

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

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**INTRODUCTION** The mismatch between the perfusion and diffusion abnormality – widely considered to approximate the ischemic penumbra – indicates tissue at risk for infarction but potentially salvageable [1]. The perfusion-diffusion mismatch has been utilized to guide thrombolytic therapy and offers predictive value of ischemic tissue fate. Predictive models have employed multiple acute MRI parameters [2]. These predictive models, however, have been limited to using data from only a single time point. In principle, understanding the temporal evolution of apparent diffusion coefficient (ADC) should help to improve prediction accuracy. For example, tissue with mild ADC reduction followed by further ADC reduction will be more likely to infarct than not, whereas tissue with mild ADC reduction followed by ADC returning toward a normal value at a subsequent time point will likely recover. In this study, we propose a novel approach to incorporate quantitative temporal profiles of acute ADC changes to characterize tissue fate on a pixel-by-pixel basis. Analysis was performed on stroke rats subjected to permanent and 60-min middle cerebral artery occlusion (MCAO).

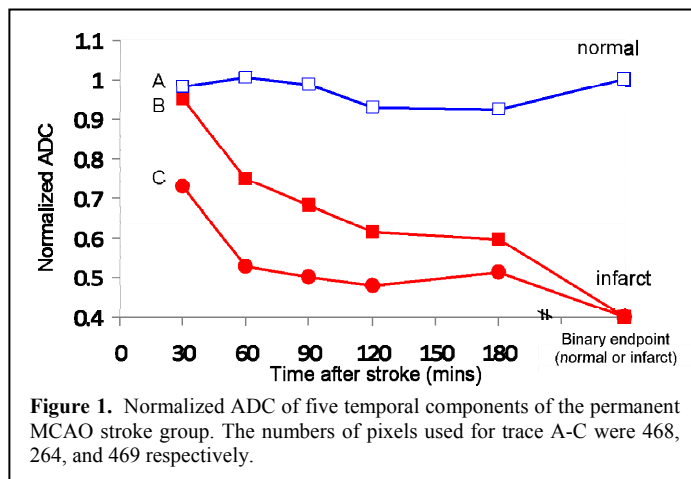
**METHODS** Male Sprague-Dawley rats were subjected to 60-min (n = 4) and permanent (n = 2) intraluminal middle cerebral artery occlusion (MCAO) [2]. Quantitative cerebral blood flow (CBF), ADC and T<sub>2</sub> data (eight 1.5-mm slices, 0.4x0.4 mm in-plane resolution) were acquired every 30 minutes during the acute phase up to 180 mins post-ischemia, immediately after reperfusion for the reperfusion group, and again at 24 hours, followed by histology, as described previously [2]. CBF was acquired using cASL. Image data were co-registered across multiple time points. Time courses from each pixel were analyzed and grouped into similar temporal components. The fate of each pixel (normal versus infarct) was determined using automated ISODATA analysis of ADC, CBF and T2 endpoint imaging (3 hrs in permanent MCAO, 24 hrs in 60-min MCAO) [4]. ADC was normalized with respect to normal tissue in the right hemisphere to correct for potential minor drift of the whole-brain ADC values. ADC temporal patterns with similar temporal characteristics were grouped together into multiple apparent components. Normalized ADC values for these components were plotted versus time after stroke onset. Tissue outcome (normal or infarct) for each component was plotted.

**RESULTS & DISCUSSION** For permanent MCAO, there were three apparent temporal components. **Figure 1** shows the ADC time courses for these components. ADC of component A (468 pixels) did not change significantly across all time points. ADC of component B (264 pixels) started at normal value but decreased monotonically with time. These pixels were likely of the perfusion-diffusion mismatch at the 30 mins time point. ADC of component C (469 pixels) started at a low ADC value and continued to decrease monotonically with time. These pixels were likely of the ischemic core at the 30 mins time point. In sum, in the permanent MCAO group, pixels with any significant ADC decrease would eventually become infarct.

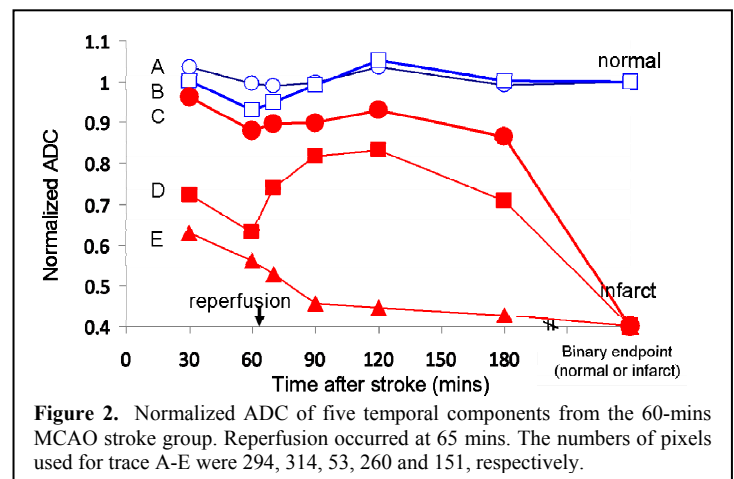
For 60-min MCAO, the temporal dynamics were more interesting. There were 5 apparent temporal components (**Figure 2**). ADC of component A (294 pixels) showed no changes across time and these pixels were not infarcted. ADC of component B (314 pixels) decreased only mildly (~5% below normal) at 60 mins after stroke. Immediately after reperfusion and at 90 and 120 mins, ADC of this component increased and remained high at subsequently time points. These pixels were salvaged. ADC of component C (53 pixels) decreased to 88% of normal at 60 mins, largely remained the same or increased slightly (up to 91% of normal) after reperfusion and at subsequent time points. This component was not salvaged. ADC of component D (260 pixels) decreased to 60% of normal at 60 mins, increased after reperfusion significantly up to 85% of normal at subsequent time points. This component was not salvaged. ADC of component E (151 pixels) started low, continued to decrease at all subsequent time points, and became infarct. In sum, pixels with ADC dropped below 90% of normal on average will become infarct. Transient recovery, if present, did not help if ADC dropped below 90% of normal. ADC below 60% of normal at 30 mins post-ischemia did not show transient recovery.

**CONCLUSION** This study presents a novel analysis approach that utilizes quantitative ADC temporal profiles to characterize ischemic tissue fate. We identify distinct temporal patterns that determined tissue salvageability. The key findings under these experimental conditions are: *i*) only tissue with ADC within 90% of normal on average can be salvaged by reperfusion, and *ii*) transient recovery does not help if ADC drops below 90% of normal. This finding, if confirmed, could have important implications. Future studies will include CBF data, additional occlusion durations, and a quantitative predictive model [1]. Incorporating the ADC temporal characteristics in acute stroke should improve prediction accuracy. Although the ability to image multiple time points in acute stroke patients may be less practical, this approach should be helpful in animal studies. The knowledge gained will ultimately help clinical decision making in the treatment of stroke.

**REFERENCES** [1] Kidwell et al, *Stroke* 2003, 34:2729. [2] Shen et al, *JCBFM* 2005, 25: 1336. [3] Wu O, et al, *Stroke*. 2001; 32, 933. [4] Shen et al, *JCBFM* 2004, 24: 887.



**Figure 1.** Normalized ADC of five temporal components of the permanent MCAO stroke group. The numbers of pixels used for trace A-C were 468, 264, and 469 respectively.



**Figure 2.** Normalized ADC of five temporal components from the 60-min MCAO stroke group. Reperfusion occurred at 65 mins. The numbers of pixels used for trace A-E were 294, 314, 53, 260 and 151, respectively.