ROBUST INTENSITY NORMALISATION AND AUTOMATIC INTENSITY WINDOW SELECTION FOR THE CALCULATION OF THE BOUNDARY SHIFT INTEGRAL

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Introduction

The boundary shift integral (BSI) is a robust measure of regional and global cerebral atrophy rates with higher precision than manual measures [1]. It estimates the brain volume change between two time points by calculating the brain boundary shift between registered serial magnetic resonance (MR) volume scans. The intensities of cerebrospinal fluid (CSF), grey matter (GM) and white matter (WM) in the baseline and repeat brain scans are required to be normalised in order to calculate BSI. At the moment, this intensity normalisation is performed by dividing the intensity on each scan by the mean intensity of the interior region of the brain (consists mainly of WM). Therefore, the existing method can sometimes fail to normalise the intensities of CSF and GM due to image artefacts in those areas. Furthermore, an intensity window parameter must be chosen in the calculation of BSI, in order to correctly capture the intensity transitions associated with the brain boundary. The optimal value is dependent on the scan acquisition protocol, and the arrangement and intensity of tissue types. Existing methods depend on expert judgement, which is not ideal in a clinical trial setting because of user variability. In this work, we normalise the intensities of the baseline and repeat scans by performing a linear regression using the mean intensities of the CSF, GM, WM and interior brain region of each scan, and automatically derive the intensity window from voxel intensities of the scans.

Material and Methods

In order to maxmimising accuracy of the BSI, the intensities of CSF, GM and WM need to be same in baseline and repeat scans. We therefore perform a linear regression using the mean intensities of CSF, GM, WM, and the interior brain region, and use the coefficients to normalise the intensity. In addition, BSI can be seen as an estimation of tissue type change between CSF and GM/WM near the brain boundary. Since our aim is to capture most of the tissue type change between CSF and GM/WM, this implies that it is desirable to ignore the tissue type change within the same tissue type, and maximise the tissue type change between different tissue types. We therefore choose the intensity window to be $[I_{CSF\ mean}+I_{CSF\ sd}, I_{GM\ mean}-I_{GM\ sd}]$ for T1-weighted images, where $I_{CSF\ mean}$, $I_{CSF\ sd}$, $I_{GM\ mean}$ and $I_{GM\ sd}$ are the mean and standard deviation of CSF intensity, and the mean and standard deviation of GM intensity. The calculation of BSI is described below:

1. Dilate the baseline and registered repeat brain regions 3 times, to include enough voxels in CSF to estimate the CSF intensity.
2. Perform a *k*-means clustering with 3 clusters (CSF, GM and WM) on the baseline and repeat brain images inside the dilated regions.
3. Perform a linear regression between the corresponding intensities (CSG, GM, WM and interior brain region) in the baseline and repeat scans.
4. Calculate $[I_{CSF\ mean}+I_{CSF\ sd}, I_{GM\ mean}-I_{GM\ sd}]$ for each scan using the results from the *k*-means clustering. The overall intensity window is given by the median value of the intensity windows of all the baseline and follow-up images in the dataset.
5. Calculate BSI using the median intensity window and the normalised baseline and repeat scans.

We compared this method and the existing method by applying them to the baseline and 1-year repeat T1w images of 23 Alzheimer's disease (AD) (mean (sd) age 75.8 (8.0)) and 54 control (mean (sd) age 75.4 (4.7)) subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu/ADNI).

Results

The median (sd) automatic intensity windows were calculated to be [0.43 (0.027), 0.64 (0.021)], which were similar to the existing manually chosen intensity window [0.45, 0.65]. Furthermore, the existing and automatic intensity windows produced almost identical brain atrophy rates for the AD and control groups when the same normalisation method was applied (see Table 1). The brain atrophy rates (mean (sd)) of the AD and control groups using the existing and new methods are shown in Table 2. The increased separation of the average brain atrophy rates between the two groups, the decreased standard deviation in each group, and the increased effect size (measured by Cohen's *d*) suggested that our new intensity normalisation method improve group separation between AD and control groups. The differences in the brain atrophy rates calculated from the new and existing methods ordered by the imaging sites are shown in Figure 1. The largest difference in the atrophy rates was from the images acquired in site X, which was subsequently found to have had a scanner upgrade between baseline and repeat scans.

Normalisation by only interior region	Using existing intensity window [0.45, 0.65]	Using automatic intensity window [0.43, 0.64]
Control	-0.01% (1.14%)	0.00% (1.11%)
AD	0.58% (1.43%)	0.60% (1.37%)

Table 1: The brain atrophy rates using existing and new automatic intensity windows when the same intensity normalization method was used.

	Normalisation by only interior region (intensity window [0.45, 0.65])	Normalisation by CSF, GM, WM and interior region (intensity window [0.43, 0.64])
Control	-0.01% (1.14%)	0.23% (0.88%)
AD	0.58% (1.43%)	1.04% (0.77%)
AD - Control	0.59% (p = 0.076)	0.81% (p = 0.0001)
Effect size	0.49	0.97

Table 2: The brain atrophy rates and group separations using existing and new methods.

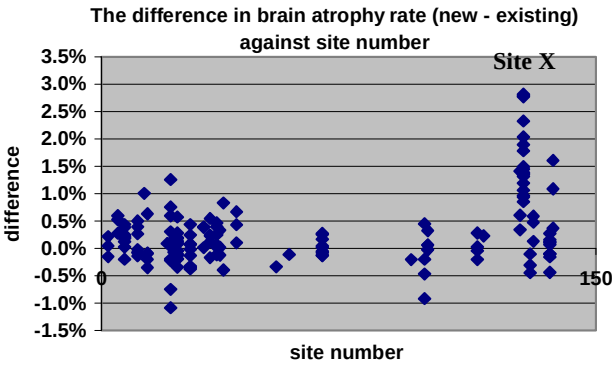

Figure 1: The difference in brain atrophy rates between the new and existing intensity normalisation methods ordered by site number.

Discussion and Conclusions

We have described a new intensity normalisation method to calculate the BSI with automatic intensity window selection, and applied it to a subset of images from the ADNI database. Initial results suggested that the new method improved group separation between AD and control groups, by better handling the intensity normalisation of images after a scanner upgrade (site X), since the effect of just using the automatic intensity window is minimal. Furthermore, the difference of the BSI values calculated using the two intensity normalisation methods may provide an automatic and endpoint-specific image quality control metric, which will be useful in large AD studies such as ADNI. Our method is closely related to the work by Nyul and Udupa [2], which suggested that intensity in MR image could be mapped to a standardised range by using the modes in the histogram. In this work, we used k-means clustering to automatically find these modes which correspond to CSF, GM and WM, although our method is not dependent on specific classification technique. Future work includes validation on the whole ADNI dataset and our own datasets. In conclusion, we demonstrate that the robustness, sensitivity and reproducibility of BSI can be improved by using the method described in this abstract.

Reference: [1] Freeborough, et al. IEEE TMI, 1997, [2] Nyul and Udupa, MRM, 1999.