Seizure: European Journal of Epilepsy 70 (2019) 63–70

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

SEEG-guided radiofrequency thermocoagulation of epileptic foci in the paediatric population: Feasibility, safety and efficacy

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ARTICLE INFO

Keywords:
Epilepsy surgery
Thermocoagulation
Children
Epilepsy
Invasive EEG
stereoEEG
Paediatrics

ABSTRACT

Purpose: Focal epilepsy in children may be refractory to pharmacological treatment and surgical resection may be an appropriate option. When invasive electroencephalogram is required in the presurgical evaluation, depth electrodes can be used to create focal lesions in the epileptogenic zone using radiofrequency thermocoagulation (RFTC), to disrupt the epileptogenic zone.

Methods: This study aimed to assess the efficacy and safety of RFTC in a paediatric population of 46 patients.

Results: The mean age of onset was 3.3 years and the mean age at SEEG was 8.2 years. MRI lesions were identified in 71.7% of the series, among them 60% of malformation of cortical development. 43.5% of the patients were seizure free at 1 month, 26.1% were responders. The mean duration of improvement was 6.8 months. 8 children were seizure free for > 8 months and among them, 6 are currently seizure free for 8–24 months. 5 patients had functional deficits post-procedures, transient in 4 patients and prolonged in one of whom. 3/5 were anticipated following the results of cortical stimulation. Multivariate analysis found 3 independent criteria linked to RFTC efficiency one month after RFTC: frequency of the seizures before RFTC, age and number of contacts used.

Conclusion: RFTC is a safe method for the paediatric population providing important predictive information for surgical resection. An improvement in seizure frequency, often transient, is seen in 2/3 of our patients. RTFC could be useful as a palliative technique for children with an epileptogenic zone overlapping with eloquent areas, with minimal risk of sequelae.

1. Introduction

Focal epilepsy in children may be refractory to pharmacological treatment in up to 30% of cases and surgical resection may be an appropriate treatment option in a subset of these cases. However, successful resection relies on the accurate identification of the epileptogenic zone. If it is not possibly to do this via conventional clinical methods (3T structural MRI and videoEEG telemetry), stereoelectroencephalography (SEEG) in which a number of depth electrodes are implanted into the brain under stereotactic guidance may be considered to record seizures, as a means to locate the epileptogenic network [1,2]. Although the aim of SEEG is to identify the brain region for resection, the depth electrodes can also be used to create small focal lesions in the epileptogenic zone using radiofrequency thermocoagulation (RFTC), using the ictal activity recording during SEEG to guide RFTC [3,4]. The aim of RFTC is the disorganization of the epileptogenic zone [3] resulting in: a/ improvement in seizure frequency or seizure freedom, often transient and b/ predictive information to aid planning of surgical resection. Benefits of the approach include the fact that RFTC can be directly targeted to the epileptogenic zone as defined by SEEG, considered to be the gold standard in presurgical evaluation, RFTC is carried out at the same time as SEEG [5]. The safety of the technique is enhanced by functional mapping through cortical stimulation prior to the procedure, to avoid eloquent cortex, minimising the occurrence of a postlesional neurological deficit. The procedure does not require anesthesia in most cases, meaning the child can be monitored throughout. In addition, this technique does not preclude surgery should this be required at a later date. The largest studies of RFTC in the adult

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https://doi.org/10.1016/j.seizure.2019.07.004
Received 5 February 2019; Received in revised form 28 May 2019; Accepted 2 July 2019

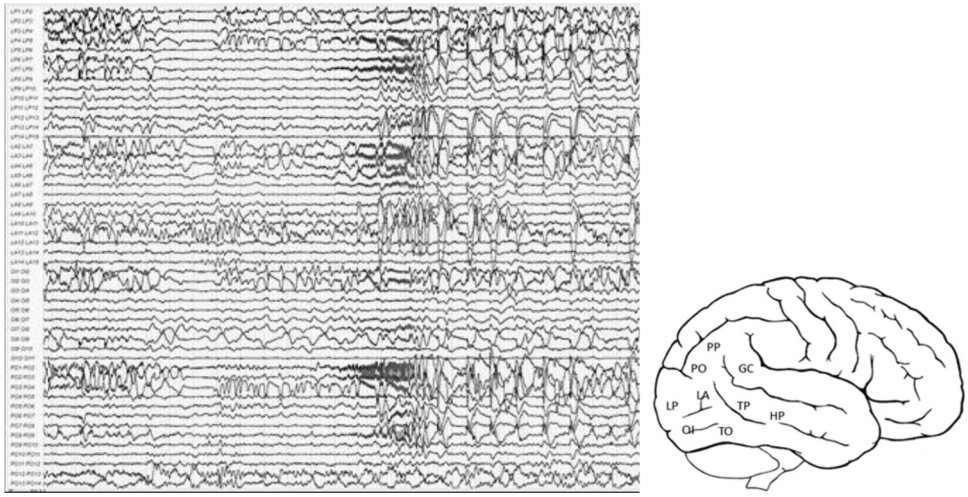

Fig. 1. SEEG recording Example showing a limited epileptogenic zone, defined by low amplitude fast rhythmic discharges over occipital contacts in a patient who was offered RFTC. On the right, SEEG implantation scheme.

population reported efficacy, (defined as a reduction of at least 50% in the seizure frequency) in 67% of the patients at two months [6] with 25% seizure freedom at the same time point. At 12 months, 28–77% remained responders [6–8]. More recently, RFTC has been suggested as a palliative procedure in patients with drug-resistant epilepsy ineligible for conventional surgical resection because of the proximity of a functional area to the region of seizure onset or an epileptic network that is too extensive [5,6,9]. This indication is still controversial. Others techniques of lesion guided RFTC and laser ablation have been applied mostly in mesio-temporal epilepsies, hypothalamic hamartoma and tumors [8,10,11]. SEEG-guided RFTC is associated with 1.1% risk of permanent deficit and 2.4% risk of transient side effect [6].

The importance of minimally invasive techniques and optimisation of cortical resection for focal epilepsy in children is particularly relevant owing to the need to preserve developmental outcomes associated with reduction in seizures as well as the importance of avoiding prolonged anti-epileptic medication where possible [12]. However, to date, only one small study of RFTC in children has been reported [13] which seemed to indicate a lower proportion of responders than in adults. The current study aimed to assess the efficacy and safety of RFTC in a large consecutive group of paediatric patients undergoing SEEG across two major children's epilepsy surgery centres in Europe.

2. Methods

2.1. Patients

All children referred to Rothschild Foundation Hospital in Paris and to Great Ormond Street Children Hospital in London undergoing SEEG between the ages of 18 months and 18 years between 2014 and 2017 were included in the study. All patients had standard presurgical non-invasive investigation, including ictal videoelectroencephalography (EEG), 3T magnetic resonance imaging (MRI) including volumetric T1-, T2 and FLAIR sequences, followed by a contras-enhanced T1 sequence, and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) as previously described [2,3]. When data obtained at this stage was insufficient to define a surgical resection, and in particular when limits of MRI lesions were unknown, the decision for SEEG was taken by a trained multidisciplinary team and offered to the family. A tailored electrode implantation schema was designed for each child in order to determine the epileptogenic zone and their relationships to the functional cortex as previously described [2,3]. Electrodes were implanted according to the hypothesis formulated after electro-clinical correlations and were placed inside the MRI lesion, in the adjacent anatomic sites around the lesion and at specific distant sites according to our hypothesis of potential propagation, in order locations to discriminate the epileptogenic zone. The results of the SEEG recordings were discussed at a multidisciplinary conference, in order to decide on whether to undertake RFTC and/or a cortical resection [2,3]. RFTC responders were defined as having a decrease of at least 50% in the seizure frequency. Post-operative seizure control was assessed using the Engel classification [14]. Patients were informed of the aims and risks of SEEG recordings including functional mapping by cortical stimulation and the risks of RFTC.

2.2. Indications for SEEG-guided RFTC and choice of targets

Intracerebral exploration was conducted with DIXI Medical® (Besancon, France) or ALCIS® (Besancon, France) electrodes according to the technique described by Talairach and Bancaud [15], and reported in detail in previous publications [2]. A post-implantation CT scan was co-registered with the preimplantation MRI, allowing visualisation of all electrodes and their contacts. SEEG recording of interictal data and spontaneous seizures were analysed by the clinical team along with the results of cortical stimulation to define the epileptogenic zone and the epileptic network. Following this, target contacts for RFTC were chosen inside the epileptic zone and determined using the following criteria: a/ within the epileptogenic zone, showing either a low amplitude fast pattern or spike-wave discharges at the onset of the seizures [2,3] (Fig. 1), in intralesional location, and/or in contacts where electrical stimulation induced habitual seizures, b/interictal paroxysmal activities were considered only in case of continuous spikes suggesting focal cortical dysplasia (FCD), c/ Limited to electrodes with cortical localisation (on MRI co-registered with CT), d/ not in close proximity ($>$ 2 mm) to a major blood vessel identified on angiography, e/ demonstrated not to lie within eloquent (supporting primary motor or language function) cortex (identified by high frequency cortical stimulation at 50 Hz, 0.5 msec pulse duration 1–8 seconds or slow (1 Hz) stimulation). A safety distance of 1 contact (i.e., 3.5 mm including the electrode isolation gap) between eloquent cortex and RFTC was mandatory. The exception to this was when the RFTC was undertaken as a palliative procedure in patients for whom conventional cortical resection was considered too high risk. SEEG-guided RFTC was not considered in patients with an extensive epileptogenic zone, a frequent situation in young children with large focal cortical dysplasia, as RFTC alone would not be expected to have an impact on the disruption of a diffuse epileptogenic network.

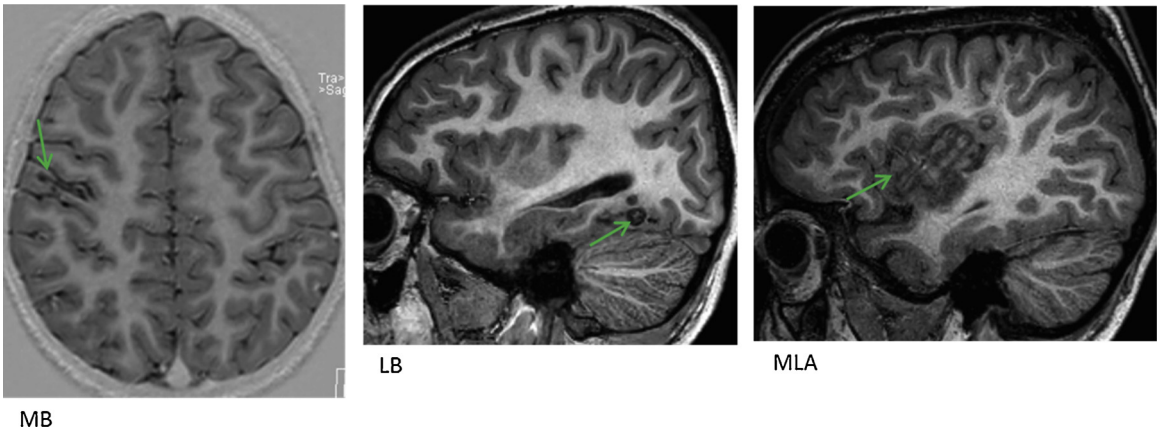

Fig. 2. Examples of post-RFTC MRI in three different patients. Lesions are indicated with an arrow.

2.3. SEEG-guided RFTC procedure

SEEG-guided RFTC was performed at the end of the recording period and before electrode removal, without anaesthesia when the child was able to cooperate, which enables clinical monitoring of the patient during the procedure. SEEG recording was performed immediately before and after the RFTC. Lesions were made using a radiofrequency lesion generator system (Neuro N50, INOMED, Emmendingen, Germany or G4, Cosman Medical, Burlington, USA), connected to the SEEG electrodes. Lesions were produced between two adjacent contacts of the selected electrodes using a 50 V, 120 mA current known to increase the local temperature up to 78–82 °C within a few seconds (in vitro), thus producing a lesion around the electrode contacts in 10–30 s [3,6]. SEEG monitoring was sometimes continued for few hours after the coagulations, in particular in patients having 2 types of seizures. In one case, when discharges close to the motor cortex persisted after the first SEEG-guided RFTC procedure, a second RFTC was performed the following day. In all other cases, the electrodes were removed 0.5 up to 5 h after the RFTC, and patients were discharged after 1–2 days of clinical follow up. MRI was performed within 3 months after RFTC (Fig. 2). The indication for subsequent surgery was decided at 1 month post-RFTC in case of seizure persistence (i.e. non-responders and responders but not seizure-free patients) and most of these children underwent cortical resection in case of seizure persistence between 2 and 3 months after SEEG. Surgery was decided also later on as soon as a recurrence of the seizures after RFTC was reported.

2.4. Statistical analysis

Group comparisons (responders versus non-responders or seizure free) were performed using Mann-Whitney U test (continuous variables) and the Fisher test (categorical variables) and univariate analysis were carried out to identify relevant factors. Variables (factors) with a $p < 0.20$ in the univariate analysis were entered in multivariate logistic regression model, applying a significance level of $p < 0.05$. The association between responders to RFTC and Engel score was tested using a Fisher test and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were also calculated. Statistical analysis was conducted using R version 3.4.3 (RFoundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Patients (Table 1)

46 patients from 2 European paediatric epilepsy surgery programs were included, all with drug-resistant focal seizures. Inclusion was prospective at Rothschild Foundation, Paris (n = 41) and retrospectively at GOSH, London (n = 5). The mean age of seizure onset was 3.3 years +/− 2.9 (0–11 years). The mean age at SEEG was 8.2 +/− 4.3 years (1–17 years). The seizure onset zone was defined by SEEG as fontal (n = 14), parietal (n = 11), pure insular (n = 7), temporal (n = 4) or occipital (n = 1). It could also be bi-lobar (n = 6) or tri-lobar but mainly insular contacts (n = 3). The mean number of coagulated contacts was 17.3 +/− 12.2 (3–57). MRI lesions were identified in

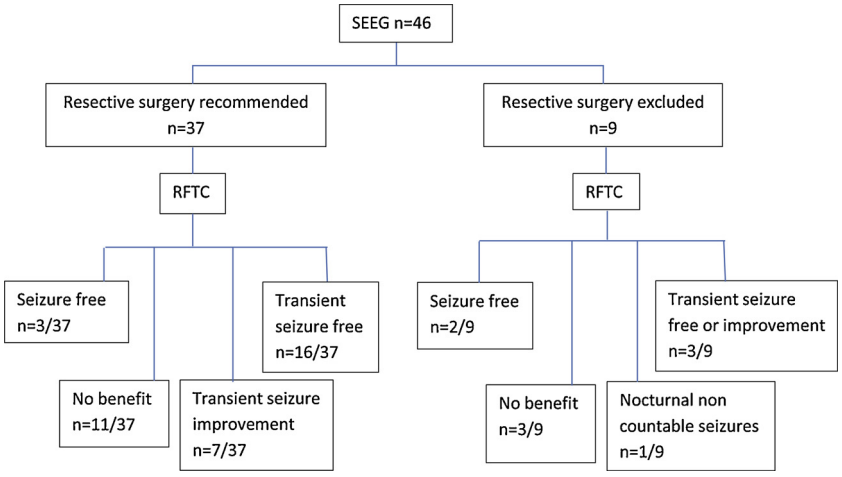

Fig. 3. Flow chart of the results of RFTC treatment (n = 46).

Table 1
Clinical features of patients in the 3 groups defined at 1 month after RFTC: seizure-freedom, responders (i.e seizure reduction > 50%) and non-responders.

	Seizure-free group at 1 month	Responder group at 1 month	Non responder group at 1 month
number	20	12	14
Age of onset (years)	3.6 +/− 3.1	2.5 +/− 2.0	3.6 +/− 3.2
Age at RFTC (years)	9.8 +/− 4.0 (p = 0.03)	6.1 +/− 3.0 (p = 0.03)	7.8 +/− 5.0
Seizure frequency	2 patients monthly, 1 weekly, 13 daily and 4 non countable seizures (subtle or nocturnal)	0 monthly, 1 weekly, 8 daily, 2 non countable (subtle or nocturnal) (p = 0.01)	1 patient monthly, 1 weekly and 12 daily seizures (p = 0.04)
Number of coagulated contacts	20.4 +/− 15.4	14.3 +/− 9.4 (p = 0.03)	15.6 +/− 8.4
Age at surgery (Years)	10.4 +/− 3.9	7.4 +/− 3.9	8.1 +/− 4.6
Delay between epilepsy onset and surgery (years)	7.3 +/− 3.7	5.9 +/− 3.6	4.5 +/− 2.2
Number of patients operated on	11	8	11
Engel 1/2	9	6	8
Engel 3/4	2	2	3
Pathology	1 FCD1, 5 FCD2a, 2 FCD2b, 1 DNET, 2 normal	1 FCD1, 2 FCD 2a, 3 FCD2b, 2 normal	4 FCD1, 5 FCD2a, 2 FCD2b
MRI	11 FCD, 1 TSC, 1 DNET, 1 heterotopia, 6 normal	9 FCD, 1 hippocampal sclerosis, 2 normal	8 FCD, 1 TSC, 5 normal

71.7% (33/46) of the series. The remaining 13/46 (28.3%) were 3 T MRI lesion negative. Among the MRI lesions, 28/33 (84.9%) were FCD, 2/33 had TSC, 1 patient had a DNET, another one had heterotopia, another one had hippocampal sclerosis. 9/46 patients were not recommended for surgery (Fig. 3). At the end of the presurgical evaluation, 30 children were operated on. The mean delay between RFTC and surgery was 5.1 +/− 3.1 months (1–14 months). Four children were operated on within the 2 months after RFTC, 19 were operated on between 3 and 6 months after surgery and 7 were operated on more than 8 months after surgery (8–30 months) mostly because of seizure relapse. Among them, FCD was found in 86.7% of the cortical samples (n = 26/30) including FCD1 = 20% (n = 7), FCD2a = 48% (n = 12), and FCD2b = 26.9% (n = 7). Another patient had a DNET. Histopathology was normal or non-diagnostic in the remaining 3 children.

3.2. Seizure outcome after RFTC

The mean duration of improvement was 6.8 months +/− 6.7 months (0.7–28 months). Eight children were seizure free for > 8 months and of these, 6 are currently seizure free for 8–24 months. No worsening of the seizure was reported by patients/carers after RFTC. At 1 month after RFTC, 69.6% (n = 32/46) of the patients were responders, including 43.5% being seizure free. At 6 months, 23 children were still evaluable, among them, 73.9% (n = 17/23) were responders, including 56.5% (n = 13/23) being seizure free (Table 2). At 12 months, 73.3% (n = 11/15) of the patients were still responders, including 26.7% being seizure free.

Focusing on children excluded for resective surgery (n = 9), 2/9 patients were seizure free at the end of the follow-up (20 and 24 months) and 3/9 had no benefit of RFTC (Fig. 3). In the group of children recommended for resective surgery at the end of the presurgical evaluation (n = 37), 3/37 were seizure free at the end of the follow-up (5, 13 and 16 months) and 11/37 had no benefit (Fig. 3).

Immediately after RFTC, EEG recording showed a dramatic decrease of interictal discharges at the site of the procedure in all patients (Fig. 4). This was also seen on scalp EEG recordings several months after RFTC. Especially in seizure free cases, interictal abnormalities improved or resolved with normal recording (Fig. 5).

The presence or absence of a MRI lesion did not influence the outcome. Among the MR lesion negative 13 patients, 8/13 (61.5%) were responders with a mean efficacy duration of 7.5 +/− 7.8 months. Thirty-three patients had a lesion on preoperative MRI and 24/33 (72.7%) responded with a mean duration efficacy of 6.2 +/− 5.3 months. On the other hand, the histopathology type seemed to influence the outcome, FCD2 responded better than type 1 and FCD2b responded better than FCD2a. Among the 7 patients with FCD2b, 5/7 (71.4%) were responders with a mean efficacy of 6.2 +/− 3.3 months. Among the 8 patients with FCD2a, 7/12 (58.3%) were responders with a mean duration of 3.03 +/− 3.17 months. Among the 7 patients with FCD1, 3/7 (42.9%) were responders with a mean efficacy of 5 +/− 2.8 months. The efficacy was not linked to the topography of the cortical structure involved. Patients with very small epileptogenic lesions did not respond differently after RFTC (n = 9): 3/10 did not respond, 3/10 were responders for less than 3 months, and 3/10 were seizure-free for 8, 8 and 26 months respectively.

The only independent variable for seizure freedom at 1 month after RFTC (in multivariate analysis) was the age at RFTC (p = 0.02) as older children responded better.

Multivariate analysis found 2 independent criteria linked to seizure reduction (> 50%) one month after RFTC: frequency of the seizures before RFTC and number of contacts used for RFTC. The responder rate in children with daily seizure was lower than in children with fewer seizures (p = 0.03). Eighty-six percent of the children in the non-responder group had daily seizures before RFTC compared to 65% (21/32) in responders and seizure free groups (Table 1). And finally, the number of contacts where RFTC were applied is an independent factor for the efficacy of the RFTC. The more contacts treated, the lower the frequency of seizures at 1 month (p = 0.03).

3.3. Safety

No seizure was elicited by RFTC. No stroke occurred. 5 patients had functional deficits post-procedures, transient in 4 patients and more prolonged in one, of whom 3/5 were anticipated following the results of cortical stimulation. The first patient experienced a transient (< 7 days) hemicorporal sensory deficit after RFTC in the precentral and

Table 2
Clinical response after RFTC.

	1 month	3 months	6 months	12 months	24 months
Total	46	37	23	15	13
Operated on	0	9	23	31	33
Responders	32 (69.6%)	27 (73.0%)	17 (73.9%)	11 (73.3%)	10 (76.9%)
Including seizure free	20 (43.5%)	14 (37.8%)	13 (56.5%)	4 (26.7%)	7 (53.8%)
Non-responders	14 (30.4%)	10 (27.0%)	6 (26.1%)	4 (26.7%)	3 (23.1%)

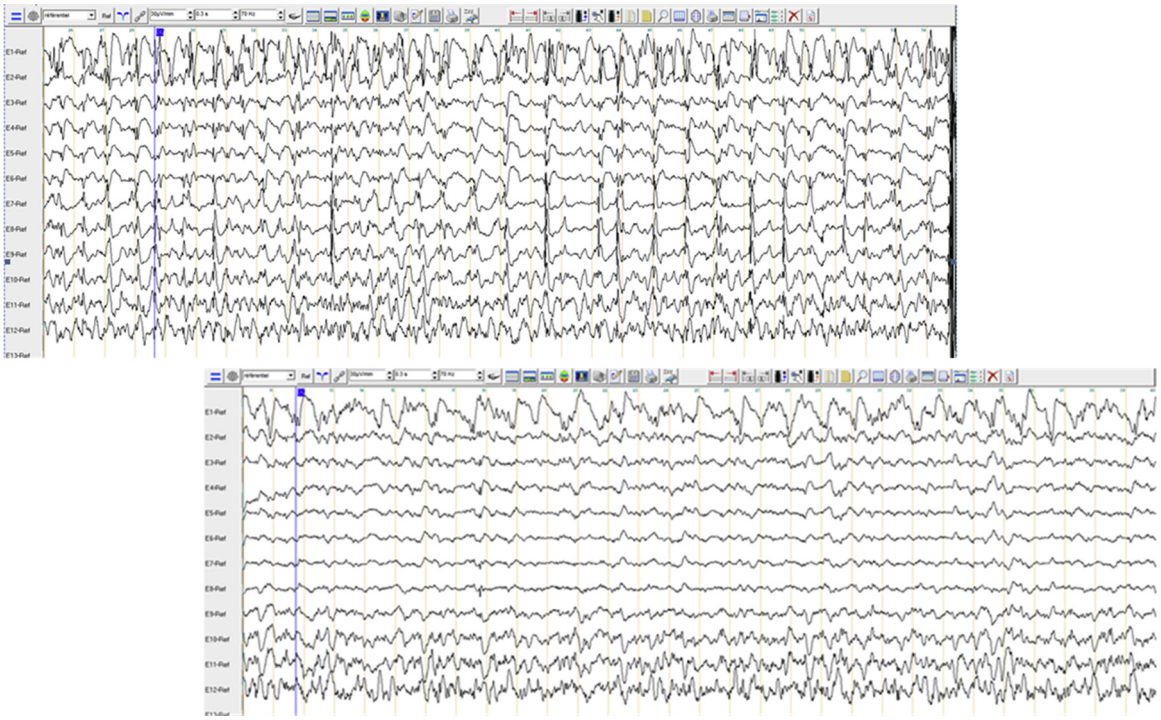

Fig. 4. Example of invasive EEG recording immediately before RFTC and the same invasive EEG recording 10 mn after RFTC of the 1–9 first contacts of the electrodes. Note the disappearance of continuous spikes over the internal and mid contacts of the electrode.

postcentral gyri. The second patient experienced transient hemiparesis after RFTC in the precentral gyrus, lasting less than 10 days. The third experienced transient worsening of his existing left arm deficit after extensive RFTC in an abnormal precentral gyrus. Six months after RFTC, he gained motor skills of his left arm with improvement compared to function prior to RFTC. For 2 other patients, complications were unexpected as electrical stimulations during invasive monitoring did not show any functional response. The first experienced very discrete transient speech difficulties after RFTC near Broca's area. The second experienced permanent paresthesia and dysesthesia over her right foot. Electrical stimulations during SEEG had not demonstrated sensory responses in this adolescent with normal cognitive skills. One patient had a cortical haemorrhage and another had a subarachnoid haemorrhage with transient motor deficit following removal of the electrodes.

3.4. Seizure outcome after surgery

Thirty of 46 patients (65%) underwent subsequent epilepsy surgery. The duration between RFTC and resective surgery was 6.9 +/− 3.8 months (2–14 months) for initially seizure-free patients (at 1 month after RFTC, n = 20). The duration was 5.0 +/− 1.9 months for the responder-group defined at 1 month (3–8 months, n = 12).

At a mean follow-up of 20.1 +/− 9.7 months, Engel 1 outcome was recorded in 73.3% of the patients (22/30) and Engel 3–4 was recorded in 20% (6/30).The last 2 patients were Engel 2. The reasons for 16/46 patients not undergoing surgery were as follows: a/ 6 patients were still seizure free after RFTC (1 patient was not completely seizure free but had only 2 short auras after 9 months of seizure freedom), b/ 9 patients were not recommended for surgery (4 with multifocal epilepsy, 4 with functional area primarily involved and 1 because of posterior insular involvement with relatively low seizure burden so the risks of the surgery were considered unreasonably high), c/ 1 patient because his parents were not prepared to proceed to surgery.

3.5. Predictive value of SEEG-guided RFTC outcome on post-operative outcome

The positive predictive value of RFTC at 1 month for Engel 1 outcome following subsequent resective surgery was 0.83. Among the non-responder group (n = 14/46), 11 patients underwent respective surgery. Eight of eleven patients (72.7%) were seizure free after surgery (Engel 1). Among the short-lasting responder group (n = 14/46), (efficacy < 6 months), 11 patients underwent surgery and 8/11 (72.7%) were seizure free. Among the long-lasting responder group (efficacy sustained more than 7 months, n = 5/46), 4/5 (80%) children who underwent surgery were seizure free and the last one was Engel 2. FCD2a was the main etiology in responders as well as in the non-responder group.

3.6. Palliative thermocoagulations in functional cortex

Four patients were excluded for resection surgery after SEEG because the epileptic zone included functional motor areas, as determined with electrical stimulations applied during SEEG. These patients were not offered surgery because of the high risk of additional post-surgical motor deficits. RFTC was performed as a palliative intervention for these highly drug-resistant patients. All the RFTC were applied inside the epileptic zone and 7 RFTC (n = 3 patients) were applied inside the functional motor area (as defined by cortical stimulations during the SEEG period). Three of four children were still seizure free 13–24 months post-RFTC, and one experienced a 4 month seizure free period with significant improvement of his pre-existing motor deficit.

4. Discussion

RFTC is a safe method for the paediatric population providing important predictive information for surgical resection. An improvement in seizure frequency, often transient, is seen in 2/3 of our patients.

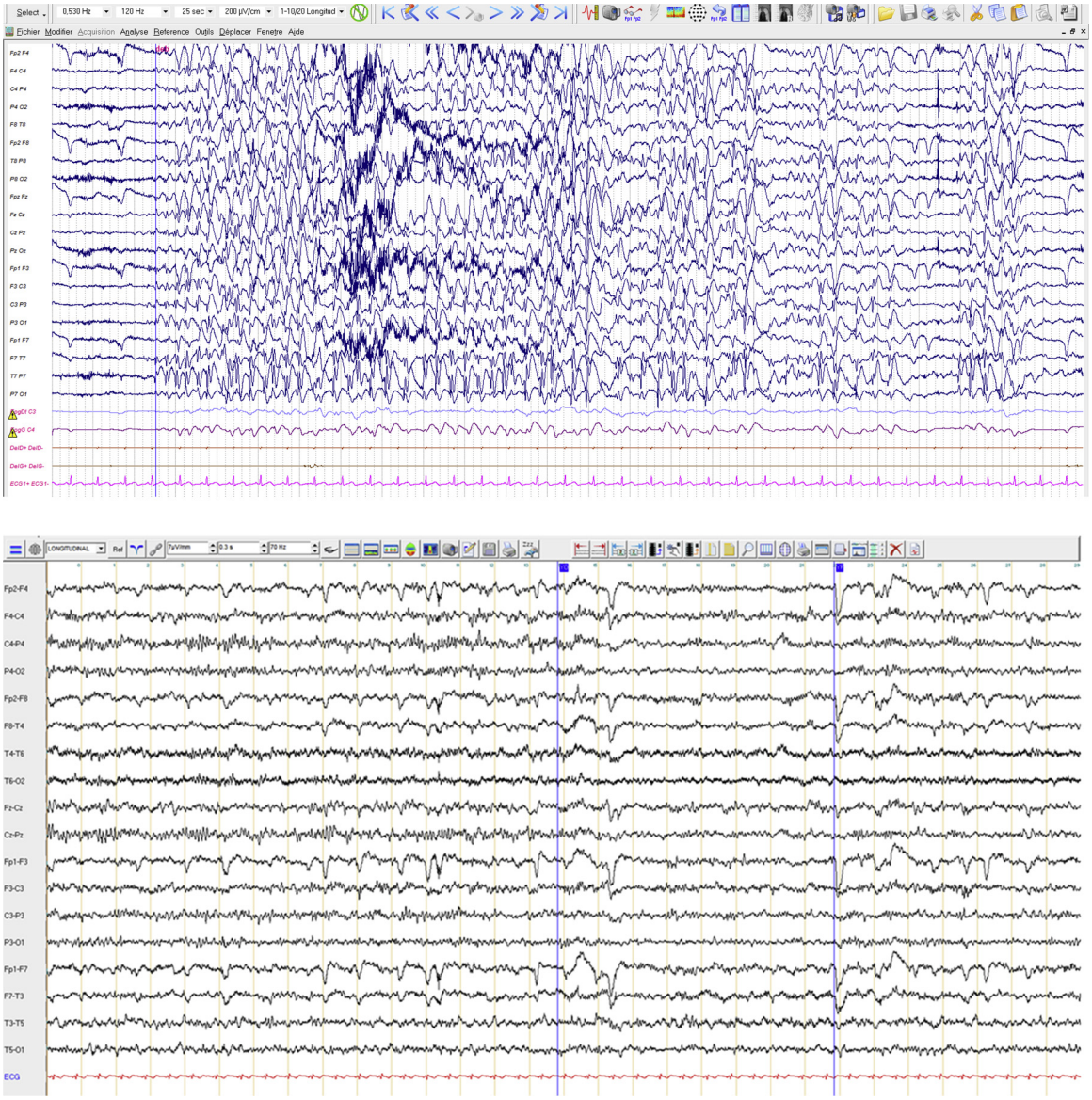

Fig. 5. Example of scalp EEG during presurgical evaluation in a longitudinal montage. Second scalp EEG was recorded 4 months after RFTC as the child was seizure free. Note the disappearance of diffuse interictal abnormalities particularly over left temporal area.

4.1. Seizure outcome

After RFTC, 43.5% and 69.6% of the patients were respectively seizure free and responders at 1 month. And so were respectively 26.7% and 73.3% of the patients (n = 15) at 12 months. And Thirty-one patients were operated on during the first year after RFTC because of the lack of efficacy of RFTC or because of seizure recurrence. The need of a surgery for persistent seizure after RFTC had to be considered as a failure of RFTC. In previous reports, 15–25% adult patients have become seizure free after SEEG-guided RFTC, and 40–67% patients experienced a ≥50% decrease of their seizure frequency [3,4,6,8,15]. The responder rate remained between 36–77% at 1 year [8]. Between one and two thirds of responders maintain their status during long-term follow-up (mean 5.4 years) [6,7]. Worsening of seizure burden has not been observed in any patients [3–6,8,16,17]. In comparison our follow-up period of responder group is shorter, because the ultimate aim in the paediatric group would be to achieve seizure freedom early to optimise cognitive outcomes and hence perform epilepsy surgery as early as possible for those with persistent seizures.

4.2. Efficacy regarding the etiology

RFTC seems to be particularly efficient in patients with gray matter nodular heterotopia–related epilepsy [8,18,19], whereas patients treated with frontal RFTC showed poorer seizure outcomes [4,8,13]. We did not observe any differences in outcomes following RFTC between cortical lobes or regarding the etiology. We recruited only one patient with periventricular nodular heterotopia, who is still seizure free (except occasional non disabling auras), 9 months after RFTC. In this particular etiology, Scholly et al. demonstrated in a single patient that RFTC modified the aberrant connections of the epileptogenic network involving heterotopia and adjacent cortex [18]. Catenoix et al. reported that good results of RFTC were obtained in patients with malformations of cortical development [5]. We could not test this hypothesis in our paediatric study group, as FCD was found in the majority (86.7%) of the cortical samples. However, we found a trend showing that histopathology type affect the outcome, as FCD2 responded better than type 1 especially FCD2b.

Regarding hypothalamic hamartomas, a recent paper showed that SEEG-guided RFTC could be efficient. This paper reported 5/9 patients

(55.6%) achieving Engel's class I recovery, and the other 4/9 achieved Engel's class II recovery (10). We did not include patients with hypothalamic hamartoma, as they were operated on with frameless stereotactic trans-ventricular endoscopic disconnection with similar outcome. Seizure free patients (Engel 1) was achieved for about 57% of our 136 patients and 21% of our patients were almost seizures free (Engel 2) (personal data). The morbidity and efficiency of the 2 techniques seem identical.

The outcome after SEEG-guided RFTC could be better for patients with a lesion on preoperative MRI [7,8]. In our series, the presence or absence of a MRI lesion did not seem to influence the outcome. We found that older children had a significantly greater response to RFTC compared to those at a younger age. One hypothesis could be that the epileptogenic zone is less extensive when the epilepsy begins at an older age [20] and RFTC might therefore more effectively disrupt the epileptogenic network. The frequency of the seizures also played a statistically independent role in the efficacy of the RFTC as children with daily seizures responded poorly. It is well known that younger children have higher seizure frequency than older children. Consequently, as stated above, RFTC are less efficient in younger children. We also find that the number of contacts where RFTC were applied is a statistically independent factor for the efficacy of the RFTC. On the contrary, Guenot et al. reported no obvious correlation between outcome and the number of lesions in an adult series [4]. But they examined a population with smaller lesions.

4.3. Prognostic value of RFTC efficacy

In adults, SEEG-guided RFTC is predictive, with a high PPV (93%) of a good outcome after conventional corticectomy [6]. Therefore, seizure control after RFTC is now routinely taken into account as a therapeutic test in clinical practice in some teams, before the final surgical decision [6]. In our series, 4/5 children with a long-lasting (> 7 months) efficacy period after RFTC were seizure free after resective surgery and the last was Engel 2. A long lasting efficacy period seems to predict the efficacy of the later resective surgery, and the PPV is 88%. RFTC could therefore be routinely used in seizures even in the context of seizure improvement.

4.4. Safety

In previous papers as in our series, the procedure was completely painless [3] except for one patient with RFTC applied adjacent to the choroidal fissure [4]. In 10–12.3% patients a typical seizure occurred during RFTC [7,13]. We did not observe any elicited seizure, but most of our patients were under general anesthesia with halogenated inhalational anesthetics and opiate medication only, in order to minimise the effect on the EEG signals. In adults, 3.3% of the procedures led to transient side effects, most often transient motor deficit or paraesthesia [4,6,7]. These are predictable by functional mapping [6]. In their review in 2018 Catenoix et al. reported only 1 patient (out of 251) who suffered unexpected permanent neurological deficit post RFTC [3,7]. When an unexpected post-RFTC neurological deficit occurred, 2 possible explanations were suggested in adults: a/ oedema of a larger volume than that of the targeted contacts, b/ lesions of areas where the induced clinical impairment is difficult to test during functional mapping (notably associative areas). In these regions, functional mapping during SEEG may have a poor predictive value regarding the post RFTC deficit [3]. The second reason is of particularly importance in children as electrical stimulations for functional mapping can be more difficult than in adults when the child is not completely cooperative. For motor mapping, stimulations can be applied during sleep for the less cooperative children i.e. younger and/or more severely impaired children. We only had 2 unexpected functional deficits: one transient very discrete speech disturbance and one more prolonged sensory impairment. These results are in line with the adult data and corroborate the fact that electrical stimulations for functional mapping is reliable in a paediatric population.

4.5. Palliative RFTC in functional cortex

RFTC is recommended when resective surgery carries a high risk of subsequent deficits. Catenoix et al. reported 22 patients not eligible for resective surgery after SEEG submitted to RFTC, three (13.6%) were seizure-free and six (27.3%) were significantly improved, suggesting that this procedure might be offered as an alternative to open surgery when patients are not ideal candidates for cortical resection [5]. In the unique paediatric series, 8/22 patients were excluded for surgery and among them, only one was seizure free after RFTC [13]. We reported 9 patients excluded for resective surgery and 2/9 (22.2%) are still seizure free 20 and 24 months after RFTC. Three other patients experienced transient seizure freedom or improvement lasting 1–9 months. So for those patients who are not candidates for cortical resective surgery after SEEG, RFTC can be considered as an alternative therapeutic option, although the chance of long-term cure is relative small.

4.6. Limitations of RFTC in paediatric population

Compared to previous paediatric series with SEEG, the ages at seizure onset and at surgery are greater in this series [2,20]. The reason is that younger children usually have wider epileptogenic zones or multiple areas of seizure onset within a larger lesion [20]. In this scenario RFTC is not effective as the areas of tissue ablation are too small to effectively disrupt the diffuse epileptogenic network. Of 216 paediatric patients, who underwent stereo EEG in the same time period in our 2 paediatric epilepsy surgery programs 46 children patients (21.3%) were eligible for RFTC, demonstrating that only a small selected group of the paediatric population would be candidates for this new technique.

4.7. Identify patients suitable for SEEG guided RFTC

This study helped identifying patients suitable for SEEG-guided RFTC. First, the SEEG trace should strongly evoked a limited FCD, showing either a low amplitude fast pattern or spike-wave discharges at the onset of the seizures in intralesional location, and/or in contacts where electrical stimulation induced habitual seizures. Secondly, the epileptogenic zone should not lie within eloquent (supporting primary motor or language function) cortex (identified by high frequency cortical stimulation). The RFTC should not be applied to white-matter contacts and stay few millimetres away from a major blood vessel identified on angiography. In the contrary, SEEG-guided RFTC was not considered in patients with an extensive epileptogenic zone, a frequent situation in young children with large focal cortical dysplasia, as RFTC alone would not be expected to have an impact on the disruption of a diffuse epileptogenic network.

5. Conclusion

In this series we have shown that RFTC is a safe method for the paediatric population combining diagnostic and therapeutic intervention, in that it provides important predictive information for surgical resection planning, and can also result in a period of improved seizure control lasting several months with improved life quality. The option of performing RFTC with the same electrodes used for SEEG has additional benefits: 1/ electrodes are already in place and therefore the risk of further implantation used for RFTC in a second session is eliminated, and 2/ EEG recording allows the use of specific ictal EEG patterns to better delineate the targeted contacts for RFTC. An improvement in seizure frequency, often transient, is seen in 2/3 of our paediatric patients as is reported in adults. Moreover, RFTC can be a therapeutic procedure, with no additional placement of intracerebral devices besides those used for diagnostic SEEG recording. Of course, RFTC is not a

contraindication to future surgery if needed. Finally, RTFC could also be useful as a palliative technique for children with an epileptogenic zone overlapping with eloquent areas, with minimal risk of sequelae.

Acknowledgments

We would like to thank all the clinicians who referred the patients to the 2 epilepsy surgery programs in Paris and London and also the neurophysiologists who performed the invasive monitoring and the RFTC. We are grateful to K.Zuber, who did the statistical analysis.

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