In-vivo Longitudinal Relaxation Enhancements (LREs) of Central-Nervous-System Metabolites at 21.1 T upon Stroke

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Target Audience. Researchers and clinicians interested in stroke and MR spectroscopic characterizations.

Introduction. The effective T1 of macromolecular resonances may be shortened significantly by harnessing spectrally selective excitations1, which focus on specific (e.g., amide) resonances while leaving a large reservoir of solvent and/or macromolecular magnetization unperturbed. This phenomenon–termed Longitudinal Relaxation Enhancement (LRE)–is driven by exchange or cross-relaxation in slowly tumbling molecules, and can be used to enhance NMR spectral sensitivity2. A recent study directly measured the apparent T1s of non-labile metabolic resonances in intact ex vivo mice brains by a similar approach2, revealing unexpected apparent T1 reductions even for methyl resonances of endogenous metabolites upon switching from broadband excitation with active water suppression to a spectrally selective sequence targeting only the resonances of interest3. Here, we implement an in vivo localized version of the ensuing LRE-MRS sequence. The potential of LRE as a biomarker in a rat model of in vivo ischemia is evaluated.

Purpose. To employ LRE for detecting superior in vivo metabolic spectra and as a potential biomarker.

Methods. All experiments were performed in the National High Magnetic Field Laboratory’s 21.1 T MRI operating at a 1H frequency of 900 MHz and equipped with a Bruker Avance III console. The middle cerebral artery of juvenile Sprague-Dawley rats (N=6) was occluded for 1.5 h, followed by reperfusion. Rats were scanned at 3 h, 24 h, and 1 w post ischemia. 1H MRS spectra were acquired using a localized LRE sequence4, which spectrally targeted only four prominent resonances of interest (Lac, NAA, Cre and Cho) by means of SLR-designed polychromatic excitation and single-band refocusing pulses, 8 and 4 ms long, respectively. Spatial localization was achieved by a 3D LASER module inserted just prior to acquisition (Figure 1). Metabolic apparent T1s were measured by a progressive saturation (PS) approach5. In separate acquisitions on the same rats, LRE-MRS data were collected from 5x5x5 (mm3) voxels positioned in the ipsi- and contralateral hemispheres.

Results and Discussion. Localized LRE-MRS acquisitions from the in vivo stroked rat brain at 21.1 T show clear resonances from the targeted metabolites with no excitation of water (Figure 2). SNR for the shortest TR was typically very high exceeding 100 for Cho in only 48 repetitions. Marked increases of Lac and decreases of NAA levels in the ipsilateral hemisphere were noted upon stroke (Figure 2). The peaks’ TR dependence of water (Figure 2). SNR for the shortest TR was typically very high exceeding 100 for Cho in only 48 repetitions. Marked increases of Lac and decreases of NAA levels in the ipsilateral hemisphere were noted upon stroke (Figure 2). The peaks’ TR dependence

Figure 1. Localized LRE MRS sequence, involving a selective excitation and refocusing of Lac, NAA, Cre and Cho resonances, and 3D LASER spatial localization. Localizing gradients are shown in black and crushers in gray.

Figure 2. Progressive saturation of localized LRE MRS. Only the metabolites of interest are excited; no active water suppression was used, and the signal was averaged with 48 repetitions (~30 minutes to acquire the entire curve). Spectra allow for robust quantification of apparent T1s.

Figure 3. LREs and apparent T1s in stroked rats for the four resonances of interest. *p<0.05, **p<0.01 (ANOVA, Fisher means). * indicates LRE; # indicates differences between ipsi- and contralateral.

Figure 4. Time-dependent post ischemia metabolic changes. The effective T1 of macromolecular resonances may be shortened by LRE-MRS and the subsequent apparent T1 decrease may reflect a release of Lac to an environment in which it undergoes fewer interactions with macromolecules or membranes, and the subsquent apparent T1 decrease may reflect the transport of excess Lac.

Conclusions. Superior MRS traces and differential LRE effects were detected for the first time in vivo via a novel localized MRS sequence. The spectra arising from the spectrally-selective excitation obviate water suppression, significantly enhancing MRS quality while providing a commensurate increase in SNR per unit time. LRE was also found to be time-dependent post ischemia, highlighting the complex nature of interactions between metabolites and their tissue under dynamic conditions in normal and diseased states.

Acknowledgements. This work was supported by an ERC Advanced Grant (#246754), a Helen and Martin Kimmel Award for Innovative Investigation, and the generosity of the Perlman Family Foundation, as well as the American Heart Association (10GRNT3860040) and NHMFL (NSF DMR-0654118), including a visiting scientist grant (#12601).