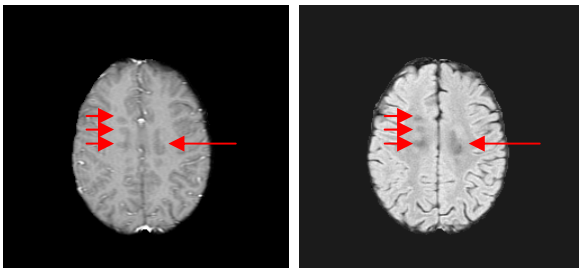
ADVANCED IMAGES ALGEBRA (ADIMA): A NOVEL METHOD FOR LESION HETEROGENEITY ENHANCEMENT IN MULTIPLE SCLEROSIS

M. C. Yiannakas[1], D. J. Tozer[1], K. Schmierer[1], D. T. Chard[1], V. M. Anderson[1], D. H. Miller[1], and C. A. Wheeler-Kingshott[1]
[1]**UCL - Institute of Neurology, London, United Kingdom**

INTRODUCTION: Multiple Sclerosis (MS) is characterised by the presence of lesions in white matter (WML), which appear hyper-intense on proton density (PD) and T2-weighted MRI scans. Histological examination has shown that the tissue damage underlying PD/T2 hyper-intense WML is heterogeneous and reflects various pathological features (e.g. inflammation, axonal loss, demyelination). However, this heterogeneity of WML cannot be assessed by using PD/T2-weighted MRI alone. A subset of PD/T2 WML appear hypo-intense on T1-weighted scans which indicates more severe tissue destruction [1]. We have developed a new post-processing analysis method "ADvanced IMages Algebra (ADIMA)", which utilises existing data sets applied to PD- and T2-weighted scans to produce a wider dynamic range of intensities over WML and surrounding tissues.

METHOD: The ADIMA method is an extension of a previously described method for "*pseudoT1*" image contrast generation [2]. The *pseudoT1* is obtained by subtracting the late echo in a conventional fast spin echo (FSE) dual-echo (i.e. PD/T2-weighted) data set from the corresponding early echo, yielding an image which appears qualitatively similar to a T1-weighted image i.e. the cerebrospinal fluid (CSF) and lesions with long T2 relaxation time appear hypo-intense relative to normal-appearing white matter (NAWM) (see figure 1a and 1b). The *pseudoT1* image shown on figure 1b can be described mathematically as follows:



a b

Figure 1. a) T1-weighted image with b) the corresponding *pseudoT1* image produced from the subtraction of the late echo from the early echo in a conventional FSE dual-echo acquisition. Red arrows indicate the presence of MS lesions

$$PDimage - T2image = pseudoT1 \qquad \textit{eq. 1}$$

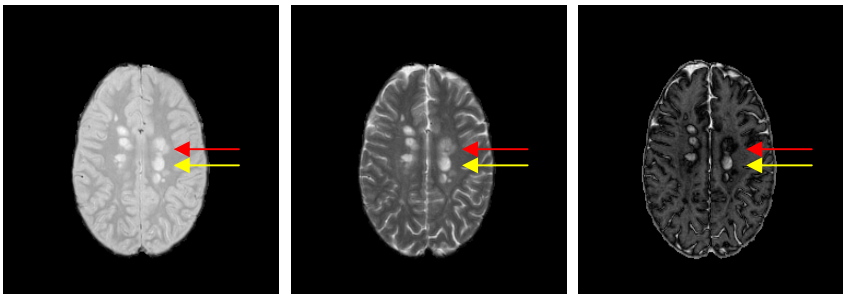
However, the subtraction of the *T2image* from the *PDimage* (***eq. 1***) results in the presence of negative pixel values within the *pseudoT1* image. The ADIMA method has its rationale in utilising the negative pixel values of the *pseudoT1* in order to increase the diversity of signal intensities in the final image. In order to achieve this result, an initial normalisation step is applied to both the *pseudoT1* and the original *PDimage* (referred to as *image* in *eq. 2*):

$$\begin{aligned} max\_a &= max\ (image\ ) \\ min\_a &= min\ \ (image\ ) \\ image\_normalised &= (image - min\_a)\ /\ (max\_a - min\_a) \end{aligned} \qquad \textit{eq. 2}$$

After the normalisation operation (*eq 2*) of the *PDimage* and *pseudoT1* image, the absolute intensity difference is calculated to obtain the ADIMA image as follows:

$$ADIMA\_image = \left| PDimage\_normalised - pseudoT1\_normalised \right| \qquad \textit{eq. 3}$$

The ADIMA images are characterised by a wide dynamic range of intensities over the MS lesions and surrounding tissue (as opposed to the conventional PD- and T2-weighted images). It is in fact possible 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 (see figure 2 – Note: the images in figure 2 are also of the same slice location as figure 1 and can be directly compared). The 'bright' and 'dark' regions can be quantified (i.e. total lesion volume) separately by using manual or semi-automated contouring methods. In order to evaluate the method images from 10 MS patients were analysed retrospectively and 'bright' and 'dark' regions contoured using an existing semi-automated method [3]. These volumes were correlated with the lesion volumes obtained using the same contouring method from the corresponding PD/T2-weighted images and the T1-weighted hypointense lesion volume using the Pearson correlation coefficient (PCC). To evaluate the reproducibility of the lesion contouring from the ADIMA images five of the patients were reanalysed by a single rater who contoured the lesions on each image type three times over a period of 1 month.



a b c

Figure 2. a) A PD-weighted image with the corresponding b) T2-weighted image and c) ADIMA image. The yellow arrow shows the same "hyperintense" MS lesion across all image types whereas the red arrow shows "hyper-" and "hypo-" intense areas of heterogeneity in the ADIMA image which are not well defined from the PD and T2 weighted images alone.

RESULTS: Lesion volume coefficient of variation (COV) and intra-class correlation coefficient (ICC) for the T2 images were calculated as 9.1% and 0.98, respectively. For the ADIMA 'bright' lesions COV and ICC were 6.1% and 0.97 whereas for the 'dark' lesions 5.3% and 0.99. The PCC correlating the T1 and *pseudoT1* lesion volumes was 0.98, 0.97 when correlating the ADIMA dark and T1 lesion volumes and reduces to 0.91 when correlating the T1 and ADIMA bright lesion volumes indicating that there may be slightly different information contained in these measures. Although the PCC is still very high for the T1/ADIMA bright volume correlation this may be due to the small number of patients imaged and their having a homogeneous lesion load and pathologies. Further subjects would be needed to investigate this further.

CONCLUSION: ADIMA images represent a new form of contrast that enhances MS WML heterogeneity in a reproducible way by utilising existing FSE dual-echo data sets. Further work will include identification of the pathological processes underlying the 'bright' and 'dark' regions of the ADIMA images.

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REFERENCES: 1) Van Walderveen MA, Neurology. 1998 May;50(5):1282-8, 2) Hickman et al, Multiple Sclerosis 2002; 8: 433-435, 3) Molyneux et al, *J Neurol Neurosurg Psychiatry* 1998; 65: 42–47.