Prediction of hemorrhagic transformation in acute ischemic stroke using DCE MRI: delayed AUC measures versus quantitative estimates of permeability

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Introduction: DCE MRI has been proposed to assess human acute ischemic stroke (AIS) patients, by evaluating leakage of contrast across the compromised blood brain barrier (BBB), and correlating these findings to clinical outcomes including hemorrhagic transformation (HT). Previous work has shown a correlation between the quantitative permeability measure, KPS, and HT [1]. However, successful estimation of KPS requires the measurement of an arterial input function (AIF) as well as pharmacokinetic modeling [2]. Recent work has suggested that semi-quantitative parameters such as the initial area under the signal intensity-time curve (IAUC) may allow rapid assessment of dynamic contrast behaviour without extensive mathematical modelling. IAUC measures have been assessed in various tumour types including brain tumours [3]; this method has been applied more recently to AIS but failed to discriminate between HT and non-HT cases [4]. One explanation for this lack of discrimination is that the time interval over which the IAUC signal is measured is too short (0-90s following contrast arrival in tissue) to adequately capture contrast-leakage associated with HT [5]. The purpose of this study was to review previous data and modify the IAUC measure to better account for the underlying physiology of AIS. We have chosen to use a delayed starting point to improve the prediction of AIS outcomes. Our hypothesis is that a delayed AUC measure is more reflective of contrast-leakage associated with HT in AIS and is similar to model-based estimates of quantitative permeability (KPS).

Materials & Methods: Twenty-nine AIS patients (aged 40-89y) were examined within 6 hours of symptom onset. Thirteen patients received thrombolytic therapy (i.e. rtPA). MRI was performed on a 1.5T clinical MR system (GE Healthcare, Milwaukee, USA) equipped with Echo-Speed gradients and an 8-channel head coil. DCE-MRI using a 3D-GRE sequence was performed as part of the AIS protocol. DCE parameters are: TR 5.9 ms, TE 1.5 ms, FOV 240 mm, matrix 128 × 128, flip angle 20º, slice thickness 7 mm, temporal resolution 5 s × 31 volumes. Gadodiamide was injected as a bolus (0.1 mmol/kg) following initiation of the 3D-GRE sequence. HT was determined by follow-up CT and/or MRI 24-72 h after initial imaging. Data were analyzed using custom in-house software (MR Analyst v. 4.0 and v. 5.0) developed in MATLAB (The Math Works, Natick, MA). Regions of interest (ROIs) for the lesion were defined on DWI images within the core region of the ADC abnormality. ROIs were then copied to the corresponding DCE images. Signal intensity - time curves were generated for all ROIs and adjusted for a standard T1 measure (0.67 for blood vs tissue). Trapezoidal integration of the ROI was performed to yield the area under the curve beginning at 50s after scanning initiation and continuing for 90 consecutive seconds (AUC_{50-140}). In addition, voxel-by-voxel maps of permeability coefficients (KPS) were derived from the same data using a uni-directional two- compartment model as described previously [2]. Mean AUC_{50-140} as well as mean KPS values for patients who proceeded to HT and those who did not were compa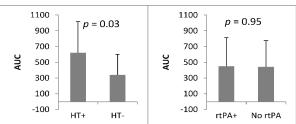red using a Student's t-test. A p-value of < 0.05 was considered statistically significant. A similar comparison was performed for patients treated with and without rtPA.

Results: Eleven out of 29 patients proceeded to HT, including 5 who also received rtPA. The mean AUC_{50-140} ± SD was significantly higher in patients who proceeded to HT (620.48 ± 394.51 versus 341.63 ± 259.12, P = 0.03). Mean KPS measures were similarly elevated in HT cases (1.21 ± 0.53 versus 0.56 ± 0.27 mL/min/100 g, P = 0.0002). AUC_{50-140} was not significantly different between patients who did or did not receive rtPA (451.82 ± 360.58 versus 443.81 ± 333.48, P = 0.95). In contrast, mean KPS values were significantly increased in patients who received rtPA (1.01 ± 0.39 versus 0.63 ± 0.52, P = 0.04). All results are summarized in Figure 1.

Figure 1. KPS and AUC measurements from AIS patients.

Conclusion: Both quantitative and semi-quantitative DCE parameters (i.e. KPS and AUC_{50-140}, respectively).are capable of differentiating AIS patients who proceeded to HT versus those who did not. Although KPS analysis is more computationally demanding it does provide more accurate results. However, measuring the AUC_{50-140} seems to be a good surrogate of KPS and is definitely superior to a previously reported IAUC which only measured the first 90s after contrast injection [4]. The AUC_{50-140} seems to reduce the likelihood that the signal is confounded by other hemodynamic parameters aside from contrast-leakage associated with HT in AIS. This study highlights the importance of optimizing AUC analysis towards the underlying pathophysiology of BBB breakdown in AIS.

References: (1) Kassner A. *et al. AJNR* 2009 30;5:933-941 (2) Roberts HC. *et al. ANJR* 2000 21;5:891-9. (3) Ferl *et al. MRM* 2010 63;5:1366-75. (4) Kassner A. *et al. ISMRM* 2010 511. (5) Vidarsson L *et al. MRI* 2009 27;9:1216-22.