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Technique, safety profile, and seizure outcomes after laser ablation for insular epilepsy: a multicenter cohort study

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OBJECTIVE The objective of this study was to assess the incidence of complications and seizure outcomes of laser interstitial thermal therapy (LITT) in the treatment of drug-resistant insular epilepsy, with a specific focus on complication rates after ablation of the posterior insula.

METHODS The authors retrospectively analyzed the diagnostic workup and outcomes of all patients treated with LITT for the treatment of insular epilepsy at three centers. The hypothesis of insular origin was based on a combination of semiology, MRI, and FDG-PET/CT and/or magnetoencephalography in MRI-negative cases. Twelve of 14 patients underwent stereoelectroencephalography (SEEG), in which 3 patients underwent radiofrequency thermocoagulation following SEEG. Additionally, 2 patients underwent a secondary LITT procedure.

RESULTS Following LITT, 9 patients (64.3%) achieved complete seizure freedom (International League Against Epilepsy [ILAE] class 1), 2 (14.3%) achieved seizure freedom but retained auras (ILAE class 2), and 3 (21.4%) saw no improvement in their epilepsy (ILAE class 5) at 6 months' follow-up. The patients who underwent a secondary LITT procedure achieved ILAE class 1 and 5, respectively. The overall transient complication rate was 18.8% for all 16 LITT cases and 21.4% for the 14 procedures that included ablation of the posterior insula. The permanent complication rate was 6.3% for all 16 LITT cases and 7.1% for 14 procedures that included ablation of the posterior insula.

CONCLUSIONS LITT is a safe and effective intervention for controlling insular epilepsy. Although the study is limited by its relatively short follow-up period, the seizure freedom rate observed in this cohort is comparable to that following open insular resection, with a low incidence of complications.

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KEYWORDS magnetic resonance–guided laser interstitial thermal therapy; MRgLITT; insular epilepsy; seizure outcome; surgical complication

Epilepsy is one of the most common diseases of the brain, with approximately 1% of the global population suffering from the disease.[1] Approximately 30% of these patients have drug-resistant epilepsy, characterized by persistent seizures despite an optimal antiseizure drug regimen.[2] Insular epilepsy is a rare form of epilepsy in which the origin of the epilepsy starts in the insula. Surgical intervention for insular epilepsy poses significant challenges due to its intricate anatomical location deep within the sylvian fissure, covered by the frontal, temporal, and parietal operculum and dense arterial and venous vasculature.[3,4] As a result of the deep location of the insula combined with the vast neural networks associated with the insula, diagnosing insular epilepsy is complex and often necessitates the use of invasive diagnostic studies such as stereoelectroencephalography (SEEG). Moreover, traditional resection of the insula is notorious for high rates of motor complications.[5] These motor complications can arise due to retraction injury following occlusion of the lenticulostriate arteries or the insular arteries, causing ischemic injury or direct damage to the pyramidal tract.[6] Notably, the posterior-superior region, where many long insular arteries traverse, plays a crucial role in supplying the corona radiata, thereby heightening the risks associ-

ABBREVIATIONS AED = antiepileptic drug; CRW = Cosman-Roberts-Wells; ILAE = International League Against Epilepsy; LITT = laser interstitial thermal therapy; MEG = magnetoencephalography; RFTC = radiofrequency thermocoagulation; SEEG = stereoelectroencephalography; UPMC = University of Pittsburgh Medical Center.

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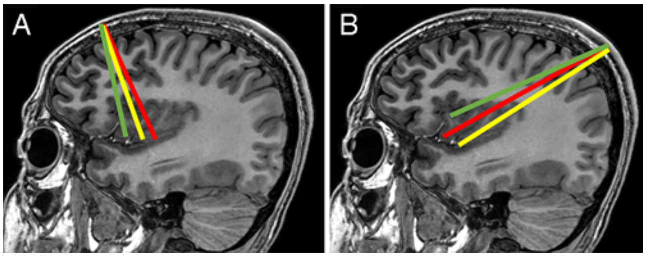

FIG. 1. Schematic view of insular LITT with a sagittal MRI view of the insula and trajectories to treat the anterior (**A**) and posterior (**B**) insula. The same entry point can be used for all three trajectories in the respective approaches. Figure is available in color online only.

ated with resections in this area.[7] Minimally invasive techniques, including laser interstitial thermal therapy (LITT) and radiofrequency thermocoagulation (RFTC), can also be used for the treatment of insular epilepsy. LITT is a minimally invasive procedure where a laser diode is inserted through a small hole in the cranium and near-infrared light from the laser is absorbed by the surrounding tissue, resulting in increased heat and a thermal ablation.[8] However, because LITT is a relatively new technique, surgical outcome data after LITT for insular epilepsy are scarce and data that specifically analyzed outcomes after LITT for posterior insular epilepsy are nonexistent. This study seeks to contribute to the existing body of knowledge by presenting new data on the outcomes of LITT in the treatment of insular epilepsy, with a specific focus on cases involving ablation of the posterior insula.

Methods

Study Population and Presurgical Evaluation

A retrospective review was conducted of all cases where LITT was used for the treatment of insular epilepsy at three academic hospitals: Sahlgrenska University Hospital (Sweden), Rigshospitalet (Denmark), and the University of Pittsburgh Medical Center (UPMC). Data were collected retrospectively under the IRB-approved protocols of each respective institution. All patients with at least 6 months of follow-up data were included. No exclusion criteria were applied. Energy usage data were unavailable for 8 cases (cases 5b and 6–12).

SEEG

SEEG to explore insular epilepsy was tailored individually for each patient. Electrode implantation typically included the insula with 2–3 oblique and 3–4 lateral trajectories, along with coverage of additional brain regions (e.g., frontal, opercular, temporal, parietal, mediotemporal, and frontoorbital), based on the multidisciplinary team's hypothesis regarding the location of the epileptogenic zone (Fig. 1).

LITT Surgery

Patient selection criteria for LITT varied between centers. At UPMC, only patients with a highly localized seizure onset, involving a maximum of two contacts on a single SEEG electrode, were considered candidates for LITT (cases 7–12). In contrast, Sahlgrenska University Hospital and Rigshospitalet included patients with more extensive epileptogenic zones, such as those involving multiple SEEG electrodes or more than 3 contacts on a single electrode.

Under general anesthesia, a laser catheter (3 or 10 mm; Visualase, Medtronic) was inserted via a 3.2-mm burr hole. The insertion trajectory was planned using pre- or intraoperative contrast-enhanced MRI to visualize the insula and adjacent cortical and subcortical vasculature, ensuring precise avoidance of critical structures. Trajectories were selected based on lesion location: parasagittal frontal for anterior insular targets, parietal for posterior insula targets, or lateral for insulo-opercular lesions.

Neuronavigation systems (StealthStation or Brainlab) were used for preoperative planning and intraoperative guidance of the laser fiber placement. The insertion process utilized one of the following robotic or stereotactic systems: Autoguide (Medtronic, n = 5), ClearPoint (n = 3), ROSA (n = 6), or Cosman-Roberts-Wells (CRW) head frame (n = 2).

Following laser catheter placement, MRI was performed to confirm accurate positioning. Ablation was initiated with laser power typically set between 4.5 and 6 W. Lesioning was monitored and guided in real time using thermography and damage prediction maps provided by the Visualase software. For larger or irregularly shaped lesions, catheter pullbacks were performed to extend the ablation volume, and multiple catheters were used as needed to achieve the desired lesion coverage. The LITT procedure is illustrated in Fig. 2.

Surgical Outcome Definitions

Seizure outcomes were assessed using the International League Against Epilepsy (ILAE) classification scale.[9] Complication outcomes were defined as transient if they were transient within 6 months and permanent if they were persistent for 6 months or longer, based on the classification system by Rydenhag and Silander,[10] with a modified timeframe following the more recent complication protocol by Bjellvi et al.[11] Energy usage was calculated by summing the watts used for each ablation multiplied by the time for each position of the catheter. Deviation in fiber placement was initially included as outcomes but later withdrawn due to data availability issues.

Statistical Analysis

The data were processed using Microsoft Excel and analyzed using the R statistical program (version 4.3.1, The R Project for Statistical Computing)[12] together with the *readxl* package (version 1.4.3)[13] and *tidyverse* package (version 2.0.0).[14] Descriptive statistics served to provide a summary of the patients' demographic and clinical characteristics. Seizure outcomes and the incidence of complications were calculated using proportions.

Results

Population Studied

The cohort included 14 patients who underwent 16 LITT procedures, consisting of 8 male and 6 female pa-

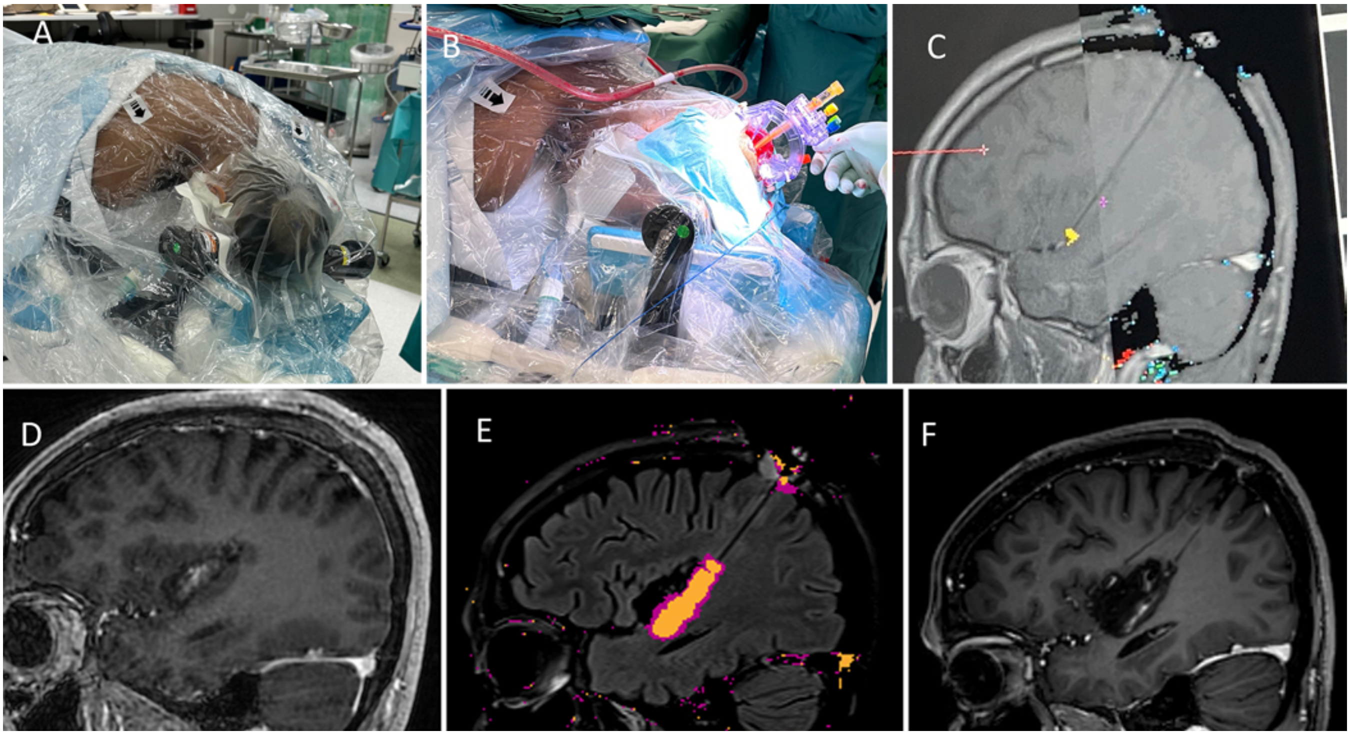

FIG. 2. Case 5. LITT procedure with posterior right insular target. **A:** Prone positioning to allow parietal access and accommodate the patient in the intraoperative MRI suite. **B:** ClearPoint frame placement. **C:** First lesion created during initial LITT, using a 3-mm Visualase catheter. Safety markers (48°C) were placed near the corticospinal tract and a branch of the middle cerebral artery. The patient experienced mild hand weakness for 2 weeks postoperatively. **D:** MRI 6 months after the first procedure. Seizures recurred after 4 months. **E:** Second LITT procedure with damage model as calculated by the Visualase system. *Yellow* indicates permanent damage and *purple* represents partially damaged tissue. **F:** MRI 6 months after the second LITT procedure. The patient is now seizure free without neurological deficits. Figure is available in color online only.

tients. Cases 1–6 were from Sahlgrenska University Hospital, cases 7–12 from UPMC, and cases 13 and 14 from Rigshospitalet. The average patient age at the time of surgery was 21.2 (range 1–43) years. The mean duration from diagnosis to surgery was 13.2 (range 1–37) years, and patients had tried an average of 4.6 (range 2–7) antiepileptic drugs (AEDs) prior to surgery. Detailed patient demographics are presented in Table 1.

Diagnostic Workup

The semiology in the insular epilepsy cohort included motor symptoms, sensory symptoms, visceral sensations, autonomic-related symptoms, and vocalization. Motor symptoms were the most common, affecting 57.1% of the cohort, followed by sensory symptoms in 42.9% of the cohort. Two patients experienced autonomic sensations, 1 patient experienced visceral symptoms, and 1 patient experienced vocalization at seizure onset. On MRI, 3 patients (18.8%) had an identifiable insular lesion. Magnetoencephalography (MEG) was used in 8 cases but did not indicate an insular epileptogenic zone in any of these cases, although data were missing from case 13. Detailed results from the diagnostic workup are presented in Table 2.

SEEG Procedure

SEEG was used in 12 patients, revealing insular activity in all 12. Specifically, seizure onset was detected in the posterior insula and/or anterior dorsal insula in 10 patients (83.3%) and in the anterior insula in 2 patients (16.7%). Case 14 experienced a subclinical hemorrhage as a complication of the SEEG procedure. Cases 3, 5, and 6 underwent a subsequent SEEG ablation/RFTC and initially achieved complete seizure freedom for 3 weeks, 6 weeks, and 18 months, respectively, after which they had a complete remission to their pre-RFTC seizure frequency. A detailed summary of the SEEG outcomes is provided in Table 3.

LITT Procedure

The LITT procedure targeted the posterior insula in 8 cases (50%), the anterior dorsal insula in 5 cases (31.3%), the anterior insula in 2 cases (12.5%), and the mid-insula in 1 case (6.3%). The mean ablation volume achieved was 2.9 (range 0.9– 8.2) cm^3. The mean energy usage was 5112 (range 1936–12,603) J. Detailed information on the LITT procedures and patient outcomes is presented in Table 4.

Seizure Freedom Rate

At 6 months following LITT, 9 patients (64.3%) achieved ILAE class 1, 2 patients (14.3%) achieved ILAE class 2, and 3 patients (21.4%) achieved ILAE class 5. No patients were ILAE class 3 or 4. Individual patient outcomes are presented in Table 4.

TABLE 1. Summary of demographic and clinical data in 14 patients who underwent LITT for insular epilepsy

Case No.	Age (yrs), Sex	Age at Seizure Onset (yrs)	Seizure Frequency	No. of AEDs Tested	Prior Surgery
1	8, M	4	50/day	5	
2a	2, F	0	10–30/day	6	
2b	2, F	0	10–30/day	6	LITT (case 2a)
3	30, F	16	1–3/day	3	
4	1, M	0	15/day	7	
5a	20, M	4	2–3/wk	4	
5b	20, M	4	2–3/wk	4	LITT (case 5a)
6	43, F	6	5–10/day	2	
7	32, M	10	10/day	5	
8	34, M	23	30/day	4	
9	41, F	25	5/day	6	
10	23, F	11	15/day	3	
11	18, M	15	5/day	7	
12	35, F	10	10/day	6	
13	9, M	0	1/day	3	
14	21, M	8	2/wk	3	

Complications

Three transient complications were reported: transient mild paresis of the left hand in case 5a, transient hemiparesis in case 11, and transient mild right-sided hemiparesis in case 13 (Table 4). The overall transient complication rate was 18.8% for all 16 LITT cases and 21.4% for the 14 procedures that included partial or complete ablation of the posterior insula. One patient (case 14) experienced a permanent complication, presenting as mild paresthesia of the right leg, corresponding to a permanent complication rate of 6.3% for all 16 LITT cases and 7.1% for the 14 procedures that included partial or complete ablation of the posterior insula.

Discussion

Following LITT of the insula, 11 (78.6%) of 14 patients became seizure free (ILAE class 1 or 2). Two patients continued to experience auras, while 3 (21.4%) of 14 patients saw no improvement in their epilepsy (Table 4). In comparison, previous studies on LITT for insular epilepsy had a mean seizure freedom rate of 52%,[15–18] while the seizure freedom rates after open resection were 64.4% and 67% as reported by Kerezoudis et al.[5] and Obaid et al.,[19] respectively. Although our cohort had a higher seizure freedom rate compared to previous LITT studies or the open resection meta-analyses, this difference could be due to our limited follow-up of only 6 months.

TABLE 2. Results from noninvasive diagnostic studies

Case No.	Semiology	MRI	FDG-PET/CT	MEG
1	Motor	Normal	Positive	NA
2	Motor	Dysplasia of lt posterior insula & parietal operculum	NA	NA
3	Motor, epigastric sensation	Normal	Positive	NA
4	Motor	Dysplasia of rt frontal insula & frontal operculum	NA	NA
5	Motor, pain in shoulder region	Normal	Positive	NA
6	Choking sensation, laryngeal contraction, pain	Dysplasia of lt middle short gyrus	NA	NA
7	Facial movement	Normal	Normal	Temporal
8	Sensations in hand	Normal	Normal	Temporal
9	Autonomic	Normal	Normal	Perisylvian
10	Autonomic	Normal	Normal	Perisylvian
11	Throat sensation	Normal	Normal	Frontal
12	Motor	Normal	Normal	Frontal
13	Motor, sensory hand & vocalization	Asymmetry in temporal lobes, including lt-sided arachnoid cyst & small encephaloceles	Positive	Data missing
14	Sensory rt side	Normal	Normal	Normal

NA = not applicable.

TABLE 3. Summary of SEEG

Case No.	SEEG Seizure Onset Region	SEEG-Related Complications	SEEG Ablation/RFTC
1	Anterior insula	None	NA
2a, 2b	NA	NA	NA
3	Anterior dorsal insula	None	RFTC w/ seizure freedom for 2–3 wks
4	NA	NA	NA
5a, 5b	Posterior insula	None	RFTC w/ seizure freedom for 6 wks
6	Mid-insula	None	RFTC w/ seizure freedom for 18 mos
7	Posterior insula	None	NA
8	Posterior insula	None	NA
9	Anterior dorsal insula	None	NA
10	Anterior dorsal insula	None	NA
11	Posterior insula	None	NA
12	Anterior insula	None	NA
13	Anterior dorsal insula	None	NA
14	Posterior insula	Subclinical hemorrhage	NA

Ten of the 14 patients had normal MRI, and all 10 underwent preoperative SEEG to map the epileptogenic onset. An isolated insular onset was identified in all 10 patients, and the involved electrodes were targeted in the LITT procedure. As noted in the *Methods*, patient selection criteria varied across centers, with UPMC favoring LITT for highly localized seizure onsets while other centers included cases with more extensive epileptogenic zones. All patients from UPMC (cases 7–12) achieved an ILAE class 1 or 2 outcome. In these SEEG-guided cases, the ablation volume was planned to encompass the entire seizure onset zone, using postimplantation SEEG reconstructions to ensure coverage of all active contacts. For the 2 patients who did not undergo SEEG, both had suspected dysplasias in the insulo-opercular region clearly seen on initial MRI at 6 or 8 months of age (Fig. 3). SEEG was not considered necessary due to the MRI findings and was also deemed technically difficult and high-risk given the skull bone thickness of only 1–2 mm. In these cases, the target was the lesion visible on early MRI. However, these lesions disappeared on later imaging, and MRI fusion was complicated by skull growth, making targeting more challenging. One patient (case 4) achieved seizure freedom for 8 months before relapse and underwent open resection at

TABLE 4. Summary of laser ablation and outcomes

Case No.	LITT Target (side)	LITT Technique	Ablation Vol (cm^3)	Energy Usage (J)	ILAE Outcome Class	FU (mos)	Complications
1	Anterior insula (lt)	Autoguide	2.0	3833	1	36	
2a	Posterior insula (lt)	Autoguide	0.9	1936	5	6	
2b	Posterior insula (lt)	Autoguide	2.3	3655	5	6	
3	Anterior dorsal insula (lt)	Autoguide	2.5	2639	5	7	
4	Anterior dorsal insula (rt)	Autoguide	2.6	2840	1	9	
5a	Posterior insula (rt)	ClearPoint frame	8.2	4572	5	6	Transient lt hand mild paresis
5b	Posterior insula (rt)	ClearPoint frame	6.0	Data missing	1	6	
6	Mid-insula (lt)	ClearPoint frame	3.0	Data missing	1	6	
7	Posterior insula (lt)	ROSA robot	2.0	Data missing	1	6	
8	Posterior insula (lt)	ROSA robot	2.5	Data missing	1	6	
9	Anterior dorsal insula (lt)	ROSA robot	2.5	Data missing	2	6	
10	Anterior dorsal insula (rt)	ROSA robot	2.0	Data missing	1	6	
11	Posterior insula (rt)	ROSA robot	2.0	Data missing	2	6	Transient hemiparesis
12	Anterior insula (lt)	ROSA robot	2.5	Data missing	1	6	
13	Anterior dorsal insula, upper part of insula/capsula externa (lt)	CRW frame	2.9	12,603	5	24	Transient mild rt-sided hemiparesis
14	Posterior insula (lt)	CRW frame	1.9	8822	1	24	Permanent rt leg mild paresthesia

FU = follow-up.

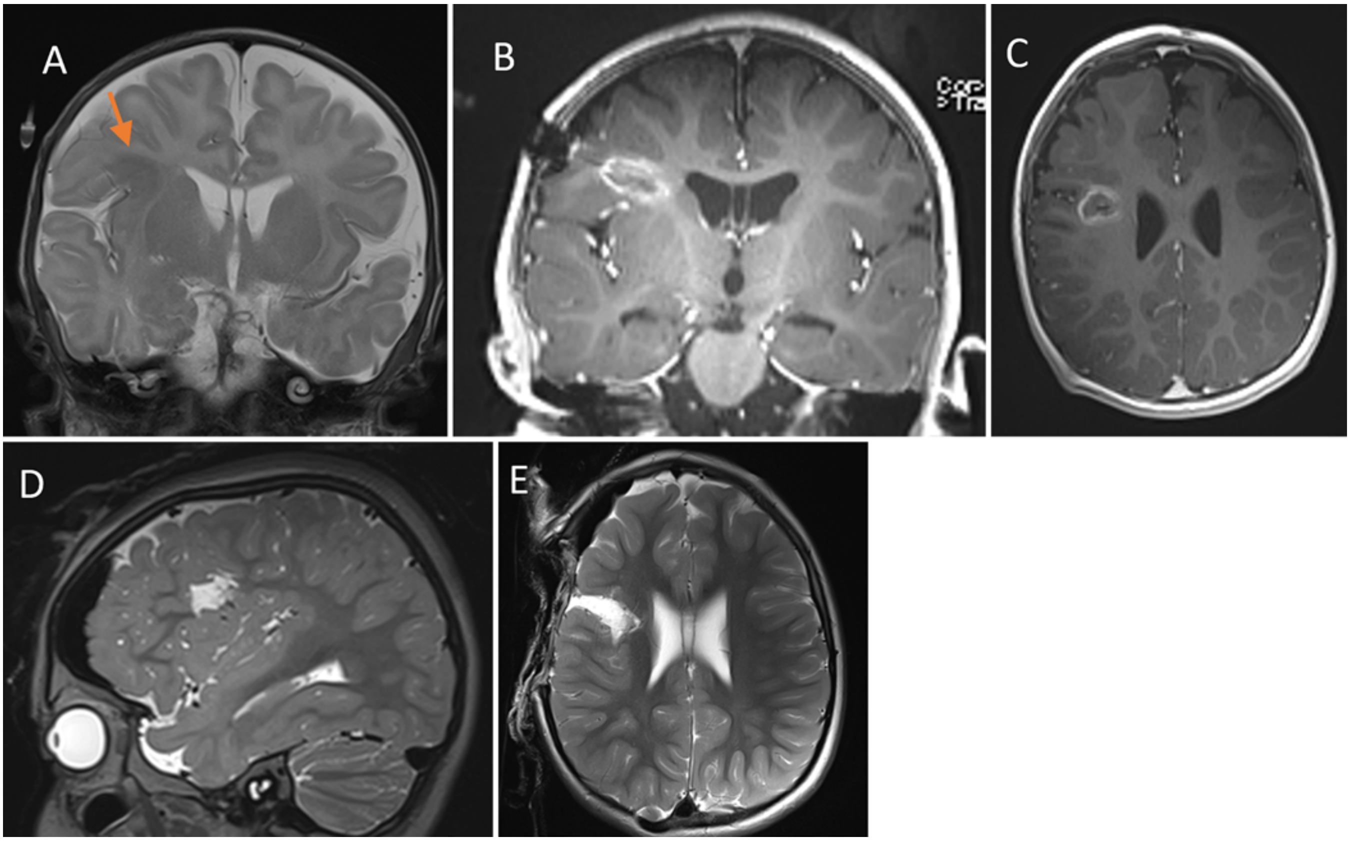

FIG. 3. Case 4. **A:** Coronal MRI at 8 months of age showing presumed dysplasia in the anterior insula (*arrow*); this finding disappeared on later imaging. **B and C:** Intraoperative MRI during LITT at 20 months of age, using a 10-mm Visualase catheter inserted via a lateral trajectory. Seizures recurred gradually after 8 months. **D and E:** Intraoperative MRI during resection at age 4 years. The patient experienced a postoperative hemiparesis, which resolved after 3 months, and is currently seizure free. Figure is available in color online only.

age 4 years. The other patient (case 2) had no improvement after two LITT procedures and has a planned resection. The disappointing effect of LITT in these insular dysplasias likely reflects that the seizure onset zone was larger than the MRI-visible lesions. Open resection, with or without preceding SEEG, might have been a more effective surgical option, although not without risks, particularly in these very young children.

Overall, these findings suggests that the best candidates for insular LITT are patients with a well-localized intrainsular seizure onset confirmed by SEEG. In cases with a broader epileptogenic zone or a lesion extending into the operculum, LITT remains a minimally invasive option, but open surgery may offer a better likelihood of seizure freedom.

Technical Considerations in Young Children

In young children, skull bone thickness must be considered. The Visulase skull bolt typically requires a minimum 3-mm bone thickness. At Sahlgrenska University Hospital, the ClearPoint frame is used for all LITT procedures involving deep, small targets, including the insula, and has been successfully applied in a 16-month-old child with 2-mm skull thickness, demonstrating excellent stability and precision. These patients were immobilized in the intraoperative MRI suite using an IMRIS HFD100 head fixation device, with pediatric head pins and a maximum pin pressure of 20 lbs/in^2. Another consideration is the increased fragility of brain tissue in this age group. Lower safety temperature thresholds may therefore be warranted. In some cases, the temperature safety marker was reduced from 48°C to 46°C. However, such adjustments must carefully balance the need to maximize lesion coverage while minimizing collateral injury to healthy tissue.

Complications

Because the objective of this study was partly to assess the complication rate of posterior insular ablation, we included insular target cases in this category, as ablation of the anterior dorsal insula, upper part of the insula/capsula externa, or mid-insula inevitably involves ablation of the posterior insula. The incidence of transient reported complications after LITT of the insula was 18.8% (n = 3), and 6.3% (n = 1) for permanent complications. For the posterior insular ablations, the transient and permanent complication rate was 21.4% and 7.1%, respectively. Notably, 75% of the reported complications involved some form of paresis. For case 13, the hemiparesis was attributed to direct thermal damage to adjacent white matter. This injury mechanism diverges from open resection, where hemiparesis is believed to be predominantly caused by end-artery damage to the long insular arteries supplying the corona radiata.[6,7]

Previous studies on LITT for insular epilepsy reported a transient complication rate of 36% with no reports of permanent complications.[15–18] In contrast, two meta-analyses on open resection by Kerezoudis et al.[5] and Obaid et al.[19] reported transient complication rates of 33.9% and 34%, and permanent rates of 9.8% and 8.0%, respectively. Neither the previous LITT studies nor the open insular resection meta-analyses used the exact same cutoff duration for transient versus permanent complication types that we used or did not provide a definition. Because no other study has presented cases for posterior insular ablations, there is no comparison we can make. Given the predominance of ablations including the posterior insula in this study (14 of 16 cases), a direct comparison to nonposterior ablation is very limited and thus not concluded.

The average insular ablation volume in our study was 2.9 cm^3, which is lower than the volumes reported by Gireesh et al.[16] (13.2 cm^3) and Alexander et al.[18] (3.2 cm^3) using LITT for insular epilepsy. This discrepancy could be due to differences in LITT technique, patient selection, or methods of measuring postoperative ablation volumes. For total energy usage, our cohort used an average of 5112 J per LITT, while the study of Alexander et al.[18] reported an average of 3859 J per LITT. They also presented a trend between ablation size and energy usage ($p = 0.06$). Notably, despite this trend and our higher average energy usage (5112 J vs 3859 J), the ablation volumes between the studies were comparable (2.86 vs 3.2 cm^3). The different ratios of energy usage and ablation volume between our study and that of Alexander et al. could reflect variations in technique, where a longer ablation time with lower heat could lead to higher total energy usage without necessarily achieving larger ablation volumes, and vice versa. Successful LITT treatment of insular epilepsy must treat the epileptogenic zone or lesion completely, making lesion size and accurate identification of the epileptogenic zone critical. Larger ablation volumes, potentially achieved using two or three catheters, might improve seizure control, but the number of patients in this study was too small to make any conclusions regarding this factor.

Limitations of the Study

This study has several limitations, including its cohort size, even though it is one of the largest cohorts to date and is notably the only study with a posterior insular laser ablation subgroup. Another limitation is the retrospective nature of the cohort study, which carries a risk of missing data. There were incomplete data on energy usage for half the patients in this cohort, which may impact the reliability of certain findings. It is also important to note that this study used a relatively short patient follow-up duration of only 6 months related to the seizure freedom outcome.

Conclusions

This study demonstrated that LITT for insular epilepsy can effectively control seizures, matching the efficacy of open insular resection, albeit with a shorter follow-up period. The transient complication rate was 18.8% overall and 21.4% for posterior insula ablations, while the permanent complication rate was 6.3% overall and 7.1% for posterior insula ablations. This study enriches the existing data on LITT for insular epilepsy and establishes a foundation for future research, particularly on posterior insular treatments, where limited prior data restricted comprehensive evaluations of open resection.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Nilsson, Gonzalez-Martinez, Rasmussen. Acquisition of data: all authors. Analysis and interpretation of data: Nilsson, Ekman, Gonzalez-Martinez. Drafting the article: Nilsson, Ekman. Critically revising the article: all authors. Reviewed submitted version of manuscript: Nilsson, Ekman, Haahr Nielsen. Approved the final version of the manuscript on behalf of all authors: Nilsson. Statistical analysis: Ekman. Study supervision: Nilsson, Gonzalez-Martinez.

Supplemental Information

Previous Presentations

The results from Sahlgrenska University Hospital (cases 1–5) were part of a presentation on surgical outcomes after laser ablation at the euLITT conference in Copenhagen, Denmark, May 16–17, 2024.

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