MAGNETIC RESONANCE IMAGE-GUIDED NEUROSURGERY

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The combination of advanced neuro-navigation, 3D multi-modality image fusion and intra-operative MRI can fulfill the promise of an integrated image guidance system for neurosurgery. The concept of MRI-guided neurosurgery is now widely accepted and preliminary evidence suggests that MRI guidance greatly improves the safety and effectiveness of neurosurgical procedures. The application of intra-operative MRI is especially helpful in the surgical excision of low grade gliomas (tumor resection control). Among the currently developed thermal therapy methods, focused ultrasound (FUS) appears to be the most promising method for non-invasive neurosurgery.

Keywords: magnetic resonance imaging, navigation, brain tumor, focused ultrasound

Introduction

Since its introduction as a diagnostic tool in the mid-1980s, MRI has evolved into the premier neuroimaging modality; and with the addition of higher field magnets, we are able to achieve spatial resolution of such superb quality that even the most exquisite details of the brain's anatomy can be visualized. Indeed, particularly within neurosurgery, Magnetic Resonance Imaging (MRI) has emerged as a supremely useful diagnostic tool; and similarly, the implementation of intraoperative neurosurgical MRI has had a major impact on conventional surgical approaches. We not only can monitor brain shifts and deformations, we can achieve intraoperative navigation using intraoperative image updates. In the near future, intraoperative MRI will be used to localize, target, and resect brain tumors and other lesions as well as elucidate the surrounding functional anatomy. In addition to the inclusion of new imaging methods, such as diffusion tensor imaging (DTI) and functional MRI, new therapeutic methods will be applied. For example, within MRI-guided focused ultrasound surgery, among the most promising new therapeutic approaches is the non-invasive thermal ablation of tumors, which uses

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MRI guidance to control and monitor the area of interest. With the clinical introduction of these advances, intraoperative MRI is rapidly changing the face of neurosurgery today [1, 2].

In modern neurosurgery, however, there is a growing need for imaging both brain morphology *and* function. To achieve this, imaging must be comprehensively integrated with surgery and the various components of the operating environment must be completely reassessed. Successful integration entails the introduction of interactive dynamic imaging, high performance computing, and real time image processing in the operating room. Novel intraoperative imaging techniques are being aggressively developed and tested for their diagnostic and clinical utility. These techniques, in turn, will be applied to several revolutionary image-guided therapy methods that are currently being explored, and which will eventually be incorporated into standard neurosurgical practice.

Image-guided Neurosurgery

The fundamental principle of image-guided neurosurgery is to target, access, and remove intracranial lesions without injuring normal and functioning brain tissue or intact blood vessels. The overall concern is the preservation of neurological function, which requires precise delineation of functional anatomy and correct definition of tumor margins. During surgery, the visual appearance of the infiltrating malignant tumors is sometimes indistinguishable from the adjacent normal brain tissue. Because of the difficulty in recognizing exact tumor margins, complete resection is, in most cases, problematic.

Early work with brain stereotaxis has established the importance and value of image guidance through better determination of tumor margins, better localization of lesions, and optimization of the targeting. In current practice, computer-assisted, image-guided surgery has replaced stereotactic neurosurgery. Frame-based and frameless stereotaxis using 2-D and 3-D images have shown that neurosurgery can be performed less invasively, yet with greater precision and accuracy.

For the neurosurgeon, the goal is to achieve complete tumor resection while maximally preserving normal brain tissue and function. Ideally, the physician should be able to precisely localize the lesion, choose the optimal trajectory of approach, and accurately determine the margins of the tumor and its separation from the normal brain. Using advanced computing technologies, these surgical "steps" are now undertaken with a remarkable degree of confidence and accuracy. Specifically, surgical planning uses multimodality and multiparametric lesion characterization, and includes the full depiction of the relevant anatomical structures and their related functions. The 3D multimodality image fusions represent an enrichment of the information provided by the MRI slices alone. They do not change the diagnosis, but can contribute substantially to surgical planning by providing additional information regarding a) the optimal craniotomy and corticotomy sites; b) surgical excision margins; and c) access trajectories to the targeted tumors. In addition to image-guidance, the most novel aspect of neurosurgical planning is the *intraoperative* use of the 3D model for interactive surgical simulation such as trajectory optimization, access route selection, and in the case of thermal therapy, 3D thermal dosimetry. Surgical planning also includes various avoidance strategies in the proximity of the lesion to the sensory and motor tracts and deep brain structures (basal ganglia) and to essential vascular structures or cranial nerves. All the available and relevant anatomical and functional information should play a role in the construction of 3D models. Surgical planning is also linked to co-registration (multimodality fusion) and should be completed in the operating room with the registration of the 3D surgical planning model to the patient anatomy.

Current advances in MRI, specifically functional MRI (fMRI) and diffusion tensor imaging (DTI) significantly improve localization and targeting within the cortical grey matter (functional anatomy) and along deep white matter structures (connectivity). In addition, contrast enhanced dynamic MRI, magnetic resonance spectroscopy (MRS), positron emission tomography (PET), and the single photon emission computed tomography (SPECT) provide complementary physiologic and/or metabolic data, allowing further differentiation of brain tissue and improved characterization of brain tumors [2, 3].

Multimodality and multiparametric model generation requires extensive image processing of the preoperative data, including image segmentation, parameter extraction, and parameter mapping and co-registration of data from multiple sources. The same tasks can be performed before or during the procedure. The multiple different data sets are aligned using a multimodal registration method based on the maximization of the inherent mutual information contained by the images originating from the same patient.

Image acquisition and intraoperative image processing have improved steadily in recent years. In parallel, this has resulted in increasingly sophisticated multimodality image fusion and registration, although most methods are confined to rigid structures. Moreover, clinical experience with image-guided therapy in deep brain structures and with large resections has revealed the limitations of existing rigid registration and visualization approaches. For example, the deformations of brain anatomy during surgery obviously require the application of non-rigid registration algorithms and the updating of anatomic changes using intraoperative imaging.

Intraoperative MRI-guided Neurosurgery

Surgical manipulations and maneuvers result in a change in the anatomic position of brain shifts and deformations that occur frequently during surgery. The leakage of cerebrospinal fluid (CSF) after opening the dura, hyperventilation, the administration of anesthetic and osmotic agents, and retraction and resection of tissue all contribute to shifting of the brain parenchyma. This makes information based upon preoperatively acquired images somewhat unreliable, and this unreliability increases substantially as a surgical procedure continues. Intraoperative imaging, on the other hand, allows accurate updates of changes and the use of correct localization and targeting coordinates. The challenge of intraoperative MRI is not only to update the position of the continuously deforming brain tissue, but also to provide the interactivity required for an image-guided therapy system. Interactive intraoperative MRI guidance allows the physician to accurately localize and target the lesion during neurosurgical procedures and to optimize surgical approaches to avoid critical structures and decrease exposure of surrounding normal, functionally critical tissues.

Intraoeprative MRI can facilitate surgical localization and targeting and, at the same time, using interactive multiplanar imaging, improve intraoperative navigation. Moreover, MRI can provide real time feedback information intraoperatively. This conceptual approach has been made feasible with an appropriately configured, open access MRI system (SIGNA SP, General Electric Medical System, Milwaukee, WI). This system incorporates several objectives of intraoperative guidance. First, it represents an attempt to overcome the restrictions of closed configuration MRIs. Second, in addition to providing access to the patient's exposed anatomy, intraoperative MRI gives the neurosurgeon an opportunity to "see" beyond the exposed surfaces. Third, it offers a more sensitive method than direct visualization for distinguishing diseased tissue from normal tissue. Finally, it can monitor and detect changes in brain anatomy and tissue integrity that occur during surgical procedures.

Operating with interactive MRI guidance offers neurosurgeons several advantages over stereotactic guidance systems including *tissue characterization* that effectively aids the surgeon in distinguishing normal from abnormal tissue during resection. However, to identify tumor, especially residual tissue that remains following resection, sufficient spatial and contrast resolution is necessary. Unfortunately, this cannot be accomplished with low field MRI systems. Only relatively high field MRI can produce images with superior resolution; and only completely open systems can offer optimal surgical access. Thus, magnet configuration and field strength require a compromise between image quality and accessibility. An optimal system for neurosurgical guidance, in fact, may have several options from mid-field to high field and from closed to completely open scanners.

From the navigational point of view, intraoperative MRI does not require a frame of reference for transformation and registration. It offers direct image coordinates in localizing a lesion in three-dimensional space and allows this localization to be updated in a dynamic fashion. This has major implications on the ability to obtain accurate biopsies or correct resections of margins. Interactive use of MRI also allows the selection of the optimal trajectories for various neurosurgical approaches. Brain surgeries can be carefully planned and then executed under MRI guidance, which, in turn, minimizes the surgical exposure and the related damage to the normal brain. The maximal preservation of normal tissue may contribute to decreased surgical morbidity. Specifically, intraoperative MRI can decrease surgical complications by identifying normal structures, such as blood vessels, white matter fiber tracts, and cortical regions with functional significance. However, intraoperative complications, such as hemorrhage, ischemia, or edema are possible and can directly affect the outcome.

Special features unique to MRI both enhance the information available during a procedure and guide therapy [1, 2, 3]. These include flow sensitivity, evaluation of perfusion, administration of contrast agents to detect a breakdown of the blood-brain-barrier (BBB), or communication among CSF compartments. In addition, the ability of MRI to detect temperature changes can be exploited to monitor and control thermal ablations. Images acquired intraoperatively can also be combined and correlated with preoperatively acquired studies such as SPECT or PET scans, prior CT studies, and functional MRI studies. *The ultimate goal of intraoperative image guidance is to combine preoperative and intraoperative image data into a comprehensive "package" of information that is indispensable to accurate surgical decision making.* Indeed, this "data package" offers several benefits: (1) with intraoperative MRI, images can be obtained at each stage of a given procedure without moving the patient and without significantly extending the surgery; (2) a lesion can be accurately and even more importantly, directly localized; (3) changes in the anatomy due to brain shifting can be immediately recognized; (4) the correlation between the surgeon's field of view and the image allows confirmation of the exact location of pathologic tissue; and (5) serial images allow evaluation of the extent of excision and aids complete removal when possible.

Intraoperative Navigation

In current neurosurgical practice, the localization of a brain lesion and the surrounding anatomy relies exclusively upon preoperative image data and intraoperative electrophysiological measurements. Although preoperative image data can be used for surgical planning and intraoperative navigational guidance, the use of this information is limited because of the unavoidable deformation of the brain during surgery. Fortunately, intraoperative MRI can resolve this problem if appropriate navigational tools are implemented. For example, by using advanced computer technology, neurosurgery can overcome the inherent inconvenience of frame-based systems. Frameless, computer-assisted navigational systems, however, require image-processing methods such as segmentation, registration, and interactive display. Using various image-processing methods, a computer-based model of the brain can be generated, and within this model, structures can be highlighted.

"Tracking" is the process by which interactive localization is achieved within the patient's coordinate system. Methods of tracking include articulated arms, optical tracking, passive systems, sonic digitizers, and electro-magnetic sensors. Active optical trackers use multiple video cameras to triangulate the 3D location of flashing light emitting diodes (LEDs) that can be mounted on any surgical instrument. Passive tracking systems use a video camera (or multiple video cameras) to localize markers that have been placed on surgical instruments. These systems do not use a power cable attached to the handheld localizer. Moreover, both LED and passive vision localization systems require at least a *partial* line of sight between the landmarks or emitters and imaging sensor at all times when an object is tracked. Electro-magnetic digitizers operate without such restrictions and further, can track instruments placed inside the body or objects that are out of view.

An ideal intraoperative MRI combines MRI imaging with interactive localization of the surgical instruments, intra-operative displays, and computer workstations. However, software tools for visualizing the segmented models and the MRI scans in concert with the tracked instruments are needed to provide direct feedback to the surgeon. The 3D model of the patient must correlate directly to the actual images. The tracked probe enables the physician to depict the position of the probe relative to the segmented structures and to the original scan. The surgeon is thus equipped with an enhanced view of the surgical field relative to the entire anatomical model of the patient.

Intraoperative MRI has a number of applications with specific requirements for dynamic MRI, particularly MR fluoroscopy, which can operate on an "open" MR scanner without extraordinary gradient coil or RF coil hardware parameters in place. The typical interventional "open" magnet configuration disallows current dynamic MRI methods. For example, it cannot be outfitted with specialized gradient coils with the high slew rate necessary for echo planar-based fast MRI. Thus, the need exists for innovative, dynamic MRI approaches. The most important applications that have specific requirements for dynamic MR, particularly MR fluoroscopy, include (1) monitoring thermal therapies, (2) catheter tip tracking, and (3) monitoring the progress of surgical resections. With 2D fluoroscopic imaging capability, the surgeon can visually, or with computer-assistance, guide and monitor therapy or surgery for greater effectiveness and safety.

MRI-guided Thermal Ablations and Focused Ultrasound Surgery

With the introduction of magnetic resonance imaging (MRI) as a monitoring method for thermal therapies, a novel mechanism for controlling energy deposition was developed [4]. Many MRI parameters are sensitive to temperature changes that make MRI suitable for monitoring thermal ablations by noninvasive means. Furthermore, the physician can take advantage of diffusion MRI, which detects changes in water mobility and compartmentalization and identifies reversible as well as irreversible thermally induced tissue changes. However, MRI monitoring of thermal ablations is only feasible if the imaging and therapy delivery systems are integrated.

The role of MRI during thermal ablations is to monitor temperature levels, to restrict thermal coagulation to the targeted tissue volume, and to avoid heating of normal tissue. MRI can also detect irreversible tissue necrosis and demonstrate permanent changes within the treated tissue. Physiologic effects such as perfusion or metabolic response to elevated temperature can also be used for monitoring the ablation. Both flow and tissue perfusion can affect the rate and extent of energy delivery and the size of the treated tissue volumes [5]. Monitoring can optimize treatment protocols. Since the original description of MRI monitoring and control of laser–tissue interactions, MRI-guided interstitial laser therapy (ILT) and other MRI-guided thermal ablation methods have been clinically tested and accepted as minimally invasive treatment options [6]. ILT is a relatively simple, straightforward method, which can be well adapted to the interventional MRI environment. Overall, these early results suggest that "interstitial laser therapy" (ILT) is a safe therapy method. Although no definitive conclusion can be drawn based on the currently available data, it appears that ILT can be of benefit in patients with low-grade gliomas. In malignant gliomas, thermal therapy has been essentially unsuccessful, a predictable outcome, since such tumors extend far beyond the area of MRI contrast enhancement [7, 8, 9].

Among the currently developed thermal therapy methods, focused ultrasound (FUS) appears to be the most promising, since its use does not require any invasive intervention. The potential therapeutic use of ultrasound energy for intracranial pathology has long been acknowledged [10]. There is no more convincing example for the FUS benefits than in the brain, where deep lesions can be induced without any associated damage along the path of the acoustic beam. In the brain, where most injuries have detectable functional consequences, it is extremely important to limit tissue damage to the targeted area. This necessitates the use of an imaging technique for localization, targeting, real-time intraoperative monitoring, and control of the spatial extent. Indeed, by combining FUS with MRI-based guidance and control, we might well achieve complete tumor ablation without any associated structural injury or functional deficit.

Beyond thermal coagulation of tissue, FUS has various other effects that can be therapeutically exploited and thus may open the way for potentially innovative vascular and functional neurosurgery applications as well as targeted drug delivery to the central nervous system [11]. Among the most important is focused ultrasound's ability to occlude vessels, which could make FUS a viable therapeutic tool for the treatment of vascular malformations [12]. Groundbreaking studies also show that FUS can also open the blood–brain barrier selectively without damaging the surrounding brain parenchyma [13]. To achieve this effect, preformed gas bubbles must be introduced into the vasculature, as is routinely done with ultrasound contrast agents. The gas bubbles implode and release cavitation-related energy, which transiently inactivates the tight junctions [14]. Consequently, large molecules can pass through the artificially created "window" in the blood–brain barrier. These large molecules can be chemotherapeutic or neuropharmacological agents. FUS-based, targeted selective drug delivery to the brain could result in novel therapeutic interventions for movement and psychiatric disorders. Such MRI-guided focal opening of the blood–brain barrier, combined with ultrasound technology that permits sonications through the intact skull will open the way for new, noninvasive, targeted therapies [15]. Specifically, it would provide targeted access for chemotherapeutic and gene therapy agents, as well as monoclonal antibodies, and could even provide a vascular route for performing neuro-transplantations.

Since the skull bone scatters and attenuates the propagation of the ultrasound beam, most clinical trials have been performed following craniotomy in order to provide an ultrasound window. However, the transcranial application of FUS, although challenging, is not impossible. Although bone scatters and absorbs most of the acoustic energy, a small fraction can penetrate through the skull. Recent simulation and experimental studies have demonstrated the feasibility of accurately focusing ultrasound through the intact skull by using an array of multiple ultrasound transducers arranged over a large surface area [16]. To correct for beam distortion, the driving signal for the transducer elements of the array is individually adjustable, based on measurements obtained with an invasive hydrophone probe, or better, based on detailed MRI. Because of the large surface area, the ultrasound energy is distributed in such a manner as to avoid heating and consequent damage of skin, bone, meninges, or surrounding normal brain parenchyma, while at the same time, is able to coagulate the tissue at the focus. The experimental data are extremely promising and a clinical trial is in progress at Harvard Medical School. Based on these preliminary results, the thermal coagulation of brain tumors through the intact skull under MRI thermometry control using MR-compatible arrays appears feasible.

By applying multiple, smaller transducers around the skull in a helmet-like phased-array system, sufficient amounts of energy can be deposited in the target tissue. Unfortunately, the skull thickness is uneven, causing variable delays of the acoustic waves originating from individual phased array elements. Phase incoherence can be corrected, however, if the skull thickness is known from preoperative X-ray computed tomography scans. In an experimental setup successful focusing through the skull has been achieved and verified by MRI, and this provides the foundation for developing the first human MRI-guided FUS system for brain tumor treatment.

Conclusion

Clearly, the broad medical community has accepted the role of imaging in both diagnosis and therapy. Increasingly, minimally invasive procedures are viewed favorably and there is a strong demand for their widespread implementation across numerous surgical disciplines. Nowhere is this demand more evident than in neurosurgery where advances in intraoperative MRI and computing technology have marshaled in a new and exciting era in the treatment of brain tumors. We are especially encouraged by the ability of MRI-guided Focused Ultrasound to penetrate the blood brain barrier selectively. This breakthrough technology holds great promise for a host of interventions from vascular occlusion to targeted drug delivery for brain cancer (and other CNS diseases) to gene therapy.

Although radiology has combined imaging with various novel therapeutic methods, the full utilization of advanced imaging technology has not yet been accomplished. The current trend is focused on the creation of *integrated* therapy delivery systems in which advanced imaging modalities are closely linked with high performance computing. Obviously, the operating room of the future will accommodate various instruments, tools, and devices that are attached to the imaging systems and controlled by image-based feedback. We are confident these innovative technologies when applied in an integrated, multimodality imaging environment will produce a range of minimally and non-invasive therapies for the brain and as well as other organs and systems.

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