Determination of the ischemic threshold for cell death in acute stroke

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Introduction: The goal in imaging stroke is to determine whether enough penumbral tissue is present to warrant the risk associated thrombolysis. However, accurate and reliable quantification of cerebral blood flow (CBF), a key parameter in identifying the degree of CBF reduction, remains challenging. We have developed a method to quantify CBF (qCBF) in acute stroke patients, and for the first time, determined the ischemic threshold for cell death in humans. We present the ischemic threshold in white and gray matter separately as well as the diagnostic accuracy for predicting ischemia in a series of stroke patients.

Methods: We have added the previously reported "Bookend Technique" for qCBF into the clinical acute stroke protocol at our institute. The Bookend technique has been shown to be correlated strongly (r=0.80,P<10-7)) with colored microsphere CBF in an animal model of acute stroke [1]. The Bookend Technique calibrates relative whole brain rCBF images based on a calibration determined on a case-by-case basis using steady-state T_1 changes which reflect cerebral blood volume (CBV_{SS}) [2]. However, CBV_{SS} has been shown to depend strongly on the water exchange rates and the T_1 change of the blood pool [3]. We have implemented an improvement over the existing bookend technique that improves the accuracy of the qCBF measurement by including water exchange effects in the model [4].

Bookend qCBF Protocol: To date, nine confirmed acute MCA stroke patients were scanned on a clinical 1.5T (Siemens Medical Solutions). For the T_1 measurement, true FISP readout of inversion recovery (IR true FISP, non-selective IR pulse, 20 linear ramp preparation pulses before train of ± 30º pulses, TR/TE = 2.91ms / 1.46 ms, 3 lines per segment, total scan time = 2.08 min) were scanned before and after a GRE perfusion scan (TR/TE=1500/46ms , slice thickness = 5 mm, 13 slices, Acq time = 1:10) acquired with a single dose contrast injection (Magnevist).

Statistical analysis: Infracted regions were defined as hyperintense on diffusion weighted image (DWI) images. qCBF distributions of normal and infarcted tissue were accumulated voxel-by-voxel, and pooled over patient. An ROC analysis [5] was used to determine the diagnostic accuracy of the qCBF parameter to identify the ischemic threshold for cell death (Figure 1 a, b). From the ROC curve, which was determined in increments of 1 ml/100g-min, the sensitivity, specificity and area under the curve (AUC) were calculated.

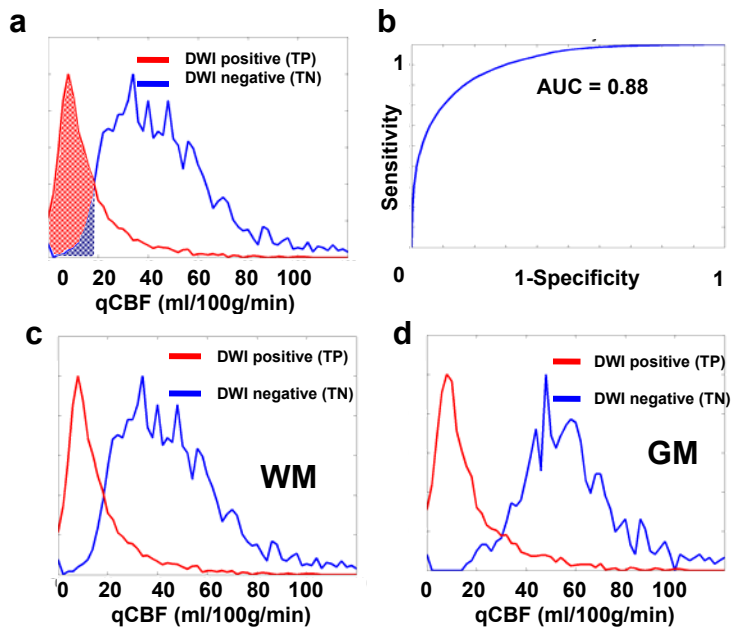

Figure 1: We have determined the diagnostic accuracy of qCBF to detect the ischemic threshold for cell death in stroke patients (n=9) a) qCBF values were compared in diffusion positive and diffusion normal regions (True/False Positive/ (TP/FP)) b) The Area under the ROC curve was high (AUC=0.88). Analyzed separately White Matter (WM) and Gray Matter (GM) ischemic thresholds are: (c) 17.5 ± 5 and (d) 30.0 ± 10 ml/100 g –min, respectively, reflecting the higher metabolic demand of gray matter.

Results: The mean value of CBF was found to be significantly different in the normal and infarcted regions (p<0.05). The ischemic threshold for cell death in WM and GM were estimated as 17.5 ± 5.0 and 30.0±10.0 ml/100g-min, respectively (Figure 1 c, d). For a threshold of 17 ml/100g-min, we find sensitivity / specificity for detecting infarcted tissue of: 83.3% / 80.8% respectively. The diagnostic accuracy for our technique to qCBF exhibited high diagnostic accuracy (AUC = 0.88).

Discussion/Conclusions: Our estimates of the ischemic threshold for cell death agree with prior findings of 18 ml/100g-min in a primate model of stroke [6]. We have shown that the Bookend technique has the potential to quantify cerebral perfusion is a setting of acute stroke. Furthermore our qCBF values show a high diagnostic accuracy (AUC =0.88) for identifying ischemic tissue.

Reference

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