

Direct Comparison of T2 and T2 ρ Image Contrast in a Rat Model of Acute Cerebral Ischemia

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Introduction: Metabolic and structural changes occur in brain tissue within minutes of ischemia. Changes in the relative concentration of oxy- and deoxy-hemoglobin, blood volume, and cell microstructure within ischemic tissue may also initiate specific metabolic processes and lead to changes in tissue magnetic susceptibility. The Localization by Adiabatic Selective Refocusing (LASER) MR localization sequence (1), has shown promise in detecting tissue ¹H₂O changes within the first few minutes of ischemia (2,3). This sequence is sensitive to the diffusion of spins through tissue regions with different magnetic susceptibility (3), and has demonstrated novel image contrast by combining sensitivity to T₂, T_{2 ρ} and diffusion (T₂[†], 3,4). LASER can also be used to create high resolution, reduced field of view images. The purpose of this study was to make a direct *in-vivo* comparison of T₂, T_{2 ρ} and diffusion image contrast during acute ischemia. It was hypothesized that T_{2 ρ} weighted images acquired using LASER would show enhanced contrast in ischemic tissue, compared to T₂ weighted images acquired with a Carr-Purcell Meiboom Gill (CPMG) sequence and diffusion-weighted images. Acute ischemia by electrocoagulation of the left Middle Cerebral Artery (MCA).

Methods: Fourteen male Sprague-Dawley rats were studied within 1.5 hours of attempted left MCA occlusion by electrocoagulation. Measurements were made using a Varian/Siemens 4T whole body MR scanner. A 3D echo-planar imaging readout was incorporated following the LASER localization pulse sequence (TR/TE = 4000/29 ms, image matrix size 128 x 128 x 8, FOV 4 x 4 x 4 cm³ (EPI), 2 x 3 x 4 cm³ LASER excitation, 4 shot EPI readout, total acquisition time 4 min 50 s) to obtain reduced field of view, 3D images of the entire brain. LASER T₂[†]-weighted images were obtained at an echo time of 110 ms by inserting 16 nonselective phase cycled, 180 degree, AFP pulses (1) prior to the LASER localization while maintaining a constant refocusing time (2 τ_{cp} =5.3 ms). T₂-weighted images were obtained with a 2D CPMG pulse sequence with 22 echoes and TE ranging from 6 ms to 122.6 ms (3000 TR, 4 x 4 FOV, 128 x 64 acquisition matrix, total acquisition time : 3 min 15 seconds). The slice thickness, field of view and interpulse delay time (2 τ_{cp}) were matched to the LASER sequence. For image and contrast comparison the closest echo time of the series (TE = 108 ms, 17 echoes) was selected to compare to the LASER echo time of 110 ms. Diffusion-weighted images were acquired by varying the pulsed gradients (G_{diff}) in a conventional pulsed gradient spin echo (PGSE) sequence while keeping the diffusion time (Δ) and the pulsed gradient width (Δ) constant (TR/TE = 2000 /60 ms, Δ = 40 ms, Δ = 10 ms, G_{diff} = 0.4 G/cm, b-values in the range of 4 to 269 (only 105 s/mm² was used in data analysis)). Animals were divided into two groups (stroke and control) based on the results of TTC staining, which shows non-viable tissue damage by stroke as white and viable tissue as pink. Contrast in the MR images defined using signal intensity (SI) ((SI (ipsilateral)- SI (contralateral))/SI contralateral) within regions of interest (ROIs) selected based on histology was compared using a two tailed *t*-test (p<0.05 considered significant).

Results: Stroke was successfully initiated in six animals confirmed by TTC staining, four animals without strokes were used as controls, and four animals could not be included in the analysis because of excessive bleeding. Figure 1 shows a TTC stained histology image (Fig 1A) and the corresponding high-resolution LASER-EPI image (TE =110 ms, Fig 1B), CPMG image (TE =108 ms, Fig 1C), and diffusion image (TE = 60 ms, Fig 1D) of rat brain at 1.5 hours post ischemia. Figure 2 shows average contrast in LASER, CPMG and diffusion images in non-viable tissue determined by TTC staining (blue, N=6 animals) and control tissue (red, N= 4 animals). Asterisks denote significance differences (p < 0.035). All data in this plot was acquired within 1.5 hours of the occlusion onset.

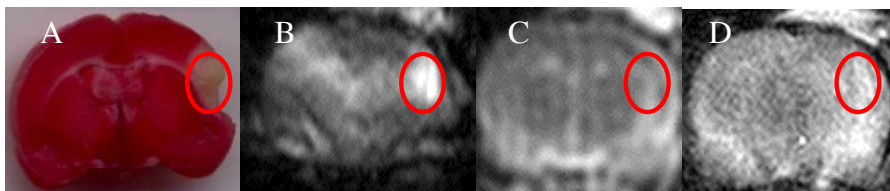


Figure 1

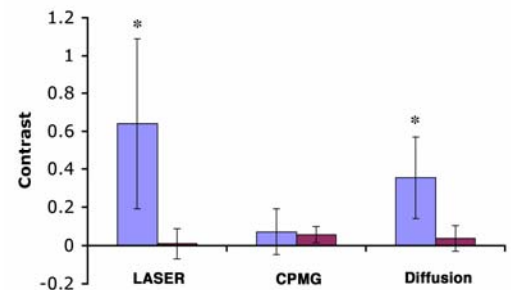


Figure 2

Discussion: A LASER localized 3D-EPI sequence was successfully implemented to acquire reduced FOV images of the rat brain at 4T (3,4). LASER, CPMG and diffusion weighted MR image contrast was directly compared during acute focal ischemia to evaluate their effectiveness in the early detection of stroke. Increased signal intensity was observed in LASER images within 1.5 hours after ischemia onset in histologically confirmed regions of tissue damage, while similar changes were not observed in CPMG images. Increased signal intensity was also observed in the diffusion-weighted images. However, the bright regions in the LASER images were more localized than in the diffusion weighted images, suggesting a different mechanism of contrast was responsible for the changes. The CPMG sequence still did not show notable contrast in ischemic regions 3 hours after occlusion (data not shown). The greater sensitivity of LASER was attributed to the known sensitivity of LASER to changes in microscopic susceptibility (4,5). The LASER pulse sequence has therefore demonstrated the ability to detect signal changes due to acute ischemia and may complement other MR imaging techniques such as diffusion and perfusion weighted imaging in the evaluation of tissue damage due to stroke.

Acknowledgements and References: Funding was provided by the Heart and Stroke Foundation of Canada, the Canadian Institutes of Health Research (MME-15594), and the Ivey BMO-Financial Group Scientist in Brain Disorders Imaging Award. (1) Garwood and DelaBarre. J Magn Reson 2001; 153: 155-177. (2) Bartha et al. ISMRM abstract 2002; 1238. (3) Nikolova et al. T₂[†] Measurement during Acute Cerebral Ischemia by Carr-Purcell MRI at 4T. Magnetic Reson Med 2005; 54:1448-1454. (4) Nikolova et al. Experimental Validation of a T_{2 ρ} Transverse Relaxation Model using LASER and CPMG acquisitions. J Magn Reson 2006; 181: 35-44. (5) Kavec et al. Dynamic Dephasing Changes in Developing Ischemic Cerebral Infarction in Rats Studied by Carr-Purcell T₂ MRI. Magn Reson Med 2005;53:960-964.