A Rapid, Robust, Anatomy and Atlas Guided Lesion Quantification Framework from Diffusion Weighted MR Images

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Introduction: Rapid assessment of the lesion location and volume using standard techniques is critical to diagnose and make treatment or clinical trial enrollment decisions in acute stroke patients [1] [2] [3]. Efforts to develop post-processing methods to segment and automatically measure lesions from DWI images are emerging (c.f., [3][4]). In [3, 4], a heuristic-based histogram thresholding was proposed to segment potential regions of ischemia. As we show later, this approach may lead to false positives arising from hyper-intense regions manifesting themselves in certain regions of the brain (e.g., cerebellum). The authors propose a strategy of removing these artifacts by observing contra-lateral statistics [3]. However this approach may lead to false negatives when detecting instances of bilateral stroke. We propose an automated hybrid approach to reliably segment potential acute stroke lesions without using *a priori* information of the absence of bilateral strokes. This approach is composed of an anatomical split-and-merge strategy to segment lesions in the cerebellum and cerebrum, separately, and then generating a composite segmentation result. This unified approach may lead to enhanced robustness of our algorithm when compared with a non-split and merge algorithm.

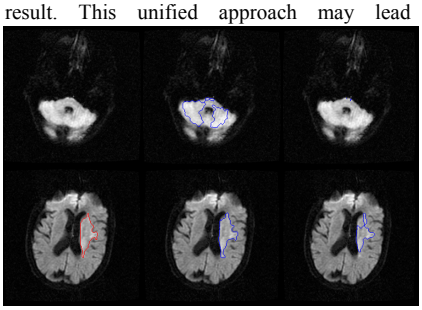

Fig. 1: Seg. (Blue) results when compared with GT (red) for two slices in a volume. 1st column – GT, 2nd column – Seg w/o anatomical split-and-merge, 3rd column – Seg. with anatomical split and merge (See text for details)

Methods: *Patient Data*: From February 2000 through October 2007, patients treated with standard IV-tPA after a baseline, pre-treatment MRI were considered for this analysis. The study was approved by the appropriate institutional review boards. *Image Acquisition*: We applied our approach on 25 acute stroke patients a range of lesion abnormalities as visualized on DWI. All patients were imaged on a clinical 1.5T GE MR scanner using an 8-channel head coil. Axial DWI images were acquired using a SE-EPI sequence (TR/TE = 4.5s-7.0s/60ms-100ms, FA = 90°, NEX = 2, matrix size = 256 x 256, FOV = 240x 240 mm^2, slice thickness = 7 mm, b = 0 s/mm^2 and 1000 s/mm^2, diffusion encoding along axial, sagittal and coronal directions). The DWI data was retrospectively processed using our algorithm. *Algorithm:* To implement the *split-and-merge* (S-n-M) algorithm on the cerebrum, and cerebellum separately, we need to isolate them from the brain, after brain masking. This was achieved by registering the subject to a T1-weighted atlas [9] on the b0 image. A rigid transform was sufficient to coarsely partition the two regions. In the first part of the hybrid approach, we employ a multi-level, histogram-based, maximum-entropy thresholding [5] on the cerebrum and select the top two threshold levels. These were determined empirically from the underlying assumption that regions of acute stroke lesion are hyper-intense and lie on the right-hand side of the histogram, and manifest as higher intensity values on the histogram. Simultaneously, in the second part, a bottom-up clustering using a disjoint-set forest algorithm [6] is employed on the cerebrum. In the third part, we superimpose the top-down clustering on the bottom-up clustered regions and keep those contiguous regions which contain "seeds". Seeds, in this context, are cues that are obtained from the calculated ADC image [1]. Finally, morphological post-processing (opening, closing) is applied to remove holes and small islands that may develop during the segmentation process. The same pipeline is applied with different parameters to obtain potential lesions in the cerebellum, and composed with those from the cerebrum leading to a final lesion segmentation mask for the entire brain.

Ground Truth (GT) and Evaluation: A trained imaging scientist marked lesion locations on DWI images which formed the ground truth [3]. The performance of the algorithm with and without split and merge schemes was measured using: (a) Spearman correlation (ρ) between algorithm segmented lesion and GT volumes, (b) Repeated measures ANOVA (c) Bland-Altman analysis to measure repeatability with GT, (d) Dice-coefficient, and (e) Linear-weighted inter-rater agreement statistic. All statistical analyses were performed using MedCalc®(v. 10.4). In addition, absolute differences between segmented lesion volumes and GT volumes were also calculated.

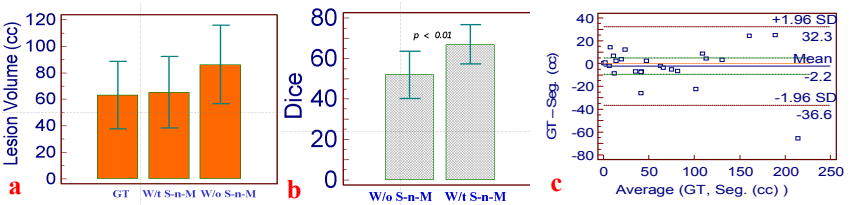

Fig. 2: Statistical analysis of Seg (S-n-M and non S-n-M) Vs GT. (See text for details).

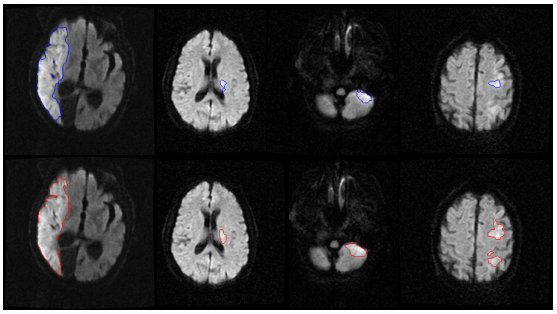

Fig. 3: Seg. (Blue) and GT (Red) for various types of lesions in cerebrum and cerebellum, including potential failure modes.

Results and Discussion: Image artifacts that affect DWI lesion segmentation, especially in the cerebellum, are readily removed with a S-n-M scheme (Fig. 1). The end-to-end processing time of the algorithm was ~10-12 sec that included time taken to read and write images. A repeated measures ANOVA showed that the mean GT volume (63±60 cc) was similar to that obtained from the S-n-M scheme (65±64 cc, p =1.0, ρ = 0.95), compared to those with a non S-n-M scheme (86±70 cc, p =0.03, ρ = 0.76) (Fig.2a). The improvement with an S-n-M scheme for lesion segmentation was also substantiated with improved Dice (Median = 71, IQR = 67-82), compared to a non S-n-M variant (Median = 64, IQR = 30-75) (Fig. 2b). When using a S-n-M scheme, Bland-Altman analysis suggested a mean bias of 2.2cc with the limits of agreement of ±36cc, while the inter-rater agreement was 0.83. These results compare favorably with prior published work [3, 4]. Notwithstanding these improvements, we observed a few unaddressed challenges. These include: (i) Lacunar or small lesions (typically < 2-3 cc) and their resolution-limited detectability, (ii) Poor contrast or acute image artifacts that affect the algorithm performance (Fig. 3, 1st column from the right), and (iii) Scope for minimal user-intervention that may dramatically improve the performance of the algorithm [7, 8]. Dynamic contrast-enhancement algorithms (e.g., adaptive histogram enhancement, etc.,), and recent inhomogeneity correction algorithms can aid the outcome of the lesion segmentation algorithm in a time-unconstrained situation. However, this is counter-intuitive in the current scenario when time is a critical factor for localizing acute stroke lesions [10]. Additionally, perfusion weighted images (PWI) may be used to refine the lesion segmentation if they are available during a study [3, 8].

Conclusions: A fully automated and robust acute stroke lesion segmentation algorithm is proposed that performs satisfactorily on a vast majority of the cases with various DWI lesion sizes (5cc – 200cc). Multi-parametric, or learning-based approaches, coupled with a final review or user-initiation can render this approach to be integrated into the clinical workflow for rapid stroke assessment.

References: [1] M. Wintermark et al., Stroke, 39(5), 2008, [2] V. Gupta et al, Acad. Rad.,15(1), p.24-39,2008 [3] M. Luby et al., Stroke; 37, p.2951-2956, 2006 [4] M. Straka et al, ISMRM, 17, p.728, 2009, [5] M. Luesi et al., J. Elec. Imaging, 18(1), p. 013004:1-10,2009, [6] P. Felzenswalb and D. Huttenlocher, IJCV, 59(2), 167-181,2004, [7] S. Nath et al., Proc. ISMRM, 17, p. 4675, 2009, [8] J. R. James et al., Comp. in Bio. & Med. 36, p.1268-1287, 2006, [9] I. Talos et al., SPL-PNL Brain Atlas, March, 2008, [10] J. L. Saver, Stroke, 37, p.263-266, 2006.