Improving the Prediction of Infarct Evolution in Acute Stroke with Diffusion and Bolus delay corrected Perfusion MRI Measures

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Introduction: Multivariate-modeling algorithms utilising diffusion and dynamic susceptibility based perfusion MRI measures are useful for predicting infarct evolution in acute stroke patients. Such information is important for acute patient management and aiding the evaluation of the efficacy of novel drug therapies [1,2]. Although deconvolution of the concentration-time course can in theory provide accurate measures of tissue perfusion [3], recent studies have shown that significant error can arise in the measures of cerebral blood flow (CBF) and mean transit time (MTT) due to effects of delayed arrival and dispersion of the bolus of contrast agent within ischemic brain tissue [4,5,6]. An important assumption with the DSC method is that the arterial input function (AIF) represents the exact input to the tissue being examined. Clearly in this patient group with occlusive vascular disease, this assumption may not be valid. In this present study we investigated whether perfusion measures corrected for bolus delay enabled better prediction of infarct evolution in a cohort of acute stroke patients.

Methods: 13 patients with acute focal neurological symptoms consistent with hemispheric ischemic stroke were studied. Patients were imaged within 3.8 ± 1.7 hours of onset of symptoms using either a 1.5T GE Echospeed scanner or a 1.5T Siemens Sonata scanner. Full brain coverage diffusion images (17 – 21 slices, 5 mm slice thickness 1 mm gap) were acquired using a diffusion tensor EPI sequence and apparent diffusion coefficient (ADC) and isotropically weighted diffusion maps [7] generated from the trace of the diffusion tensor. Cerebral perfusion maps [3] were obtained by the dynamic tracking of a double dose of GdDTPA (30ml, injector rate 5 ml s^{1}) using a single shot EPI (13-19 slices, 5 mm slice thickness 1 mm gap, TE 60ms TR <1.9 ms, 50 frames per slice). Arterial input functions were selected from the MCA within the contralateral hemisphere. Diffusion and perfusion maps were registered using a 6-parameter rigid body transformation. A second DTI series was acquired at 30 days. The final lesion volume was determined by subtracting the registered 30-day B0 images from the initial B0 maps. Bolus delay corrected perfusion maps were generated by calculating the arrival time of the bolus in a given pixel of interest and shifting the profile of the concentration time course curve by an integral value of the arrival time to best match the AIF. Following correction of the bolus delay, perfusion measures were evaluated using standard deconvolution methods.[3] We implemented a parametric classifier algorithm to predict infarct evolution that uses a combination of K-means and Expectation maximization (EM).[2] To test the hypothesis that bolus delay corrected perfusion measures improve prediction of infarct evolution, we compared model performance using as input parameters ADC, DWI,T2 metrics in conjunction with either CBF and MTT or bolus delay corrected perfusion (cCBF, cMTT) and bolus delay. Predicted infarct volumes were compared with final lesion volumes and 30 day NIHSS scores.

Results and Discussion: Mean measures of sensitivity, specificity and similarity index for modeling (DWI, ADC,T2, CBF and MTT) were 0.77 ± 0.12, 0.87 ± 0.13 and 0.65 ± 0.12, respectively. The performance of the model significantly improved when cCBF, cMTT and bolus delay measures were employed; 0.84 ± 0.07 ($p < 0.02$), 0.90 ± 0.10 ($p < 0.04$) and 0.74 ± 0.09 ($p < 0.001$), respectively. The mean Pearson correlation coefficient for the predicted lesion volume derived from diffusion, CBF and MTT measures compared with the final lesion volume was 0.88 ($p<0.001$). When corrected perfusion measures were used the correlation increased to 0.94 ($p<0.001$). Correlations for predicted lesion volumes based on diffusion, non-corrected and bolus corrected measures and outcome NIHSS scores were 0.73 ($p<0.001$) and 0.83 ($p<0.001$), respectively. The effect of delayed arrival of the bolus of contrast agent to cerebral tissue is demonstrated in Figure 1. For this acute patient the bolus delay map (F) reveals a significant lag in the time between arrival of the contrast agent in the contralateral MCA and tissue within the effected hemisphere. The CBF and MTT maps show a large perfusion abnormality extending into the non-effected hemisphere. In comparison, cCBF and cMTT maps show a much reduced hypoperfused region which better reflects the extent of neuronal injury shown on the follow-up 30 day T2 scan. In addition, the predicted lesion derived from bolus delay corrected perfusion measures better correlates with tissue outcome.

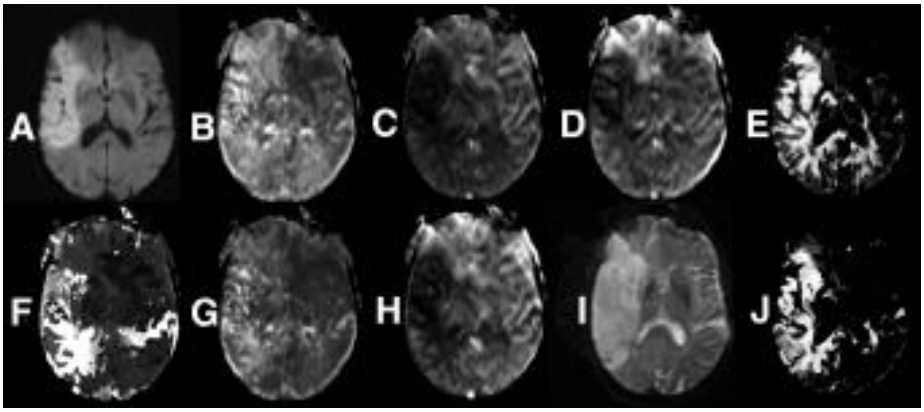

Figure1. Images represent (A) initial diffusion image (3 hrs after onset of symptoms), (B) MTT, (C) CBF, (D) CBV, (E) predicted lesion derived from non-corrected perfusion measures (F) bolus delay map (G) bolus delay corrected MTT, (H) bolus delay corrected CBF, (I) 30 day T2 scan and (J) predicted lesion derived from bolus corrected perfusion measures.

Conclusion: Bolus delay corrected perfusion measures enable an improved prediction of infarct evolution and evaluation of hemodynamic status of neuronal tissue in acute stroke.

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