Automatic Mean Transit Time Lesion Outlining in Acute Stroke Using Level Sets

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Introduction MRI is widely used in the assessment of acute stroke patients, with the mismatch between perfusion weighted- and diffusion weighted imaging an emerging target for thrombolytic therapy in clinical management and large clinical trials [1,2]. Maps of tissue mean transit time (MTT) are commonly used in visualizing hypoperfused tissue. However, the critical delineation of the boundary of the perfusion lesion suffers extreme interobserver variability [3]. This is due in part to the variations and gradients in tissue perfusion from core lesion to unaffected tissue, and experimental noise in underlying raw EPI images. We propose estimating the perfusion lesion by finding a smooth contour, which minimizes variation around a patient-specific elevated MTT value inside the contour, and variation around a normal value outside the lesion, using variational calculus. We show that, in contrast to simple thresholding, this technique compares excellently with lesion outlines by four expert neuroradiologists in typical clinical stroke image data.

Materials and methods In the hypoperfused area, MTT values will vary around en elevated MTT value M_{hypo}, while in normal tissue MTT is close to a normal value M_{norm}. We seek a contour C, which minimizes

$$\mathbf{E}(C) = \lambda_1 \int_{\text{inside } C} (\text{MTT}(x,y) - M_{hypo})^2 dxdy + \lambda_2 \int_{\text{outside } C} (\text{MTT}(x,y) - M_{norm})^2 dxdy + \alpha \text{length}(C)$$

where MTT(x,y) is the mean transit time at coordinates (x,y). Smoothness is ensured by adding a cost for the length of the contour (last term). The contour C minimizing this expression was found using the level set approach in [4]. The tuning weights were fixed at $(\lambda_1, \lambda_2, \alpha) = (1.0, 1.25, 0.5)$. N=14 patients with acute ischemic stroke (NIHSS 12.5 ± 5.64) underwent standard dynamic susceptibility contrast MRI (3.0T) within 3 hours of onset. MTT was calculated by block-circulant singular value decomposition (oSVD). Four neuroradiologists were asked to delineate the extent of hypoperfused tissue, and were blinded to all clinical and other imaging data. In the absence of gold-standard lesion outline, we compared the proposed methodology to the extent of lesion outline confidence, as assessed by varying extent of consensus among experts. Thus, four lesion-estimates were generated, with the largest corresponding to voxels classified as being hypoperfused by at least one expert, and the most conservative including only voxels classified unanimously as being hypoperfused by all experts.

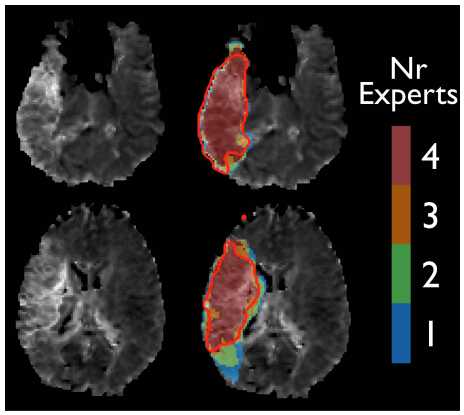

Figure 1 MTT images. Overlay: number of experts assessing each voxel as ischemic. Red contour represents level set algorithm.

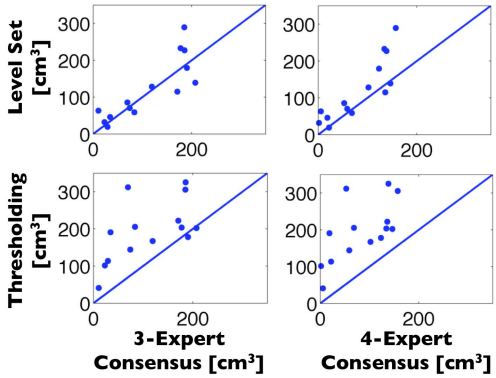

Figure 2 Correlation between volume of expert consensus lesions and, respectively, the level set algorithm and thresholding.

Results The median single-slice computation time across all patients in this study using 600 iterations was 10.0 sec [9.9, 10.1]. In all patients, the difference between the largest and smallest expert-estimated volume is greater than 10% of the average lesion size, and in 6 of 14 cases this difference exceeded 30%. Top row in Figure 1 illustrates the algorithm's ability to estimate a spatially coherent lesion matching the rater consensus despite a diffuse gradient between hypoperfused and normal tissue. Bottom row shows an example with clear interrater variation, with the algorithm identifying the consensus lesion. Close agreement between level set lesions and manual delineation is observed for lesions with consensus between 3 and 4 experts, while thresholding leads to increased bias and variance (Figure 2). The smallest average volume difference -9.3±45.2cm^3 (manual-automatic) was observed with lesions marked by at least three of four experts. For thresholding, the smallest volume difference was observed when voxels were judged ischemic by just one expert, average difference of -23.9±89.2cm^3.

Conclusion Our results confirm earlier findings of substantial interrater variation in perfusion lesion delineation, while demonstrating that with a simple variational calculus framework, lesions defined by expert consensus can be reliably and efficiently estimated. Thus the technique shows promise as a means for reproducible perfusion lesion determination. **References** [1] Davis, Lancet Neurology 2008. [2] Hacke, Stroke 2005. Coutts, Stroke 2003. Chan, Image Processing 2001.