In vivo Quantitative evaluation of brain tissue damage in Multiple Sclerosis using Gradient Echo Plural Contrast Imaging technique

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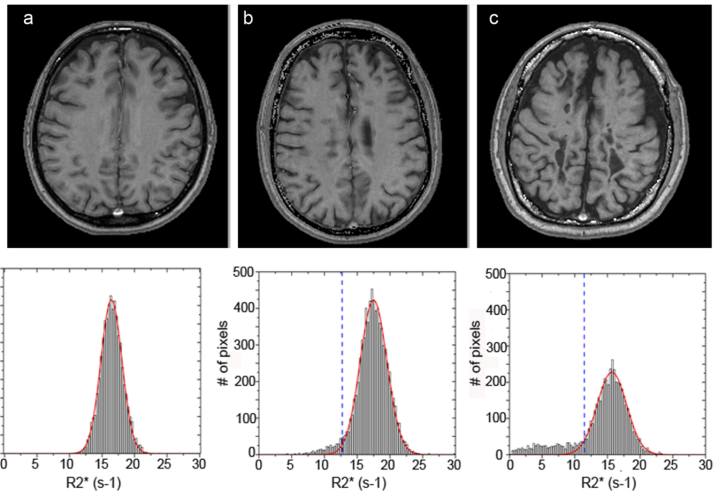
Introduction: Conventional MRI based on T1 and T2 weighted spin-echo (SE) sequences aids in the diagnosis of multiple sclerosis (MS). However, MRI markers derived from these SE sequences provide limited information about tissue damage and correlate poorly with patient disability assessed with clinical tests. In this study, we introduced a method for estimating the severity of brain tissue damage in MS lesions which is based on quantitative R2* maps produced by the Gradient Echo Plural Contrast Imaging (GEPCI) technique [1,2,3].

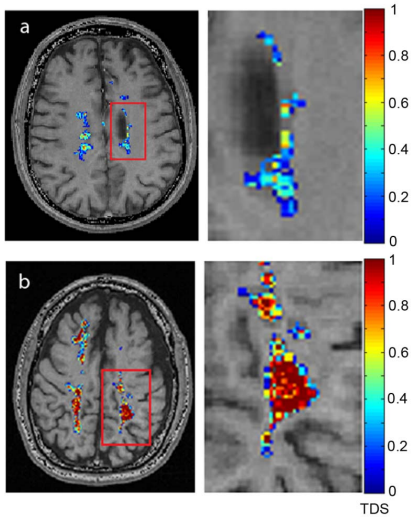
MRI method and Image analysis: Brain images of 5 subjects with MS and 5 healthy controls were acquired using a Siemens 1.5T Magnetom Sonata system. 3D version of GEPCI sequence was used with a resolution of 1×1×3mm^3 and 8min32s acquisition time. From GEPCI dataset, quantitative T2* maps, T1w images and GEPCI-FLAIR images were generated by post-processing methods. Masks containing only normal appearing white matter (NAWM) and MS lesions (or WM for controls) were applied, and R2* histograms of the selected pixels were generated using a bin width of 0.3 s^{-1} For subjects with MS, physical disability was rated using the expanded disability status scale (EDSS) during a clinical examination on the same day.

Results: The successive steps of the proposed scoring method are illustrated in the Figure on the right with three subjects: (a) control, (b) subject with Relapsing-Remitting (RRMS) and (c) subject with Secondary Progressive (SPMS). Upper row represents T1W-GEPCI images. The corresponding R2* histograms of segmented pixels belonging to NAWM and MS lesions (or WM for the control) are displayed in the lower raw. The R2* distribution for the healthy control has a symmetric Gaussian peak (fitting line is shown in red). The R2* histograms for the subjects with RMMS and SPMS display tails of pixels with lower R2* values on the left of the NAWM peak. In this study, the control subjects had higher mean Gaussian peak center values than subjects with MS [mean difference = 0.32 (1.69 to -1.05, 95% confidence interval)] but the difference was not significant (P = 0.60). The subjects with MS had higher mean Gaussian peak width values than control subjects [mean difference = 0.3 (0.70 to -0.10, 95% confidence interval)], the difference was not significant (P = 0.12). For the subjects with MS, to define abnormal tissue, a threshold on R2* histograms (blue dot lines) was selected to provide similar lesion load as defined by T1 and T2 weighted clinical images. Only clusters of three or more pixels having R2* smaller than the threshold value are considered as abnormal pixels. The tissue damage score of each abnormal pixel was then calculated using equation [1]:



$$TDS = \frac{R2^*_{Peak\ center} - R2^*}{R2^*_{Peak\ center} - R2^*_{CSF}} \qquad [1]$$

An illustration of the scores obtained for the brain slices of the subjects with RRMS and SPMS is provided on the right figure (a for RRMS and b for SPMS). The abnormal pixels, which define the lesion areas in the slice of interest, are colored and overlaid on the T1W-GEPCI images (first column). Colors correspond to score ranging from 0 (normal tissue) to 1 (full tissue destruction)..The magnified view of the lesions (second column) for the subject with RRMS shows scores in the blue color range which indicate low severity of tissue damage. On the other hand, the magnified view of the lesions for the subject with SPMS displays many scores with the red color indicating very severe tissue damage. The tissue damage load (TDL) which combines both volume and severity of lesions, and the mean tissue damage score (MTDS) which provides an average MS lesion severity, were then calculated using equations [2] and [3]:



$$TDL = V \cdot \sum_{i=1:N} TDS_i \qquad [2]$$

$$MTDS = \frac{\sum_{i=1:N} TDS_i}{N} \qquad [3]$$

These calculations were performed by taking into account all the slices containing MS lesions. Statistical analysis of the correlations between clinical EDSS and each of the two MRI markers for the 5 subjects with MS revealed significant correlation (Spearman rank =1 with P < 0.05).

Conclusion: This pilot study introduces for the first time a new scoring method for MS evaluation using R2* histograms acquired by means of GEPCI technique. This method is sensitive not only to lesion load, but also to the degree of tissue damage within the MS lesions thus holding promise for improving the quantitative evaluation of MS pathology, both in the clinic and as a research tool.

References: **1.** Yablonskiy DA, ISMRM (2000); **2.** Bashir A and Yablonskiy DA, ISMRM (2006); **3.** Sati P, Cross AH, Bashir A, Yablonskiy DA., World Congress on MS (2008).