Single-shot Lactate Editing using Foci-Laser and a Multiple Quantum Filter

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Introduction

Lactate is elevated in many cancers, largely as a consequence of the Warburg effect. Changes in lactate are expected and observed with several treatments, including PI3k[1] and MEK[2] pathway inhibitors, making lactate an important potential treatment biomarker. However lactate is difficult to measure in many tissues owing to the overlap with strong lipid resonances at 1.3 ppm. Methods to overcome this problem include use of long echo times (TE), spin-echo difference editing, and multiple-quantum filters. Using long TE is only partially selective, while in the presence of motion spin-echo difference editing is liable to serious subtraction errors. While MQF CSI has been demonstrated, single voxel localisation with multiple quantum filters has been limited by the chemical shift displacement artefact, owing to the different RF pulses experienced by the lactate CH spins compared with the CH3 spins in different parts of the selected region[3]. FOCI pulses have high bandwidth with very sharp slice profiles[4,5]. In this work the implementation and evaluation of the multiple quantum filter method using a single-voxel semi-Laser sequence[6] with FOCI slice selection is described.

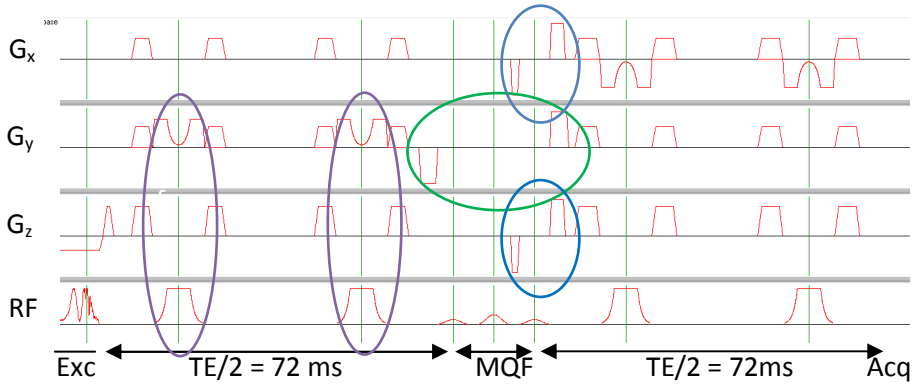
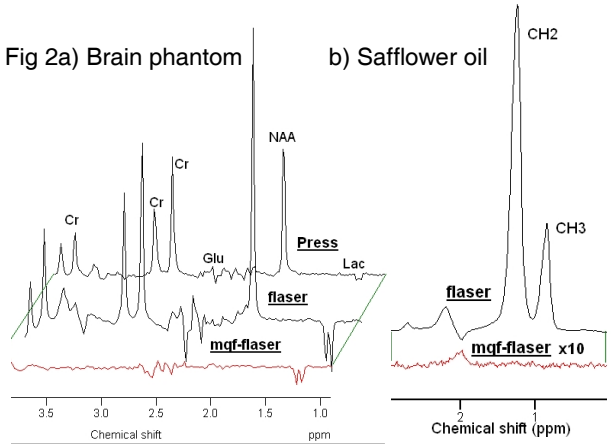


Figure 1. MQF-flaser Sequence

Methods

Semi-laser sequences comprise slice-selective excitation followed by two pairs of identical adiabatic inversion RF pulses (usually hyperbolic secant) with corresponding slice-select and spoiler gradients. Since the maximum bandwidth permitted for HS pulses on our system is ~1200 Hz, resulting in poor slice profiles and a 1/3 voxel shift between lactate CH and CH_3, we replaced them with 12 kHz FOCI RF-and-gradient pulses (1st pair ringed in purple). We call this "flaser". The mqf-flaser sequence (Fig 1) was created by inserting a multiple quantum filtering segment (based on that of Mellon[7]) at TE/2. This segment includes 6 ms sinc-gauss 90°, 180° and 90° RF pulses. The 90° pulses are at the frequency of water and lactate CH; the 180° pulse is offset by 434 Hz (lactate CH_3). Coherence selection gradients (ringed in blue) in the ratio -1:2 are placed before and after the 2nd selective 90° read pulse. These are at the magic angle (54.7° to z) to avoid refocusing intermolecular multiple quantum coherences from water[8]. A further pair of spoiler gradients is placed around the MQF period along y (green).

Measurements were performed on a 3T Philips Achieva, using a cardiac array receive coil. The flaser and mqf-flaser sequences were compared with standard PRESS in a 15cm-diameter spherical phantom of brain metabolites, including 5 mM lactate, and in a 50-ml tube of safflower oil. Voxel size $(2cm)^3$; NS 128.



Results and Discussion

In the brain phantom (Fig2a) PRESS lactate signal was low owing to the chemical shift displacement effect creating subvoxels of lactate in antiphase[9]. This effect was much reduced with flaser, with a large increase in lactate signal. MQF-flaser eliminated singlets, and yielded 35-40% lactate signal compared with flaser (the theoretical maximum is 50%[10,11]). In mqf-flaser spectra of the oil phantom (Fig 2b) no signal remained above the noise level at 1.3ppm; the 2ppm allyl peak was detected as expected[7]. SAR is dominated by the FOCI pulses with only 1% added by the mqf pulses, yielding a minimum TR of 1040 ms. Placing the mqf selection gradients at the magic angle eliminated large near-resonant artefacts otherwise observed. The good lactate detection and lipid suppression suggest this mqf-flaser sequence should be suitable for lactate measurement in a wide range of applications.

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References 1. CS Ward Cancer Res 70:1296 (2010); 2. M Falck-Miniotis Proc AACR p5083 (2010); 3. H Lei JMR 150:17 (2001); 4. RJ Ordidge MRM 36:562 (1996); 5. GS Payne MRM 38:828 (1997); 6. TWJ Scheenen MRM 59:1 (2008); 7. EA Mellon MRM 62:1404 (2009); 8. RB Thompson MRM 62:796 (2009); 9. Kelley JMRI 9:732 (1999); 10. Q He JMR B106:203 (1995); 11. LA Trimble JMR 86:191 (1990);