Quantitative Prediction of Ischemic Tissue Fates: Incorporating Spatial Information to Improve Prediction Accuracy

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INTRODUCTION Diffusion and perfusion MRI obtained during the acute phase have the potential to predict final tissue outcomes on a pixel by pixel basis and the ability to do so could aid clinical decision-making in the treatment of acute ischemic brain injury. In addition, some regions of the brain 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. Thus, utilizing spatial information to account for regional susceptibility should improve prediction accuracy. The aims of this study were: 1) to develop and test a prediction algorithm by documenting the probability profiles and probability-of-infarct density profiles for three representative (30-min, 60-min and permanent) intraluminal MCAO durations in a rat stroke model, 2) to predict ischemic tissue fate using only the acute stroke data, validate with histology, and quantify prediction accuracy using performance measures, and 3) to improve prediction accuracy by accounting for regional susceptibility.

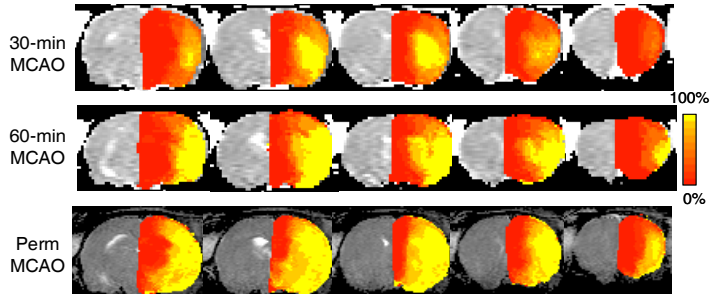
METHODS Quantitative perfusion, diffusion and T_2 image data were acquired every 30 minutes during the acute phase up to 180 mins post-ischemia, and again at 24 hours followed by histology. Three different occlusion durations were studied: 30-min (n = 12), 60-min (n = 12), and permanent MCAO (n = 12). For each occlusion group, half of the animals were randomly assigned to the training group for generating probability profiles; predictions were made on the remaining half, the experimental group. Using the training group, profiles of the probability of infarct (P_I) contour plots were derived as a function of ADC versus CBF by determining the percentage of pixels within each grid that migrated to the ischemic core at 24 hrs post-ischemia. Predictions of subsequent infarction were made on the experimental group using only the 30-min data by looking up the corresponding P_I contour plots of training group on a pixel-by-pixel basis. Sensitivity, specificity, receiver operating characteristic (ROC) were obtained to evaluate prediction performance.

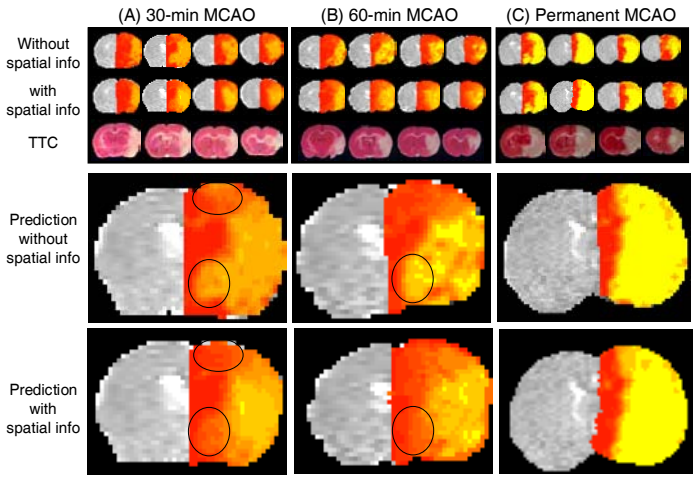
To take into account the regional susceptibility to ischemic injury, spatial frequency-of-infarction maps were obtained by counting the frequency of infarction pixel-by-pixel. Predictions were made by taking the weighted average of the probability-of-infarct map and the frequency-of-infarct map. ROC analysis was performed to determine the optimal weighting coefficients by plotting the areas under the ROC curves as a function of the spatial information weighting coefficients. Comparisons were made among histology, endpoint imaging, and predictions made with and without spatial information.

RESULTS & DISCUSSION To account for regional heterogeneity in statistical prediction, spatial frequency-of-infarct maps were constructed for the three MCAO groups (**Figure 1**). Spatial frequency of infarct and the extent of infarction were heterogeneous. Predictions were made by taking the weighted average of the probability-of-infarct map and spatial frequency-of-infarct map. To derive the optimal weighting coefficients, ROC analysis of the prediction accuracy was performed as a function of the weighting coefficients for spatial information. The optimal coefficients were 10% for permanent MCAO group and 40% for 30-min MCAO and 60-min MCAO group, indicating that spatial information was important for accurate prediction in reperfusion stroke, whereas ADC and CBF data, although critically important, appeared insufficient.

Figure 2 shows the probability-of-infarct maps predicted without spatial information and with the optimal weighting coefficient of spatial information. Regional differences between predictions made with and without spatial information were most apparent in the reperfusion groups, specifically, in the cortical tissues close to the anterior communicating artery and caudate tissues near the midline. Importantly, predictions made with spatial information consistently corresponded better with end-point imaging and histology than those made without spatial information. These results suggested that incorporating spatial information significantly improved prediction accuracy. The sensitivities were 82 ± 6, 82 ± 7, and 86 ± 4%, the specificities were 83 ± 5, 86 ± 5, and 89 ± 6, and the area under the ROC curves were 87 ± 3, 90 ± 4, and 93 ± 3%.

Conclusion This study documents the probability-of-infarct profiles of ischemic brain injury and reveals pixel-by-pixel the likelihood of infarction. We conclude that spatial information is important for accurate prediction in reperfusion stroke, whereas ADC and CBF data, although critically important, appeared insufficient. Spatial information is likely to be more important in human stroke because of human stroke is more heterogeneous. This predictive approach could provide quantitative frameworks for clinicians to tailor treatment options for individual acute stroke patients.





⇑ **Figure 1.** Spatial frequency of infarct maps. Color bar = probability of infarct from 0% to 100%.

⇒ **Figure 2**. Predictions with and without spatial information. Probability-of-infarct prediction maps with and without spatial information for three different occlusion durations. Optimal weighting coefficients for spatial information were used. Histological TTC slides are shown for comparison.