Simultaneous *In Vivo* ^{1}H and ^{31}P MRS Acquisition in Ischemic Rat Brain at Ultrahigh Field

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INTRODUCTION The wealth of information contained in *in vivo* MR spectroscopy (MRS) and its importance to understanding brain metabolism under physiopathological conditions is becoming increasingly apparent. However, the inability to measure signal from more than one nucleus at a time and the slow acquisition limit the amount of information that can be obtained from a single MRS scan using conventional acquisition strategies. While paradigm repetition allows different types of MR signal to be collected, it is not always a feasible option, particularly when dynamic conditions cannot be exactly replicated or when time is of the essence. We propose a new MR technique capable of simultaneous multiple channel acquisition of ^{1}H and ^{31}P MRS, thus allowing the study of the dynamic relationship of ^{31}P metabolites with BOLD signals or ^{31}P metabolites with ^{1}H metabolites from a single measurement.

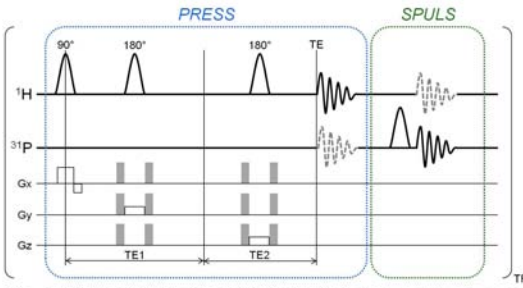

Fig. 1 ^{1}H PRESS (blue) and ^{31}P SPULS (green) pulse sequence. SPULS inserted into delay time at the end of PRESS. Hardware constraints require acquisition from both receivers, noise FIDs (dashed grey) are discarded from analysis.

METHOD MRI/MRS data was acquired on a 9.4T/31 cm horizontal animal MR scanner (Agilent Technologies, CA) with a dual-channel ^{1}H (butterfly loop) and ^{31}P (single loop) RF surface coil probe. Modifications were made to the scanner to allow for acquisition from multi-nuclei channels simultaneously. To optimize signal collection from both the ^{1}H and ^{31}P channels, standard pulse sequences were combined utilizing the "down time" between sequence completion and end of TR. This strategy is similar to that used by Schnall et al.[1] and Eleff et al.[2], who had more complicated console and coil requirements than used here, and by Price et al.[3], who acquired muscle spectra using a double-tuned RF coil. For this study, localized spin echo ^{1}H MRS (PRESS) and global single-pulse acquire ^{31}P MRS (SPULS) sequences were combined (Fig. 1). Each FID acquisition collects signal from both active receivers, resulting in FIDs of the desired signal and FIDs of the un-optimized signal (dashed grey FIDs shown in Fig. 1). All processing was performed with MATLAB (MathWorks, Inc., MA) with un-optimized or "noise" FIDs discarded from analysis.

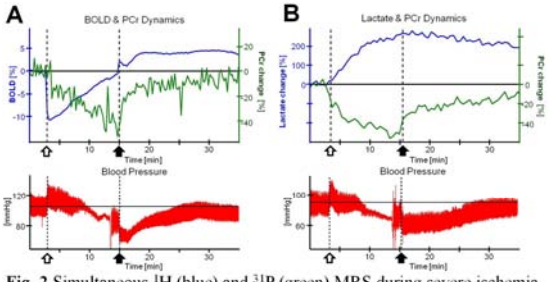

Fig. 2 Simultaneous ^{1}H (blue) and ^{31}P (green) MRS during severe ischemia. Dashed lines indicate occlusion start (open arrow) and end (closed arrow). Dynamic changes in (A) BOLD and PCr intensity, temporal resolution 16 sec, and (B) Lactate and PCr intensities, temporal resolution 32 sec. Bottom graphs show corresponding blood pressure changes. The decreased BP range (starting at 8 mins) is due to a partially blocked arterial line, which was recovered following a line flush (at 12 mins).

Rats with acute global forebrain ischemia preparation were used for this study. Ischemia was induced with a 4-blood-vessel-occlusion (4BVO). Vertebral arteries were electrically cauterized 48 hours prior to the experiment, and carotid arteries occluded during the experiment with plastic vessel occluders[4]. The rat was intubated and catheterized, then secured with ear and bite bars. The animal was kept under 2.0% isoflurane, and its condition was monitored and maintained throughout the experiment. After the animal was stable, two 12-minute occlusions were induced, with a 70 min recovery period between them. Simultaneous *in vivo* ^{1}H and ^{31}P MR spectra were acquired during the occlusion and recovery periods. All procedures and protocols were performed according to the guidelines of the National Institutes of Health and approved by the Institutional Animal Care and Use Committee of the University of Minnesota.

RESULTS and DISCUSSION To assess the capabilities of this new acquisition approach for monitoring the temporal variation of the MR signals, an ischemia rat model was used for its robust metabolic and hemodynamic (BOLD) response. For the first occlusion, localized BOLD and global ^{31}P MRS signals were measured simultaneously. Fig. 2A shows the time courses of BOLD and relative PCr intensity changes (top), and corresponding blood pressure changes (bottom). For the second occlusion, ^{1}H metabolites and ^{31}P MRS were acquired, with lactate and PCr relative changes shown in Fig. 2B. It is noticed for both experiments that changes in all traces begin to occur immediately following occlusion onset (open arrow), with slow recovery of metabolite levels and an overshoot in BOLD following reperfusion (closed arrow). The changes during occlusion follow expected ischemia trends of decreased PCr, decreased BOLD, and increased lactate. The PCr change was not as dramatic as expected due to a partial volume effect and large muscle contribution to the global ^{31}P signal in this rat. The PCr trace appears noisier in Fig. 2A than 2B due to the higher temporal resolution (16 s/spectrum vs. 32 s/spectrum, respectively). The responses of the two channels during the second occlusion (Fig. 2B) are examined in detail in Fig. 3, where the stacked spectra of ^{31}P (Fig. 3A) and ^{1}H (Fig. 3B) are shown. The PCr and lactate changes can easily be seen, with peak intensity traces plotted for additional visualization of occlusion start (open arrow) and end (closed arrow). Average baseline ^{31}P (Fig. 3C) and ^{1}H (Fig. 3D) MR spectra are displayed for reference.

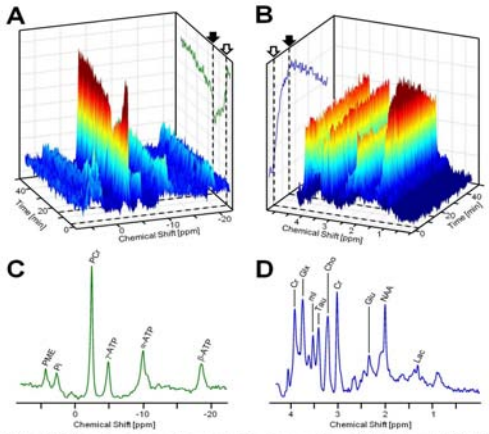

Fig. 3 Visualization of spectral changes in (A) ^{31}P and (B) ^{1}H MRS during and following ischemia. Occlusion start (open arrow) and end (closed arrow) indicated by dashed lines on PCr (A, green) and Lactate (B, blue) traces. Temporal resolution is 32 sec. (C-D) Average baseline spectra for (C) ^{31}P and (D) ^{1}H MRS.

CONCLUSION We have demonstrated here the utility of the simultaneous dual channel acquisition for the study of dynamic *in vivo* ^{1}H and ^{31}P spectra of rat brain under an ischemic condition. This technique opens up exciting new avenues for exploring various metabolic and/or hemodynamic activities simultaneously under many different paradigms and animal conditions. It also reduces the number of subjects and scanning time for the same study, while improving the study reliability.

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REFERENCES [1]Schnall et al, *MRM*, 1988; [2]Eleff et al, *MRM*, 1988; [3]Price et al, *PNAS*, 1996; [4]Sugio et al, *Stroke*, 1988.