

Identification of Cortical Pathology in Multiple Sclerosis with 7T MRI

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Introduction

Neocortical lesions (NLs) are an important component of disease pathology in multiple sclerosis (MS). However, the limited resolution and contrast of conventional MRI techniques compromise their ability to detect the subtle pathological changes occurring at the inception of NLs and successive tissue loss. In the present work, we aimed at (1) visualizing neocortical lesions (NLs) in brains of patients with multiple sclerosis (MS) using multi echo gradient echo (ME-GRE) T2*-weighted magnetic resonance imaging (MRI) at 7.0 Tesla¹ and (2) assessing the sensitivity of ME-GRE in depicting NLs compared to myelin and iron staining.

Methods

Brain Samples

- 2 MS brain samples
 - MS-1: M, 70 yrs, Secondary Progressive MS, 30 yrs of MS
 - MS-2: F, 61 yrs, Secondary Progressive MS, 24 yrs of MS
- Tissue preparation
 - 10 mm-thick coronal slices, fixed in 4% paraformaldehyde

Image Acquisition & Processing

- GE 7 T whole body scanner, 24-channel phase array coil
- 3D Multi-Echo GRE
 - 0.2 mm isotropic resolution, TE = 8.7/25.2/41.7/58.2 ms, TR = 200 ms, flip angle = 20°, bandwidth = 62.5 kHz, SENSE rate = 2
- R₂* map was derived from a mono-exponential fit to the TE-dependent signal intensity¹

Histology

- 16 randomly selected tissue blocks (30 x 20 x 5 mm each)
- PLP stains for myelin and Turnbull blue stains for iron

Results

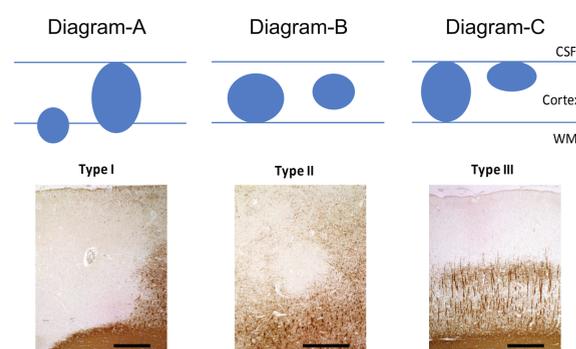


Fig. 1: (A) Type-I leucocortical lesion with demyelination of the whole width of the cortex and adjacent white matter. PLP staining. (B) Type-II intracortical lesion evolving around a vessel. PLP staining. (C) Type-III subpial lesion. Demyelination spreads from the pial surface until cortical layer 3. PLP staining. Scale bars represent 500 μ m.

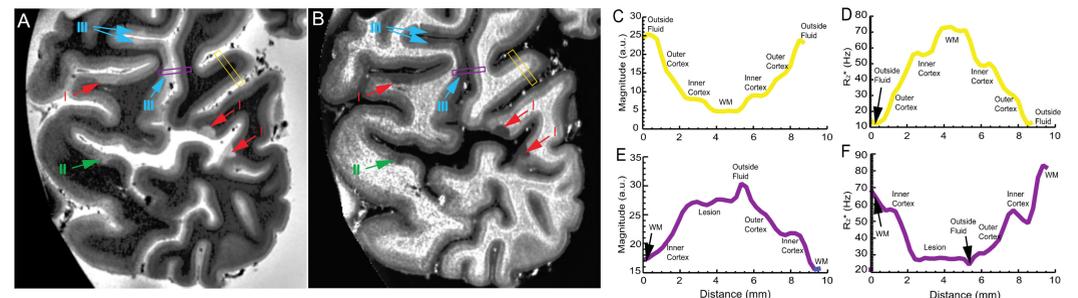


Fig. 2: Examples of NLs from tissue MS-2 identified on MRI (A) magnitude and (B) R₂* images. Arrows point towards different types of NLs. Examples of intensity profiles on both magnitude (C, E) and R₂* maps (D, F), corresponding to the yellow (C,D) and purple box regions (E, F, cross through a NL), respectively.

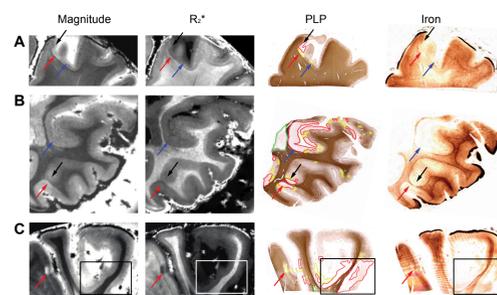


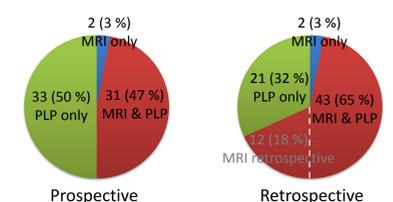
Fig. 3: Comparison between MRI and histology. Red arrows: NLs identified by MRI and confirmed by PLP staining; Blue arrows: NLs identified by PLP and only retrospectively identified by MRI; Black arrows and block box: NLs only identified by PLP.

Table 1: NL occurrence by MRI

| | Type-I NLs | Type-II NLs | Type-III NLs | Total |
|--------------|-------------------|-------------------|-------------------|-----------|
| MS-1 | 29 | 17 | 2 | 48 |
| MS-2 | 16 | 20 | 9 | 45 |
| Total | 45 (48.4%) | 37 (39.8%) | 11 (11.8%) | 93 |

Table 2: NL occurrence by histology

| | Type-I NLs | Type-II NLs | Type-III NLs | Total |
|--------------|-------------------|-------------------|-------------------|------------|
| MS-1 | 26 | 38 | 56 | 120 |
| MS-2 | 2 | 1 | 5 | 8 |
| Total | 28 (21.8%) | 39 (30.5%) | 61 (47.7%) | 128 |



Discussion and Conclusions

Our data suggested that detection of cortical lesions might be improved substantially with susceptibility contrast at high field as compared with conventional (T1, T2) contrast at low field². Our observations further indicate that lesion size may not be the main factor contributing to the difference in ability of histology and MRI to detect lesions. We found non-subpial NLs to be the predominant type of NLs disclosed by MRI. Conversely, a detailed analysis of NL occurrence by histopathology showed type-III NLs to occur most frequently. The results may explain the known discordancy between *in vivo*^{3,4} and post mortem findings⁵⁻⁷. Our results clearly demonstrate that a substantial portion of cortical pathology in MS is not captured by MRI, and this is attributed to lack of contrast.

References

1. Yao B et al. 2012, *Radiology* 262:206-15;
2. Seewann A et al. 2012, *Neurology* 78:302-8;
3. Bo L et al. 2003, *J Neuropathol Exp Neurol* 62:723-32;
4. Kutzelnigg A et al. 2005, *Brain* 128:2705-12;
5. Mike A et al., 2011, *AM J Nueoradiol* 32:515021;
6. Pitt D et al. 2010, *Arch Neurol* 67:812-8;
7. Bagnato F et al. 2006, *Am J Neuroradiol* 27:2161-7

