

# Probabilistic Prediction of Tissue Fates in Acute Ischemic Brain Injury

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**INTRODUCTION** Tissue signatures based on perfusion and diffusion characteristics in acute stroke provide critical information regarding tissue fates and could assist in clinical decision making. Previous studies had demonstrated that multiparametric analysis of  $T_1$ -,  $T_2$ -, and diffusion-weighted images (DWI) outperformed analysis of any single parameter alone in correlating with histology or stroke outcomes (NIH stroke scale). A natural extension would be to include perfusion-weighted imaging (PWI). Wu et al. [1] used a general linear model to combine DWI and PWI and predicted 66% sensitivity and 84% specificity that proceeded to infarct in humans. In this study, we propose a different statistical algorithm to determine the probability and probability density of infarction based on quantitative perfusion and diffusion imaging on a pixel-by-pixel basis. Probability maps of infarction in the image space determined at each time point were tested against lesion volumes determined at 3 hrs and histology at 24 hrs on stroke rats subjected to permanent ischemic brain injury.

**METHODS** Permanent focal brain ischemia was induced on 8 male SD rats (300-350g) (Group I: 4 rats in training set, and Group II: 4 rats used for prediction). Imaging at 4.7T was performed under 1% isoflurane at 30, 60, 90, 120, 180 mins, and followed by TTC staining at ~24 hrs. Blood pressure, heart rate, respiration rate, rectal temperature, blood gases were maintained within physiological ranges.

ADC was measured using spin-echo echo-planar imaging (EPI) with matrix=128x128, 4 segments, FOV=2.56x2.56cm<sup>2</sup>, eight 1.5-mm slices, TE=37ms, TR=2s, 16 averages, b = 10, 1270 s/mm<sup>2</sup> along each of the 3 principle axes. CBF was measured using the continuous arterial spin-labeling technique with gradient-echo EPI, with parameters similar to the ADC measurement except TE=15ms.

ADC(trace) and CBF maps were calculated at each time point. Lesion volumes were resolved using an improved unsupervised ISODATA (iterative self-organizing data analysis technique [2]) clustering method based on both ADC and CBF maps [3]. Probability contour plots of the CBF and ADC scatterplots were computed (**Group I**) by determining the percentage of pixels at each grid (grid width:  $0.05 \times 10^{-3}$  mm<sup>2</sup>/s for ADC and 0.1 ml/g/min for CBF) that migrated to the ISODATA-defined lesion volumes at 180 mins. Probability was calculated in steps of 10% from 0 to 100%. Normalized probability density contour plots were also computed by multiplying the probability contour plots by the number of pixels in each grid. Prediction was made (**Group II**) and compared with ADC-defined and ISODATA-defined lesion volume at 3 hrs (both were correlated with infarction at 24 hrs [3,4]; lesion volumes stopped evolving after 3hrs of occlusion in this stroke model). Accuracy of prediction was evaluated based on visual spatial correspondence and based on the ratio of numbers of correctly predicted lesion pixels to the numbers lesion pixels determined by ISODATA method.

**RESULTS & DISCUSSIONS** Fig. 1a shows the contour plots of probability of becoming infarct ( $P_1$ ) at 30, 60, 90 and 120 mins computed based on the ADC and CBF maps (Group I). The probability was determined with reference to the 180min time point. For the 4 time points,  $P_1$  of pixels with high ADC and CBF (i.e.,  $ADC > 0.7 \times 10^{-3}$  mm<sup>2</sup>/s,  $CBF > 1.0$  ml/g/min) was essentially zero whereas  $P_1$  with very low ADC and CBF ( $ADC < 0.52 \times 10^{-3}$  mm<sup>2</sup>/s,  $CBF < 0.3$  ml/g/min) was very high (>90%). The “mismatch” zone where the ADC was normal or close to normal but the CBF was reduced [4] showed a non-zero probability of becoming infarcted (>20%) at 30 and 60 mins. Generally, lower ADC and/or CBF showed a higher probability of becoming infarcted. Fig. 1b shows the probability density  $P_D$  contour plots. At 30 mins, there appeared to be two modes in the  $P_D$  plots relative to other time points. As ischemia progressed, the contour plots became narrower (more defined) with the peak (highest probability density) remained at the same CBF (0ml/g/min) and ADC ( $0.42 \times 10^{-3}$  mm<sup>2</sup>/s).

Based on the probability contour plot, the probability of pixels becoming “infarcted” at 3 hrs was computed on a separate group of animals (Group II) based on the ADC and CBF maps at 30 mins only. Fig. 2 shows the results from one representative animal (red: 0-10% and yellow: 90-100% probability). The predicted tissue fates showed excellent spatial correspondence to the lesion volumes defined by ADC abnormality and ISODATA analysis at 3hrs. Prediction was 87% (group average =  $83 \pm 7\%$ ) accurate on a pixel-by-pixel basis for this animal (>90% probability of becoming infarcted was used). The average predicted  $P_1$  of 30mins “core” and “mismatch” pixels are 97% and 84%, respectively.

**CONCLUSION** This study demonstrated a probability-based estimate to evaluate tissue at risk of infarction. Probability and probability density of tissues becoming infarcted were derived on a pixel-by-pixel basis. The derived probability maps of tissues at risk of infarction showed good correlation with ADC-defined and ISODATA-defined lesion volumes at 3 hrs (both were correlated with infarction at 24 hrs). This approach has the potential to assist in therapeutic drug testing in animal models and clinical decision making.

## REFERENCES

[1] Wu et al., Stroke 2001, 32:933. [2] Jacobs et al. JMRI, 2000; 11: 425. Theiler et al., Proc SPIE, 1997; 3159:108. [3] Ren et al., submitted 2003. [4] Shen et al, JCBFM 2003, 23:1479.

