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BRIEF COMMUNICATION

Disrupting the epileptogenic network with stereoelectroencephalography-guided radiofrequency thermocoagulation

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Abstract

Stereoelectroencephalography-guided radiofrequency thermocoagulation (SEEG-guided RF-TC) is a treatment option for focal drug-resistant epilepsy. In previous studies, this technique has shown seizure reduction by ≥50% in 50% of patients at 1 year. However, the relationship between the location of the ablation within the epileptogenic network and clinical outcomes remains poorly understood. Seizure outcomes were analyzed for patients who underwent SEEG-guided RF-TC and across subgroups depending on the location of the ablation within the epileptogenic network, defined as SEEG sites involved in seizure generation and spread. Eighteen patients who had SEEG-guided RF-TC were included. SEEG-guided seizure-onset zone ablation (SEEG-guided SOZA) was performed in 12 patients, and SEEG-guided partial seizure-onset zone ablation (SEEG-guided P-SOZA) in 6 patients. The early spread was ablated in three SEEG-guided SOZA patients. Five patients had ablation of a lesion. The seizure freedom rate in the cohort ranged between 22% and 50%, and the responder rate between 67% and 85%. SEEG-guided SOZA demonstrated superior results for both outcomes compared to SEEG-guided P-SOZA at 6 months (seizure freedom $p = .294$, responder rate $p = .014$). Adding the early spread ablation to SEEG-guided SOZA did not increase seizure freedom rates but exhibited comparable effectiveness regarding responder rates, indicating a potential network disruption.

KEYWORDS

drug-resistant epilepsy, radiofrequency thermocoagulation, stereoelectroencephalography

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1 | INTRODUCTION

Radiofrequency thermocoagulation (RF-TC) is a minimally invasive procedure used for the treatment of focal drug-resistant epilepsy (DRE). This technique involves applying RF energy to produce a targeted lesion in the areas associated with seizure generation. RF-TC can be coupled with stereoelectroencephalography (SEEG) evaluation using depth electrodes that are already implanted, which we refer to as SEEG-guided RF-TC. In previous studies, SEEG-guided RF-TC has shown a reduction of seizures by more than 50% in at least 50% of patients at 1 year, with a low risk for complications.[1–3]

The underlying mechanism that supports the effectiveness of SEEG-guided RF-TC remains poorly understood. Some studies have highlighted the relevance of local tissue destruction in the seizure-onset zone (SOZ),[4,5] and others have focused on the epileptogenic network.[6–8] However, the relationship between the location of the ablation within the epileptogenic network and clinical outcomes has not been carefully explored.

The primary goal of this study is to assess the seizure freedom and responder rate after SEEG-guided RF-TC in our cohort of patients. The secondary objective is to analyze outcomes depending on the location of the ablation within the epileptogenic network. This study aims to provide valuable information on whether achieving optimal clinical outcomes is more closely associated with an extensive ablation of the epileptogenic focus or the disconnection of multiple nodes within the network.

2 | METHODS

Adult patients with DRE who underwent SEEG-guided RF-TC at the epilepsy program at Western University (London, Ontario, Canada) from November 2020 to July 2023 were included. All patients underwent comprehensive pre-surgical evaluation, with video-EEG monitoring, brain magnetic resonance imaging (MRI), neuropsychological assessment, 18-fluorodeoxyglucose positron emission tomography (FDG-PET), and single photon emission computed tomography (SPECT), as required. The SEEG investigation and implantation strategy were determined during the multidisciplinary epilepsy surgery conference.

The epileptogenic network was defined as all SEEG sites involved in seizure generation and propagation, including epileptogenic lesions. We categorized the ablated contacts based on their involvement in the seizure into two distinct categories: (1) SOZ and (2) early spread. The SOZ was the region with the SEEG contacts showing the first evident SEEG changes. The early spread was the distinct anatomic-functional region reached by seizure propagation within 3 s.[9] The epileptogenic lesion was identified as any structural abnormality considered to be the underlying cause of the seizures.

RF-TC was performed using an RF lesion generator (Diros OWL URF-3AP RF Lesion Generator, Diros Technology, Inc., Markham, Canada). Lesions were made by delivering a monopolar or bipolar current (see Table S1).

SEEG-guided seizure-onset zone ablation (SEEG-guided SOZA) was defined as the ablation performed in all contacts involved in the SOZ as identified on SEEG. In contrast, SEEG-guided partial seizure-onset zone ablation (SEEG-guided P-SOZA) corresponded to the ablation that did not encompass all SOZ contacts. SEEG-guided P-SOZA was performed selectively based on clinical judgment as the initial step before a surgical resection (e.g., temporal plus insula epilepsy), as a palliative procedure when encountered with a sizable SOZ, when there was overlap with eloquent cortex, or when not amenable to RF-TC due to proximity to blood vessels. The seizure outcomes included seizure freedom and responder rate. Seizure freedom refers to the absence of any seizure type at follow-up. Responder rate was defined as the percentage of patients with ≥50% reduction of the seizure frequency for at least one seizure type at follow-up.

We used Fisher's exact test to compare categorical variables. The statistical significance was set to $p < .05$. The analysis was performed using IBM SPSS v22.0 (Chicago, IL). The institutional research ethics board approved this project (R-19-603).

3 | RESULTS

3.1 | General characteristics

Forty-four patients underwent SEEG, and 18 had RF-TC performed. The median age at implantation was 35 years (interquartile range [IQR] 25.5), and 55.6% were female ($n = 10$). Eight patients (44.4%) had SEEG-guided RF-TC only, six patients (33.3%) underwent resective surgery after SEEG-guided RF-TC, and four patients (22.2%) had SEEG-guided RF-TC following a recurrence of seizures after resective surgery. The most frequent location of the SOZ was the insula in 50% ($n = 9$), either as temporal plus 27.8% ($n = 5$) or alone 22.2% ($n = 4$). The region of the ablation was in the insula in 38.9% ($n = 7$) of the patients and involved more than one lobe in 33.3% ($n = 6$). The mean number of contacts ablated was 9.8 (standard deviation [SD] ± 6.6). SEEG-guided SOZA was performed in 66.7% ($n = 12$) of patients, and SEEG-guided P-SOZA in 33.3% ($n = 6$). Ablation of the early spread was performed in 16.7% ($n = 3$) of the SEEG-guided SOZA patients. No

patients underwent SEEG-guided P-SOZA plus an early spread ablation. Five patients (27.8%) had ablation of a lesion. No ablation was performed for late propagation or another independent seizure focus. The number of patients who had follow-up appointments to assess outcomes after SEEG-guided RF-TC at 1, 3, 6 and 12 months were 18, 16, 13, and 9, respectively. No complications occurred. Table S1 shows additional information regarding each patient's RF-TC procedure, post-ablation recording, and MRI segmentation.

3.2 | Cohort seizure freedom rates and across subgroups

Seizure freedom at 1-month post-SEEG-guided RF-TC was seen in 50% ($n = 9/18$) of the patients, at 3 months in 38% ($n = 6/16$), at 6 months in 23% ($n = 3/13$), and at 12 months in 22% ($n = 2/9$). The two patients who achieved seizure freedom at 1 year had SEEG-guided SOZA of a lesion (one with a tuber and one with an old stroke).

At 3 months, 37% (3/8) of the SEEG-guided SOZA patients and 67% (2/3) of SEEG-guided SOZA plus early spread ablation patients were seizure-free. At 6 months, 43% (3/7) of the patients who underwent a SEEG-guided SOZA alone were seizure-free, whereas no patient achieved seizure freedom when the early spread ablation was added to the SEEG-guided SOZA. Twenty percent (1/5) of the patients who underwent an SEEG-guided P-SOZA achieved seizure freedom at 3 months. No patients were seizure-free at 6 months when an SEEG-guided P-SOZA was performed. There was no difference between SEEG-guided SOZA compared to SEEG-guided P-SOZA regarding seizure freedom at three (SOZA $n = 5/11$) (P-SOZA $n = 1/5$) and 6 months (SOZA $n = 3/9$) (P-SOZA $n = 0/4$), ($p = .346$ and $p = .294$, respectively). At 3 months, more patients achieved seizure freedom following a combination of SEEG-guided SOZA plus early spread ablation compared to SEEG-guided SOZA alone. However, the trend observed at 6 and 12 months indicated no additional benefit from including the early spread ablation; for more results, see Table 1. See a case example in Figure 1.

3.3 | Cohort responder rate and across subgroups

The responder rate at 1-, 3-, 6-, and 12-months post-SEEG-guided RF-TC was 67% ($n = 12/18$), 69% (11/16), 85% (10/13), and 78% (7/9), respectively. Regarding specific seizure types, all responders exhibited improvements in all pre-ablation seizures, except for three individuals who experienced a reduction in more severe seizures, namely focal to bilateral tonic–clonic and focal with impaired awareness, but continued with focal aware seizures.

At 3 months, 87% ($n = 7/8$) of the patients who underwent SEEG-guided SOZA alone and all (3/3) who underwent SEEG-guided SOZA plus an early spread ablation were responders. At 6 months, all the patients who underwent SEEG-guided SOZA either with an early spread ablation ($n = 2/2$) or in isolation ($n = 7/7$) were responders. One of the six patients (16%) who underwent SEEG-guided P-SOZA was a responder at 3 months. There were no responders at 6 months when SEEG-guided P-SOZA was performed. There was a statistically significant difference between SEEG-guided SOZA and SEEG-guided P-SOZA regarding responder rate at 3 months (SOZA $n = 10/11$) (P-SOZA $n = 1/5$) and 6 months (SOZA $n = 9/9$) (P-SOZA $n = 1/4$), ($p = .005$ and $p = .014$, respectively). A higher percentage of patients were responders after adding the early spread to the SEEG-guided SOZA compared to SEEG-guided SOZA alone at 3 months ($p = .72$). At 6 months, there was no difference in adding

TABLE 1 Seizure freedom and responder rate at 1, 3, 6, and 12 months after SEEG-guided RF-TC, depending on the extent of ablation.

	SEEG-guided SOZA		SEEG-guided P-SOZA	
Seizure freedom	**Early spread**	**No early spread**	**No early spread**	**Total seizure-free patients**
1 month	67% (2/3)	67% (6/9)	16% (1/6)	50% (9/18)
3 months	67% (2/3)	37% (3/8)	20% (1/5)	38% (6/16)
6 months	0% (0/2)	43% (3/7)	0% (0/4)	23% (3/13)
12 months	0% (0/2)	40% (2/5)	0% (0/2)	22% (2/9)

	SEEG-guided SOZA		SEEG-guided P-SOZA	
Responder rate	**Early spread**	**No early spread**	**No early spread**	**Total of responders**
1 month	100% (3/3)	89% (8/9)	16% (1/6)	67% (12/18)
3 months	100% (3/3)	87% (7/8)	20% (1/5)	69% (11/16)
6 months	100% (2/2)	100% (7/7)	25% (1/4)	85% (10/13)
12 months	100% (2/2)	100% (5/5)	0% (0/2)	78% (7/9)

Note: Ablation was performed on all contacts involved in the SOZ guided by SEEG. SEEG-guided P-SOZA: Ablation did not encompass all SOZ contacts guided by SEEG.

Abbreviations: SEEG-guided SOZA, SEEG-guided seizure-onset zone ablation; SEEG-guided P-SOZA, SEEG-guided partial seizure-onset zone ablation; SOZA, seizure-onset zone; P-SOZA, partial seizure-onset zone; SEEG-guided, Stereoelectroencephalography-guided; SEEG-guided RF-TC, stereoelectroencephalography-guided radiofrequency thermocoagulation.

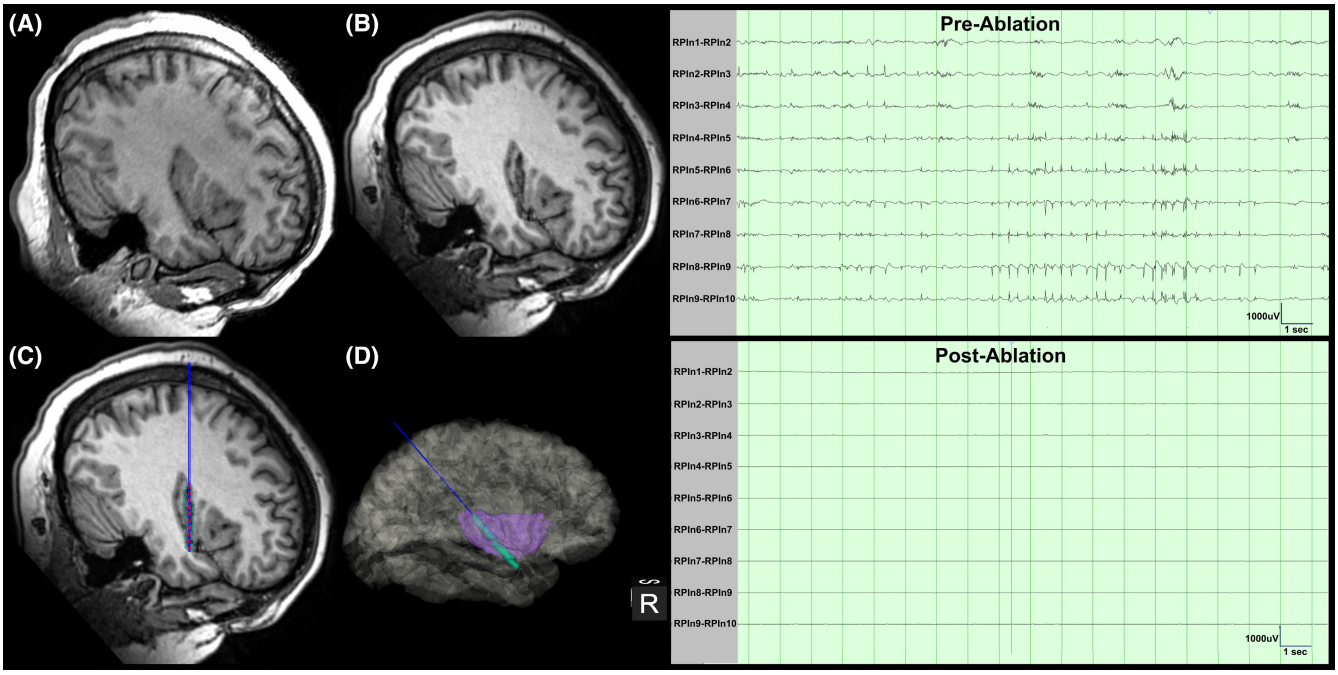

FIGURE 1 A case example of a patient who underwent an SEEG-guided SOZA over the right posterior insula (RPIn) electrode contacts 1 to 10. Images A, B, C. Sagittal T1-MRI images. (A) Pre-ablation. (B) Six months post-ablation. (C) Representation of the ablation (green), the electrode (blue), and the contacts (red). Image D. Three-dimensional representation of the brain, including the segmentation of the insula (purple), segmentation of the volume of ablation (green), and electrode (blue).[11] SEEG epoch. Pre-ablation: persistent interictal spikes over RPIn 9–10 > 1–8. Post-ablation: Flattening of the signals over RPIn 1–10, absence of spikes. The patient is currently 10 months seizure-free after SEEG-guided RF-TC. SEEG-guided SOZA: stereoelectroencephalography-guided seizure-onset zone ablation; RPIn: Right posterior insula; T1-MRI: Magnetic Resonance Image; SEEG-guided RF-TC: stereoelectroencephalography guided radiofrequency thermocoagulation.

the early spread to the SEEG-guided SOZA. For more results, see Table 1.

4 | DISCUSSION

The seizure freedom rates were 50% or less, which is concordant with what has been reported previously. The two seizure-free patients at 12 months had a well-defined SOZ and a lesion.[2] Previous studies have shown that the subgroup of patients with lesions—particularly nodular heterotopias, hypothalamic hamartomas, or small focal cortical dysplasia—have higher rates of seizure freedom.[3] Despite the ongoing debate on the treatment potential of SEEG-guided RF-TC without resective surgery, it remains a valuable tool for predictive purposes. This is attributed primarily to the observed longer seizure-free periods post-SEEG guided RF-TC, leading to improved outcomes after a resective surgery.[10]

Most patients within our cohort exhibited positive responses to treatment at 1, 3, 6, and 12 months, with responder rates ranging between 67% and 78%. Notably, our patient population achieved a higher responder rate than reported previously in other cohorts, where rates typically range between 23% and 58%. This discrepancy may be attributed, in part, to the smaller size of our sample and the inclusive definition of treatment response, encompassing any seizure type.

For both outcomes, SEEG-guided SOZA demonstrated superior results compared to SEEG-guided P-SOZA. At the 1- and 3-month marks, adding the early spread to the SEEG-guided SOZA showed improved outcomes compared to SEEG-guided SOZA alone, but these results were not significant. Of interest, at the 6- and 12-month follow-ups, the addition of the early spread did not increase seizure freedom rates but exhibited comparable effectiveness in terms of responder rates.[9] Our findings highlight that the ablation of the SOZ is the most influential predictor of outcome. Although the tissue implicated in early spread likely contributes to the epileptogenic network, our preliminary results suggest that its ablation may contribute to the reduction of clinical seizures, possibly interfering with the symptomatogenic zone. Nevertheless, it does not inherently possess seizure-generating potential, and its ablation does not lead to seizure freedom. Additional considerations that account for individual differences encompass the duration since seizure onset (secondary epileptogenicity), etiology, and other lesions not discernible in MRI (independent seizure focus).

Most patients underwent ablation in the insula. This aligns with a growing trend toward less-invasive procedures in this area, which carries inherent risks with conventional open surgical approaches. However, most of these patients did not achieve seizure freedom, likely due to the prevalence of temporal plus insula epilepsy, where a two-step approach with SEEG-guided RF-TC followed by resective surgery may be preferred.

The main limitations of our study include the small sample size, the retrospective nature, pending 1-year follow-up appointments, and the inherent sampling bias of the SEEG. We acknowledge that the sampling bias provides, at best, an approximation of the SOZ, potentially contributing to suboptimal outcomes in some patients after SEEG-guided RF-TC. The definition of early spread also presents a challenge, as it lacks a well-established criterion.[9]

5 | CONCLUSION

A complete ablation of the contacts involved in the SOZ was associated with higher rates of seizure freedom and responder rate. Ablating the early spread improved the responder rate but not the seizure freedom rate, indicating a potential network disruption.

AUTHOR CONTRIBUTIONS

Hellen Kreinter, Poul H. Espino, and Sonia Mejía: Study Design, data recollection, data analysis and project draft. Khalid Alorabi and Greydon Gilmore: Volume segmentation, data recollection, data analysis, and project draft and revision. Jonathan C. Lau, Jorge G. Burneo, David A. Steven, Giovanni Pellegrino, Keith MacDougall, Michelle-Lee Jones, David Diosy, and Mirsattari SM: Data analysis, project draft, critical review, and final approval. Ana Suller-Marti: Study design, data analysis, project draft, critical review, and final approval.

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CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose for this paper. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ETHICS STATEMENT

Our institution's institutional research ethics board approved this project (R-19-603).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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