

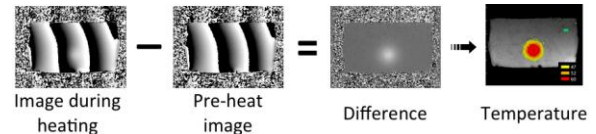
MR-Guided Focused Ultrasound

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Investigators throughout the world are currently applying MR-guided focused ultrasound (MRgFUS) for non-invasive treatments of a variety of diseases and disorders. Typically, focused ultrasound uses a large area ultrasound transducer array outside the body, focused either geometrically or electronically, to a point within the body. The amplification provided by focusing (which can be on the order of 1000-fold) provides the means to generate significant ultrasound intensities deep within the body, with insignificant ultrasound intensities in the intervening tissue. Current clinical systems for body applications are made by InSightec, who makes a variety of systems that are integrated into General Electric MR-scanners,¹ and Phillips, who has a system integrated into their own scanners.² An alternative is to use an ultrasound transducer within the target organ or tissue, with little or no focusing, an example of which is the Profound Medical transurethral ultrasound device for prostate treatments,³ which is currently in clinical trials on Siemens scanners. For brain applications, InSightec has a hemisphere array, which is currently in clinical trials, and Supersonic Imagine⁴ is developing a similar system, which will soon begin clinical trials on Siemens scanners.

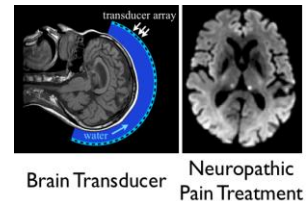


Magnetic resonance imaging provides the means to target the ultrasound beam to the tissue of interest, monitor the therapy with MR thermometry, and assess the treatment through the variety of contrast mechanisms available with MRI. While some targeting and assessment could alternatively be done with ultrasound, MRI is the only imaging modality that provides quantitative temperature mapping over a wide range of temperatures. The key to MR thermometry is the change in hydrogen bonding with temperature, which results in a change in the electron shielding of water protons, and changes the resonant frequency by approximately $-0.01 \text{ ppm}/^{\circ}\text{C}$. In practice, temperature images are calculated from the change in phase on gradient echo images.



There are several clinical applications of MRgFUS in the body. The first is the ablation of uterine fibroids. This application has regulatory approval in a number of countries, including by the FDA in the United States. With 24 month follow-up, MRgFUS provides a durable relief of symptoms.⁵ Second is the treatment of palliation of painful bone metastases. The ultrasound beam destroys the periosteum lining the bone, which then decreases pain. At the time of this writing, results from early trials have been submitted to the FDA. A number of other trials are ongoing in various body parts including breast,⁶ prostate, liver, and other abdominal organs.

A challenge in brain applications is the absorption of ultrasound by the skull. In order to minimize heating of the skull, cooled water is circulated about it. A second challenge is the variable thickness of the skull, which leads to phase aberrations and a reduction in the intensity of the ultrasound at the focus. These can be reduced through calculations of the phase aberrations on presurgical CT images.



Clinical trials in the brain have included neuropathic pain,⁷ essential tremor,⁸ both of which require target specific locations in the thalamus. An example diffusion-weighted image demonstrating FUS lesions is shown. In both applications, specific patients have experienced immediate symptom relief. A third clinical trial of focused ultrasound in the brain was a small study of ablation of brain tumors.⁹

MRgFUS has a role in innovative new drug delivery methods. Celsion makes a heat sensitive liposome containing doxorubicin (Thermodox), which can be combined with focused ultrasound and is in clinical trials.¹⁰ Another method for improved drug delivery addresses the selectivity of the blood brain barrier. In the presence of microbubbles, focused ultrasound can selectively open the blood brain barrier, allowing large molecules to enter the brain.¹¹

While these clinical trials are ongoing, there is an immense amount of research across the world in a number of areas. Technical areas of research to support clinical applications include improved thermometry (especially in moving organs), focal spot visualization, improved phase aberration correction, and workflow improvements. New transducers and geometries are being investigated. In addition, basic science research in ultrasound-based neuromodulation is showing that ultrasound can modulate neuronal firing.^{12,13} Thus, the future of MRgFUS holds new non-invasive treatments for a variety of diseases and disorders and also an exciting array of technical and scientific innovations.

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