Incorporating ADC temporal profiles to predict ischemic tissue fate in acute stroke

Qiang Shen[1], Virendra Desai[1], and Timothy Q Duong[1]
[1]*Research Imaging Institute, University of Texas Health Science Center at San Antonio, San Antonio, Texas, United States*

INTRODUCTION It is important clinically not only to identify the extent of ischemic brain injury but also to render accurate and objective prediction of the likelihood of infarct on a pixel-by-pixel basis because such prognoses impact therapeutic regimen. Sophisticated algorithms have been developed to predict ischemic tissue fate and they included predictive models based on generalized linear model [1, 2], probability-of-infarct [3, 4], artificial neural network (ANN) [5] and support vector machine [6]. These predictive models provide statistical or probabilistic maps of infarct likelihood on a pixel-by-pixel basis utilizing only the acute MRI data. None of these studies accounted for the multiple time points. We previously reported a method to incorporate the apparent diffusion coefficient (ADC) temporal characteristics to improve prediction accuracy [7]. In this report, we provided quantitative evaluation of the prediction accuracy using ADC data of multiple time points and compared results across three middle cerebral artery occlusion (MCAO) durations.

METHODS Male Sprague-Dawley rats were subjected to 30-min (n = 13), 60-min (n = 12) and permanent (n = 10) intraluminal MCAO [3]. Quantitative perfusion, diffusion and T_2 image data were acquired every 30 minutes during the acute phase up to 180 mins post-ischemia, immediately after reperfusion for reperfusion group, and again at 24 hours, followed by histology. Image data were co-registered across multiple time points. Time course from each pixel were analyzed and grouped into similar temporal components via k-means clustering method using ADC of the first time point only or ADC of all time points. The fate of each pixel (normal versus infarct) was determined using automated iterative self-organizing data (ISODATA) analysis [7] of ADC and T2 endpoint imaging (3 hrs in permanent MCAO, 24 hrs in 60-min and 30-min MCAO). ADC patterns with similar temporal characteristics were grouped together into 4 apparent components. ADC values for these components were plotted versus time after stroke onset. Tissue outcome (normal or infarct) for each component was analyzed. Prediction sensitivity (true positive ration, TPR) and specificity (true negative ratio, TNR) were calculated. Statistical pair t-test was performed to compare the results using single and multiple time points. $P<0.05$ was taken as significant different.

RESULTS AND DISCUSSION ADC maps of different time points were shown on top row and followed by ISODATA clustering method determined final infarct and k-means clustering map (using all time points). For all groups, there were four apparent temporal clusters. The time courses of averaged ADC for these clusters are shown below the images. The numbers at the right side of the time courses are the percentage of each cluster becoming infarct at end point. For instance, 96% of the tissues in red cluster of the permanent group clustered with single time point data became infarct at end point.

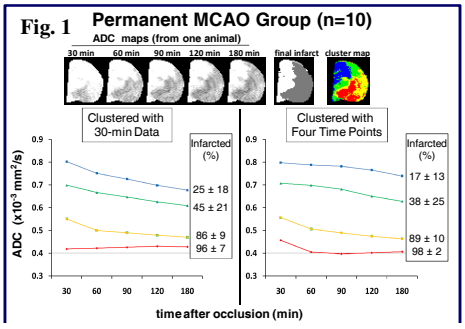
For the permanent MCAO group (**Fig.1**), the percentage to infarct of the red and yellow clusters clustered with single or multiple time points were similar. But, when using multiple time points, the blue and green clusters had significantly lower infarct percentages than when using a single time point, which demonstrated improved clustering of survival tissue via multiple time points analysis. The prediction accuracy analysis shown in the table below this graph demonstrated a statistically significant improvement in prediction sensitivity when using multiple time points ($p = 0.018$ for TPR).

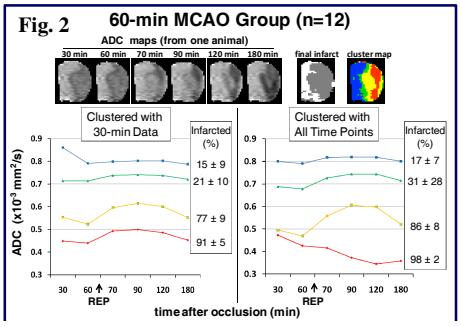
For the 60-min MCAO group (**Fig. 2**), using multiple time points, an ADC monotonically decreasing cluster (red) was clustered and with almost 100% certainty that tissues in this cluster went to infarct at the end point. The percentage to infarct of the yellow cluster was also improved when using multiple time points. The prediction accuracy analysis shown in the table below this graph demonstrated a statistically significant improvement in specificity ($p = 0.004$ for TNR) when using multiple time points, but a decrease in sensitivity ($p = 0.032$ for TPR).

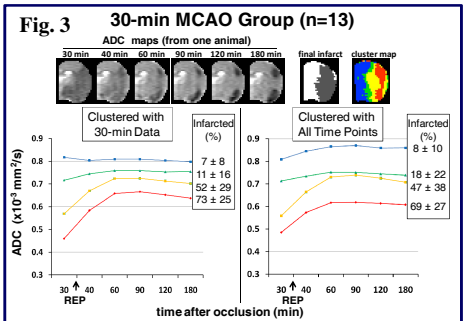
For the 30-min MCAO group (**Fig. 3**), with both methods, the yellow and red clusters showed recovery after reperfusion and the blue and green clusters were relatively stable across time. Furthermore, with both methods, each cluster had similar rates of infarction with high variability across individual rats. The prediction accuracy analysis shown in the table below this graph demonstrated no statistically significant difference in prediction with either method ($p = 0.18$ for TPR and 0.58 for TNR).

This study presents a novel analysis approach that utilizes the ADC temporal characteristics to characterize ischemic tissue fate. We identify distinct temporal patterns that determined tissue salvageability. Utilizing data from multiple time points increases prediction accuracy for the permanent group while it increases specificity but decreases sensitivity for the 60-min group and has no difference for the 30-min group. These results for the reperfusion groups likely stem from the ADC recovery post-reperfusion interfering with the clustering analysis. Future studies will focus on pre-reperfusion data alone and then include CBF data, incorporating these results into a predictive model. Although the ability to image multiple time points in acute stroke patients is likely limited, this approach should be helpful in animal studies and the knowledge gained will ultimately help clinical decision making in stroke treatment.

REFERENCES [1] Wu O, et al. Stroke. 2001; 32, 933. [2] Wu O, et al., JCBFM 2007; 27: 196. [3] Shen Q, et. al., JCBFM 2005, 25: 1336. [4] Shen Q et al., NMR Biomed. 2008; 21:839. [5] Huang et al., JCBFM 2010; 30: 1661. [6] Huang et al., BR 2011; 1405: 77. [7] Shen Q, et al, JCBFM 2004; 24:887.







ROC Analysis – Permanent Group			ROC Analysis – 60 min Reperfusion Group		ROC Analysis – 30 min Reperfusion Group	
	Single Time Point	**Four Time Points**	**Single Time Point**	**Multiple Time Points**	**Single Time Point**	**Multiple Time Points**
TPR	**73 ± 16 %**	**80 ± 19 %**	**80 ± 8 %**	**67 ± 15 %**	**84 ± 12 %**	**76 ± 14 %**
TNR	85 ± 10 %	89 ± 5 %	86 ± 9 %	94 ± 3 %	75 ± 11 %	71 ± 18 %