Automated 3-D Segmentation of Radiation-induced Cerebral Microbleeds on Susceptibility Weighted Imaging at 3T and 7T

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Introduction:

Cerebral microbleeds (CMBs) appear as small, round foci of low signal intensity on T2*-weighted MRI. The diagnostic and prognostic value of these lesions has recently been explored in many diseases, mainly through quantification of their number and location [1-3]. However, a clear relationship between CMB size and spatial distribution in different disorders has not been well established[4]. Therefore, CMB volumes and their derivatives might be independent biomarkers of clinical interests. Unfortunately, manual CMB segmentation is a lengthy and laborious task due to their small size, large number, three-dimensional nature, varying contrast, and imperfect spherical profile [5]. These characteristics make CMB segmentation even more difficult than CMB identification, which is known to be prone to human error, as manifest by high intra- and inter-rater variability [6, 7]. Therefore, automated CMB detection and segmentation is highly desirable. In this study, we propose an automated 3-D CMB segmentation algorithm that is applied after automated CMB detection[8]. Our preliminary results show that the proposed method can efficiently, robustly and consistently segment CMB regions, offering a reliable alternative to manual definition.

Methods:

MR Imaging: Ten patients with gliomas who received radiation therapy between 2 and 15 years prior to the date of imaging were retrospectively selected for this study. Patient with fewer than 10 CMBs were excluded. All patients were scanned on 3T and 7T GE scanners on the same day using eight-channel phased array coils. High resolution 3-D susceptibility-weighted imaging (SWI) was performed with flip angle 20°, 24 cm FOV, in-plane resolution of 0.5 x 0.5 mm, and 2 mm slice thickness on both 3T and 7T. Echo time/repetition time was 28/46 ms at 3T and 16/50 ms at 7T. A GRAPPA-based parallel imaging acceleration was applied two-fold at 3T and three-fold at 7T. CMB candidates were first identified using a previously-described automated CMB detection algorithm [8] and then corrected by an experienced rater on minimum-intensity projected (mIP) SWI. A binary mask in mIP SWI coordinate system was generated in the identification process. To examine the performance of the algorithm in extreme conditions, two patients with more than 200 CMBs who were scanned on a 7T GE scanner using a 32-channel phased array coil, were also included as a separate test set.

CMB 3-D segmentation: The proposed segmentation algorithm is based on the local image intensity and morphology of lesions in SWI images. The binary mask in mIP SWI coordinates was first projected back into SWI coordinates. For each CMB, a cubic region of interest (ROI) with edge length L and centered on the minimal intensity voxel within the masked area was selected. As radiation-induced CMBs often have radii smaller than 2 mm [2], L = 4 mm was used in this study. The segmentation was then achieved by combining two models. The first model assumes that in a small ROI where tissue is relatively homogenous, tissue intensity approximately follows a Gaussian distribution introduced by noise while the other structures such as CMBs and veins are presented as low-intensity outliers[9]. A local intensity threshold $T = \bar{X}_{ROI} - \alpha \cdot \sigma_{ROI}$ is iteratively calculated by excluding $x_{outlier} < T$, where x is individual voxel intensity, $\bar{X}_{ROI}$ and σ_{ROI} are mean intensity and standard deviation, and α is the thresholding degree. In this study, α was tested from 1.5 to 2.5. Gray-scale SWI images can also be modeled as topological surface with intensity level as altitude. As CMBs have lower signal intensity than surrounding brain parenchyma, they can be thought of as 'catchment basins' that can be distinguished using a 3-D watershed algorithm[10]. After applying both local threshold and wtershed transform models, the 6-connected 3-D neighborhood containing the center voxel is segmented as CMB region.

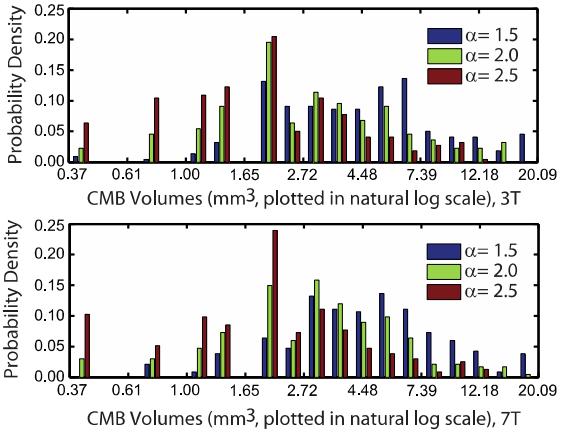

Figure 1: Distribution of CMB volumes on 3T and 7T using the automated segmentation method with varied α. Volumes are plotted in natural log scale.

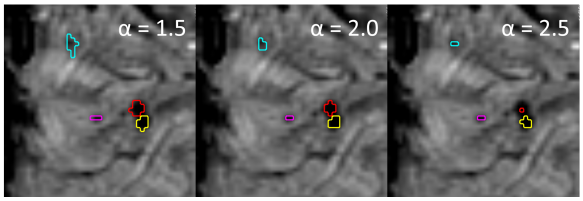

Figure 2: Segmentation results on one test dataset using α = 1.5, 2.0, and 2.5. The segmented regions of four CMBs are highlighted in four different colors.

Results:

A total of 220 CMBs and 234 CMBs were identified in ten patients at 3T and 7T, respectively. The average computation time was approximately 2s for a single SWI volume. No CMBs were merged into each other. The mean and standard deviation of the volumes of all segmented regions smoothly and monotonically decreased as α increased at both field strengths. The distribution of segmented CMB volumes were roughly the same between 3T and 7T using the same α (Fig. 1). The correlation coefficient between volume distribution at 3T and 7T was 0.94, 0.94, 0.89 for α = 1.5, 2.0, and 2.5, respectively. These findings suggest that the performance of the proposed 3-D segmentation algorithm is consistent even between different field strengths.

In the 2 test datasets with high CMB counts, one patient had 309 CMBs and the other 217 CMBs. The average computation time of the segmentation algorithm on these two patients was approximately 30s for each SWI volume. Only 3/309 and 1/217 CMBs were merged into nearby CMB regions when α = 1.5, and only 1/309 and 0/217 CMBs were merged when α = 2.5. The segmentation results of four CMBs on one test dataset are shown in Fig. 2. The shape of all CMBs was nearly but not perfectly spherical. The segmentation algorithm was even able to distinguish the two bordering CMBs that were visually distinct (red and yellow regions in Fig. 2).

Discussion:

The proposed 3-D segmentation algorithm for quantification of CMB volumes shows efficient, robust, and consistent performance in this study of patients with radiation-induced microhemorrages. The high correlation coefficient between segmented CMB volume distribution at 3T and 7T using the same α indicates that the local threshold model can appropriately accommodate regional contrast variation. Empirically, α = 2 had the most reasonable segmentation. The watershed algorithm detected every regional minimum and thus nearby CMBs and veins were well segmented. Consequently, over-segmentation occurs when a CMB has internal intensity fluctuation. Our preliminary algorithm will be further improved by removing too shallow local minima and region merging, and validated by comparing with manual definition from multiple experienced raters. The algorithm will ultimately facilitate investigation of the relationship between CMB size, radiation dose, and cognitive outcome.

References:

[1] Greenberg, S.M., et al., Neurology, 1999. [2] Lupo, J.M., et al., Int J Radiat Oncol Biol Phys, 2012. [3] Werring, D.J., et al., Neurology, 2005. [4] Cordonnier, C., et al., Brain, 2007. [5] Schenck, J.F., Med Phys, 1996. [6] Cordonnier, C., et al., Stroke, 2009. [7] Gregoire, S.M., et al., Neurology, 2009. [8] Bian, W., et al., Neuroimage Clin, 2013. [9] Barnes, S.R., et al., Magn Reson Imaging, 2011. [10] Meyer, F., Signal Processing, 1994.