137) resection was not extended despite obvious residual tumor on intraoperative imaging due to the infiltration of eloquent brain cortex or critical anatomical structures. In total, in 41% of all patients (56 of 137) the resection was extended due to intraoperative MRI, leading to a completion of resection in 32% (18 of 56) of this subgroup. The additional further resection in the other 68% (38 of 56) led to a distinct reduction in the percentage of final tumor volume compared with first intraoperative MRI.

A volumetric analysis had shown that extended resections due to intraoperative MRI resulted in a significant reduction in the percentage of final tumor volume compared with first intraoperative MRI. Additional further resection significantly reduced the percentage of final tumor volume compared with the first intraoperative MRI scan ($6.9\% \pm 10.3\%$ versus $21.4\% \pm 13.8\%$; $P < 0.001$). Percentages of final tumor volume also were significantly reduced in both low-grade ($10.3\% \pm 11.5\%$ versus $25.8\% \pm 16.3\%$; $P < 0.05$) and high-grade gliomas ($5.4\% \pm 9.9\%$ versus $19.5\% \pm 13.0\%$; $P < 0.001$) [33].

Comparing our low-field with the high-field experience, it can be stated that the clearly improved image quality will result in greater reliable information regarding the extent of resection, i.e., about the presence of residual tumor tissue and its exact location. The percentage of patients benefiting from intraoperative MRI in respect to extended resections was 41%, indicating a distinct increase compared to the numbers obtained with the low-field system of 26% [45]. These numbers support the impression that the clearly improved im-

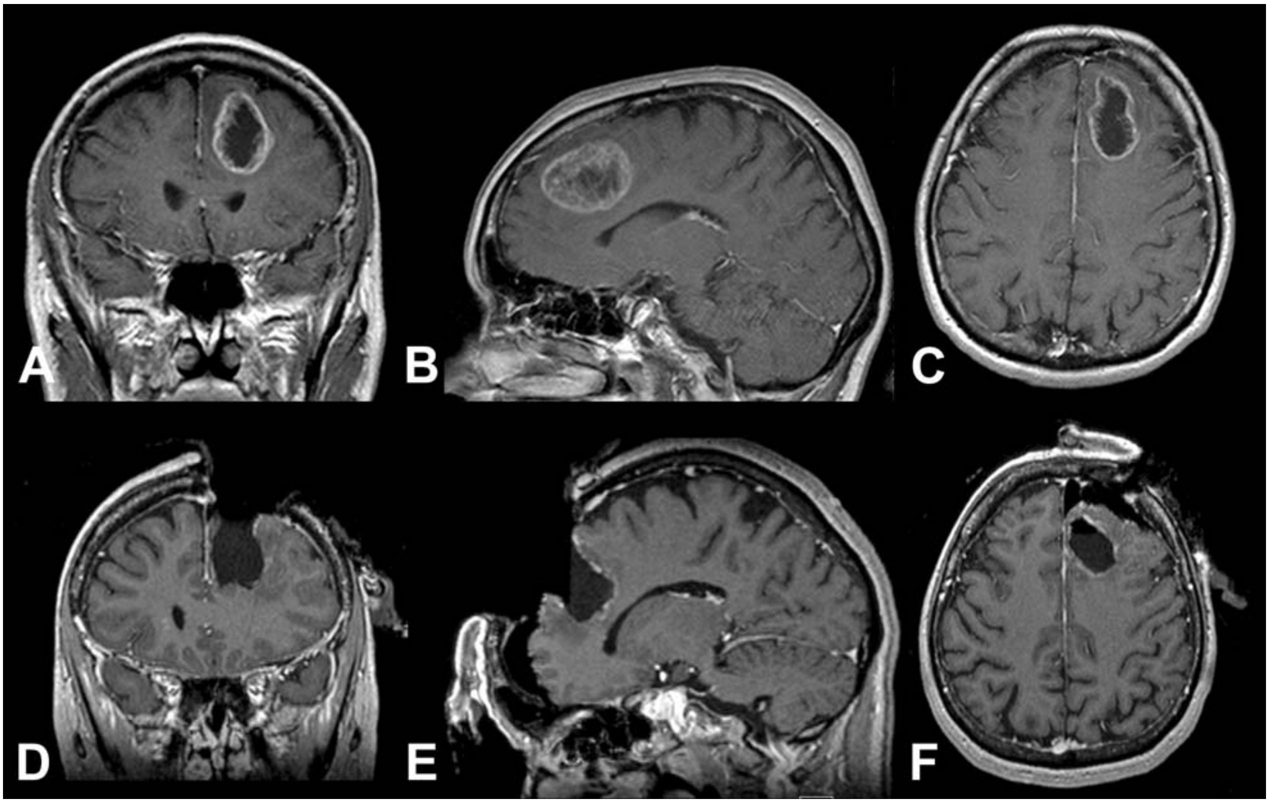

Fig. 1. 52-year-old female patient with a left frontal WHO grade IV glioblastoma. (A–C) preoperative coronal, sagittal, and axial T1-weighted images after contrast enhancement; (D–F) corresponding intraoperative images depicting complete removal of the contrast-enhancing tumor parts

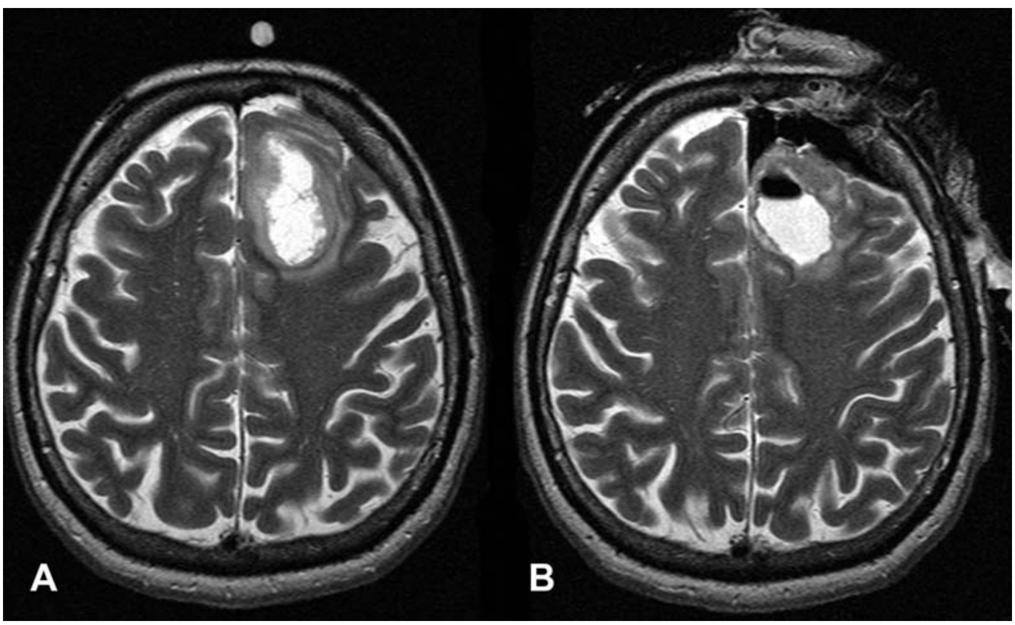

Fig. 2. Same patient as in Fig. 1, pre- (A) and intraoperative (B) imaging with T2-weighting

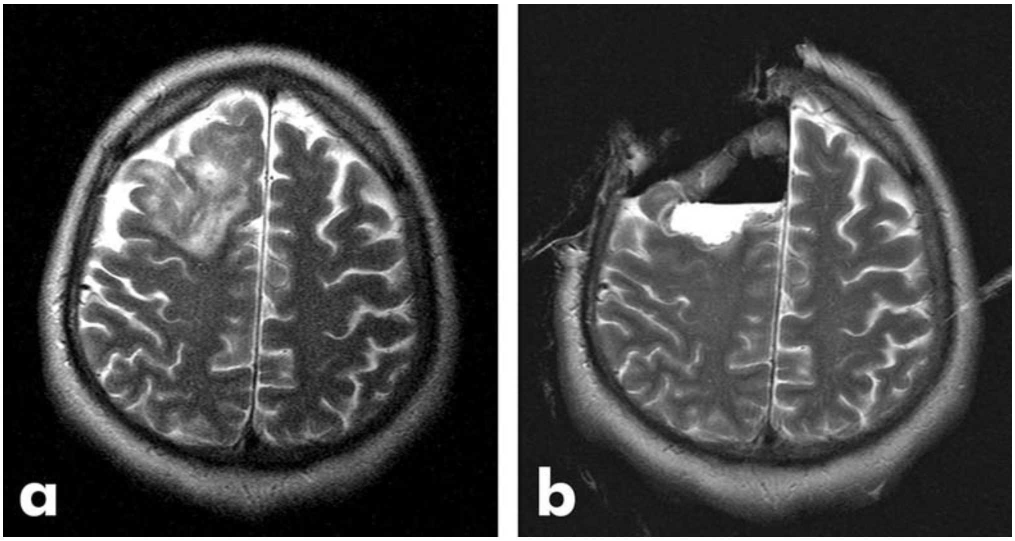

Fig. 3. 54-year-old male patient with a right frontal WHO grade II oligoastrocytoma; T2-weighted imaging confirms complete removal (a: Pre-, b: intraoperative T2-weighted axial scan)

age quality of the high-field system may also result in increased rates of extended resections. However, it is too early to decide whether these increased rates translate into long-term patient benefit, i.e. longer progression free intervals and increased overall survival.

Compared to the low-field setup the high-field MRI implementation provides an improved workflow. Navigation and imaging are closely integrated, so that in all cases intraoperative imaging and microscope-based navigation were applied in parallel. Navigational accuracy estimated by the localization error of an additional independent fiducial, allowed documenting a low target registration error ranging from 0 to 3.4 mm with a mean of 1.1 ± 0.63 mm. Intraoperative image data were registered with the preoperative data, so that the effects of brain shift could be compensated for. The navigation update, performed in 41% (56 of 137), led to a reliable identification of the residual tumor parts.

In addition to anatomical data, functional data from MEG ($n = 37$) or fMRI ($n = 65$), identifying motor ($n = 65$) or language related ($n = 43$) cortex, were co-registered in the glioma patients investigated with the 1.5 T MR scanner. In 55 patients data from DTI were also integrated, either as color-encoded fractional anisotropy maps or as 3-D objects representing the pyramidal tract generated from a bundle of fibers calculated by tracking algorithms (Figs. 4 & 5) [39, 40, 44, 46]. The application of functional neuronavigation was associated with low postoperative morbidity. In 8.8% (12 of 137) a new or aggravated paresis was encountered in the immediate postoperative course, which resolved in two thirds, so that only in 2.9% (4 of 137) there was a new permanent neurological deficit. In two further patients (1.4%) a transient speech dysfunction was documented, we did not encounter any permanent speech deficits. Furthermore, data from PET imaging ($n = 8$) and metabolic maps form MRS ($n = 28$) were integrated in the navigational datasets allowing to take correlated biopsies at the tumor border [15, 50, 51].

Discussion

Intraoperative imaging for resection control

Considering pituitary tumor surgery it can be stated that the extent of resection in transsphenoidal surgery can be assessed reliably by intraoperative MRI. Besides the suprasellar compartment also intra- and parasellar structures are visualized in great detail by intraoperative high-field MRI. Intraoperative imaging acts as immediate intraoperative quality control allowing not only increasing the extent of resection, but also increasing the percentage of completed removals [5, 12, 13, 30, 38].

In contrast to pituitary tumor surgery there is still no definite common agreement for the role of surgical treatment in low grade [10, 23] as well as high grade gliomas [28]. Despite modern technologies that may

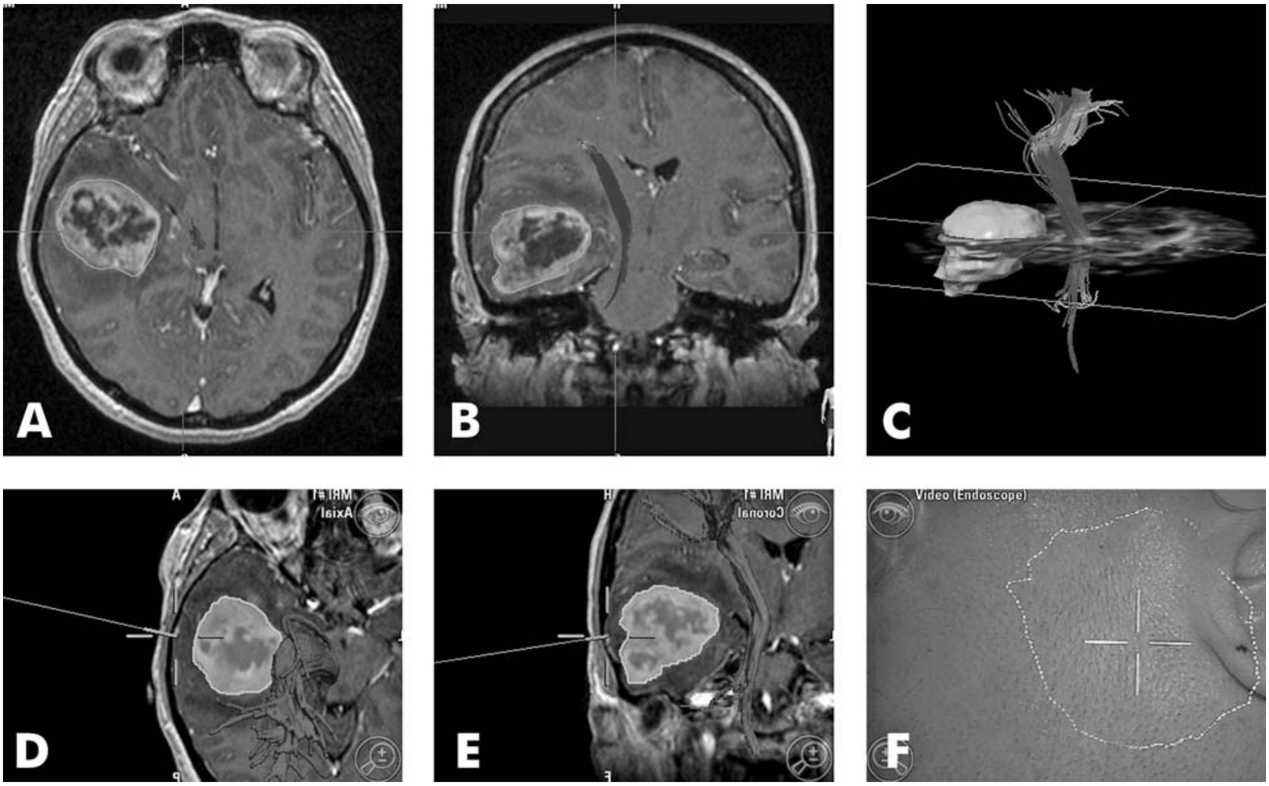

Fig. 4. 50-year-old female patient with a right temporal WHO grade IV glioblastoma. (A/B) segmented tumor outline and reconstructed pyramidal tract by diffusion tensor imaging based fiber tracking (axial and coronal) in the navigation planning software; (C) color-encoded fractional anisotropy map with the segmented 3-D tumor object; (D/E) 3-D rendering of an object representing the pyramidal tract displayed in the navigation software during surgery; (F) microscope-view at the beginning of surgery with the dotted yellow-line depicting the extension of the contrast enhancing tumor parts, as well as the course of the pyramidal tract superimposed on the surgical field in blue

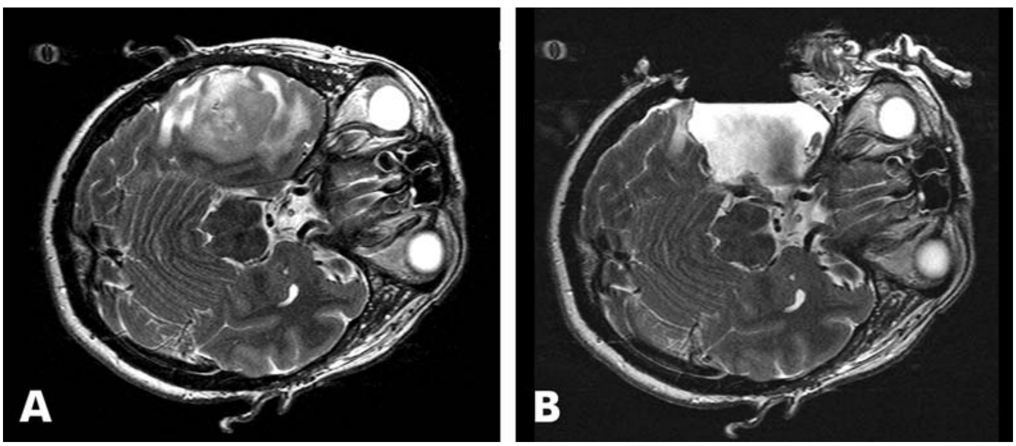

Fig. 5. Same patient as in Fig. 4 corresponding pre- and intraoperative axial T2-weighted scans depicting the extent of resection

solve the challenges of glioma surgery, like the difficulty to reliably identify the extent of the tumor during surgery, it is obvious that imaging alone will not solve the challenge of glioma treatment. MR-guided removal of local tumor remnants may be critical in an interdisciplinary concept of glioma treatment where the maximum extent of tumor volume reduction with least neurological deficits is the optimal starting point for further sophisticated adjuvant therapeutic regimens.

There are many powerful arguments in favor of attempting a radical resection of all gliomas of the brain, including both the "malignant" and "benign" varieties [28]. In the vast majority of studies that address the role of surgery in the management of high-grade gliomas, the degree of tumor removal accomplished is solely based on the intraoperative perception of the neurosurgeon. Despite its fundamental importance for a comparison of different treatment modalities, little systematic effort has been made to evaluate the residual gross tumor volume by neuroimaging methods immediately after surgery. Albert *et al.* analyzed in a prospective study the effect of early postoperative magnetic resonance imaging after resection of malignant glioma [2]. The neurosurgeon's estimation of gross tumor burden reduction could be shown to be much less accurate (by a factor of 3) than the postoperative assessment by modern neuroimaging. Our own results comparing the estimation of the surgeon about the extent of imaging confirm these results with intraoperative MRI data. Especially in the low grade tumors there was a discrepancy of up to 30% where the estimation of the surgeon did not compare well to the result of intraoperative imaging [34]. In Albert's series [2], residual tumor enhancement was the most predictive prognostic factor of survival in patients with glioblastoma, followed by radiotherapy. Patients with a residual tumor postoperatively had a 6.6-times higher risk of death in comparison to patients without a residual tumor.

Several recent studies provide data for the beneficial effect to reduce the tumor burden in high-grade gliomas seeing the extent of surgery as positive prognostic factor [7, 8, 27, 29, 52, 53]. However, there are also several reports that did not support aggressive resection as a major factor in good prognosis in high-grade gliomas [26, 31, 54]. The same controversy [23, 32, 56] is true for the low grade tumors despite the fact that there should be little question that a complete removal of all tumor tissue would be an ideal treatment because if residual tumor is left behind, it eventually degenerates into a glioblastoma limiting life expectancy of the patient [6].

There are only few studies on long-term patient outcome after glioma resection under intraoperative MRI control. However, it is without doubt that intraoperative MRI allows to increase the extent of a glioma resection, as well as it increases the number of completed resections. If a gross total resection of a glioma is of benefit then intraoperative MRI will greatly help to achieve this goal.

A study comparing a group of patients (n = 32) undergoing intraoperative MRI control with a matched group undergoing conventional surgery could not demonstrate an increased efficacy of surgery although MRI was effective to visualize residual tumor [21]. Unfortunately, this study did not compare the extent of resection, so that the real effect of intraoperative MRI cannot be elucidated. In a small but homogeneous patient group of 31 glioblastoma patients the Leipzig group could show a significant difference in the mean survival time comparing the group with complete and incomplete resection [49]. The recently published Boston experience on the resection of low grade gliomas favors a possible association between surgical resection and survival under MRI guidance [10].

In an analysis of 97 glioma patients undergoing intraoperative low-field MRI resection control Wirtz *et al.* could show that for high grade gliomas, the percentage of cases in which residual tumor was identified by MRI could be significantly reduced from 62% intraoperatively to 33% postoperatively, which was paralleled by a significant increase in survival times for patients without residual tumor [24, 55].

By intraoperative MRI the unwanted occurrence of finding residual tumor on a postoperative scan is thus practically eliminated. As a result, the surgical goal of complete or optimal resection can be achieved without any guesswork. Ultimately, this means for the glioma patient an increased likelihood of longer survival brought about by a more thorough tumor resection [47].

Imaging beyond anatomical imaging

Low postoperative neurological deficits are mandatory, especially in surgery of high grade tumors it is of no benefit for the patient to maximize the extent of resection to potentially increase the survival time by only some weeks, when risking permanent neurological deficits right after surgery. It is absolutely mandatory to combine the goal of maximum resection with the goal of preservation of function. Intraoperative imaging helps not only maximize the extent of resection but in combination with functional multi-modality navigation also minimization of postoperative neurological deficits is possible [36, 37]. With the advances in surgical techniques and perioperative technology, it is now possible to maximally resect malignant intrinsic glial neoplasms, even within functionally critical areas, without increased morbidity. Studies have demonstrated a survival advantage with 98% or greater resection of these lesions, particularly in younger patients with good Karnofsky scores [20].

To achieve this, functional neuronavigation, i.e. integrating functional data into anatomical navigational datasets, is an important add-on to intraoperative MRI since it prevents too extensive resections, which would otherwise result in new neurological deficits. Up to now, data from MEG and fMRI are routinely integrated in functional neuronavigation allowing identification of eloquent brain areas such as the motor area and speech related areas [14, 43]. Functional data from MEG and fMRI only localize function at the brain surface. However, neurological deficits can occur during tumor resection due to damaging of deeper structures, such as major white matter tracts. DTI can be used not only to delineate tumor borders, but also to display the course of white matter tracts, such as the pyramidal tract. The knowledge of the course of major white matter tracts in relationship to a tumor helps prevent new postoperative neurological deficits [9, 18]. Registration of diffusion data with the navigational dataset [11, 44, 46] facilitates the intraoperative preservation of these eloquent structures. A prerequisite is that intraoperative changes of the brain anatomy, known as brain shift, are taken into account. Intraoperative functional imaging, i.e. intraoperative DTI, revealed a marked shifting of the pyramidal tract due to tumor resection [39, 40]. As a consequence of this shifting the preoperative functional data are no longer valid, so navigation can no longer be relied on, if this shifting is not compensated for. Therefore, it is necessary that not only intraoperative anatomical data are used to compensate for the effects of brain shift but also functional data have to be updated. Intraoperative acquisition of DTI data enables intraoperative fiber tracking to visualize how a tumor remnant is localized in relation to major white matter tracts [39, 40]. Even intraoperative fMRI applying electrical stimulation of median and tibial nerves as a passive stimulation paradigm is possible and enables identification of the somatosensory cortex [16].

Besides functional data further information is available for a multi-modal navigation setup. PET, MRS, and diffusion weighted imaging may provide information on the diffuse tumor border. Integration of metabolic maps into the neuronavigation datasets enables a spatial correlation of metabolic data and histopathological findings [50, 51]. The question whether these techniques can also be used intraoperatively so that these data can also be updated, is under investigation. Furthermore, upcoming techniques such as MR-based molecular imaging may find its role in the intraoperative imaging armamentarium.

Conclusion

- Intraoperative MRI enables anatomical visualization of the extent of resection. In contrast to early postoperative scanning that can only document the extent of tumor removal, in case of tumor remnant that seems to be further removable intraoperative imaging allows extending resection during the same surgical procedure. The unwanted occurrence of finding residual tumor on a postoperative scan is thus practically eliminated. As a result, the surgical goal of complete or optimal resection can be achieved without any guesswork.
- Intraoperative image data can be used to update the navigation system, compensating for the effects of brain shift. So tumor remnants can be easily localized with updated navigation.
- Intraoperative functional imaging is possible, allowing an immediate intraoperative evaluation of the spatial relation of the resection cavity and potential remnants to eloquent cortical and subcortical brain regions depicted by intraoperative fMRI and intraoperative DTI-based fiber tracking.
- Intraoperative diffusion imaging can be used to evaluate the invasion of normal white matter tract structures. Whether even intraoperative MR spectroscopy for a better identification of tumor borders is technically feasible is an open question, as well as whether MRI-based molecular imaging techniques will find their way into the operating room.

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Intraoperative MR imaging: preliminary results with 3 tesla MR system

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Summary

Aim of this study is to present the initial clinical experience with 3 tesla intraoperative MR (ioMR).

Material and methods. The 3T MRI suite is built adjacent to the neurosurgical operation theatre. The magnet room and the operation theatre are interconnected by a door and both RF-shielded. Before the operation, the magnet (3T Trio, Siemens) and the console rooms are disinfected. Whenever imaging is needed during the operation, the door is opened and the patient is transferred from the operation table to the magnet cradle. Axial, sagittal and/or coronal TSE T2, SE T1 and 3D Flash T1 weighted images (4–6 mm section thickness, 1 mm interslice gap) are obtained according to the lesion. Total examination time is approximately 10 minutes.

Results. Twenty-six patients were examined with ioMR. There were ten female and seven male patients. Lesions were pituitary adenoma in 10, low grade glial tumor in 9, meningioma and high grade glial tumor in 2 each and metastasis, haemangioblastoma and chordoma in one each. Follow-up time was 1 to 9 months. In 16 patients the first intraoperative examination revealed gross total tumor excision. However, in 10 patients due to tumor remnants surgical intervention was continued and a second examination revealed gross total tumor excision in all. Postoperative routine MR examinations confirmed total tumor excision in all patients. No complication occurred in this series.

Conclusion. This small group of patients examined with ioMR demonstrated that the procedure is simple, helpful in achieving gross total tumor excision without complications.

Keywords: 3 tesla; intraoperative MR; magnetic resonance imaging.

Introduction

Intraoperative MR technology is one of the recent improvements in neurosurgery [1, 6, 10, 18]. The main aim of intraoperative MR usage is to minimize morbidity and mortality while achieving total tumor resection. Even though there are some concerns regarding the effectiveness of intraoperative MR examinations, so many systems are in use the world over [1, 7]. Costs of the system, perioperative problems regarding a system in use, long-term follow-up of patients should be discussed to reach a conclusion for this technology.

Short term results of intraoperative MR imaging in different pathologies such as pituitary adenomas, low and high grade glial tumors, epilepsy surgery, suprasellar tumors are very encouraging [3–5, 12, 13, 17, 20, 24].

There is no report in the literature on 3 tesla ioMR systems. In this paper the preliminary results of 3 tesla intraoperative MR system are reported, which has been in use in our hospital for more than one year.

Material and methods

MR imaging system

Our 3T MRI site is built next to the operating theatre that is dedicated to neurosurgical operations. The magnet room and the operation theatre are interconnected by a door and are both RF-shielded. In daily practice, we use the 3T MRI (3T Trio, Siemens, Erlangen) as a clinical scanner. Before the operation, the magnet and console rooms are properly disinfected. Whenever the neurosurgeon needs imaging during the operation, the door between the magnet room and the operating theatre is opened, and the patient is transferred from the operation table to the magnet cradle with a floating table in not more than 3 minutes. All equipment in the magnet room is compatible with 3T MR. Since all surgical equipment including the microscope are outside the 5 gauss-line, we can manage every kind of equipment safely. We used a body coil to transmit and receive signals in these patients because the head coil was not compatible with the head holder. In the last three months we organised a dedicated head holder with a specially designed 8-channel head coil. Axial, sagittal and/or coronal TSE T2, SE T1 and 3D Flash T1 weighted images (1–6 mm section thickness, 0–1 mm interslice gap, $192–256 \times 256–512$ matrix, 200–260 mm FOV) are obtained according to the lesion. Total examination time including transfer of the patient, analysis of the images and the final decision takes approximately 10 minutes. At the end of the examination we decide to continue or terminate the operation. If we decide to go on, the examination procedure is repeated. If the operation is terminated, the door between the magnet room and the operating theatre is closed, and routine outpatient examinations begin immediately.

Patients

A total of 26 operations have been performed with intraoperative MR since November 2004. There were 16 female and 10 male patients. Of these 26 operations, 10 were pituitary adenomas, 9 low grade glial tumors, 2 meningiomas, 2 High grade glial tumors, and one each metastasis, chordoma and hemangioblastoma. The follow-up time was between 1 to 9 months (mean 3 months). The first intraoperative exam demonstrated gross total removal in 16 patients. In 10 patients (4 with pituitary adenomas, and 6 with low grade glial tumours) surgical intervention was continued due to the demonstration of remnants. A second intraoperative exam in these patients revealed total tumor excision in all.

Discussion

Aim of any neurosurgical intervention is the correct localisation, targeting and treatment of intracranial pathologies while preserving normal neural tissues [26]. To achieve this goal, numerous techniques are applied in the operating room. Intraoperative ultrasonography, ioCT, neuronavigation techniques have been developed in the recent history of neurosurgery [1, 2, 19, 22]. All these techniques have their own advantages and disadvantages.

Intraoperative MR imaging is a new but rapidly developing technique in neurosurgery [11, 14, 23, 25].

Low-field systems

The first ioMR system was established in Brigham and Women's Hospital in Boston [1]. The system is widely known as the General Electric "double doughnut" with two vertically oriented superconducting magnets with radiofrequency coils in two separate but communicating cryostats, resulting in a 56-cm wide vertical gap at the center of the magnet. The major advantages of this system are: the whole surgical procedure takes place in one room, two surgeons may have access to the patient at the same time, and it gives near real-time images. The disadventages of the system are: lower image quality, increased cost due to usage of MR-compatible non-ferromagnetic surgical equipment and limited space for the surgeons. Since results of operations in this suite are very encouraging, many centers have started to use different types of ioMR systems.

The Toronto GE system is a single donut system [6]. This system consists of a 0.2 tesla vertically open, biplanar standard magnet which is integrated into a tracking system. Limited patient access, insufficient image quality and mobilisation of the patient in and out of the magnet field during interactive scanning are major disadvantages of this low-field system.

The Siemens low-field system was first used in the University of Erlangen and Heidelberg [17]. It was a 0.2 tesla system requiring patient movement during the procedure. Surgery is performed in a twin operating theathre consisting of a conventional operating room and an RF-shielded room designed for the ioMR scanner. The patient is transferred to the MR unit on a specially designed air cushion and back to the surgeon. The ability to use MR compatible surgical instruments, and increased access to the patient are the major advantages of this system. However requirement for intraoperative transport of the patient to the MR room increases the time of surgery and a possible risk of infection.

The Odin system from Israel is completely different from the above mentioned systems [1]. This system is very low-field (0.12 tesla). The magnet is formed by two vertical, parallel disk-shaped arms, and the permanent magnet docks under a standard OR table. This system is less expensive than other systems. However image quality is very weak and the area which can be imaged is very narrow.

It was tried to overcome the weaknesses of these systems by using high-field systems.

High-field systems

The Philips system at the University of Minnesota is a 1.5 tesla unit and has been in use since 1997 [6]. It requires a dedicated theatre. Movement of the patient in and out and limited patient access are the major disadvantages.

The Calgary crane was built in 1999 [1]. Unlike other high-field systems, it is able to move along a ceiling mounted crane obviating the transfer of the patient in and out of the magnet; instead the magnet goes to the patient. Sliding magnet keeps the patient immobile and standard surgical instruments and equipment can be used safely. The image quality is better. The operating table should be constructed from titanium and fiberglass.

The high-field system from Siemens consists of a standard 1.5 tesla magnet scanner in a dedicated OR [18]. A rotating operating table permits the rotational movement of the head, enabling placement of the patient out of the 5-gauss safety line so that any standard neurosurgical operation can be carried out by standard instruments.

All these high-field systems offer the advantage of intraoperatively performing fMRI, DwMRI, MRA, MRV and MR spectroscopy [7, 15, 16].

TRIO 3 tesla ioMR system

This system is based on the twin room concept. The operating theatre is adjacent to the MR unit. The magnet of the MR unit is at the far end of the OR side. The head side of the operating table is directed to side of the MR unit. When the surgeon decides to take an intraoperative MR image, the patient is tansfered onto a transporting table. The distance between the operating table and the MR cradle is only 3 meters. As soon as the patient has been transported to the MR unit, he is connected to an MR compatible anaesthesia unit which is stationary in this room. An anesthesiologist observes the patient and monitoring during that time period. When MR examination is completed, the same steps are done conversely.

Advantages of the Acibadem system are:

1. It is an ultra high-field system: there is debate in neuroradiological practice on the advantages of 3 tesla MR imaging for routine application [21]. The ultra high-field systems generate a high signal intensity-to-noise ratio. This results in high image quality. Due to the surgical manipulations and blood and foreign bodies in the surgical field, images in low-field systems sometimes can be confusing. Also, the high signal intensity-to-noise ratio shortens scanning time, which is very important in ioMR imaging. In our system, completion of the whole imaging procedure takes not more than 10 minutes . This obviates long interruptions of the operating time. In this short time period different image sequences can be obtained. One of the advantages of high field systems is to be able to perform diffusion tensor imaging and tractography intraoperatively. Tumors situated close to important tracts such as corticospinal tract, optic tract, etc. can very easily be seen with these systems. This results in decreased morbidity connected with tumor removal in these patients.
2. Twin room concept: One of the main disadvantages of ioMR systems is their expensiveness. To use an MR unit only for intraoperative purposes increases the cost of the system. Our system is designed as to be used not only intraoperatively but also for outpatient clinics. The special design of twin rooms opened this possibility to us. A disadvantage of other high-field systems is that MR compatible instruments are needed. However, the twin room concept enables the use of standard instruments for surgery, which also lowers costs of the system.

The disadvantages of the Acibadem system are:

1. Need to transport the patient: Even though the transportation time is not more than 3–4 minutes, this systems requires transferal of the patient to the neighbouring MR room. No problem was encountered in our small patient group. This is a minor problem only and we think it may be ignored.
2. Infection rate: no infections were observed in the 26 patients. However, composition of the system may affect the infection rate. Our patient group was to small to draw a conclusion.

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