ROBUST REPRODUCIBLE SEMI-AUTOMATED PERFUSION-DIFFUSION MISMATCH ASSESSMENT IN ACUTE ISCHEMIC STROKE SETTING

Venkata Veerendranadh Chebrolu[1], Dattesh D Shanbhag[1], Arun Govinda Rao[2], Patrice Hervo[3], Marc-Antoine Labeyrie[4], Catherine Oppenheim[4,5], and Rakesh Mullick[1]
[1]*Medical Image Analysis Lab, GE Global Research, Bangalore, Karnataka, India,* [2]*GE Healthcare, Bangalore, Karnataka, India,* [3]*GE Healthcare, Buc, France,*
[4]*Departments of Radiology and Neurology, Centre Hospitalier, Sainte-Anne, Paris, France,* [5]*Université Paris Descartes, Paris, France*

Target Audience: Physicists and radiologists interested in acute ischemic stroke and perfusion-diffusion mismatch.

Purpose: Stroke is a leading cause of death and disability, with more than 15 million people suffering from stroke each year. In acute ischemic stroke, MRI perfusion (PWI)-diffusion (DWI) mismatch (PDM) has been used to estimate the salvageable brain tissue that is at risk of infarction [1-2]. Accurate and fast quantification of the mismatch volume is critical for timely treatment decision and several automated stroke lesion segmentation methods have been reported [3-7]. However, it is known that histogram distributions of ADC and DWI of normal and infarcted tissues overlap [8]. Hence, manual intervention might be needed in some cases as reported recently [9]. Manual intervention is expected to bring subjectivity into stroke lesion assessment. For example, in semi-automated lesion segmentation methods based on user defined seed inputs, the location and shape of the input could vary. The purpose of this work is to develop robust and reproducible semi-automated DWI and PWI lesion segmentation algorithms and to evaluate their performance and reproducibility in assessing perfusion-diffusion mismatch in a cohort of acute ischemic stroke patients as compared to manual segmentation, considered as a reference.

Methods: *DWI Lesion Segmentation*: DWI lesion segmentation was performed using both DWI images and ADC map. DWI data was processed using histogram-matching filter and was partitioned into two regions: cerebrum and cerebellum [5]. Each of the two regions was further partitioned in to four classes based on DWI intensity (three brain segments and a fourth background region). The regions that belonged to the highest intensity class on DWI data with corresponding low value in the ADC map ($< 0.65\times10^{-3}$ mm^2/s for cerebrum and $< 0.6\times10^{-3}$ mm^2/s for cerebellum) were selected as probable DWI lesion regions. The regions connected (6 - connectivity) to the above selected regions and with an ADC threshold ($< 0.59\times10^{-3}$ mm^2/s for CBM and $< 0.51\times10^{-3}$ mm^2/s for CBLM) were also included as probable DWI lesion regions. These regions were checked for the presence of seed point inputs that were provided by the radiologist before the segmentation was started. If there was no seed within any of the probable infarct regions or if the regions were not in proximity (measured using Euclidian distance transform) to another region that had a seed, then the region was discarded and removed to generated the final DWI lesion segmentation. *PWI Lesion Segmentation*: Tmax (time at which the deconvolved residue function maximizes) based PWI lesion segmentation with DWI feedback was performed as follows: The PWI lesion hemisphere was identified using results from DWI lesion segmentation. Then, regions with Tmax < 6sec [9] and regional cerebral blood volume (rCBV) greater than 12 mL/100g were removed. Additionally, regions without contralateral support were removed [10]. The final PWI lesion marking was obtained after removing the ventricular regions (using the ventricle mask generated by registering DWI to PWI data). *Reproducibility Analysis*: 30 stroke patients were imaged with DWI and PWI before treatment with thrombolysis according to rt-PA guidelines (< 4.5 hours after onset) on a 1.5T GE scanner (Signa HDx, GE Healthcare, Chalfont St Giles, UK) with an 8-channel head coil. The reproducibility of the above described semi-automated segmentation methods was tested with three different kinds of user-defined-inputs (Figure 1): i) A line on the central slice of the infarct on the DWI data (CSL) ii) A point on the central slice (CSP) and iii) A point on the extremity slice of the infarct on the DWI data (ESP). The ground-truth was generated by a senior radiologist who manually delineated the stroke infarct on DWI images (using ADC to avoid false-positive) and ischemic hypo-perfused area on Tmax map. The results of semi-automated DWI and PWI lesion segmentation and PDM assessment with three different user inputs were compared with ground-truth. The user-interaction, Tmax map and ground-truth generation was done using functionality available in READY View tool within the Advantage Workstation platform (GE Healthcare, Buc, France). *Mismatch Criteria*: Target mismatch was calculated using DWI and PWI lesion volumes by applying criteria similar to DEFUSE 2 study [9]. *Statistical Analysis*: Statistical analysis for reproducibility and mismatch agreement was performed using the MedCalc tool (v.12.3). Repeated measures ANOVA was performed to analyze the difference between segmentation results from the three user inputs. The kappa coefficient (κ) was used to analyze the dichotomous agreement between ground-truth mismatch and the mismatch obtained from the semi-automated approach.

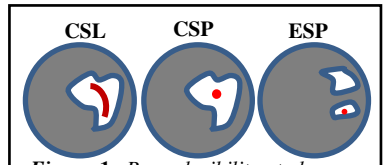

***Figure 1**: Reproducibility study was performed with three different user inputs i) A line on the central slice of the infarct on the DWI data (CSL) ii) A point on the central slice (CSP) iii) A point on the extremity slice of the infarct on the DWI data (ESP).*

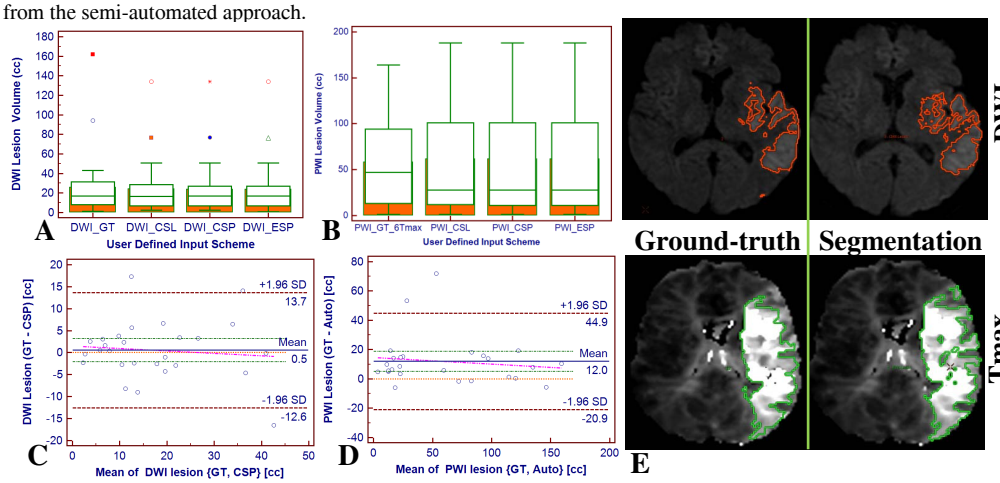

***Figure 2**: A) and B) demonstrate reproducibility of the DWI and PWI lesion segmentation using the proposed semi-automated algorithms with different user-inputs (CSL, CSP, ESP). C) and D) show the Bland-Altman analysis comparing ground-truth (GT) with results from CSP based segmentations of DWI and PWI lesions. E) shows DWI and PWI lesion markings obtained using the proposed approaches with their corresponding ground-truths for a representative case.*

Results and Discussion: Results in Figure 2 show Box-and-Whisker plots demonstrating excellent reproducibility of the DWI lesion segmentation for the three different user inputs. Repeated measures ANOVA did not show any statistically significant differences between ground-truth lesion volumes and those obtained using the semi-automated methods ($p < 0.05$). Bland-Altman plots show good agreement between ground-truth and semi-automated DWI and PWI lesion segmentation. The differences observed in lesion volumes compared to ground-truth were similar to those reported earlier for intra and inter observer variability with manual marking [11]. Mismatch agreement was achieved in 88% of the cases with a kappa (κ) of 0.766. The overall processing time including user-interaction was less than two minutes. In summary, we have successfully demonstrated semi-automated DWI and PWI lesion segmentation algorithms which are robust to variations in user-inputs.

References: [1] Kane I et al, J Neurol Neurosurg Psychiatry 2007;78:5 485-491. [2] Albers GW, Stroke. 1999;30:2230-2237. [3] Straka M et al, JMRI 2010; 32:1024–1037. [4] Lansberg M et al, Stroke 2011; 42: 1608-1614. [5] Nath SK et al, ISMRM 2010: p. 678. [6] Nargenthiraja K et al, ISMRM 2012: p. 756. [7] Montiel N et al, Acad Radiol 2008; 15:77–83. [8] Chebrolu et al, ISMRM 2012: p. 3097. [9] Lansberg M et al, Lancet Neurol 2012; 11: 860–67. [10] Shanbhag D et al, ISMRM 2010: p 59. [11] Luby M et.al, Stroke 2006;37;2951-2956;