A NEW MRI ANALYSIS METHOD FOR LESIONAL HETEROGENEITY CHARACTERISATION IN MULTIPLE SCLEROSIS AS DEMONSTRATED BY QUANTITATIVE MRI.

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INTRODUCTION: Multiple Sclerosis (MS) is characterised by the presence of lesions in white matter which are shown as areas of high signal intensity on proton density (PD) and T2-weighted MRI scans. While the volume of these lesions can be readily quantified by means of manual segmentation or semi-automated segmentation algorithms [1], the high signal intensity may be due to a number of pathologies, and subtle signal intensity variations within and between these areas of high signal intensity [2] are usually not well depicted. Therefore, attempts to assess these underlying tissue heterogeneities from the PD or T2-weighted images alone is likely to suffer from operator dependent errors or errors arising from the criteria set within possible semi-automated algorithms used. While quantitative MRI methods including magnetisation transfer (MTR), T1 and T2 mapping may be more pathologically specific, these require more refined acquisition protocols that may not be readily available. A new MR image processing method is presented here, which utilises conventional fast spin echo (FSE) dual-echo (i.e. PD/T2-weighted) data sets in order to display a wider dynamic range of intensities within MS lesions and surrounding tissue, which cannot be assessed using PD/T2-weighted images alone. The method uses advanced image algebra (ADIMA) to classify the hyper-intense lesions seen on the PD and T2-weighted images into subsets of 'bright' (or hyper-intense) and 'dark' (or hypo-intense) regions. In this work, the ADIMA method is described along with the results from preliminary investigations to characterise the pathological pattern of the tissue within these bright and dark regions by means of quantitative MRI.

METHOD: i) MRI acquisition protocols: 10 patients were scanned on a 1.5 T Signa (GE, Milwaukee, WI, USA) scanner with the following sequences all acquired with a 24x24 cm field of view, a matrix size of 256x256 and coverage of 28 x 5 mm slices: 1) dual echo FSE giving PD and T2-weighted images (TR 2000ms; TE1/2 19/95 ms; number of excitations (NEX)=1; echo train length (ETL)=8). These images were also used to calculate T2 maps based on a two point estimation; 2) An interleaved dual echo spin echo sequence for MTR calculation (TR 1720 ms; TE1/2 30/80 ms; both echoes with and without an MT pulse; NEX= 0.75). MTR maps were then calculated from the short echo data; 3) Two gradient echo sequences used for T1 maps as previously described [3] (1st acquisition: TR 1500 ms; TE 11 ms; flip angle 45 ; NEX=1.5 (i.e. partial filling of k-space); 2nd acquisition: TR 50 ms; TE 11 ms; flip angle 45; NEX=3). All images were registered to the PD-weighted images using a normalised mutual information cost function [4]; ii) ADIMA image creation: The ADIMA method is an extension of a previously described method for "*pseudoT1*" image contrast generation [5]. Firstly, the "*pseudoT1*" is obtained by subtracting the late echo (T_2-weighted) of a dual-echo FSE from the corresponding early echo (PD-weighted), yielding an image which appears qualitatively similar to a T1-weighted image. Following the image subtraction, the "*pseudoT1*" image contains negative pixel values. Before dealing with the negative pixels, both the original *PD image* and the "*PseudoT1"* image are normalised to a range 0-1. After the normalisation operation of the *PD image* and "*pseudoT1"* image, the absolute intensity difference between the two is calculated to obtain the ADIMA image. ADIMA images were created using MATLAB 6 (Mathworks, Natick, MA, USA); iii) Lesion contouring: Conventional lesion masks were obtained by one rater from the PD/T2-weighted images using a well established semi-automated technique [1]. Secondly, lesion masks were drawn around the ADIMA hyper-intense and hypo-intense regions by the same rater using the same technique. The reproducibility of the lesion volume quantification was assessed by repeating the semi-automated contouring process 3 times in 5 patients over a period of 1 month; iv) Quantitative analysis of lesion masks: The bright and dark ADIMA masks as well as the conventional lesion masks were applied to the MTR, T1 and T2 parameter maps and the mean ± SD values were measured for each lesion mask.

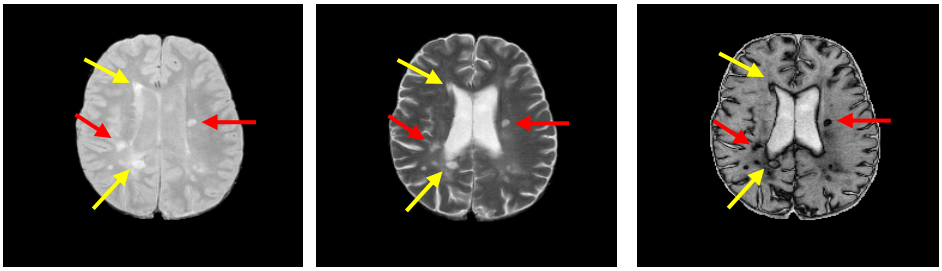

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Figure 1. a) A PD-weighted image with the corresponding b) T2-weighted image and c) ADIMA image. The yellow arrows show the hyper-intense MS lesions across all image types whereas the red arrows show hyper-intense lesions on the PD and T2-weighted images but appear hypo-intense on the ADIMA image.

Measurement	ADIMA – bright (n=10)	ADIMA – dark (n=10)	T2 lesions (n=10)	NAWM (n=10)
T1, Mean (SD), ms	1248.4 (223.2)	893.2 (156.7)	719.6 (299.9)	632.3 (47)
T2, Mean (SD), ms	228.2 (104)	121.8 (18.3)	175.14 (12.4)	79.3 (4.5)
MTR, Mean (SD), %	23.49 (4.2)	31.4 (3.4)	29.1 (4.8)	39.8 (1.6)

Table 1. Quantitative MRI measurements

RESULTS: An example of the ADIMA images is shown on figure 1 along with the corresponding PD and T2-weighted images for comparison. Table 1 shows the results from the quantitative measurements obtained from the ADIMA bright and dark masks, which confirms the presence of tissue heterogeneity in MS lesions. Also shown in the table for comparison are the values from NAWM and the conventional T2 lesions. ADIMA bright lesions exhibit the longest T1 and T2 and lowest MTR suggesting more severe tissue disruption. For T2 and the MTR the conventional lesions show values between the bright and dark ADIMA lesions suggesting that it is made up of both dark and bright lesions, whereas for T1 the conventional lesions have the shortest T1, probably due to the effect of isointense lesions on T1. Lesion volume coefficient of variation (COV) and intra-class correlation coefficient (ICC) for the T2-weighted lesions, ADIMA bright and ADIMA dark were calculated as COV = 9.1%, 6.1%, 5.3% and ICC = 0.98, 0.97, 0.99 respectively.

CONCLUSIONS: ADIMA images represent a new form of contrast based on FSE dual-echo data sets and characterises MS lesion heterogeneity in a novel and reproducible way. It is a simple post processing technique that can be used with existing or historical data sets without the need for additional data collection. Further work will be directed at investigating the exact pathological processes that can be quantified from the hyper-intense and hypo-intense regions of the ADIMA images.

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