A Novel Strategy for Predicting Tissue Outcome in Acute Human Stroke

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INTRODUCTION

Several MRI-based algorithms for predicting tissue outcome following acute ischemic stroke have been proposed, with varying degrees of success [1-3]. Generally, these algorithms utilize a number of MRI parameters (diffusion- and perfusion-based) to predict tissue outcome on a voxel-by-voxel basis. The search for improved strategies for prediction of tissue fate has largely focused on the inclusion of additional MRI parameters (e.g., flow heterogeneity, bolus delay) [4,5] and/or on novel mathematical models for combining these parameters [4]. We present here a different strategy for improving prediction of tissue fate, the inclusion of spatial information. In doing so, we take advantage of the richness of the imaging dataset by incorporating knowledge about the location of each voxel, in addition to its parameter values.

METHODS

Patients were included in this study if they had acute MR imaging within 12 hours following the onset of first-ever ischemic stroke and follow-up imaging a minimum of 5 days later. Patients receiving thrombolytics or non-standard therapeutics were excluded. MR imaging was performed at 1.5 T. A total of 74 patients met these inclusion criteria. Acute diffusion weighted images (DWI) were obtained using a b-value of 1000. From these, apparent diffusion coefficient (ADC) and T2 (b=0) maps were calculated. Acute perfusion imaging using dynamic susceptibility contrast was also obtained. From these, maps of cerebral blood flow and blood volume (CBF, CBV) and the mean transit time (MTT) were obtained. For each patient, diffusion and perfusion images were coregistered to each other and to that patient's follow-up T2 images using FLIRT software (FMRIB, Oxford, UK). These 6 MRI parameters were then used as input parameters into a supervised learning algorithm that utilizes a generalized linear model to determine the likelihood of infarction (expressed as a percentage) on a voxel-by-voxel basis to produce a Risk Map. The model was trained on (n-1) patients using these 6 input parameters and follow-up imaging, on which a neuroradiologist had outlined the infarcts, as outcome, and the results were then applied to the remaining patient to produce predictions of tissue outcome. This process (i.e., leave-one-out cross validation, or, jacknifing) was then repeated for each of the n=74 patients. The performance of the model, i.e., its predictive ability, was evaluated using receiver operator characteristic (ROC) curves in which the true positive ratio (sensitivity) is plotted against the false positive ratio (1-specificity). The area under the ROC curve (AUC, values can range from 0 to 1) serves a numerical performance metric.

This model (i.e., the MRI-only Model) was then compared to one that included spatial information (Spatial Model). Spatial information was implemented as an additional input parameter in which the (Euclidean) distance from the acute DWI lesion was calculated for each voxel to produce a map.

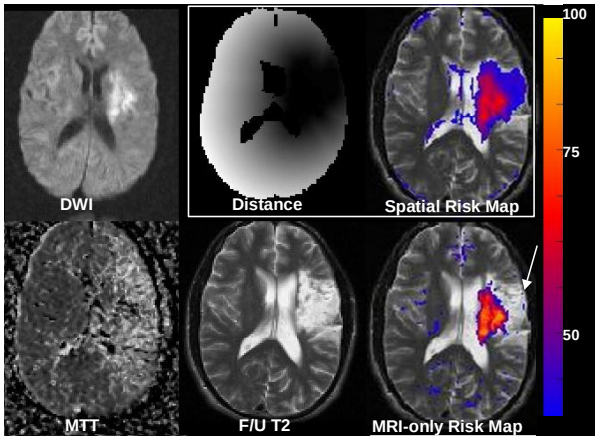

Figure 1: Comparison of Risk Maps for a typical patient. Acute DWI and MTT are shown. These, along with acute T2, ADC, CBF and CBV (not shown) were used to predict risk of infarction (MRI-only Risk Map, color bar indicates likelihood of infarction, expressed as a percentage). Compare this Risk Map (overlaid onto the follow-up T2 image) to the voxels that actually infarcted shown on follow-up. The arrow indicates a large region missed on the MRI-only Risk Map that did go on to infarct. Shown in the inset are the Distance map (distance from acute DWI lesion) and the effect of including this map as an additional parameter in the model (Spatial Risk Map). Note that the Spatial Risk Map captures more voxels that went on to infarction than the MRI-only Risk Map.

RESULTS

The MRI-only Model resulted in an AUC of 0.749 ± 0.132 (mean ± SD) whereas the inclusion of spatial information increased the mean AUC to 0.823 ± 0.135, a significant improvement (p=0.00093, n=74). A typical example of the improvement seen by including spatial information is seen in Figure 1. The ROCs corresponding to this example are shown in Figure 2. For the clinically acceptable range of false positive ratios (i.e., 0 to 0.3, corresponding to specificity ranging from 100 to 70%), the MRI-only Model had a maximum sensitivity of 67 ± 22% (which occurred at a false positive ratio of 0.3, specificity=70%), whereas the Spatial Model had a maximum sensitivity of 79 ± 23%, a significant improvement (p=0.0027, n=74).

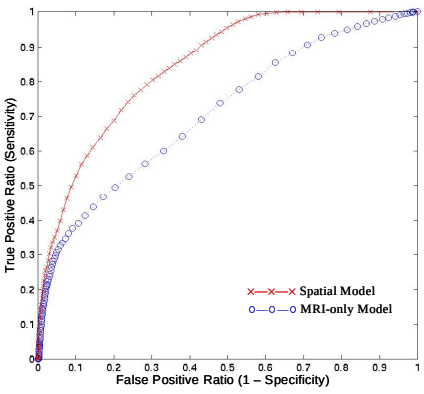

Figure 2: Comparison of model performance for the same patient as in Figure 1. The area under the curve (AUC) for the Spatial Model is substantially higher than the AUC for the MRI-only Model (0.846 vs. 0.712), a fact that can be visually appreciated from the curves themselves which shows that the Spatial Model has higher sensitivity for each value of specificity than the MRI-only Model. For the clinically acceptable range of false positive ratios (i.e., 0 to 0.3), the Spatial Model has a maximum sensitivity of 80% vs. 58% for the MRI-only Model (at false positive ratio=0.3, specificity=70%).

DISCUSSION

Although it is agreed upon that the likelihood of a voxel of tissue proceeding to infarction depends, in part, on its proximity to other tissue voxels that will infarct, or on a more basic level, on whether or not it is located within the vascular territory or even the hemisphere at risk, no such knowledge has thus far been incorporated into tissue outcome predictive models. Some of this information is presumably reflected in the parameter values themselves, explaining the success of prior algorithms. However, the input tissue signatures are not perfectly sensitive or specific, leading to normal voxels that sometimes have abnormal values in one or more parameters, and lesion voxels that sometimes have normal values.

Incorporating knowledge of the location of a given voxel, in the fullest sense, could potentially be prohibitively complex from a computational standpoint. In this work, spatial information was included as a simple distance metric, the lowest possible order implementation of location data. The acute DWI lesion was used as the focal point of this measure in order to exploit the fact that infarcts usually grow outwards from the DWI lesion. The inclusion of this information led to a substantial and significant improvement in predictive ability. There may be other variations on this theme that could result in similar improvements. Nevertheless, to our knowledge, this is the first time that a predictive algorithm with high sensitivity and specificity has been applied to such a large (n=74), heterogeneous patient dataset.

1. Wu et al, Stroke 2001; 32:933. 2. Rose et al, Magn Reson Imaging 2001; 19:1043. 3. Mitsias et al, AJNR Am J Neuroradiol 2004; 25:1499. 4. Mouridsen et al, Proc 12th ISMRM 2004, #410. 5. Rose et al, Proc 12th ISMRM 2004, #411. *This work was supported in part by Public Health Service grant NS38477, the National Center for Research Resources (P41RR14075) and the Mental Illness and Neuroscience Discovery Institute.*