Tissue Outcome Prediction in Ischaemic Stroke with Diffusion, Perfusion and pH Sensitive CEST Imaging at Three Different Time Points

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Target Audience: Researchers interested in MRI applications in stroke, tissue outcome prediction, pH-weighted MRI and machine learning (demonstration included).

Purpose: Recent randomised stroke trials using the diffusion-perfusion mismatch as enrolment criteria have been negative. This study assesses the quantitative value of individual hyper-acute MRI modalities in predicting tissue outcome 1 month following ischaemic stroke. Machine learning combining MRI modalities is demonstrated.

Methods: Patients who presented with an ischaemic stroke within 6 hours of symptom onset to Oxford University Hospitals, UK, were recruited into an MRI-based observational cohort study (UK National Research Ethics Service committee 12/SC/0292). Informed consent or agreement from next of kin was obtained at the time of patient enrolment. Patients were imaged at 5 time points (3T Siemens): at presentation, 2 hours later, at 24 hours, at 7 days and at 1 month. Final tissue outcome was defined by regions-of-interest (ROIs) manually drawn by a clinician around the infarct assessed by fluid attenuated inversion recovery (FLAIR) imaging. Imaging sequences were co-registered and included diffusion weighted imaging (DWI), perfusion weighted imaging (PWI) and a single slice pH sensitive amide proton transfer (APT) image [1] that exploits the chemical exchange saturation transfer effect. Receiver operating characteristic (ROC) curve analysis was performed in Matlab (Mathworks, Inc.) on a per voxel basis on each of the acute phase MR imaging modalities to assess their ability to predict final tissue outcome. A semi-automatic interactive tool allowing an imaging researcher to define the boundary separating the contralateral and ipsilateral hemispheres was used to normalize each voxel by the interpolated signal intensity from the opposite side of the brain. A support vector machine (SVM) tissue outcome prediction demonstration was also performed combining MRI modalities with LIBSVM [2] using a radial basis function kernel in regression mode to produce a range of predictive values instead of a binary output.

Results: ROC analysis included 41939 pixels from 32 imaging examinations from 7 subjects. ROC analysis results are provided in figure 1 for DWI, PWI and APT imaging. Figure 2 provides example imaging data with a clinician defined red overlaid ROI on follow-up FLAIR and on acute (scan 2) DWI, PWI, and APT. A demonstration of regression SVM results combining the acute images at scan 2 is provided in the final pane. Bright voxels on the SVM map indicate an increased likelihood of infarction. The machine learning demonstration was able to predict an additional 6% of FLAIR assessed tissue damage not suspicious on DWI alone.

Discussion: As expected, the prediction of final tissue outcome using DWI improves and PWI deteriorates as the time following stroke onset increases and the infarct matures. APT, as an individual variable, is less predictive of final tissue outcome than DWI or PWI. The yellow arrow in figure 2 points to tissue within the final infarct volume that is normal on DWI but exhibits tissue acidosis based on APT. The SVM regression demonstration is provided combining DWI, PWI and APT images (all at scan 2) to form a tissue outcome prediction map that highlights tissue at risk. The regression SVM outputs a range of predictions with elevated values indicating a high likelihood of infarction. A standard binary output (infarct or not) can be obtained by applying a threshold to the regression output map (figure 2 final pane).

Conclusion: Individual MRI modalities have varying success in defining final tissue outcome and the SVM demonstrates the results of the first attempt to incorporate pH-weighted imaging using APT. Future work will validate machine learning [2] on a larger patient population to create tissue-at-risk maps on presentation.

References: [1] Chappell *et al.*, *MRM*, 2013, 70:556-567. [2] Chang and Lin, LIBSVM, *ACM Transactions on Intelligent Systems and Technology*, 2(3):1-27, 2011.

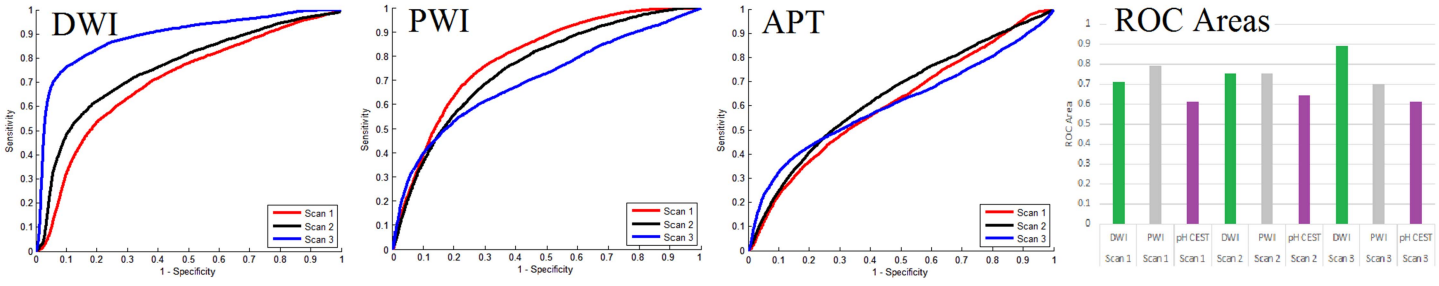

Fig. 1 Receiver operating characteristic curve analyses assessing the FLAIR predictive capacity of DWI, PWI and pH APT. ROC Areas are provided in the final pane.

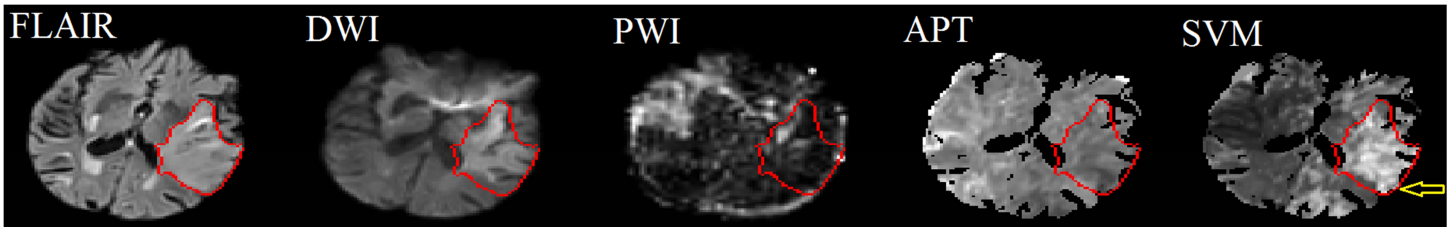

Fig. 2 A red clinician-defined damaged tissue ROI is provided on FLAIR, DWI, PWI, APT, and a demonstration SVM regression image. Bright voxels on the SVM demonstration image indicates increased likelihood of tissue damage. DWI, PWI and APT were acquired at scan 2 and served as inputs to the SVM.