Three Compartment Magnetic Resonance Diffusion Imaging in Early Ischemia

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Introduction: We have shown that our magnetic resonance diffusion imaging (MRDI) technique allows quantitative assessment of three unique diffusion rates (D) in brain tissue [1]. The slow and intermediate rates, D1 and D2, arise from water in tissue while the fast rate, D3, arises from the pseudo-diffusive motion of microcirculatory flow. Many questions continue to surround the quantitative assessment and interpretation of diffusion rates (D) in ischemic brain tissue, in particular, immediately after the onset of ischemia. Our MRDI technique measures quantitatively 3 D's that provide new information about the changes in tissue architecture and microcirculatory flow in brain tissue during the first 4 hours post-onset of ischemia.

Hypothesis: We hypothesize that changes occur in all 3 D's measured in brain tissue during the first 4 hours post-onset of ischemia.

Methods: Ten New Zealand white rabbits were a□nesthetized by isofluorane inhalation. Blood pressure, arterial blood gases (pH, PO_2, PCO_2, HCO_3) and temperature were monitored continuously. Ischemia was achieved by injection of an autologous blood clot into the left internal carotid artery followed by 5cc of saline [2]. Imaging was performed on a 1.5T GE CV/i MRI system with 400mT/m gradient strength and a quadrature surface RF coil (4cm loops). DW images (single shot SE-EPI, TE/TR=94.8ms/1500ms, FOV=10x5cm, matrix=80x80, slice thickness=5.0mm, 6 averages) were acquired with 18 b-values (0, 5, 10, 20, 30, 60, 90, 130, 230, 360, 530, 740, 1000, 1500, 2000, 2600, 3300, 4100s/mm^2, encoding along xz, -xz, yz, -yz, xy, -xy). Images were acquired prior to ischemia, and 10, 30, 60, 90, 120, 180, and 240 minutes post-onset of ischemia. Immediately post-imaging (~5 hours post-ischemia), rabbits were euthanised and brains removed and stained with 2% 2,3,5-triphenyltetrazolium chloride (TTC). Trace images were formed and then filtered using a scale-space filter [4]. For each pixel, the diffusion decay curve (Si/So versus b where Si is the signal at the ith b-value (i=0,…,17)) was fit using the non-negative, least squares (NNLS) algorithm (75 logarithmically spaced D-values submitted between 0.1x10^{-3} and 50x10^{-3}mm^2/s; 3 weighted averages calculated for D's chosen between 0.10–0.80x10^{-3}mm^2/s (D_1), 0.80-2.50x10^{-3}mm^2/s (D_2), and 2.50-50.0x10^{-3}mm^2/s (D_3), and corresponding fractional volumes (f1, f2, f3) were determined). Average Ds and fs were obtained for regions of interest (ROIs) drawn on the ischemic area in the diffusion weighted image, b=2600s/mm^2, and on a similar area on the contralateral side of the brain. For average D's only, pixels with f=0 were not included in the calculation of the average.

Results: Average Ds and fs in the ROIs are plotted versus time post-ischemia in Figures 1 and 2, respectively. Error bars represent standard error of the mean, and solid lines represent contralateral ROIs and dotted lines, ischemic ROIs for slow (D1, f1=green), intermediate (D2, f2=blue), and fast (D3, f3=red) diffusion. Images acquired prior to injection of the blood clot are plotted at time=0. Student t-tests showed that ischemic and contralateral ROIs were: 1) not significantly different ($p \geq 0.2$) pre-ischemia for all Ds and fs; 2) not significantly different ($p \geq 0.1$) at all time points for D3; 3) significantly different ($p < 0.001$) at 10 minutes post-ischemia for D2, f1, and f2; and 4) significantly different ($p \leq 0.001$) at all time points >10 minutes post-ischemia for D1, D2, f1, f2, and f3.

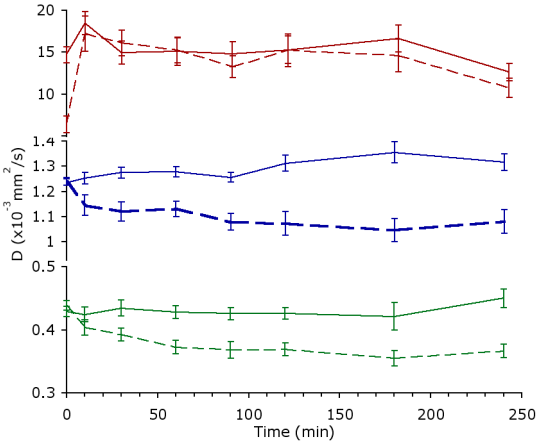

Fig 1: Average Ds in ischemic (dotted lines) and contralateral (solid lines) ROIs for D1 (green), D2 (blue), and D3 (red) vs time post-onset of ischemia.

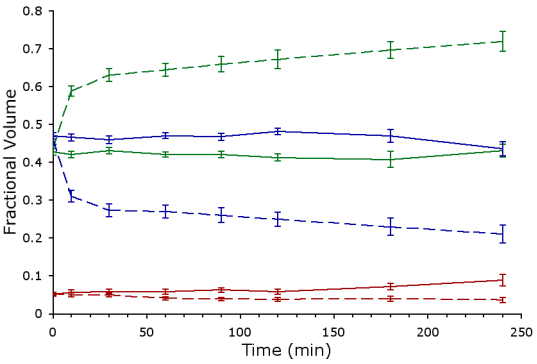

Fig 2: Average fs in ischemic (dotted lines) and contralateral (solid lines) ROIs for f1 (green), f2 (blue), and f3 (red) vs time post-onset of ischemia.

Discussion: D1 and D2 decrease post-ischemia suggesting increased restriction of water diffusion in tissue. The increase in f1 and corresponding decrease in f2 suggest a shift of water from the intermediate to the slow diffusion rate compartment. While f3 changes post-ischemia, D3 does not. This may be due to the ROI containing pixels outside the ischemic area, noise, or incomplete occlusion of microvessels in the area that appears ischemic in diffusion weighted images and D1 and D2 maps. This suggests a net reduction in the number of patent microvessels post-stroke, but those microvessels that remain patent sustain blood flow at the same average velocity as pre-stroke. The slow decrease in f3 compared to D1, D2, f1, f2 (within 10 min.) and the lack of change in D3 suggest changes in perfusion may be slower than changes in tissue micro-architecture.

Conclusions: In the first 4 hours post-onset of ischemia, changes were observed in slow and intermediate diffusion rates and fractional volumes of brain contributing to slow, intermediate, and fast diffusion rates. Ongoing work involves correlating the "pseudo-diffusion" rate and fractional volume of the microvascular compartment to contrast enhanced perfusion images.

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References:

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