Thin Slice Magnetic Resonance Histological Imaging and Co-Regisitration of Beta-Amyloid Plaques

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Introduction: Our prior study in the development of histological coil at 3.0 T addressed a long-standing difficulty in co-registration of MRI data with histological tissue images (1). Using this coil, a one-to-one relationship between image parametric maps and the histological chemical stains can be achieved. Aberrant regulation of iron leading to its focal concentration in brain tissue is believed to be associated with the neurodegenerative process in neurological disorders such as Alzheimer's disease (AD), Parkinson's Disease (PD) and Restless Legs Syndrome (2). Using the histological coil, here we present data demonstrating unambiguously that MR image parametric maps closely correlate with tissue iron content and the hallmark Beta-Amyloid (Aβ) plaques found in AD by histological staining.

Methods: The histological samples were dissected from the entorhinal, occipital, and frontal cortices from two pathologically confirmed AD brains and sliced at 60μm using a Leica cryostat. The slices were rinsed with PBS and placed between two 24 x 30 mm coverslips with 7.5μl of PBS. The edges of the coverslip were coated with a hydrophobic barrier PAP pen to maintain tissue hydration during scans. The sample was then placed into a histological coil matched and tuned to 125.44 MHz. MRI studies were undertaken on a 3.0 T imaging-spectrometer (Medspec S300 MR Bruker, Ettligen) with a home-built gradient insert (9.5 cm aperture and 100 G/cm). Multi spin-echo for T_2 mapping, and the mGESEPI protocol (3) for T_2* mapping were acquired with in a plane resolution of 179 x 179μm and a through plane of 60μm. After MR imaging, the tissue samples were removed from the coverslips and co-stained with a modified Perl's with 3'3-diaminobenzine enhancement for iron content and Thioflavin-S for Aβ detection. High resolution images of the stained tissue were taken under visual light spectra and fluorescence at 430nm excitation and 550nm emission for respective iron and Aβ plaque analysis.

Results: Figure 1 shows the whole tissue histological iron stain (a), T_2- (b), and T_2*- (c) weighted images. The darker contrast in T_2 image shows a close relationship with the dark brown of iron staining in the white matter tissue in gross histology. Of particular interest in the T_2* images are corona regions of dark intensities that overlap the location of the Aβ plaques in the gray matter. These regions are also seen in the T_2 image as iso-intense with those in white matter. The correlation between the dark corona region on the MR image (top), iron (middle), and Aβ plaques staining (bottom), is shown in the magnified images in Figure 2. However, the correlation between the discrete iron distributions with Aβ plaques can only be appreciated when zooming into a specific plaque as shown in Figure 3.

Figure 1: The dark brown Perl's stain for uniform iron in white matter (a) correlates to the darker intensity in T_2 image (b). The darker intensity in T_2* image (c) in gray matter correlates well with patchy iron and Aβ plaques.

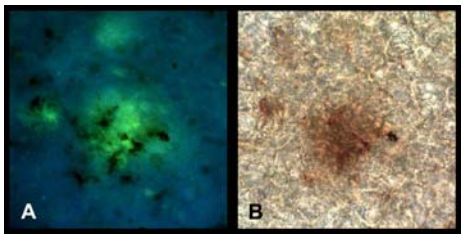

Figure 3: 200X magnification of a plaque in Fig. 2 (A) and iron staining (B).

These images in the same field view revealed a large type 2 plaque taken under fluorescence (A) and stained iron under visual light (B).

Conclusions: With the aid of histological coil, an unambiguous correlation of T_2* contrast with elevated focal issue iron associated with Aβ plaque is established. Iron in normal white matter appears distributed uniformly, which is correlated well with T_2 contrast. Patchy high iron content is observed overlapping with Aβ-plaque formation, which correlates specifically with T_2* contrast and non-specifically with T_2 contrast. These results indicate that, in addition to the absolute iron content, the morphology of iron in tissue plays an important role in MR contrast formation. Thus, T_2* contrast may be more specific for detection of abnormal brain iron distribution related to the Aβ plaques.

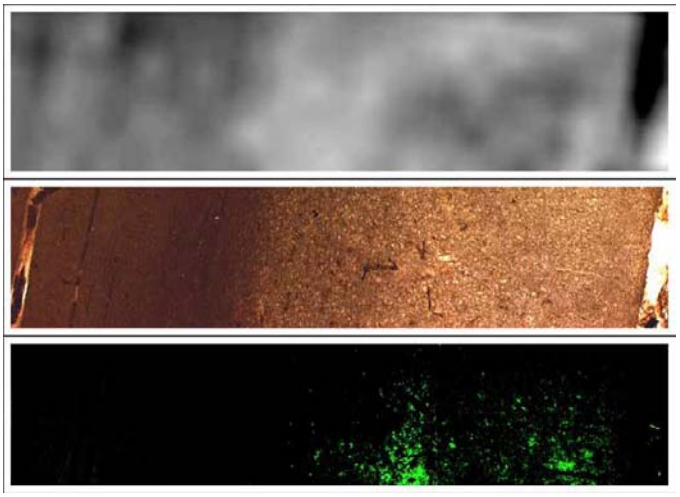

Figure 2: Precise co-registration of MRI T_2 weighted (top), Perl's iron staining (middle) and Thioflavin-S for Aβ plaques. The images extend from white matter into gray matter from left to right. All images are at 40x magnification.

References:

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