Correlative Analysis of Anisotropy Diffusion Coefficient and Magnetization Transfer Ratio with Serum Antibody Brain Binding and Antiphospholipid Antibodies in Multiple Sclerosis

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OBJECTIVE:

Magnetization Transfer Ratio (MTR) and Diffusion Tensor Imaging (DTI) are used individually and together to investigate abnormalities associated with a variety of neurological disorders including Multiple Sclerosis (MS). Numerous studies have shown, as compared to normal subjects, MTR and DTI value were found to be abnormal in similar areas of the brain. For patients with MS, MTR and DTI together enable us to quantify the extent of specific structural changes in the brain. Antiphospholipid and antimyelin antibodies have been associated with MS, to varying degrees.

Correlative analysis of multiparametric tests of MS may contribute to improved differential diagnosis of this heterogeneous disease. We investigated relationships between DTI, MTR, brain-binding serum IgM, and serum antiphospholipid antibody levels in MS and control subjects. Our objective is to determine if correlations between these parameters exist, and of what significance they may be.

SUBJECTS AND METHODS:

This study included 42 Normal subjects and 48 subjects diagnosed with MS. **MR methods:** Subjects were scanned with a 1.5 T GE Signa MRI scanner and images required to process DTI and MTR data were acquired. Corresponding ROIs were created on the ADC and MTR maps, irrespective of the presence or absence of lesions. Mean ADC and mean MTR for the ROIs were calculated. The ROIs were as shown in fig.1.

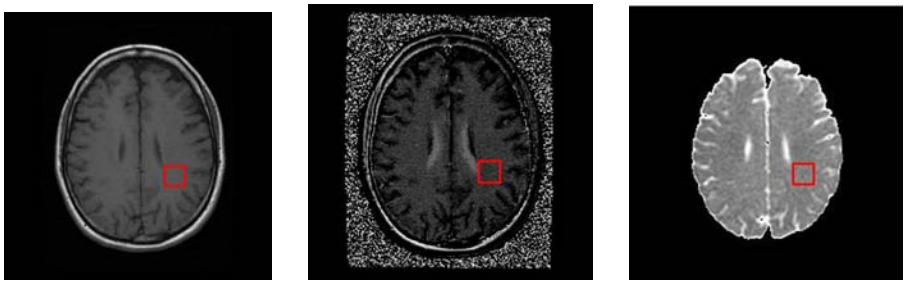

Figure.1. White Matter ROIs drawn on the regular T1 images, MTR images and ADC images.

Brain-binding serum antibodies were tested with standard HRP Immunoperoxidase methods on paraffin-embedded sections of normal control brain tissue (generously provided by the Harvard Brain Tissue Resource Center) and evaluated by light microscopy. **Antiphospholipid Antibodies** were evaluated by commercial ELISA kits

Statistical analysis was performed with student's t-test and Spearman's correlations.

RESULTS:

Variable	By Variable	Spearman Rho	Prob>|Rho|
Normals - ADC BB-	Normals - mean MTR BB-	0.4	0.0258*
MS - ADC BB-	MS - mean MTR BB-	0.3483	0.047*
Normals - ADC BB+	Normals - mean MTR BB+	-0.0238	0.9554
MS - ADC BB+	MS - mean MTR BB+	0.1879	0.6032

* Significant correlations.

Table 1. Correlations between ADC and mean MTR.

Correlations were found between ADC and MTR values for Normal BB- subjects and the MS BB- subjects, whereas ADC and MTR did not correlate significantly for Normal BB+ subjects and for MS BB+ subjects. Other immunological differences between BB+ and BB- were the presence of elevated serum aPLs, independent of MS; and whether MS subjects in specific had elevated serum aPLs. No significant difference between BB+ and BB- was found for normal subjects, with or without elevated serum aPLs.

CONCLUSIONS:

We found a significant correlation between ADC and MTR values in subjects **without** concomitant brain-binding serum antibodies. ADC and MTR values did not correlate in subjects **with** concomitant brain-binding serum antibodies. This was independent of disease.

Correlations between ADC and MTR were found for BB- subjects, but not for BB+ subjects, irrespective if the subject was normal or diagnosed with MS. ROIs were drawn blind to lesions. This suggests that the correlation does not depend on the presence or absence of lesion in the brain, but rather on the presence of serum IgM antibodies capable of binding brain tissue. The absence of correlation with the presence of BB IgM suggests that these antibodies may be a marker of a specific subtype that ADC and MTR may be useful in characterizing by both neuroimaging and immunological methods. Further investigations are needed to clarify the significance of these relationships.