Delineating the Boundary between the Ischemic Penumbra and Regions of Oligaemia Using pH-weighted MRI (pHWI)

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INTRODUCTION

Recent progress in the field of ischemic stroke has shown that thrombolysis treatment increases survival and reduces disability, but that early intervention is the key to successful therapeutic outcome.1 The classical definition of ischemic penumbra is that of a region of hypoperfusion that is still viable but at risk of infarction, restricted to an area in which metabolism is impaired, but still sufficient to maintain cellular polarization. Modern MRI technologies, such as perfusion and diffusion weighted imaging (PWI, DWI), can identify regions of reduced perfusion and cellular depolarization, respectively, but it may be unclear whether reduced perfusion corresponds to benign oligaemia or a true penumbra. Recently, amide proton transfer (APT) imaging2 has been shown to be able to monitor tissue pH and protein content through indirect detection of exchangeable amide protons via magnetization transfer asymmetry analysis (MTR asym). We hypothesized that the pH-weighted imaging (pHWI) acquired using the APT technique may be able to subdivide the PWI-DWI mismatch into the penumbra and the region of oligaemia.

MATERIALS AND METHODS

Adult male Wister rats (n = 31) underwent middle cerebral artery occlusion (MCAO) and were imaged on a 4.7 T animal scanner during the hyperacute period every half hour from 0.5 or 1 hr up to 3.5 hr post MCAO as well as at 24 hr for follow-up T2 MRI. Multi-parametric MRI including pHWI, perfusion-weighted (PWI), diffusion-weighted (DWI), and T1 and T2 images were acquired using single shot EPI. In two rats only minimal hypoperfusion, and no pH and ADC abnormalities were detected during either the hyperacute stage or at 24 hr follow-up MRI. For three additional animals (n = 3) high signal fluctuations were measured, which could be traced to a malfunction of the active coil decoupler. These five animals were excluded from the data analysis. In addition, six animals (n = 6, mainly group I and group II to be defined below) died within 24 hr and no follow-up MRI study performed, but the evolution in the first hours was included in the group study.

RESULTS

All 26 animals included in the analysis showed the expected maximum perfusion deficit on PWI, but, due to the variability of the model, different animals showed different deficits on pHWI and ADCave [= (1/3)trace(ADC)] images. CBF, ADC and MTR asym from the contralateral brains of eight animals (n = 8) were used as the reference values. CBF, pH (i.e., MTR asym), and ADC deficits were defined as values falling outside two standard deviations from the mean value. To reflect the different types of evolutions in the pHWI and ADCave maps, animals were assigned to three groups based on the correspondence of the deficits on these image types during the initial 3.5 hr of ischemia:

Group I (n = 8, severe ischemia): the spatial pHWI and ADCave deficits are within 20% at the start of the first MRI scans.

Group II (n = 11, severe ischemia at 3-3.5 hr): spatial difference between the pHWI and ADCave deficits evolved to within 20% up to 3.5 hr.

Group III (n = 7): PWI deficit > pHWI deficit >> ADCave deficit during the 0.5-3.5 hr initial period.

Fig. 1 shows results of processed images (Fig. 1a-d) and a schematic drawing of the principles of subdivision (Fig. 1e).

Fig. 2. Temporal evolutions of pHWI (filled squares) and ADCave deficits (circles) normalized by the PWI deficit for the three ischemic groups. The final infarct volume is indicated by a triangle. The mean standard error over the group is displayed. It can be seen that, for this permanent occlusion model, pHWI predicts well the final T2 deficit, which is smaller than the initial perfusion deficit.

REFERENCES