Utility of 7 tesla MRI brain in 16 “MRI Negative” epilepsy patients and their surgical outcomes

Himanshu K. Sharma a,⇑,1, Rebecca Feldman b, Bradley Delman a, John Rutland a, Lara V. Marcuse c, Madeline C. Fields c, Saadi Ghatan d, Fedor Panov d, Anuradha Singh c,2, Priti Balchandani a,e

a Icahn School of Medicine at Mount Sinai, Department of Diagnostic, Molecular and Interventional Radiology, New York, NY, USA
b University of British Columbia, Computer, Math, Physics, and Statistics, 3187 University Way, Kelowna, BC CAN V1V 1V7, USA
c Icahn School of Medicine at Mount Sinai, Neurology, New York, NY, USA
d Icahn School of Medicine at Mount Sinai, Neurosurgery, New York, NY, USA
e Icahn School of Medicine at Mount Sinai, BioMedical Engineering and Imaging Institute, New York, NY, USA

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Abstract

The objective is to quantitatively assess surgical outcomes in epilepsy patients who underwent scanning at 7T MRI whose lesions were undetectable at conventional field strengths (1.5T/3T).

16 patients who underwent an initial 1.5T/3T scan that was marked as non-lesional by a neuroradiologist and were candidates for epilepsy surgery were scanned at 7T. The 7T findings were evaluated by an expert neuroradiologist blinded to the suspected seizure onset zone (sSOZ). The relation of the neuroradiologist’s findings compared with the sSOZ was classified as non-definite (no 7T lesion or lesion of no epileptogenic significance, or lesion of epileptogenic potential which localizes to the patient’s sSOZ but is not the definitive cause), or definite (7T lesion of epileptogenic potential that highly localizes to the sSOZ and is confirmed through surgical intervention). Each patient underwent neurosurgical intervention and postoperative Engel outcomes were obtained through retrospective chart review by an epileptologist.

Of the 16 patients, 7 had imaging findings of definite epileptogenic potential at 7T while 9 had non-definite imaging findings. 15 out of 16 patients had Engel I, II, or III outcomes indicating worthwhile improvement. Patients with definite lesion status achieved Engel I surgical outcomes at higher rates (57.1%) than patients with non-definite lesion status (33.3%). Patients with normal clinical diagnostic scans at lower field strengths who have definite radiological findings on 7T corresponding to the sSOZ may experience worthwhile improvement from surgical intervention.

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1. Introduction

About 20–30% of patients with focal epilepsy are “MRI-negative” at conventional field strengths (1.5 or 3T), i.e., they lack a detectable lesion [1]. “Non-lesional” cases have been associated with poor surgical outcomes [2]. Advanced imaging techniques can better define the lesion, which may improve surgical outcomes. Preliminary studies using ultra-high field MRI scanners operating at 7T or higher confer better resolution due to improved signal to noise ratio (SNR) compared to lower field strengths, which may aid detection of more subtle structural abnormalities in epilepsy cases previously labeled non-lesional [3,4]. However, the role of 7T MRI in the neurosurgical management of MRI-negative epilepsy patients remains poorly described in the literature. Prior work has reported qualitative surgical outcomes for 10 patients scanned at 7T [7]. Here, we present our quantitative 6-year single-institution experience in the management of 16 epilepsy patients with MRI-negative epilepsy who underwent imaging with 7T and subsequent epilepsy surgery. We assessed Engel outcomes of epilepsy surgery in our MRI-negative case series at follow-up, and analyzed differences in 7T findings and surgical outcomes.

2. Methods

2.1. Patient population

Following approval from the Icahn School of Medicine Mount Sinai Institutional Review Board, 37 patients were prospectively
recruited to undergo 7T imaging between 2013 and 2018. 16 out of 37 patients were MRI-negative focal epilepsy patients who were candidates for epilepsy surgery. These patients underwent subsequent epilepsy surgery and were included in the analysis. Patients with recent neurosurgical intervention or contraindications to MRI were excluded. Demographics, clinical presentation, MRI findings, and long-term surgical outcomes were obtained through review of electronic medical records.

### 2.2. Imaging methods

The 7T imaging protocol was comprised of T1-weighted, T_{2}-weighted and susceptibility-weighted MRI sequences. Four sequences were obtained at a coronal-oblique angle and two sequences were obtained in the axial plane. Sequence details are provided as a supplementary endnote. 3

In our case series, 16 patients qualified (6 males, 10 females), with a mean age of 38.5 years (range 23 – 68). The mean age of patients at surgery was 35.5 years and the mean age at follow-up was 37.9 years. To qualify, patients had prior 1.5T and/or 3T MRI scans at our institution reported as non-lesional by neuroradiologists with a certificate of added qualification (CAQ). 7T imaging obtained in this protocol was also evaluated by a CAQ-neuroradiologist blinded to the suspected seizure onset zone (sSOZ) as determined by clinical data, scalp EEG, and other neuroradiologic findings (including PET and SPECT). The relation of the neuroradiologist’s findings compared with the sSOZ was classified as non-definite (no 7T lesion or lesion of no epileptogenic significance) or definite (7T lesion of epileptogenic potential that highly localizes to the sSOZ) as determined by clinical data, scalp EEG, and other neuroradiologic findings (including PET and SPECT). The relation of the neuroradiologist’s findings compared with the sSOZ was classified as non-definite (no 7T lesion or lesion of no epileptogenic significance) or definite (7T lesion of epileptogenic potential that highly localizes to the sSOZ and is confirmed through surgical intervention) [7]. Each patient underwent neurosurgical intervention with intention of curing seizures through resection, ablation, or RNS or VNS implantation. Engel outcomes were determined at 12 months follow-up through retrospective chart review by our epileptologists [5]. Any findings on the 7T scans prompted re-evaluation of conventional field-strength imaging to validate and confirm the potential new seizure focus. No additional invasive measures were performed on 7T data alone without validation of either scalp EEG and/or standard-of-care clinical diagnostic data.

### 3. Results

#### 3.1. Clinical presentation and imaging findings of patients

Table 1 lists MRI abnormalities identified on 7T. Nine out of 16 patients exhibited hippocampal or cortical malformations (cortical...
dysplasia, cortical thickness abnormalities, or polymicrogyria). Five of those nine patients exhibited hippocampal asymmetry, two exhibited cortical malformations, and two demonstrated hippocampal asymmetry as well as cortical dysplasia. Three patients exhibited ventricle asymmetry. One patient had an arachnoid cyst and a meningioma, and one patient had a cavernoma. Two patients lacked overt imaging abnormality at any field strength. Fig. 1 depicts examples of lesions visible at 7T not identified at lower field strengths.

Of the 16 patients, seven (43.8%) had imaging findings judged to be of epileptogenic potential (definite). Nine patients (56.3%) had imaging findings without epileptogenic potential (non-definite). Of these nine patients, three demonstrated ventricular asymmetry, three demonstrated hippocampal asymmetry, one had a meningioma and an arachnoid cyst, and two had no imaging findings.

3.2. Surgical interventions and Engel outcomes

The surgical interventions performed on the patients and their Engel outcomes at 12-month follow-up are also summarized in Table 1. Eleven patients received invasive stereo EEG implantation (SEEG) and an additional surgical intervention. Four patients

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Fig. 1. Sample imaging of lesions visible on 7T imaging. 1a. Patient 14, Polymicrogyria. Axial T2-weighted imaging at 1.5T (A) and 7T (B). The posterior insular polymicrogyria was not detected at 1.5 T but is clearly resolved at 7T (see lobulated gray matter pattern emphasized by arrows in magnified 7T inset, B1) 1b. Patient 8, Hippocampal Asymmetry. Coronal T2 weighted images at 3T (A) and 7T (B). The 7T image has superior visualization of both hippocampal formations, and in particular more precisely highlights the contours of the smaller left side hippocampus better than the 3T scan was able to.
underwent resection, three underwent laser ablation, one received a VNS, and eight were implanted with RNS.

Note that 11 out of 16 patients had their lesion findings targeted during neurosurgical intervention. Of those 11, seven had definite imaging findings, and four had non-definite findings. In 13 patients, the surgical intervention matched the sSOZ as defined by SEEG. Five of seven patients with definite imaging findings received surgical interventions that matched the sSOZ confirmed by SEEG. Two of the seven patients with definite findings did not have an SEEG implanted and therefore the sSOZ was not confirmed. Eight of nine patients with non-definite findings underwent surgical interventions that matched the sSOZ as defined by SEEG. One patient with a non-definite finding was treated with a VNS and their intervention did not match the sSOZ as defined by SEEG.

To analyze surgical outcomes, we grouped patients by Engel class. Postoperative Engel outcomes were obtained through evaluation of medical records by our epileptologists. Following surgery, seven patients were classified as Engel I, one as Engel II, seven as Engel III, and one as Engel IV (see Table 1). Of seven patients with definite lesion status, four patients (57.1%) were free of disabling seizures (Engel I), with two of those four achieving complete seizure freedom (Engel IA). Three patients (42.9%) showed reduction in seizure burden (Engel III). All patients with definite lesion status demonstrated ‘worthwhile improvement’ after surgery. Of the nine patients with non-definite lesion status, eight (88.9%) demonstrated ‘worthwhile improvement’ (Engel III and above). Three of these nine patients (33.3%) were free of disabling seizures (Engel I). One patient (11.1%) showed ‘no worthwhile improvement’ (Engel IV).

4. Discussion

This study analyzed patients with epilepsy with no structural abnormalities detected at 1.5 or 3T MRI. Results suggest that in general 7T imaging, which may be leveraged for higher SNR and/or improved resolution, enabled detection of possible epileptogenic abnormalities not clearly identifiable at lower field strengths. In drug-resistant focal epilepsy patients, localization of a structural lesion on MRI is critical for pre-operative planning and is associated with better surgical outcomes [6].

7T imaging was found to be well-tolerated among the patient population. Prior studies have shown 7T imaging have a similar safety profile to 3T, except for increased acoustic noise and transitory physiological effects [7]. This study was limited to adults over the age of 18 because the 7T scanner used for the case series was approved with respect to the specific absorption rate (SAR) for adults. However, the increased SNR of 7T imaging could be a useful tool in revealing sources of epilepsy in children. Additional technical and safety considerations are required to ensure 7T imaging in children is within conservative SAR limits.

Of the 16 patients studied, a neuroradiologist could detect a definite lesion in seven patients (44%), and a non-definite lesion in nine patients (56%). 7T imaging was used to complement clinical data to identify neurosurgery candidates. We found 7T MRI a useful additional tool to clinical and electrographic data for planning SEEG electrode placement and identification of the sSOZ, because focal targeting of a potentially epileptogenic lesion may confer lower collateral morbidity. 7T MRI data was not used independently to guide surgical decision making. Findings on 7T were validated with conventional field-strength imaging and clinical data.

Of the 16 patients in the study, 15 (93.8%) had Engel I, II, or III outcomes indicating worthwhile improvement following surgery. Patients with definite imaging findings experienced freedom from disabling seizures after neurosurgical intervention at a greater rate (57.1%) than patients with non-definite imaging findings (33.3%). This preliminary investigation suggests that patients with epilepsy that is non-lesional at conventional field strength may benefit from 7T imaging. 7T imaging, in conjunction with clinical and EEG data, may be a useful tool in determining whether MRI-negative epilepsy patients are candidates for neurosurgical intervention. Additionally, our study suggests that enhanced detectability of lesions at 7T MRI may be predictive of the likelihood of achieving seizure freedom in patients with MRI-negative drug resistant epilepsy. Further study of 7T imaging in MRI-negative epilepsy patients is warranted to determine its potential role in clinical practice.

5. Limitations

This study does have some limitations. The relatively small number of patients in this case series prevents statistical validation of the diagnostic value of 7T compared to lower field strength imaging.

Additionally, the study is limited by the strength of the patients’ initial diagnostic scan. Patients underwent 1.5T or 3T MRI scans at the time of enrollment based on the scanning protocol of the clinical or referring site. Retrospective re-examination of some of the initial scans, particularly those obtained at 3T, may have been read as lesional and not qualified for inclusion. However, the initial scans were deemed sufficient clinically when interpreted and non-lesional by the care team. The study was not designed as a comparative 3T vs. 7T study as we did not have control over initial clinical field scans.

This analysis applied only to patients who received surgery. A larger subset of patients did not undergo surgery. In some cases, abnormalities were found and surgery was not pursued. 7T imaging was not conducted postoperatively to objectively measure the effect of surgical intervention because it was beyond the scope of this study and many patients were ineligible due to implanted RNS electrodes at the time of the study. Heterogeneity among patients in the epileptogenic structural abnormality undergoing surgical intervention also limits our assessment of surgical outcomes.

6. Conclusions

Here we detail our institutional experience with surgical treatment of epilepsy patients following imaging using 7T MRIs. We demonstrate that focal epilepsy patients with non-lesional clinical diagnostic scans at lower field strengths who have definite radiological findings on 7T corresponding to the sSOZ are likely to experience worthwhile improvement from surgical intervention. Patients whose 7T findings had non-definite lesion status in relation to the sSOZ benefited from surgical intervention at lower rates. Our preliminary findings in this case series suggest that there is value in performing a larger study with a greater sample size to assess the utility of 7T in surgical treatment of patients with focal epilepsy.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2020.100424.

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