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FOCUSED ULTRASOUND: A NEW ERA IN TREMOR CONTROL

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Functional neurosurgery for the treatment of tremor and Parkinsonism dates back to as early as 1912.[1] Since then, it has evolved significantly, transitioning from open surgeries (e.g., cortectomies and cerebellar dentatectomies) to stereotactic closed surgeries targeting subcortical nuclei, primarily the globus pallidus and thalamus. The focus has since shifted to how these procedures can be performed with greater precision, minimizing side effects and, ideally, without making any surgical incision.

Ultrasound's capability to create precise, targeted lesions has been recognized since the 1940s.[2] By focusing acoustic energy into specific brain regions, modern focused ultrasound technology, combined with high-resolution imaging, enables accurate, incision-less stereotactic lesioning.[3] Initial pilot trials of MR-guided Focused Ultrasound (MRgFUS) VIM thalamotomy reported significant reductions in hand tremors and improvements in quality of life, with minimal side effects.[4-6] These promising results led to a larger, sham-controlled trial that confirmed the effectiveness of MRgFUS in treating medication-resistant ET for up to 12 months.[7] Longer follow-up studies have demonstrated that the benefits of MRgFUS are sustained over time, with tremor suppression and quality of life improvements maintained for up to three years post-treatment.[8] Although some patients experienced side effects such as gait disturbances and sensory changes, most of these effects were transient, with only a small percentage persisting long-term.7 Based on these findings, the U.S. FDA approved MRgFUS unilateral VIM thalamotomy for medically refractory ET in 2016.[9] In 2023, the FDA also approved MRgFUS VIM thalamotomy for the opposite side, but the two surgeries must be performed at least nine months apart.[10]

MRgFUS thalamotomy is also used in the symptomatic management of tremor-predominant Parkinson's disease (TD-PD) and combined ET-PD phenotype.[11] A double-blinded, sham-controlled clinical trial involving 27 TD-PD patients demonstrated a 62% median improvement in contralateral hand tremor for those who underwent MRgFUS thalamotomy, compared to 22% in the sham group.[12] Beyond the thalamus, MRgFUS has also been used to target other brain structures in PD, such as the pallidothalamic tract, globus pallidus pars interna, and subthalamic nucleus.[11] These procedures have shown effectiveness in treating motor fluctuations, dyskinesias, and other PD symptoms but are accompanied with more adverse effects than thalamotomy. A multicenter trial found that unilateral MRgFUS pallidotomy significantly improved motor function or reduced dyskinesia in PD patients compared to a sham procedure over three months. The active-treatment group demonstrated significantly greater improvements in both Unified Dyskinesia Rating Scale (UDysRS) (mean difference: 2.5 points; 95% CI, 1.2 to 3.9) and MDS-UPDRS III scores (mean difference: 3.9 points; 95% CI, 1.1 to 6.6) compared to the control group. Adverse events were typically mild, with the most common being dysarthria, gait disturbance, and loss of taste, most of which resolved within 3 months.[13] The FDA has currently approved MRgFUS thalamotomy (for tremor) and pallidotomy (for motor symptoms or dyskinesia) for treating PD symptoms, but the approval is limited to unilateral lesions only.[14]

Regarding the procedure details, the MRgFUS process begins with screening eligible candidates using a skull density ratio (SDR) based on head CT scans. An SDR <0.40 often leads to exclusion due to difficulty in focusing the ultrasound beams. During the procedure, the patient's head is shaved and secured in a stereotactic frame under local anesthesia. In the MRI suite, a FUS transducer and a silastic cap with cooled water circulation are used to protect the scalp. Baseline MRI scans are taken to target the VIM nucleus of the thalamus. Ultrasound energy is gradually delivered while the patient remains awake for tremor testing, allowing for adjustments based on clinical effects. Once the optimal target is confirmed, higher energy is applied to create a permanent lesion.[11] MRgFUS is mostly performed as a daycare procedure and the tremor response is immediately evident. For developing countries like ours, MRgFUS treatment appears to be an attractive option on paper, offering a same-day, incisionless procedure without the need for implants or repetitive programming. However, its utility is hindered

by the high cost of equipment, limited infrastructure, and a shortage of trained specialists, which remain the primary barriers.

Beyond its proven efficacy in treating ET and PD tremors, MRgFUS is being investigated for multiple applications, including the management of chronic pain, temporary disruption of the blood-brain barrier for enhanced drug delivery, and the breakdown of blood clots. These promising research areas could broaden the therapeutic potential of MRgFUS, opening up new possibilities for non-invasive treatments.

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