Magnetic Resonance–Guided Focused Ultrasound

A New Technology for Clinical Neurosciences

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KEYWORDS

• Magnetic resonance imaging • Focused ultrasound • Neurosurgery • Brain tumor • Targeted drug delivery • Chemotherapy • Neuromodulation • Blood-brain-barrier

KEY POINTS

- Transcranial MRI-guided focused ultrasound (TcMRgFUS) is an old idea but a new technology that may change the entire clinical field of the neurosciences.
- TcMRgFUS has no cumulative effect, and it is applicable for repeatable treatments, controlled by real-time dosimetry, and capable of immediate tissue destruction.
- Most importantly, it has extremely accurate targeting and constant monitoring.
- It is potentially more precise than proton beam therapy and definitely more cost effective.
- Neuro-oncology may be the most promising area of future TcMRgFUS applications.

INTRODUCTION

Diseases of the central nervous system (CNS) account for more hospitalizations and a greater need for long-term care than most other clinical areas. Most currently available therapeutic interventions are suboptimal. Surgery, radiation therapy, and drug delivery all have significant limitations; therefore, completely new approaches and technologies are desperately needed.

Over the past 2 decades, the authors and other investigators have developed the fundamentals of TcMRgFUS, a noninvasive technology that, according those who

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are familiar with it, will have a profound impact on all aspects of the clinical neurosciences.[1–7] TcMRgFUS is a disruptive technology that can improve on or replace existing treatments and enable therapies that are not possible today. It is a radical departure from current treatment methods and involves expertise from multiple disciplines. Although the full potential that focused ultrasound (FUS) can have for disorders of the CNS is not widely known, the transformational process has already begun.

As described in this article, FUS has the ability to precisely focus acoustic energy to anatomically and functionally targeted locations in the brain and noninvasively induce a broad range of bioeffects that can be utilized to develop new diagnostic and therapeutic methods. Despite this great promise, this new enabling technology has several critical hurdles to overcome before widespread clinical translation is possible; a large-scale concentrated multidisciplinary effort is necessary. Currently, a diverse team of physicists, neuroscientists, engineers, and clinicians is working to advance FUS in clinical applications with the greatest impact. This review is based on innovations made by the authors' group and other investigators who have demonstrated the promise of TcMRgFUS. There are only a few prior examples of any other technology that has the same disruptive and transformative potential in any other field of medicine. If translated into everyday clinical practice, this enabling technology will change all aspects of clinical neuroscience.

FUS is uniquely capable of producing changes that can be used for the treatment of a potentially extensive range of CNS diseases and disorders. It is a completely noninvasive, targeted, and repeatable method that can be integrated with MRI to enable the necessary precise anatomic and functional guidance and control of energy deposition.[8,9] MRgFUS has been applied to treat benign and malignant tumors, such as uterine fibroids, breast tumors, prostate and liver cancer, and bone metastases.[8–10] The capabilities of FUS include the ability not only to noninvasively ablate tissue volumes (potentially replacing neurosurgery and radiosurgery) but also to deliver drugs to targeted brain regions through a temporary disruption of the blood-brain barrier (BBB).[11] This FUS-mediated method can revolutionize both neuro-oncology and neuropharmacology. In addition, FUS can reversibly modulate neuronal function (providing a tool that can be used in diagnosis and treatment in basic or clinical neuroscience).[12–14]

In recent years, with the development of a commercial TcMRgFUS device that is capable of FUS through the human skull, the feasibility of the technology was proved in humans in brain tumor ablation and functional neurosurgical applications.[7,15] Also, through a large number of preclinical studies that have been published recently, it has become clear that this technique has matured and is ready to be translated into clinical practice. This translation will be difficult however, because, to most clinicians, the therapeutic use of ultrasound in the brain is a radical concept. Therefore, significant work is needed to prove that FUS can be applied safely. Progress has been slow, with the feasibility of TcMRgFUS thermal ablation in humans reported only within the past few years.[7,15]

HISTORY OF BRAIN FUS

FUS has been investigated for more than 50 years, primarily for noninvasive ablation in the brain as a potential alternative to surgical resection, functional neurosurgery, and radiosurgery.[16–21] The enormous benefits of applying FUS as a noninvasive method for treating brain tumors, epilepsy, and movement disorders have been understood for many years, but the need for a craniotomy and the absence of imaging technologies delayed its development. Until recently, clinical tests of the method have required the removal of a section of the skull[22] to allow for ultrasound propagation into the brain