Neurosurgical Applications of High-Intensity Focused Ultrasound with Magnetic Resonance Thermometry

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KEYWORDS

- MRgFUS • Focused ultrasound • Brain • Glioma
- Magnetic resonance–guided focused ultrasound surgery

KEY POINTS

- Magnetic resonance–guided focused ultrasound surgery (MRgFUS) is a noninvasive, image-guided therapy method that treats neoplasms and target tissue using thermal ablation and/or nonthermal effects.
- Thermal ablation involves the heating of target tissues using ultrasound waves to yield cellular damage and coagulative necrosis.
- Nonthermal effects include modulation of cellular permeability and cavitation, which can contribute to enhanced drug delivery through the blood-brain barrier.

INTRODUCTION

Magnetic resonance–guided focused ultrasound surgery (MRgFUS) is a therapeutic modality that has gained interest in recent years for its potential use in noninvasive tumor ablation and treatment, and more recently in the treatment of essential tremors. Although surgery and radiation therapy currently provide the standard of care for many oncological conditions and have been more extensively implemented in the clinic, these are associated with differential outcomes and long-term toxicities. The benefit of MRgFUS is its potential to establish a treatment that can be maximally effective with minimal side effects.

MRgFUS is the integration of 2 widely used imaging and therapy processes, MRI and focused ultrasound surgery (FUS), respectively. MRI is a long-established imaging methodology that provides high-contrast resolution for planning treatments and quantifying effects, namely through accurate target delineation, real-time monitoring of temperature changes, and modulation of energy deposition in the tissue of interest.[1] Whereas MRI is the monitoring component of MRgFUS, FUS is the therapeutic component; ultrasound beams can cause cellular damage in a thermal ablative or nonthermal manner. Together, MRI and FUS provide an unparalleled ability to directly visualize

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tumors as they are treated with ultrasound waves and monitor effects in near real-time. With further research, this has the potential to serve as an adjunct or even replace current invasive surgery and radiotherapy therapeutic courses for specific tumors and diseases. This article discusses the principles and applications of thermal ablation and nonthermal effects in cancerous and noncancerous central nervous system (CNS) disease.

THERMAL ABLATIONS

The mechanism of thermal ablation of tumors involves the conversion of mechanical energy into heat through the steering of multiple ultrasound waves to a targeted location of tissue.[2] These waves, also called sonications, are highest and most intense at their point of convergence. When the tissue is heated to approximately 57°C to 60°C for at least 1 second at the target tissue's point of conversion, protein denaturation, coagulative necrosis, and eventual complete ablation of the tissue will occur.[2–4] This location is typically 2 mm (very precise) and thus multiple simultaneous or parallel sonication points can be done for larger ablation zones.

As mentioned, a benefit of FUS is its noninvasive nature and that it is unique in its ability to generate mechanical energy from ultrasound waves, which is converted to heat and hits the target focal area without harming adjacent tissue in its trajectory. With surgery and radiation therapy, excision of the tumor region without affecting surrounding normal tissue is not possible; MRgFUS can act as an alternative in patients for whom these other options may not be feasible due to the associated risks.[1] In fact, this method becomes even more relevant for neoplasms that are located in regions of the body where affecting nearby tissues incidentally can yield severe, long-lasting damage, such as deep-seeded neoplasms in the brain. Given the highly invasive nature of accessing the brain in surgery, and the nonspecificity and scatter issues that plague radiation therapy, using MRgFUS for thermal ablation in the brain can provide an accurate and efficient modality to access more sensitive and hard to reach tumors. Early in the implementation of this method, the skull provided a challenge to the accurate convergence of sonications to tissues of interest given the irregular thickness of the skull that leads to phase distortions and aberrations. In addition to these irregularities, there was excessive heating of the skull caused by the bone being able to absorb up to 50 times more acoustic energy than soft tissues.[1,4,5] These issues have led to the establishment of hemispherically configured phased-array transducers that can evenly distribute the heat across the skull while delivering the appropriate amount to the focal point. Another modification has been the addition of a cold water cap placed between the patient's head and transducer to aid in the cooling of the scalp and skull (**Fig. 1**).[4,6,7]

Although using FUS alone is effective, it is often nonspecific and can lead to tissue ablation of both normal and neoplastic cells. This necessitates the use of a spatial and temporal monitoring modality, which is where MRI comes in. One of the components of MRI is its thermometry capability. MR thermal mapping can generate near real-time temperature-sensitive maps that help monitor and maintain appropriate temperature levels during focused ultrasound and focus on the region of interest while preventing any damaging heating of adjacent or trajectorial tissue. Additionally, an advantage of MRgFUS over radiotherapy is the lack of ionizing radiation and the capacity to administer repeated treatments within a short amount of time, with minimal side effects.[1,2,4] Unlike surgery, MRgFUS is not invasive and is a

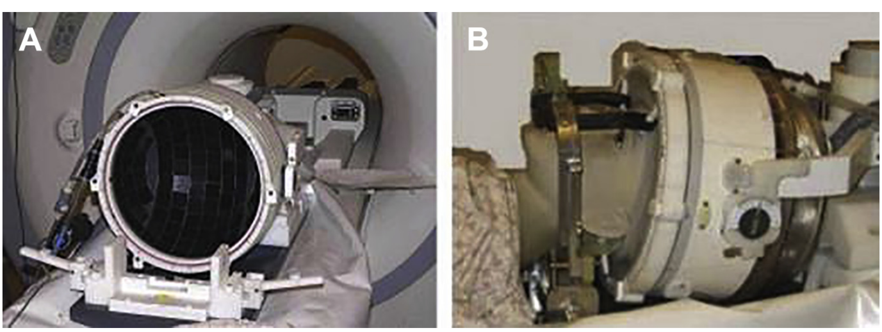

Fig. 1. Transcranial therapeutic system (Exablate 4000). (*A*) Helmet-type, hemispherically configured phased array transducer; it results in spatial spreading of the transducer elements and distributes heating across a larger surface area. (*B*) This is placed over the patient's head. A degassed cold-water cap is placed between the patient's head and the transducer. (*Courtesy of* Insightec, Haifa, Israel; with permission.)