Lesion guided stereotactic radiofrequency thermocoagulation for palliative, in selected cases curative epilepsy surgery

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ABSTRACT

Introduction: Resective epilepsy surgery is an established treatment option in patients with pharmaco-resistant, lesion related epilepsy. Yet, if the presurgical work-up proves multi-focal organization of the epileptogenic zone, or the area of intended resection is close to eloquent brain areas, patients may decide against resections because of an unfavorable risk–benefit ratio. We assess if lesion guided cortical stereotactic radiofrequency thermocoagulation (L-RFTC) is a potential surgical alternative in these patients.

Methods: We performed seven procedures of L-RFTC. Three patients had monofocal epilepsy arising close to eloquent structures; in four, invasive pre-surgical workup documented monofocal seizure onset but strong interictal epileptic activity also independent and distant from the seizure onset zone. L-RFTC was restricted to the lesional area (=seizure onset site).

Results: 12 to 37 months after RFTC worthwhile seizure improvement was achieved in 6 patients. One patient became seizure free following complete coagulation of a focal cortical dysplasia, two had had 1–2 auras under tapered but not under continued medication. In one patient only subclinical seizures persisted. In one patient hypermotor seizures were transformed into milder short tonic seizures and another one had a seizure reduction by 50%. Only one patient did not profit at all. One patient developed a persisting neurological deficit.

Significance: In patients with complex epileptogenic zones L-RFTC can lead to worthwhile seizure reduction. This qualifies this procedure as a palliative surgical technique with potential good risk–benefit ratio. In patients with small focal cortical dysplasias L-RFTC may even allow minimal-invasive surgery with curative intention.

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Introduction

Resective epilepsy surgery is an established treatment option for patients with pharmaco-resistant focal epilepsy resulting in significantly better seizure free outcomes than continued medical treatment alone (Jobst and Cascino, 2015). Yet, not every patient who enters a formal presurgical work-up can finally be recommended resective epilepsy surgery. Some patients suffer from multifocal epilepsy or have vast, badly demarcated, or complex organized epileptogenic zones with only a low chance for seizure freedom. Others have overlapping or closely neighboring epileptogenic zones and eloquent brain structures and are in danger of intolerable neurological or cognitive deficits. In these cases palliative epilepsy surgery can be considered (Fauser and Zentner, 2012; García et al., 1982).

The term palliative epilepsy surgery is usually used when a surgical intervention does not offer a high chance for complete seizure
freedom but aims at ceasing particularly disabling seizure types or at decreasing the global seizure frequency at a lower risk than open resective surgery would have in the individual case.

Surgical techniques that are often applied with palliative intention are: intentional incomplete resective surgery of the epileptogenic zone, multiple subpial transactions, corpus callosotomy, stereo-electroencephalography (SEEQ) guided radiofrequency thermocoagulation (RFTC), radiosurgery, deep brain stimulation, and vagus nerve stimulation (for overview see Beniﬁla et al., 2006; Catenoi et al., 2015; Cassou et al., 2015; Englot et al., 2011; Guénot et al., 2011; Ilyas et al., 2014; Malmgren et al., 2015; Novy et al., 2010; Rolston et al., 2015). Palliative thalamotomy via stereotactic thermocoagulation was also applied in patients with non-resectable lesions but was eventually abandoned because of insufficient reduction of seizure frequencies (Wieser, 1994). However, neither of the listed surgical techniques can approximately compete with the seizure freedom rates of resective epilepsy surgery. Therefore, it would be important to have a technique sharing the usually low procedural risk with the established palliative procedures but coming closer to the seizure outcomes of resective surgery. A strategy to improve outcomes could be transferring one of the keys of recent successful developments of resective epilepsy surgery to palliative surgery: magnetic resonance imaging (MRI) guidance of interventions.

In 2014 we published lesion guided stereotactic radiofrequency thermocoagulation (L-RFTC) of two eloquently located bottom-of-sulcus focal cortical dysplasias (FCD) type IIB with favorable outcomes (Engel class 1a and 1b) (Wellmer et al., 2014). We now report our experience with L-RFTC in seven patients with a follow up of 12 to 37 months (mean 22.3 months) in whom four had a clear palliative indication and three were treated with curative intention but risk-considerations argued against classical resective surgery.

**Patients and methods**

**Patient selection**

Between November 2012 and November 2014 seven patients with pharmacoresistant focal onset epilepsy underwent stereotactic, lesion guided RFTC. For biographical data see Table 1. In summary, patients had a disease duration of 3 to 57 years (mean 30.7), had had an average of 11 life-time antiepileptic drugs (range 3–18) but still experienced 10 to 300 seizures per month. All patients were recruited at the Ruhr-Epileptology, Department of Neurology, University Hospital Knappschaftskrankenhaus Bochum and underwent their presurgical work-up there.

**Presurgical work-up**

**Non-invasive work-up**

The presurgical work-up included non-invasive video-EEG-monitoring with seizure registration and 3-Tesla MRI (Verio, Siemens, Erlangen, Germany) following an epilepsy specific protocol (Wellmer et al., 2013 + 3D-FLAIR 1 × 1 × 1 mm) and a morphometric MRI analysis (MAP07; Huppertz et al., 2005). Three patients had an additional 3 Tesla Siemens Prisma MRI examination with a newly developed T2-ZOOMit® sequence (Siemens, Erlangen, Germany; Riffel et al., 2015) to unveil formerly not sufficiently displayed lesions or to show the margins of lesions. In two patients non-invasive work-up was sufficient to allocate the epileptogenic zone to a circumscribed FCD IIB. In these and all other patients the etiological lesion diagnosis was based on MRI morphology. Examples of the lesions before and after L-RFTC are shown in Fig. 1.

In five patients the results of the non-invasive work-up were not conclusive. In addition to the documentation of epileptogenic lesions by MRI (FCD IIB in three patients, suspected FCD type IIA or B in one patient, small cystic lesion in one patient) we found additional epileptogenic lesions in two patients (a contralateral FCD IIB and an ipsilateral temporo-polar encephalocoele, discordant EEG in 4 patients, discordant EEG or magnetoencephalography (MEG) source localization in 3 patients, and discordant positron emission computed tomography (PET) or single photon emission computed tomography (SPECT) in 2 (Table 1).

**Invasive work-up**

The applied invasive work-up in patients 3–7 followed the combined principles of confirmation (that the detected lesion is in fact the site of seizure onset) and exploration (excluding that sites which could alternatively explain the results of non-invasive work-up are involved in seizure onset; Wellmer et al., 2012). Therefore, implantation schemes were very individualized and comprised 1

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**Table 1**

<table>
<thead>
<tr>
<th>Age, gender</th>
<th>Duration [y]</th>
<th>Seizures per mo</th>
<th>Lifetime AED</th>
<th>Lesion</th>
<th>Lesion location</th>
<th>Surface EEG concordant</th>
<th>EEG/MEG SL concordant</th>
<th>PET/SPECT concordant</th>
<th>Invasive EEG concordant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39, f</td>
<td>30</td>
<td>30–60</td>
<td>18</td>
<td>FCD IIB</td>
<td>Right precentral gyrus</td>
<td>Yes</td>
<td>Yes/Yes</td>
<td>–/–</td>
</tr>
<tr>
<td>2</td>
<td>45, m</td>
<td>27</td>
<td>10–20</td>
<td>3</td>
<td>FCD IIB</td>
<td>Left fronto-orbital</td>
<td>Yes</td>
<td>Yes/–</td>
<td>–/–</td>
</tr>
<tr>
<td>3</td>
<td>49, f</td>
<td>47</td>
<td>100–200</td>
<td>8</td>
<td>FCD IIB</td>
<td>Left fronto-lateral but 2nd FCD IIB right frontal</td>
<td>No</td>
<td>No/No</td>
<td>–/–</td>
</tr>
<tr>
<td>4</td>
<td>31, m</td>
<td>21</td>
<td>150–300</td>
<td>12</td>
<td>FCD II</td>
<td>Left temporo-occipital mesial</td>
<td>No</td>
<td>Yes/–</td>
<td>No/No</td>
</tr>
<tr>
<td>5</td>
<td>44, m</td>
<td>30</td>
<td>30–210</td>
<td>14</td>
<td>FCD IIB</td>
<td>Left insular</td>
<td>Yes</td>
<td>Yes/–</td>
<td>–/–</td>
</tr>
<tr>
<td>6</td>
<td>25, f</td>
<td>10</td>
<td>3</td>
<td>4</td>
<td>FCD IIB</td>
<td>Left temporo-occipito-mesial</td>
<td>No</td>
<td>No/–</td>
<td>–/–</td>
</tr>
<tr>
<td>7</td>
<td>57, f</td>
<td>57</td>
<td>20</td>
<td>17</td>
<td>FCD IIB</td>
<td>Left parietal but also encephalocoele left temporo-polar</td>
<td>No</td>
<td>No/Yes</td>
<td>No/–</td>
</tr>
</tbody>
</table>

**AED:** antiepileptic drugs; **FCD:** focal cortical dysplasia, classification according to Palmini and Lüders 2002; **EEG:** electroencephalography; **PET:** 18-Fluorodeoxyglucose positron emission computed tomography; **SPECT:** 99 Technetium single photon emission computed tomography, performed bothly and interictally, computed as SISCOR (subtraction ictal SPECT co-registered with MRI); **second IZ = zone of interictal epileptic activity independent from the seizure onset zone;** – = not applied.

Concordant in the meaning of a prove of mono-focal, lesion-restricted functional pathology.

Concordant in the meaning of a prove of seizure onset within the lesion.
Fig. 1. Three representative examples of pre- and post-operative 3 Tesla MRI of patients undergoing L-RFTC. Upper row—left: FCD IIB of patient 1 located in the right precentral gyrus;—right: one year after L-RFTC at the place of the former lesion only a substance defect remains. Outcome: Engel 1a despite near complete tapering of the medication. Middle row—left: left fronto-orbital FCD IIB of patient 2;—right: postoperative coagulation defect. Outcome: Engel 1b—the patient had one aura when trying to taper his medication. Lower row—left: patient 4 showed a badly demarcated blurring of the gray–white-matter junction and subcortical FLAIR hyperintensity suspicious for an FCD type II. Invasive EEG was able to prove the onset of habitual seizures here but also documented abundant interictal activity left temporo basal where the MRI was negative for additional lesions;—right: Despite intraoperative EEG-based extension of the coagulation not all local epileptic activity could be removed. After 6 months of complete seizure freedom the patient’s preoperative seizures returned. Outcome Engel 3.

to 3 (mean 2) depth electrodes combined with 0 to 7 (mean 4) strip electrodes.

In all implanted patients we documented only one seizure onset zone (SOZ) each. In patients 3, 4, 6 and 7, however, we found one additional remote, highly active interictal discharge area each which did not show coherence with the activity in the SOZ (confirming the discordant non-invasive findings). In patient 5 onset of interictal and ictal activity were restricted to the MRI-detected FCD, remote strip electrodes showed only propagation of this activity.

Decision for L-RFTC and classification of surgery as curative or palliative

In the first two patients (already published with shorter follow-up in Wellmer et al., 2014) the motivation to perform L-RFTC instead of classical open resection was the eloquent localization of the FCD IIB. The intervention was performed with curative intention. This was also the case for patient 5 with a FCD IIB in the dorsal left insula. In patients 3, 4, 6 and 7 our intention was palliative. According to invasive EEG all had complex organized
epileptogenic zones without option for complete resection at good risk–benefit ratio. We explained to all patients that L-RFTC was an individual treatment attempt in the expectation of a lower procedural risk than open resection but a given chance for worthwhile seizure improvement. All patients decided for L-RFTC after repeated information about alternative surgical and non-surgical options mentioning that a later open resection or re-RFTC could be discussed if the first surgery fails. Because of the very individualized treatment decisions in every case this report is a successive case collection and not a prospective study. The publication of our observations is in accordance with the rules of the local ethics committee.

Operative procedures

Operations 1–5 were performed at the Department of Stereotactic Neurosurgery, University of Magdeburg, Germany (surgeon: JV), procedures 6 and 7 were performed at the Department of Neurosurgery, University Hospital Knappschaftskrankenhaus Bochum (surgeon: YP).

L-RFTC was planned based on the lesion extent recognizable on 3 Tesla 3D-FLAIR, co-registered to a contrast-enhanced T1 weighted volume sequence to prevent penetration of blood vessels by the electrodes. For the definition of coagulation sites and trajectories, we used in patients 1–5 a stereotactic brachytherapy treatment planning software (Praezis-Plus, Precisis AG, Walldorf, Germany), developed for stereotactic brachytherapy of intracerebral tumors with iodine-125 seeds, simulating multiple lesions with 4.5 mm diameter each referred to a hypothetical therapeutic isodose line, which finally covered the pathology in total. Lesion size prediction was done relying on the empirically known volume and shape of lesion visible on MRI—follow ups after RFTC (80 °C for 60 s = 60 mm^3) in thalamus and globus pallidum in movement disorders with the same probe as used in this study (TCB013, Inomed, Emmendingen, Germany) (Schmitt et al., 2011). In patients 6 and 7 we simulated same size spheric lesions of 4.5 mm diameter in Iplan Stereotaxy Software (Brainlab, Feldkirchen, Germany). Resulting lesions consisted of multiple single lesion sites along several trajectories. Because of the complex lesion anatomy, 3–7 (mean 5.8) trajectories were necessary in each patient. Coagulations were carried out by a 500 kHz radiofrequency generator (NeuroNSO, Inomed, Emmendingen, Germany).

RFTC was performed under general anesthesia in presence of an epileptologist (JW) who read the intraoperative SEEG recorded directly from the lesioning electrode. The lesioning electrode was inserted via a Riechert–Mundinger frame in cases 1–5 (Tamed, Precisis AG, Walldorf, Germany) and a Leksell G Frame, (Elekta, Sweden) in cases 6 and 7. During the successive insertion of the electrode along the pre-planned trajectories, invasive bipolar 1 channel EEG was recorded via the bipolar contacts every 4.5 mm to recognize interictal discharges outside and within the lesion. When it was possible without putting critical structures at risk, the electrode trajectory was continued for one or two 4.5 mm steps beyond the deepest planned coagulation. EEG was recorded by an XLTEK 32 IOM system (Natus Medical, San Carlos, CA) or an ISIS (Inomed, Emmendingen, Germany).

By reading the intraoperative EEG we recognized that in most patients some epileptic activity was also present in the vicinity of the planned coagulation volume. Although this could not be definitely classified as locally generated or propagated from the lesion we performed few additional coagulations. However, any EEG recording and extra coagulation was restricted to the trajectories since planning and insertion of additional electrodes is not easily done once the surgery had started.

In patient 1 we also performed motor evoked potentials during the surgery to detect the proximity of the pyramidal tract (for details see: Wellmer et al., 2014). This was not necessary in any of the following patients.

The number of coagulations finally performed in these seven patients ranged from 14 to 27 (mean 18.6), with 0 to 9 (mean 2.8) additional coagulation sites because of intraoperative EEG. A single planned coagulation site was left out in patient 1 because motor evoked potentials documented close proximity of the pyramidal tract.

Results

Seizure outcome

The results of the lesion oriented, partially EEG–extended coagulations are summarized in Table 2. One patient achieved complete seizure freedom (Engel 1a), three patients had an outcome of Engel 1b. In two patients, clinical seizures persisted but the improvement was worthwhile (Engel 3). Only in one patient, L-RFTC did not result in any improvement of the seizures.

Detailed commenting on outcomes is necessary for the following cases.

Patient 3 reported to be completely seizure free for 22 months after RFTC although only one of two FCD IIb (the left fronto-lateral in Fig. 2(A1 and A2) and (B1 and B2)) was coagulated. She then complained of morning tiredness and sleep disturbance. Subsequent video-EEG-monitoring revealed up to ten seizures from sleep as before surgery but the post-operative seizures consisted only of very short (<10 s) right arm and leg dystonias and arousals. The previous hypermotor seizure component did not exist any more (in concordance with the observations of her husband). Whether the shorter seizures persisted since surgery or reoccurred later is not clear. The patient herself classifies her outcome as worthwhile improvement (therefore rated as Engel 3).

Patient 7 reports freedom from her pre-operative seizures 12 months after L-RFTC, but an EEG 3 months after surgery recorded a hyperventilation induced subclinical seizure. One year after surgery another EEG documented at the same site (electrode T3) intermittent repetitive spikes and spike-waves typical for a remnant of the focal cortical dysplasia. In fact, during surgery strong epileptic activity was recorded outside the planned coagulation volume at the entry point of one coagulation trajectory. Re-analysis of a pre-operative ZOOMit T2 MRI sequence (but not a standard 3 Tesla with 3D-FLAIR) showed a pale, initially overseen extension of the bottom of sulcus dysplasia to the neighboring crown of sulcus (Fig. 2(C1 and C2) and (D1 and D2)). We classify this outcome as Engel 1b.

Patient 5 is the only one without benefit from L-RFTC. Early after surgery he experienced again around 15–20 seizures per day. The extent of his FCD IIb was underestimated on the pre-operative MRI and the L-RFTC destroyed only a small lesion part. After subsequent open resection of the complete left insula the patient became seizure free (for now 12 months). Histology confirmed the suspected FCD IIb. Patient 5 is the only patient in this series who developed a neurological deficit from the L-RFTC. He suffers from a mostly expressive aphasia most likely due to injury of the arcuate fascicle by the thermocoagulation.

Radiological results

Comparison of the coagulation planning and post-operative MRIs shows a match of anticipated and achieved cortical coagulation volumes in 6 of 7 cases. Only in patient 3 a small piece of lesion between two trajectories questionably remained uncoagulated—possibly explaining the seizure persistence. In patients 5 and 7 the lesion was definitely incompletely coagulated. This
Fig. 2. Importance of optimal MRI for L-RFTC. A and B: In patient 3 the 3 Tesla 3D-FLAIR showed a pale but recognizable bottom of sulcus FCD right frontal (A1) which could be confirmed by morphometric MRI analysis (A2, MAP07). However, the hint for a second left supra-insular FCD could not be confirmed in the FLAIR. The T2 ZOOMit sequence in contrast showed morphological correlates for both lesions (B1 and 2, arrows). C and D: The left parietal FCD IIB of patient 7 in a 3 Tesla 3D-FLAIR sequence (C) and a 3 Tesla T2-ZOOMit sequence (D). Whereas the typical bottom of sulcus part of the FCD IIB is clearly seen in both sequences (C1 and D1), only the ZOOMit shows an extension of the lesion to the adjacent crown of gyrus (C2 at lower end of dashed arrow), explaining the FCD-like epileptic discharges documented here.
Table 2
Outcomes of L-RFTC and suspected mechanisms of action.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Indication</th>
<th>Outcome (Engel classification)</th>
<th>Follow up (months)</th>
<th>Comment on outcome</th>
<th>Suspected mechanism of outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Curative</td>
<td>1a</td>
<td>37</td>
<td>No epileptic seizures since surgery*</td>
<td>Complete destruction of the FCD IIB and the EZ</td>
</tr>
<tr>
<td>2</td>
<td>Curative</td>
<td>1b</td>
<td>29</td>
<td>Two auras under attempt to taper medication, now &gt;18 months aura and seizure free</td>
<td>Incomplete destruction of the EZ but transformation of epilepsy from pharmacoresistant to—sensitive</td>
</tr>
<tr>
<td>3</td>
<td>Palliative</td>
<td>3</td>
<td>22</td>
<td>No improvement of seizures following L-RFTC. Only since open resection Engel 1a (&gt;12 months)</td>
<td>Lesion extent was underestimated on pre-OP MRI. EZ was coagulated only insufficiently</td>
</tr>
<tr>
<td>4</td>
<td>Palliative</td>
<td>3</td>
<td>18</td>
<td>No persisting seizure reduction but short tonic instead of hyper motor seizures</td>
<td>Incomplete destruction of the EZ but truncation of the pathway of propagation of ictal discharge activity</td>
</tr>
<tr>
<td>5</td>
<td>Palliative</td>
<td>1b</td>
<td>18</td>
<td>First 6 months post-op seizure free, then reoccurrence of seizures at 50% of pre-op frequency</td>
<td>Badly demarcable lesion, incomplete coagulation of the EZ</td>
</tr>
<tr>
<td>6</td>
<td>Palliative</td>
<td>1b</td>
<td>18</td>
<td>One aura under forgotten medication, now &gt;12 months aura and seizure free</td>
<td>Incomplete destruction of the EZ but transformation of epilepsy from pharmacoresistant to—sensitive</td>
</tr>
<tr>
<td>7</td>
<td>Palliative</td>
<td>1b</td>
<td>12</td>
<td>Free of clinical seizures but documentation of 1 subclinical seizure 3 months post op and persisting strong spike-focus over FCD at 12 months</td>
<td>Incomplete destruction of the EZ but truncation of the pathway of propagation of ictal discharge activity (now restricted to non-symptomatogenic cortex)</td>
</tr>
</tbody>
</table>

EZ = epileptogenic zone.
* Patient 1 is rated Engel 1a although she reported two events at days 56 and 57 after surgery and in the 2014 paper we judged these as possibly epileptic seizures. Yet, the atypical semiology of these two events (jerks propagating from the left hand to the right hand), and the subsequent 35 months long complete seizure freedom despite near complete tapering of the medication argues that these events were non-epileptic.

was due to the underestimation of the extent of the lesion on the preoperative MRI.

There were neither neurosurgical complications nor unexpected post-operative neurological deficits. Patient 5 with the post-operative aphasia was informed preoperatively about the high possibility of aphasia but decided to accept this risk because of up to 20 tonic seizures per day.

A separate paper on the lesioning technique will cover further aspects of coagulation planning and performance.

Discussion

Our case series indicates that neocortical, lesion guided RFTC can deliver favorable seizure outcomes. The heterogeneity of epileptogenic zones and outcomes in our patients, however, makes a detailed case analysis necessary to understand the possible mechanisms of antiepileptic action of L-RFTC.

Antiepileptic mechanism of L-RFTC in multifocal epilepsies

Four patients had complex organized epileptogenic zones. These patients received L-RFTC in truly palliative intention and achieved nevertheless favorable outcomes (Engel 1b, 1b and 3). This is noteworthy since in each of these patients pre-operative invasive EEG documented strong and independent interictal epileptic activity remote from the later coagulated lesional area. With regard to the underlying mechanisms our interpretation is that in patient 6 (as in the monofocal patient 2) L-RFTC transformed epilepsy from pharmacoresistant to pharmacosensitive—possibly by destroying the medically uncontrollable core of the epileptogenic zone leaving a better to control shell or a medically controllable second epileptogenic zone in place.

In patient 7 with incomplete FCD IIB coagulation and a secondary left tempo-polar encephalopathy one can speculate that the documented post-operative sub-clinical seizure (and interictal discharge activity) arose from a non-symptomatic part of the incompletely coagulated FCD IIB and did not spread to symptomatogenic brain areas. In patient 3 with two FCD IIB and continued seizures but truncated seizure semiology one can discuss if the incomplete coagulation of the left suprasylvian epileptogenic lesion is responsible for the prevention of a spread of seizure activity to areas responsible for the pre-RFTC hypermotor behavior.

Finally, in patient 4, seizures reappeared following the L-RFTC despite six months of complete seizure freedom. The pre- and post-operatively identical seizure semiology indicates that the volume of L-RFTC was obviously not sufficient to destroy his complete epileptogenic zone or to transform his epilepsy from pharmacoresistant to persisting pharmacosensitive.
Summarizing the patients with complex epileptogenic zones it appears that lesion oriented but with regard to interictal activity incomplete thermocoagulation is worth being applied under the prerequisite of continued anticonvulsive medication. Possible mechanisms are the destruction of the pharmacoresistant core of the epileptogenic zone or a block of seizure spread close to its onset. Yet, the long-term outcome of all patients remains to be assessed to learn if seizure remission or truncation is enduring.

Antiepileptic mechanism of L-RFTC in other epileptogenic lesion entities—Comparison with the literature

Comparable effectiveness of lesion guided RFTC has previously been shown in other settings with usually widespread, often multifocal interictal EEG activity. The largest experience (although mostly from a single research group) exists with hypothalamic hamartomas (Homma et al., 2007; Kameyama et al., 2015). It is well known, that pre-operative EEG in hypothalamic hamartomas often shows wide-spread or multifocal interictal and ictal activity. Despite this, the group of Kameyama reports around 70% seizure freedom after L-RFTC of the hypothalamic hamartomas. There is no report about postoperative EEG and medication. However, as in our cases it appears reasonable to presume either a destruction of the epileptogenic zone or its pharmacoresistant core, or a truncation of the pathway of ictal activity from the hypothalamic hamartoma as mechanisms of action.

Publications about patients with periventricular heterotopias (PNH) are less extensive. The largest experience comes from Milan, Italy (Cossu et al., 2015). In a series of 89 patients receiving primarily SEEG-guided RFTC, 12 had PNH as epileptogenic lesion. Following coagulation, 8 became seizure free. In addition to the above mentioned mechanisms of action, in these cases another has to be taken into consideration: a destruction of an essential node in network of PNH and overlying cortex. That study is remarkable not only for the comparatively good outcome in patients with PNH. It also indicates a turning point in the application of traditional SEEG-guided interventions: Cossu and colleagues describe that the arrangement of depth electrodes was progressively implemented in a fashion that allows destroying the lesion as completely as possible and that this may have contributed to the favorable outcomes. This supports our argument for lesion guidance of RFTC. Schmitt et al. reported the application of L-RFTC on a single patient with PNH in a protocol very similar to ours (Schmitt et al., 2011). One year after surgery the patient is classified as Engel class Ib (seizure free besides isolated aura). Further cases have to be collected to judge the final value of L-RFTC in PNH patients.

The role of invasive EEG in defining coagulation sites

What role invasive EEG should play for tailoring of coagulations in patients with poorly demarcated lesions or when epileptic activity is found outside circumscribed lesions remains to be clarified. From our limited data we cannot conclude to what extent strong interictal activity documented outside the coagulation zone predicts poor seizure outcome. At least in midterm a transformation from pharmacoresistant to pharmacosensitive was possible when only a part of strong, quasi-continuous interictal activity was coagulated.

Ictal EEG changes recorded via depth electrodes, which were for a long time understood to be essential to guide SEEG-RFTC is also increasingly recognized as an imperfect coagulation guide. Cossu et al. (2015) and Catenoix et al. (2015) both report mostly unfavorable outcomes following traditional SEEG-RFTC procedures that were applied without strong lesion guidance. They explain this with the fact that a complete destruction of an epileptogenic zone cannot be achieved due to the restricted spatial sampling of SEEG.

However, same as Cossu et al. and us, Catenoix et al. expect that with increasing density of RFTC within intrinsically epileptogenic lesions (such as dysplasias) the chance to achieve seizure freedom might ameliorate. This would mean a development of SEEG-RFTC in the direction of L-RFTC as applied in our case series.

The role of MRI in defining coagulation sites

A very critical point in planning and execution of L-RFTC is optimal pre-surgical MRI. Although in our series all patients had state of the art 3 Tesla MRI including a highly sensitive 3-dimensional (3D) FLAIR with a resolution of 1 × 1 × 1 mm we had two cases in which this was not sufficient. In patient 3 the finally coagulated FCD was not recognizable by visual evaluation of the MRI, even retrospectively (Fig. 2(A1 and A2) and (B1 and B2)). It was depicted only by the automated morphometric analysis MAP07 (Huppertz et al., 2005) and confirmed on the recently developed ZOOMit parallel transmit T2 sequence with isotropic 0.5 mm voxels acquired on a 3 Tesla MRI Scanner (Prisma, Siemens, Erlangen, Germany). In patient 7 the retrospective evaluation of the ZOOMit sequence but again not the standard 3 Tesla 3D FAIR showed a pale extension of the bottom of sulcus dysplasia to the next crown of gyrus as explanation for the strong interictal epileptic activity that was unexpectedly recorded at the entry point of one coagulation electrode trajectory (Fig. 2(C1 and C2) and (D1 and D2)). In patient 5 we underestimated the size of the FCD IIb based on the initial evaluation. Only after the non-successful coagulation of a FCD in the dorsal left insula we understood that a pale signal increase in the complete left insula (recognizable only in one sagittal plane of the 3D-FLAIR) was a correlate of a whole insula FCD (that was later confirmed histologically). This patient did not have a preoperative ZOOMit MRI. The critical role of MRI recognized in our study should prompt epileptologists and neurosurgeons to apply lesioning methods (but also resective epilepsy surgery) only on grounds of optimal imaging.

Comparison of L-RFTC with other lesioning techniques

There is currently not enough evidence to estimate whether L-RFTC might have advantages over other lesion guided minimal invasive epilepsy surgery techniques. For both laser ablation and radiosurgery more promising results than for non-lesion oriented procedures (SEEG-RFTC, callosotomy, multiple subpial transections, vagus nerve stimulation, deep brain stimulation) have been reported, but usually worse outcomes than following classical resections (Levis et al., 2015; Quigg and Harden, 2014). We expect the effectiveness of L-RFTC to be in the range of laser ablation and radiosurgery. Further studies are required to examine this. Beyond seizure freedom, these studies must address also the incidence of procedure associated early and late complications, the immediateness of seizure ceasing effects, the maximal possible ablation volume, and economic issues.

In the context of the different lesion guided techniques L-RFTC might have two advantages (when the currently questionable value of intraoperative EEG is not included): one argument for L-RFTC is the possibility to perform motor evoked potentials via the tip of the coagulation device (Wellmer et al., 2014). This might perform better than only including tractography into neuronavigation to prevent damage to the pyramidal tract. Also language mapping with intraoperative electrical stimulation should be possible with L-RFTC under the conditions of awake surgery to prevent postoperative aphasia as we observed in our case 5. A disadvantage of L-RFTC, however, is the restricted tissue volume that can be destroyed with a single coagulation procedure. In larger lesions laser ablation and radiotherapy with bigger coagulation volumes might prove advantageous.
Outlook of L-RFTC

Summarizing the results of our patient series it appears justified continuing research on seizure outcomes and tolerability of L-RFTC. Based on current understanding, candidates for the palliative application of L-RFTC are patients with circumscribed, well MRI-demarcated epileptogenic lesions which are either difficult to access for resection or close to eloquent structures and patients who have additional epileptogenic zones and therefore an unfavorable risk–benefit-ratio for resections. To what extent it will be justified in the future to apply L-RFTC to neocortical lesions alternatively to open resection as minimal invasive intervention with curative intent also remains to be examined.

Disclosure

None of the authors has any conflict of interest to disclose.

Ethical publication statement

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.

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