Transcranial magnetic resonance–guided focused ultrasound surgery for trigeminal neuralgia: a cadaveric and laboratory feasibility study

Laboratory investigation

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Object. Transcranial MR-guided focused ultrasound surgery (MRgFUS) is evolving as a treatment modality in neurosurgery. Until now, the trigeminal nerve was believed to be beyond the treatment envelope of existing high-frequency transcranial MRgFUS systems. In this study, the authors explore the feasibility of targeting the trigeminal nerve in a cadaveric model with temperature assessments using computer simulations and an in vitro skull phantom model fitted with thermocouples.

Methods. Six trigeminal nerves from 4 unpreserved cadavers were targeted in the first experiment. Preprocedural CT scanning of the head was performed to allow for a skull correction algorithm. Three-Tesla, volumetric, FIESTA MRI sequences were performed to delineate the trigeminal nerve and any vascular structures of the cisternal segment. The cadaver was positioned in a focused ultrasound transducer (650-kHz system, ExAblate Neuro, InSightec) so that the focus of the transducer was centered at the proximal trigeminal nerve, allowing for targeting of the root entry zone (REZ) and the cisternal segment. Real-time, 2D thermometry was performed during the 10- to 30-second sonication procedures. Post hoc MR thermometry was performed on a computer workstation at the conclusion of the procedure to analyze temperature effects at neuroanatomical areas of interest. Finally, the region of the trigeminal nerve was targeted in a gel phantom encased within a human cranium, and temperature changes in regions of interest in the skull base were measured using thermocouples.

Results. The trigeminal nerves were clearly identified in all cadavers for accurate targeting. Sequential sonication of 25–1500 W for 10–30 seconds were successfully performed along the length of the trigeminal nerve starting at the REZ. Real-time MR thermometry confirmed the temperature increase as a narrow focus of heating by a mean of 10°C. Postprocedural thermometry calculations and thermocouple experiments in a phantom skull were performed and confirmed minimal heating of adjacent structures including the skull base, cranial nerves, and cerebral vessels. For targeting, inclusion of no-pass regions through the petrous bone decreased collateral heating in the internal acoustic canal from 16.7°C without blocking to 5.7°C with blocking. Temperature at the REZ target decreased by 3.7°C with blocking. Similarly, for midcisternal targeting, collateral heating at the internal acoustic canal was improved from a 16.3°C increase to a 4.9°C increase. Blocking decreased the target temperature increase by 4.4°C for the same power settings.

Conclusions. This study demonstrates focal heating of up to 18°C in a cadaveric trigeminal nerve at the REZ and along the cisternal segment with transcranial MRgFUS. Significant heating of the skull base and surrounding neural structures did not occur with implementation of no-pass regions. However, in vivo studies are necessary to confirm the safety and efficacy of this potentially new, noninvasive treatment.

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Key Words • magnetic resonance–guided focused ultrasound surgery • trigeminal neuralgia • pain

There are several surgical treatments for TN, each with an associated failure rate and morbidity. Microvascular decompression remains the gold-standard treatment when feasible and directly addresses the vascular structure causing impingement on the trigeminal nerve. While it was Taarnhøj in 1952 who first described the procedure, Jannetta refined the

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
Stereotactic radiosurgery for TN using the Gamma Knife or modified linear accelerator devices has demonstrated comparable efficacy to the percutaneous techniques but with lower complication rates. With radiosurgery, there is, however, a small risk of radiation-induced injury to the pons, which can result in facial numbness and even anesthesia dolorosa. The risk of radiosurgical complications increases with repeat treatment.

Magnetic resonance-guided focused ultrasound surgery is a rapidly developing technology that has already been used in clinical trials for the treatment of chronic pain via thalamotomy and in the treatment of brain tumors. With the ExAblate Neuro (InSightec), 1024 ultrasound transducers transmit ultrasound energy through the skull that converges onto a focal spot and causes a highly focused region of heating, thereby creating a lesion in the target tissue. Until now, the trigeminal nerve was considered beyond the existing treatment envelope or range of the ExAblate Neuro system due to its deep location within the brain. The aim of this study was to determine if the transcranial MRgFUS system is able to create a clinically relevant thermal increase in the human trigeminal nerve and trigeminal REZ without appreciable heating of important surrounding structures.

Methods

Part 1: Cadaveric Experiments

Acquisition of all cadaveric materials was performed in accordance with standard institutional policy for human tissue. Whole cadavers were acquired unpreserved within 1–3 days of death. Whole cadavers were used to prevent the introduction of intracranial air, which impedes ultrasound waves. The head was closely shaved to allow transduction of ultrasound energy without causing interface heating on the scalp caused by hair.

Preprocedural Neuroimaging Protocol. Thin-slice (0.5-mm) CT scans of the head with bone windows were obtained and input into the skull correction algorithm of the ExAblate Neuro software system. This process corrects for the attenuation caused by the irregular shape and density of the skull and allows for transcranial focusing to a single spot. Axial and coronal T2-weighted spin echo images of the entire brain were obtained using a 3-T MRI scanner (General Electric) followed by 3D FIESTA sequences (TR 4.8 msec, TE 1.4 msec, slice thickness 0.5 mm, FOV 20 × 20 cm, matrix 352 × 192, number of excitations 4) through the region of the trigeminal nerve for preoperative planning and visualization of the target. Measurements of anatomical structures of interest, such as the length of the cisternal segment of the trigeminal nerve, were obtained (Table 1). The FIESTA sequences were obtained and demonstrated vascular impingement in several specimens.

MRgFUS Protocol. To reach the depth in the brain required to effectively target the trigeminal nerve, the stereotactic frame (Radionics) was pinned low with the occipital pins positioned below the external occipital protuberance. The treatment envelope was further expanded by tilting the ExAblate transducer backward 15°, thereby allowing the head to be positioned deeper within the curvature of the transducer (Fig. 1). The transducer was adjusted laterally such that the focus was centered over the REZ and encompassed the cisternal segment of the trigeminal nerve and part of the pons (Fig. 2). Final positioning was confirmed with T2-weighted imaging.

Once the transducer was positioned, the silicone membrane was applied to the scalp and filled with chilled, degassed water (dissolved oxygen < 1.2 parts per million). Confirmatory T2-weighted and 3D FIESTA planning images were then obtained in 3 orthogonal planes. The CT imaging bone correction algorithm was overlaid and applied to the MR images. Short, low-energy (150-W, 10-second, 650-kHz) thermal test sonications were performed in the pons to confirm accurate focusing. Real-time MR thermometry using the proton resonance frequency shift temperature measurement method was used to correct for targeting discrepancy (difference in the region of actual thermal increase compared with location of target spot) in 2 frequency directions. Confirmation of accurate electrical steering of the focus was then performed at the level of the pons.

Treatment sonications were then performed along the trigeminal nerve starting at the REZ and moving out along the cisternal segment (25–1500 W, 10–30 seconds, 650 kHz). Figure 2 demonstrates a typical planning image with targets at the REZ and in the cisternal segment. The treatment was then initiated after the target was confirmed in all 3 planes of imaging (Fig. 3). Real-time MR thermometry using the proton resonance frequency shift temperature measurement method was used to correct for targeting discrepancy (difference in the region of actual thermal increase compared with location of target spot) in 2 frequency directions. Confirmation of accurate electrical steering of the focus was then performed at the level of the pons.

Part 2: Calculating Temperature of Skull Base Structures Using Simulation Data

Post hoc MR thermometry was simulated on a workstation by the device manufacturer (InSightec) to analyze temperature changes in the skull base and other areas of interest, such as the basilar artery, the entrance to the Meckel cave, and the IAC. This system used an FDA-approved MR thermometry algorithm. This algorithm overestimates bone heating as there is no circulation of CSF or blood flow to account for heat dispersion. Two-dimensional acoustic simulation of ultrasonic fields using the physical parameters of a cadaveric skull and physiological brain parameters was performed. Simulations with a section of trilaminar skull at 10 and 20 mm distal to the focal point were performed to simulate the skull base. Temperature maps were simulated for a range of target focal spot temperatures (Tables 2 and 3). Temperatures of interest were noted at the focal spot and the skull (including areas of maximum heating), as well as at distances between the focus and the skull (temperature falloff from the focal point). These results were then scaled to MR images and overlaid to demonstrate the results in a visual format for easier interpretation and clinical implementation. These simulations assume an energy of 600 J.
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**TABLE 1: Measurements of various anatomical regions of interest and thermal sonication results**

<table>
<thead>
<tr>
<th>Specimen No.</th>
<th>Cistern Length in mm (lt/rt)</th>
<th>Distance From REZ to Basilar Artery in mm (lt/rt)</th>
<th>Bone Distance From MC to IAC (lt/rt)</th>
<th>Power Range (W)/Duration (sec)</th>
<th>Target Tmax Change (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.8/7.9</td>
<td>23.4/19.7</td>
<td>11.4/13.5</td>
<td>250–400/10–30</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>11.2/11.3</td>
<td>19.8/20.8</td>
<td>13.8/15.8</td>
<td>150–1500/10</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>8.7/7.9</td>
<td>21.8/20.8</td>
<td>11.8/11.5</td>
<td>250–500/10</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>12.2/12.3</td>
<td>20/17.6</td>
<td>8.9/8.5</td>
<td>25–800/10–20</td>
<td>6</td>
</tr>
<tr>
<td>mean</td>
<td>10.5</td>
<td>20.5</td>
<td>11.9 (11.5/12.3)</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

* MC = Meckel cave; Tmax = maximum temperature.

Part 3: In Vitro Thermocouple Testing to Assess for Bony Heating

To validate the MR thermometry data and predicted temperature increases in bone adjacent to anatomical structures of interest, thermocouple experiments were performed. A degassed human skull was custom fitted with a compatible gel for transcranial sonication. The CT correction algorithm was implemented. The thermometry-compatible gel allowed accurate MRI-guided targeting for ultrasound delivery. Using MRI data from the cadaveric studies, the average relative location of the trigeminal nerve (REZ, cisternal segment, and distal segment) in 3D space relative to the IAC was simulated.

Rapid sensing (sample rate = every 50 msec) MR-compatible thermocouples were fixed to the skull to monitor temperature changes in the bone adjacent to the following areas of interest (Fig. 5): 1) contralateral carotid canal, 2) clivus, 3) ipsilateral carotid canal, 4) ipsilateral IAC, 5) ipsilateral anterior temporal fossa, and 6) ipsilateral midportion of the temporal fossa. After placement of the thermocouples, the skull was degassed and the gel was placed inside the skull while it was submerged in degassed water. The entire apparatus was transferred underwater into the ExAblate system. The skull was rigidly attached to a jig on the transducer and suspended in degassed water. Dissolved gas content in the water was less than 1.2 parts per million.

The calculated location of the “virtual” trigeminal nerve in 3D space was targeted in the gel in a similar fashion to the cadaveric study. Sequential 800-W sonications for 10 seconds were performed targeting the REZ and midcisternal segment. Temperature changes in the gel were monitored using MR thermometry, and temperature changes in the thermocouples were recorded every 50 milliseconds by a computer system. The sonication began after 8 seconds of baseline temperature recording. Each sonication was repeated at each location 3 times and the results were averaged. A temperature profile in bone regions of interest before, during, and after sonication was created as a function of time.

**Results**

Part 1: Mechanical Feasibility to Target the REZ of the Trigeminal Nerve—Cadaveric Study

Adequate focusing of the ultrasound transducer was

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**Fig. 1.** Lateral (A) and anterior (B) views of the positioning. The frame should be pinned low as described, just above the orbital rim anteriorly and below the level of the inion posteriorly. The frame should be positioned almost as far laterally in the transducer as possible, and the frame should be advanced deep into the transducer. Final adjustments are made following MRI. The transducer is tilted backward 15° to allow further advancement of the head deeper into the transducer and is critical to facilitate targeting.

**Fig. 2.** Planning image. A treated sonication spot is shown as a blue diamond at the REZ. A second sonication spot is placed along the cisternal segment (open light blue circle). The target is then checked in all 3 planes of MRI planning. The green circle indicates the viable treatment envelope. The treatment envelope should include the pons (for calibration) as well as the REZ and cisternal segment.
achieved in all cases. A total of 38 sonications in the 4 cadavers were performed. The mean length of the cisternal segment was 10.5 mm, and the mean distance from the REZ to the basilar artery was 20.5 mm. The mean distance from the REZ to the internal acoustic meatus was 11.5 mm. The mean bony distance measured on CT (0.5-mm cuts) from the trigeminal nerve entry into the Meckel cave to the internal acoustic meatus was 11.9 mm.

The pons was targeted 10 times to calibrate the system and to perform electrical steering to correct for error in focal point prior to performing the treatment sonications. Low-power sonications into the pons created a discrete thermal increase in all 4 cases, indicating that the region of treatment was within the scope of the transducer. It should be noted that the tissue condition of the cadaver appeared to impact the ease with which a thermal increase in brain tissue could be achieved. Due to cavitation, less fresh specimens in poorer conditions were less likely to achieve higher temperatures, most likely due to cavitation from gas formation in the brain tissue.

No ultrasound beam blocking of regions of concern such as the IAC was performed in the cadaver studies. The REZ was targeted in 13 (34%) of 38 sonications, and the cisternal segment was targeted in 15 (39.5%) of 38 sonications. The results are summarized in Table 1. Power settings ranged from 25 to 1500 W for durations from 10 to 30 seconds. The average discrete thermal increase achieved in the REZ or cisternal segment was 10°C, with a range from 6°C to 18°C.

Part 2: Calculating the Temperature of Skull Base Structures Using Simulation Data

Simulation data assumes a body temperature of 37°C. The simulation does not take into account the thermal dissipation effect of CSF flow or blood flow in vessels or in bone. This therefore tends to overestimate the temperature increase seen in the bone. The predicted focal point area was 3 × 2 mm based on thermometry data. Placing the sonication within 10 mm from the skull results in a minimal temperature increase between the skull and focal point (Table 2). As a possible treatment example, the peak temperature in bone 10 mm from the focal point was 47.4°C for a treatment temperature of 48°C, with a rapid falloff to less than 39.4°C at approximately 6 mm

<table>
<thead>
<tr>
<th>Focal Spot</th>
<th>Temp From Focus</th>
<th>Temp of Bone w/ Bone Distance 10 mm From Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>38</td>
<td>41</td>
</tr>
<tr>
<td>44</td>
<td>39</td>
<td>43.5</td>
</tr>
<tr>
<td>46</td>
<td>39</td>
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<tr>
<td>52</td>
<td>40.2</td>
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<td>54</td>
<td>40.4</td>
<td>53.4</td>
</tr>
<tr>
<td>56</td>
<td>41</td>
<td>55.4</td>
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<td>58</td>
<td>41.5</td>
<td>57.3</td>
</tr>
</tbody>
</table>

* Values are in degrees Celsius. Abbreviation: Temp = temperature.
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TABLE 3: Predicted temperatures in soft tissue and bony interface for given thermal doses with the bone 20 mm from focus without beam blocking*

<table>
<thead>
<tr>
<th>Focal Spot Temp</th>
<th>Temp 5 mm From Focus</th>
<th>Temp 10 mm From Focus</th>
<th>Temp 15 mm From Focus</th>
<th>Temp of Bone w/ Bone Distance 20 mm From Focus</th>
</tr>
</thead>
<tbody>
<tr>
<td>42</td>
<td>38</td>
<td>37.3</td>
<td>37.2</td>
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<tr>
<td>44</td>
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<td>46</td>
<td>38.7</td>
<td>37.6</td>
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<tr>
<td>48</td>
<td>39.1</td>
<td>37.7</td>
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<td>50</td>
<td>39.55</td>
<td>37.8</td>
<td>37.6</td>
<td>37.2</td>
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<tr>
<td>52</td>
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<td>37.8</td>
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<tr>
<td>58</td>
<td>41.2</td>
<td>38.4</td>
<td>37.9</td>
<td>37.3</td>
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</table>

from this point (Fig. 6A). Overlaying these data on the MR images and calculated distance measurements (Table 1) demonstrated a predicted peak bone temperature at the entrance to the Meckel cave of approximately 47°C over a 2-mm area of bone, with rapid thermal dispersion (Fig. 6A). Along the trigeminal nerve itself, the temperature decreased steeply from 48°C at the focal point to less than 39.4°C at 5 mm (Fig. 6A). The maximum temperature calculated at the IAC based on the thermometry measurements was less than 47°C (Fig. 6B). With the skull placed 20 mm from a 48°C focal point, the peak temperature in the clivus reached 37.2°C, with a rapid falloff to 45°C. The temperature increase of the bone was therefore insignificant. The predicted temperature of the basilar artery did not change significantly from baseline (0.5°C) (Fig. 6C).

Part 3: In Vitro Thermocouple Testing to Assess Bony Heating and Accompanying Temperature Changes at Adjacent Neuroanatomical Structures

The calculated location of the trigeminal nerve could be targeted, and a discrete thermal increase at the target spot was achieved in all cases (Fig. 7). Preliminary experiments demonstrated minimal collateral temperature increases in bony areas of interest except for the IAC. To negate the unwanted temperature increase in this region, blocking of ultrasound beams was performed using the ExAblate software. The area to be blocked is highlighted on the skull CT scan on sequential slices until a 3D no-pass volume is created. Blocking algorithms prevented any waves passing through the petrous bone (Fig. 8). Elements that would propagate ultrasound energy through unwanted regions pretarget as well as those posttarget were turned off. Sonications were performed at the REZ and the midcisternal segment without blocking and with blocking (petrous bone blocked) (Fig. 9A). In the IAC blocking experiments, additional thermocouples were placed as internal controls. The results are shown in Fig. 9.

Without blocking, an 800-W sonication for 10 seconds resulted in a thermal increase at the REZ target of 11°C with a thermal increase occurring in the IAC of 16.7°C (Fig. 9A). With blocking of the petrous bone, the temperature increase in the IAC decreased dramatically to 5.7°C while a target temperature change of 7.3°C was still achieved at the same power (Fig. 9B). Temperature increases in the other bony areas of interest were minimal, and therefore no blocking was required for these areas. Targeting the midcisternal segment with 800 W for 10 seconds resulted in a 12.2°C temperature increase at the target with a 16.3°C temperature increase at the IAC (Fig. 9C). With blocking of the petrous bone, a much lower temperature increase at the IAC of 4.9°C was demonstrated while a target temperature change of 7.8°C was still achieved at the same power (Fig. 9D).

Discussion

Thermal Effects on the Trigeminal Nerve in Established Treatments for TN

This study demonstrates focal heating up to 18°C in a cadaveric trigeminal nerve at the REZ and along the cisternal segment with transcranial MRgFUS. Significant heating of the skull base and surrounding neural structures did not occur with implementation of no-pass regions along the petrous temporal bone. The data presented here demonstrate that it would be feasible to treat TN in a noninvasive fashion with this technology.

In comparing MRgFUS, the mechanism of pain relief in radiofrequency thermocoagulation is of particular interest. The primary mechanism of pain relief in radio-
frequency thermocoagulation for TN is heating of neural tissue. Secondary effects from the radiofrequency field itself have also been reported to be responsible for pain-relieving effects. Pulsed radiofrequency is a nondestructive method whereby short bursts of radiofrequency current at 42°C are generated with long pauses between bursts. This pause allows heat to dissipate. There is some evidence that A-beta and A-delta fibers may demonstrate less significant changes compared with C fibers with pulsed radiofrequency bursts. With conventional radiofrequency, changes in temperature up to 45°C are considered reversible; however, protein irreversibly denatures at 60°C. In an autopsy study of a patient treated with multiple radiofrequency ablations, this irreversible effect on the nerve was demonstrated by wallerian degeneration with associated myelin breakdown.

Due to the shape of the radiofrequency electrode, the heating effect creates a pear-shaped area of thermal energy, and heat dissipation occurs due to absorption, CSF, and blood flow. The neural tissue on the far side of the electrode does not receive the same energy as that closest to the electrode. Early animal studies in cats by Letcher and Goldring demonstrated that smaller unmyelinated nerves were more susceptible to moderate temperatures than were larger nerves. However, Smith et al. found that in dogs, the lesion was more indiscriminant, and destruction of small unmyelinated, small myelinated, and large myelinated fibers occurred. In 1974 Sweet and Wepsic hypothesized that the residual touch sensation following thermocoagulation of the gasserian ganglion was due to preservation of the heavily myelinated A-beta fibers. From a practical standpoint, in a typical treatment, localization is performed with an electrical stimulation. Following appropriate placement of the electrode the lesion is then made at 55°C–70°C. The procedure is considered completed if the patient demonstrates appropriate hypalgesia in the targeted branch of the nerve and the pain can no longer be triggered in the same fashion as preoperatively.

MRgFUS as a Tool for Pain Associated With Intracranial Disorders

The concept of using focused ultrasound energy as a lesioning method in the brain was demonstrated by Fry et al. through a craniectomy window in 1954. Later, for Lars Leksell, the imaging technology available was unable to allow visualization of deep targets, and there was still a need for a craniectomy to allow ultrasound energy passage. Leksell realized that ionizing radiation did not suffer these limitations, and this culminated in the development of the Gamma Knife in 1967. He had a particular interest in the use of noninvasive techniques for the treatment of pain disorders, including stereotactic radiosurgery for the treatment TN. Since then, stereotactic radiosurgery has developed into an effective noninvasive treatment alternative for patients with TN.
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The development of modern imaging, particularly MRI, has brought focused ultrasound–based lesioning back into consideration. Use of MRgFUS for the treatment of painful bone metastases has been performed with an excellent efficacy and safety profile. Gianfelice et al. reported a 92% (p < 0.01) decrease in visual analog pain scores for patients treated with MRgFUS. Similarly, Liberman et al. treated 31 patients with at least 3 months of follow-up in a multicenter trial, and 72% of patients reported significant pain improvement. Furthermore, 67% of patients decreased their opioid usage. No device-related complications or adverse events were recorded.

Transcranial MRgFUS now has commercially available systems that have been used effectively in the clinical setting, including the ExAblate Neuro (InSightec). Similar transcranial systems have been used in the experimental treatment of brain tumors, including glioblastoma. Such a system was also used to safely and effectively perform noninvasive centrolateral thalamotomies in 9 patients with chronic pain. Discrete thermal lesions of 4 mm in diameter were produced in the medial thalamus of awake patients with peak temperatures of 51°C–60°C under MRI guidance and continuous MR thermometry. Similar, a multicenter, FDA-approved Phase 1 trial utilizing the ExAblate Neuro 650-kHz system (InSightec) to perform unilateral ventral intermediate nucleus thalamotomy lesioning in patients with essential tremor who do not respond to medical treatment has been designed. Trials such as these demonstrate the feasibility of transcranial sonication and provide safety profile data that will be necessary for future brain applications of MRgFUS for other diseases like TN.

There are specific concerns with the potential use of MRgFUS for TN. The distance to adjacent bony anatomy from the target tissue is small, especially in the case of patients with a short cisternal segment of the trigeminal nerve. Critical brain structures may be susceptible to collateral heating, including the pons, cranial nerves VII and VIII, the basilar artery, and basilar branches including those causing microvascular impingement on the nerve itself, such as the superior cerebellar artery.

A sufficient thermal energy dose to achieve thermal coagulation in soft tissues is approximately 55°C peak temperature or 240 equivalent minutes at 43°C (TEM 43). To investigate safety concerns, simulated results with supramaximal treatment sonications were explored in the current study, with intervening soft tissue and bone heating calculated and correlated at critical structures. A sonication of 58°C would create a thermal lesion in nervous tissue, something that would not be intended in the treatment of TN. This simulation therefore represents the extreme limits of temperature increase to investigate safety. The simulated data demonstrate that the temperature encountered at the basilar artery will essentially be at baseline (Fig. 6C). The average distance from the REZ to the site of vascular impingement was described by Hardy et al. and averaged 3.7 mm in 50 cadaveric trigeminal nerves. Additional studies have found that temperatures in excess of 60°C are necessary to cause thermal coagulation within blood vessels by high-intensity focused ultrasound, with focal point temperatures up to 80°C. From the data in Tables 1 and 2, temperature increases 5 mm from the focal point are not significant, indicating that vessels impinging on the nerve are extremely unlikely to be under significant...
Fig. 9. A: Root entry zone target (800 W for 10 seconds) with no bone blocking resulted in an 11°C temperature increase at the target with a 16.7°C temperature increase in the bone of the IAC (Thermocouple 4). Sonication begins at 8 seconds. Trivial heating is seen at other skull base regions of interest. Refer to Fig. 5 for other thermocouple locations. B: Root entry zone target with blocking of the petrous bone. With the same ultrasound delivery parameters (800 W for 10 seconds), a 7.3°C temperature increase at the target results in a 5.7°C temperature increase at the IAC (Thermocouple 4). C: Midcisternal target without blocking of the petrous bone. With the same ultrasound delivery parameters (800 W for 10 seconds) a 12.2°C temperature increase at the target results in a 16.3°C temperature increase at the IAC (Thermocouple 4). D: Midcisternal target with blocking of the petrous bone. With the same ultrasound delivery parameters (800 W for 10 seconds) a 7.8°C temperature increase at target results in a 4.9°C temperature increase at the IAC (Thermocouple 4).

The simulations and in vitro thermocouple experiments demonstrate that targeting of the trigeminal nerve would result in adjacent bony heating in the IAC. This is likely due to the “shadow” of beams intersecting on the trigeminal target pointing in the direction of the IAC. With the introduction of petrous bone no-pass regions (volumes of the skull deliberately highlighted and excluded from any ultrasound beam paths) the average temperature increase in the IAC could be decreased from 16.7°C to 7.3°C for the REZ target. This maneuver did result in a slightly smaller target temperature increase for a given power (from 11°C to 7.3°C), although not as significant as that seen at the bone (Fig. 9A and B). In a similar fashion, for the midcisternal segment an improvement of bony heating at the IAC from 16.3°C to 4.9°C could be achieved. A less dramatic decrease in the target temperature was again noted (from 12.2°C to 7.8°C) (Fig. 9C and D). Magnetic resonance thermometry data did not demonstrate any additional skull surface heating as a result of the blocking compensation. Such compensatory measures would be an important part of the planning process in the treatment of patients. Further studies will investigate optimum combinations of power and sonication duration that result in the maximal target temperature increase, with the least amount of collateral bony heating after petrous blocking has been added to the treatment plan.

The sonication target, exact dose of ultrasound energy, and parameters required to create a long-lasting treatment effect in patients can only be adequately tested in the setting of a clinical trial. Parameters, such as power,
duration of sonication, and whether to use continuous or pulsed sequences, will need to be determined. A likely initial target would be the REZ. This target decreases the chances of encountering issues of skull heating due to a cisternal target more closely approximated to the bone and permits decreased bone heating at the IAC by creation of no-pass regions. Previous studies have demonstrated energy requirements to irreversibly lesion neural tissue with this system; however, in the case of TN the surgeon does not wish to completely lesion the nerve with MRgFUS. Preservation of the motor fibers, in addition to light-touch sensation combined with adequate pain relief, is the ideal treatment result. As with radiofrequency ablation, it is likely a combination of temperature increase (as monitored with real-time MRI thermometry) and real-time clinical examination and demonstration of hypesthesia in the awake patient will determine adequate treatment completion.

There are several limitations in using a cadaveric model in studying MRgFUS. It is difficult to control for the tissue quality of the specimens. The specimens that had longer to decay or those that had lost small volumes of CSF are less effective at permitting a clear thermal increase due to interface issues (intracranial air caused by CSF leak) and microbubble formation caused by the decay process. This tends to smudge the thermal spot in poor specimens and may not fully reflect the human situation. The temperature in the MRI room (16°C) is lower than body temperature. The cadavers also do not demonstrate the same extent of heat exchange manifested in living patients with well-perfused brain parenchyma, blood flow through blood vessels and bone, and CSF pulsations. Such additional fluid movement may improve heat dissipation; however, this is speculative. It was also noted that more distal targeting of the trigeminal nerve resulted in less signal for proton resonance frequency thermometry.

Despite these limitations, there are some potential benefits of MRgFUS for the treatment of TN. These include avoidance of the complications associated with percutaneous techniques, the noninvasiveness of the procedure (which can be performed on an outpatient basis), absence of the harmful effects of ionizing radiation (vs radiosurgery), the movability of the target in real time using subtherapeutic sonications with both patient response and MR thermometry feedback, and the possibility of repeat treatment with less risk to surrounding structures (the dose is not cumulative compared with radiosurgery). Potential disadvantages of the treatment include initial setup cost of the equipment, the current need to shave the head, the possibility that patients with extremely short cisternal segments may not be able to be treated, a longer treatment duration (on the order of 2 hours), and potential claustrophobia in the MRgFUS system for a prolonged period.

Conclusions

This is the first study to demonstrate feasibility of MRgFUS to noninvasively heat the trigeminal nerve. The results of this study demonstrate that focal heating of the trigeminal nerve and REZ can be achieved with transcranial MRgFUS. This novel treatment permits the possibility of repeated treatments for TN without the concerns of ionizing radiation to the brainstem seen with radiosurgery, and it avoids the complications encountered with traditional percutaneous techniques. Significant heating of the skull base and surrounding neural structures can be limited by appropriate ultrasound beam blocking during treatment planning. However, further studies will need to demonstrate the safety and histological effects of this treatment.

Disclosure

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