## Automatic segmentation of diffusion MRI from the Genes Associated with Stroke Risk and Outcomes Study

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Background and purpose: Acute ischemic stroke lesions are reliably detected as abnormalities on diffusion-weighted MRI (DWI) [1,2]. Clinical decision-making and

trial design could be improved with a fast and reproducible method for delineating such areas and determining their volume. Genome wide association studies seeking to link genetic variants with imaging phenotypes that require thousands of subjects would benefit from automated lesion segmentation techniques. We compared two algorithms for automatic segmentation of DWI lesions in an independent dataset.

**Methods**: DWI from ischemic stroke patients enrolled in the Genes Associated with Stroke Risk and Outcomes Study (GASROS) who were imaged within 48 h of admission were retrospectively analyzed. Cases were included if a manual lesion outline,  $b_0$  (b-value=0 s/mm<sup>2</sup>) volume and isotropic DWI (iDWI) volume (b-value=1000 s/mm<sup>2</sup>) were available. Apparent diffusion coefficient (ADC) maps were calculated from the slope of the linear regression fit of the log of the iDWI and  $b_0$  images versus their b-values. Manual outlines took approximately 5-30 min for each patient depending on lesion size. The cerebellum was removed from analysis by resampling (MNI Autoreg [3]) the ICBM152 atlas [4,5] to the  $b_0$  image and excluding tissue with >90% probability of being part of the cerebellum [6]. Two algorithms were evaluated: an ADC thresholding-based algorithm similar to RAPID [7] and a Naive Bayes approach that had been trained on an independent dataset [8-10]. Performance was compared in terms of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN). Sensitivity (TP/(TP+FN)), specificity (TN/(TN+FP)) and Dice similarity metric (DSM, (2TP)/(2TP+FP+FN)) were computed and evaluated using a two-sided Wilcoxon test. Pearson correlations between manually and automatically determined volumes were compared using a Fisher transformation. Results are specified as median [interquartile range]. For all analyses, p < 0.05 were considered significant.



Fig. 1.Top: Manual outline of stroke lesion overlaid on isotropic DWI. Middle: concomitant ADC map. Bottom: automatic segmentation by NB algorithm

**Results**: 289 cases met inclusion criteria. Lesion volumes on manual outlines were median [IQR] 2.2 [0.39 – 8.4] cm<sup>3</sup>. The NB algorithm was significantly more sensitive (p < 0.001) than the ADC thresholding based algorithm and also had superior DSM (p < 0.001). Both algorithms took 20–40s/subject to segment the lesion. There were no significant differences between both algorithms in terms of specificity (p = 0.21) and correlation between automatically and manually determined volumes (p = 0.35).

**Discussion**: Although highly correlated and spatially coincident with manual outlines, both algorithms performed less reliably than reported in two other datasets [9,10]. A critical difference with those data is that patients in this study were included based on time from admission to MRI, which may include patients with subacute strokes. The earlier studies included patients using a criterion of <24h last-known-well (LKW) time to MRI [9,10]. Algorithms were trained for cases seen within 24h of LKW [8–10] and DWI findings are known to change markedly after this timeframe [11,12]; it is likely that the study population included a large number of cases whose LKW was >24h before MRI. Also, the lesion sizes in this study were significantly smaller than those previously studied: 112 of the cases had lesions smaller than 1 cm<sup>3</sup>, the minimum size threshold that RAPID uses for excluding spurious noise [7]. The algorithms we investigated were optimized to detect large lesions presenting within recanalization treatment windows (<8 h) and therefore the reduced performance on a dataset including subacute strokes is not surprising. Future automatic segmentation programs should take into consideration time from stroke onset to improve performance.



Fig. 2. a) Sensitivity, b) specificity, c) Dice similarity and d) agreement in terms of lesion volume of automatic segmentations compared to manual outlines.

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