MRI Intensity Tissues Normalisation for Longitudinal Surface Based Analysis of the WM/GM Contrast, application to Alzheimer's Disease

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Introduction.
MR imaging has been widely used to highlight the brain changes occurring in neurodegenerative diseases by comparing affected patients to healthy individuals. However, most of these studies focused on the cortical thickness and/or cortical volume; and only few of them studied contrast changes between gray matter (GM) and white matter (WM) [1]. To our knowledge, no longitudinal study of tissue intensities has been reported. We hypothesize that tissue alteration as measured by WM/GM could provide insights into the etiology of Alzheimer's disease (AD). MR image intensity I may be affected by a intensity change F, called contrast transform [2]. The resulting observed image I_0 becomes $F(I)$ (Fig. 1). These intensity changes between different MR data do not allow tissues intensities comparisons. The normalisation with a tissue mean value is not sufficient for latter statistical comparison and at least the two first statistical moments should be normalised. Different strategies have been proposed to normalise the greyscale intensity between MRI scans. A simple linear approximation does not adequately represent the contrast transform since, as argued in [2], changes in contrast are non linear and such methods may not be sufficient. Non-linear model as proposed in [2], [3] is based on a mean histogram and hence does not account for tissue volume differences between patients, which occurs in AD in the presence of atrophy. We assume the contrast transform to be a smooth function, which can be linearly approximated for each tissue. In this paper, we define an intensity space free from the contrast transformation where tissues intensities can be compared. After segmentation each tissue is considered separately. For each tissue, all the scans from the patient population are mapped into the space defined by the first two intensity moments. The contrast transform affects this space only along a vector direction and is easily identifiable. The tissues moments are then projected onto the space orthogonal to the contrast transform where the population can be reasonably compared.

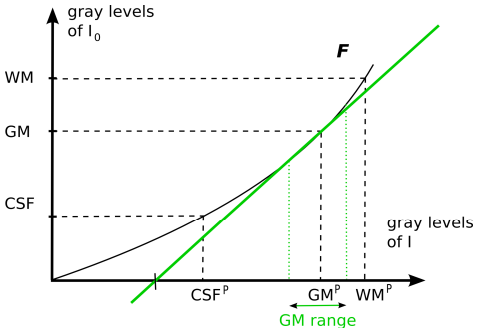

Fig. 1: *Representation of the contrast transform and the linear approximation in the GM intensity range*

Methods.
95 subjects were imaged on a 3T Siemens Trio using a 3D MPRAGE sequence as part of the Australian Imaging, Biomarker and Lifestyle study [4]. 28 were affected by Alzheimer's disease (AD), while the other 89 were healthy controls (HC) elderly subjects. All subjects received 2 scans 18 months apart.
We denote by $T_t^P=(a_t^P,b_t^P)$ the local linear approximation of the contrast transformation F in the t tissue range of patient p, where a_t^P and b_t^P are respectively its slope and its y-intersect. When measuring the mean and standard deviation of tissue t on the MRI, one measures $M_t^P=a_t^P m_t^P+b_t^P$ and $S_t^P=|a_t^P|s_t^P$. An estimation of b_t^P is given by the tangent of the second order polynomial function joining the individual means of the CSF, GM, WM to their mean values estimated over the whole population. By plotting M_t^P-b_t^P against S_t^P (Fig. 2) for all patients p, the contrast transformations act on the observed means and standard deviations along a line, crossing the origin. For each patient, the point $(M_t^P-b_t^P,S_t^P)$ is projected on the orthogonal line crossing the population barycentre. This line L is the space where the contrast transformation influence is the less important. For all patients, both tissues are then renormalised based on the projected values of their mean and standard deviation. For both MRI (baseline and follow-up), the local WM/GM contrast is calculated as the ratio of the local means of the WM and GM corrected intensities. In a surface based approach [5], a mesh is created from the WM/GM interface with scalar value representing WM/GM contrast difference between baseline and follow-up. All meshes are then registered to a common template. A point-wise general linear model (GLM) is performed to test if an intensity difference between the AD and the HC groups could be detected; Age, years of education and time between scans are controlled as covariates.

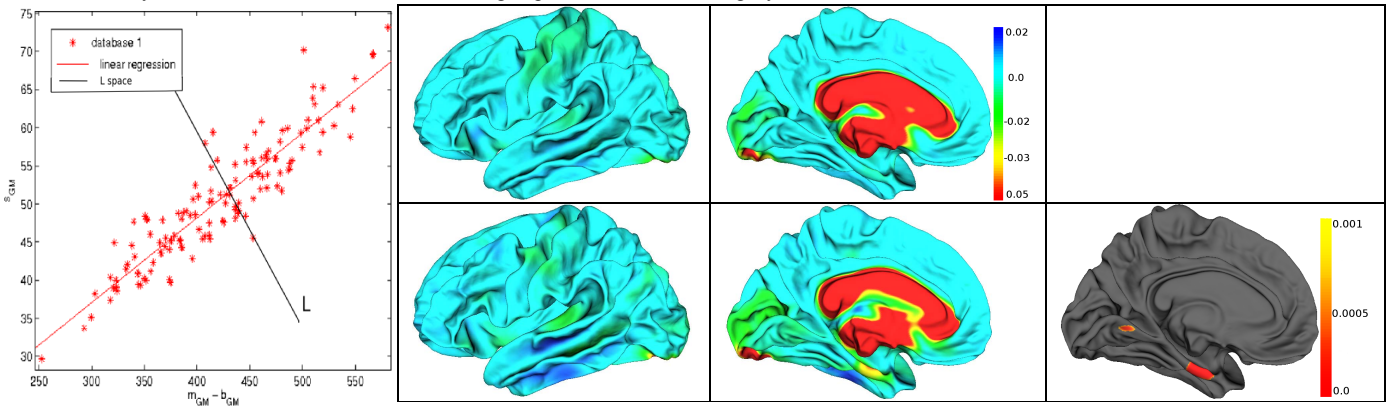

Fig. 2: *The left graph plots M_{GM}^P-b_{GM}^P against S_{GM}^P for the whole population. The red line shows the direction on which the contrast transformation is the most important. All points are projected on the orthogonal of this line to renormalise the GM intensities. The 4 meshes in the middle panel present the annual rate of change(interior and exterior of the right hemisphere) for the HC group (top row) and the AD group (bottom row). The right panels shows location with significant differences ($p<0.05$, FDR corrected)*

Results and discussion.
Figure 2 shows M_{GM}^P-b_{GM}^P as a function of S_{GM}^P for all patients. On the orthogonal space L, the AD population distribution differed from the HC one (not shown) but this was not statistically significant. The 4 first meshes of Fig. 2 show the mean annual rate of change for the HC and AD group on the right hemisphere. The main differences appeared in the temporal lobe. The AD group exhibits a decrease of contrast (around 2%/year) in the gyri of the lateral view and an increase of the contrast in the hippocampus (>3%/year). The left hemisphere had the same patterns but with lower rate of change (1%/year). The FDR-corrected p-values right hemisphere mesh of the longitudinal GLM test are shown on Figure 2. No significant regions were found on the left hemisphere. One region in the temporal lobe on the medial was significant ($p<0.005$). Without correction, no regions were significantly different, suggesting that the proposed tissue normalisation increased the separation between AD and HC. The rate of cortical atrophy has been reported to be higher in the AD population than in the HC, in the temporal lobe and special in the hippocampus [6]. Measuring contrast changes might provide a new biomarker for early diagnosis of Alzheimer's disease, but further investigations are needed.

Conclusion.
We have investigated the longitudinal evolution of the WM/GM contrast in the context of Alzheimer's disease using a new tissue normalisation method. The MRI intensity normalisation enable to measure significant change in contrast over time between AD patient and HC elder.

References
[1] Salat, D.H. et al., Neuroimage 14:721 (2009); [2] Angelini, E. et al., ISBI (2007); [3] Cox. I.J et al., ICIP 2:366 (1995) ; [4] Ellis KA et al. Int Psychogeriatric Association 21(4):672 (2009) ; [5] Acosta, O. et al., ISBI (2010) ; [6] Fejll, A., et al. Neuroscience 29(48) (2009)