Technical Notes and Surgical Techniques

Endoscopic laser ablation of clival chordoma with magnetic resonance-guided laser induced thermal therapy

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Background: Chordomas are rare malignant tumors that are difficult to treat and have high recurrence rates despite aggressive therapy.
Objectives: We present the first case of a patient with a clival chordoma in which complete tumor ablation was achieved using Magnetic Resonance guided Laser Induced Thermal Therapy (LITT) delivered via an endoscopic endonasal approach. We analyzed the safety and feasibility of this approach and quantified the response of this pathology to thermal energy. This novel technique is intended to provide chordoma patients with an alternative to surgery and radiotherapy.
Methods: A 54 year-old female with a newly diagnosed clival chordoma elected MRI-guided LITT. She underwent placement of the laser catheter into the chordoma via an endoscopic endonasal approach. With real-time MR thermometry monitoring, laser-generated thermal energy was delivered to the tumor. We defined several parameters to quantify the thermal ablation response: the thermal damage ratio and the thermal ablation constant.
Results: Post procedure contrast-enhanced MRI demonstrated a complete thermal ablation of the mass. The patient tolerated the procedure well and is being followed with serial imaging. The tumor continues to regress beyond 4 months. Additionally, chordoma cells seem to be sensitive to LITT, as indicated by a complete ablation in less than 60 s.
Conclusion: The endoscopic endonasal approach to MRI-guided laser ablation is both technically feasible and safe. As a result, this therapy may be a useful alternative in hard-to-reach chordomas, or in recurrent cases that have failed other conventional treatment modalities.
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Introduction

Chordomas are rare, slow-growing, locally-invasive tumors occurring mostly at the sacrococcygeal region and spheneno-occipital junction [1]. Treatment typically consists of en bloc surgical resection with adjuvant radiation therapy. Despite such aggressive treatment, the recurrence-free 5-year survival rate in patients with a skull base chordoma is only 60–70% [2]. In recent years, advances in endoscopic endonasal skull base surgery have allowed more complete surgical resections with reduced morbidity.

One such method employs the use of thermal energy in treating intracranial malignancies and has been achieved with radio waves, ultrasound, microwaves, and lasers. Laser thermal ablation has been successfully used in treating a variety of tumors outside the nervous system [3] by destroying tumor cells within a well-defined tissue volume while sparing healthy peripheral tissue.

However, the unpredictability of the ablation size and volume as well as the irregular heating pattern and distribution has largely limited the application of laser thermal ablation for intracranial lesions. The development of magnetic resonance (MR) thermometry has recently made it possible to target abnormal tissue and limit the amount of heat distributed to surrounding tissues by acquiring real-time thermal information during the procedure [4]. By combining these two techniques, MRI-guided Laser Induced Thermal Therapy (LITT) is a minimally-invasive method for delivering thermal energy delivered through a fiber optic laser under stereotactic guidance and real-time thermal feedback. The use of LITT in neurosurgery is gaining popularity due to the ability to apply precise amounts of thermal energy to target lesions that are difficult or impossible to access with standard surgical techniques. We present the first application of MRI-guided LITT to a clival chordoma, report short-term radiographic follow-up, and describe ablation dynamics with respect to chordoma cells.

Patients and methods

The patient is a 54 year-old female with several months of progressive dysphagia and changes in her voice. As part of her
neurologic workup, brain MRI revealed a clival mass. T1-weighted MRI with gadolinium contrast showed a 1.8 × 1.35 × 1.3 cm well-circumscribed, heterogeneously enhancing mass arising from the ventral surface of the clivus and extending anteriorly into the posterior nasopharynx (Fig. 1). There was mild T2 signal hyperintensity within the lesion and no significant FLAIR signal in the surrounding tissue. A CT-guided needle biopsy established the diagnosis of chordoma. She was referred for neurosurgical evaluation and treatment. Further radiographic evaluations revealed that the posterior wall of the clivus was intact with no disruption of the skull base anatomy.

The standard treatment option, en bloc surgical resection with or without adjuvant radiation was offered to the patient. MRI-guided LITT was offered as an alternative treatment option. The family was thoroughly counseled that although this approach may be less disruptive, and require less operative time, the effect of thermal energy on chordoma cells is not known. The patient and her family decided to undergo LITT as part of an institutional IRB-approved study.

**Intervention**

The patient was placed in the supine position under general anesthesia. The setup was similar to all endoscopic endonasal skull base cases performed at our institution. A single-nare approach was utilized. The cooling catheter was introduced into the nose after passing it through the guidance bolt (Fig. 2A). We achieved excellent visualization of the exophytic endonasal portion of the mass. A 1.65 mm diameter coaxially-cooled diffusing tip laser applicator (VCLAS-400, BioTex, Inc., Houston, TX, USA) was then introduced through the surface of the mass until the bony clivus was felt at the posterior margin of the mass (Fig. 2B). The plastic guidance bolt typically used to anchor the laser to the skull was then advanced down the applicator and seated in the left nostril (Fig. 2C). A 2-0 silk suture was sewn to the nasal septum and tightly tied to the bolt to restrict any migration during transport to MRI (Fig. 2D). The blue cap of the guidance bolt was then screwed tightly over the clear base in order to secure the laser catheter’s position within the lumen of the guidance bolt.

The patient was then transferred to the MRI scanner (GE, 1.5 Tesla) to initiate therapy. The laser applicator tip was connected to the Visualase Thermal Therapy System (BioTex Inc., Houston, TX, USA), which provides up to 15 Watts of 980 nm laser energy and software that allows real-time MR thermal monitoring of the selected MR slice. Oblique sagittal sequences in line with the laser catheter were obtained and confirmed optimal laser placement. A reference image in the sagittal plane was selected as the monitoring slice for proton resonance frequency (PRF) based magnetic resonance temperature imaging (MRTI) on the Visualase workstation (Fig. 3A). This allows for temperature information to be superimposed over live treatment images in real-time (Fig. 3B). Target temperature limits were set to 90 °C near the catheter and 50 °C at the posterior and superior borders of the clivus. Based on the temperature and time history, the software predicted cell kill, utilizing the Arrhenius damage model. A test dose was delivered at 3.1 W for 33 s. This confirmed the laser location within the targeted lesion. Once confirmed, a total of 4 ablations were performed at 12 W for a combined total of 311 s.

Post-ablation MR imaging confirmed that the zone of ablation encompassed the entire tumor and therapy was concluded. The laser was removed and post-operative imaging confirmed no hemorrhage within the nasal cavity. The patient was then transferred to recovery where she was extubated in stable condition. She was admitted overnight and discharged the next day without any postoperative complications. After 4 months, her dysphagia has resolved and she reports no further voice changes. The patient is being followed closely with serial imaging.

**Results**

**Radiographic evaluation**

Prior to thermal ablation, the lesion heterogeneously enhanced consistent with viable tumor. There was no edema or hematoma seen around or within the lesion. Gadolinium enhanced MRI scans were obtained immediately after ablation, and at various time points after therapy. All post-ablation scans demonstrate a peripherally enhancing lesion with a central focus of low signal that encompasses the entire region of enhancement that was seen on pre-operative MRI. These findings are consistent with complete thermal ablation [5]. An MRI performed at 136 days post-ablation shows a reduction in lesion size.

Volumetric analysis was performed on all images to quantify changes in the size of the tumor mass. The lesion volume was estimated by evaluating it as an ellipsoid structure \( V = \frac{4}{3} \pi r_1 r_2 r_3 \). The tumor lesion diameter was measured in 3 dimensions based on the largest diameter in axial, coronal, and sagittal planes. The pre-ablation estimate of the lesion volume was 1.65 cm³. The immediate post-ablation lesion volume was 2.85 cm³. The lesion volume at 1 day was 2.47 cm³, at 25 days it was 1.34 cm³, at 73 days it was 0.59 cm³, and at 136 days the lesion volume was 0.35 cm³.

**Ablation dynamics**

The Visualase software provides a real-time estimate of thermal damage area. This information is routinely used to guide the duration of treatment. The damage estimate is derived from the Arrhenius equation:

\[
\Omega(t) = \int_0^t Ae^{-E_d \frac{dT}{RT(\tau)}} d\tau.
\]
Eₐ and A are the activation energy and the frequency factor, respectively. T(τ) is the tissue temperature over time, R is the universal gas constant, and t is time. In the Visualase software, voxels are assumed to have reached the threshold for thermal damage when Ω ≥ 1 and are displayed in orange (Fig. 4). Once the damage estimate that is superimposed on the reference image indicates that the entire lesion has been ablated, treatment is concluded. The number of damage voxels is converted into damage area (mm²) by the following formula:

\[ \text{Damage area} = \frac{\text{No. of pixels} \times (\text{FOV} \times \text{FOV})}{256 \times 256} \]

FOV is the field of view; 256 × 256 is the specified image acquisition matrix. The first ablation for this patient produced an estimated damage area of 156 mm². Ablation plateau was reached at approximately 60 s. The time to reach 50% of the total ablation area (t₅₀) was 7.4 s (Fig. 5). The subsequent three treatments that were performed did not significantly increase the estimated damage area.

**Discussion**

Clival chordomas present many challenges to the neurosurgeon. Complete tumor resection at the skull base may be difficult to achieve. Radiation therapy may reduce local recurrence but is associated with complications such as radiation necrosis, cranial nerve injury, and pituitary dysfunction. MRI-guided laser induced thermal therapy (LITT) is a novel treatment modality that has not yet been applied to chordomas. In this report we demonstrate the safety and technical feasibility of utilizing MRI-guided LITT for skull base pathologies and report the responsiveness of a chordoma to thermal energy.

The reduction in lesion volume over time indicates that chordomas are responsive to thermal ablation and follow a response profile similar to those of other pathologies. The immediate post-ablation lesion volume is almost always larger than the pre-ablation volume due to hyperacute thermal-induced edema [5].

Upon resolution, a steady decline in lesion volume may be observed for at least 4 months. As a result, LITT may be useful as an adjunctive treatment or even palliative measure in patients who require local tumor control but are not operative candidates.

In an effort to guide future ablation procedures, we attempt to define parameters define tumor response to thermal energy. We propose two parameters: the thermal damage ratio and the thermal ablation constant.

We define thermal damage as the ratio of the estimated thermal damage area to the pre-ablation lesion area based on the reference...
Thermal damage area estimate versus time by using the standard logarithm formula \( A = \log_a(t) \), as previously reported. To quantify the response, we correlated ablation area limitation are currently under development.

Software upgrades that overcome this irregular-shaped tumor volume may also decrease the accuracy of single-plane estimation. There are certain limitations to this measurement. The pre-treatment lesion area is calculated from the reference image, which is an elliptical approximation of the lesion and is susceptible to overestimation, possibly explaining an underestimation of the damage ratio. While our damage ratio (0.821) suggests incomplete ablation, our post-ablation imaging showed complete ablation, also indicating an overestimation of pre-ablation area. Additionally, an irregular-shaped tumor volume may also decrease the accuracy of single-plane estimation. Software upgrades that overcome this limitation are currently under development.

Thermal ablation dynamics for chordomas have not been previously reported. To quantify the response, we correlated ablation area versus time by using the standard logarithm formula \( A = \log_a(t) \), where \( A \) represents ablation damage area, \( t \) represents time in seconds, and \( a \) is the thermal ablation constant. When the laser power is held constant (12 W), the area of ablation increases logarithmically with duration. Our data suggested a maximum ablation area of 156 mm\(^2\). Using our intraoperative data, a can be estimated to be 1.026. This allows us to calculate the predicted ablation area based on duration \( t \). This basic regression model fits the observed data with an \( R^2 \) of 99.2%. We hypothesize that different lesions have unique thermal ablation constants. In a chordoma ablated under 12 W of laser power with a thermal ablation constant of 1.026, the damage area estimate is:

\[
\text{Damage area} = \log_{1.026}(t)
\]

Even though more sophisticated regression techniques may generate a more refined model, we seek to prove our concept with this simplified version.

Several conclusions may be drawn on the inherent susceptibility of the tumor to thermal ablation. Variations in vascularity, water content, density and proximity to fluid collections or bone all affect a particular tissue's response to laser ablation. We have attempted to quantify the overall effect of these variables as the thermal ablation constant. Theoretically, as the constant approaches 1, the ablation area increases with shorter ablation times. Therefore, we hypothesize that tumor thermal ablation constants closer to 1 represent a higher susceptibility to thermal ablation and a more favorable response to LITT.

The thermal ablation constant also provides physicians with a tool to calculate laser dosimetry. Knowing a particular tumor's thermal ablation constant and area enables a clinician to estimate treatment time and determine the tumor's amenability to laser ablation. In a chordoma with an area of 200 mm\(^2\), our model predicts total ablation with a 12 W laser for approximately 170 s, which are reasonable operative conditions. However, in a 400 mm\(^2\) chordoma, our model predicts an ablation duration of over 7 h. Our group has shown other tumors of this size to be easily ablated in significantly less time, suggesting that the current model may be inaccurate for larger lesions. Additionally, due to the unique anatomy of this particular case (tumor surrounded by nasopharyngeal air and bone), the tumor may have been completely ablated when the damage area reached 156 mm\(^2\). If the tumor were surrounded by brain tissue, ablation may have continued, yielding a model that may better account for larger lesions.

Further studies to evaluate the utility of the thermal ablation constant are required. Each tumor will have some variability in its tissue composition and it is unlikely that even two chordomas would have exactly the same thermal ablation constant. As previously discussed, variations in the tissue composition of a tumor may change its response to thermal ablation. We therefore aim only to introduce the idea to the literature and prompt further investigations into the dynamic response of various tumors to LITT.

The long-term efficacy of MRI-guided LITT in chordoma treatment is yet to be established. The short-term results presented in this case are promising and demonstrated the susceptibility of chordomas to thermal ablation. Chordomas have high water content and low vascularity, features that make them ideal targets for thermal ablation. Our patient also benefited from having a rim of intact clivus, which may have shielded vital neural structures from unintended thermal damage. Our technique is minimally invasive with short
procedure duration and can be monitored with real-time temperature feedback. The possibility of thermal ablation as a primary treatment option is unknown at this time. Nonetheless, thermal ablation therapies show potential as an alternative or adjunctive treatment modality for chordomas.

Conclusion

MR-guided LITT is technically feasible for skull-base lesions permissible to endonasal approaches. Chordoma cells are highly sensitive and responsive to thermal energy. MR-guided LITT may be a useful adjunct in select clival chordomas. Longer term follow-up and larger series will be necessary to determine whether this technique can improve non-recurrence rates in clival chordomas.

References