Preclinical assessment of a noncooled MR thermometry–based neurosurgical laser therapy system

*Hargunbir Singh, MBBS,1 Christian R. Osswald, PhD,2 Aaron Rossmann, BBA,2 Verena Knappe, Dipl-Ing,3 Lonnie Schneider, PhD,4 Candace L. Floyd, PhD,4 and John D. Rolston, MD, PhD1

1Department of Neurosurgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts; 2ClearPoint Neuro, Inc., Solana Beach, California; 3Clinical Laserthermia Systems LLC, Berlin, Germany; and 4Department of Emergency Medicine, Emory University, Atlanta, Georgia

OBJECTIVE MRI-guided laser interstitial thermal therapy (MRgLITT) has recently gained interest as an ablative stereotactic procedure for intractable epilepsy, movement disorders, and brain tumors. Conventionally, a LITT system consists of a laser generator and cooled laser applicator, which is a fiber optic core surrounded by a sheath through which cooled fluid is pumped. However, this footprint can make the system bulky and nonmobile, limit the maximum depth of targeting, and increase the chances of breakdown. Herein, the authors conduct a preclinical assessment of a noncooled MRgLITT system in a porcine model.

METHODS Three-tesla MRI was used to guide the in vivo placement of noncooled laser applicators in the porcine brain. The study consisted of a survival arm and terminal arm. The laser was activated at a power of 4–7 W for ≤ 180 seconds. Temperature changes were monitored using the MR thermometry software ThermoGuide in the survival arm (n = 5) or both ThermoGuide software and adjacently inserted thermal probes in the terminal arm (n = 3). Thermal damage was determined by the software using the temperature-time relationship of cumulative equivalent minutes at 43°C (CEM43). Temperatures calculated by the software were compared with those recorded by the temperature probes. The dimensions of thermal damage thresholds (TDTs; 2–9, 10–59, 60–239, ≥ 240 CEM43 isolines) given by MR thermometry were compared with the dimensions of irreversible damage on histopathological analysis.

RESULTS There was a strong correlation between temperature recordings by ThermoGuide and those by thermal probes at both 4 mm (r = 0.96) and 8 mm (r = 0.80), with a mean absolute error of 0.76°C ± 2.13°C and 0.17°C ± 1.65°C at 4 and 8 mm, respectively. The area of 2–9 CEM43 was larger than the area of irreversible damage seen on histopathological analysis. The dimensions of the 10 and 60 CEM43 correlated well with dimensions of the lesion on histopathological analysis. A well-defined border (≤ 1 mm) was observed between the area of irreversible damage and healthy brain tissue.

CONCLUSIONS This preclinical assessment showed that the noncooled LITT system was able to precisely reach the target and create well-defined lesions within a margin of safety, without any adverse effects. MR thermometry software provided an accurate near-real-time temperature of the brain tissue, and dimensions of the lesion as visualized by the software correlated well with histopathological findings. Further studies to test the system’s efficacy and safety in human subjects are in progress.


KEYWORDS MRgLITT; laser interstitial thermal therapy; laser ablation; noncooled laser applicator; neurosurgery; MR thermometry; surgical technique

Magnetic resonance imaging–guided laser interstitial thermal therapy (MRgLITT) is an emerging and innovative technique to thermally ablate deep tissues within the brain. LITT has garnered increasing attention in recent years, with researchers investigating its use in a variety of conditions such as intractable epilepsy, movement disorders, and brain tumors. Although the concept of LITT was introduced in the 1980s, its use was limited because of the inability to accurately monitor tissue temperature during the procedure. However, ad-
vances in imaging technology, such as MR thermography, have allowed for real-time monitoring and precise control of tissue ablation.12

One of the major advantages of MRgLITT, particularly when combined with MRI-guided navigation, is its ability to treat otherwise inaccessible or difficult-to-reach brain lesions.13 Additionally, MRgLITT can be used in cases in which traditional treatments are not feasible, such as in patients with medical comorbidities that preclude open surgery.14 MRgLITT has been useful for the treatment of drug-resistant focal epilepsy, demonstrating a significant reduction in seizure frequency with limited morbidity.15 Another notable exploration by Mohammadi et al. suggested the efficacy of LITT in managing difficult-to-access high-grade gliomas, an often challenging condition with limited therapeutic options.16 LITT has also been tried for the percutaneous treatment of epidural spine tumors.17 Ongoing research and development of MRgLITT technology will be important in improving its efficacy and expanding its applications.

In the United States, there are currently two established LITT ablation systems approved for clinical use by the Food and Drug Administration (FDA): Visialase (Medtronic) and NeuroBlate (Monteris Medical). In September 2022, the ClearPoint Prism Neuro Laser Therapy System (ClearPoint Neuro, Inc.), described in detail below, received FDA clearance. Prism utilizes the laser technology behind the TRANBERG Thermal Therapy System and the TRANBERG ThermoGuide Workstation (both manufactured by Clinical Laserthermia Systems AB, SE).

An MRgLITT system conventionally consists of a laser unit along with a laser applicator, a workstation, which is used for trajectory planning and real-time visualization of the temperature and damage estimation surrounding the laser applicator. The procedure is performed in an MRI suite. During treatment, a laser generator is used to heat tissue via the laser applicator to temperatures that are high enough to cause thermal damage. The procedure is monitored with MR thermometry to provide near real-time temperature feedback from tissue in the ablation zone.18 The extent of thermal damage depends on the temperature reached and the duration of exposure. The time and temperature history data from each voxel are used by the software to estimate tissue damage in the ablation zone.19 The Prism system utilizes cumulative equivalent minutes at 43°C (CEM43), which is a standardized metric to indicate the thermal dose delivered.20 21 It represents the amount of time that tissue has been exposed to temperatures of 43°C that causes thermal damage.22 Thermal damage thresholds (TDTs) are temperature-time combinations that result in a specific level of tissue damage.23 These are determined experimentally and are specific to the tissue type. Once calculated, these TDTs can be represented as CEM43 isolines.

The Prism system consists of a mobile laser unit, an MR thermometry workstation with ThermoGuide software, and noncooled laser applicators (Fig. 1A). Other LITT systems have a laser probe surrounded by a cooling sheath through which a constant stream of cold fluid or gas (saline or CO₂) is pumped. A noncooled laser ablation system presents a significant advantage in terms of efficiency, capable of creating lesions of the same size as a traditional cooled applicator but in half the time and utilizing only half the energy, which is attributed to the elimination of the heat sink effect around the applicator, making it suitable for highly vascularized tissue. Moreover, while the cooling sheaths can increase the overall footprint of some systems and can require permanent installation, a noncooled system has the advantage of being mobile with the added benefit of having fewer points of failure like leaks or running out of coolant. Additionally, the noncooled Prism system still offers the same level of safety because of a robust silica diffuser tip that absorbs minimal laser light. There are additional mandatory safety features implemented in the ThermoGuide software such as temperature guards to protect sensitive structures and the temperature close to the laser applicator, as well as automatic B₀ phase drift, which is inherent to the MR scanner and can lead to inaccurate temperature estimation.24

In this study, we conducted a preclinical assessment of the ClearPoint Prism Neuro Laser Therapy System in a porcine model. The study had three main objectives: first, to demonstrate that the damage area predicted by the thermal damage estimate (TDE) map, as measured by the 2 CEM43 isoline, provided a safety margin and was larger than the developed thermally ablated area of irreversible damage as determined by histopathological analysis at 3 days posttreatment (survival arm). The second objective was to compare the various TDTs to the morphometry of irreversible damage seen on histopathological analysis. This was important to determine the reliability of the MR thermometry software in predicting the extent of tissue damage and to evaluate the therapy’s effectiveness in thermally ablating the target tissue. The third objective was to assess the accuracy of the Prism system in predicting actual temperature changes in vivo (terminal arm). This was important to ensure that the system accurately predicted temperature change in vivo, thus enabling an accurate calculation of the TDE map without causing damage to surrounding healthy tissue. This preclinical assessment will provide valuable information on the safety and efficacy of the Prism system and pave the way for its use in clinical settings.

Methods

The MR thermometry workstation runs the MRI analysis software ThermoGuide (Clinical Laserthermia Systems AB) for the determination and visualization of relative changes in tissue temperature during therapy. As part of the Prism system, the software has been developed and validated for laser interstitial therapy in neurosurgery under 3.0-T MRI guidance.25

ThermoGuide monitors and automatically corrects for B₀ phase drift throughout the procedure. This enables more accurate temperature prediction over the duration of the ablation. Additionally, ThermoGuide provides “temperature guard” functionality whereby several temperature limit regions of interest (set as points, lines, or areas) may be associated with prescribed anatomical image locations, which can then be used to automatically deactivate the laser if the limits set by the user are reached or
can be used to simply monitor the temperature of various voxels.

TDTs are represented as color-coded CEM43 isolines, with the tissue damage predicted by 2–9, 10–59, 60–239, or ≥ 240 CEM43 TDTs (Table 1). These TDTs are used to create a TDE map in which the color of the voxel represents the TDT of that voxel based on the CEM43 isolate (Fig. 1B). The default voxel size of the thermometry imaging sequence is 1.6 × 1.6 × 3 mm, which can be interpolated or resampled to 0.8 × 0.8 × 3 mm to offer a better spatial resolution. TDE maps can be visualized in up to three user-defined planes. The refresh rate for temporal resolution is ≤ 3.1 seconds for two planes at 3T and is therefore faster than the 5–9 seconds in conventional systems. Thus, the Prism system offers better intraoperative visualization of the therapy, which can lead to more precise estimates of

**TABLE 1. TDTs displayed by ThermoGuide**

<table>
<thead>
<tr>
<th>TDT</th>
<th>CEM43 Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>2–9</td>
<td>Exposure to thermal equivalent of 43°C for at least 2 mins’ duration; tissue outside green area has high probability of receiving no thermal damage; tissue in green area may experience thermal damage, but cell death is not guaranteed</td>
</tr>
<tr>
<td>Yellow</td>
<td>10–59</td>
<td>Exposure to thermal equivalent of 43°C for at least 10 mins’ duration; tissues w/ a yellow thermal dose are likely to experience irreversible cell damage</td>
</tr>
<tr>
<td>Orange</td>
<td>60–239</td>
<td>Exposure to thermal equivalent of 43°C for 60 mins’ duration; all tissue w/in this boundary experiences cell death w/in ≤48 hrs</td>
</tr>
<tr>
<td>Red</td>
<td>≥240</td>
<td>Exposure to thermal equivalent &gt;43°C for 240 mins’ duration; immediate, irreversible damage has occurred</td>
</tr>
</tbody>
</table>
the thermal dose delivered to the tissue and improve the safety and efficacy of the treatment.

Noncooled Laser Applicators

Noncooled laser applicators (Clinical Laserthermia Systems AB) are 15 G/1.7 mm in diameter and are available in two types: radial and diffuser (Fig. 1C). The radial laser applicator design delivers light in all directions in a plane perpendicular to the fiber axis. With heat conduction, a spherical ablation zone is achieved. The diffuser applicator design delivers light in all directions along a cylinder, which is available in 15- and 25-mm lengths, and provides an ellipsoid ablation zone. Both the laser power level and the emission time are user controlled within safety limits set by the associated radiofrequency identification (RFID) tag, included with each laser applicator. The laser unit has additional safety systems to prevent unintended misuse of the system.

Laser applicators have a 550-μm quartz glass core, 12-mm length, and standard subminiature version A (SMA) connector. The length of the laser applicator is marked every 1 cm to aid in pullback ablations, and the applicator is intended to be used with a compatible introducer or catheter. Laser applicators and SMA connectors are MRI conditional up to 3-T systems.

In Vivo Validation Study

This study aimed to evaluate the efficacy and accuracy of the Prismo system in a porcine model, selected for its gyrencephalic nature and cytoarchitecture, which are similar to those of the human brain.26,27 The in vivo study had two arms: a survival arm and a terminal arm. The survival arm was intended to demonstrate that the ThermoGuide software provides an accurate prediction of damage 3 days posttreatment as compared to histopathological findings. The terminal arm was intended to demonstrate that the ThermoGuide software provides an accurate temperature estimate as compared to reference physical temperature probes.

An overview of the methodology is provided in Fig. 2. The sample size was determined to have at least five results per study arm.

Anesthesia

Animals were sedated with a cocktail of Telazol (4.4 mg/kg), ketamine (2.2 mg/kg), and xylazine (2.2 mg/g) through either intramuscular or subcutaneous injection. Subsequently, the animals were intubated for anesthesia with inhaled isoflurane (1.5%-3%) continuously for the duration of surgery. Approximately 3–5 minutes prior to incision, a local dose of lidocaine (1–3 mg/kg) was administered subcutaneously at the planned incision site. The depth of anesthesia was monitored approximately every 15 minutes by looking for changes in heart rate in response to deep pain stimulus (toe pinch). For supplemental heat, an MRI-compatible, recirculating water blanket was placed on the MRI table under the animal.

MRI and Targeting

Intraoperative MRI (3T Magnetom Trio system, Siemens) was used for navigation and thermometry in combination with a 4-channel large flex coil. Animals were positioned prone and pinned in a multipositional head fixation frame (ClearPoint Neuro, Inc.) to prevent motion artifact and maintain MRI space throughout the procedure. The SmartFrame Array and associated software (ClearPoint Neuro, Inc.) were used to place the laser applicators.

Placement of Laser Applicators

For the terminal study arm, bilateral craniotomies were conducted in 3 animals. A custom-made device guide for the SmartFrame Array was used to place the laser applicator (15-mm diffuser) and two MRI-compatible temperature probes (Rugged Monitoring) in the parietal and/or occipital lobes under MRI guidance. Ablations were performed at ≤ 7 W for up to 3 minutes while temperature monitoring was conducted. The procedure was then mirrored in the other hemisphere and repeated so that two sets of data were collected per animal, for a total of six replicates.

For the survival study arm (n = 5), radial tip laser applicators were navigated to the caudate nucleus unilaterally. The procedure was performed through a 3.4-mm twist drill hole using the standard SmartFrame Array hardware and software, with laser applicators inserted through a 5-Fr peel-away sheath (ClearPoint Neuro, Inc.). Ablations were performed at 4 W for up to 3 minutes.

Temperature Recording: Terminal Arm

Reference MRI-compatible fiber optic temperature probes were calibrated prior to the study. The probes were inserted to a depth corresponding to the center of the laser applicator window and were placed radially at 4 and 8 mm from the applicator. The temperature probes were connected to a 4-channel temperature monitor (Rugged Monitoring), and data were recorded using the Rugged Connect software.

Since the temperature probe creates an artifact within the MR thermometry image, a concordant voxel was selected at the same distance, and the calculated temperature was exported from ThermoGuide. To determine the accuracy of the ThermoGuide software in predicting actual temperature changes, the mean absolute error (MAE) was calculated for each ablation. The MAE was defined as the mean of the difference between temperature recordings from the temperature probes and the concordant ThermoGuide temperature measurement over the duration of the ablation.

Lesion Dimensions Determined by TDE Maps: Survival Arm

The dimensions of the lesion were calculated from TDE maps. The area, height, and width of CEM43 isolines (2, 10, 60, and 240 CEM43) were measured by three independent raters for each subject. An example of this process of measuring one lesion is shown in Fig. 3 upper and Video 1.

VIDEO 1. Clip demonstrating a laser ablation procedure using the ThermoGuide software in conjunction with the Prismo laser ablation system in a porcine brain. A 15-mm diffuser-type laser applica-
FIG. 2. Overview of the study methodology. In the terminal study arm, temperature probes were inserted in parallel to the laser applicator to assess the accuracy of the Prism system in predicting actual temperature changes in vivo. In the survival study arm, animals were permitted to survive for 3 days. Histopathological analysis was performed to ensure that ThermoGuide provided a safety margin; that is, the damage area predicted by ThermoGuide was larger than the area of irreversible damage on histopathological analysis.
**FIG. 3.** Upper: Dimensions (height, width, and area) measured for one lesion. The height and width were defined as the length that included all the voxels of that CEM43 isoline (dashed lines). The area was defined as all voxels enclosed within the respective CEM43 isoline (dashed squares). Lower: Histological images of the lesion from one of the subjects in the terminal arm. The area of irreversible damage was delineated using amino cupric silver staining. The left image shows the tracing method used to calculate the area of the lesion. The central void in these images comes from the laser probe and the immediate, irreversible damage. The right image shows the border between irreversibly damaged brain tissue and viable area surrounding it. A sharp border (≤ 1 mm) between the lesion and healthy brain tissue was achieved. Figure is available in color online only.

<table>
<thead>
<tr>
<th>Height</th>
<th>Width</th>
<th>Area</th>
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</thead>
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<td><img src="image2.png" alt="Image" /></td>
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<tr>
<td>10-59 CEM₄₃</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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<tr>
<td>60-239 CEM₄₃</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
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<tr>
<td>&gt;240 CEM₄₃</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
</tbody>
</table>
Targeting Accuracy and Precision

Results were used to determine the area (mm²), height, and width measurements provided by a board-certified histopathologist.

Lesion Dimensions Determined by Histopathological Analysis: Survival Arm

Three days after ablation, subjects in the survival arm were humanely euthanized and exsanguinated, and their brains were extracted. Brain tissue was immersion fixed in 10% formalin and then shipped to NeuroScience Associates for processing, sectioning, and histopathological analysis. The brains were trimmed to the area of interest, cryoprotected, embedded, and frozen for sectioning in an oblique coronal plane, aligned with the trajectory of the laser fiber, using a microtome setting of 40 μm. A set of every 24th section (an interval of 960 μm) was processed using amino cupric silver stain with neutral red counterstain.

In all animals, the 2D radial error, defined as the absolute scalar distance between the intended target planned in the ClearPoint Array software and the actual laser placement, was 0.96 ± 0.4 mm. Insertion depth was also accurate, with an average depth error of 0.62 ± 0.55 mm. No revisions were necessary to reach the target in any animal.

Comparison to Histopathological Analysis

In all cases, the 2 CEM43 TDT area was 32.66 ± 24.9 mm² larger than the area of irreversible damage measured on histopathological analysis. The 10 CEM43 TDT best represented the area measured on histological analysis with a mean difference of 0.34 ± 6.9 mm². In 2 of the 5 animals, the area of 10 CEM43 TDT was larger than that measured on histopathology. Lastly, given the anatomical constraints of the porcine caudate nucleus limiting the desired size of ablation, in some subjects, the ablation did not yield a TDT at 60 or 240 CEM43. These data are summarized in Table 2.

The study also compared linear dimensions of the TDTs with dimensions of the lesion on histopathology. For the TDTs, the maximal length (i.e., along the laser applicator fiber axis) and width (i.e., perpendicular to the laser applicator axis) were compared with the measurements of the greatest vertical (length) and horizontal (width) dimensions of the brain region of irreversible damage on histopathological analysis. Among the different CEM43 isolines, the 60 CEM43 TDTs showed the greatest similarity to the vertical and horizontal dimensions from histopathology in 3 of 5 animals. The 10 CEM43 TDTs had the next highest similarity, with 2 of 5 animals showing the closest resemblance. In 1 subject, both the 10 and 60 CEM43 TDTs had similar width measurements compared to the horizontal dimension from histological analysis. These values are summarized in Table 3.

Table 2. TDE area compared to morphometry: survival arm

<table>
<thead>
<tr>
<th>Subject</th>
<th>CEM43 (mm²)</th>
<th>Histological Analysis (mm²)</th>
<th>% Difference Compared to Histopathology</th>
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<tbody>
<tr>
<td></td>
<td>2</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
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<td>115.2</td>
<td>64.7</td>
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<td>26.0</td>
<td>3.3</td>
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<td>P21-070</td>
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<td>20.5</td>
<td>NA</td>
</tr>
<tr>
<td>P21-072</td>
<td>26.0</td>
<td>14.7</td>
<td>8.5</td>
</tr>
</tbody>
</table>

NA = not assessable, as that TDE was not achieved during ablation; +/- = area of the TDE map was larger/smaller than the area of irreversible damage on histological analysis, respectively.

Ethics Committee Approval

This study involving a porcine model was conducted in accordance with the guidelines set by the University of Utah Institutional Animal Care and Use Committee. Ethical approval was duly obtained prior to commencement of the research, ensuring adherence to all animal welfare standards.

Results

Targeting Accuracy and Precision

In all animals, the 2D radial error, defined as the abso-
TABLE 3. TDE dimensions compared to morphometry

<table>
<thead>
<tr>
<th>Subject &amp; Measurement Source</th>
<th>Length (mm)</th>
<th>Width (mm)</th>
<th>Closest Length to Histology</th>
<th>Closest Width to Histology</th>
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<tbody>
<tr>
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<td>2 CEM43</td>
<td>13.0</td>
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<tr>
<td></td>
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<td>8.2</td>
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<td></td>
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<td></td>
<td>Histopathology</td>
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<td></td>
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<td>Histopathology</td>
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<td>Histopathology</td>
<td>3.0*</td>
<td>3.6*</td>
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<td>Histopathology</td>
<td>3.9*</td>
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* Estimated due to excessive sectioning artifact.
† Both measurements similar.

Discussion

In this preclinical assessment of the ClearPoint Prism Neuro Laser Therapy System, we evaluated the safety, accuracy, and efficacy of the device in a porcine model. The study had three main objectives: first, to demonstrate that the damage area predicted by the ThermoGuide TDE map, as measured by the 2 CEM43 isoline, provided a safety margin and was larger than the developed thermally ablated area of irreversible damage as determined by histopathological analysis at 3 days posttreatment. The second objective was to compare the TDE to the morphometry of irreversible damage on histopathological analysis. The third objective was to assess the accuracy of the Prism system in predicting actual temperature changes in vivo.

The accuracy of the SmartFrame Array in placing the Prism system laser applicators was determined by measuring the 2D radial error (i.e., the distance between the target and laser applicator placement) and the depth error. Both errors were consistently less than 1 mm, which is in line with current accuracy and precision reported in other intraoperative MRI–guided stereotactic procedures like deep brain stimulation lead placement.28 High accuracy was especially important while targeting small structures in preclinical animal models.

The first goal of the study was to establish that the 2 CEM43 isoline provided a margin of safety while creating these lesions. For this, morphometry of the TDTs and lesion on histopathological analysis were compared in the survival arm (n = 5). In all cases, the area of the 2 CEM43 TDT was larger than the area of irreversible damage measured on histopathological analysis, highlighting its crucial role in offering the surgeon a reliable point to decide when to halt treatment. Said another way, the 2–9 CEM43 isoline represents the area surrounding the lesion that exhibited an increase in temperature during the procedure, but where there was no irreversible damage seen on histological analysis. From a clinical perspective, this provides surgeons with an additional buffer or safety margin during procedures. Further, a sharp transition (approximately 200 μm) was observed between the area of damage and surrounding healthy tissue.

A subsequent goal of our study was to understand which TDE most reliably predicted irreversible tissue damage. For all animals, the percentage difference between the 10 CEM43 TDE map was the least, indicating that the damage area predicted by the 10 CEM43 TDE map was most similar to the area of irreversible damage observed in histomorphometry. The length and width of the TDTs were also compared to those measured in histopathology. In 3 of the 5 animals, the 60 CEM43 isoline height and width measurements had the greatest similarity to the vertical and horizontal dimension measurements from histology. The 10 CEM43 isoline height and width measurement was the next most similar, with data from 2 of the 5 animals being most similar. In 1 subject, both the 10 and 60 CEM43 isolines had similar measurements. These findings are consistent with previous studies that have shown that TDTs from MR thermometry can be used as a reliable predictor of irreversible tissue damage during laser ablation procedures.16,23,29 As the 10 CEM43 isoline is a more conservative threshold, it should be preferred for clinical scenarios to predict irreversible damage; however, more trials are needed to answer definitively whether the 10 or 60 CEM43 isoline is clinically more relevant for assessing irreversible damage.

Lastly, temperature recordings provided by ThermoGuide were compared to recordings from the thermal probes in the terminal arm (n = 5). Although previous studies have shown that MR thermometry can be used to predict temperature changes in real time while performing a thermal ablation,16,31 to our knowledge, this preclinical assessment...
is the first of its kind to incorporate two thermal probes that measured the in vivo temperature of brain tissue during the ablation. Our results showed that there is a strong correlation between the temperature recorded by ThermoGuide and that recorded by the thermal probes, both at 4 and 8 mm away from the laser applicator.

Compared with other FDA-approved LITT systems like Visualase and NeuroBlate, the ClearPoint Prism Neuro Laser Therapy System demonstrated distinct benefits in this preclinical trial. The refresh rate of < 3.1 seconds offers a better temporal resolution, which ultimately translates to a more controlled lesion, as compared to 5–7 and 7.8 seconds for Visualase and NeuroBlate, respectively. Further, the highest in-plane resolution offered by Prism, with an MR thermometry voxel size of $0.8 \times 0.8 \times 3.0$ mm, helps to create a precise lesion, as compared to a voxel size of $1 \times 1 \times 3$ mm for Visualase and $2 \times 2 \times 5$ mm for NeuroBlate. The strong correlation between temperature recordings from the intracranial thermal probes and ThermoGuide ensures predictable lesioning with a margin of safety, as confirmed by histology. When paired with the ClearPoint SmartFrame Array, the radial and depth errors in applicator placement were consistently < 1 mm in this trial. Our preliminary data also suggest that the decreased energy deposition inherent to the noncooled Prism system may contribute to a reduction in perilesion edema, particularly noticeable when conducting larger ablations, although further research is required to substantiate these findings and validate the performance of ClearPoint Prism in a broader clinical context.

There were some limitations of this study. For instance, although the study was performed in a porcine model, which allowed us to simulate the properties of human brain tissue, the small size of the porcine brain makes creating larger lesions, as would be done in many clinical procedures, difficult. Additionally, the sample size was limited, as was the duration of follow-up. A larger sample with more time to evaluate the chronic effects of ablation would be of great interest as MRgLITT becomes more widely used.

**Conclusions**

This preclinical assessment provides valuable insights
into the performance of the ClearPoint Prism Neuro Laser Therapy System in an in vivo brain model. This preclinical assessment in a porcine model showed that the Prism system can both precisely reach the target and create well-defined lesions with a margin of safety, without any adverse effects. The Prism system provides an accurate, near-real-time temperature of the brain tissue with an MAE of < 1°C, as determined by implanted temperature probes. The area and dimensions of the lesion, as visualized by Thermoguide, correlated well with histopathological findings. The development of a safer, faster, and more streamlined MRgLITT system represents a welcome new treatment option for patients with intractable epilepsy, movement disorders, and brain tumors.

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**Disclosures**

Dr. Osswald and Mr. Rossman were salaried employees of ClearPoint Neuro Inc. during the conduct of the study and outside the submitted work. Ms. Knappe was a salaried employee of Clinical Laserthermia Systems GmbH during the conduct of the study. Dr. Rolston received grants from ClearPoint Inc. during the conduct of the study. While funding was provided by ClearPoint Neuro Inc. and Clinical Laserthermia Systems GmbH and the authors are affiliated with these entities, the analysis presented in this study was conducted independently and was subjected to external auditing to ensure the integrity of the results.

**Author Contributions**

Conception and design: Osswald, Knappe, Floyd, Rolston. Acquisition of data: Osswald, Rossman, Knappe, Schneider, Floyd, Rolston. Analysis and interpretation of data: Singh, Osswald, Rossman, Schneider, Floyd, Rolston. Drafting the article: Singh, Osswald, Knappe, Rolston. Critically revising the article: Singh, Osswald, Knappe, Rolston. Reviewed submitted version of manuscript: Singh, Osswald, Rossman, Rolston. Approved the final version of the manuscript on behalf of all authors: Singh. Statistical analysis: Singh, Rossman. Administrative/technical/material support: Rossman, Floyd, Rolston. Study supervision: Floyd, Rolston.

**Supplemental Information**

**Videos**


**Correspondence**

Hargunbir Singh: Brigham and Women’s Hospital, Harvard Medical School, Boston, MA. hsingh12@bwh.harvard.edu.