# IMPACT OF ACCURACY AND RELIABILITY OF DIFFUSIVITY IN ASSESSING ACUTE ISCHEMIC STROKE

Venkata Veerendranadh Chebrolu[1], Dattesh D Shanbhag[1], Ek Tsoon Tan[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 Global Research, Niskayuna, NY, 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**: In acute ischemic stroke, diffusion weighted MRI (DWI) forms the basis for clinical assessment of infarct core [1]. Treatment decisions based on the perfusion-diffusion mismatch (PDM) criteria [2] depend on accurate determination of diffusion/perfusion lesion volumes. Several groups have developed automated algorithms [2-6] for diffusion and perfusion lesion segmentation. These are based on apparent diffusion coefficient (ADC) and/or DWI contrast, both of which depend on the accuracy of the diffusion sensitivity b-factor realized during imaging experiment. The b-factor used for DWI imaging could vary due to factors such as gradient non-linearity [7] and concomitant field effects [8]. These system imperfections may differ between different vendors and MRI systems [7]. This variation would impact multi-center studies evaluating the efficacy of the PDM criteria for thrombolysis treatment decision. In this work we demonstrate the effect of b-factor variations on automated diffusion lesion segmentation and PDM assessment.

**Theory**: The signal intensity ($S$) of a voxel in a DWI image is given by the equation: $S = M\exp(-TE/T_2)\exp(-b \times D_a)$, where $M$ is the magnetization, $TE$ is the echo-time, $T_2$ is the transverse relaxation time, $D_a$ is the ADC and $b$ is the diffusion sensitivity factor $[b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)]$. When $b$ is zero, we obtain a $T_2$-weighted or the so called $S_0$ image. If we define a dimension less exponential decay factor $f = b \times D_a$, then the estimated ADC ($ADC_e$) is calculated as: $ADC_e = [-\log(S/S_0)] \times [f/b]$. A variation in $f$ could occur because of factors such as gradient nonlinearities and/or $\Delta$. If these variations are represented by a scaling factor $\varepsilon$ (i.e. $f$ changes to $\varepsilon \times f$), then % change in $ADC_e$ would be $100(\varepsilon - 1)$ and the % change in the measured DWI signal would be $100[e^{-f(\varepsilon-1)} - 1]$. Therefore, for a given variation in $f$, the % change in measured DWI signal is lower than the % change in $ADC_e$. Hence, a variation in $f$ would have different impact on diffusion lesion segmentation methods based on ADC and/or DWI intensities.

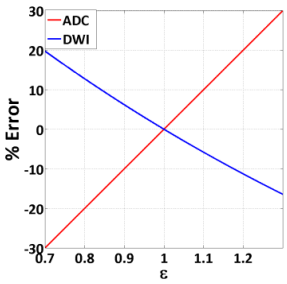


***Figure 1**: % Error in estimated ADC and measured DWI signal at different ε. A typical b-factor of 1000 s/mm² and ADC of 0.6×10⁻³ mm²/s were used in the computations.*

**Methods**: 40 acute ischemic stroke patients in the anterior circulation (Sainte-Anne Stroke unit, Paris) were imaged were imaged with DWI and PWI within 4.5 hours of onset on a 1.5T GE scanner (Signa HDx, GE Healthcare, Chalfont St Giles, UK) with an 8-channel head coil. ***DWI***: The imaging parameters include: echo-time/repletion-time=81-102/6600ms, flip-angle=90°, NEX=2, Acquisition matrix=256×256, FOV=240×240mm², slice thickness of 6 mm, no gap, b=0 s/mm², and b=1000 s/mm² diffusion encoding along axial, sagittal and coronal directions. ADC was computed using b=0 ($S_0$) and trace b=1000 data ($b_{1000}$). Using this ADC map and $S_0$, 8 different DWI data sets ($b_k$) were synthesized as follows: $b_k = S_0 \exp(-k \times ADC)$. Where $k$ = 800, 850, 900 … 1150 and 1200. These data sets represent a ε of 0.8, 0.85, 0.9 … 1.15 and 1.2 respectively. ***DWI Lesion Segmentation:*** Two different methods were tested: (A) *Based on ADC only*: i) Compute $ADC_e$ using $b_k$ and $S_0$ ii) Generate a brain mask and apply to $ADC_e$ iii) Apply ADC threshold of 0.6×10⁻³ mm²/s iv) Remove regions with volume less than 1cc v) Perform morphological open operation with structuring element of disk shape with radius of 1 to generate the final ADC based diffusion lesion mask. (B) *Based on DWI and ADC:* An algorithm described in [4] was modified to perform lesion segmentation. The modifications included use of user-provided seed point(s) to guide DWI lesion segmentation. ***PWI***: Dynamic susceptibility contrast weighted axial oblique slices were acquired using a GE-EPI sequence, TE=19–60ms, TR=1000–2275ms, FA=90°, number of phase measurements varying from 40 to 100, slice thickness=5 mm–7mm, matrix size=64×64 to 128×128, FOV=240×240mm². The PWI images were processed using READY View tool within the Advantage Workstation platform (GE Healthcare, Buc, France) to generate deconvoluted Tmax maps. ***Ground-Truth (GT)***: An experienced radiologist marked the lesions on DWI and Tmax images. ***Mismatch Criteria***: A dichotomous PDM was calculated at different ε using a criteria similar to the DEFUSE 2 study [9] for both the segmentation methods. The same GT PWI volumes were used for PDM calculation at different ε. ***Statistics***: Repeated measures ANOVA was performed for each of the segmentation methods to assess the DWI lesion volume variation with ε. Agreement between GT mismatch and the mismatch obtained for both segmentation methods at each ε was estimated using the kappa coefficient (κ). The statistical analysis was performed using the MedCalc tool (v.12.3).

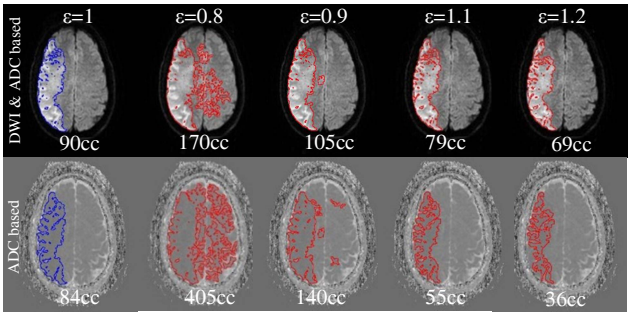


***Figure 2:** Comparison of diffusion lesion segmentation, for a representative case, by the method that uses both ADC and DWI with the method that uses ADC alone. Error in lesion volume for ADC based segmentation was higher than segmentation that used both DWI and ADC. GT =91cc.*

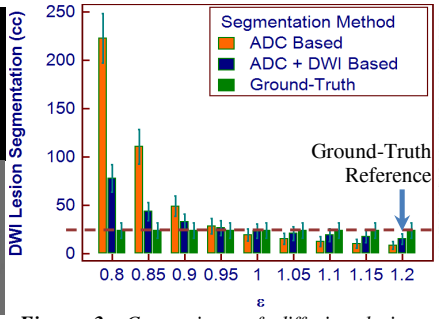


***Figure 3**: Comparison of diffusion lesion segmentation results for the complete cohort using repeated measures ANOVA. Methods that use both ADC and DWI demonstrate better robustness to system imperfections.*

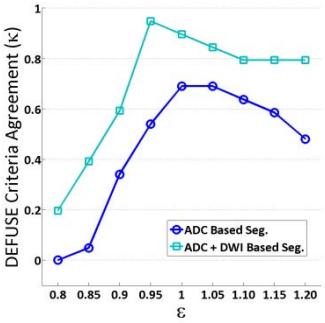


***Figure 4**: Agreement (κ) between GT PDM and the PDM obtained using the two segmentation methods at different ε. ADC+DWI based method shows strong agreement above ε of 0.95.*

**Results and Discussion**: Figure 2 demonstrates relative stability of DWI and ADC approach to b-factor variability. Figure 3 shows the comparison of the segmentation results for the complete cohort at different ε. In the case of ADC based segmentation, repeated measures ANOVA showed statistically significant differences ($p < 0.05$) in DWI lesion volumes compared to GT for ε other than 1 and 0.95. Similarly, for DWI and ADC based methods ε other than 1.05, 1 and 0.95 showed statistical difference. For all values of ε we observed better PDM agreement with GT for ADC+DWI based method compared to ADC only based method (Figure 4). Interestingly, the maximum value of agreement (κ) was obtained for ε = 0.95 with ADC+DWI based method. This suggests a potential preprocessing step for ADC+DWI based DWI lesion segmentation. In this work, spatial variation of b-factor was not considered. The results shown in this work demonstrate the maximum possible errors in the assessment of diffusion lesion volume and PDM. The results indicate that in presence of b-factor variability a joint DWI and ADC based method may offer more robust perfusion-diffusion mismatch assessment compared to ADC alone based DWI lesion segmentation method.

**References**: [1] Campbell BCV et al, JCBFM 2012; 32, 50–56. [2] Straka M et al, JMRI 2010; 32:1024–1037. [3] Lansberg et al, Stroke 2011; 42: 1608-1614. [3] [4] Nath SK et al, ISMRM 2010: p. 678. [5] Nargenthiraja K et al, ISMRM 2012: p. 756. [6] Montiel N et al, Acad Radiol 2008; 15:77–83. [7] Malyarenko D et al, JMRI 2012; (early view). [8]Baron CA et al, MRM 2012; 68(4): 1190-1201. [9] Lansberg et al, Lancet Neurol 2012; 11: 860–67.