Comparison of the Temporal and Spatial Evolution of the Water Apparent Diffusion Coefficient and T2 Following Transient Middle Cerebral Artery Occlusion in Rats

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Introduction
Diffusion-weighted imaging (DWI) is an accepted research and clinical tool for the detection and evaluation of acute stroke. Studies have shown that regions of abnormality visible on DWIs are completely reversible if reperfusion is performed soon after the onset of stroke (1,2); however, subsequent work has demonstrated clearly that the acute ADC reversal is not permanent and can be followed by a secondary ADC decline (3,4). Further, it has been shown that the secondary ADC results in varied lesion volume relative to the initial lesion volume during stroke (5). The purpose of this study was to characterize the temporal and spatial evolution of the ADC of water and T2 in a 30-minute transient middle cerebral artery occlusion (MCAO) model.

Methods
Seven male Sprague-Dawley rats were subjected to 30 minutes of transient MCAO. DWI and T2-weighted images (T2WI) were performed immediately before and after reperfusion and every 30 minutes for 12 hours following reperfusion. MR imaging was performed with a GE CSI-II 2.0T/45 cm imaging spectrometer (GE NMR Instruments, Fremont, CA) operating at 85.56 MHz for 1H and equipped with ±20 G/cm self-shielding gradients. MRI data consisted of eight contiguous, coronal 2-mm-thick slices, centered about the optic chiasm with FOV = 25.6 mm × 25.6 mm and a 64 × 64 pixel resolution.

Multislice, diffusion-weighted spin-echo echo planar imaging (DW-EPI) was employed to estimate the average ADC on a pixel-by-pixel basis from three separate diffusion-weighted (x, y, and z) images. Diffusion weighting was achieved by incrementing the gradient amplitude from 2 to 18 G/cm in 2 G/cm steps. Other parameters were TR=1 s, NEX=2, δ=72 ms. A multislice, double spin-echo EPI pulse sequence that contains a Hahn spin-echo preparation pulse sequence followed by a spin-echo echo-planar acquisition sequence was used to acquire T2WI. TE of preparation pulse provided the T2 weighting and was incremented in 9 steps from 20-110 ms. The second TE period was 74 ms. Other parameters were TR=5 s and NEX=4. T2 maps were constructed from nine T2-weighted EPIs on a pixel-by-pixel basis using a linear least-squares regression. The natural logarithm of the signal intensity was fitted to the TE values, where the slope of the fitted line is inversely proportional to the T2 value.

Using the ADC and T2 maps, pixels ipsilateral to the insult were compared to the corresponding contralateral pixel. The initial lesion volume was calculated from ADC maps using a 15% reduction as abnormal. On pixel-by-pixel basis, ADC and T2 maps were interrogated to determine the time point after 2 hrs (time point when all pixels usually normalized) at which the ADC or T2 value changed by 15% (and thus were considered to exhibit a secondary change). Pixels identified as abnormal during MCAO (>15% ADC reduction) were then grouped according to their secondary characteristics: no secondary ADC decline and no T2 increase (-SADC, -T2), secondary ADC decline but no T2 increase (-SADC, +T2), secondary ADC decline accompanied by a T2 increase (+SADC, +T2).

Results
3x3 Region-of-interest analysis in Figure 1 shows the ADC and T2 parameter changes in the caudoputamen during the study (hour and half-hour time points merged for display). The ADC declined during occlusion, renormalized by 2 hrs after reperfusion, and secondarily declined during the remainder of the experiment. T2 values did not begin to increase until 5 hrs post reperfusion and continued to increase through the 12-hr time point.

Figure 2 illustrates the regions of the secondary ADC decline and T2 increase following transient MCAO. The initial lesion during MCAO, as determined by the ADC maps, is demarcated by the combined dark gray regions, which also denote the conditions of that tissue at the 12-hr time point.

Statistical analysis was performed on pixels initially defined as abnormal (>15% ADC reduction) to determine if any differences could be observed between the secondary ADC characteristics. Pixels that exhibited secondary ADC decline by 3 hrs were not statistically different, in terms of ADC or T2, from pixels that decline secondarily by 12 hrs. Further, there was no statistical difference, in terms of ADC or T2, in regions with secondary ADC decline (+SADC, +T2) to regions without secondary ADC (-SADC).

Discussion
Acute reversal of brain tissue ADC values in ischemic brain does not necessarily protect tissue from chronic ischemia and infarct. Further, initial ADC changes during MCAO do not appear to correlate with the secondary events. By 24 hrs, the ADC-derived lesion following 30 min of temporary ischemia is maximized and matches histological analysis (6). Although the chronic lesion as determined by T2 evolves to include the region of secondary ADC, the final lesion volume is variable and may not match the initial MCAO lesion volume (5).

Further study of the heterogeneous progression of secondary lesion could assist in understanding cerebral tissue response to ischemic events and to treatment.

References