Improved deep gray matter segmentation using anatomical information from quantitative susceptibility maps

Ferdinand Schweser[1], Xiang Feng[1], Rosa Mach Batlle[1], Daniel Güllmar[1], Andreas Deistung[1], Michael G Dwyer[2], Robert Zivadinov[2,3], and Jürgen R Reichenbach[1]
[1]*Medical Physics Group, Institute of Diagnostic and Interventional Radiology I, Jena University Hospital - Friedrich Schiller University Jena, Jena, Germany,* [2]*Buffalo Neuroimaging Analysis Center, University at Buffalo SUNY, Buffalo, New York, United States,* [3]*Jacobs Neurological Institute, University at Buffalo SUNY, Buffalo, New York, United States*

TARGET AUDIENCE – Researchers interested in brain segmentation.

PURPOSE – Brain image segmentation followed by region-of-interest (ROI)-based analyses is a way to quantify subtle variations of MR image intensity. With the recent advent of imaging techniques that provide excellent contrast of deep brain nuclei, such as quantitative susceptibility mapping (QSM)[1-3], research interests focus on subtle pathologic variations of deep gray matter (DGM) tissue properties. In particular, QSM promises to provide information on the tissue iron concentration[4], which is supposed to be an important biomarker in several neurodegenerative diseases[5,6]. While manual outlining represents the gold standard segmentation technique this approach is prohibitive for large cohort studies. Several sophisticated tools are available to perform the segmentation automatically based on T_1-weighted (T_1w) images. However, the contrast of DGM relative to white matter (WM) is generally very low in T_1w images (see **Figure 1** left). The T_1-based segmentation of deep brain nuclei using algorithms such as FMRIB's Integrated Registration and Segmentation Tool (FIRST)[7], consequently, often fails to identify the nuclei and falls back to an inaccurate atlas-based segmentation. This has a substantial degrading effect on the ROI analysis and may result in misleading biases due to disease-related effects such as atrophy[8]. **In this contribution we present an approach to improve the automated segmentation of deep gray matter with FIRST that relies on the incorporation of prior anatomical information from secondary image contrasts with high-contrast in the critical brain regions.** The proposed technique is solely pre-processing-based and, thus, does not require modification of the actual segmentation algorithm. We demonstrate the approach with quantitative susceptibility maps as secondary images due to their exquisite DGM contrast[1-3].

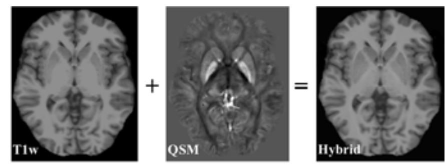

FIGURE 1. T_1w image (left), susceptibility map (middle) and (proposed) hybrid image (right) of the diencephalon of an exemplary volunteer. The contrast in the T_1w image is low for the DGM nuclei compared to the other images.

THEORY – We propose to use a special *hybrid contrast* as input for the segmentation algorithm instead of conventional T_1w images. The hybrid contrast is created by mathematically combining T_1w images with the secondary high-contrast images, i.e. the susceptibility image. Since segmentation algorithms, such as FIRST, require T_1w image contrast (because they were trained with T1w data), we propose to combine the images such that the resulting image contrast is similar to the T_1w brain atlas template in MNI space that is used by FIRST. To demonstrate the technique, we combined the two contrasts using a weighted sum approach (see Methods). When intensity normalized or quantitative images are used for the combination optimal weights can be determined once and for all in a separate *training step*. The resulting weights can then be used for all images of the cohort to create the hybrid images that are fed to the segmentation algorithm. This is illustrated in **Figure 2**.

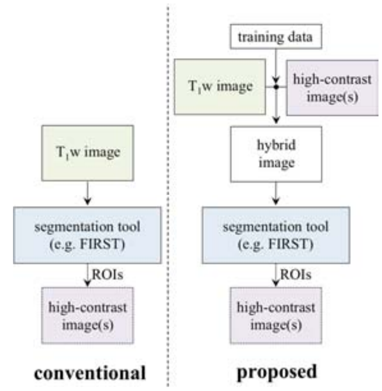

FIGURE 2. Flowchart of image segmentation. The left part illustrates the conventional processing; the right part is the proposed algorithm.

METHODS – *Data acquisition:* Data were acquired from seven healthy volunteers (21–41 years) on a 3T whole-body MRI scanner (Tim Trio, Siemens Medical Solutions, Erlangen, Germany). The local ethics committee approved the experiment and informed written consent was obtained from each recruited subject. The T_1w data was acquired with a magnetization prepared rapid gradient echo (MP-RAGE) sequence using the following sequence parameters: TE=3.03 ms, TR=2300 ms, TI=900 ms, FA=9°, voxel size=(1 mm)^3. Acquisition parameters of the gradient echo acquisition used for QSM were: $TE_1/TE_2/TR$=12 ms/40 ms/46 ms, flip angle 20°, and 0.47 x 0.47 x 0.94 mm^3 voxel size. *Data processing:* The T_1w images were intensity normalized using the mri_normalize utility in Freesurfer. Susceptibility maps were reconstructed by applying SHARP[2] and HEIDI[9]. *Training step:* ROIs were manually defined in various brain regions (caudate, globus pallidus, putamen, thalamus, white matter, cortical gray matter) in the T_1-weighted images of all subjects, in the corresponding susceptibility maps, and in the brain atlas. The mean values m_j (j=1…N) of the intensities in the ROIs were calculated for all three image types. The optimal weights w_k were determined by solving the following equation system in a least-squares sense: $[\boldsymbol{m}_{\mathrm{T1w}}\ \boldsymbol{m}_{\mathrm{QSM}}] \cdot \boldsymbol{w} = \boldsymbol{m}_{\mathrm{atlas}}$, where $\boldsymbol{m}_{\mathrm{T1w}}$, $\boldsymbol{m}_{\mathrm{QSM}}$, and $\boldsymbol{m}_{\mathrm{atlas}}$ are 1xN vectors that concatenate the mean values m_j of the image intensities in the ROIs and the 1x2 vector $\boldsymbol{w}$ concatenates the desired weights. *Hybrid contrast generation*: The hybrid images I_{hybrid} were created by, first, registering all susceptibility maps I_{QSM} to the corresponding T_1w-images I_{T1w} and, then, multiplying the contrast as follows: $I_{\mathrm{hybrid}}=I_{\mathrm{T1w}}\cdot \mathrm{w}_1 + I_{\mathrm{QSM}}\cdot \mathrm{w}_2$. *Analysis*: FIRST was applied subsequently to both the T_1w images and the hybrid contrast images of all subjects. Resulting ROIs were compared to each other and to manually defined ROIs using the Jaccard index, the kappa index, the dice index, sensitivity and specificity.

RESULTS – The mean Jaccard index over all subjects is summarized in **Figure 3.** The hybrid images yielded a substantially improved segmentation of the nuclei compared to the conventional T_1w images. All other measures yielded comparable results and are, thus, omitted here. **Figure 4** illustrates the improvement in an exemplary dataset.

DISCUSSION – The presented approach overcomes the limited contrast on T_1w images as well as the poor image segmentation resulting from it. The similarity of the hybrid contrast with a conventional T_1w contrast allows using image analysis tools such as FIRST that were originally designed for T_1w data and, consequently, generally do not yield satisfactory results when other image contrasts are used as input. As an example, FIRST relies on a large training dataset with manually defined (T_1w) deep brain nuclei[7]. Creating new training data for FIRST, e.g. with the high-contrast susceptibility maps, is an extremely laborious task with uncertain success. The presented method however is a simple preprocessing step for the FIRST input data. The technique is not restricted to using susceptibility maps but could be used, in principle, also with other contrasts such as R_2*. Future improvements may include non-linear combination and extending the approach to using more than one high contrast image, potentially providing even a better match of the hybrid contrast with the typical appearance of T1w images.

CONCLUSION – By combining conventional T_1-weighted contrast with susceptibility maps a novel hybrid contrast can be created that substantially improves FIRST segmentation of deep brain regions. Modifying the segmentation algorithm is not required.

REFERENCES – [1] Deistung A et al., 2013. *NeuroImage*. 65:299-314. [2] Schweser F et al., 2011. *NeuroImage*. 54(4):2789-807. [3] Deistung A et al., 2013. *Front Hum Neurosci*. 7:710. [4] Langkammer C, 2012. *NeuroImage*. 62(3):1593-99. [5] Hagemeier J, et al., 2012. *Expert review of neurotherapeutics*. 12(12):1467-80. [6] Langkammer C et al., 2013. *Neurodegener Dis*. (epub). [7] Patenaude B et al., 2011. *NeuroImage*. 56(3):907-22. [8] Zivadinov R, 2013. *Front Biosci*. E5(2):525. [9] Schweser F et al., 2012. *NeuroImage*. 62(3):2083-100.

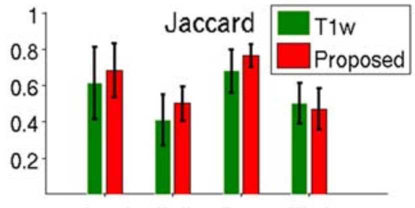

FIGURE 3. Quantitative analysis of the segmentation results using Jaccard coefficient.

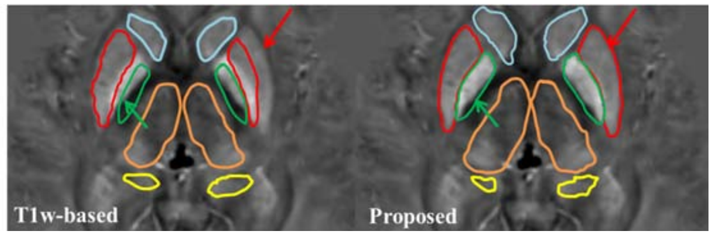

FIGURE 4. Outlines of segmented deep GM regions obtained using the conventional T_1w image contrast (left) and the hybrid contrast (right) (superimposed on the susceptibility map) The arrows mark regions with poor segmentation based on T_1w images and improved segmentation using the hybrid contrast.