Tissue-Based Intensity Standardization Technique: Application to the ADNI Multi-Centric Dataset

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Introduction

Intensity standardization in magnetic resonance imaging (MRI) aims at correcting scanner-dependent intensity variations to ensure correspondence between different tissue classes. Existing techniques for the most part are aimed at matching input image histograms onto that of a given standard [1-4]. In particular, the simple and robust technique of Nyul et al. [1], referred as L_4, linearly interpolates intensities between matched decile histogram landmarks. Our experience convinced us, however, that standardization should be aimed at matching spatially corresponding tissue intensities rather than non-spatially specific histogram information. In this study, we present a novel automatic technique called STI (STandardization of Intensities), which incorporates tissue spatial intensity information and compare STI to L_4 on the large, multi-centric Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset (www.adni-info.org), based on the mean absolute intensity error (MAE).

Method

Dataset and initial image processing. The ADNI dataset consisted in 797 baseline MRIs from controls, mild cognitive impairment and probable Alzheimer's disease subjects, acquired on 56 different 1.5T scanners using the ADNI 3D T1-weighted MP-RAGE protocol [5]. All MRI volumes were pre-processed in a similar fashion using the MINC image processing toolbox (http://www2.bic.mni.mcgill.ca) before standardization: a) noise removal [6]; b) raw scanner intensity inhomogeneity correction [7]; c) global registration (12 degrees of freedom) to the standard image [8], maximizing the mutual information between the two volumes [9]; d) resampling to a 1-mm^3 isotropic grid; e) clamping. In this last step we 1) set to zero all intensity values below percentile values 0.01; 2) set to 100 all intensity values above the percentile value 99.99; and 3) linearly interpolate intensities between those limits. This step removes low and high intensity outliers and rescales image intensities on a common 0 to 100 scale. The standard image taken as a reference throughout this study was obtained from BrainWeb [10] (normal brain, T1 image, 1-mm resolution, 0% noise, 0% non-uniformity).

Intensity standardization. STI uses available BrainWeb tissue masks for the background, white matter (WM) and grey matter (GM) to determine tissue-specific intensity correspondences. For each tissue mask, STI performs the following steps: 1) mask both input and standard images, i.e. keep only the voxels contained in the tissue mask; 2) from the masked voxels, compute and smooth the standard-vs.-input joint intensity histogram; 3) find the two-dimensional (2D) position of the maximum in the joint histogram. The maximum corresponds to the most frequent intensity correspondence between the input and standard images, i.e. the mode, for the current tissue. The 2D intensity points obtained for each tissue are then used as control points in the mapping function. To this set, STI adds two extra points: the first maps both minimum intensities in the input and standard images, and the second, the maximum values. STI finally completes the mapping function by linearly interpolating intensities between 2D points.

Technique comparison. We compared STI to the L_4 histogram-matching technique described in [1], which uses decile (10%-spaced percentile) landmarks. To allow direct image comparison, the standardized images were non-linearly registered [11] onto the standard. The comparison was based on the mean absolute error (MAE), with respect to the standard, i.e. the mean absolute intensity difference between the standardized and the standard images, over 1) the entire image, 2) the brain, consisting in WM and GM, 3) only WM and 4) only GM. The brain, WM and GM regions were determined using the same BrainWeb tissue masks.

Results

Over the 797 subjects of the ADNI dataset, both intensity standardization methods gave significantly lower mean MAE compared to no standardization at all. STI gave lower mean MAE for the entire image, the brain and WM, while L_4 gave lower mean MAE for GM. A one-way ANOVA test showed that the difference was significant for WM ($p < 0.0001$, see box-plot in Figure 1) but not for other regions (entire image: $p = 0.7527$, brain: $p = 0.2662$, GM: $p = 0.3320$). Qualitatively, this is also reflected in the four image examples of Figure 2, where WM intensity is underestimated when using L_4.

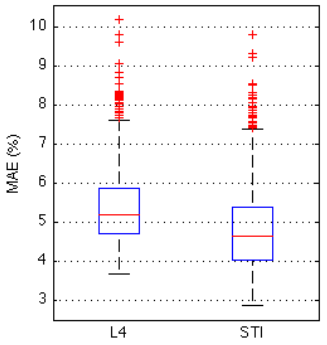

Figure 1. Box-plot of MAE for WM. Since intensity values range from 0 to 100, MAE can be interpreted as a percentage value.

Conclusion

Compared to L_4, STI gave improved intensity standardization when compared on the basis of mean MAE, especially with respect to white matter. Those results demonstrate that standardization methods should not be aimed solely at matching histograms and that spatial information must also be incorporated. A major strength of the current study is the use of a large, multi-centric dataset.

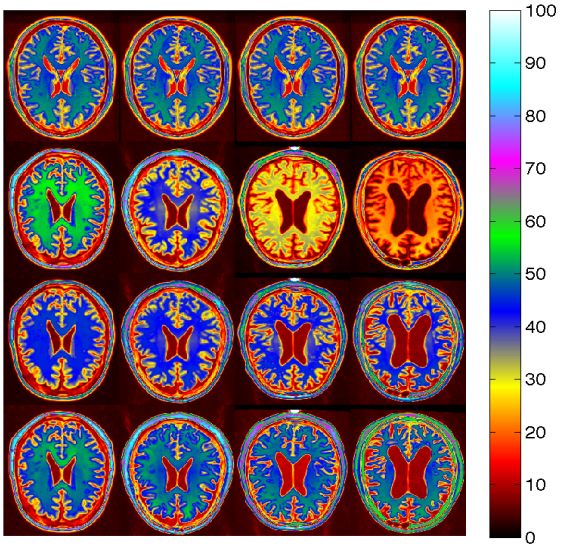

Figure 2. From left to right: four intensity standardization examples of ADNI images, before non-linear registration. From top to bottom: standard image, input image, and images standardized with L_4 and STI, respectively.

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