Predicting Infarct Growth With Multi-parametric Modeling in Acute Ischemic Stroke

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Purpose

Diffusion-weighted imaging (DWI) can identify cytotoxic edema in acute ischemic stroke. Also, perfusion-weighted imaging (PWI) measures can indicate the depth and extent of ischemia. Multivariable, voxel-based analysis can predict tissue outcome based on DWI and PWI but these studies have only distinguished final infarct from ultimately salvaged tissue [1]. The region of infarct growth that corresponds to the penumbra, the target of stroke therapy, has different physiological characteristics from both the core infarct and from benign oligemia [2]. Our hypothesis was that a different multi-parametric logistic regression model optimally distinguishes infarct growth from core infarct compared to the model that best distinguishes infarct growth from benign oligemia. Since gray and white matter (GM and WM) have different diffusion and perfusion thresholds for infarction, we also tested for interaction between tissue type and the apparent diffusion coefficient (ADC), cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) [3]. We also tested for interaction between ADC and CBF since a correlation between these parameters has been reported previously but has not been tested in multivariable analysis [4].

Methods

Diffusion- and perfusion-weighted MR imaging was acquired from 13 acute ischemic stroke patients less than 6 hours from stroke onset. The imaging data was processed to obtain a voxel-based dataset with the following parameters: T2, DWI, ADC, CBF, CBV, MTT, and time-to-peak (TTP). Each voxel was labeled as GM or WM by segmentation of images from a custom-designed sequence that was designed to optimize contrast between the tissue types. Each voxel was assigned to one of the following three regions: CORE (part of acute and 30-day infarcts), GROWTH (part of 30-day infarct, but not acute infarct), or OLIGEMIA (region of perfusion abnormality not part of either the acute or 30-day infarcts). We used logistic regression analysis to build models that distinguish GROWTH from CORE and from OLIGEMIA. The final models were selected based on the Wald statistic and the area under the curve (AUC) from receiver operating characteristic analysis was evaluated by cross-validation. The models were applied to patient data to generate probability maps highlighting the regions at risk of core infarct and infarct growth.

Results

The final model for differentiating GROWTH from CORE included DWI, ADC, CBF and tissue type (AUC = 0.9392, standard error = 0.0076, 11,937 voxels). Significant interaction was found between ADC and CBF ($p < 0.001$) and between CBF and tissue type ($p = 0.001$). Given a certain level of ADC, voxels at a lower level of CBF are at a higher risk of being part of the core infarct and this relationship was more evident in WM than GM (Figure 1). A decrease in CBF from 25 to 15 mL/100g/min at an ADC of 500 x 10^{-6} mm^2/s increases the probability of core infarction in GM from 54% to 58%. In WM, on the other hand, a similar decrease in CBF increases the probability of core infarction from 35% to 47%. The final model for differentiating GROWTH from OLIGEMIA included DWI, CBF and TTP (AUC = 0.7967; 51,393 voxels). Interaction was also found between ADC and CBF ($p = 0.036$). Different multi-parametric models were important in distinguishing GROWTH from CORE compared to GROWTH from OLIGEMIA. Figure 2 shows an example of applying the models to imaging data from one patient.

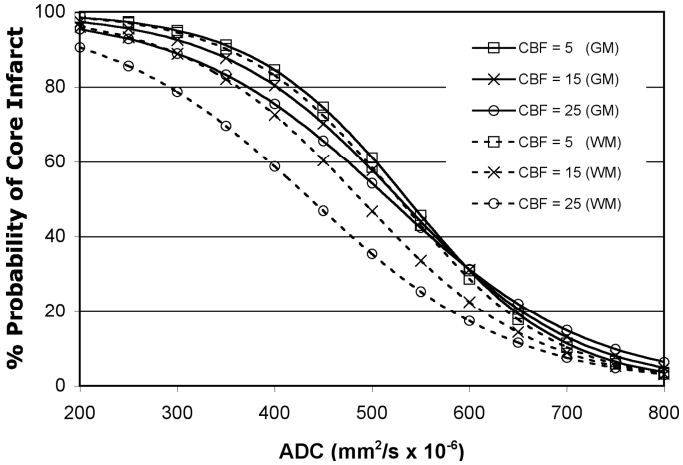

Figure 1. Interaction among ADC, CBF and tissue type. At a given value of ADC, the probability of core infarct depends on the level of CBF. GM is at higher risk than WM at the same level of CBF. The increase in probability of core infarction attributed to a decrease in CBF is more evident in WM than in GM.

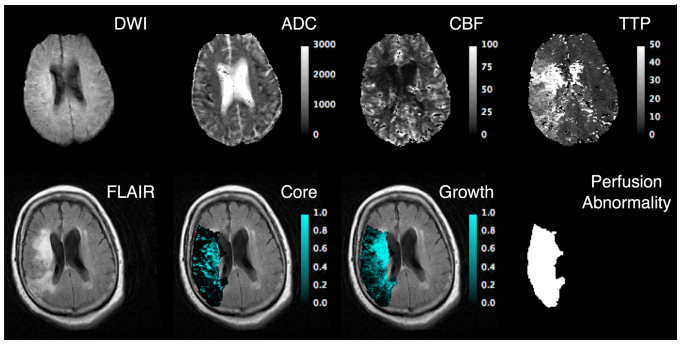

Figure 2. Application of logistic regression models to MR imaging. The top row shows the acute images. The bottom row shows the final follow-up fluid attenuated inversion recovery (FLAIR) image, the probability maps generated by the CORE/GROWTH model (Core) and GROWTH /OLIGEMIA model (Growth) overlaid on the FLAIR, and the region of perfusion abnormality selected for analysis. Probability values range between 0 and 1, where 0 (dark) is at low risk of infarction and 1 (bright) is at high risk. The logistic regression models generate probability maps that highlight the tissue destined for infarction regardless of acute intervention (Core) and the tissue likely to become infarct if acute recanalization is not achieved (Growth). The difference between these two represents tissue potentially amenable to acute stroke therapy.

Conclusion

Different magnetic resonance-derived DWI and PWI parameters are important for distinguishing infarct growth from core infarct and from benign oligemia. At a given level of ADC, the probability of infarction depends on the CBF. At a given level of low CBF, GM is at higher risk of core infarct than WM. Multivariable, voxel-based, logistic regression modeling of DWI and PWI parameters can reliably distinguish infarct growth from both core infarct and from benign oligemia and may aid the evaluation of treatment options for individual patients with acute ischemic stroke.

References

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