Transcranial magnetic resonance-guided focused ultrasound for tremor

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Magnetic resonance-guided focused ultrasound (MRgFUS) has emerged as a leading noninvasive therapy for tremor, offering a precise, lesion-based alternative to deep brain stimulation (DBS) and traditional lesioning techniques. By using phased ultrasound arrays to focus energy at intracranial targets, MRgFUS allows for real-time visualization and monitoring, improving safety and efficacy. Initially developed for essential tremor (ET), MRgFUS-VIM-thalamotomy has gained widespread acceptance and is now a first-line option for tremor-dominant Parkinson's disease (TDPD) and other tremor syndromes.

Davidson and Lozano's review discusses the fundamental physics of focused ultrasound, key anatomical targets, and the clinical application of MRgFUS thalamotomy, pallidotomy, and subthalamotomy. Skull density ratio (SDR) and energy efficiency are highlighted as crucial factors affecting treatment outcomes. The evolution of MRgFUS as a bilateral treatment, along with the exploration of novel targets such as the pallidothalamic tract, is examined. Additionally, we discuss advancements in FUS neuromodulation, which could complement lesioning by providing temporary or reversible symptom relief.

Expert opinion: MRgFUS is poised to further revolutionize tremor treatment with frameless technology, staged bilateral procedures, and the integration of neuromodulation. Future developments may allow for precise, adaptive therapies that enhance both efficacy and patient experience [1).

How MRgFUS Works

Patient Preparation: The patient lies on a specially designed bed that fits into an MRI scanner. A frame is placed on the patient’s head to keep it still during the procedure, and a helmet filled with water is positioned over the head. This helmet allows the ultrasound waves to pass through the skull without causing damage.

MRI Guidance: The MRI provides real-time images of the brain, allowing the medical team to identify the precise target area. For tremor control, the target is typically the Vim (ventral intermediate nucleus) of the thalamus, a brain region involved in motor control.

Focused Ultrasound: High-intensity ultrasound waves are then focused on the target area. These waves converge on a small focal point, generating enough heat to create a thermal lesion in the targeted brain tissue.

Monitoring and Adjustment: The MRI continuously monitors the treatment area, allowing for real-time adjustments to the position, intensity, and duration of the ultrasound waves. This ensures precise targeting and minimizes the risk of damage to surrounding brain tissue.

Feedback from the Patient: Throughout the procedure, the patient is awake and able to provide feedback. This interaction helps the medical team fine-tune the procedure for maximum effectiveness and safety.

Benefits of MRgFUS for Tremor

Non-Invasive: Unlike deep brain stimulation (DBS) or surgical thalamotomy, MRgFUS does not require incisions or implanted hardware. Real-Time Imaging: MRI guidance allows for precise targeting and monitoring, reducing the risk of damaging surrounding brain tissue. Immediate Results: Many patients experience a significant reduction in tremor symptoms immediately following the procedure. Outpatient Procedure: MRgFUS is usually performed on an outpatient basis, allowing patients to return home the same day.

Indications

MRgFUS is primarily used to treat:

Essential Tremor: A common movement disorder characterized by rhythmic shaking, usually in the hands, that can interfere with daily activities. Parkinson's Disease Tremor: Tremor associated with Parkinson's disease, which may not respond adequately to medication.

Risks and Considerations

While MRgFUS is generally safe, it is not without risks. Potential complications may include:

Temporary or Permanent Sensory Changes: Such as numbness or tingling in the fingers or face. Weakness: In rare cases, patients may experience weakness in the treated area. Balance Issues: Some patients report temporary balance problems post-treatment. Headache and Pain: During or immediately after the procedure, patients might experience headaches or pain at the target site.

Conclusion

Transcranial MRgFUS is a promising treatment for tremor, offering a non-invasive alternative to more traditional surgical approaches. It provides immediate and often long-lasting relief from tremor symptoms, significantly improving the quality of life for patients who are suitable candidates. However, careful patient selection and thorough pre-procedure planning are essential to minimize risks and maximize outcomes.

Transcranial magnetic resonance guided focused ultrasound is increasingly used to non-invasively treat a wide variety of neurological disorders including essential tremors, Parkinson's disease and neuropathic pain. Although this treatment is an MRI-guided procedure, the current pre-treatment screening and planning involve a CT of the head to obtain three-dimensional skull images. These images are necessary for estimating the proportion of absorbed energy and the acoustic phase shift associated with the skull and determining the transmit energy of ultrasonic wave to create thermal lesions at a desired focal spot. Ultrashort Echo Time MRI sequences are able to capture signals from tissues such as bone which has a very short transverse relaxation time [2)].

An additional strength of transcranial MRgFUS surgery is its ability to focus acoustic energy through the intact skull onto deep-seated targets, while minimizing adjacent tissue damage. Even though the established indications of MRgFUS include bone metastases, uterine fibroids, and breast lesions, several promising preclinical and phase I clinical trials of neuropathic pain, essential tremor, Parkinson's disease (PD), and obsessive-compulsive disorder have demonstrated that the delivery of focused ultrasound energy promises to be a broadly applicable technique. For instance, this technique can be used to generate focal intracranial thermal ablative lesions of brain tumors, or to silence dysfunctional neural circuits and disrupt the blood-brain barrier for targeted drug delivery and the modulation of neural activity [3)].

Focused ultrasound (FUS) produces a region of high intensity at the focal zone of the beam but with minimal effects at adjacent areas, allowing the sonication of deep targets throughout the body. Despite early obstacles to transmitting ultrasound energy through the skull, recent advances in ultrasound technology, software, and real-time monitoring have resulted in a renewed interest in the clinical applications of transcranial FUS. Following extensive pre- clinical studies, ultrasound-induced thermal ablation has been approved by several countries for the treatment of essential tremor, Parkinson's disease, obsessive-compulsive disorder, depression, and neuropathic pain. Ongoing clinical trials involving patients with brain tumors, Alzheimer's disease, or epilepsy, and pre-clinical work involving stroke and hydrocephalus have the potential to significantly expand the possible indications for transcranial FUS in the future [4)].

Progressively less invasive neurosurgical approaches for the treatment of movement disorders have evolved, beginning with open craniotomy for placement of lesions within pyramidal structures followed by refined stereotactic ablation of extrapyramidal targets that encouraged nondestructive electrode stimulation of deep brain structures. A noninvasive approach using transcranial high-energy focused ultrasound has emerged for the treatment of intractable tremor. The ability to target discreet intracranial sites millimeters in size through the intact skull using focused acoustic energy marks an important milestone in movement disorders surgery [5)].

Weintraub and Elias, discuss ongoing trials and future avenues of investigation [6].

Magnetic resonance guided focused ultrasound thalamotomy for essential tremor

Magnetic resonance guided focused ultrasound thalamotomy for essential tremor.

Transcranial magnetic resonance-guided focused ultrasound for Parkinson's disease

Transcranial magnetic resonance-guided focused ultrasound for Parkinson's disease.

Exclusion Criteria

Severe Medical Conditions: Patients with severe, uncontrolled medical conditions, such as heart disease, respiratory issues, or infections, may not be eligible for MRgFUS due to the risks associated with prolonged immobilization and the procedure itself.

Coagulation Disorders: Patients with bleeding disorders, such as hemophilia, or those taking anticoagulant medications (e.g., warfarin, clopidogrel) that cannot be temporarily discontinued are at a higher risk of bleeding complications during the procedure.

Implanted Metallic Devices: Patients with certain types of implanted metallic devices or hardware, such as pacemakers, aneurysm clips, cochlear implants, or any other non-MRI-compatible devices, may not be eligible for MRgFUS because these devices can interfere with the MRI or be affected by the focused ultrasound.

Poor Skull Density: The effectiveness of MRgFUS relies on the ability of ultrasound waves to pass through the skull. Patients with skulls that are too thick, too thin, or have poor bone density may not be good candidates because the ultrasound may not adequately penetrate to reach the target area.

Psychiatric or Cognitive Impairment: Patients with significant psychiatric disorders (e.g., severe depression, psychosis) or cognitive impairment that prevents them from providing informed consent or cooperating during the procedure may be excluded from MRgFUS.

Inability to Tolerate MRI: Patients who are unable to tolerate MRI due to claustrophobia, severe anxiety, or inability to lie still for extended periods may not be suitable candidates for MRgFUS, as the procedure requires precise imaging guidance.

Pregnancy: MRgFUS is not recommended for pregnant women due to the potential risks to the developing fetus from both the MRI and focused ultrasound.

Other Neurological Conditions: Patients with other neurological conditions that may cause tremor or movement disorders (e.g., multiple sclerosis, stroke, or brain tumors) might be excluded if the condition could complicate the diagnosis or treatment of tremor.

Conclusion

The exclusion criteria for MRgFUS are important to ensure patient safety and the effectiveness of the procedure. It is crucial for patients to undergo thorough screening and evaluation by a medical team to determine their eligibility for MRgFUS, considering both the potential benefits and risks.

1)
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