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Staged Laser Interstitial Thermal Therapy (LITT) Treatments to Left Insular Low-Grade Glioma

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BACKGROUND AND IMPORTANCE: Low-grade insular gliomas remain challenging tumors for aggressive resection because of the numerous functional and vascular structures surrounding them. Because of the potential morbidities associated with open surgical resection, less invasive techniques may confer a more optimal balance between cytoreduction and surgical complications. For this reason, we evaluated the use of laser interstitial thermal therapy (LITT) for resection of a dominant hemisphere oligodendroglioma World Health Organization (WHO) grade II in a 68-yr-old patient by use of multiple staged surgeries for its resection.

CLINICAL PRESENTATION: Patient KK was a 68-yr-old female who was found to have a large, left-sided insular mass that was shown to be an oligodendroglioma WHO grade II, positive for codeletion 1p/19q and IDH1 mutant on biopsy. Over the course of 3 mo, KK underwent 2 stages of LITT, targeting different areas of the 5-cm tumor. The 60-d magnetic resonance imaging (MRI) demonstrated a reduction in size of the tumor from 5.2 × 3.3 × 2.4 cm to 3.6 × 1.9 × 1.4 cm. She returned for a second stage targeting the anterior portion of the tumor. KK did well postoperatively and went on to postsurgical chemoradiation. At the 2-yr follow-up, the lesion showed near resolution on MRI.

CONCLUSION: This case report demonstrates successful use of LITT for staged surgeries to treat a left hemisphere-dominant insular lesion. This establishes the use of LITT as a viable, minimally invasive option to treat tumors that are difficult to access or pose concerns for increased morbidity through an open surgery.

KEY WORDS: LITT, Laser, Insular tumor, Craniotomy, Minimally invasive, Oligodendroglioma

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Low-grade insular gliomas remain challenging tumors for aggressive resection because of the numerous functional and vascular structures surrounding them.¹ For this reason, the Berger-Sanai insular glioma classification system was designed to help classify tumor types that may benefit from more aggressive surgery, depending on their location and size.² More aggressive open surgical resection, however, may increase the risk for deficits in language, cognition, memory, affect, and sensation, such as olfaction/taste.¹⁻⁴ Because of the potential morbidities associated with open surgical resection, less invasive techniques

may confer a more optimal balance between cytoreduction and surgical complications. Specifically, laser interstitial thermal therapy (LITT) using the NeuroBlate system (Monteris Medical) provides minimally invasive access, thus sparing surrounding healthy tissue, while performing focused and precise ablation of the targeted pathology. The NeuroBlate system employs a 3-mm diameter, CO₂-cooled laser that can treat 1 to 2 cm of tissue surrounding the probe. This has been used successfully for the treatment of high-grade gliomas, metastatic lesions, and epilepsy in difficult-to-access areas of the brain.⁵⁻⁹ Typically, these lesions are treated in a single operation. Lesion volume with diameters of 3 cm or greater may require multiple trajectories to treat the entire target. These large volumes, however, are associated with higher risk of surgical complications (eg, symptomatic edema and seizures).⁹ Given the slow growing

ABBREVIATIONS: FLAIR, fluid-attenuated inversion recovery; LITT, laser interstitial thermal therapy; MRI, magnetic resonance imaging; RSN, resting-state network; WHO, World Health Organization

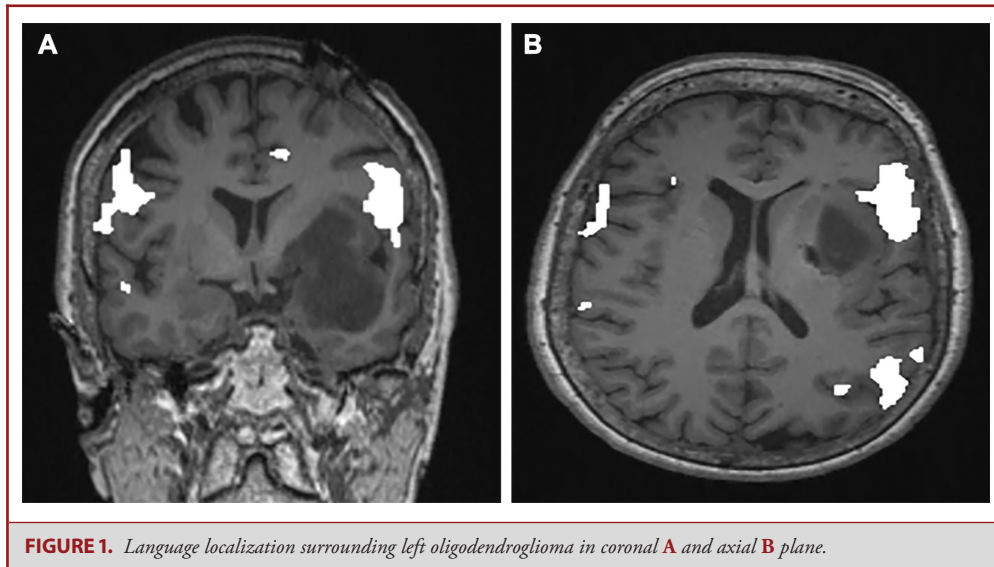


FIGURE 1. Language localization surrounding left oligodendroglioma in coronal **A** and axial **B** plane.

nature of low-grade gliomas and the minimally invasive nature of LITT, we have employed a novel staged approach to treat a select patient with large, low-grade insular glioma. Thus, the patient trades off a single, higher-risk surgery for multiple, lower-risk procedures. This case report, with consent from the patient, describes the use of multiple staged LITT therapies to treat a left-sided insular oligodendroglioma with no permanent clinical deficit and near resolution of the tumor on postoperative magnetic resonance imaging (MRI).

CLINICAL PRESENTATION

The patient is a 68-yr-old female (KK) who initially presented to her primary doctor with an episode of right hand twitching and eventually progressing to altered mental status. An MRI performed demonstrated left-sided insular mass, approximately 5 cm in maximal dimension, nestled within language regions demonstrated on functional MRI imaging (Figure 1). She subsequently underwent a biopsy at an outside hospital, and pathology was an oligodendroglioma World Health Organization grade II, positive for codeletion 1p/19q and IDH1 mutant. Although open surgery was discussed, she did not feel comfortable and opted for a more minimally invasive treatment. Therefore, she was offered staged laser ablation of the insular mass.

To identify the language network, an advanced brain MRI was obtained as described in Mitchell et al, 2013 and Leuthardt et al, 2018.¹⁰⁻¹² Briefly, the topography of resting-state networks (RSNs) in individual patients is defined using a multilayer perceptron that is trained to assign RSN membership (eg, motor, language, and vision) to each brain voxel on the basis of resting state functional MRI correlations.¹¹ This method is not specific for stimulation loci that produce speech arrest, but it is highly sensitive, identifying eloquent speech areas that should be avoided during surgical planning. Thus, if the tumor is far from the

“language” RSN map, the data show that it is extremely unlikely that awake stimulation mapping would have yielded a positive result that would alter the surgical plan.

Using StealthStation navigation (Medtronic, Minnesota), the first stage of the procedure targeted the posterior half of the tumor. Using intraoperative MRI, the location of the laser probe was verified prior to each staged treatment (Figure 2). Treatment of the tumor progressed until the thermal dosage thresholds maximally covered the area of interest, while avoiding nonpathologic and functional regions of the brain. Postoperatively, she tolerated the procedure well and was observed in the intensive care unit overnight. Having no deficits following her laser ablation, she was discharged to home on postoperative day 1.

KK followed up in clinic 1 wk after the ablative procedure. At that time, she had mild difficulty with word repetition. She returned for her 60-d MRI prior to her second stage procedure. At this time, the left insular mass was reduced in size, now $3.6 \times 1.9 \times 1.4$ cm compared to the preoperative size of $5.23 \times .3 \times 2.4$ cm (Figure 3A-3F). Clinically, she was back to her neurologic baseline. The amount of vasogenic edema was also reduced. Three months later, KK returned for the second stage of treatment. The second ablative procedure used a trajectory that encompassed the anterior portion of the insular glioma and its extension into the anterior temporal lobe, paying special attention to avoid the branches of the middle cerebral artery. Again, the procedure was tolerated well. She had mild expressive aphasia postoperatively, which eventually resolved after a 2-wk steroid taper. The patient’s fluid-attenuated inversion recovery (FLAIR) signal continued to reduce at the 60-d postprocedure MRI (Figure 3G-3I). She then went on to have concurrent chemoradiation with temozolomide at 75 mg/m^2 , followed by 6 cycles of high-dose adjuvant temozolomide. At 2 yr follow-up, she had near resolution of the initial FLAIR

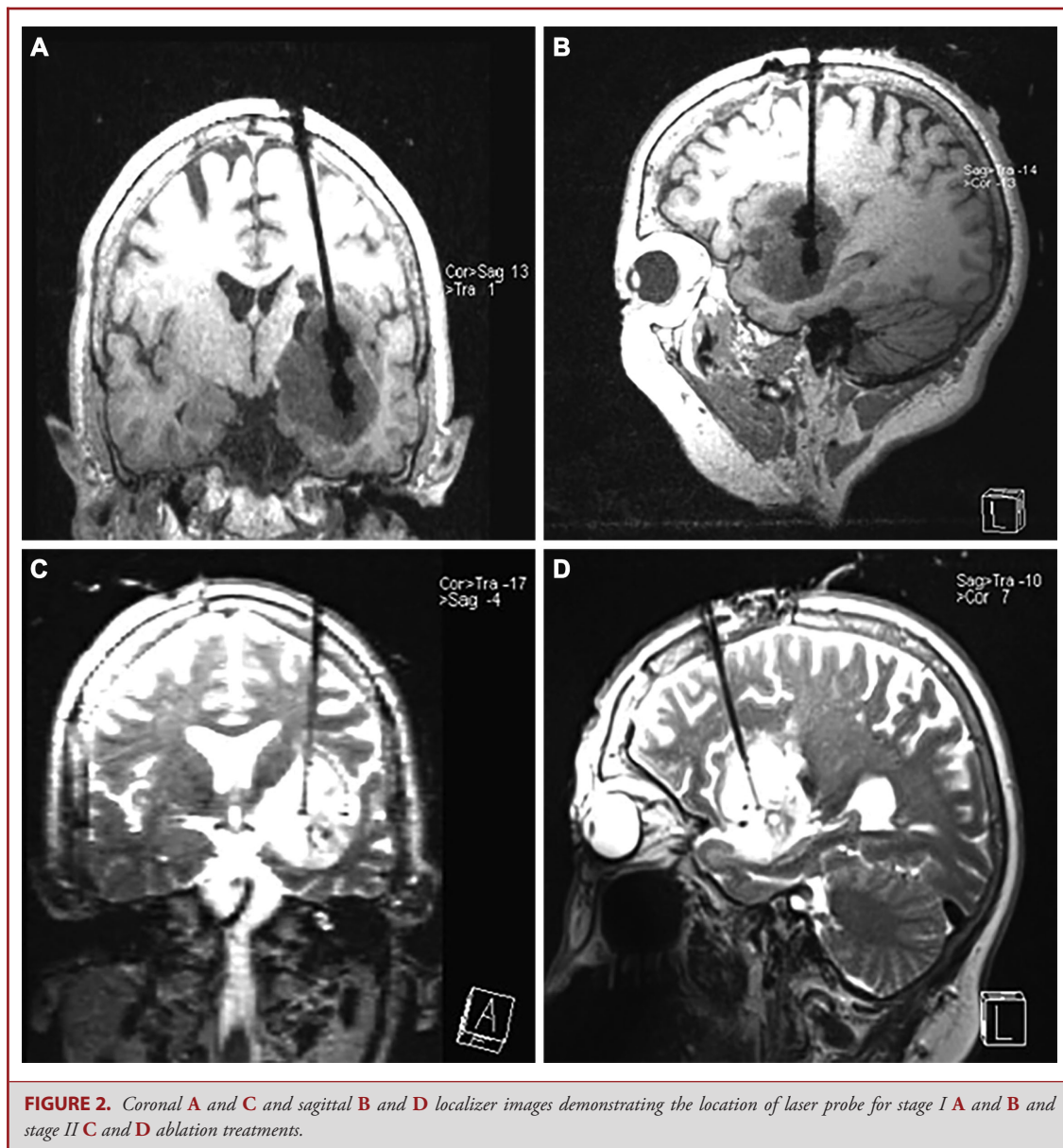


FIGURE 2. Coronal **A** and **C** and sagittal **B** and **D** localizer images demonstrating the location of laser probe for stage I **A** and **B** and stage II **C** and **D** ablation treatments.

signal, which neuroradiology believed to be post-treatment effects (Figure 3J-3L). To analyze the treatment volumes, tumor and treatment models were created using StealthStation software. The tumor prior to treatment had a volume of 40 cm^3 , and the initial treatment trajectory treated a volume of about 10 cm^3 (Figure 4A-4C). The volume of the tumor at the start of the second treatment was about 28 cm^3 (Figure 4D-4F). The second treatment trajectory had a larger treatment volume than the first treatment, treating about 20 cm^3 . At the 2-yr follow-up, the residual hyperintensity volume was around 5 cm^3 (Figure 4G-4I), which was stable over 3 MRIs spanning 18 mo since the initial follow-up.

DISCUSSION

This case represents the confluence of a new way of thinking about low-grade insular gliomas and about LITT. Typically, insular tumors are considered through the lens of open surgical resection.² LITT therapies have historically been performed as a single procedure for a given pathology.⁹ This case demonstrates a good clinical outcome can be achieved with a slow growing larger lesion, which may be less risky than a single, upfront open craniotomy or a single laser procedure (with multiple trajectories) treating a large volume. By performing multiple, staged, well-tolerated single trajectory LITT procedures with

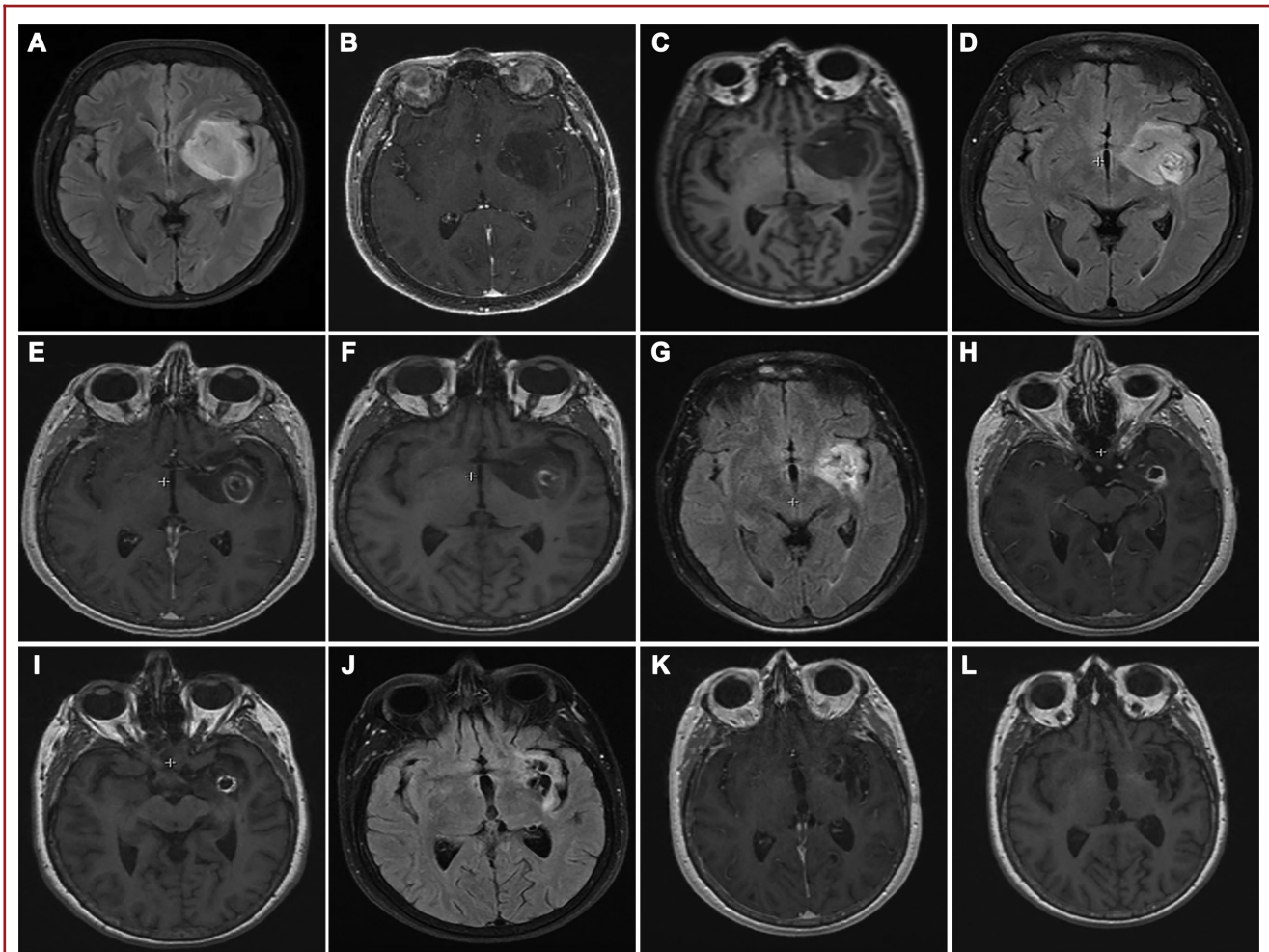


FIGURE 3. FLAIR, T1 with, and T1 without images demonstrating treatment of left insular oligodendroglioma. Lesion size and FLAIR signal noticeably reduce in size from preoperation A-C, 60 d after stage I ablation D-F, 60 d after stage II ablation G-I, and 2 yr after stage II ablation J-L.

more moderate volumes (<3 cm in diameter), the surgeon can take a modular approach that could be less morbid for the patients with comparable cytoreduction accomplished with a craniotomy.

Insular lesions, particularly in the dominant hemisphere, have increased complexity with surgical resection because of the functional anatomy in proximity to these lesions. By staging the procedures, the patient was allowed time between sessions to evaluate the treatment effect, as well as modifications to the plan and treatment aggressiveness. Using different trajectories, each staged surgery allowed for a new area to be targeted, as well as additional treatments to the already-treated areas, thus maximizing the cytoreduction. Moreover, gliomas necessarily are diffusely infiltrating and even with optimal resection, will most likely recur. Therefore, alternatives that provide successful cytoreduction with limited invasiveness and surgical footprint

may provide benefit for tumors when possibility of a need for retreatment is high.

It is important to note, however, although the described approach has numerous potential benefits in the treatment of insular low-grade gliomas, it will be important to further validate this surgical strategy in the form of larger clinical experience and outcome assessments. The use of advanced brain imaging identifying neural networks involved in speech has been reliably and successfully used at our institution, allowing for use of the minimally invasive approach in specific cases. However, depending on the location of the tumor, performing an awake craniotomy may be necessary, and this minimally invasive approach would not be a viable option if language mapping was essential for increasing the safety of the tumor resection. Therefore, LITT therapy should continue to be used in a case-by-case basis.

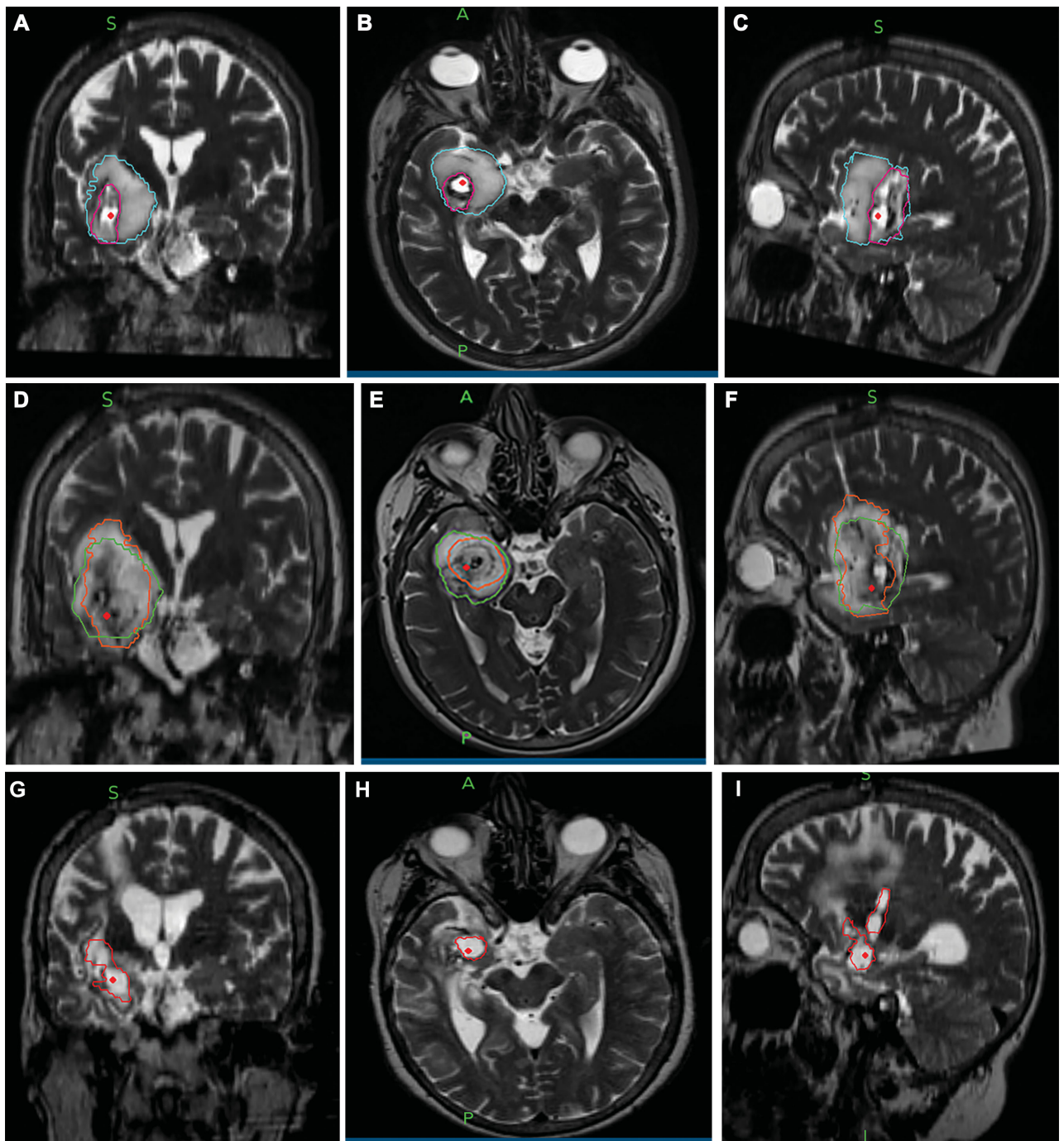


FIGURE 4. Volumetric analysis using StealthStation neuronavigation software. Coronal, axial, and sagittal images demonstrating the initial tumor volume (blue line; $\sim 40 \text{ cm}^3$) and the first staged treatment volume (pink line; $\sim 10 \text{ cm}^3$) **A-C**. Images **D-F** demonstrate the tumor volume at the start of the second treatment (green line; $\sim 28 \text{ cm}^3$) and the second stage treatment volume (orange line; $\sim 20 \text{ cm}^3$). The volume of the residual at the 2-yr follow-up was stable over 18 mo (red line; $\sim 5 \text{ cm}^3$) **G-I**.

CONCLUSION

This case report demonstrates the versatility of LITT therapy to treat a patient with left insular glioma with multiple staged treatments. The treatments were well tolerated, and side effects that were encountered resolved during the routine follow-up period. Stereotactic laser therapy can be considered as an alternative for insular tumors in appropriately selected patients.

Disclosures

Dr Leuthardt is a consultant for Monteris Medical. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENT

Laser ablation is a novel treatment modality being used more and more in neuro-oncology as well as epilepsy surgery. As a minimally invasive cytoreductive treatment, it has a big advantage over open craniotomy in the setting of recurrent and postradiated cases because of its minimal wound healing issues compared with large incisions. In addition, it has been used as initial treatment for a number of intracranial tumors, including high-grade glioma. However, in most of the cases, its usage is limited to smaller tumors. In the case of large tumors, because of increased edema and temporary worsening mass effect, its role is limited to combined cases with surgery.

This is a very well-written paper; it describes successful treatment of a large insular tumor by laser interstitial thermal therapy. In this case report, which is the very first one of its kind, staged laser ablation has been used to minimize increased mass effect associated with laser ablation in the early postoperative period. Especially in such a highly eloquent area, because open surgery has its own risks and limitations, using a minimally invasive procedure like laser ablation has a potential advantage in treatment planning. Several cases of successful laser ablation for smaller insular lesions had been reported before, and with this technique of staged ablation, size would not be a major issue for selecting patients.

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