Evaluation of cortical lesions conspicuity in multiple sclerosis: 7T vs 3T MRI

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Introduction. The ability of MRI using standard field strength scanners (1.5, 3T) to visualize cortical pathology in multiple sclerosis (MS) is still significantly lower compared to neuropathology. Previous studies have investigated the potential of higher field strengths scanners (4.7 and 8T) to detect cortical pathology in autoptic cases of MS[1,2], however none of them directly addressed whether the contrast properties of the cortical lesions *in vivo* will allow them to be visualized using ultra-high field MRI. Preliminary data have demonstrated that phase reconstruction techniques at ultra-high field strengths may provide useful information about MS white matter (WM) pathology[3]. Here, we assessed the use of 7T MRI to (1) visualize cortical lesions, including all histopathological types, in MS; (2) characterize the contrast properties of cortical lesions including T_2*, T_2, T_1, and phase images to assess which MR contrasts at ultra-high field MRI are more sensitive to the presence of cortical pathology; (3) compare the ability of the 7T images that showed higher contrast for cortical plaques with that from 3T in disclosing cortical MS pathology.

Methods. Sixteen patients (nine with relapsing-remitting MS, RRMS; seven with secondary progressive MS, SPMS; mean±SD age=38.8±12.4 years; median Expanded Disability Status Scale=3.5, range=1.0-6.5; mean±SD disease duration=8.7± 3.1 years) and eight age-matched controls were scanned on a human 7T Siemens scanner using an in-house developed 8- or 32-channel phased array coil. We collected 2D FLASH-T_2* spoiled gradient-echo weighted images (TR/TE=1000/22 ms, 20, 0.33×0.33×1mm^3 slices), and T_2 turbo spin-echo, TSE, (TR/TE = 6890/78 ms) with the same resolution and orientation as the FLASH-T_2* scans. For each modality two to three slabs were acquired, allowing coverage of the supratentorial brain. A 3D MPRAGE (TR/TE/TI=2600/3.26/1100ms, 0.60×0.60×1.5 mm slices) with the same orientation as the FLASH-T_2* and T_2-TSE scans was also acquired. Fourteen patients and all controls were scanned, within an interval of maximum a month, on a 3T Siemens Tim Trio scanner using the Siemens 32-channel coil. T_2-TSE (TR/TE=7560/111 ms, turbo factor=9, 2 averages, 0.33×0.33×1.5 mm^3 slices), and Fluid Attenuated Inversion Recovery (FLAIR, TR/TE/TI=9000/2500/89 ms, 0.7×0.7×1.5 mm^3 slices) allowing the same coverage as 7T scans. Cortical lesions were defined as focal cortical hyperintensities on 7T FLASH-T_2* and T_2-TSE scans, and on the 3T T_2-TSE and FLAIR scans by two independent experienced observers and considered for further analyses only if there was consensus between the two observers. 7T phase images were post-processed using PRELUDE (www.fmrib.ox.ac.uk) to generate a full-range phase image. The contrast-to-noise ratio (CNR) of the different types of cortical lesions was calculated on data from five patients (three with SPMS and two with RRMS). For each image (FLASH-T_2*,T_2-TSE, T_1) regions of interest (ROIs, ~24 mm^3) were placed in 15 lesions (five leukocortical, five intracortical, and five subpial), in adjacent ROIs of normal appearing cortical gray matter (NACGM), and in regions outside the brain and away from imaging artifacts (background noise, BN). The CNR was calculated as the following: $(S_{LES} - S_{CNAGM})/BN$, where S_{LES} and S_{CNAGM} represent the mean signal intensities in cortical lesions and in adjacent NACGM respectively. For phase images BN was calculated as the variance of signal intensity in NACGM ROIs since the actual variance would be meaningless for background (zero signal) regions.

Results. None of the controls showed cortical abnormalities on any scan. Overall, 199 cortical lesions were detected on both 7T FLASH-T_2* and T_2-TSE scans. 7T MRI allowed for characterization of cortical plaques into Type I, (leukocortical), Type II (intracortical), and Type III/Type IV (subpial extending or not through the whole width of the cortex) lesions as described neuropathologically[4]. Type III/IV were the most frequent type of cortical plaques observed (50.7%), followed by type I (35.2%), and type II (14.1%) lesions. Cortical plaques were mostly observed in patients with SPMS compared to patients with RRMS for either type I (mean±SE: 6.2±4.0 vs), type II (mean±SE: 2.8±1.5), or type III/IV (mean±SE: 10±2.3). This difference, however, was only statistically significant for subpial lesions ($p<0.03$ by Mann-Whitney test). FLASH-T_2* scans showed the greatest mean±SE CNR for either type I (mean±SE: 7.7±1.5), type II (mean±SE:8.6±1.9), or type III/IV (mean±SE:10.5±4) cortical plaques compared to T_2 , T_1, and phase images (**Fig. 1-A**). When individual types of cortical lesions were considered, the CNR of FLASH-T_2* scans was significantly higher only for type I lesions when compared to the CNR of phase images ($p<.004$ by ANOVA). However, when all types of lesions were taken into account the CNR of FLASH-T_2* scans was significantly higher than that of either T_2 ($p<.02$), T_1 ($p<.01$), or phase images ($p<.0001$ by ANOVA).

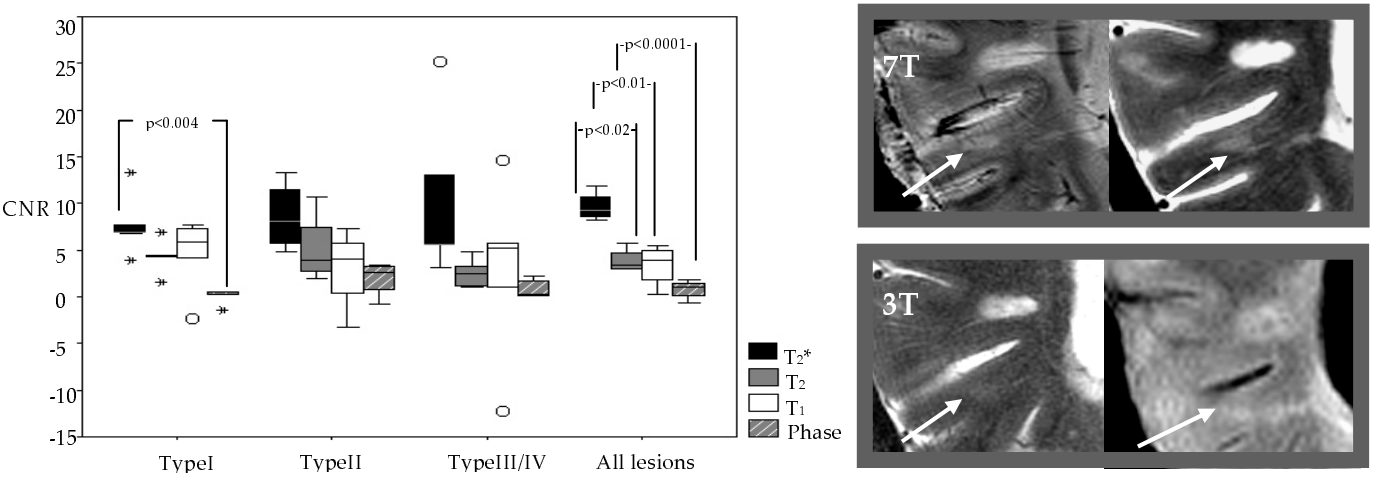

Fig 1. **A (left)**. Mean CNR of different MR contrasts for type I, type II, type III/IV, and all types of cortical lesions in 15 patients with MS. Asterisks represent extreme points (cases with values more than 3 box lengths from the upper or lower edge of the box). **B (right)**. Example of leukocortical lesion appearance on a 7T scan (superior rectangle) and on a 3T scan (inferior rectangle) in a patient with SPMS. In the superior rectangle (7T), left image is FLASH-T_2*, right image is TSE; in the inferior rectangle (3T) left image is TSE, right image is FLAIR.

3T MRI did not allow a clear characterization of the different histopathological types of MS cortical lesions as seen on 7T scans (Fig. 1-B). Lesions were therefore classified as leukocortical or intracortical. In the 14 patients that underwent both 7T and 3T MRI, FLASH-T_2* and TSE 7T scans could detect a significantly higher number of cortical lesions (n=188) than either 3T TSE (overall cortical lesions=40, 19 of which were leukocortical, $p<0.002$ by ANOVA) or FLAIR (overall cortical lesions=57, 29 of which were leukocortical, $p<0.007$ by ANOVA) scans.

Conclusions. Ultra-high field MRI, and particularly FLASH-T_2* scans, show greater potential than standard field strength scanners (3T) not only in detecting cortical lesions but also in characterizing them histopathologically. Indeed the ratio of lesion types seen on 7T scans was nearly identical to that documented by previous seminal neuropathological data.

References. **1.** Geurts JJ et al, 2008. **2.** Kangarlu A. et al, 2007 **3.** Hammond et al 2008 **4**. Peterson et al, 2001