Artificial Neural-Network Prediction of Ischemic Tissue Fate in Acute Stroke Imaging

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INTRODUCTION Multimodal MRI of acute stroke provides clinically relevant data and predictive value to guide stroke therapy. Combined perfusion- and diffusion-weighted MRI is remarkably sensitive in detecting acute stroke changes and is becoming the method of choice for diagnosis, staging and characterization of ischemic brain injury. The anatomical mismatch between perfusion and diffusion abnormality (*1, 2*) approximates the potentially salvageable "ischemic penumbra" (*3*).

Artificial neural network (ANN) (*4*), inspired by the neuronal networks in the central nervous system, is widely used in science and engineering for prediction and classification. ANN consists of nodes that are connected together to form a network with variable strengths (weights) between different connections. Through training, the relationship between inputs and outputs can be mapped by altering the weights within the network. The goal of the present study is to develop and test a flexible predictive algorithm based on ANN to predict ischemic tissue fate using acute ADC and CBF data. ANN prediction algorithms were evaluated on rat stroke models subjected to three different occlusion durations (30-min, 60-min and permanent MCAO). Predictions using ADC alone, CBF alone and ADC+CBF were evaluated. In addition, the effects of neighboring pixels and regional tissue susceptibility to ischemic injury on prediction accuracy were also evaluated. Prediction accuracy was quantified using receiver operating characteristic (ROC) analysis. Comparisons of prediction accuracy were made with end-point T2-weighted MRI.

METHODS Three experimental groups (*5*) were analyzed: 30-min (n = 10), 60-min (n = 12) and permanent (n = 8) MCAO. ANN was trained and tested using leave-one-out method – that is one animal was used as the "test" subject and the remaining animals in the same MCAO group was used as "training" subjects. This was cycled for all animals in the same group. ANN predictions were made for the 30-min, 60-min, and permanent MCAO groups using the corresponding ANN basis set, namely, that: *i)* permanent MCAO ANN basis set was trained and applied to permanent MCAO animals for prediction, *ii)* 60-min MCAO ANN basis set was trained and applied to 60-min MCAO animals for prediction, and *iii)* 30-min MCAO ANN basis set was trained and applied to 30-min MCAO animals for prediction. For each MCAO data set, predictions were made using only data obtained at 30 mins after stroke onset for six conditions: 1) CBF alone, 2) ADC alone, 3) ADC+CBF, 4) ADC+CBF+2D adjacent pixels, 5)ADC+CBF+3D adjacent pixels, and 6) ADC+CBF+3D adjacent pixels+spatial information. Adjacent pixels referred to 8 and 26 immediate neighbor pixels in 2D and 3D, respectively. Spatial information referred to the spatial frequency of infarct described above. To further evaluate the hypothetical treatment effects, prediction was also made for permanent, 60-min and 30-min MCAO groups using only permanent MCAO ANN training basis set. Predictions were made for six conditions described above. ROC analysis (*5*) was performed to evaluate prediction accuracy. Sensitivity and specificity at the optimal point and the area under the ROC curves (AUC) were tabulated for comparison.

RESULTS & DISCUSSION **Figure 1** shows the pixel-by-pixel ANN predictions of subsequent infarction for three experimental stroke groups under various conditions. Predictions using acute stroke data *obtained at 30 mins post ischemia*. The conditions evaluated were: CBF alone, ADC alone, ADC+CBF, ADC+CBF+2D, ADC+CBF+3D, and ADC+CBF+3D +spatial information). For references, ADC, CBF maps and ISODATA analysis of lesion volume based on ADC and T2 are also shown. ISODATA analysis of lesion volume was taken as the endpoint measure which had been previously correlated with histology. The major findings are as followed. The predicted infarct maps showed generally good prediction, with the exception of CBF data alone which poorly predicted infarct. With additional information (going from top to bottom), predictions were more accurate with respective to lesion location and volume, as well as slightly more certain (i.e., stronger yellow pixels). Predicted maps are in general agreement with ISODATA analysis of lesion volume.

Figure 2 shows the AUC's for predictions of each MCAO group with the model trained with only permanent MCAO ANN training basis set. The key findings were: 1) CBF alone at 30 mins poorly predicted infarct across three experimental groups. 2) ADC alone adequately predicted infarct. 3) CBF+ADC improved prediction accuracy. 4) Addition of neighboring pixel information in 2D and 3D further improved prediction accuracy. 5) Addition of spatial information of regional tissue susceptibility to ischemic injury further improved prediction. 6) Finally, AUC's for the 30-min and 60-mins MCAO predictions were smaller than the permanent MCAO prediction, suggesting that the 30-min and 60-mins MCAO groups were more amenable to treatment. These findings are consistent with those reported using threshold method (*6*), GLM (*7*) predictive and probabilistic (*5*) models.

CONCLUSION A flexible artificial neural network algorithm was developed to predict ischemic tissue fate pixel-by-pixel based on multimodal MRI data of acute stroke. Efficacy of the ANN prediction algorithm was evaluated by employing reproducible rodent stroke models of various occlusion durations. Predictions showed the likelihood of future infarction on a pixel-by-pixel basis. Moreover, accounting for neighboring pixels and regional tissue susceptibility to ischemic injury significantly improved prediction accuracy. ANN prediction model has the potential to provide quantitative and objective frameworks to aid clinical decision-making in the treatment of acute stroke, test therapeutic treatments, tailor individual treatment.

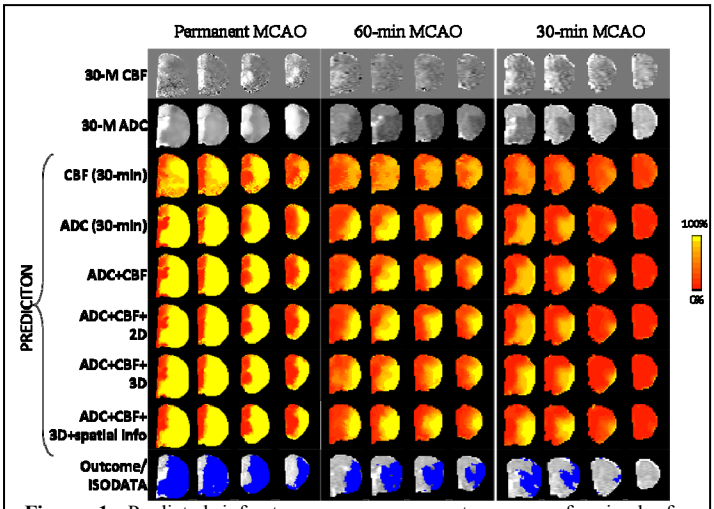

Figure 1. Predicted infarct maps on a separate group of animals for permanent, 60-min, and 30-min MCAO. From left to right, images are arranged posterior to anterior. Color bar = probability of infarct 0% to 100%.

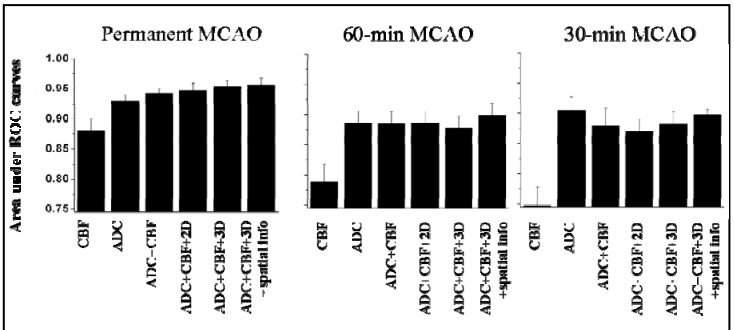

Figure 2. The areas under ROC curves for three different occlusion durations: permanent, 30-min and 60-min MCAO. Small area under the ROC in 60-min and 30-min MCAO indicated they are more amenable to treatment.

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