In vivo characterization of cortical lesions in multiple sclerosis by 7T MRI

C. Mainero[1], A. van der Kouwe[1], T. Benner[1], G. Wiggins[1], B. R. Rosen[1], and R. P. Kinkel[2]

[1]A. A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, United States, [2]Neurology, Beth Israel Deaconess Medical Center, Boston, MA, United States

Introduction. Although the development of cortical lesions has emerged as a major component of disease progression in multiple sclerosis (MS) [1], the underlying pathogenic mechanisms, and the relation between cortical lesions and white matter (WM) pathology are still poorly understood. Indeed, it has been hypothesized that cortical GM degeneration may, at least in some patients, represent an initial target of MS leading to axonal degeneration and subsequent demyelination (the "inside-out" model of MS) [2]. The *in vivo* study of cortical lesions in MS is constrained by the technical limitations of currently available MR techniques including limited image resolution and low contrast between small cortical lesions and surrounding normal cortical GM. Recent data at ultra-high field (7 T) indicate, however, the ability to visualize cortical structure in great detail) [3], potentially improving the detection of cortical lesions in patients with MS.

Neuropathological examinations of MS brains have identified three main types of cortical lesions: 1) type I (leukocortical) lesions that extend across both WM and gray matter (GM); 2) type II (intracortical) lesions located within the cerebral cortex but not extending to the surface of the brain or to the subcortical WM; 3) type III (subpial) wedge-shaped lesions that extend from the pial surface to cortical layers 3 and 4. Some lesions, however, might affect the entire width of the cortex from pial surface to WM (type IV). The objective of this study was to assess the ability of 7T MRI to characterize the different types of cortical MS lesions.

Methods. Six patients with clinically definite MS (one patient with benign MS, one with relapsing-remitting (RR) MS, and four patients with secondary progressive (SP) MS; mean±SD age=44.8±5 years; mean±SD Expanded Disability Status Scale, EDSS, score=4.4±2, range 2.0-6.5; mean±SD disease duration=10±2 years) and 3 age matched healthy controls were scanned on a 7 T scanner (Siemens, Erlangen, Germany) with 40mT/m maximum gradient amplitude using an in-house developed 8-channel phased array coil. In each subject we collected 2D Flash, T_2* spoiled gradient-echo weighted images (TR/TE=1000/21, flip angle=55°, FOV=800x1724, bandwidth=30 Hz, 1.0-1.5 mm thick slices with an in-plane resolution of 330 x 330 µm), and T_2 turbo spin-echo, TSE, (TR/TE = 6890/58, turbo factor=9, 2 averages) with the same resolution and orientation as the Flash-T_2* scans, allowing a whole brain coverage from the level of the junction of the brainstem with the cerebellum. An MPRAGE (TR/TE/TI=2600/3.59/1100, bandwidth=205 Hz, 1.5 mm thick with an in-plane resolution of 600 x 600 µm slices) with the same orientation as the Flash-T_2* and T_2 TSE scans was also acquired to improve GM/WM boundary identification. Real time shimming was performed before each anatomical scan to minimize magnetic field B_0 inhomogeneities.

An experienced radiologist and a neurologist interpreted the images by consensus. Cortical lesions were identified on the Flash-T_2* magnitude images, and then confirmed on the corresponding T_2 TSE scans. Cortical lesions were considered for further analyses only if there was a full agreement between the two observers.

Results. Imaging at 7T was well tolerated in all subjects. None of the controls showed cortical lesions. Data from one patient with SP MS were discarded due to gross motion artifacts. A total of 22 cortical lesions were identified in the remaining three patients with SP MS (mean±SD, 7.1±3.3), while we did not observe any lesion in the cortex of the patient with benign MS and in the one with RR MS. Out of 22 lesions, five (22.7%) were subpial, three were type IV lesions (13.6%), three leukocortical (13.6%), 10 intracortical (45.5%), and one lesion was classified as "undefined". In patients with SP MS, in the Flash-T_2* images, we also observed a pattern of increased signal intensity involving the superficial layers of a gyrus or multiple gyri of the frontal and temporal cortex. This pattern is commonly observed in healthy controls in the occipital cortex, but less commonly in other cortical areas. Neuropathological studies have indeed described extensive subpial demyelination involving multiple gyri. However, whether the pattern we observed in SP MS patients really underlies a pathological disease process or simply reflects "normal" signal heterogeneities needs to be further investigated.

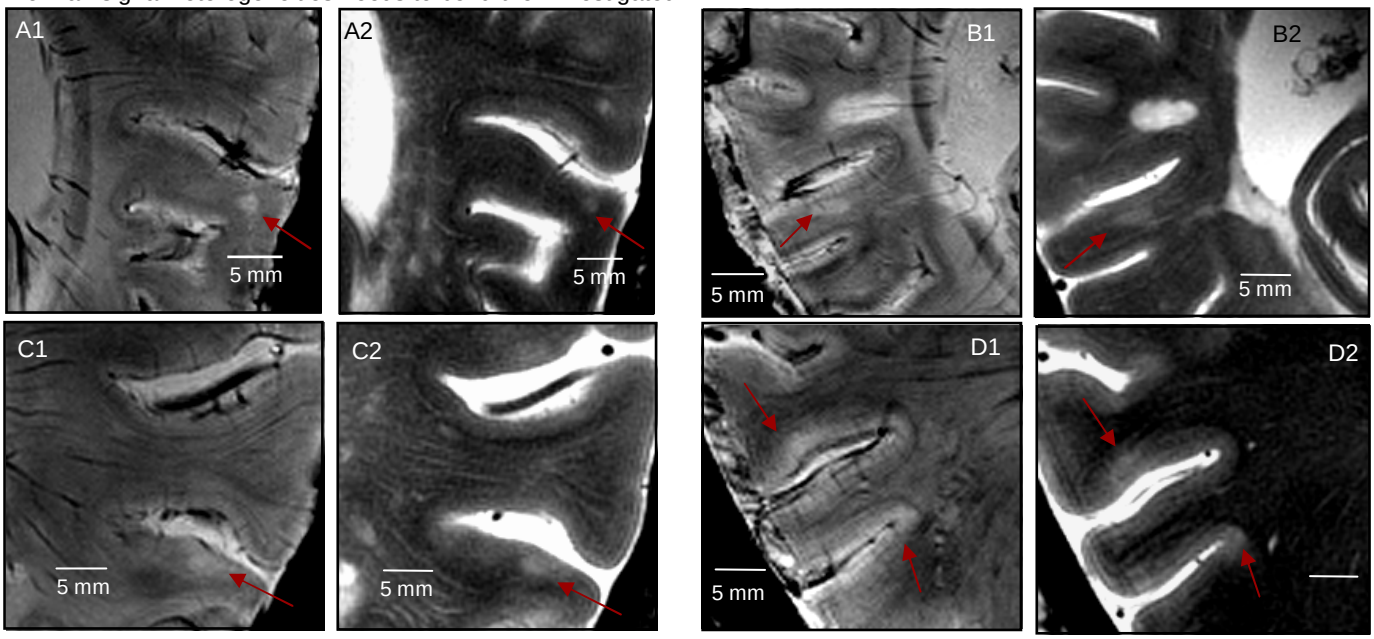

Fig. A1-D4. Illustration of Flash, T_2* TSE **(A1, B1, C1, D1)** and T_2 turbo spin-echo **(A2, B2, C2, D2)** images in two patients with SPMS scanned at 7 T. Intracortical lesion as seen on **(A1)** Flash, T_2* spoiled gradient-echo and **(A2)** T_2 TSE images. Leukocortical lesion as seen on **(B1)** Flash, T_2* spoiled gradient-echo and **(B2)** T_2 TSE images. Signal hyperintensities suggestive of subpial lesions in **C1-C2** and **D1-D2**

Conclusions. Although in a small series of patients, these preliminary data show the ability of high field MRI at 7T to detect and characterize cortical lesions heterogeneity in patients with MS. Different type of cortical lesions might have different pathogenesis and impact on disease outcome. Future studies will assess whether cortical pathology heterogeneity is a patient- or stage-dependent process.

References

1. Kidd D, et al. Brain 1999; 122:17-26. **2**. Tsunoda I, et al. Am J Pathol 2003 ; 162 :1259-69. **3**. Duyn JH, et al. PNAS 2007 ;104 :1179-11801.