7T MRI detection of epileptogenic foci in previously non-lesional patients with focal epilepsy

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Introduction: Epilepsy, a chronic condition characterized by recurrent seizures, affects almost 3 million people in the United States. 15% to 30% of these individuals are refractory to pharmacotherapy [1, 2]. In many of these cases, surgical resection of the brain abnormality acting as the source of seizure activity is recommended to eliminate or reduce seizures. Magnetic resonance imaging (MRI), in conjunction with electroencephalography (EEG), plays a vital role in the preoperative localization and characterization of epileptogenic abnormalities [3]. Higher field MRI scanners, such as those operating at 7 Tesla (7T), have been found to be useful in characterizing hippocampal sclerosis [4, 5], cortical dysplasias [6], and vascular malformations [7] associated with epilepsy. Here we report preliminary results for a study designed to assess the value of 7T imaging to reveal subtle abnormalities acting as epileptogenic foci in patients with idiopathic focal epilepsy who have non-lesional diagnostic MRI scans. We report all abnormalities detected at 7T, including those that have had an impact on surgical planning and treatment course as well as findings that could assist with better understanding the etiology of the disease.

Methods: 17 healthy controls and 20 epilepsy patients (14 male, ages 19-57 years) with previous normal MRI scans were recruited for the 7T imaging study. Each subject had indications of focal epilepsy, identified through semiology and EEG, of unknown etiology with no record of family history, traumatic brain injury, brain infection, or febrile incident. The images were acquired on a 7T MAGNETOM scanner (Siemens, Erlangen) using a 32-channel receive Nova Medical head coil. The MRI protocol consisted of: A) 4 sequences acquired at a coronal oblique angle perpendicular to the hippocampus: MP-RAGE (TR 3000 ms, TI 1050 ms , TE 2 ms, voxel 0.7x0.7x0.7 mm^3), MP2RAGE [8] (TR 6000 ms, TI1 1050 ms , TI2 3000, TE 5.06 ms, voxel 0.8x0.8x0.7 mm^3), T_2 TSE (TR 6000 ms, TE 69 ms, voxel 0.4x0.4x2.0 mm^3), and FLAIR (TR 9000 ms, TI 2600 ms, TE 123 ms, voxel 0.36x0.36x3 mm^3); and B) 2 sequences acquired axially: Susceptibility weighted imaging (SWI) (TR 23 ms, TE 14 ms, voxel 0.21x0.21x1.5 mm^3), and T_2 TSE (TR 6000 ms, TE 69 ms, voxel 0.4x0.4x2.0 mm^3). The 7T images were inspected by an experienced neuroradiologist, and the findings were reported to the patient's referring epileptologist. Changes in treatment plan, if any, resulting from these findings, were reported as an endpoint of this investigation.

Results: In 7 of the patients, no significant abnormalities were reported on the 7T scans. The remaining scans showed abnormalities that were either not visible or ambiguous on the previous lower-field clinical MRI scan. These findings include: prominent perivascular spaces, partially empty sella, prominent arachnoid granulations, hippocampal asymmetry, Meckel's ectasia, oculomotor ectasia, polymicrogyria, cortical thickness defect, developmental venous anomaly, and ventricular asymmetry. We will focus on three exemplar cases labeled Patients 1, 2 and 3 for which the 7T scans revealed significant abnormalities. The 7T images for Patient 1 revealed a temporal occipital cortical polymicrogyria as shown in the axial TSE and coronal oblique MP2RAGE in Figs. 1A and C. The axial SWI image in Fig 1 B shows abnormal venous vasculature associated with this cortical abnormality. These findings resulted in a complete change of surgical plan for Patient 1. For Patient 2, hippocampal asymmetry was detected at 7T, for which coronal-oblique TSE images are shown in Fig 2. The left hippocampal volume loss (indicated by the arrows in Fig. 2) for Patient 2 was contralateral to the EEG results, indicating the need for further testing including repeat EEGs. For Patient 3, a subtle cortical thickness abnormality was detected on the 7T T_2 TSE (Fig. 3 A) and this cortical defect was correlated with an ovoid focus on the SWI (Fig. 3 B). This focus was also contralateral to the EEG findings for Patient 3, suggesting the potential for bilateral seizures but no immediate change in treatment plan.

Discussion: Prior to the 7T scans, there was no clear indication of seizure focus location for any of the patients enrolled in this study. From the initial cohort of subjects, there have been 6 patients with findings concordant with the suspected seizure onset zone. In two of these patients for which the abnormality and other findings detected through the 7T images have significantly altered the treatment plan. for Patient 1, the two invasive studies planned to assist in localization of the focus have been reduced to a single admission combined study and scheduled interventional surgery. In retrospect, the polymicrogyria may have been visible in previous MR examinations, but the reduced contrast and resolution made the findings ambiguous and suggested an overall normal reading. For Patient 2, with subtle hippocampus asymmetry (Fig. 2), seizures have been adequately controlled with medication; however, 7T results could be valuable in planning if the patient requires neurosurgery in the future. In summary, abnormalities were found in 6/9 of the 7T scans, resulting in one change in treatment plan. Although the abnormalities in the MRI images were not always concordant with EEG and semiology, the information revealed by the improved resolution and contrast of the 7T scanner will be valuable in providing new insights into the etiology of idiopathic focal epilepsy. Future work involves scanning a larger number of patients as well as age- and gender-matched controls to better characterize and quantify the subtle brain alterations associated with epilepsy.

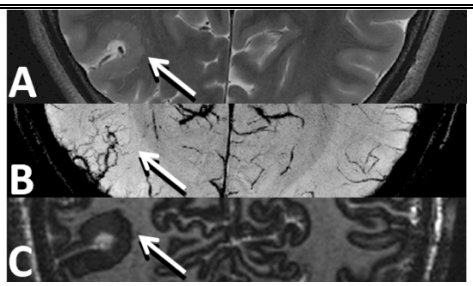

Figure 1: **Patient 1: Polymicrogyria visualized using A) axial T_2-TSE, B) a MIP through an axial SWI image, and C) a coronal-oblique MP2RAGE.**

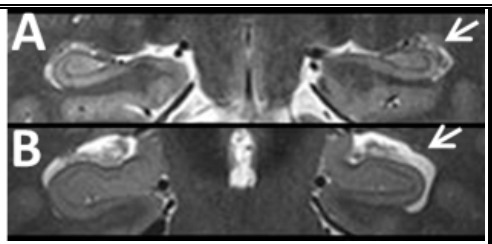

Figure 2: **Patient 2: Hippocampal asymmetry visualized using coronal oblique T_2-TSE. A) Slice showing subtle loss in left hippocampal volume and structural integrity. B) Different slice showing increase in fluid space surrounding left hippocampus.**

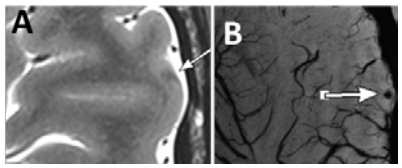

Figure 3: **Patient 3: A) Subtle cortical thickness defect detected in 7T T_2-TSE image which correlates with ovoid focus in B) 7T SWI MIP.**

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Acknowledgement: NIH-NINDS R00 NS070821, Icahn School of Medicine Capital Campaign, Translational and Molecular Imaging Institute and Department of Radiology, Siemens Healthcare