# *In vivo* quantitative evaluation of Multiple Sclerosis progression using Gradient Echo Plural Contrast Imaging technique

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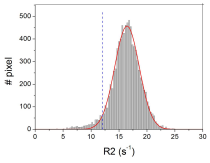
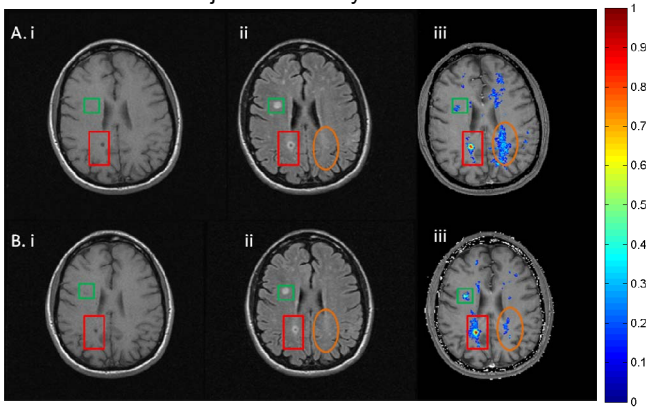
**Introduction:** Although conventional MRI, based on T1 and T2 weighted (T1w and T2w) images, has been used for probing Multiple Sclerosis (MS) disease, correlation between MRI and clinical findings remains weak (1). One reason for this is the inability of conventional MRI to quantify the extent of tissue damage. A recently introduced new MRI technique, Gradient Echo Plural Contrast Imaging (GEPCI) (2,3), demonstrated substantial improvement in image quality and MRI acquisition time as compared to clinical sequences for evaluation of MS white matter damage in humans (4). Herein, we present preliminary results showing that GEPCI, allowing quantitative evaluation of degree of tissue injury in MS lesions, has tremendous potential to serve as an efficient tool for monitoring disease progression.

**Methods and Data Analysis:** Brain images of six Relapsing Remitting MS (RRMS) subjects under treatment were acquired twice (with half-year time interval) using a Siemens 1.5T Magnetom Sonata system. Standard clinical 2D T1w, T2w and FLAIR images were first obtained with a resolution of 1×1×3mm$^3$ and total acquisition time 15min49s. 3D version of GEPCI sequence was then used with a similar resolution and 8min32s acquisition time. From GEPCI dataset, quantitative T2* maps, along with T1w images were generated by post-processing methods. T1W-GEPCI images provide substantial contrast for segmentation of white matter (WM). Such generated WM masks are applied on GEPCI-T2* maps and the R2*(=1/T2*) histogram of all the slices (covering the whole cerebrum) is generated using a bin width of 0.3 s$^{-1}$ ranging from 0 s$^{-1}$ up to 30 s$^{-1}$. The R2* histograms for the subjects with RRMS display as a quasi-Gaussian shape, with tails of pixels on the lower R2* side corresponding to MS lesions (see example on the right). To define abnormal tissue, a threshold on R2* histograms (vertical dotted line) was selected to provide similar lesion load as defined by T1 and T2 weighted clinical images. The tissue damage score (TDS) of each abnormal pixel was then calculated using Eq. [1] , which reflects the fact that the tissue R2* relaxation rate constant decreases when tissue regresses from normal condition corresponding to R2* of peak center to cerebral spinal fluid (CSF). 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 tissue damage severity, were then calculated using equations [2] and [3] where *V* is imaging voxel volume.




$$TDS = \frac{R2^*_{Peak\ center} - R2^*}{R2^*_{Peak\ center} - R2^*_{CSF}} \quad [1]\ ; \qquad TDL = V \cdot \sum_{i=1:N} TDS_i \quad [2]\ ; \qquad MTDS = \frac{\sum TDS_i}{N} \quad [3]\ ;$$

**Results and Discussion:** Figure on the right shows an example of two scans for the same subject with half year interval: upper row A represents first visit, and second row B is from second visit. First column (i) shows standard T1w spin-echo images; second (ii) - standard FLAIR images; and third (iii) are GEPCI score maps (TDS) of abnormal tissue superimposed on T1w-GEPCI images. Colors correspond to score ranging from 0 to 1. We hypothesize that as tissue destruction becomes more severe, accompanied by demyelination and axonal loss, the R2* value decreases, leading to increasing TDS score (red color).




As we compare images A and B, the lesion score map based on quantitative T2* information showed clearer details of lesions changes as compared to the weighted clinical images. For example, the isointense lesion (green square) showed very small changes on T1w and FLAIR images, yet demonstrated increased TDS GEPCI score (became 'worse'). The black hole (red rectangle) looks practically the same on T1w and FLAIR clinical images but shows increased volume of surrounding dirty WM on TDS GEPCI score map which could indicate progression of the lesion. On the other hand, the dirty-appearing WM in the right hemisphere (orange circle) displayed significant 'improvement' in the lesion score map. A similar pattern is also seen on FLAIR, but is less obvious.

| patient | visit | Peak center | Relative width (2σ/peak center) | TDL /mm$^3$ | MTDS | Lesion Load/mm$^3$ |
|---|---|---|---|---|---|---|
| 1 | 1 | 16.36 | 0.246 | 2856.2 | 0.343 | 8325 |
| | 2 | 17.59 | 0.198 | 887.4 | 0.245 | 3615 |
| 2 | 1 | 16.12 | 0.248 | 1275.7 | 0.315 | 4044 |
| | 2 | 16.13 | 0.203 | 1158.1 | 0.282 | 4113 |
| 3 | 1 | 15.79 | 0.219 | 462.3 | 0.272 | 1701 |
| | 2 | 16.11 | 0.269 | 853.7 | 0.305 | 2799 |
| 4 | 1 | 16.41 | 0.236 | 942.1 | 0.302 | 3123 |
| | 2 | 16.57 | 0.212 | 1045.5 | 0.295 | 3549 |
| 5 | 1 | 16.59 | 0.245 | 730.9 | 0.283 | 2586 |
| | 2 | 16.57 | 0.337 | 1077.4 | 0.376 | 2868 |
| 6 | 1 | 17.76 | 0.217 | 533.0 | 0.251 | 2121 |
| | 2 | 16.49 | 0.237 | 333.4 | 0.262 | 1272 |

Longitudinal comparison of all 6 subjects is shown in the left table. Peak center varied between subjects. The peak center either increased or remained the same in most patients. Similar variation has been reported on T2 histograms (5). We also observed that the relative width of R2* Gaussian shape is wider for MS patients than for healthy volunteers (data not shown here). While center and width of R2* Gaussian distribution reflect global changes of the brain tissue, the last three columns in the table provide information from the distribution tail, which reflects local changes in the MS lesions. Note that trends of different R2* characteristics could provide important complimentary information on the disease progression. For example, data for patient #2 show an increase in the lesion load (total volume of abnormal voxels), but a decrease in the 'tissue damage load' and 'mean tissue damage score', which indicates improvement over the whole cerebrum, with appearance of new lesions or growth of old lesions.

**Conclusion:** In this study, we demonstrated an efficient method based on GEPCI technique that might be used for monitoring progression of MS. This method not only depicts MS lesions similar to conventional T1w and FLAIR images, but also allows quantitative evaluation of disease progression based on R2* histograms. Combining characteristics of main peak in R2* distribution and quantitative score assigned to MS lesions, allows the evaluation not only of the volume of cerebral MS lesions, but incorporates the degree of tissue damage as well.

**References:** 1. Mainero C, et al., Neurology (2001); 2. Yablonskiy DA, ISMRM (2000); 3. Bashir A and Yablonskiy DA, ISMRM (2006); 4. Sati P, et al., World Congress on MS (2008); 5. Neema M, et al., Neuroimage (2009).