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Case Report

Delayed clinical response to focused ultrasound thalamotomy in essential tremor in a patient with suboptimal skull density ratio – A case report

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ABSTRACT

Background: Magnetic resonance imaging-guided focused ultrasound (MRgFUS) thalamotomy offers incision-less treatment for essential tremor or tremor-dominant Parkinson's disease, gaining acceptance as an alternative to deep brain stimulation. Compared to other methods, it offers real-time efficacy assessment without ionizing radiation.

Case Description: A 63-year-old male underwent MRgFUS, initially yielding subtle results due to skull limitations. However, significant tremor relief emerged 6 hours post-procedure, sustained for 5 days. Imaging confirmed thalamotomy effect. A second treatment was delivered at day five for longevity.

Conclusion: For patients with challenging skull characteristics and initial suboptimal outcomes, staged procedures may be considered, with potential delayed benefits and the need for lesion expansion for long-term relief.

Keywords: Case report, Delayed clinical response, Essential tremor, Focused ultrasound, Staging, Thalamotomy

INTRODUCTION

Magnetic resonance imaging-guided focused ultrasound (MRgFUS) thalamotomy has been Food and Drug Administration-approved for the treatment of upper extremity tremor in patients with essential tremor (ET) or tremor-dominant Parkinson's disease (PD).[5] The thalamotomy is created by ultrasound waves emitted from up to 1024 transducers focused on an intended target. The accumulated energy raises the tissue temperature at the target, resulting in permanent cell disruption.

This technique is attractive as subthreshold temperature elevations allow for reversible changes at the target and thus for "mapping" of the target area to assess for response. Temperature elevations up to 52°C allow for this reversible change. Once target assessment has been made, sonications resulting in temperatures above 55°C create permanent and irreversible changes at the target.[4]

A significant portion of the delivered energy is lost as the ultrasound waves traverse the skull.[10] The skull density ratio (SDR), obtained from a pre-procedure computed tomography (CT), is used as a measure of the skull's capability to transmit the ultrasound effectively. The SDR is a measure of the ratio of average Hounsfield units of the cortical layer of the skull to that of the cancellous portion. The lower the SDR, the less efficient the transmission of the ultrasound, and the more energy is required to reach optimal temperatures. The consensus for the optimal SDR in the US is 0.40, although this threshold varies globally.[3]

ILLUSTRATIVE CASE

Clinical presentation

A 63-year-old male with over a 20-year history of ET, with disabling tremors affecting activities of daily living and work, was referred for evaluation. Medication trials in the past were unsuccessful due to lack of efficacy, side effects, or both. He underwent testing for candidacy for either MRgFUS or deep brain stimulation (DBS) for the treatment of his tremors. A magnetic resonance imaging (MRI) of the brain was unremarkable, and a CT scan demonstrated an SDR of 0.39. Although initially offered DBS due to his borderline SDR and bilateral tremors, the patient and his family chose to proceed with MRgFUS. As a non-U.S. resident, he had concerns about long-term monitoring, maintenance, and generator changes required with DBS.

Intraoperative findings

After preparations, including placement of a stereotactic frame, he was placed on the MRI table, and after ensuring comfort and securing the head frame, a volumetric T1-weighted study was obtained. Internal landmarks were identified (AC-PC distance of 22.31), and the target coordinates were selected (X: −14.0, Y: 5.3, Z: 1.5). Table 1 summarizes the targets, sonication phases, and energy breakdown despite delivering 23,000 joules (J) to verify the target, the average temperature plateaued at 49°C. There was a small degree of tremor relief and mild transient paresthesias of the face.

The target was moved slightly anteriorly and the parameters were set for a thalamotomy as there was some clinical improvement with the prior preceding sonication. 40,000 J were delivered, and an average temperature of 52°C was reached. The patient had mild tremor relief again with transient paresthesias. An intraoperative T2-weighted scan was obtained to assess the target [Figure 1]. Parameters were set to create another lesion 1 mm anteriorly. 52,000 J were delivered, and we reached an average temperature of 55°C with marginal tremor relief without any side effects. Imaging revealed some changes at the target [Figure 2].

The next target was placed 1 mm anterior and 1.5 superior to the prior target to expand the lesion. The prescription was set to deliver 52,800 J to the target; however, with cavitations, only 26,000 J were delivered, and the average temperature reached only 47°C. Cavitation is a phenomenon where the propagating ultrasonic waves can expand small amounts of gas in tissues. When transient, the expanded gas bubbles collapse and release high energy, damaging surrounding tissue. The FUS technology is able to detect acoustic signatures of this phenomenon and will not proceed with further energy delivery once cavitations are detected to ensure the safety of the procedure.[7,12,15]

At this point, with high energy delivery being required and with a drop off in the skull efficiency, we decided to conclude the procedure. The patient had a small degree of

Table 1: The operative characteristics of the MRI-guided focused ultrasound procedures at the initial stage and the second stage at postoperative day 5.

Sonication Number	Target coordinates			Treatment Step	Sonication parameters		Prescribed dose (J)	Delivered dose (J)	Average temperature (°C)	Maximum temperature (°C)
	X	Y	Z		Power (W)	Time (s)				
1st-day treatment										
1	−14	5.3	1.5	Align	300	11	3000	3027	41	43
2	−14	5.3	1.5	Align	450	13	5400	5435	42	44
3	−14	5.3	1.5	Align	696	23	15,312	15,351	46	49
4	−14	5.3	1.5	Verify	942	27	23,292	24,542	49	51
5	−14	5.6	1.5	Treat	1,200	35	40,800	40,822	52	52
6	−14	6.2	1.5	Treat	1,200	45	52,800	49,913	55	57
7	−14	7.0	3.0	Treat	1,200	45	52,800	26,090	47	47
2nd-day treatment										
1	−13.8	7.1	3.0	Align	450	13	5,400	5,406	42	43
2	−13.8	7.1	3.0	Align	650	14	8,450	8,471	42	43
3	−13.8	7.1	3.0	Align	900	18	15,300	15,392	43	43
4	−13.8	7.1	3.0	Treat	1200	45	52,800	50,297	52	55

MRI: Magnetic resonance imaging

thalamotomy effect and demonstrated some lesion formation that was visible on imaging.

Delayed findings

Six hours later, while the patient was at home, he noticed a significant improvement in the ability to use his right hand to drink and eat without any tremors. As the patient intended to leave the U.S. a week after the procedure, he was brought back on day 5 after the initial treatment for additional imaging to delineate lesion versus edema.

Second session

On postoperative day 5, the patient still had excellent tremor relief. Imaging revealed lesion formation and some associated edema [Figure 3]. After considering the options and implications with the patient and his family, the stereotactic frame was re-applied to proceed with additional sonications to expand the lesion for long term efficacy. The targeting and parameters of the sonications on the second treatment day are demonstrated in Table 1. Post-procedure imaging is demonstrated in Figure 4. One more treatment was delivered with 52,000 J. The patient tolerated this without any adverse effects.

DISCUSSION

Observations

In this case review, we present a patient with a delayed clinical and radiological efficacy of thalamotomy. The treatment was more challenging as the patient required significantly higher energy delivery to reach the intended temperatures, and the clinical and radiological findings during the procedure were not optimal. The decision to conclude the procedure proved fortuitous, as the patient developed a delayed arrest of the tremor 6 hours after the procedure. We confirmed radiological findings 5 days after the procedure and decided to proceed with more treatments to ensure the longevity of

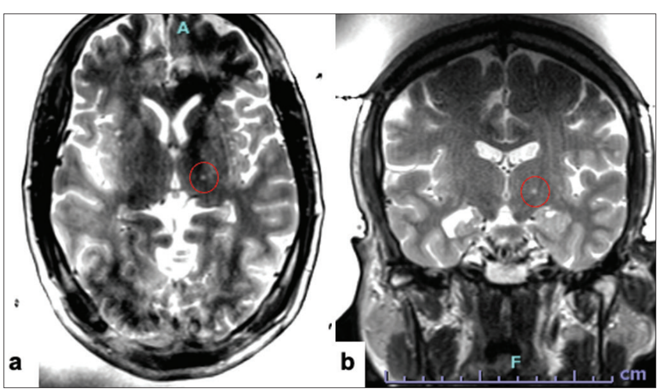

Figure 1: (a) Axial and (b) coronal T2 images demonstrating a small lesion forming in the left thalamus (encircled in red) with the delivery of the initial treatment sonication.

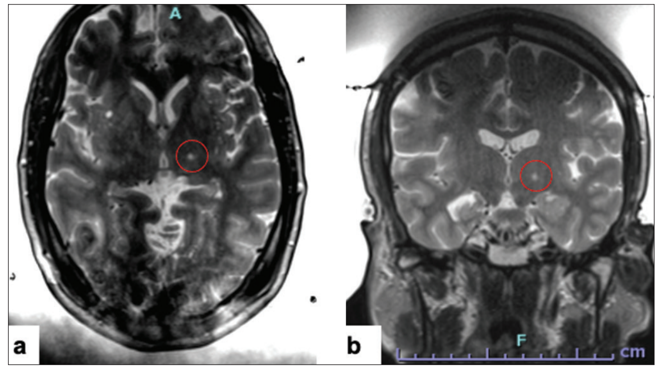

Figure 2: (a) Axial and (b) coronal T2 images demonstrating the left thalamic lesion (encircled in red) after delivery of the second treatment sonication.

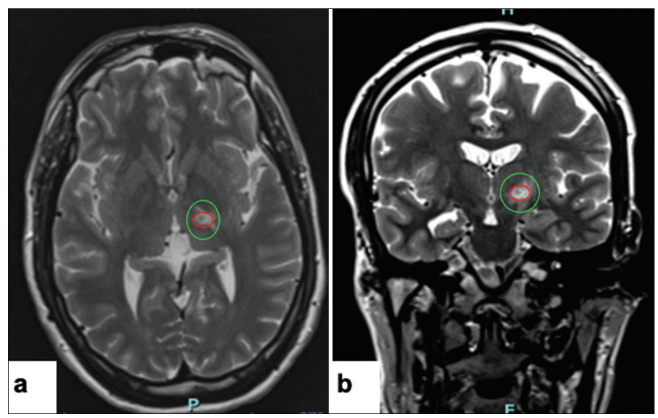

Figure 3: (a) Axial and (b) coronal T2 images on postoperative day 5 demonstrating enlargement of the lesion (encircled in red) and surrounding edema (encircled in green).

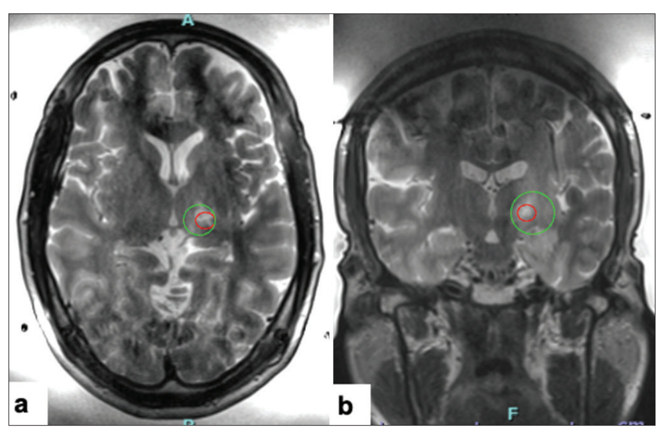

Figure 4: (a) Axial and (b) coronal T2 images after the treatment sonication on the second day of treatment, showing further expansion of the lesion (encircled in red) and surrounding edema (encircled in green).

the results. The patient is now 9 months from his treatment with sustained benefit.

Lessons

MRgFUS is becoming more accepted as an option for addressing upper extremity tremors in those with ET and tremor-dominant PD.[1,5,8] The ambulatory nature of these procedures, the relatively low-risk profile, the longevity of the treatment, and the ability to obtain near-immediate results have contributed to the growth of this technique.

"Mapping" the target of interest with subthreshold sonications is important in assessing side effects of paresthesias related to the proximity of the sensory ventral caudal nucleus of the thalamus as well as efficacy before the creation of more permanent lesions. A successful procedure is based on the ability of the ultrasound waves to penetrate the skull and reach the intended target, with enough remaining energy to produce a rise in the temperature of the target tissue. Several skull characteristics affect this[9,18,19]; however, the most important is the SDR. The preferred SDR in the United States is 0.4, although practitioners in other countries have different thresholds.[3] Several authors have demonstrated good efficacy with lower SDRs.[2,13,14,16] There are other factors, such as head size, angle of the impact of ultrasound, skull thickness, or irregularity, which have not been delineated as well but likely also contribute to the efficiency of ultrasound delivery during these procedures.[9,18,19]

Another interesting observation during focused ultrasound procedures is the degradation in the efficiency of the sonications, where each subsequent sonication requires more energy delivery.[17] This phenomenon limits the ability to continue "mapping" the area of interest, especially in those with less favorable skull characteristics.

CONCLUSION

This case report illustrates the clinical course of a patient with a delayed clinical and radiological efficacy of the treatment. This may be the first documented instance of delayed clinical improvement after MRgFUS thalamotomy, as previous literature documents typically immediate clinical benefits.[1,6,11] Delays in clinical impact may be due to suboptimal skull characteristics. With the treatment requiring significant energy to bypass the skull, perhaps the focal accumulation of energy may not be rapid enough for immediate efficacy. This illustrative case suggests the consideration of staging a procedure where skull characteristics or other factors demand high energy delivery, limiting mapping potential and decision-making. It is important to consider the possibility of delayed clinical improvement to guide appropriate management as MRgFUS thalamotomy becomes more widely adopted.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

Dr. Hooman Azmi has a consulting agreement with Insightec as part of the Infocus program.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Chang JW, Park CK, Lipsman N, Schwartz ML, Ghanouni P, Henderson JM, *et al*. A prospective trial of magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: Results at the 2-year follow-up. Ann Neurol 2018;83:107-14.
2. Chang KW, Park YS, Chang JW. Skull factors affecting outcomes of magnetic resonance-guided focused ultrasound for patients with essential tremor. Yonsei Med J 2019;60:768-73.
3. D'Souza M, Chen KS, Rosenberg J, Elias WJ, Eisenberg HM, Gwinn R, *et al*. Impact of skull density ratio on efficacy and safety of magnetic resonance-guided focused ultrasound treatment of essential tremor. J Neurosurg 2019;132:1392-7.
4. Elias WJ, Huss D, Voss T, Loomba J, Khaled M, Zadicario E, *et al*. A pilot study of focused ultrasound thalamotomy for essential tremor. N Engl J Med 2013;369:640-8.
5. Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, *et al*. A randomized trial of focused ultrasound thalamotomy for essential tremor. N Engl J Med 2016;375:730-9.
6. Fishman PS, Elias WJ, Ghanouni P, Gwinn R, Lipsman N, Schwartz M, *et al*. Neurological adverse event profile of magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor. Mov Disord 2018;33:843-7.
7. Gateau J, Aubry JF, Chauvet D, Boch AL, Fink M, Tanter M. *In vivo* bubble nucleation probability in sheep brain tissue. Phys Med Biol 2011;56:7001-15.
8. Halpern CH, Santini V, Lipsman N, Lozano AM, Schwartz ML, Shah BB, *et al*. Three-year follow-up of prospective trial of focused ultrasound thalamotomy for essential tremor. Neurology 2019;93:e2284-93.
9. Jung NY, Rachmilevitch I, Sibiger O, Amar T, Zadicario E,

Chang JW. Factors related to successful energy transmission of focused ultrasound through a skull: A study in human cadavers and its comparison with clinical experiences. J Korean Neurosurg Soc 2019;62:712-22.
10. Kim C, Eames M, Paeng DG. Improving sonication efficiency in transcranial MR-guided focused ultrasound treatment: A patient-data simulation study. Bioengineering (Basel) 2023;11:27.
11. Langford BE, Ridley CJ, Beale RC, Caseby SC, Marsh WJ, Richard L. Focused ultrasound thalamotomy and other interventions for medication-refractory essential tremor: An indirect comparison of short-term impact on health-related quality of life. Value Health 2018;21:1168-75.
12. Leighton TG. The acoustic bubble. London: Academic Press; 1994.
13. Tsai KW, Chen JC, Lai HC, Chang WC, Taira T, Chang JW, *et al*. The distribution of skull score and skull density ratio in tremor patients for MR-guided focused ultrasound thalamotomy. Front Neurosci 2021;15:612940.
14. Vetkas A, Boutet A, Sarica C, Germann J, Gwun D, Yamamoto K, *et al*. Successful magnetic resonance-guided focused ultrasound treatment of tremor in patients with a skull density ratio of 0.4 or less. J Neurosurg 2023;140:639-47.
15. Xu Z, Carlson C, Snell J, Eames M, Hananel A, Lopes MB, *et al*. Intracranial inertial cavitation threshold and thermal ablation lesion creation using MRI-guided 220-kHz focused ultrasound surgery: Preclinical investigation. J Neurosurg 2015;122:152-61.
16. Yamamoto K, Ito H, Fukutake S, Kamei T, Yamaguchi T, Taira T. Ventralis intermedius thalamotomy with focused ultrasound for patients with low skull density ratio. Mov Disord 2019;34:1239-40.
17. Yang AI, Hitti FL, Alabi OO, Joshi D, Chaibainou H, Henry L, *et al*. Patient-specific effects on sonication heating efficiency during magnetic resonance-guided focused ultrasound thalamotomy. Med Phys 2021;48:6588-96.
18. Yuen J, Goyal A, Kaufmann TJ, Jackson LM, Miller KJ, Klassen BT, *et al*. Comparison of the impact of skull density ratio with alternative skull metrics on magnetic resonance-guided focused ultrasound thalamotomy for tremor. J Neurosurg 2023;138:50-7.
19. Yuen J, Miller KJ, Klassen BT, Lehman VT, Lee KH, Kaufmann TJ. Hyperostosis in combination with low skull density ratio: A potential contraindication for magnetic resonance imaging-guided focused ultrasound thalamotomy. Mayo Clin Proc Innov Qual Outcomes 2022;6:10-5.

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