

# Influence of hypointense white matter lesions in segmentation based assessment of brain volume. Implications for clinical MS studies.

M. Battaglini<sup>1</sup>, A. Giorgio<sup>1</sup>, M. L. Stromillo<sup>1</sup>, and N. De Stefano<sup>1</sup>

<sup>1</sup>Department of Neurological and Behavioral Sciences, University of Siena, Siena, Toscany, Italy

**Introduction:** Measurement of brain volumes from T1-weighted (T1-W) MR images is becoming a widely accepted marker of tissue loss, useful for charting disease progression and response to treatment in multiple sclerosis (MS). In tissue segmentation-based analysis, however, it is not clear yet whether and to what extent the presence of T1 hypointense lesions can bias volume estimation in different brain compartments. We assessed here the impact of T1 hypointense lesions on measurements of brain tissue volumes such as cortical grey matter (GM) and white matter (WM).

**Methods:** We selected 10 MS patients who underwent the same MR protocol: a dual echo, turbo spin-echo sequence (TR/TE1/TE2 = 2075/30/90 msec, 50 contiguous 3-mm slices) for T2 lesion volume (T2-LV) measurement and a T1-W gradient-echo image (TR/TE=35/10 msec, 50 contiguous 3-mm slices) for brain volumes' measurement. Five patients had very low T2-LV ( $< 0.6 \text{ cm}^3$ ), and five patients had T2-LV ranging from 2.3 to  $26.3 \text{ cm}^3$ . The T2 lesion masks of the latter group were used to create binarised lesion masks from T2/PD images and were applied on each patient of the first group. For each patient of the first group we created 20 "artificial" T1-W images obtained as follows: the 5 masks with increasing T2-LV of the second group were registered on the "original" T1-W image using FLIRT, the registration tool of FSL, and each of these lesion masks was filled with 4 different intensities (WM-GM interface, GM, GM-CSF interface and CSF). These lesion intensities (LIs) were obtained from an intensity distribution built up from mean and standard deviation values of intensity computed using segmented tissue-types (WM, GM, CSF) of the "original" T1-W image. Values of normalised WM volume (NWMV) and cortical volume (NCV) from the "original" and from the new "artificial" T1-differences between "original" and "artificial" NWMV (NW-PVDs) and NCV (NC-PVDs) were computed. Shapiro-Wilks and Levene tests were used to assess normality and homoscedasticity of PVDs data, respectively. A repeated-measures analysis of variance (ANOVA) was carried out to test the effects of LV (5 levels) and LIs (4 levels) on PVDs.

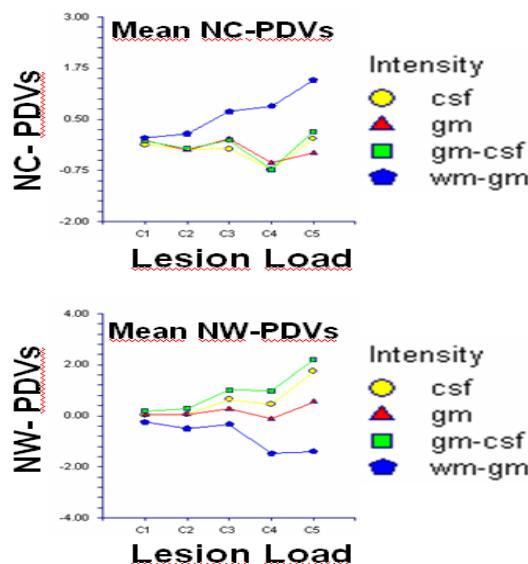


Fig 1

**Fig 1** Scatter-plots showing, for a given LV and LI, the average values of NC-PVDs (top) and NW-PVDs (bottom) in 5 patients.

We can notice how quantification of cortical GM is underestimated in presence of T1 hypointense lesions with intensity intermediate between GM and WM. By contrast, the various LIs have different effects on NW-PVDs: at the highest LV this effect is maximal between WM-GM and GM-CSF LIs.

**Results:** There was a significant main effect of LV and LI on PVDs for NWMV ( $p<0.01$  and  $p<0.001$ , respectively) and NCV ( $p<0.01$  and  $p<0.001$ ). Interaction between LV and LI was significant for NW-PVDs ( $p<0.001$ ) and NC-PVDs ( $p<0.001$ ) (Fig 1)

**Conclusions:** Both high volume and intensity of T1 hypointense lesions influence tissue segmentation-based analysis of brain volumes. In particular, quantification of cortical GM is underestimated in presence of T1 hypointense lesions with intensity intermediate between GM and WM. Segmentation algorithms used for quantification of brain volume on T1-W images should take into account both volume and intensity of T1 hypointense lesions.