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Magnetic Resonance Guided Focused Ultrasound Surgery: Part 2 – A Review of Current and Future Applications

Ricky Medel, M.D.¹, Stephen J. Monteith, M.D.¹, W. Jeffrey Elias, M.D.¹, Matthew Eames, Ph.D.², John Snell, Ph.D.², Jason P. Sheehan, M.D., PhD¹, Max Wintermark, M.D., M.A.S.³, Ferenc A. Jolesz, M.D.⁴, and Neal F. Kassell, M.D.^{1,2}

¹Department of Neurosurgery, University of Virginia Health Sciences Center, University of Virginia, Charlottesville, Virginia, 22908

²Focused Ultrasound Surgery Foundation, Charlottesville, Virginia, 22903

³Department of Radiology, University of Virginia Health Sciences Center, University of Virginia, Charlottesville, Virginia, 22908

⁴Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02445

Abstract

Magnetic Resonance guided Focused Ultrasound Surgery (MRgFUS) represents a novel combination of technologies that is actively being realized as a non-invasive therapeutic tool for a myriad of conditions. These applications are reviewed with a focus on neurological utilization. A combined search of Pubmed and Medline was performed to identify the key events and current status of MRgFUS, with a focus on neurological applications.

MRgFUS signifies a potentially ideal device for the treatment of neurological diseases. As it is nearly real-time, it allows monitored provision of treatment location and energy deposition, is noninvasive, thereby limiting or eliminating disruption of normal tissue, provides focal delivery of therapeutic agents, enhances radiation delivery, and permits modulation of neural function. Multiple clinical applications are currently in clinical use and many more are under active preclinical investigation.

The therapeutic potential of MRgFUS is expanding rapidly. Although clinically in its infancy, preclinical and early phase I clinical trials in neurosurgery suggest a promising future for MRgFUS. Further investigation is necessary to define its true potential and impact.

Keywords

Focused Ultrasound; Ultrasound; MRI; Therapy; Neurosurgery

Corresponding and Reprint Author: Neal F. Kassell, M.D., Department of Neurological Surgery, University of Virginia Health Sciences Center, Box 800212, Charlottesville, VA 22902, Phone: (434) 924-2735, Fax: (434) 924-9656, nfk8g@virginia.edu.

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Disruptive technologies are by nature transiently less refined, in addition to being briefly confined in applicability compared to their established counterparts¹. However, with persistent scrutiny, investigation, and enhancement, it is these technologies that revolutionize current practices. The therapeutic potential of ultrasound, in particular high intensity focused ultrasound (HIFU), has been apparent for decades. More recently, through progressive innovation in radiographic modalities, magnetic resonance (MR) imaging has provided superior resolution of soft tissue structures, especially within the central nervous system (CNS). Neither in itself represents novelty, but through the integration of these technologies, the field of MR guided focused ultrasound surgery (MRgFUS) has been conceived^{2,3}. While easily dismissed as an inferior alternative to existing medical and surgical standards, MRgFUS is auspiciously placed to usurp these same practices across multiple clinical disciplines.

Throughout history, the therapeutic limitations of neurosurgery have largely been derived from concerns for damage to adjacent and overlying tissue. MRgFUS permits precise targeting of structures in multiple areas of the central nervous system in a noninvasive fashion. Although there have been substantial improvements in the conformity of radiosurgical dosing, there remains concerns with repetitive dosing. Concerning MRgFUS, cumulative dosing from multiple treatments has not been demonstrated to pose a significant risk to the surrounding tissue⁴⁻⁶. Additionally, its action is not limited to ablation, thus extending applicability to include: thrombolysis; augmentation of existing therapies (targeted drug delivery, blood brain barrier disruption, and moderate hyperthermia for enhancement of radiation); modulation of neural function; and coagulation. Overall, it is an exciting technology with an expansive therapeutic potential undergoing active realization. The purpose of this review is to outline the current status and future prospects of MRgFUS, focusing on its neurological applications.

Methods

A combined search of Pubmed and Medline was performed to identify the key events and current status of MRgFUS, with a focus on neurological applications.

Mechanisms

The physical principles underlying focused ultrasound surgery have been well outlined previously⁷⁻¹⁰ and will only be briefly recounted as they pertain to therapeutic applications.

Thermal Effects

The creation of thermal energy via focused ultrasound underlies both the ablative effects, as well as those associated with mild hyperthermia, such as radiosensitization. In either instance, the mechanisms of heat generation are similar, only its degree is different.

Tissue heating can be brought beyond the threshold for protein denaturation (57-60 degrees Celsius) with resulting necrosis depending upon a very predictable temperature-time relationship¹¹⁻¹³. As an ultrasound wave travels through tissue, pressure variations lead to microscopic shearing of tissue with consequent conversion of the mechanical energy into

heat¹⁴. This process accounts for a significant portion of the heat deposition that occurs during sonication. Non-linear wave propagation also plays a substantial role in the production of thermal lesions¹⁵⁻¹⁷. As a single frequency wave travels through a heterogeneous medium, supraharmonic leakage occurs from the fundamental frequency, with the energy from the latter being readily absorbed by surrounding tissues¹⁸. As this process is dependent on the amplitude of the wave, medium characteristics, and distance traveled, it is also a substantial contributor to heat generation when using high-intensity focused ultrasound⁹.

A final source of heat generation is through the induction of cavitation. At sufficient amplitudes, gaseous cavities form (predominantly at tissue interfaces), with the subsequent behavior of these being divided into two categories: stable and inertial. Stable cavitation refers to sustained oscillation of the intact bubble, whereas inertial cavitation is a rapid expansion of the cavity with a consequent violent collapse and rupture, which is associated with the release of broadband acoustic emissions^{9, 19}. Heating occurs both through the absorption of this energy in the latter circumstance, as well as through scattering and preferential absorption of ultrasound within the cavitating region, resulting in a focal deposition of the acoustic energy.

Mechanical Effects

In addition to the concentration and amplification of thermal energy deposition, cavitation also has mechanical effects that are important for sonothrombolysis, blood brain barrier disruption, and sonoporation²⁰⁻²⁵. These effects are due both to the direct mechanical impact of bubble oscillation on cells and the formation of local eddies within fluid. These forces can disrupt fibrin strands in the setting of clot or induce changes at the tight junctions of the blood brain barrier, depending on the clinical setting.

Of utmost concern is careful focal control of this process, as the induction of inertial cavitation has the potential to produce adverse effects. One method of improving the safety profile of cavitation is with the administration of microbubbles, which are commonly used as an ultrasound imaging contrast agent. In this instance, lower power ultrasound can be delivered to achieve similar cavitation effects, because one is not relying on ultrasound-induced nucleation of gas bubbles within the tissue²⁶⁻³⁰.

Acoustic streaming also possesses a role in the effect of sonication. As a wave traverses a fluid medium, particles contained within the medium are propelled in the direction of wave propagation³¹. This can be used to facilitate targeting of agents³², as well as contributing to the mechanical effects as described for cavitation.

MRgFUS for Diseases outside the brain

Given the technical challenges of transcranial sonication, various diseases were chosen for preliminary investigations. After feasibility testing of the initial integrated MRgFUS delivery system, ablation of breast fibroadenomas was chosen as the first clinical application in 2001³³. This pathology was chosen for the following reasons: the breast is easily accessible to the ultrasound beam without obstruction of the acoustic window; MRI

precisely defines the well marginated benign fibroadenomas; and although benign, these lesions can be exceedingly symptomatic. In this study, 11 fibroadenomas in nine women were treated with an early non-commercial MRgFUS system containing a single element ultrasound transducer using local anesthesia and MRI-based thermometry. Following treatment, eight of the 11 lesions treated demonstrated complete or partial loss of contrast material uptake on T1-weighted images³³. Further investigations have focused on the effectiveness of MRgFUS in breast cancer. Although these have proven feasible to ablate, there remains some concern for viable tumor at the margins³⁴⁻³⁸.

Additional application has been found for MRgFUS in the treatment of uterine fibroids³⁹, and it is for this indication that it acquired its CE Mark in Europe in October 2002 and Food and Drug Administration (FDA) approval in the United States in October 2004^{40, 41}. Stewart et al⁴² reported that 71% of patients who underwent MRgFUS for uterine fibroids had a significant reduction in symptoms for at least 6 months, with 51% achieving improvements for at least 1 year. Further reports have also documented improved quality of life⁴³, significant reduction in fibroid size⁴⁴, as well as the positive effect on fertility following treatment⁴⁵⁻⁴⁹.

MRgFUS can also be an effective palliative solution for the treatment of pain caused by bone metastases, and obtained CE Mark certification in Europe for this indication on November 17, 2007⁴¹. Since bone absorbs 50 times more acoustic energy than soft tissues, FUS treatment can significantly increase bone temperature so that the periosteum and the bone around a metastasis can be heated, with subsequent denervation and analgesia. Catane et al.⁵⁰ noted pain relief (on a visual-analog scale) in 10 of 12 patients with bone metastases at 59-days follow-up. Other active areas of investigation with promising results include prostate lesions, hepatocellular carcinoma, colon cancer, bladder cancer, testicular carcinomas, ocular tumors, and inflammatory disorders⁵¹⁻⁶⁴.

Current Neurological Applications

MRgFUS is well suited for intracranial neurosurgical applications, allowing real-time visualization and treatment of a target with directed deposition of acoustic energy, while minimizing or eliminating injury to the normal brain. A brief summary of the procedure is described below.

Prior to therapy, a planning computed tomography (CT) scan of the head is obtained for the correction of phase aberrations caused by irregular skull thickness and bone density that prevents focusing^{65, 66}.

For many applications this is inconsequential; however, for the treatment of time-sensitive conditions such as stroke, direct acquisition of bone parameters would optimally be obtained directly from the planning MRI. In the hemispheric phased-array transducer (ExAblate Neuro, InSightec Ltd., Tirat Carmel, Israel), each element is driven separately affording individual correction for bony distortion, as well as electronic steering. The geometric and density information obtained from the CT scan, combined with acoustic simulations, allow for phase adjustments to compensate for skull-induced phase aberrations. This CT correction allows the ultrasound beams to converge on a highly focused target point. A stereotactic

head frame is placed for patient immobilization during the procedure, and the head is shaved to provide an acceptable acoustic window. A silicone diaphragm is then fitted to the scalp and the transducer filled with degassed water (dissolved oxygen below 1.2 ppm). The cooled (15 to 20 degree Celsius) degassed water is circulated between sonications to prevent thermal injury to the scalp. A pretreatment MRI is acquired to allow definition of the target for treatment planning. Calibration and monitoring of treatment is performed using MR-thermometry. Once calibration is complete, therapeutic sonications are delivered with the parameters dependant upon the goal of treatment. The procedure can be performed with minimal analgesia as necessary for patient comfort.

Brain Tumor Ablation

Complete excision or local destruction of malignant or benign lesions, without associated injury to the surrounding parenchyma, is the preferred, often difficult to achieve goal of open surgery, radiosurgery, and radiation therapy. Although CT- and ultrasound guided studies on thermoablation of brain tumors has been reported previously with mixed results ^{67, 68}, recent studies have focused on using the improved visualization provided by MRgFUS for the treatment of malignant gliomas.

Ram et al., used a craniectomy to treat three patients with recurrent glioblastoma ⁶⁹. Craniectomy was performed 7 to 10 days before the sonication to create an acoustic window. MRgFUS therapy produced immediate lesions on MRI, with subsequent histopathological evidence revealing thermocoagulation. Patient survival times of 10, 31, and 33 months were reported; however, the limited population prevents any generalization. Additionally, in one patient, heating of brain tissue in the sonication path resulted in a secondary focus outside the target, which caused neurological deficits. Consequently, changes have been made to the therapeutic system in order to improve the safety profile.

Park, et al reported successful ablation of an anaplastic astrocytoma transcranially in a 17 year-old female in whom no other therapeutic options were available. On follow-up imaging six months later, a decrease in the tumor volume and surrounding edema was noted ⁷⁰. Further research evaluating another transcranial treatment system (ExAblate 3000; InSightec, Tirat Carmel, Israel) was performed on three patients with deep-seated primary brain tumors at the Brigham and Women's Hospital ^{71, 72}. These procedures incorporated CT-based planning for aberration correction with MRI-based pretreatment planning and intraoperative guidance. This study demonstrated focusing of ultrasound-induced thermal energy at the desired targets. However, the clinical trial was halted when a fourth patient treated with the same approach suffered a cavitation induced intracranial hemorrhage and subsequently died.

In these studies, MRI monitoring was instrumental to guide sonication paths away from critical intracranial structures and to give real-time feedback on the spatial and temporal distributions of thermal energy deposition. Unfortunately, despite accurate focusing, thermocoagulation was not obtained due to technical limitations of the prototype system.

Based on these early works, transcranial MRgFUS for tumor ablation appears feasible; however, further investigation is clearly necessary. Additionally, although high-grade

gliomas were included in the studies described, they likely do not represent the optimal population for this modality, with better applications being well-circumscribed lesions such as metastasis or benign tumors in locations that are difficult to access surgically. Current trials in the United States and Switzerland in patients with metastases and gliomas are expected to provide more evidence regarding treatment efficacy.

Limitations presented by the current system include the inability to target superficial skull base, or posterior fossa lesions secondary to bone heating and difficulties in beam focusing. Studies have shown that ultrasound contrast agents can create the thermal effect with a lower time-averaged power level^{26, 73}. By systemically injecting an ultrasound contrast agent such as preformed microbubbles, cavitation enhanced tissue ablation can be optimized. These agents have been shown to enhance focal heating during sonication and have been suggested as a means to reduce the time-averaged power needed during transcranial focused ultrasound ablation. Preformed microbubbles act as cavitation nuclei and the pressure amplitudes required for heating and lesion creation are greatly reduced. McDannold et al. have demonstrated that the administration of a microbubble-based ultrasound contrast agent reduces the acoustic power threshold required to induce lesions in rabbit brains with high-intensity focused ultrasound⁷⁴. The time-averaged acoustic power needed to produce localized necrotic lesions in the brain was less than one tenth of what was needed to produce thermal lesions without contrast agents under otherwise identical experimental conditions.

Neuropathic Pain

Drs. Jeanmonod, Martin, and other collaborators have conducted a phase I feasibility study on patients with chronic therapy resistant neuropathic pain^{4, 75}. Twelve patients underwent transcranial MRgFUS with a commercial system (ExAblate 4000; InSightec, Tirat Carmel, Israel) containing a hemispheric 1,024-element phased array transducer functioning at 650 kHz to yield precise lesioning of the central lateral nucleus of the thalamus. One patient with prior radiofrequency lesioning suffered a hemorrhagic lesion next to the target, which resulted in dysmetria that partially resolved over the three-month follow-up. Pain relief forty-eight hours following the procedure averaged 68% (30-100%).

Movement Disorders

Currently, phase I clinical trials utilizing the ExAblate Neuro 650 KHz system (InSightec, Israel) to evaluate the safety of unilateral ventralis intermedius lesions in patients with medically refractory essential tremor are ongoing⁷⁶. The preliminary results are very encouraging and were recently presented at the 2011 Congress of Neurological Surgeons annual meeting⁷⁶. A similar study is also being instituted in Solothurn for patients suffering from Parkinson's disease, by targeting the pallidothalamic tract.

Facet Rhizotomy

Since its introduction in 1974, facet rhizotomy has been utilized with variable success to alleviate chronic back pain associated with degeneration of the zygo-apophyseal joints^{77, 78}. The procedure is commonly performed using radiofrequency thermal ablation or glycerol, both with the goal of denervating the joint. As described for palliation with painful bony

metastases, thermocoagulation of the periosteum can be achieved with MRgFUS. Seventeen patients have been treated in St. Mary's Hospital, London, England by Dr. Gedroyc with as much as a 60% reduction in pain with the current follow-up and a similar improvement on the Oswestry Disability Index. Currently, a randomized clinical trial is ongoing comparing the efficacy of MRgFUS ablation versus radiofrequency ablation ⁷⁹.

Future Neurological Applications

As previously described ⁷, the utility of MRgFUS is being investigated for numerous applications, including blood brain barrier disruption and targeted drug delivery, clot lysis, coagulation, and HIFU-induced immunomodulation. A summary of these topics is provided below.

Sonothrombolysis

Stroke, both ischemic and hemorrhagic, remains a common affliction in modern society with substantial morbidity and mortality ^{80, 81}. Current therapeutic options are limited, especially when considering deep-seated intracranial hemorrhage ⁸²⁻⁸⁶. Innovative modalities utilizing HIFU have the potential to revolutionize current treatment paradigms. A full review of sonothrombolysis has been published ⁸ and will only briefly be recounted here.

Concerning ischemic stroke, low intensity ultrasound in the presence of tissue plasminogen activator (tPA) has been demonstrated to significantly improve the rates of recanalization. Alexandrov, et al ^{87, 88} performed a multicenter trial, enrolling 126 patients with middle cerebral artery occlusion. Patients were randomly assigned to receive either tPA alone or tPA plus isonation with a 2 MHz transcranial doppler 2 hours following administration of tPA. Rates of recanalization improved from 18% to 46% ($P < 0.001$) in the ultrasound group without a significant increase in hemorrhagic or other complications. An improvement in clinical outcome as defined by a Rankin score of 0 to 1 at 90 days was observed, but was not statistically significant. Limited publications exist regarding the use of HIFU for ischemic stroke; however, in vitro models such as that employed by Rosenschein, et al ⁸⁹ have demonstrated the ability of HIFU to completely lyse intra-arterial clot independent of tPA without damage to the surrounding arterial wall.

The therapeutic options for hemorrhagic stroke are remarkably limited and, given the poor associated prognosis, there exists significant impetus for the development of novel technology ^{80, 90}. Harnof, et al ⁹¹ and others have sonicated thrombi in gel phantoms, revealing the ability to liquefy 90% of the clot within 10 seconds (Figure 1). Currently, studies utilizing both porcine ⁹² and cadaveric intracerebral hemorrhage models are underway and have confirmed the ability to not only liquefy, but also percutaneously aspirate the lysate ⁹³.

Through persistent improvement in technology, MRgFUS may allow for lysis of clot within the main intracerebral arteries while potentially minimizing the hemorrhagic complications associated with the use of thrombolytics. However, as has been realized with systemic thrombolytics and mechanical thrombectomy, the time limitations associated with ischemic stroke represent a substantial constraint on the application of treatment. Concerning ICH,

this technology will afford clinicians the ability to lyse an intracerebral thrombus with a high degree of accuracy. Subsequent aspiration could then be performed in a minimally invasive fashion, with MRI providing immediate information regarding clot removal, all without the need for indwelling catheters. Clinical trials are expected to begin in the near future.

Targeted Drug Delivery

Modification in sonication parameters from those used for ablation can permit reversible effects on the blood brain barrier (BBB), allowing leakage of targeted chemotherapeutic agents, nanoparticles and other systemically administered substances. This is possible by implementing low-duty cycles that allow for dissipation of heat between pulses. Instead of heat deposition, acoustic radiation forces and the mechanical effects of cavitation displace tissue, reorganize and allow increased delivery of liposomal doxorubicin, nanoparticles, fluorophores, and naked DNA injected systemically to locally sonicated tumor tissue in vivo²⁰⁻²⁴.

Reversible cell membrane poration has been well demonstrated in vitro using HIFU treatment^{94, 95}. This technique provides a potential alternative method to treating tumors by incorporating heat-activated chemotherapy, gene therapy, nanoparticles or liposomes locally where it is needed while theoretically avoiding side effects of systemic drug or gene therapy administration.

The earliest pre-clinical trials on selective drug delivery involved antibody targeting. Following MRgFUS disruption of the blood brain barrier in mice, injected anti-dopamine 4 antibodies (anti-D4) were only found in the area of blood brain barrier (BBB) disruption, indicating a high degree of selectivity⁹⁶. Pre-clinical studies involving chemotherapeutic agents have shown similar promise. Bendell et al⁹⁷ demonstrated that when the anti-Her-2 antibody Herceptin was injected into mice using ultrasound-induced BBB disruption technique, the agent was successfully delivered into the brain, with a concentration gradient that correlated with the expected BBB disruption magnitude measured using MRI. This phenomenon opens the possibility of estimating the actual concentration of a drug at the target location using MRI-guided blood brain barrier opening⁹⁸.

Although these studies clearly demonstrate the feasibility of targeted drug delivery using MRgFUS, the clinical efficacy of this approach use remains unclear. While internalization of small molecules (less than 37 nm in diameter) has been shown to be extremely efficient, the effectiveness of delivery of larger macromolecules has been shown to be less efficient⁹⁴.

HIFU-induced Immunomodulation

Aside from delivery of antibodies and other immunologic agents, early data appears to show that endogenous danger signals from HIFU-damaged cells in tumor models can enhance the anti-tumor response^{99, 100}. Several clinical studies have provided evidence that immunomodulation occurs following HIFU treatment, which could affect the patient's immune status^{94, 100}. Furthermore, this systemic anti-tumor immunity has been confirmed in animal studies. In unresectable murine neuroblastomas, HIFU treatment coupled with adriamycin caused a significant reduction in tumor growth, and delayed tumor regrowth

compared with HIFU or adriamycin alone, a phenomenon that was thought to be related to immunomodulatory activity ¹⁰¹. Hu et al ⁹⁹ demonstrated an enhanced systemic immune reaction in an animal model that was related to dendritic cell activation. This study also found that dendritic cell activation was more pronounced when tumor cells were mechanically lysed, indicating that mechanical HIFU may be a particularly attractive option when the host's tumor immunity needs to be enhanced.

Neuromodulation and Epilepsy

Neuromodulation refers to the ability to selectively manipulate neuronal circuits in a reversible fashion. Multiple in vitro and in vivo studies have demonstrated the ability of focused ultrasound to both reversibly and irreversibly block nerve conduction ¹⁰²⁻¹⁰⁵. Other US parameters may in fact activate neural tissue, both peripherally and in the central nervous system ¹⁰⁶. These effects are posited to occur as a result of mechanical stimuli (reversible) and thermal ablation (potentially irreversible). Tufail, et al ¹⁰⁷, stimulated the murine motor cortex with pulsed ultrasound (500 kHz, 100 cycles per pulse 1.5 kHz PRF, 80 pulses) and achieved muscular contraction by EMG in 92% of the mice without any evidence of histological damage or adverse motor impairment.

A similar set of experiments were conducted in New Zealand white rabbits by Yoo and colleagues ¹⁰⁸. Using a 690 kHz transducer, various parameters were manipulated in an effort to both stimulate and suppress neural transmission. Sonication for greater than or equal to 1 second with an acoustic intensity of 12.6 W/cm² (TBD 50 msec, 10 Hz PRF) to the motor cortex resulted in a motor response detectable both visually and by EMG. They then examined visual evoked potentials before and after exposure to sonications of the visual cortex for approximately eight seconds with an acoustic intensity of 6.4 W/cm² (TBD 0.5 msec, 100 Hz PRF). This revealed a reduction in the magnitude of the response that completely recovered within 10 minutes of the sonication. Again, histological analysis was performed and did not demonstrate any evidence of permanent tissue injury.

This technique of modulating neural transmission also had potential application in the treatment of epilepsy. Epilepsy is a common disabling condition with significant personal and societal ramifications. MRgFUS has been shown in a murine epilepsy model using pentylentetrazol to decrease epileptic activity ¹⁰⁹. The animals underwent transcranial pulsed sonication at an intensity (130 mW/cm²) within the range of clinical imaging. The epileptic activity on EEG was significantly decreased from the presonation state, as well as in comparison to controls. This technique could afford clinicians the potential to target an epileptic focus prior to permanent ablation if necessary.

Trigeminal Neuralgia

Although many modalities exist for the treatment of trigeminal neuralgia, there remain patients who are refractory to conventional therapy. Previously, transcranial MRgFUS for the treatment of this disease was not thought to be feasible due to the deep-seated location of the trigeminal nerve target and its proximity to critical basilar structures. However, recent investigations using a cadaveric model with real-time MR thermometry, in addition to experimentation with thermocouples in a transcranial in vitro setup, have challenged this

notion. These studies demonstrated the ability to produce a focal temperature rise within the trigeminal nerve with acceptable bony heating and minimal changes in the temperature of surrounding structures (Stephen J. Monteith, M.D., personal communication, August 2011) (Figure 2). Although further investigation is needed, this illustrates the expansive potential of MRgFUS.

Hyperthermia for Radiation Enhancement

The application of hyperthermia to enhance radiation delivery is not a novel concept; however, the advantages afforded by focused ultrasound have provided a new impetus for exploration. Cells vary in their sensitivity to hyperthermia depending on temperature, exposure duration, and internal milieu ¹¹⁰. Absolute temperature and exposure can be precisely manipulated with MRgFUS, while exploiting the more unfavorable environment (i.e. lower pH and energy state) within tumor tissue. Additionally, cells that are in the S-phase of reproduction, and relatively more radioresistant, have a higher sensitivity to hyperthermia ¹¹⁰.

Prior attempts at combining these modalities have been plagued by the need for craniectomy and placement of internal probes for measuring temperature elevation, with their associated morbidity ¹¹⁰. As previously illustrated, this is obviated with current MRgFUS technology. This potential approach represents another area for which MRgFUS may have future clinical utility

Conclusion

The field of MRgFUS remains in its infancy, but it seems poised to broaden the neurosurgical armamentarium. The lack of adequate imaging and the need for a craniectomy previously constrained the use of acoustic energy, but modern magnetic resonance imaging and computer technology have overcome these limitations. The result is a novel therapeutic device that appears to have expansive potential in the treatment of neurological disorders as has been demonstrated above. Although relatively few clinical trials have been performed, this number is expected to increase dramatically. Considerable opportunity exists to exploit this technology across medical disciplines, with a consequent abundance of research opportunities.

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This is a complete review where Magnetic resonance image-guided focused ultrasound surgery (MRGFUS) was deeply analyzed by Authors, especially regarding current and future applications. MRGFUS represents an innovative technology in the panorama of new treatment using ultrasound with ablative intent. MRGFUS, as promising and non-invasive technique, can potentially minimize mortality, cut medical costs, and open new opportunities for the treatment of patients with CNS diseases. It combines two well-known and distinct components: high-intensity focused ultrasound (HIFU) and a magnetic resonance imaging system (MRI). Nevertheless, MRGFUS is still in its infancy. The possible side effects such as skin burns, coagulative necrosis of adjacent heat-sensitive tissues can be dangerous and not negligible. More data on patients are needed to consolidate the definitive feasibility of the MRGFUS approach in CNS. Thus, this technology still remains only an experimental approach.

Filippo Alongi, Milan, Italy

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Figure 1.

Transcranial sonothrombolysis of clotted blood in a phantom setup with 230Khz, 30seconds, 10% duty cycle, 3950W. After performing a calibration sonication in the center of the middle column of clotted blood, lysis parameters can be tested at additional locations. Pre (A) sonication T2 MRI. In (B) the blue spots are completed sonications. In figure C, discrete areas of clot lysis at the target areas are demonstrated by increased T2 signal.

Figure 2.

Demonstration of focal heating of the trigeminal nerve root entry zone in a cadaveric laboratory setup. In this example a discrete 8 degree temperature rise as measured by realtime MR thermometry (top panels) was achieved with the ExAblate 650Khz system with 750W for 10s. Such a MRgFUS system could be used to focally heat the trigeminal nerve for the treatment of trigeminal neuralgia.