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ORIGINAL COMMUNICATION

SEEG-guided radiofrequency coagulation (SEEG-guided RF-TC) versus anterior temporal lobectomy (ATL) in temporal lobe epilepsy

Alexis Moles[1,2,3] · Marc Guénot[1,4,5] · Sylvain Rheims[4,6,7] · Julien Berthiller[8] · Hélène Catenoix[6] · Alexandra Montavont[9] · Karine Ostrowsky-Coste[9] · Sebastien Boulogne[4,6] · Jean Isnard[6] · Pierre Bourdillon[1,4,10,11]

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Abstract

Background Stereoelectroencephalography-guided radiofrequency thermocoagulation (SEEG-guided RF-TC) is a super-selective procedure. Hippocampus has a limited volume and is widely accessible to SEEG so that SEEG-guided RF-TC could be an alternative to the anterior temporal lobectomy (ATL) in case of temporal lobe epilepsy (TLE) syndrome.

Objective To compare seizure-free rate at 1-year follow-up between patients undergoing SEEG-guided RF-TC and patients undergoing ATL in TLE over a 15-year period.

Methods All patients had a drug-resistant epilepsy and underwent SEEG after non-conclusive phase I investigations suspecting a TLE. Two groups were selected according to the procedure which the patients underwent (ATL or SEEG-guided RF-TC); TLE had to be confirmed by SEEG in the two groups. The primary outcome was seizure freedom at 1 year. The secondary outcome was response (at least 50% reduction of seizure frequency) at 1 year. In case of persistent seizures after SEEG-guided RF-TC, ATL was performed.

Results A total of 21 patients underwent SEEG-guided RF-TC and 49 ATL. At 12 months, none of the patients of the SEEG-guide RF-TC group was seizure free, while 37 (75.5%) in the ATL group were so ($p < 0.001$). Ten patients (47.6%) were responders after 12 months of follow-up after SEEG-guided RF-TC; all patients in the ATL group who were seizure free were responders.

Conclusion SEEG-guided RF-TC is not as effective as ATL in TLE. As no memory impairment following SEEG-guided RF-TC was found, patients with dominant mesial involvement for whom hippocampectomy is not an option could benefit from the technique.

Keywords Epilepsy surgery · Hippocampo-amygdalectomy · Mesio-temporal · Drug resistant · Stereotactic lesioning

✉ Alexis Moles
pierre.bourdillon@neurochirurgie.fr

1 Department of Neurosurgery, Hospices Civils de Lyon, Neurology and Neurosurgery Hospital Pierre Wertheimer, 59, Bd Pinel, 69677 Bron, France

2 Department of Neurosurgery, Nantes University Hospital, Nantes, France

3 University of Nantes, Nantes, France

4 University of Lyon, Université Claude Bernard Lyon 1, Lyon, France

5 NEUROPAIN Team, Lyon Neuroscience Research Center, INSERM U1028, CNRS, Université Claude Bernard Lyon 1, 5292 Lyon, France

6 Department of Functional Neurology and Epileptology, Neurology and Neurosurgery Hospital Pierre Wertheimer, Hospices Civils de Lyon, Lyon, France

7 TIGER, Neuroscience Research Center of Lyon, INSERM U1028, CNRS, Université Claude Bernard Lyon 1, 5292 Lyon, France

8 Hospices Civils de Lyon, Pôle Information Médicale Evaluation Recherche, Lyon, France

9 Department of Sleep, Epilepsy and Pediatric Clinical Neurophysiology, Hospices Civils de Lyon, Lyon, France

10 Sorbonne Université, Paris, France

11 Brain and Spine Institute, INSERM U1127, CNRS 7225, Paris, France

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Introduction

Temporal lobe epilepsy (TLE) syndrome is a frequent and well-circumscribed cause of focal epilepsy, characterized by typical clinical, radiological, and electrophysiological features. This syndrome is known to become readily drug resistant, and therefore many patients may be candidates for epilepsy surgery which aims, in this particular case, at removing at least the mesial part of the temporal lobe, in addition to a more or less extended part of the temporal pole and of T5 (parahippocampal) gyrus. Such a surgical procedure, which consists in performing an amygdalo-hippocampal resection, is known to provide 58–83% chance of seizure freedom [1–3].

From the 1970s to the early 1990s, radiofrequency thermocoagulation (RF-TC) had been developed as a possible alternative to resective surgery for the treatment of TLE but was later abandoned due to poor results [4–7]. The rather disappointing feature of these results can be explained by the limited size of the hippocampal lesion, which was obtained by means of one or two dedicated stereotactic approaches using classical monopolar stereotactic lesioning probes. Therefore, despite some other attempts to generate more extensive hippocampal lesions by means of stereotactic radiosurgery, or, more recently, by means of laser interstitial thermal therapy (LITT), surgical resection remains the gold standard for TLE syndrome.

In 2004, the new approach of SEEG-guided Radiofrequency Thermocoagulation (SEEG-guided RF-TC, also called "thermo-SEEG") was proposed as a treatment of some drug-resistant epilepsies [8]. This technique takes advantage of the implanted SEEG electrodes to perform multiple stereotactic lesions that are spatially placed on the basis of the findings provided by the SEEG recordings. This technique offers multiple advantages: (i) there is no additional bleeding risk when compared to a conventional stereotactic procedure as the same electrode is used for both SEEG and RF-TC (all bleedings reported in the literature were related to removal of SEEG electrodes, and these were not those used for RF-TC [9]), (ii) it allows a very accurate targeting of the seizure-onset zone, previously delineated by intracranial recordings, (iii) multiple lesions can be performed, instead of the single or double lesions usually performed in a conventional stereotacic lesioning procedure, and (iv) a functional mapping, through direct electrical stimulation on SEEG electrodes, is done prior to any lesion being made, thus allowing to anticipate the possible adverse effects in detail [10]. Recent literature confirmed the value of SEEG-guided RF-TC when the ictal onset zone is limited in size or when it is located in highly functional areas so that resective surgery is not feasible [11, 12].

Hippocampus has a limited volume, is widely accessible to SEEG; and multiple stereotactic lesioning appears as a super-selective lesional procedure, which could be particularly interesting when functions of the involved hippocampus are not impaired. In this context, multiple SEEG-guided RF-TC could be an alternative to surgical resection in case of TLE syndrome. The aim of this study was, therefore, to compare the effectiveness of SEEG-guided RF-TC to that of anterior temporal lobectomy (ATL) for TLE in our institution. The 15-year period chosen for this investigation includes patients with typical TLE who were treated in both before and after invasive investigation became no longer necessary [13], but which is still performed when an extra-mesial onset zone is suspected on phase 1 investigation [14, 15].

Materials and methods

Patient selection

For this retrospective single-centre study, patients were identified from a prospective institutional database collecting information about all epilepsy patients (declared to the national data protection agency, CNIL). All patients between 2001 and 2016 who presented with disabling focal drug-resistant epilepsy for which the data obtained from non-invasive presurgical investigation (consisting of long-term scalp video-EEG monitoring, high-resolution MRI, metabolic imaging ^{18}F-fluorodeoxyglucose-positron emission tomography—FDG-PET, and neuropsychological testing) were compatible with a TLE.

For identified patients, data including demographics, seizure frequency, and complications of the SEEG-guided RF-TC procedure or the ATL (initial state, and at 2 and 12 months of follow-up) were retrospectively analyzed.

Patients were included when the data obtained from these non-invasive investigations were not sufficiently congruent to allow direct resective surgery without performing invasive recordings with SEEG, and SEEG confirmed the diagnosis of TLE syndrome. SEEG-guided RF-TC was a newly developed procedure that was not available in all cases. Consequently, in the population of selected patients, some of them underwent the standard ATL procedure while the others underwent SEEG-guided RF-TC. Among the latter, ATL was performed in case of non-favorable outcome. No criteria differentiate the two groups in terms of selection.

End-points

The primary endpoint was seizure freedom (Engel's Class Ia) at 1 year for both SEEG-guided RF-TC and ATL groups. Patients who required an ATL following SEEG-guided

RF-TC before the first year post SEEG-guided RF-TC were classified as failure. The secondary endpoint was responder rate at 1 year, defined as a reduction of at least 50% in seizure frequency in comparison with to before SEEG (among those who were not seizure free).

SEEG-guided RF-TC modus operandi

Multiple SEEG-guided RF-TC methodology was similar to that been previously reported in detail elsewhere [8, 12]. In brief, targets were defined, based on the SEEG recording, by either spike wave discharges or low amplitude fast pattern at the onset of the seizures. Bipolar electric stimulations were then performed on each eligible site to provide a functional mapping prior to any lesion. Bipolar RF-TC were then obtained on all the relevant electrode contacts (Fig. 1). During the procedure, patients underwent a real-time clinical evaluation by a neurologist. Patients were discharged 24 h after the procedure, and their epilepsy treatment was not to be changed during the year following the SEEG-guided RF-TC.

ATL group modus operandi

ATL was performed by a single neurosurgeon experienced in surgery for epilepsy (M.G.). The temporal pole was resected at a maximum of 3 cm in the non-dominant side, and 2 cm in the dominant temporal lobe (Fig. 1). The mesial resection included the amygdala, the head and the anterior tail of the hippocampus, and the parahippocampal cortex. Patients were discharged 5 days after surgery, and their epilepsy treatment was not to be changed during the year following the surgery.

Statistical analysis

Categorical variables were expressed as number (n) and percentage. Quantitative variables were expressed as means ± standard deviation when the distribution was normal or median and minimum and maximum when the distribution was not normal. The hypothesis of normal distribution of quantitative variables was tested using the Kolmogorov–Smirnov and graphically confirmed with a histogram. Categorical variables were compared using the χ^2 test or Fisher's exact test when the conditions of application of the χ^2 test were not met. Quantitative variables were compared between groups using Student's t test after verification of equality of variances when data were normally distributed, and with the nonparametric Wilcoxon test when the hypothesis of normality of distribution was not verified. The statistical test is bilateral and the level of significance was set to 5% ($p < 0.05$). Statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA).

Ethics

Each patient or his/her legal guardian(s) gave informed consent to both implantations of the electrodes for SEEG as well as RF-TC procedures and ATL. This study received the approval of the local ethics committee.

Results

Population characteristics

From 2001 to 2016, 261 patients were screened and 70 were included (mean age: 33 years, range 12–60; 40 female and

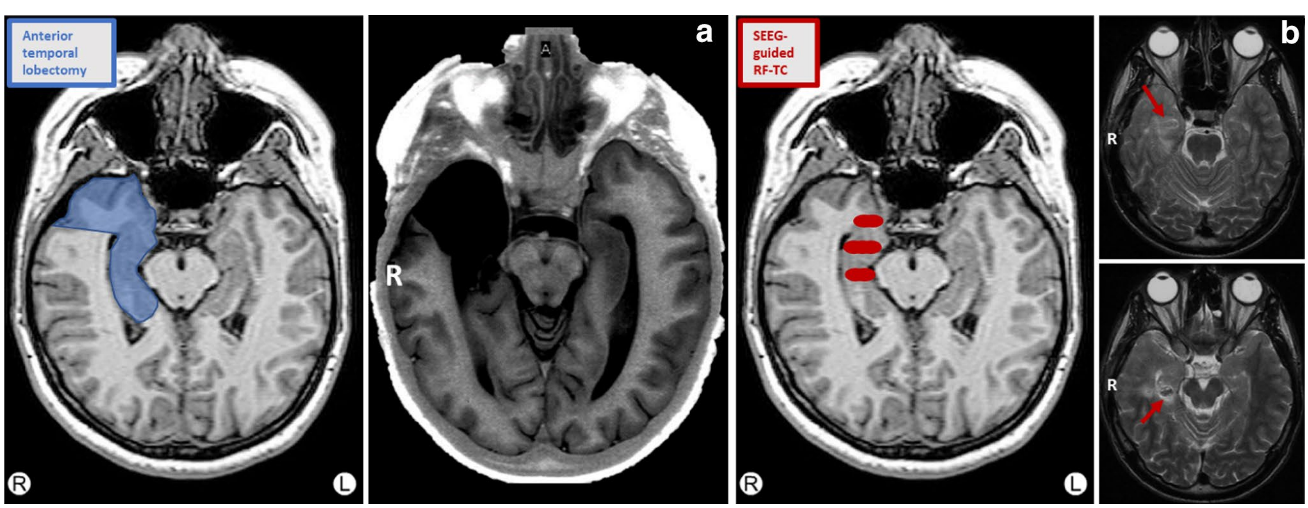

Fig. 1 **a** Schema (blue) and example of anterior temporal lombectomy. **b** Schema (red) and example SEEG-guided RF-TC

30 male). In all of those included, SEEG confirmed that the ictal onset zone involved the temporo-mesial structures; 21 patients underwent SEEG-guided RF-TC and 49 ATL alone (Fig. 2). The mean duration of epilepsy among the total population was 22.1 years (SD 10.0, range 4–49), and 59 (84.2%) had an abnormal MRI. The characteristics of the two groups were similar, with the exception of mean epilepsy duration that was longer in the ATL group (24.0 years, SD 9.4 vs 17.8 years, SD 10.2; $p=0.02$, Table 1).

Outcome

At 12 months, none of the patients of the SEEG-guided RF-TC group was seizure free while 75.5% ($n=37$) of the surgical group were ($p<0.0001$; Fig. 1); 47.6% ($n=10$) of the patients of the SEEG-guided RF-TC group were responders at 12 months while all the non-seizure-free patients ($n=12$) were responders in the ATL group ($p<0.0001$).

A mean 11 (SD 6.6; range 2–28) RF-TC lesions were made. In 3 cases (patients 9, 11, and 15), temporal RF-TC were associated with extra-temporal impacts (insula, orbitofrontal cortex, and occipital lobe; Table 2); these impacts were located on propagation pathways and did not correspond to an extra-temporal ictal onset zone.

Nineteen of the 21 patients in the SEEG-guided RF-TC group subsequently underwent ATL because they were not seizure free at 12 months, 14 of whom (73.7%) were seizure free at 12-month follow-up after ATL. Among the 2 patients who have not undergone ATL, 1 is about to undergo this procedure, and the other has been a responder following a 2-month seizure-free period. For this patient, the involved temporal lobe is the dominant one, and as the verbal memory

Table 1 Patient characteristics

	SEEG-guided RF-TC	ATL	*P* Value
	$n=21$	$n=49$	
Female (%)	12 (57.1%)	28 (57.1%)	
Men (%)	9 (42.8%)	21 (42.8%)	
Age (year (SD))	31,3 (9.7)	34,22 (8.0)	0.2‡
Mean duration of epilepsy [years (SD)]	17,8 (10.2)	24,0 (9.4)	0.02‡
Negative MRI (%)	5 (23.8%)	6 (12.2%)	0.2*
TLE subtypes (%)			0.6*
MTLE	16 (76.1%)	43 (87.7%)	
TPE	5 (23.8%)	6 (12.2%)	
Etiology (%)			0.9*
HS	11 (52.3%)	28 (57.1%)	
Cryptogenic	5 (23.8%)	11 (22.4%)	
Dysplasia	3 (14.2%)	6 (12.2%)	
Others	2 (9.5%)	4 (8.1%)	

ATL anterior temporal lobectomy, *RF-TC* radiofrequency thermocoagulation, *MRI* magnetic resonance imaging, *TLE* temporal lobe epilepsy, *MTLE* mesio-temporal lobe epilepsy, *TPE* temporal pole epilepsy

‡Student's test

*Fisher's exact test

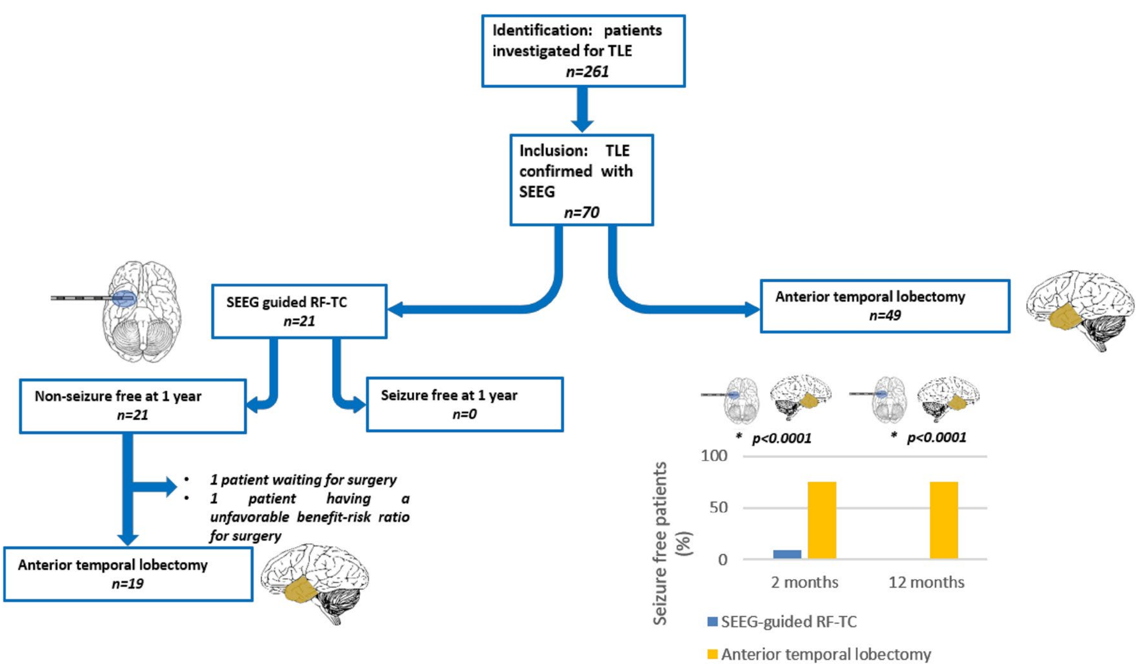

Fig. 2 Flow chart and main results

Table 2 SEEG-guided RF-TC population

No	Sex	Age at RF-TC	Epilepsy duration (year)	Dominance	Targets	Number of RF-TC	Seizure control at 12 months
1	F	45	17	ND	H; AN; Ext	9	NR
2	M	23	22	D	H; Pole; Ext	18	NR
3	M	34	29	ND	H; AN; EC	10	R
4	F	30	25	ND	H; AN; EC	13	R
5	M	32	17	ND	H; AN	9	R
6	M	55	49	D	H; AN; Pole	15	R
7	M	27	19	ND	H; AN	9	NR
8	F	37	19	D	H; AN	8	NR
9	M	28	9	D	H; AN; Insula	7	NR
10	F	25	11	ND	H; AN; EC	17	NR
11	M	18	16	ND	H; AN; Occipital	26	NR
12	F	29	27	D	H; EC	7	R
13	M	26	15	D	H; AN	8	R
14	F	32	5	D	H; AN; EC	12	R
15	M	34	9	D	H; EC; Insula; ObF	28	NR
16	F	29	26	ND	H; AN; EC	10	R
17	F	26	10	ND	H; AN	8	NR
18	F	28	24	ND	H; AN; EC	7	R
19	F	48	9	ND	H	6	NR
20	F	12	4	ND	H	3	NR
21	F	40	12	D	H; AN; EC	2	R

RF-TC radiofrequency thermocoagulation, *ND* non-dominant, *D* dominant, H hippocampus, *AN* amygdala nucleus, *EC* enthorinal cortex, *ObF* orbito-frontal cortex, *NR* decrease in seizure frequency $\leq$ 50%, *R* decrease in seizure frequency $\geq$ 50%, *SF* seizure free (Engel's Class Ia)

functions are intact the benefit-risk ratio is presently not in favor of resective surgery.

Complications

No complication was reported following the SEEG procedure, or the SEEG-guided RF-TC. In particular, no verbal or visuo-spatial memory alteration was reported. In the ATL group, 5.8% ($n = 4$) of patients had a post-operative complication. None of these was responsible of a neurological impairment; all were transient and included one case of chronic subdural hematoma, one case of post-operative hydrocephalus, and two cases of post-operative meningitis.

Discussion

The present study found that seizure outcome following SEEG-guided RF-TC is significantly worse than that following ATL for the treatment of drug-resistant TLE. No patient having undergone SEEG-guided RF-TC became seizure free; however, almost half of them were responders at 12 months. The groups were well balanced with the exception of longer epilepsy duration in the ATL group, but this is unlikely to explain the results as this is a risk factor for failure. Furthermore, no complication occurred in this group, which confirms the previously reported safety of this technique [8, 9, 16].

As far as resective surgery is concerned, the seizure outcome reported in this study is similar to that reported in the literature [3, 17–19], as is the complication rate [20]. These are expected, but notable results, as the diagnosis of TLE syndrome was not straightforward, necessitating SEEG before any surgical decision. Moreover, the very similar results after direct ATL and ATL following SEEG-guided RF-TC failure suggest that the two groups had a similar prognosis, close to classical TLE, which could indicate that their comparison is relevant.

Concerning SEEG-guided RF-TC, the outcome reported herein is poor when compared not only to that reported after resective surgery (both herein, and elsewhere), but also with that reported after conventional stereotactic RF-lesioning, or after treatment by stereotactic radiosurgery or laser interstitial thermotherapy (LITT). Since the initial description of temporal lobectomy in 1958 by Niemeyer in Charles [21], there have been numerous reports of procedures more selective than ATL, focusing on the epilepogenic tissue, and aiming to obtain the same seizure-free rate with a better neuropsychological outcome [22]. Selective amygdalohippocampectomy, advocated by Yasargil et al. in 1982 [23], is one of the more selective of these procedures. Some studies have suggested better neuropsychological outcomes [24], but meta-analyses have found a worse seizure control [25, 26]. Similarly, stereotactic procedures have been proposed to be more selective and less invasive. Stereotactic RF-TC using a single monopolar probe was extensively studied in the 1970s up to the 1990s [6, 7, 27, 28], and is still being developed. A recent study of monopolar RF-TC that included 61 patients presenting with TLE, reported 70% Engel's Class I at 2-year follow-up [29]. Nevertheless, the same team in another study reported that only 13/32 (40%) patients were seizure free (Class Ia) at 2-year follow-up [30]. These results strongly suggest the limited success rate of stereotactic monopolar RF-TC conducted without electrophysiological guidance in TLE; they are, however, better than those reported herein. More recently, LITT, which also produces tissue coagulation but by laser, has been developed. Two systems are FDA-approved (but still not CE marked) for use in neurosurgery. LITT is a real-time MRI-guided (for monitoring probe placement and thermal dose delivery) treatment [31]. Only small-sized studies have been published: Willie et al. reported 13 cases of LITT amygdalo-hippocampectomy for TLE, leading to a seizure-free rate of 54% (Engel's Class I) after 5–26 months of follow-up [32]; Kang et al. obtained 53% of Engel's Class I in 15 TLE cases after 6 months of follow-up [33]; Jermakowiscz et al. reported, in a series of 23 patients, 65% of patients free of disabling seizures, and 39% of Engel's Class Ia at 12-month follow-up [34]. Youngerman et al. reported that a series of 30 patients in which 58% of patients were Engel's Class I at 12-month follow-up [35]. The complication rate of these stereotactic procedures is not possible to quantify owing to the small number of patients studied; cerebral edema, hematomas, hydrocephalus, partial visual field deficit, III and IV nerve palsy, and psychiatric disorders have been reported [25, 32, 33, 36].

The reasons for which SEEG-guided RF-TC outcomes herein are worse than those obtained after monopolar RF-TC or LITT remain to be clarified. One explanation could be that, whereas the latter techniques provide extensive coagulation of the mesial temporal structures as a result of an electrode placement along the hippocampal axis by means of an occipital approach to perform radially distributed lesions spanning from 30 to 45 mm [30, 33, 34], the size of the lesions produced by bipolar RF-TC using SEEG electrodes is smaller (5–7 mm around the probe [8]) and placed orthogonally to the hippocampal axis. The multiple lesions targeting the core structure of the mesial epileptic network, such as the entorhinal cortex, that are known to be a risk factor for seizure control failure if spared [37, 38], are certainly smaller than those that LITT can provide (which are able to almost destroy the entire hippocampus). The volume of hippocampal lesion appears to be an essential factor of seizure control in any stereotactic procedure, especially concerning the head of the hippocampus [34]. Another explanation for the poor outcome reported herein could be that it may be due to the presence of a more complex and robust epileptic network in TLE than in extra-temporal epilepsy. A perspective for improvement would be to develop a stereotactic procedure coupling intracranial recordings to a highly efficient hippocampal lesionning technique.

Conclusion

SEEG-guided RF-TC is not as effective as ATL. As no memory impairment following SEEG-guided RF-TC was found, patients with dominant mesial involvement for whom hippocampectomy is not an option could benefit from the technique.

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Compliance with ethical standards

Conflicts of interest All the authors declare that they have no conflict of interest.

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