T_1 tissue specific imaging in multiple sclerosis: Sensitivity and specificity issues

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Introduction: The processes of inflammation, development of edema and neuronal degeneration, characteristic of many diseases of the central nervous system such as multiple sclerosis (MS), affect proton relaxation times and density. However, in the case of MS, the lesion load as depicted by traditional MRI techniques shows a rather limited correlation with the clinical condition of the patient. From the available MR contrast modifiers, T_1 has thus far shown the best, albeit weak, correlation with the clinical symptoms of MS [1]. An increase in T_1 is usually associated with myelin loss and subsequent fluid accumulation at the later stages of lesion evolution, so T_1 weighted imaging is considered to depict areas with severe damage, known as "black holes" due to their appearance in such images. However, areas with milder damage can go undetected by traditional T_1 weighted imaging, and are described with the ill-descriptive term "normal appearing white matter". Improved sensitivity to T_1 changes can be achieved with double inversion recovery (DIR) techniques[2, 3], which utilize two inversion pulses for zeroing signal from two different tissue types, thus producing for the brain a "single tissue type" image. A by-product of zeroing two tissue types is that the resulting images show very strong contrast for specific ranges of T_1 values. In this work, we apply a recently introduced variant of DIR MRI to the study of MS. The technique allows collection of tissue specific (TS) images with optimized contrast, with the potential of improving the characterization of MS lesions.

Theory & Methods By intermixing 2 inversion pulses and 3 image acquisitions, 3 single tissue type images (white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF)) with optimal contrast can be obtained simultaneously [4], one for each major tissue type of the brain, dubbed triple Tissue Specific Imaging (TSI). Figure [1] shows images and corresponding contrast curves for the resulting three images.

The sequence was implemented on a GE 3T magnet, equipped with a GE 8 channel receiver head coil. Image resolution was $(1.5\text{mm})^3$ isotropic for a 12 minute scan. Six MS patients (5 female – 1 male, 3 relapsing remitting - 3 secondary progressive, disease duration 18.1 ±10.1 years, Extended Disability Status Scale score 1.0-7.5 (3.7±2.6)) and six healthy volunteers were scanned after giving informed consent under IRB approved protocol. Both TSI and inversion recovery prepared fast spoiled gradient recalled (IR-FSPGR) images were obtained during the same session.

Results & Discussion: Baseline contrast to noise ratio was measured in normal volunteers, where the contrast was taken between the selected tissue type and the remaining two suppressed tissue types. It was found to be about 30 in the WM image, also about 30 in the GM image and about 75 in the CSF image. These values allow for unambiguous distinction between suppressed and non-suppressed tissue.

A typical set of TSI images from a MS patient is shown in Fig. 2. Abnormal findings include hypointense areas in the WM image, hyperintense regions in the GM image, and hyperintense regions in the CSF image.

When compared to state-of-the-art IR-FSPGR images (Fig. 3), TSI GM images show systematically greater lesion load in white matter areas. This is due to the greater sensitivity of the TSI GM image to early changes in T_1, as can easily be seen in the corresponding Signal vs. T_1 diagrams in Fig. 1 and 3, which demonstrate that the curve slope for T_1 values around white matter (approximately 900 ms at 3T) is larger for the TSI sequence than the IR-FSPGR. Contrast is further enhanced by the prolonged T_2* values that are associated with MS lesions, resulting in CNR values averaging 40.

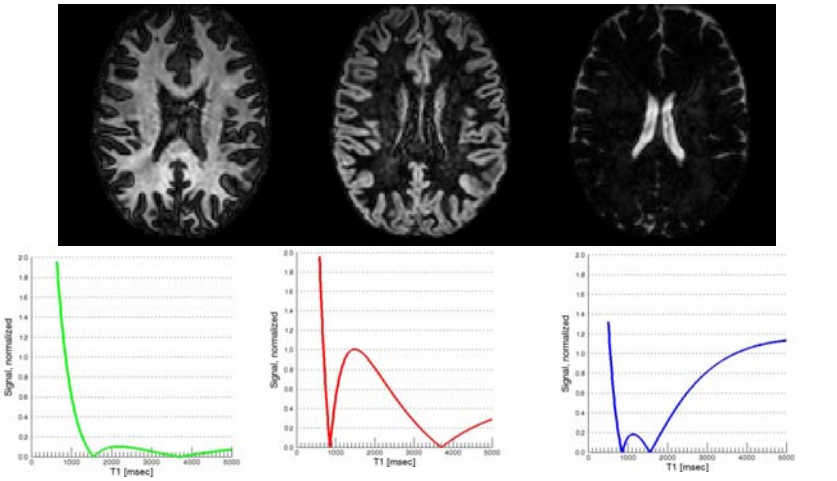

Figure 1: TSI images of a healthy volunteer (WM, GM and CSF images), and corresponding T_1 weighting curves

Compared to the T_2 weighted image shown in Fig. 3, the GM image shows that areas that appear as slightly hyperintense on the T_2 weighted image can also show T_1 abnormalities that however fall below the sensitivity threshold of a conventional T_1 weighted imaging technique like the IR-FSPGR.

When comparing the CSF images to the corresponding IR-FSPGR, the CSF image shows a smaller number and lesser volume of lesions. Given that the CSF image selectively depicts only tissues with long T_1 values, it is likely that these lesions resemble freely moving liquid, marking severe axonal loss and fluid accumulation. Average CNR values for lesions in the CSF image is about 40, but, depending on the nature of the lesion, can go up to about 80.

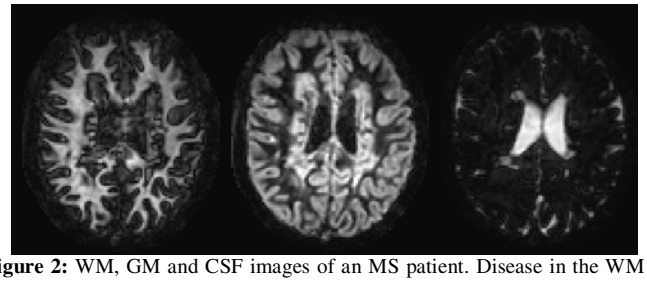

Figure 2: WM, GM and CSF images of an MS patient. Disease in the WM is evident in both the WM and the GM images, whereas the CSF image depicts only regions with advanced degeneration.

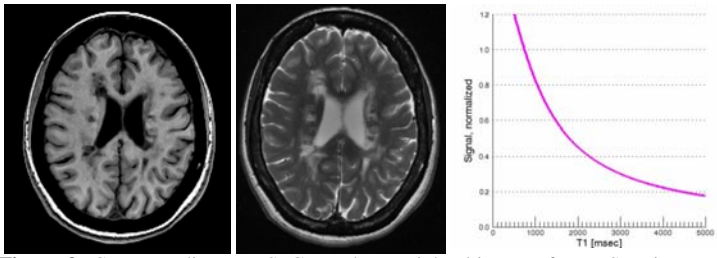

Figure 3: Corresponding IR-FSPGR and T_2 weighted image of an MS patient, and T_1 weighted contrast curve for the IR-FSPGR.

Conclusion: We have presented initial results from the application of a novel DIR based TSI technique to MS. The main advantage of the proposed implementation over normal DIR implementations for MS imaging is that it results in three simultaneously acquired images. In their primary form, these images show WM, GM and CSF, thus offering a useful anatomical framework. As far as lesions are concerned, they offer complementary information about the disease. The GM image is very sensitive in depicting early changes in T_1, and thus possibly early pathological change. On the other hand, the CSF image selectively images only the very long T_1 species, offering specificity in characterizing severe damage and fluid accumulation in older lesions (black holes). Thus, we believe that the combination of the three images is a promising tool offering both increased sensitivity and specificity in characterizing tissue pathology in MS.

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