## **Temporal Profiles of the Infarct Frequency in Acute Stroke**

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**INTRODUCTION** We and others have shown that acute diffusion and perfusion data can be used to quantitatively predict ischemic tissues fate on a pixel-by-pixel basis [1, 2]. While ADC and CBF are strong predictors of tissue infarction following acute stroke, some brain regions are known to be more susceptible to infarct than others. Factors that contribute to regional susceptibility include distance from patent afferent vessels, basal regional blood flow, and basal tissue metabolism. Therefore, utilizing spatial information to account for regional susceptibility has the potential to improve prediction accuracy. Similarly, acute stroke data obtained at multiple time points could give additional information that could help to predict tissue outcomes. In this study, we expanded our algorithm to include spatial and temporal information in order to improve prediction accuracy. The combined spatial and temporal profiles of the frequency of infarct were analyzed for two groups of rats subjected to permanent and transient MCAO.

**METHODS** Quantitative perfusion, diffusion and  $T_2$  image data were acquired every 30 minutes during the acute phase up to 180 mins postischemia, and again at 24 hours followed by histology. Two different occlusion durations were studied: 30-min (n = 12) and permanent MCAO (n = 12). All the animals in the same group were co-registered. Spatial frequency-of-infarction maps at all time points were obtained by counting the frequency of infarction pixel-by-pixel. Infarcts were determined by using ADC threshold (0.53x10<sup>-3</sup> mm<sup>2</sup>/s) [3]. The infarcts of 24-hour were determined by using ADC and T2 maps with automated ISODATA clustering method [4]. Spatial frequency of infarct maps were derived at different time points after occlusion to generate spatiotemporal profiles. In addition, time courses of frequency-of-infarct were plotted for three different ROI's: the core, mismatch and normal pixels identified at 30 mins post ischemia. The difference maps of frequency-of-infarct maps between the end time point (180-min for permanent MCAO and 24-hour for 30-min MCAO) and the first time point were obtained.

**RESULTS Fig 1A** shows the spatial frequency-of-infarct maps at different time points for the permanent MCAO group. Area of high frequency-of-infarct (yellow) grew over time. The highest frequency of infarct was in the sub-cortical area while some of the cortical areas were spared. **Fig 1B** shows the temporal dependence of the frequency-of-infarct for three tissue types (core, mismatch and normal). For the core pixels, the frequency of infarct was high and did not change significantly over time. For the normal pixels, the frequency of infarct was essentially zero and did not change significantly over time as expected. For the mismatch pixels, the frequency of infarct increased roughly linearly over the first 3 hrs. The "difference" in frequency-of-infarct map between 180-min and 30-mins (**Fig 1C**) clearly showed the pixels with the most time-dependent changes were at the boundary of ischemic core (highlighted by the green ROI).

Similarly, **Fig 2A** shows the spatial frequency-of-infarct maps at different time points for the 30-min MCAO group. Reperfusion only transiently lowered the frequency-of-infarct in the striatum. **Fig. 2B** quantifies the time courses of infarct frequency for three different regions. Importantly, the caudate near the midline showed negative infarct frequency (purple pixels in **Fig. 2C**), suggesting reperfusion has a probability of salvaging this tissues. Majority of the mismatch pixels were salvaged as indicated by the low frequency-of-infarct.

**DISCUSSION & CONCLUSION** We incorporated combined spatial and temporal information, in addition to ADC and CBF data, into our prediction model. This model identifies that the brain regions that shows the most time dependent change as well as predicting the brain regions that have a high probability of being salvaged by repefusion. We concluded that incorporating temporal and spatial information reveals unique information and has the potential to improve prediction accuracy.

REFERENCES [1] Shen et. al. JCBFM 2005, 25: 1336. [2] Wu O, et al. Stroke. 2001; 32, 933. [3] Shen et. al. JCBFM 2003, 23: 1479. [4] Shen et al. JCBFM, 2004, 24:280.



Fig. 1 (A) Spatial frequency-of-infarct maps at different time points of permanent MCAO; (B) Time courses of infarct frequency at three regions (core, at-risk and normal); (C) Difference of infarct frequency maps between 180-mins and 30-min. Green ROI highlights the pixels with largest increase frequency of infarct.



Fig. 2 (A) Spatial frequency-of-infarct maps at different time points of the 30-min MCAO group. Green ROI highlights the striatum. (B) Time courses of infarct frequency at three regions (striatum, mismatch and salvaged tissues); (C) Difference of infarct frequency maps between 24-hr and 30-min where the green ROI highlights the salvaged tissues.