Support Vector Machine 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*).

Support vector machine (SVM) (*4*), have been successfully applied in prediction and classification. SVM creates a higher dimensional separating hyperplane So that it can optimally discriminate two or more classes. During a minimization procedure (i.e., a learning process), the hyperplane is tuned so that the SVM model generalization error is minimized, therefore, achieving an optimal solution to the classification problem. The goal of the present study is to develop and test a flexible predictive algorithm based on SVM to predict ischemic tissue fate using acute ADC and CBF data. SVM 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 = 12), 60-min (n = 12) and permanent (n = 12) MCAO. SVM 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. SVM predictions were made for the 30-min, 60-min, and permanent MCAO groups using the corresponding SVM basis set, namely, that: *i)* permanent MCAO SVM basis set was trained and applied to permanent MCAO animals for prediction, *ii)* 60-min MCAO SVM basis set was trained and applied to 60-min MCAO animals for prediction, and *iii)* 30-min MCAO SVM 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 SVM training basis set. Predictions were made for six conditions described above. ROC analysis (*5*) was performed to evaluate prediction accuracy. ROC analysis was also compared with a previously published study using the artificial neural network (ANN) prediction model (6) operating on the same data sets.

RESULTS & DISCUSSION **Figure 1** shows the pixel-by-pixel SVM 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. 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 its own basis set and MRI data obtained at 30 minutes after ischemia. 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.

By comparing with our previously published prediction made using artificial neural network method (6), SVM generally showed better performance, many of the improvement were remarkable and highly statistically significant (**Fig.2**).

CONCLUSION A flexible support vector machine algorithm was developed to predict ischemic tissue fate pixel-by-pixel based on multimodal MRI data of acute stroke. Efficacy of the SVM 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. SVM outperformed ANN algorithm on the same data sets. SVM 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.

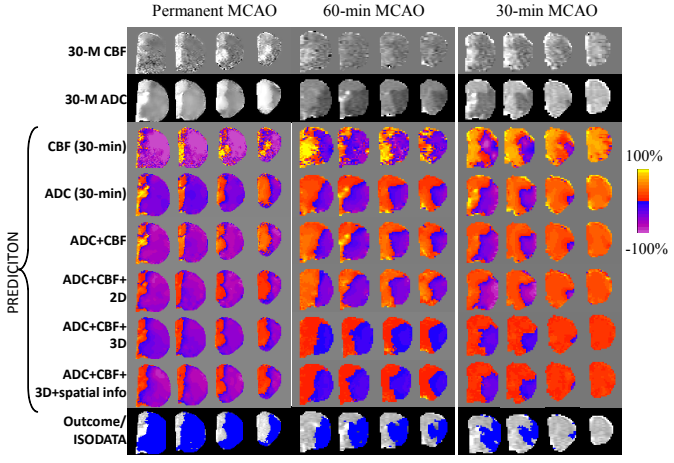

Figure 1 Predicted infarct maps on a separate group of animals for permanent, 60-min, and **3**0-min MCAO. From left to right, images are arranged posterior to anterior.

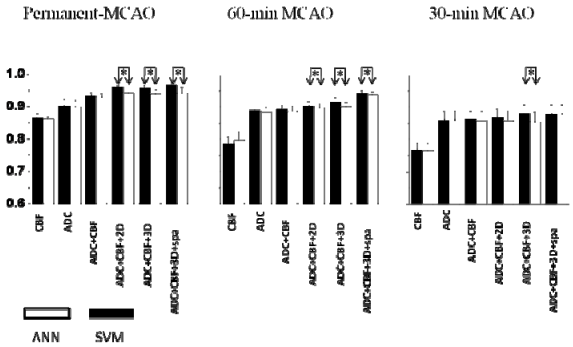

Figure 2 The areas under ROC curves for three different occlusion durations: permanent, 30-min and 60-min MCAO. Small area under the ROC in 60-min and 30-min MCAO indicated they are more amenable to treatment.

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