

## Pre-filling MS lesions on T1 and T2-weighted images for improved tissue segmentation

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**Introduction:** Lesions in multiple sclerosis (MS) brain images are known to affect automated image registration and segmentation. Improved registration of MS brains has been demonstrated, by prior in-painting of lesions with white matter (WM) signal intensity (SI) derived from neighboring voxels [1]. Here we present an alternative fully-automated approach using the whole-brain histogram and image in-homogeneity profile rather than local voxel intensities. This algorithm achieves physiologically realistic in-painting on 3D T1 and 2D T2-weighted scans, and is robust to operator variation in lesion contouring.

**Methods:** MRI acquisition: Brain T1-weighted IR-FSPGR data was collected on one healthy control (1.5T, TR/TE/TI = 13.3/4.2/450ms) and on 31 MS patients (3T, TR/TE = 7.9/3.1ms). Fast FLAIR images were acquired on two MS subjects (3T, TR/TE/TI=9000/151/2250ms).

Lesion filling method: Images were corrected for RF inhomogeneity and natural WM variation, over a length scale of 35 mm. From the corrected images, a map of the image inhomogeneity profile and a whole brain histogram were generated. The global WM SI and standard deviation (SD) were found by fitting the histogram to a four-Gaussian model. A data set of simulated WM was created based on this distribution. Realistic spatial correlation was introduced with 0.6 mm Gaussian smoothing, and the SI was spatially modulated using the previously obtained non-uniformity profile. Voxels in the target image were replaced by simulated WM in regions corresponding to a pre-defined lesion mask, producing a lesion in-painted image. The FSL and MNC image processing software is used together with in-house code; computer processing time is 1 minute per image.

Data analysis: To validate the method, artificial lesions with a similar size, intensity and distribution to MS were introduced into a T1-weighted healthy control image. These lesions were then in-painted using the above method. The SI was measured in each lesion after in-painting and compared with the SI in the original image. To investigate the effect of lesion in-painting on segmentation, GM and WM fractions (GMF & WMF) were estimated for 31 SPGR MS brain images using SPM8, with a post-segmentation lesion correction [2]. The lesions were removed from the images by in-painting, and GMF and WMF were re-estimated using SPM8. The fractions obtained with two methods were compared. In-painting was performed on two T2-weighted images, to investigate this technique with other image contrasts.

**Results:** The intensity variation across the brain of the in-painted WM SI matched the non-uniformity present in the image. For 52 lesion ROIs in both infratentorial and supratentorial regions (Figure 1), the mean in-painted value correlated strongly ( $r=0.82$ ,  $p<0.001$ ) with the mean ROI SI prior to artificial lesion generation and lesion in-painting. Deviations from the ideal values were comparable to the SD of WM values within an ROI. In-painted WM SI values had a mean within-lesion SD of 38 SI units, compared to a mean SD for these regions in the original image of 40 SI units. Qualitatively, in-painted WM has a similar appearance to normal-appearing WM, on both T1 and T2 images (Figure 2). Examining the filled regions in Figure 2b indicates that the in-painted intensity is not affected by the SI on the boundary of the lesion contours. When lesion in-painting was performed prior to segmentation, the measured GMF increased (~1%), WMF decreased (~0.75%) and total brain volume increased (~0.25%) compared to correcting for lesion volumes after segmentation, for lesion volumes of 15–20 ml. The effect of lesion in-painting was proportional to lesion volume for both GMF ( $r = 0.73$ ;  $p > 0.001$ ) and WMF ( $r = -0.77$ ;  $p > 0.001$ ).

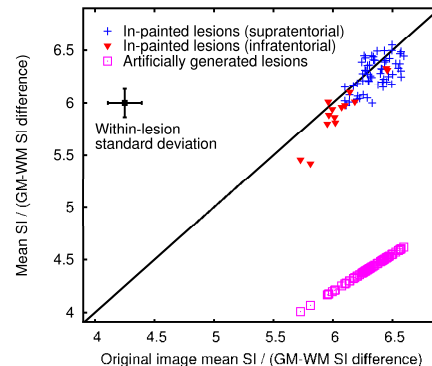


Figure 1: WM intensity values within 52 lesion ROI's after artificial lesion generation and lesion in-painting, compared to the original WM values in a healthy control image. The mean signal intensity (SI) is expressed relative to the SI difference between GM and WM.

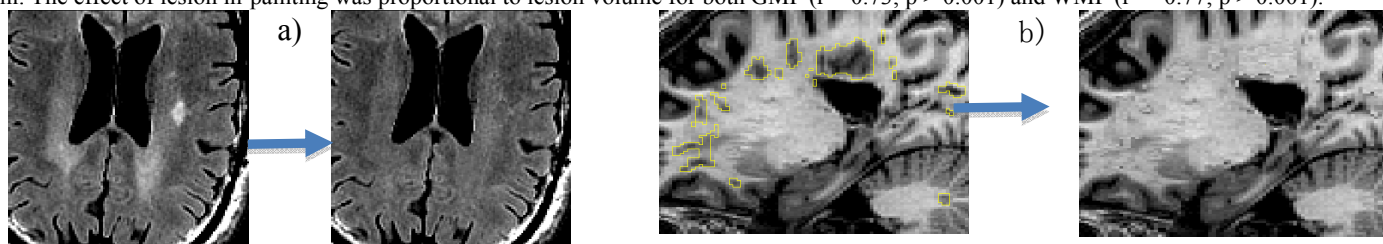


Figure 2: (a) T2 weighted images before (left) and after (right) lesion in-painting. (b) T1-weighted image before (left) and after (right) lesion in-painting, showing correction of infratentorial and supratentorial lesions.

**Conclusions:** We have introduced an automated lesion in-painting technique to address segmentation misclassification from T1 and T2-weighted images in MS. Many automated algorithms rely on accurate histograms for segmentation; therefore this approach to lesion WM correction based on the global histogram is appropriate and recommended as a pre-processing step for MS images to determine the volume of GM and WM. The inherent insensitivity to operator variation in lesion contouring is an additional benefit. The effect of lesion in-painting prior to segmentation is lesion load dependent, implying the importance of in-painting rises with advancing disease.

**References:** [1] Sdika, M. & Pelletier, D.; Hum Brain Mapp (2009), 30, 1060-1067 [2] Chard, D. T. et al.; J Magn Reson Imaging (2002), 15, 259-267