Thermal injury to corticospinal tracts and postoperative motor deficits after laser interstitial thermal therapy

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OBJECTIVE Laser interstitial thermal therapy (LITT) has been increasingly used to treat deep-seated tumors. Despite its being minimally invasive, there is a risk of LITT damaging adjacent critical structures, including corticospinal tracts (CSTs). In this study, the authors investigated the predictive value of overlap between the hyperthermic field and CSTs in determining postoperative motor deficit (PMDs).

METHODS More than 140 patients underwent an LITT procedure in our institution between April 2011 and June 2015. Because of the tumor's proximity to critical structures, 80 of them underwent preoperative diffusion tensor imaging and were included in this study. Extent of the hyperthermic field was delineated by the software as thermal-damage-threshold (TDT) lines (yellow [43°C for 2 minutes], blue [43°C for 10 minutes], and white [43°C for 60 minutes]). The maximum volume and the surface area of overlaps between motor fibers and the TDT lines were calculated and compared with the PMDs.

RESULTS High-grade glioma (n = 46) was the most common indication for LITT. Postoperative motor deficits (partial or complete) were seen in 14 patients (11 with permanent and 3 with temporary PMDs). The median overlap volumes between CSTs with yellow, blue, and white TDT lines in patients with any PMD (temporary or permanent) were 1.15, 0.68, and 0.41 cm³, respectively. The overlap volumes and surface areas revealed significant differences in those with PMDs and those with no deficits (p = 0.0019 and 0.003, 0.012 and 0.0012, and 0.001 and 0.005 for the yellow, blue, and white TDT lines, respectively). The receiver operating characteristic was used to select the optimal cutoff point of the overlapped volumes and areas. Cutoff points for overlap volumes and areas based on optimal sensitivity (92%–100%) and specificity (80%–90%) were 0.103, 0.068, and 0.046 cm³ and 0.15, 0.07, and 0.11 mm² for the yellow, blue, and white TDT lines, respectively.

CONCLUSIONS Even a minimal overlap between the TDT lines and CSTs can cause a PMD after LITT. Precise planning and avoidance of critical structures and important white matter fibers should be considered when treating deep-seated tumors.

<http://thejns.org/doi/abs/10.3171/2016.7.FOCUS16216>

KEY WORDS laser; thermal therapy; thermal-damage-threshold lines; corticospinal; motor tracts; brain tumor

LASER interstitial thermal therapy (LITT) is a minimally invasive technique that involves stereotactic implantation of a laser probe and tissue ablation using thermal energy.^{11,13,21,22} The minimally invasive nature of LITT coupled with advances in MR thermography techniques has led to the exploration of this technique's use for various neurosurgical indications such as deep-seated glioma,^{8,9,20,22} brain metastasis,^{2,5,21} radiation necrosis,^{4,16,21} and epilepsy.^{7,23} LITT has shown promising results in the management of patients with difficult-to-

access brain tumors¹² and has emerged as a potential tool in the armamentarium of neurosurgeons. Despite being minimally invasive in nature, there is a risk of LITT damaging adjacent critical structures, such as corticospinal tracts (CSTs), in eloquent brain areas. Complications such as neurological deficits (hemiparesis, aphasia), systemic complications (deep vein thrombosis, hyponatremia), and hardware-related complications (displacement) have been reported after LITT when used for a variety of indications.^{7,12,17,22} Temporary and permanent neurological defi-

ABBREVIATIONS CST = corticospinal tract; DTI = diffusion tensor imaging; GBM = glioblastoma multiforme; LEM = lower extremity (motor); LITT = laser interstitial thermal therapy; MPRAGE = magnetization-prepared rapid-acquisition gradient echo; PMD = postoperative motor deficit; ROI = region of interest; TDT = thermal damage threshold; UEM = upper extremity (motor).

SUBMITTED May 25, 2016. **ACCEPTED** July 27, 2016.

INCLUDE WHEN CITING DOI: 10.3171/2016.7.FOCUS16216.

cits after LITT in the ranges of 0%–29.4% and 0%–10%, respectively, have been reported in various published case series.^{7,12,15,17,22}

Diffusion tensor imaging (DTI) is a newer imaging technique that has been used to delineate white matter tracts during resection of brain tumors. It can be integrated with stereotactic navigation systems for preoperative and intraoperative planning to prevent postoperative neurological morbidity in patients with intraaxial brain tumors.^{3,6,18,19,24} Various brain tumors, depending on their pathology, have been shown to cause disruption, infiltration, or displacement of the white matter tracts,²⁴ which can be elucidated preoperatively and thus assist in surgical planning. This technique has been shown to have an impact on the surgical procedure, in terms of either tailoring the corticotomy or defining resection margins, in up to 82% of patients.¹⁸ With the increasing use of LITT, there has been an emerging interest regarding the effects of thermal therapy on white matter fiber tracts. There has been a paucity of literature regarding the extent of thermal injury that CSTs can sustain before clinical manifestation of motor deficits. In this study, we investigated the predictive value of surface area and volume overlap between hyperthermic fields and CSTs in determining postoperative motor deficits (PMDs) after LITT in patients with brain tumors.

Methods

Clinical Data and Inclusion Criteria

This retrospective study was approved by the institutional review board at the Cleveland Clinic. More than 140 patients underwent an LITT procedure in this institution between April 2011 and June 2015. The procedure was explained to each patient, and valid consent was obtained. Of these 140 patients, 80 patients (81 procedures) who underwent preoperative DTI (because of the tumor's proximity to critical structures) and for whom thermal-damage-threshold (TDT) line data were available were included in this analysis. Two patients with postoperative intracerebral hemorrhage and motor deficit as a direct result of the hemorrhage were excluded from the analysis. Patient charts were reviewed for demographics, operative findings, imaging details, and follow-up data. The senior authors (A.M.M. and G.H.B.) performed all the procedures, thus maintaining homogeneity in terms of surgical techniques. Patient charts were reviewed retrospectively for PMDs, which were dichotomized as temporary or permanent. Motor deficits were recorded using the standard Medical Research Council grading system.¹⁰ Temporary deficit was defined as a new-onset motor deficit that appeared immediately after the LITT procedure and improved either before discharge or during follow-up, and permanent deficit was defined as a new-onset motor deficit that appeared after the LITT procedure and did not improve during follow-up. The median ($\pm$ SD) length of hospital stay in our study was 2.0 ± 3.7 days, and the median follow-up time was 7.0 ± 9.5 months.

Image Acquisition and Analysis

Standardized preoperative 3-T MRI (Siemens AG) was performed in each patient. An axial T1-weighted

magnetization-prepared rapid-acquisition gradient echo (MPRAGE) tumor protocol with a TR/TE of 11/4.68 msec, flip angle of 25°, voxel size of $1 \times 1 \times 1$ mm³, imaging matrix of 256×256 , and FOV of 256×256 mm² was performed. Also, a coronal T2-weighted space tumor protocol using a TR/TE of 3200/412 msec, flip angle of 25°, voxel size of $1 \times 1 \times 1$ mm³, imaging matrix of 256×256 , and FOV of 256×256 mm² was performed. The DTI tumor protocol was performed in 12 diffusion gradient directions using echo planar imaging with a TR/TE of 6700/95 msec, flip angle of 90°, voxel size of $1.95 \times 1.95 \times 2.5$ mm³, imaging matrix of 128×128 , FOV of 250×250 mm², and b value of 1000 sec/mm².

The extent of the hyperthermic field was delineated by M^ovision software as TDT lines. The yellow TDT line was defined for the equivalent of a temperature of 43°C for 2 minutes, the blue TDT line for 43°C for 10 minutes, and the white TDT line for 43°C for 60 minutes. Motor fiber tracts for the upper extremities (UEMs) and lower extremities (LEMs) were created using deterministic DTI by placing appropriate region-of-interest (ROI) seeds over the motor strip (UEMs and LEMs, separately) using anatomical MRI (MPRAGE). Preoperative MRI and TDT lines were imported to iPlan software (Brainlab AG) for volumetric analysis. The maximum volume of overlaps between motor fibers of the UEMs and LEMs and the TDT lines (white, blue, and yellow) were analyzed in 3 planes of axial, coronal, and sagittal imaging. Similarly, the maximum area of surface overlap between motor fibers of the UEMs and LEMs and the TDT lines were analyzed in all 3 planes in a slice with maximum overlap. Using the volume function in Brainlab and given that the thickness of the slices was 1 mm in a volumetric scan, the maximum area of overlap in millimeters squared was calculated. Volumes and areas of overlap between the TDT lines and CSTs were correlated with PMDs (Fig. 1). There is an inherent subjectivity in the generation of motor tracts using DTI; however, to maintain uniformity of ROI seed placement and generation of CSTs, the procedure was performed uniformly by the first author (M.S.) under guidance of the senior author (A.M.M.).

Surgical Technique

We used the NeuroBlate system (Monteris Medical) for laser ablation in each of our patients. The procedure was performed using intraoperative MRI (IMRIS) system after induction of general anesthesia. The patient was intubated in an induction room and brought to the IMRIS, and his or her head was positioned on the operating table using an MRI-compatible DORO head clamp (pro med instruments GmbH). After positioning the patient's head, scalp fiducials (typically 9–11) were applied at the desired locations. We then obtained MPRAGE with contrast and/or T2-weighted volume MRI, and the images were fused with preoperative MRI sequences for planning purposes. Image space and patient head space were registered in an iPlan Curve navigation system (Brainlab AG) to plan the trajectory. After marking the proposed entry site on the scalp, the corresponding area of skin was clipped, prepared, and draped in a usual manner. The VarioGuide system (Brainlab AG) was fixed to the head clamp, and the

FIG. 1. A: Overlap between TDT lines (yellow, blue, and white) and UEM CSTs. **B:** Extent of overlap between TDT lines and LEM CSTs. The red arrows point to the extent of overlap. Note that white TDT lines are represented in red in Brainlab for better visualization.

entry point was aligned after adjusting all 3 joints on the VarioGuide while keeping a distance of at least 3 fingers breadth between the scalp and the bottom of the VarioGuide. The skin was then incised (1–1.5 cm), and bone was drilled using a twist drill (outer diameter 4.5 mm). The anchoring bolt (outer diameter 4.5 mm) was placed using the VarioGuide along the stereotactic trajectory. After placement of the bolt, the VarioGuide was removed, and a pulsed diode laser probe (side firing/diffuse tip; Nd:YAG [neodymium-doped yttrium aluminum garnet] range 1046 nm with an output of 12 W)¹¹ was introduced into the bolt after measuring the length of the laser probe required and locking at the corresponding length. The laser probe was then connected to the robotic probe drive, and the MRI coil was placed over the bolt (in a sterile manner) at the desired location for scanning. The magnet was then brought into the operating room, and M^oVision software was used for planning and treatment at a workstation outside the operating room. This software integrates with the MRI machine and enables real-time monitoring of laser ablation using MR thermometry. CO₂ is typically used at the tip of the laser probe for cooling and to prevent tissue charring/vaporization.^{11,13} The TDT lines were generated using the software and monitored throughout the procedure. Once complete tumor coverage by the blue TDT lines (43°C for at least 10 minutes)^{11–13} was achieved, the procedure was considered complete and ablation was stopped. It is prudent to monitor the temperature in the surrounding critical structures throughout the procedure. After the ablation, the bolt was removed, the patient's skin was sutured, dressing was applied in a usual manner, and the patient was transferred to the step-down unit for clinical observation. Multiple trajectories were used for larger

(> 40–50 cm³) or periventricular lesions to achieve satisfactory tumor ablation.

Statistical Methods

We analyzed 80 patients who underwent an LITT procedure. R programming language and R studio were used for statistical analysis. The t-test was used to analyze volume and area differences between the groups. We used the receiver operating characteristic (ROC) curve to find the optimal threshold. We used the Fisher exact test to analyze the classified groups by using the appropriate threshold outlined in the ROC curve. A p value < 0.05 (2 tailed) was considered significant.

Results

Patient Demographics and Tumor Characteristics

Data on 80 patients were included in this analysis during the study period. The mean $\pm$ SD age of the patients was 52.46 ± 17.18 years, and the majority of the patients were male (n = 43 [53.8%]). High-grade glioma (n = 46 [57.5%]) was the most common diagnosis, followed by low-grade glioma (n = 16 [20%]), metastasis (n = 10 [12.5%]), radiation necrosis (n = 4 [5%]), meningioma (n = 3), and schwannoma (n = 1) (Table 1). PMDs were seen in 14 patients (17.5%) (11 with permanent and 3 with temporary PMD). Of these 14 patients, 6 had both permanent UEM and LEM weaknesses, and 1 patient had transient UEM and LEM weakness that resolved during the follow-up time of 4 months. Isolated permanent or temporary UEM weakness was noted in 5 and 2 patients, respectively, whereas none of the patients had isolated LEM pare-

TABLE 1. Patient demographics and tumor characteristics

Variable	Total (n = 80)	Permanent PMD (n = 11)	Temporary PMD (n = 3)	p Value
Sex (no. [%])				0.124
Female	37 (46.3)	6 (54.5)	3 (100)	
Male	43 (53.8)	5 (45.5)	0 (0)	
Age (mean SD) (yrs)	52.46 ± 17.18	51.45 ± 14.07	55.00 ± 14.79	0.836
No. of trajectories* (no. [%])				0.592
1	50 (61.7)	8 (72.7)	3 (100)	
2	22 (27.16)	2 (18.2)	0 (0)	
3	9 (11.11)	1 (9.1)	0 (0)	
Tumor type (no. [%])				0.832
High-grade glioma (WHO Grade III or IV)	46 (57.5)	9 (81.8)	0 (0)	
Low-grade glioma (WHO Grade I or II)	16 (20)	0 (0)	2 (66.7)	
Metastasis	10 (12.5)	1 (9.09)	1 (33.3)	
Radiation necrosis	4 (5)	1 (9.09)	0 (0)	
Meningioma or schwannoma	4 (5)	0 (0)	0 (0)	
Length of hospital stay (mean [median ± SD]) (days)	3.5 (2.0 ± 3.7)	4.36 (3.0 ± 3.2)	3.0 (3.0 ± 0.0)	0.698

* The total number of procedures was 81.

sis. Upper extremity monoplegia and partial LEM paresis with facial droop were noted in 1 patient (with left parietal operculum glioblastoma multiforme [GBM]) after LITT, which improved partially during the follow-up period. Dense hemiplegia after LITT was noted in 1 patient (with preoperative right hemiparesis) with left frontal GBM, which did not improve during subsequent follow-up. Preoperative motor deficits were seen in 21 (26.25%) patients, 8 (38.10%) of whom developed worsening PMDs resulting in permanent motor deficits after LITT.

Extent of Volume Overlaps Between TDT Lines and CSTs

Overall, the mean overlap volumes between UEM and LEM CSTs with the yellow, blue, and white lines were 0.373, 0.188, and 0.089 cm³ and 0.239, 0.126, and 0.067 cm³, respectively. The median overlap volumes between CSTs and the yellow, blue, and white TDT lines in patients with any PMD were 1.15, 0.68, and 0.41 cm³, respectively. Compared with patients without PMDs, overlap volumes were significantly different in those with PMDs ($p = 0.0019$, 0.003 and 0.012 for yellow, blue, and white TDT lines, respectively). The cutoff points for overlap volume based on optimal sensitivity (100%) and specificity (almost 90%) were 0.103, 0.068, and 0.046 cm³ for the yellow, blue, and white TDT lines, respectively.

Permanent PMDs were seen in 13.75% ($n = 11$) of the patients, and the largest median overlap volumes between CSTs and the yellow, blue, and white lines were 1.08, 0.69, and 0.46 cm³, respectively, in these patients. Cutoff overlap volumes for patients with permanent deficits were 0.084, 0.064, and 0.031 cm³ for the yellow, blue, and white lines, respectively. Similarly, overlap volumes between UEM and LEM CSTs and the TDT lines were significantly different between patients with any deficits and those without deficits ($p < 0.05$). Cutoff overlap volumes for patients with UEM and LEM deficits for the yellow, blue, and white lines were 0.088, 0.067, and 0.064 cm³ and

0.049, 0.043, and 0.044 cm³, respectively (Tables 2 and 3 and Fig. 2).

Extent of Surface Area Overlaps Between TDT Lines and CSTs

The mean largest overlap surface areas between CSTs and the yellow, blue, and white lines were 19.5, 11.8, and 7.0 mm², respectively, in all patients. Mean surface area overlap volumes between the TDT (yellow, blue, and white) lines and UEM and LEM CSTs were 17.8, 10.3, and 6.3 mm² and 13.3, 7.9, and 4.6 mm², respectively. The median overlap surface areas between CSTs and the yellow, blue, and white TDT lines in patients with any PMD were 59.5, 34, and 21.5 mm², respectively, which were significantly different than those of patients with no PMDs ($p = 0.0012$, 0.001 , and 0.005 for yellow, blue, and white TDT lines, respectively) (Table 4). Based on optimum sensitivity (93%–100%) and specificity (80%–87%), cutoff points for overlap surface areas in patients with PMDs were 0.15, 0.07, and 0.11 mm² for the yellow, blue, and white lines, respectively. Similarly, overlap surface areas between UEM and LEM CSTs and the TDT lines were 47.5, 29.0, 19.0 mm² and 41, 25.0, and 12.5 mm², respectively. These overlap areas were significantly different in patients with any deficits compared with those without deficits ($p < 0.05$). Cutoff overlap areas for patients with UEM or LEM deficits for the yellow, blue, and white lines were 0.07, 0.07, and 0.12 mm² (sensitivity 92%–100%; specificity 79%–89%) and 0.06, 0.11, and 0.09 mm² (sensitivity 85%–100%; specificity 65%–86%), respectively (Tables 4 and 5 and Fig. 3).

Discussion

Laser interstitial thermal therapy is a relatively new minimally invasive technique that has shown promising results in the management of a variety of neurosurgical

TABLE 2. Extent of volume overlap between TDT lines and CSTs in patients with permanent, temporary, or no deficits

Deficit	Yellow TDT Line	Blue TDT Line	White TDT Line
Patients w/ temporary or permanent deficits or no deficits			
Temporary or permanent deficit (median overlap vol [cm ³])	1.15	0.68	0.41
No deficit (median overlap vol [cm ³])	0	0	0
p value	0.0019*	0.003*	0.012*
Cutoff overlap vol (cm ³ [sensitivity, specificity (%)])	0.103 (100, 88)	0.068 (100, 88)	0.046 (100, 90)
Patients w/ permanent deficits or temporary or no deficits			
Permanent deficit (median overlap vol [cm ³])	1.08	0.69	0.46
Temporary or no deficit (median overlap vol [cm ³])	0	0	0
p value	0.007*	0.010*	0.016*
Cutoff overlap vol (cm ³ [sensitivity, specificity (%)])	0.084 (100, 84)	0.064 (100, 84)	0.031 (100, 87)

* Significant result.

conditions in the past few years.^{2,4,5,7–9,16,20–23} NeuroBlate was first cleared by the FDA in 2009 after a multicenter Phase I clinical study that assessed the safety and efficacy of this tool in patients with recurrent GBM. Since then, there has been an abundance of literature regarding the efficacy of this modality for various neurosurgical indications. Also, a multicenter study that was designed to evaluate the efficacy of LITT in patients with brain metastasis and failed stereotactic radiosurgery is currently ongoing (the Laser Ablation After Stereotactic Radiosurgery [LAASR] study, ClinicalTrials.gov identifier NCT01651078). With this emerging utility, an understanding of the effects of thermal energy on CSTs and the extent to which CSTs can tolerate thermal effects without causing postoperative neurological deficits is essential.

In our study, permanent and temporary PMDs were noted in 13.75% and 3.75% of patients, respectively. Leonardi and Lumenta⁹ reported transient and permanent neurological deterioration in 2 (8.3%) of their 24 patients (30 procedures), each after LITT for glioma. All 4 neurological deficits were noticed in patients with tumor in an eloquent area. Carpentier et al.¹ reported transient dysphasia in 1 (25%) of 4 patients after LITT for recurrent GBM and a 28.57% incidence of transient neurological deficit after LITT for metastasis.²

A Phase I study that investigated the safety, toxicity,

and efficacy of LITT in patients (n = 10) with recurrent GBM²² found transient neurological deficits in 20% of the patients and permanent neurological deficits in 10% of the patients. Another study found transient neurodeficits in 5 (29.4%) patients with no permanent neurological deficits after LITT for GBM, brain metastasis, or epilepsy.⁷

Mohammadi et al.¹² reported transient worsening of preoperative motor deficits in 5 (14.28%) patients and permanent worsening in 2 (5.7%) patients after LITT for difficult-to-access high-grade glioma. Contralateral transient hemiparesis with residual left-hand weakness was reported in 1 (6.67%) of 15 patients after LITT for post-radiosurgical recurrent brain metastasis or radiation necrosis.¹⁷ Recently, the authors of a retrospective case series reported the incidence of transient (n = 10 [9.8%]) and permanent (n = 4 [3.9%]) neurological deficits in 102 patients (133 procedures) after LITT for primary brain tumor (n = 50), recurrent metastasis/radiation necrosis (n = 37), pain (n = 5), or epilepsy (n = 10).¹⁵ In this study, the authors hypothesized postablation edema to be the cause of transient neurological deficits and thermal injury to the white matter tracts to be the etiology of permanent neurological deficits (Table 6).¹⁵

Based on these studies, it is prudent to be cognizant of the impact of the extent of overlap between TDT lines and CSTs and PMDs. The M°Vision software displays

TABLE 3. Extent of volume overlap between TDT lines and CSTs in patients with permanent, temporary, or no UEM or LEM deficits

Deficit	Yellow TDT Line	Blue TDT Line	White TDT Line
Patients w/ temporary or permanent or no UEM deficits			
Temporary or permanent deficit (median overlap vol [cm ³])	1.02	0.51	0.24
No deficit (median overlap vol [cm ³])	0	0	0
p value	0.002*	0.006*	0.02*
Cutoff overlap vol (cm ³ [sensitivity, specificity (%)])	0.088 (100, 88.1)	0.067 (100, 88)	0.064 (100, 91)
Patients w/ temporary or permanent or no LEM deficits			
Temporary or permanent deficit (median overlap vol [cm ³])	0.95	0.77	0.36
No deficit (median overlap vol [cm ³])	0	0	0
p value	0.05*	0.041*	0.04*
Cutoff overlap vol (cm ³ [sensitivity, specificity (%)])	0.049 (100, 60)	0.043 (71, 86)	0.044 (71, 85)

* Significant result.

FIG. 2. Correlation and cutoff points between extent of volume (cubic centimeters) overlap (TDT lines and CST fibers) and postoperative neurological deficits. Figure is available in color online only.

TDT lines as white (corresponding to exposure of tissue to 43°C for 60 minutes), blue (43°C for 10 minutes), or yellow (43°C for 2 minutes). Tumor tissues located within the white and blue line zones undergo coagulation necrosis and permanent thermal injury, respectively, whereas tissue located outside the yellow line zone remains viable with no permanent or severe thermal injury.¹³ Based on this model, Mohammadi et al.¹² reported improved median progression-free survival for patients with wider coverage

of the tumor by blue and yellow TDT lines. The median progression-free survival was reported to be 9.7 months in patients with favorable coverage (< 0.05 cm³ tumor volume missed by the yellow TDT lines and < 1.5 cm³ of tumor volume between the yellow and blue TDT lines) compared with 4.6 months in patients with unfavorable coverage (< 0.05 cm³ of tumor volume missed by the yellow TDT lines and < 1.5 cm³ of tumor volume between the yellow and blue TDT lines).¹² The results of this study clearly indicate

TABLE 4. Extent of surface area overlap between TDT lines and CSTs in patients with permanent, temporary, or no deficits

Deficit	Yellow TDT Line	Blue TDT Line	White TDT Line
Patients w/ temporary or permanent deficits or no deficits			
Temporary or permanent deficit (median overlap area [mm ²])	59.5	34	21.5
No deficit (median overlap area [mm ²])	0	0	0
p value	0.0012*	0.001*	0.005*
Cutoff overlap area (mm ² [sensitivity, specificity (%)])	0.15 (92.9, 85.1)	0.07 (100, 80.6)	0.11 (92.9, 86.6)
Patients w/ permanent deficits or temporary or no deficits			
Permanent deficit (median overlap area [mm ²])	54.0	36.0	22.0
Temporary deficit or no deficit (median overlap area [mm ²])	0	0	0
p value	0.003*	0.004*	0.013*
Cutoff overlap area (mm ² [sensitivity, specificity (%)])	0.12 (90.9, 84)	0.08 (100, 84.3)	0.05 (100, 74.3)

* Significant result.

TABLE 5. Extent of surface area overlap between TDT lines and CSTs in patients with permanent, temporary, or no UEM or LEM deficits

Deficit	Yellow TDT Line	Blue TDT Line	White TDT Line
Patients w/ temporary or permanent or no UEM deficits			
Temporary or permanent deficit (median overlap area [mm ²])	47.5	29	19
No deficit (median overlap area [mm ²])	0	0	0
p value	0.001*	0.002*	0.008*
Cutoff overlap area (mm ² [sensitivity, specificity (%)])	0.07 (100, 79)	0.07 (100, 82)	0.12 (92.9, 89.6)
Patients w/ temporary or permanent or no LEM deficits			
Temporary or permanent deficit (median overlap area [mm ²])	41	25	12.5
No deficit (median overlap area [mm ²])	0	0	0
p value	0.003*	0.002*	0.008*
Cutoff overlap area (mm ² [sensitivity, specificity (%)])	0.06 (100, 65.7)	0.11 (85.7, 86.6)	0.09 (85.7, 86.6)

* Significant result.

the significance of effective coverage of tumor volume by TDT lines and reiterate the fact that coagulation necrosis occurs in the areas closest to the laser probe tip.¹⁴

The results of our study show that the extent of overlap (volume and surface area) between the TDT lines and CSTs has implications on postoperative neurodeficits that

need to be considered to avoid postoperative morbidity. It is interesting to note that optimal cutoff points for surface area overlap had lower sensitivity (93%–100%) and specificity (80%–87%) than those for volume overlap (100% sensitivity and 90% specificity). Also, cutoff points for volume overlap in LEMs had lower sensitivity (71%–100%)

FIG. 3. Correlation and cutoff points between extent of surface area (square millimeters) overlap (TDT lines and CST fibers) and postoperative neurodeficits. Figure is available in color online only.

TABLE 6. Incidence of transient and permanent neurological complications after LITT for intracranial tumors

Authors & Year	Pathology (no. of patients)	Anatomical Location (no. of procedures)	Complications
Leonardi et al., 2002	Recurrent glioma (24 [30 procedures])	Eloquent region of brain (20)	2 patients w/ Grade 2 astrocytoma in precentral areas experienced worsening of rt-sided hemiparesis after LITT, which did not resolve during follow-up; 1 patient w/ Grade 2 central astrocytoma developed rt hand paresis; another patient w/ lt parietal Grade III astrocytoma noticed worsening of apraxia after LITT secondary to development of brain abscess, which resolved after drainage
Carpentier et al., 2011	Metastasis (7 [15 lesions])	NA	1 patient each had transient aphasia & cerebellar syndrome
Carpentier et al., 2012	Recurrent GBM (4)	Rt temporal (1), lt centrum semiovale & the lower part of the face MC (1), rt frontal (1), lt temporal (1)	1 patient (w/ rt temporal location) developed GTC seizure, & another patient (w/ lt centrum semiovale & the lower part of the face MC location) developed mild transient dysphasia w/ CSF leak
Sloan et al., 2013	Recurrent GBM (10)	F (3), T (2), P (2), temporoparietal (1), temporooccipital (1)	1 patient had transient dysphasia w/ upper-limb weakness; 1 patient had transient contralateral hemiparesis w/ homonymous hemianopia in an eloquent region & near eloquent regions; 1 patient developed severe hemiparesis immediately after LITT in rt frontal area (eloquent), which had improved partially w/ physiotherapy at 3-mo follow-up
Hawasli et al., 2013	Glioma (WHO Grade III or IV) (11); metastasis (5)	Glioma: F (2), P (2), thalamus (4), insula (1), CC (1), BG (1); metastasis: F (2), P (1), insula (1), frontoparietal (1)	3 patients had transient aphasia after LITT for metastasis (insula), GBM (thalamus), & epilepsy (insula); 2 patients had transient hemiparesis after LITT for GBM (parietal) & metastasis (frontal); no permanent deficits
Mohammadi et al., 2014 ¹²	High-grade glioma (WHO Grade III or IV) (35)	F (15), T (5), P (5), thalamus (7), insula (2), CC (1)	5 patients had temporary neurological deficits; 2 patients had permanent neurological deficits
Rao et al., 2014	RN and tumor recurrence after metastasis treatment (14 [15 lesions])	F (6), C (6), Cp (1), P (1), T (1)	1 patient had transient hemiparesis w/ residual lt-hand weakness
Patel et al., 2016	Primary brain tumor (50), recurrent metastasis/radiation necrosis (37), pain (5) and epilepsy (10) (102 total [133 procedures])	NA	10 patients had transient neurological deficits, 4 patients had permanent neurological deficits

BG = basal ganglia; C = cerebellar; CC = corpus callosum; Cp = cerebellar peduncle; F = frontal lobe; GTC = generalized tonic-clonic; MC = motor cortex; NA = not available; O = occipital lobe; P = parietal lobe; RN = radiation necrosis; T = temporal lobe.

and specificity (60%–85%) than those for volume overlap (100% sensitivity and 90% specificity) in the UEMs. This finding corroborates with surface area overlap also, with better sensitivity (92%–100%) and specificity (79%–90%) in the UEMs than in the LEMs (85%–100% sensitivity and 65%–87% specificity). This finding might be attributable to the fact that the greater the extent of overlap between TDT lines and CSTs, the greater the risk of postoperative neurological deficits secondary to cumulative effects of thermal injury (although even a small area of overlap between the TDT lines and CSTs should result in thermal injury to CSTs and postoperative neurodeficits). Nevertheless, the extent of both volume and surface area overlap between TDT lines and CSTs was shown to be significant in patients with PMDs and to be a predictive value in our study. Additional studies are required to better delineate improved sensitivity and specificity in UEM CST overlaps compared to those in LEM CST overlaps.

Limitations

A small sample size and limitations inherent to retro-

spective studies are drawbacks of our study. The heterogeneous patient population with different tumor types might have had an effect on the diffusion of thermal energy and, consequently, on PMDs. Fusion between TDT images and preoperative MRI might be a potential source of error and affect the extent of overlap and results of the analysis. However, our study is, to our knowledge, the first to demonstrate a correlation between the extent of overlap between the TDT lines and CSTs and PMDs. Our study also provides the cutoff limit for the overlap between each of the TDT lines and CSTs for avoiding postoperative deficits. However, larger prospective controlled studies are needed to validate our findings.

Conclusions

Permanent postoperative neurological deficits were noted in patients with larger overlap volumes and areas between CSTs and TDT (yellow, blue, and white) lines. Even a minimal overlap between the TDT lines and CSTs can cause PMDs after LITT.

The extent of overlap volumes had better sensitivity and specificity in predicting postoperative neurological deficits than surface area overlap volumes. The sensitivity of overlap volumes and areas for predicting PMDs was higher for UEM CSTs than for LEM CSTs. Therefore, during LITT for brain tumors, it is critical to have a conformal coverage of tumor volume with TDT lines while minimizing the extent of overlap with CSTs to avoid postoperative neurological deficits. Precise planning to avoid critical structures and important white matter fibers should be considered when treating deep-seated tumors.

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Disclosures

Drs. Barnett and Mohammadi are consultants for Monteris Medical.

Author Contributions

Conception and design: Mohammadi, Behbahani, Barnett. Acquisition of data: Sharma, Behbahani, Silva. Analysis and interpretation of data: Sharma, Habboub. Drafting the article: Sharma. Critically revising the article: Mohammadi, Sharma, Habboub, Silva, Barnett. Reviewed submitted version of manuscript: Mohammadi, Sharma, Silva, Barnett. Approved the final version of the manuscript on behalf of all authors: Mohammadi. Statistical analysis: Habboub. Administrative/technical/material support: Mohammadi, Barnett. Study supervision: Mohammadi, Barnett.

Supplemental Information

Videos

Video Abstract. <https://vimeo.com/179781058>.

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