Evaluation of acute hepatic ischemia in rats using 23Na and 1H diffusion-weighted MRI

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Introduction

Acute ischemic conditions (e.g., stroke, heart attack, iatrogenic from surgical procedures) affect the majority of people world-wide at some point in life and carry high morbidity and mortality rates [1]. In many cases, reperfusion therapy is a viable option to improve chances for recovery, yet the procedures used to detect ischemia do not always give accurate results within a time frame that is narrow enough to be beneficial [2]. Diffusion-weighted ^{1}H MRI (DWI) is a gaining more attention as a noninvasive technique for ischemia detection, yet its major limitation in the liver is respiratory, cardiac, and peristaltic motion artifacts [3]. Another option for ischemia evaluation is single-quantum (SQ) and triple-quantum- (TQF) filtered ^{23}Na MRI. This technique allows estimation of total tissue and intracellular Na^+, respectively, with little sensitivity to motion artifacts. In this study, apparent diffusion coefficient (ADC) values calculated from DWI and SQ and TQF ^{23}Na MRI were used to evaluate hepatic ischemia in rats.

Methods

SQ and TQF ^{23}Na MRI and DWI were performed on Wistar rats (~250 g). The animals were anesthetized with 1.0-1.5% isofluorane. After collecting baseline images, global ischemia was produced by increasing the isoflurane dose to 5% while monitoring respiration and cardiac activity. MR images were acquired for 5 hours with a Varian 9.4 Tesla, 31-cm horizontal bore system with a 12-cm gradient insert (maximum gradient strength = 38 G/cm). 3D trans-axial SQF ^{23}Na MRI were obtained with a home-built loop-gap resonator tuned to 106 MHz using a gradient-echo (GE) imaging sequence and following imaging parameters: TR = 50 ms, TE = 4.5 ms, 64 x 64 x 16 data points over a FOV of 6 x 6 x 6 cm^3, and 10 min total imaging time. TQF ^{23}Na MRI employed the same parameters as used for SQF ^{23}Na MRI except TR = 100 ms, data size of 64 x 32 x 8, and 50 min total imaging time. A reference of 0.3% NaCl was used to normalize all data and to show that the TQF was functioning.

A 63-mm birdcage coil tuned to 400 MHz using a multi-slice DWI sequence was used to determine ADC values. The following imaging parameters were used: 1,100 ms repetition time (TR), 21 ms echo time (TE), 256 x 128 data points over a 80 x 80 mm^2 field of view (FOV), 0.5 mm slice thickness, 1.5 mm slice gap, 7 min total imaging time. Two diffusion gradient pulses of δ = 6 ms duration separated by a Δ = 11 ms period were applied along all three axes. Four interleaved *b*-factors (*b* = 0, 256, 945 and 1,679 s/mm^2) were used. To evaluate possible ways to reduce motion artifacts, the following were examined: 1), oral gavage of 2.0 mL Gastromark (Mallinckrodt, Inc., St. Louis, MO USA), a superparamagnetic iron oxide solution, 2) fat suppression applied the resonance frequency of methylene (1.3 ppm), and 3) collection while breathing 30, 45, or 60 breaths per minute (bpm).

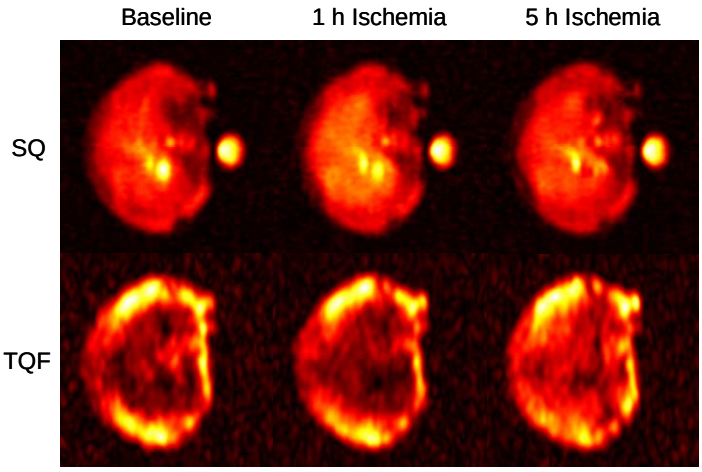

Figure 1: Representative trans-axial single quantum (SQ) and triple quantum filtered (TQF) ^{23}Na MRI of rat liver obtained before and 1 and 5 hours after onset of death. The MQF images show increasing signal intensity in the liver after death. The bright areas along the periphery in the MQ images represent skeletal muscle.

Results

The SQF ^{23}Na data (Figures 1 and 2) showed a significant increase from baseline values ($p<0.02$) for the 1 and 2 hour time points after the onset of ischemia before decreasing and plateauing to a value similar to the baseline value. The TQF ^{23}Na data (Figures 1 and 2) showed a very significant increase from baseline values ($p<0.0002$) that increased in value and that plateaued at 5 hours after ischemic onset.

The ADC values calculated from DWI ^{1}H MRI with and without fat suppression (Figure 3) show a significant drop from baseline after the onset of ischemia. Due to the affect motion has on ADC value calculation, all time points varied significantly from baseline ($p<0.05$) except the 5 min time point without fat suppression ($p=0.06$). Therefore, p-values were calculated from data collected immediately following onset of hepatic ischemia (~5 min) in order to get a better estimation of the significance of the ADC values. Yet, no statistically significant variations were observed between any two time points in either group. Additionally, no statistical significant improvement in baseline ADC values was observed between fat suppressed and non-supressed baselines (1.5±0.2 versus 1.8±0.1, $p=0.10$). No statistical variation were observed between the techniques examined to possibly decrease motion artifacts (Table 1).

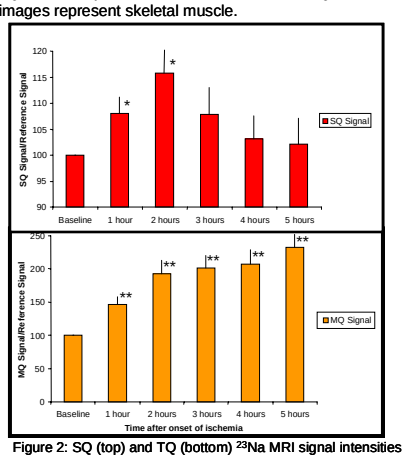

Figure 2: SQ (top) and TQ (bottom) ^{23}Na MRI signal intensities from liver at baseline and after induction of ischemia. Baseline values for each were normalized to 100. *p<0.02 **p<0.0002

Discussion and Conclusions

It was expected that at the onset of ischemia, the SQF ^{23}Na signal intensity would increase and then decrease. This is due to the liver acting like a "sponge" at death, causing an overall increase in extracellular Na^+. A decrease is then observed at later time points as the fluid equilibriates with surrounding tissues. The MQF ^{23}Na signal intensity increased and then plateaued due to the depletion of ATP stores, resulting in the inability of Na^+-K^+ ATPases to maintain the electrochemical gradient and subsequently Na^+ ions entering the intracellular space. This study shows that due to the significant affect respiratory, cardiac, and gastrointestinal motion has on ADC calculation, SQ and MQF ^{23}Na MRI is superior to DWI for acute hepatic ischemia evaluation in rats.

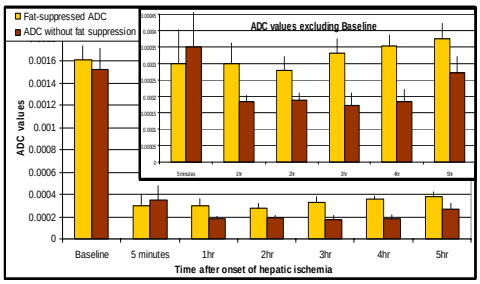

Figure 3: ADC values calculated from DWI with (gold) and without fat suppression (maroon). The inset figure amplifies the time points after the onset of ischemia. Due to motion artifacts, all time points after the onset of ischemia vary significantly from the baseline values (see larger, base figure). Therefore, p-values were calculated from data collected immediately following onset of hepatic ischemia (~5 min), yet no time points varied significantly from this 5 min time point or any other time point.

	Average ± Standard Error	p-value
Without Fat Suppression	0.0015±.0002	
With Fat Suppression	0.0018±0.001	
p-value		0.1
Without Gastromark	0.8±0.8	
With Gastromark	1.5±0.2	
p-value		0.15
30 bpm	1.8±0.1	
45 bpm	1.7±0.4	
60 bpm	2.0±0.3	
p-value: 30 vs. 45 bpm		0.89
p-value: 30 vs. 60 bpm		0.79
p-value: 45 vs. 60 bpm		0.88

Table 1:Data from the techniques examined to possibly decrease motion artifacts

References

[1] Varon J. Am J Emerg Med 2007;25:949-59

[2] Girn et al. Vasc Endovasc Surg 2007;41:277-93.

[3] Le Behan et al. JMRI 2006;24:478-88