Diffusion tensor imaging offers complementary information compared to conventional MRI for measuring degeneration in normal-appearing white matter

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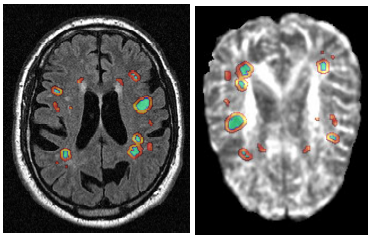
Abstract: We investigated fractional anisotropy (FA) computed from diffusion tensor images (DTI) as a measure of early detection of white matter (WM) degeneration. Our study of white matter lesions and the surrounding regions involved baseline data from 12 brain MRI's with white matter lesions. These data reveal that while fast fluid attenuated inversion recovery (FLAIR) images identify the lesions well, they are unable to characterize the extent to which the surrounding tissue has been affected. In contrast, FA values are significantly lower in WM lesions and also the partially degenerated WM around the lesions. FA may provide an excellent marker of early degeneration and thus identify a subset of individuals with WM lesions more responsive to interventions aimed at enhancing brain function.

INTRODUCTION **A**nalysis of brain MR images from patients with WM lesions, often indicative of WM degeneration due to underlying vascular disease, is important in a variety of brain diseases, including multiple sclerosis, Alzheimer's, and diabetes. While lesions in conventional MRI, such as FLAIR, present clear evidence of white matter degeneration, they represent diseased white matter which has peaked. For the purposes of diagnosis and treatment monitoring, it is often crucial to be able to identify diseased WM that is normal appearing, and which might be relatively more amenable to treatment. A better understanding of early and potentially diffuse WM changes that are not necessarily manifested by the presence of lesions and are therefore more difficult to detect and quantify is also important for a deeper understanding of the underlying disease processes. Traditional modalities (like FLAIR) used for detection of lesions at higher intensity than the surrounding brain tissue have limited ability for early identification of WM disease. DTI, which characterizes WM based on tissue microstructure, is particularly suited to WM analysis and may be more effective than any other modality in identifying appearing white matter affected by disease but appears normal-on traditional imaging methods.

METHODS Our experiments are designed to compare lesions, as well as surrounding normal-appearing white matter between FLAIR and DTI images. We analyzed 12 brain MR images that included white matter abnormalities (mean age: 62.25 years, range 55 - 69 years). Using 1.5T magnet, DTI (6 directions) and FLAIR images were acquired. The lesions were manually identified on the FLAIR images by an expert radiologist (RNB). FA maps were computed from the DTI data, where FA values range from 0 to 1[1]. The FLAIR and FA images were intensity normalized to remove biases and smoothed prior to analyses. The FA maps were registered to the FLAIR images using a mutual information based registration technique. The lesions on the FLAIR images are overlaid onto the registered FA images. We then dilated these lesions by 2 pixels into the surrounding white matter, then subtracted the lesions, thereby constructing a ring shaped area around each lesion. Fig. 1 shows the lesions (green) and the dilated regions around them (red) overlaid on the FLAIR (a) and FA (b) images. Average FA and FLAIR intensity values were computed in each of the lesions and the rings and changes were studied. WM regions were identified in the FLAIR images and values for FA and FLAIR in these areas were computed.



(a) (b)

Fig. 1: FLAIR (a) and FA (b) images overlaid with lesions (green) and dilated area (red)

EXPERIMENTAL RESULTS. The average FA value in normal WM lies in the range of 0.5 to 0.9, and that of normal gray matter lies in the range 0.1 to 0.4. We found that the average FA value of diseased WM to be in the range of 0.2 to 0.7, that is, between normal WM and GM. Lesions displayed relatively increased FLAIR signal, as compared to white and gray matter. FA values were significantly decreased in the lesions by 48%, compared to normal WM. FA values were also reduced by 38% in the dilated area surrounding the lesions. In the FLAIR images, the increase in intensity in the lesions was about 47%, however in the surrounding rings the change in FLAIR intensity was only 25%. The difference in FA and FLAIR values can be clearly seen in the graphs in Fig. 2. While the FLAIR values were closer to the normal WM, the FA values in areas around the lesions was very close to the diseased FA. The FA values in the lesions and the area around them differ by 7% on average, whereas FLAIR values differ by 15 %.

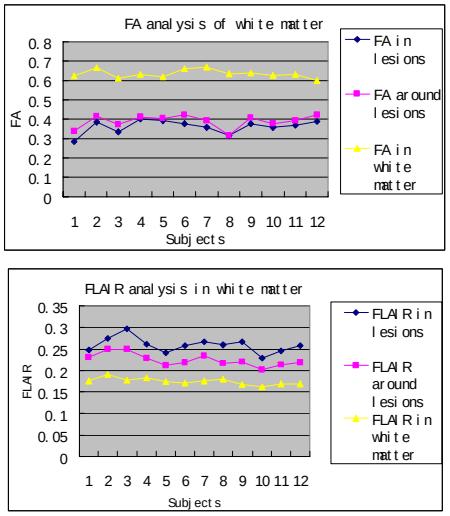


Fig. 2 Change in FA and FLAIR values in lesions, surrounding regions and normal white matter

DISCUSSION. The significant decrease in FA values of normal appearing WM around that of lesions, as compared to the change in FLAIR, demonstrates that DTI-based measures, and particularly FA, have greater sensitivity than FLAIR for identifying the spectrum of white matter degeneration on MRI. These results indicate that in the future, Fractional anisotropy might be used to identify patients with earlier stage brain changes that would be candidates for testing treatments aimed at preventing further loss of functional brain tissue. Based on the findings of multiple sclerosis based studies [2], we also investigated the effectiveness of other DTI measures, such as the principal eigenvalue, trace, apparent diffusion coefficient and the volume ratio. While volume ratio provided results similar to FA, the results from no other measure provided as significant a measure of white matter degeneration, as FA did. Therefore, we have demonstrated that FA maps in conjunction with FLAIR images, provide a characterization of white matter degeneration that significantly augments that obtained via conventional FLAIR imaging.

REFERENCES

1. D. LeBihan, J. F. Mangin, C. Poupon, C. A. Clark, S. Papata, N. Molko, and H. Chabriat, "Diffusion tensor imaging: concepts and applications," *Journal of Magnetic Resonance Imaging*, vol. 13, pp. 534-546, 2001.
2. M. Filippi, M. Cercignani, M. Inglese, M. A. Horsfield, and G. Comi, "Diffusion tensor magnetic resonance imaging in multiple sclerosis," *Neurology*, vol. 56, pp. 304-311, 2001.