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Usage of SWI (susceptibility weighted imaging) acquired at 7 T for qualitative evaluation of temporal lobe epilepsy patients with histopathological and clinical correlation: An initial pilot study

Benjamin Y.M. Kwan [b], Fateme Salehi [b], Pavlo Ohorodnyk [b], Donald H. Lee [b], Jorge G. Burneo [d], Seyed M. Mirsattari [d], David Steven [d], Robert Hammond [e], Terry M. Peters [a,b,c], Ali R. Khan [a,b,c,*]

[a] Imaging Research Laboratories, Robarts Research Institute, Western University, 1151 Richmond St. North, London, Ontario, N6A 5B7, Canada
[b] Department of Medical Imaging, Schulich School of Medicine and Dentistry, Western University, 1151 Richmond St. North, London, Ontario, N6A 5B7, Canada
[c] Department of Medical Biophysics, Schulich School of Medicine and Dentistry, Western University, 1151 Richmond St. North, London, Ontario, N6A 5B7, Canada
[d] Epilepsy Program, Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, 1151 Richmond St. North, London, Ontario, N6A 5B7, Canada
[e] Department of Pathology and Laboratory Medicine, Schulich School of Medicine and Dentistry, Western University, 1151 Richmond St. North, London, Ontario, N6A 5B7, Canada

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ABSTRACT

Objectives: Ultra high field MRI at 7 T is able to provide much improved spatial and contrast resolution which may aid in the diagnosis of hippocampal abnormalities. This paper presents a preliminary experience on qualitative evaluation of 7 T MRI in temporal lobe epilepsy patients with a focus on comparison to histopathology.
Methods: 7 T ultra high field MRI data, using T1-weighted, T2*-weighted and susceptibility-weighted images (SWI), were acquired for 13 patients with drug resistant temporal lobe epilepsy (TLE) during evaluation for potential epilepsy surgery. Qualitative evaluation of the imaging data for scan quality and presence of hippocampal and temporal lobe abnormalities were scored while blinded to the clinical data. Correlation of imaging findings with the clinical data was performed. Blinded evaluation of 1.5 T scans was also performed.
Results: On the 7 T MRI findings, eight out of 13 cases demonstrated concordance with the clinically suspected TLE. Among these concordant cases, three exhibited supportive abnormal 7 T MRI findings which were not detected by the clinical 1.5 T MRI. Of the ten cases that progressed to epilepsy surgery, seven showed concordance between 7 T MRI findings and histopathology; of these, four cases had hippocampal sclerosis. SWI had the highest concordance with the clinical and histopathological findings. Similar clinical and histopathological concordance was found with 1.5 T MRI.
Conclusions: There was moderate and high concordance between the 7 T imaging findings with the clinical data and histopathology respectively.

1. Introduction

Epilepsy is the leading neurological disorder in terms of years of life lost to disease, with more than one-third of the patients being refractory to pharmacotherapy [1]. Temporal lobe epilepsy (TLE), and in particular hippocampal sclerosis (HS), is a common form of medically refractory epilepsy [2]. Surgical intervention is the standard of care in many of these patients. In those with TLE, a randomized control trial by Wiebe et al. showed that surgery results in seizure-free status in 58%, compared to 8% with medical treatment [3]. In addition, surgical outcomes in patients with underlying lesions are more favourable [4,5]. In 20–30% of patients with refractory epilepsy, no structural abnormalities are identified on MRI, and patients with no discernible MRI lesions are more likely to have their surgery delayed than those with perceptible lesions on MRI [2]. In the absence of detectable structural lesions on MRI, patients often undergo invasive EEG recordings including insertion of subdural electrodes, which are associated with a risk of complications, prolonged hospital stay, and higher costs [6,7]. Recent studies have shown that 3 T MRI (as compared to 1.5 T MRI) improved identification of lesional abnormalities in patients previously classified as 'non-lesional' in 5% of cases and changed the diagnosis or prognosis of the underlying abnormality in 26% of the studied patients [2].

Evaluation for the presence of hippocampal abnormalities at 1.5 T and even 3 T field strengths is limited by spatial resolution and insufficient contrast (Fig. 1) [8]. Features of HS on MR imaging include the presence of atrophy, disruption of internal architecture and hyperintense signal on T2-weighted MR images [9]. A normal-appearing hippocampus occurs in up to 40% of the cases based on post-surgical histopathological study of resected temporal lobes [10]. Recent studies

* Corresponding author at: Robarts Research Institute, Departments of Medical Biophysics & Medical Imaging, Western University, 1151 Richmond St N, London, ON N6A 5B7, Canada.
E-mail address: alik@robarts.ca (A.R. Khan).

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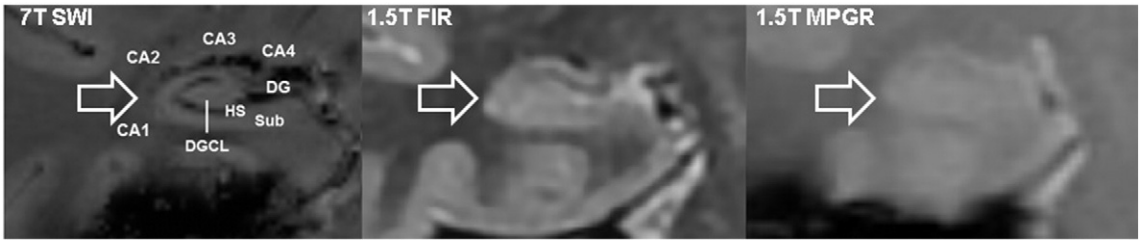

Fig. 1. A. Coronal SWI N4 image acquired at 7 T. Depiction of normal hippocampal anatomy in the normal right hippocampus of case 5 (subiculum (Sub), dentate gyrus (DG), dentate granule cell layer (DGCL), hippocampal sulcus (HS)). Comparison images at 1.5 T on FIR and MPGR are shown which do not depict the intricate hippocampal anatomy well. Note the signal drop out at the inferior temporal lobe on 7 T which is a common artifact seen.

using 7 T MR imaging have shown its superior diagnostic benefits in various pathologies including multiple sclerosis, cerebrovascular diseases, aneurysms, cavernous malformations, polymicrogyria, and brain tumors [11,12]. T2*-weighted MR images acquired at 7 T have previously been shown to depict hippocampal subfield structures as small as 100 μm [13]. However there are drawbacks to higher field strength imaging, including greater signal dropout in areas of local susceptibility differences (sinuses), and a higher level of inhomogeneities in the magnetic fields, which can cause distortions and signal loss artifacts.

The aim of the current study was to 1) determine the ability of 7 T MR imaging (and particularly susceptibility weighted images (SWI)) to detect hippocampal and mesial temporal lobe abnormalities in patients before temporal lobe resection and 2) evaluate concordance of 7 T MRI findings with post-operative histopathological results which can serve as a basis for validation of imaging findings.

2. Methods

Ethics approval was obtained through our institutional review board including participation of patients under 18 years of age. All human and animal studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Patients (male or female) with a history of drug-resistant TLE aged 16–65 years old were recruited for this study. Exclusion criteria included patients with severe coexisting or terminal systemic disease and those unsuitable for MRI evaluation. Thirteen patients undergoing evaluation for epilepsy were scanned using the 7 T MRI scanner. Each patient also underwent standard clinical 1.5 T MRI, prolonged video-EEG, and neuropsychological testing, as part of the clinical epilepsy evaluation at an academic tertiary care center. Seven patients also underwent invasive EEG electrode placement. Clinical data were collected for each patient, including age at surgery, gender, suspected epilepsy type, clinical 1.5 T MRI reports, EEG reports, subdural electrode recording reports, clinical follow-up notes post resection and corresponding histopathology reports if applicable.

Ultra high field data were acquired on a 7 T neuroimaging optimized MRI scanner (Agilent, Santa Clara, CA, USA/Siemens, Erlangen, Germany) using a 16-channel transmit-receive head coil array constructed in-house. The imaging sequences used for this study were a multi-echo gradient-echo sequence with six echoes acquired with a 0.5 mm in-plane resolution (TR = 40 ms, TE = 4.57 ms, echo spacing = 4.89 ms, flip angle = 13 degrees, NEX = 1, matrix = 256 × 360, 80 slices, slice thickness = 1.5 mm, in-plane resolution 0.5 mm, FOV = 128 × 180 × 120 mm, acquisition time = 12 min), with slices acquired perpendicular to the long axis of the hippocampus in a coronal oblique orientation, and a T1-weighted MPRAGE sequence (matrix = 256 × 512 × 172, resolution = 0.58 × 0.43 × 1 mm, acquisition time = 5:42 min). For the multi-echo image, the magnitude images for each of the six echoes were averaged to produce a T2*-weighted image. SWI were generated from the multi-echo images using a frequency mask derived from the unwrapped and filtered phase images, using a process described in detail previously [14]. These volumes (T1, T2*, SWI), three for each patient, had randomized identification numbers assigned and were converted to DICOM format for blinded review by a fellowship trained neuroradiologist with over 30 years of experience. Additionally, each volume was processed to remove shading artifact using a non-uniformity intensity normalization filter (N4) [15], which we refer to henceforth as N4, to assess the impact of viewing images with and without shading artifact removal.

Clinical MRI data was acquired on a 1.5 T MRI scanner (GE, USA). The imaging protocol for epilepsy imaging at this institution included T2 axial (2 mm contiguous slices, matrix = 256 × 256 mm, NEX = 1, TR = 12,666 ms, TE = 49 ms, FOV = 22 cm), FSEIR coronal (3.5/1, matrix = 288 × 256 Zipped to 512 × 512, TR = 5116 ms, TE = 15 ms, TI = 150 ms, FOV = 22 cm), gradient echo coronal (5/1, matrix = 256 × 192 mm, NEX = 2, FOV = 20 cm), 3D FLAIR coronal (with 1.8 mm partitions, reconstructed at 0.9 mm intervals, TR = 6000 ms, TE = 122 ms, TI = 1872 ms, FOV = 24 cm), 3D T1 axial (with 2 mm partitions, reconstructed at 1 mm intervals, FOV = 24 cm, matrix = 256 × 256 mm) and diffusion axial ((6 directions, B0, B1000), 5 mm contiguous, matrix = 128 × 192, FOV = 24 cm, TR = 8100 ms, TE = 88.8 ms).

Each of the patient's 7 T MRI data was reviewed by the neuroradiologist using a qualitative grading scale while blinded to clinical information. Volumes were graded for scan quality and the presence of artifact. Qualitative grading of the mesial temporal lobe internal architecture (including note of signal abnormality and/or architectural abnormalities), mesial temporal lobe size and temporal neocortical architecture was performed (Table 1). The rest of the brain architecture was briefly evaluated for any gross abnormalities. The results of the neuroradiologist were converted into a single rating for each category by taking the most abnormal grade assigned for each category among the six volumes evaluated. Additionally, the grades of 'normal' or 'possibly normal' were merged into a single rating value of "normal" and the grades of 'possibly abnormal' or 'definitely abnormal' were merged into a single rating value of "abnormal". A second reader (a senior radiology resident) also evaluated the 7 T MRI scans using the qualitative grading scale and assigned a single rating for each category while taking into account all the volumes. A Cohen's kappa was calculated between the two readers (GraphPad Software, La Jolla, CA, USA and StatsToDo, Australia).

The neuroradiologist also blindly evaluated the 1.5 T MRI data in a similar fashion.

Resected specimens were processed according to established protocol. Briefly, specimens were fixed in 10% buffered formalin. Fixed

Table 1
Qualitative rating scale.

Merged rating of 'Normal' or 'Abnormal' (for each hemisphere) per category
1. Mesial temporal lobe internal architecture (including signal abnormalities)
2. Mesial temporal lobe size
3. Temporal neocortical architecture
4. Rest of brain architecture