Dynamic Tracking of Tissue Fates Using Improved Unsupervised ISODATA Analysis of High-Resolution Quantitative Perfusion and Diffusion Imaging

H. Ren[1], Q. Shen[1], T. Q. Duong[1]

[1]Department of Psychiatry, CCNI, University of Massachusetts Medical School, Worcester, MA, United States

INTRODUCTION It has been postulated that the "perfusion-diffusion mismatch" seen initially after stroke approximates the "ischemic penumbra". Although multiparametric analysis of T_1-, T_2- and diffusion-weighted data had been shown to be a better predictor than any individual parameters based on correlation with histology or stroke outcome, no study employed multiparametric analysis to dynamically track tissue fates on a pixel-by-pixel basis as ischemia evolves during the acute phase. In this study, we implemented an improved multiparametric clustering technique using the unsupervised ISODATA (iterative self-organizing data analysis technique) method [1] to characterize quantitative perfusion and diffusion data in focal ischemic rats during the *acute phase*. ISODATA clustering technique can statistically determine the number of clusters in an iterative fashion, which is more suitable for analyzing stroke data because the number of clusters is usually unknown during the evolution of cerebral ischemia. Our goals were 1) to improve ISODATA method and apply it to statistically resolve different pixel clusters on the ADC-CBF scatterplots on a pixel-by-pixel basis and map these clusters onto the image spaces, and 2) to characterize the temporal and spatial dynamics of each cluster on a pixel-by-pixel basis in term of their tissue volumes, CBF and ADC values as ischemia progressed during the acute phase.

METHODS High-resolution quantitative perfusion and diffusion images were acquired with matrix=128x128, FOV=2.56x2.56cm^2, 8 1.5mm slices every 30mins for 3 hrs on 8 rats subjected to permanent MCAO. TTC histological staining was performed at 24 hours post-ischemia. The unsupervised, multi-parametric ISODATA technique was modified to include the use of Mahalanobis distance measure and spatial continuity. Since CBF distribution was wider than ADC distribution, ISODATA analysis using the Euclidean distance measure generally failed to resolve the correct number of clusters. Mahalanobis distance measure was better suited because it took into account the covariance of each parameter. Pixel spatial contiguity [2] was also implemented to correct the pixel mis-assignment due to noise. Multiple clusters were resolved using ISODATA analysis, color-coded and overlaid on the CBF-ADC scatterplots and the image spaces. Tissue volumes, ADC and CBF of each cluster were evaluated at each time point. The "mismatch" pixels at 30 mins were characterized as they evolved to different clusters with time.

RESULTS & DISCUSSIONS In all animals at 30 mins post-occlusion, three clusters were detected and were assigned to be "normal" (high ADC and CBF), "mismatch" (high ADC but low CBF) and "core" (low ADC and CBF) clusters. At 30 mins post-occlusion, all rats showed substantial "perfusion-diffusion mismatch". At 180 mins, the mismatch disappeared in some animals (Group I, n = 5) and persisted in others (Group II, n = 3). **Fig. 1A** shows representative CBF images, ADC maps at 30 mins and 180 mins post-occlusion (left column: Group I, right column: Group II). The ADC and CBF lesion volumes can be clearly visualized. There was substantial "perfusion-diffusion" mismatch at 30 mins post-occlusion. **Fig. 1B** shows the ISODATA cluster analysis of the CBF-ADC scatterplots. The normal left hemisphere exhibited a single cluster. In the right ischemic hemisphere at 30 mins, three clusters were resolved using ISODATA analysis, namely: the normal, core and mismatch cluster. At 180 mins, the scatterplots show the mismatch disappeared in Group I but persisted in Group II. Spatial locations of the different pixel clusters resolved on the scatterplots were mapped onto the image spaces (**Fig. 1C**).

Evolutions of the group-average tissue volumes for the ISODATA-resolved clusters are shown in **Fig. 2**. In both groups, the tissue volumes of the "normal" cluster remained relatively constant; the "core" volumes grew whereas the "mismatch" volumes decreased as ischemia progressed. In Group I, the "mismatch" volume disappeared and the "core" volume was not statistically different from the TTC infarct volume at 24 hrs ($P > 0.05$). In Group II, the mismatch volumes decreased with a smaller magnitude relative to that of Group I. The core volume at 3 hrs was slightly smaller than the TTC infarct volume at 24 hrs ($P < 0.05$), suggesting that some of the persistent mismatch tissues became infarcted between 3-24 hrs post occlusion.

The fate of the "perfusion-diffusion" mismatch pixels at 30mins were dynamically tracked in terms of their tissue volumes, ADC and CBF values, as these pixels migrated to different clusters following occlusion (**Fig. 3**). In Group I, the mismatch volume gradually decreased as ischemia progressed with all pixels migrated exclusively to the "core" at 180 mins. In Group II, the mismatch volume also gradually decreased as ischemia progressed but there were some mismatch pixels remained at 180 mins. Essentially no pixels migrated to "normal" zone. The ADC and CBF values at 30 mins of the pixels migrated to "core" are significant lower than those of the pixels migrated to "normal" or stay in "mismatch" (ADC: 0.66 ± 0.02 *vs* 0.72 ±.0.03 x10^{-3} mm^2/s; CBF: 0.20 ± 0.12 *vs* 0.38 ± 0.20 ml/gram/min). The CBF value was above the critical viability thresholds of 0.2-0.3 ml/g/min (3); consequently these "persistent" mismatch pixels escaped infarction. The ADC and CBF values of the pixels migrated to "core" are significant lower at 180 mins than at 30mins (ADC: 0.45 ± 0.03 *vs* 0.66 ± .0.02 x10^{-3} mm^2/s; CBF: 0.06 ± 0.04 *vs* 0.20 ± 0.12 ml/gram/min). The CBF value was below the critical viability thresholds of 0.2-0.3 ml/g/min (3); consequently these initial mismatch pixels did not escape infarction.

CONCLUSIONS Automated ISODATA analysis of the quantitative perfusion and diffusion data on a pixel-by-pixel basis yielded unique additional information that is not evident in separately analyzing the perfusion and diffusion data in the spatial and temporal domain. This approach is expected to be useful in monitoring the spatiotemporal dynamic changes in cluster membership as a function of therapeutic intervention, where such information may be critical in predicting tissue outcome.

References [1] Jacobs MA, JMRI, 2000; 11: 425. [2] Theiler J, Proc SPIE, 1997; 3159:108. [3] Hoehn et al. JCBFM 1995, 15: 1002, Kohno et al, MRI 1995, 13: 73, Shen et al. JCBFM 2003, 23: 1479.

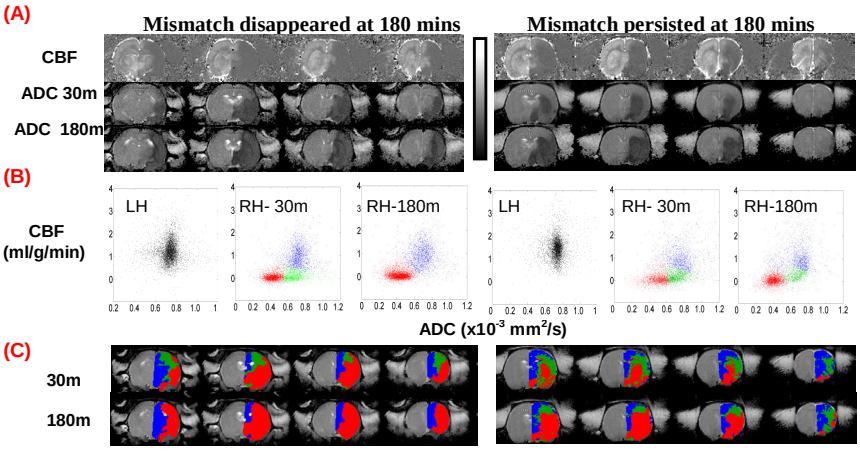

Fig.1 (A) CBF maps, ADC maps at 30 mins and 180 mins. Grayscale bar indicates ADC: 0 – 0.001 mm^2/s, CBF: -1 – 2 ml/g/min. (B) CBF-ADC scatterplots of the left hemisphere (LH) and right hemisphere (RH) at 30 and 180mins. Blue, green and red are assigned as "normal", "mismatch" and "ischemic core" clusters, respectively. (C) Pixel clusters from the CBF-ADC scatterplots were overlaid on the images at 30 & 180mins post-ischemia.

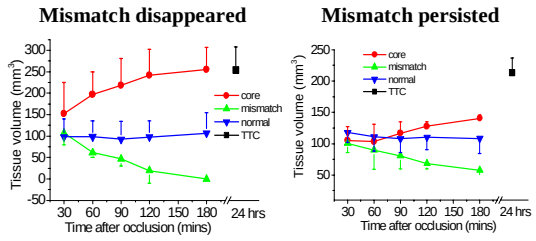

Fig.2 Group-average tissue-volume curves of different clusters.

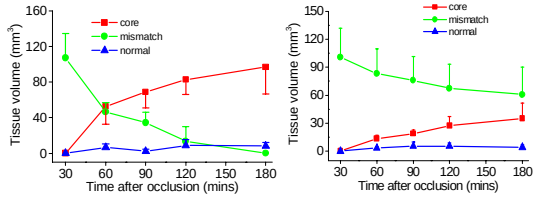

Fig.3 Group-average evolutions of tissue volumes of the mismatch cluster as ischemia progressed (mean ± SEM).