Predicting final lesion characteristics during MR-guided focused ultrasound pallidotomy for treatment of Parkinson's disease

*Timothy R. Miller, MD,¹ Sijia Guo, PhD,¹ Elias R. Melhem, MD,¹ Howard M. Eisenberg, MD,² Jiachen Zhuo, PhD,¹ Nathaniel Kelm, PhD,⁴ Mor Dayan, BS,⁴ Rao P. Gullapalli, PhD, MBA,¹ and Dheeraj Gandhi, MD^{1–3}

Departments of ¹Diagnostic Radiology & Nuclear Medicine, ²Neurosurgery, and ³Neurology, University of Maryland School of Medicine, Baltimore, Maryland; and ⁴Insightec, Tirat Carmel, Israel

OBJECTIVE Magnetic resonance–guided focused ultrasound (MRgFUS) ablation of the globus pallidus interna (GPi) is being investigated for the treatment of advanced Parkinson's disease symptoms. However, GPi lesioning presents unique challenges due to the off-midline location of the target. Furthermore, it remains uncertain whether intraoperative MR thermometry data can predict final lesion characteristics.

METHODS The authors first performed temperature simulations of GPi pallidotomy and compared the results with those of actual cases and the results of ventral intermediate nucleus (VIM) thalamotomy performed for essential tremor treatment. Next, thermometry data from 13 MRgFUS pallidotomy procedures performed at their institution were analyzed using 46°C, 48°C, 50°C, and 52°C temperature thresholds. The resulting thermal models were compared with resulting GPi lesions noted on postoperative days 1 and 30. Finally, the treatment efficiency (energy per temperature rise) of pallidotomy was evaluated.

RESULTS The authors' modeled acoustic intensity maps correctly demonstrate the elongated, ellipsoid lesions noted during GPi pallidotomy. In treated patients, the 48°C temperature threshold maps most accurately predicted postoperative day 1 lesion size, while no correlation was found for day 30 lesions. The average energy/temperature rise of pallidotomy was higher (612 J/°C) than what had been noted for VIM thalamotomy and varied with the patients' skull density ratios (SDRs).

CONCLUSIONS The authors' acoustic simulations accurately depicted the characteristics of thermal lesions encountered following MRgFUS pallidotomy. MR thermometry data can predict postoperative day 1 GPi lesion characteristics using a 48°C threshold model. Finally, the lower treatment efficiency of pallidotomy may make GPi lesioning challenging in patients with a low SDR.

<https://thejns.org/doi/abs/10.3171/2020.2.JNS192590>

KEYWORDS MR-guided focused ultrasound ablation; Parkinson's disease; globus pallidus interna; pallidotomy; MR thermometry; functional neurosurgery

MAGNETIC resonance–guided focused ultrasound (MRgFUS) ablation of the thalamic ventral intermediate nucleus (VIM) has been shown to be a safe and effective treatment for medically refractory essential tremor.^{1,2} The technique obviates the need for an open neurosurgical procedure and allows for real-time patient monitoring. Given the success with essential tremor, MRgFUS is now being investigated for the treatment of other disease entities, including advanced idiopathic Par-

kinson's disease.³ Preliminary results have been promising, and our center is participating in a pivotal, prospective, multicenter, sham control study of MRgFUS pallidotomy for the management of Parkinson's dyskinesia symptoms and motor fluctuations (registration no. NCT03319485, clinicaltrials.gov).

Nevertheless, MRgFUS is a novel treatment modality, and many questions remain regarding its use, including how to best predict final lesion characteristics during ab-

ABBREVIATIONS CEM₄₃ = cumulative equivalent minutes at 43°C; GPi = globus pallidus interna; MRgFUS = magnetic resonance–guided focused ultrasound; SDR = skull density ratio; T2WI = T2-weighted imaging; VIM = ventral intermediate nucleus.

SUBMITTED September 19, 2019. **ACCEPTED** February 10, 2020.

INCLUDE WHEN CITING Published online April 24, 2020; DOI: 10.3171/2020.2.JNS192590.

* T.R.M. and S.G. contributed equally to this work.

lation. Intraprocedural MRI is limited in visualizing the forming lesion due to poor image quality caused by several factors, including the use of a body coil and artifact generated from both the transducer and associated water bath. Consequently, accurate lesion prediction using MR thermometry data could help to further enhance the safety and efficacy of the technique by ensuring adequate treatment of the intended target, while simultaneously avoiding unintended ablation of adjacent eloquent structures. Although there have been a few recent reports evaluating thermal models for estimating the final VIM lesion during essential tremor treatment, no studies to date have been published regarding lesion prediction for globus pallidus interna (GPi) pallidotomy.^{4–6} GPi pallidotomy is likely to differ from VIM ablation due to the target's greater distance from the brain midline and possible differences in tissue composition.

In order to better understand lesion formation in the treatment of Parkinson's disease, we first performed temperature simulations to model the shape of the lesion generated when targeting the GPi and compared the resulting models with actual cases and results of VIM thalamotomy. We then retrospectively reviewed the results of patients undergoing MRgFUS pallidotomy at our institution to determine if MR thermometry data could predict final lesion characteristics, and if so, which thermal model would be most accurate. Finally, we examined treatment efficiency in our cohort, comparing it with VIM ablation, as well as whether it varied with patients' skull density ratios (SDRs).

Methods

Data were acquired from subjects participating in a prospective, IRB-approved, multicenter study of GPi pallidotomy for the treatment of motor complications of Parkinson's disease (registration no. NCT02263885). Thirteen patients (Table 1) were recruited for the study at our institution and were available for analysis. Full details of the prospective study can be found at clinicaltrials.gov.

Clinical Procedure

Details regarding MRgFUS GPi ablation have been previously described.³ In brief, whole-brain MR and CT imaging was performed at least 1 day prior to the procedure for pretreatment planning. The CT scan also served to screen patients for low SDR, which may preclude successful ablation due to inefficient acoustic transmission. Unilateral GPi pallidotomy was then performed using the Exablate 4000 midfrequency (670 kHz) head transducer system (Insightec), consisting of a 1024-element phased array configuration arranged in hemispheric geometry, integrated with a 3T clinical MRI system (Signa 750 W, GE Healthcare). During treatment, the GPi contralateral to the dominant hand was targeted by both the use of atlas-derived coordinates and direct visualization of the target on MRI. Two-dimensional monitoring of the focal spot during each sonication was performed using the MR thermometry acquisition protocol provided by Insightec. The latter consists of a multiecho gradient echo sequence (TR 27.8 msec; TE 3.13, 7.82, 12.51, 17.20, and 21.88 msec; FOV 28 × 28 cm; matrix size 128 × 256 mm interpolated

TABLE 1. Age, sex, and SDR in 13 patients who underwent GPi pallidotomy

Patient No.	Age, Sex	SDR
1	50, F	0.52
2	39, M	0.47
3	58, M	0.54
4	70, M	0.49
5	58, M	0.61
6	55, F	0.60
7	55, M	0.50
8	34, F	0.49
9	56, F	0.50
10	73, F	0.45
11	58, M	0.51
12	62, M	0.51
13	68, M	0.48

to 256 × 256, with slice thickness 3 mm), with the phase-difference images converted to temperature maps using a temperature sensitivity of -0.00909 ppm/°C.^{7,8} Initially, low-power sonications were performed to raise the target temperature to approximately 45°C for focal spot alignment, followed by a gradual increase in power to reach a peak temperature of 52°C–61°C. Patients were monitored by clinical examination throughout the procedure to assess for treatment efficacy as well as for the development of any side effects. Following treatment, MRI was performed on postprocedure days 1 and 30 for evaluation of the pallidotomy lesion and adjacent structures.

Acoustic and Temperature Field Simulation

In order to better understand lesion formation during MRgFUS pallidotomy, we first performed acoustic field simulations of GPi ablation to evaluate the resulting acoustic profile in representative cases of GPi and VIM ablation. The acoustic and temperature fields within the head were simulated using a 3D finite differences algorithm, which aims to solve the full Westervelt equation⁹ as detailed below:

$$\rho_0 \nabla \cdot \left(\frac{1}{\rho_0} \nabla p \right) - \frac{1}{c_0^2} \frac{\partial^2 p}{\partial t^2} + \frac{\delta}{c_0^4} \frac{\partial^3 p}{\partial t^3} + \frac{\beta}{\rho_0 c_0^4} \frac{\partial^2 p}{\partial t^2} = 0, \text{ [eq. 1]}$$

where p is the acoustic pressure, c_0 is the speed of sound, ρ_0 is the density of the medium, β is the acoustic nonlinearity coefficient of brain tissue, and δ is the sound diffusivity. The sound diffusivity δ is obtained through the relation

$$\alpha = \delta \omega^2 / 2c_0^3,$$

where α is the attenuation coefficient of the tissue and ω is the angular frequency of the ultrasound in that tissue. The acoustic properties of skull, along with the transducer and target locations, were modeled based on the CT images of a representative sample of Parkinson's disease and

essential tremor treatment cases.⁹ Similarly, the power and phase of each transducer element in the hemispheric array were also modeled using data stored within the Insightec Exablate system from the same treatment cases.

Temperature simulation was estimated using the inhomogeneous Pennes equation of heat conduction.¹⁰ By solving the bio-heat equation with the calculated acoustic intensity field as the input, tissue temperature distribution over the exposure time was calculated accordingly:

$$\partial T / \partial t = k \Delta(T) - (T - T_0) / \tau + Q_v / C_v, \quad [\text{eq. 2}]$$

where T is the tissue temperature, T_0 is the body temperature, C_v is the heat capacity, k is the thermal diffusivity, Q_v is the absorbed heat energy, Δ is the Laplace operator, and τ is the characteristic time of the blood perfusion. Both acoustic and temperature simulations were done at a resolution of 1 mm × 1 mm × 3 mm, to match the resolution of the MR thermometry images obtained during treatment. The resulting simulated temperature profile for GPi ablation was compared with that generated for VIM thalamotomy.

Thermal Thresholding Area Estimates From MR Thermometry

MR thermometry data from GPi ablation procedures were analyzed in the Insightec Exablate system. The average and peak voxel temperature, target location, and treatment power and duration for individual sonications were reviewed. Due to the 2D technique, thermometry imaging could only be viewed in the original plane of acquisition. Background temperatures were appropriately windowed and filtered to ensure that measured voxel temperatures were accurate and consistent. At the time peak temperature was reached during a given sonication, a temperature threshold was set to view voxels at or above 4 temperature thresholds (46°, 48°, 50°, and 52°C). These thresholds were chosen based on our anecdotal observation that post-procedure day 1 lesion size following MRgFUS pallidotomy appeared to most often correlate with target regions reaching 46°C–52°C during ablation. While it has been reported that sonications with peak temperatures > 55°C can result in tissue ablation in a few seconds, sonications at lower temperatures (50°C–54°C) have also been shown to contribute to lesion formation.^{6,11} Finally, MR thermometry data from only the 5 highest peak temperature sonications for each patient were used for comparison of postprocedure day 1 and 30 lesions. This was done to simplify the analysis and was based on the observation that a peak temperature > 50°C was reached on average in 5.7 ± 2.4 sonications in our cohort. It was therefore thought reasonable to assume that the 5 highest peak temperature sonications made the largest contribution to the resulting pallidotomy.

Lesion Size Measurements and Comparison With Thermal Thresholding Areas

T2-weighted imaging (T2WI) studies obtained on postprocedure days 1 and 30 were reviewed, and zone II of the GPi lesion was measured in the same section as MR thermometry. Zone II is a well-demarcated, hyperin-

FIG. 1. Schematic of the method used for determining thermal thresholded area accounting for target movement between sonications. x_1 and y_1 represent the long and short axes, respectively, of the thermal map region, while x_2 and y_2 represent the long and short axes, respectively, of the T2WI lesion. Figure is available in color online only.

tense region noted on T2WI that includes a necrotic core and area of cytotoxic edema but excludes a larger region of surrounding vasogenic edema (zone III).¹² Zone II has been demonstrated in animal models to correlate with the region of acute coagulative necrosis induced by thermal ultrasound injury and typically demonstrated restricted diffusion on diffusion-weighted imaging.^{13,14} Next, the T2WI scan was registered to the MR thermometry data obtained during the procedure. Due to the off-midline location of the target, GPi lesions assume an elongated shape. Consequently, 2 vectors (x and y) were chosen to compare the shape and size of the ellipsoid lesion and thermal thresholding areas, with x being the long axis of the area in question, y the short axis, and θ the angle between the x -axis and the horizontal line.

As the targeted focal spot typically is repositioned several times during MRgFUS ablation (either to achieve a greater treatment effect or to ensure its durability), we compensated for this movement when analyzing and comparing ablation lesions and thermal thresholding areas as shown in Fig. 1. Given that the 2D MR thermometry technique provides a temperature map in a single plane, movement could only be accounted for in 2 directions for a given sonication (equations 3–8) as follows.

For MR thermometry images in coronal view,

$$x_1 = x + RL \cdot \cos\theta + AP \cdot \sin\theta, \quad [\text{eq. 3}]$$

$$y_1 = y + RL \cdot \sin\theta + AP \cdot \cos\theta. \quad [\text{eq. 4}]$$

For MR thermometry images in axial view,

$$x_1 = x + RL \cdot \cos\theta + SI \cdot \sin\theta, \quad [\text{eq. 5}]$$

$$y_1 = y + RL \cdot \sin\theta + SI \cdot \cos\theta. \quad [\text{eq. 6}]$$

For MR thermometry images in sagittal view,

$$x_1 = x + SI \cdot \cos\theta + AP \cdot \sin\theta, \quad [\text{eq. 7}]$$

$$y_1 = y + SI \cdot \sin\theta + AP \cdot \cos\theta. \quad [\text{eq. 8}]$$

Again, only the 5 highest peak temperature sonications from each patient were considered for thermal threshold-

FIG. 2. Comparison of MRgFUS ablation of the VIM and GPi. Axial T2-weighted image obtained after VIM ablation for essential tremor (ET) treatment, demonstrating the postprocedure day 1 lesion (**A**, magnified in **inset**). The corresponding thermal map (**B**, magnified in **inset**) from a treatment sonication in the same patient, with the *red area* representing the target region reaching a temperature above 52°C (peak sonication temperature 56°C). Acoustic simulation of VIM thalamotomy (**C**, magnified in **inset**) using the patient's data reproduces the spherical target shape of the actual lesion. In contradistinction, the elongated, ellipsoid lesion of GPi (GP) pallidotomy is shown on an axial T2-weighted image obtained on postprocedure day 1 after treatment for Parkinson's disease (PD; **D**, magnified in **inset**). The thermal map from a corresponding treatment sonication (**E**, magnified in **inset**) in the same patient, with the *red area* representing the target region reaching a temperature above 48°C (peak sonication temperature 54°C). The *light red area* (**inset** in **E**) represents the smaller 240 CEM₄₃ region. Finally, acoustic simulation of pallidotomy using data from the same patient (**F**, magnified in **inset**) reproduces the ellipsoid target shape of the actual lesion. Figure is available in color online only.

ing analysis. Consequently, only movement of the focal spot among these sonications was evaluated.

Finally, to calculate the difference between the thermal thresholding (x_2, y_2) and the actual thermal lesion (x_1, y_1) at days 1 and 30, we used the following equation:

$$\sum \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2} / n, \quad [\text{eq. 9}]$$

where n is the number of sonications considered for the analysis. After finding the closest thermal thresholding model, the average lengths of the x- and y-axes from the selected number of sonications were used to estimate the 1-day lesion size in each patient.

Treatment Efficiency

The treatment efficiency was calculated as the average energy/temperature rise (J/°C) among all sonications for each pallidotomy procedure and compared with historical data from VIM ablation for essential tremor treatment (unpublished data from our institution). In addition, the influence of SDR on treatment efficiency was assessed.

Results

Temperature Profile Modeling

Modeled temperature maps for both VIM and GPi MRgFUS ablation are presented for 2 representative patients (Fig. 2), and the 24-hour T2WI lesions (Fig. 2A and D) and thermometry data (Fig. 2B and E) from the respective cases are compared. In both instances, the simulated thermal profiles (Fig. 2C and F) closely resemble those typically observed during GPi and VIM ablation. GPi lesions are noted to assume an elongated, ellipsoid shape extending in the inferolateral to superomedial direction due to the target's off-midline location (Fig. 2F). In contradistinction, VIM lesions, with the target located near the brain midline, are spherical (Fig. 2C).

Comparison of Thermal Thresholding Area and Lesion Areas

All 13 treatment sessions in the cohort were successfully completed, resulting in a visible lesion on postprocedure T2WI. Figure 3 shows an example of thermal thresholding areas (46°C, 48°C, 50°C, and 52°C) for a single sonication

FIG. 3. An example of thermal mapping with varying thresholds (52°C, 50°C, 48°C, and 46°C) using MR thermometry from a single sonication during GPi pallidotomy. The sonication duration was 13 seconds, and the peak temperature reached 54°C. Figure is available in color online only.

during GPi pallidotomy, with the red areas indicating the region of tissue reaching the specified threshold. Based on the difference calculation using equation 9, the 48°C thresholding area, modified to take into account target spot movement as previously described, provided the closest match to the observed postprocedure day 1 lesion in the cohort overall (2.1 ± 0.7 mm) and was the best match for 10 of 13 patients. In addition, strong correlations were found between the average lengths of the x- and y-axes (i.e., long and short axes) from the 48°C thermal thresholding areas and lesion sizes in the cohort ($R^2 = 0.62$, $p < 0.0001$; and $R^2 = 0.86$, $p < 0.0001$, respectively) (Fig. 4). Finally, no close correlation was found between the 4 thermal threshold areas and postprocedure day 30 lesions. A summary of the linear regression coefficients and paired t-test analysis is provided in Table 2. Paired t-tests failed to reject the null hypotheses that 48°C thresholding areas

were equivalent to the lesion sizes measured on postprocedure day 1 at a confidence level of 95% ($p = 0.29$ and 0.30 , for the long axis and short axis, respectively). For all other thresholding areas, paired t-tests rejected the null hypothesis of equivalence for one or both axes.

Sonication Efficiency

The average temperature rise ratio ($J/^\circ C$) among all sonications was $612 J/^\circ C$, which is higher than what we have previously noted during VIM ablation for essential tremor treatment (unpublished data from our institution). A strong correlation was noted between the patient's SDR and the average temperature rise ratio for all sonications in our cohort (Fig. 5). A decrease in energy absorption efficiency was noted as the number of sonications increased during individual treatment sessions, resulting in a greater

FIG. 4. The average of the long and short axes derived from the 48°C thermal thresholding maps provided the strongest correlation with the postprocedure day 1 lesion on T2WI. Figure is available in color online only.

TABLE 2. Summary of data comparing postprocedure day 1 T2WI lesions with thermal maps at various thresholds

Thermal Threshold	Mean Error ± SD (mm)	Long Axis			Short Axis		
		Regression Slope	Regression R ²	p Value*	Regression Slope	Regression R ²	p Value*
52°C	6.2 ± 2.5	2.05	0.47	<0.001	1.86	0.70	<0.001
50°C	4.1 ± 1.4	1.59	0.52	<0.001	1.38	0.76	<0.001
48°C	2.1 ± 0.7	1.09	0.62	0.29	0.96	0.86	0.30
46°C	3.5 ± 1.7	0.74	0.50	<0.005	0.83	0.69	0.05

* t-test.

amount of energy required per degree Celsius temperature rise over 37°C. This decrease in energy absorption was more pronounced in patients harboring low SDRs.

Discussion

The goal of MRgFUS is to induce a thermal lesion in an anatomically precise location in the brain while avoiding damage to adjacent structures.^{5,15} However, lesion formation in MRgFUS is complex and dependent on multiple factors, including, but not limited to, the skull thermal efficiency, the varying sensitivity of different regions of the brain to thermal damage, and the distance of the target from the midline.¹⁶ Given this complexity, acoustic simulations can be useful for better understanding how lesion formation varies depending on the unique characteristics of a given target site. For example, our simulation of GPi pallidotomy clearly illustrates how the off-midline location results in the elongated, obliquely oriented, thermal lesions that are observed during actual treatments. The off-midline location results in slight differences in the distances traveled by the individual element ultrasound beams, which, in turn, results in variations in the energy deposited at the target. Changes in the incident angles of individual transducer elements when targeting farther away from the midline also play a role. These same factors result in an overall reduced peak acoustic intensity generated at the GPi compared with the VIM (all other factors

being equal), with resulting lower achievable peak ablation temperatures. In contradistinction, the near-midline location of the VIM results in a more even energy deposition at the target, producing spherical lesions and (on average) higher achievable peak temperatures.

Although acoustic simulations may provide important general insights regarding focused ultrasound ablation at a given location, they currently cannot be used intraprocedurally to guide lesion formation due to the amount of time and processing required to generate the corresponding model. In contradistinction, intraprocedural MR thermometry may help guide operators in focused ultrasound lesioning following each treatment sonication. However, it remains uncertain how best to use MR thermometry to predict the final lesion characteristics in individual cases. Prior investigations regarding the use of MR thermometry to predict MRgFUS lesioning in vivo are limited to 3 recent studies evaluating VIM ablation for essential tremor. Two noted that the accumulated thermal dose profile for 100 and 200 cumulative equivalent minutes at 43°C (CEM₄₃) best correlated with the resulting VIM lesion, while the third found that a 51°C threshold model was most accurate.^{4–6} However, given the unique characteristics of the GPi (e.g., off-midline location, larger size than the VIM, possible differences in tissue composition), it was uncertain whether MR thermometry data could accurately predict lesioning in Parkinson's treatment, and, if so, which thermal model would be most accurate.

Our study is the first to demonstrate that MR thermometry data can reliably predict GPi lesioning and that the 48°C threshold areas from the 5 highest peak temperature sonications, modified to take into account target spot movement, are most accurate in predicting the resulting postprocedure day 1 lesion. We found that this 48°C threshold for pallidotomy is lower than what has been previously reported for VIM lesioning, which is likely due to the more diffuse distribution of ultrasound energy in the typical elongated GPi lesion. These findings correlate well with our prior anecdotal observations that the 240 CEM₄₃ area obtained from MR thermometry during GPi ablation often underestimates the final lesion noted on postprocedure day 1 (Fig. 2F). The clinical implication of our finding is that the thermal map region reaching at least 48°C on 5 treatment sonications can reliably be considered to reflect the ablation zone. This in turn can guide operators during lesion creation in the GPi by both confirming that a specific target has been successfully ablated and avoiding inadvertent lesioning of adjacent, nontarget structures. Al-

FIG. 5. Association between SDR and average energy/temperature rise (J/°C) demonstrating a strong correlation between SDR and treatment efficiency. Figure is available in color online only.

though we were unable to correlate MR thermometry data with the postprocedure 30-day lesion size, we speculate that this is likely due to encephalomalacia formation at the target with subsequent cavity collapse. This phenomenon has been previously demonstrated in focused ultrasound lesioning at the Vim for essential tremor where a mean reduction in lesion diameter of 11% was noted between postprocedure days 1 and 30.⁴

As expected, we observed a lower treatment efficiency of GPi pallidotomy than of Vim ablation due to the greater distance of the target from the midline. In addition, the strong correlation noted between SDR and treatment efficiency suggests that the former may be predictive of the highest temperature achievable during GPi pallidotomy. SDR has already been shown to be predictive of peak achievable temperature during Vim thalamotomy.¹⁰ Finally, a decrease in energy absorption efficiency was noted as the number of sonications increased during individual treatment sessions, which again is similar to prior results investigating Vim ablation.⁴ The mechanism for this increase in energy requirement is still under investigation, but it may be due to changes in the properties of the target tissue and overlying skull caused by thermal deposition from early sonications.⁶ However, given the inherent lower treatment efficiency of GPi ablation, this further decline in efficiency may make treatment of Parkinson's disease challenging in some instances, especially in patients with lower SDRs.

Limitations of this study include its retrospective, single-center design and the relatively small size of our cohort. In addition, we cannot exclude the possibility of further growth of GPi lesions after 24 hours (the time of our measurements), although we speculate that this phenomenon would not be substantial, as direct thermal injury should be apparent within the first day. Furthermore, the decision to limit our analysis of MR thermometry data to the 5 highest energy sonications from each treatment likely excluded some sonications that contributed to the final pallidotomy lesion. Finally, our analysis using peak temperature achieved during individual sonications does not take into account variations in repetitions and sonication duration. Despite these limitations, we believe that our results suggest that postprocedure day 1 lesion characteristics during GPi ablation may be predicted by thermal map data of the highest peak temperature treatment sonications. Our findings will need to be validated in a larger cohort of patients, possibly using thermometry data from all sonications reaching a certain peak temperature.

Conclusions

Our acoustic simulations accurately depicted the characteristics of thermal lesions encountered during MRg-FUS pallidotomy. Furthermore, a 48°C temperature threshold model most accurately predicts the resulting lesion on postprocedure day 1. Finally, the treatment efficiency of pallidotomy is less than that of thalamotomy and correlates with SDR.

References

1. Elias WJ, Huss D, Voss T, et al. A pilot study of focused

- ultrasound thalamotomy for essential tremor. *N Engl J Med*. 2013;369(7):640–648.
2. Elias WJ, Lipsman N, Ondo WG, et al. A randomized trial of focused ultrasound thalamotomy for essential tremor. *N Engl J Med*. 2016;375(8):730–739.
3. Fishman PS, Frenkel V. Treatment of movement disorders with focused ultrasound. *J Cent Nerv Syst Dis*. 2017;9:1179573517705670.
4. Bond AE, Elias WJ. Predicting lesion size during focused ultrasound thalamotomy: a review of 63 lesions over 3 clinical trials. *Neurosurg Focus*. 2018;44(2):E5.
5. Huang Y, Lipsman N, Schwartz ML, et al. Predicting lesion size by accumulated thermal dose in MR-guided focused ultrasound for essential tremor. *Med Phys*. 2018;45(10):4704–4710.
6. Jones RM, Kamps S, Huang Y, et al. Accumulated thermal dose in MRI-guided focused ultrasound for essential tremor: repeated sonications with low focal temperatures [published online May 10, 2019]. *J Neurosurg*. doi:10.3171/2019.2.JNS182995
7. Hughes A, Huang Y, Schwartz ML, Hynynen K. The reduction in treatment efficiency at high acoustic powers during MR-guided transcranial focused ultrasound thalamotomy for essential tremor. *Med Phys*. 2018;45(7):2925–2936.
8. McDannold N, Park EJ, Mei CS, et al. Evaluation of three-dimensional temperature distributions produced by a low-frequency transcranial focused ultrasound system within ex vivo human skulls. *IEEE Trans Ultrason Ferroelectr Freq Control*. 2010;57(9):1967–1976.
9. Guo S, Zhuo J, Li G, et al. Feasibility of ultrashort echo time images using full-wave acoustic and thermal modeling for transcranial MRI-guided focused ultrasound (tcMRgFUS) planning. *Phys Med Biol*. 2019;64(9):095008.
10. Pennes HH. Analysis of tissue and arterial blood temperatures in the resting human forearm. 1948. *J Appl Physiol* (1985). 1998;85(1):5–34.
11. Chang WS, Jung HH, Zadicario E, et al. Factors associated with successful magnetic resonance-guided focused ultrasound treatment: efficiency of acoustic energy delivery through the skull. *J Neurosurg*. 2016;124(2):411–416.
12. Martin E, Jeanmonod D, Morel A, et al. High-intensity focused ultrasound for noninvasive functional neurosurgery. *Ann Neurol*. 2009;66(6):858–861.
13. Chen L, Bouley D, Yuh E, et al. Study of focused ultrasound tissue damage using MRI and histology. *J Magn Reson Imaging*. 1999;10(2):146–153.
14. Chen L, Bouley DM, Harris BT, Butts K. MRI study of immediate cell viability in focused ultrasound lesions in the rabbit brain. *J Magn Reson Imaging*. 2001;13(1):23–30.
15. Schuurman PR, Bosch DA, Merkus MP, Speelman JD. Long-term follow-up of thalamic stimulation versus thalamotomy for tremor suppression. *Mov Disord*. 2008;23(8):1146–1153.
16. Yarmolenko PS, Moon EJ, Landon C, et al. Thresholds for thermal damage to normal tissues: an update. *Int J Hyperthermia*. 2011;27(4):320–343.

Disclosures

Dr. Eisenberg: clinical or research support for this study from Insightec FUS Foundation. Dr. Kelm and Mr. Dayan: employees of Insightec.

Author Contributions

Conception and design: Miller, Guo, Melhem, Zhuo, Dayan, Gullapalli, Gandhi. Acquisition of data: Miller, Guo, Eisenberg, Zhuo, Gandhi. Analysis and interpretation of data: all authors. Drafting the article: Miller, Guo, Gullapalli, Gandhi. Critically revising the article: all authors. Reviewed submitted version

of manuscript: Miller, Guo, Melhem, Eisenberg, Kelm, Dayan, Gullapalli, Gandhi. Approved the final version of the manuscript on behalf of all authors: Miller. Statistical analysis: Guo, Gullapalli. Administrative/technical/material support: Miller.

Supplemental Information

Previous Presentations

A portion of this work was previously presented at the ISMRM 27th Annual Meeting and Exhibition, Montreal, Quebec, Canada, May 11–16, 2019.

Correspondence

Timothy R. Miller: University of Maryland Medical Center, Baltimore, MD. tmiller5@umm.edu.