Enhanced polyamine detection at 7T as a possible in vivo biomarker for prostate cancer

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Introduction

^{1}H MRSI is often used to diagnose prostate cancer where the ratio of choline + creatine to citrate is taken as a marker for tumour occurrence. Although biopsy studies have demonstrated a strong correlation of decreasing polyamines (mainly spermine) in tumour compared to healthy tissue as an additional biomarker [1], in vivo detection of these metabolites is hampered by signal cancellation due to J-couplings and signal overlap with choline and creatine resonances. At higher magnetic field strengths, increased chemical dispersion will not only reduce signal overlap, but also allows the application of selective refocusing pulses to reduce signal losses due to homo-nuclear J-coupling in the 3.1 ppm spermine signal. In this work we added selective refocusing pulses to a semi LASER sequence [2], which interpulse timings were optimized for the detection of citrate, to enable a substantially higher SNR of the signal from spermine.

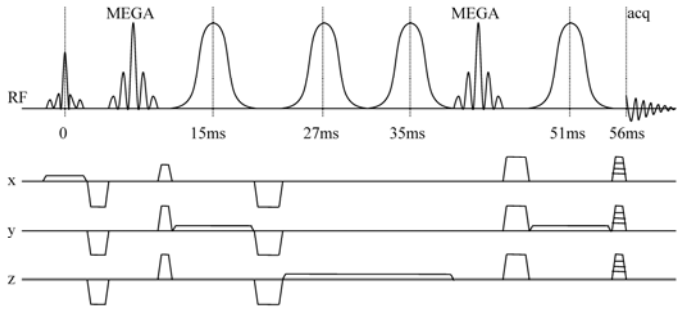

Fig 1: optimized pulse sequence for MRSI of the prostate at 7T

Methods

The interpulse timing of a semi LASER sequence was adjusted for the optimal detection of citrate, leaving room for two chemical shift selective refocusing pulses (Fig 1). The frequency profile of the pulses is calculated to refocus the 2.1 and 1.7 ppm chemical shifts of spermine without affecting its resonance at 3.1ppm and simultaneously to suppress both water and lipid signals (MEGA [3]). Quantum mechanical simulations were performed for the spin system of spermine using the semi LASER either with these refocusing pulses, without these refocusing pulses or using a pulse-acquire sequence. Phantom measurements were performed on a Philips 7T MRI system to validate the gain in spermine signal. Finally MRSI data was obtained from the prostate of a healthy volunteer using the optimized sequence at a Siemens 7T system to verify the detectability of spermine *in vivo.*

Results and discussion

The interpulse timing for optimal detection of citrate results in a TE of only 56ms, leaving space for two selective RF pulses of only 5 ms each. At 7T, the profile of these pulses is sufficient to refocus the 2.1 and 1.7 ppm resonance of spermine, but slightly affects the 2.6 ppm resonance of citrate (Fig 2). The next optimum TE of 118ms enables the use of 16ms pulses (Fig 3a), which transition zone is small enough to maximally enhance the spermine resonance at 3.1 ppm and optimally detect the citrate resonance at 2.6 ppm. In both sequences, quantum mechanical simulations show fully refocused evolution of spermine spins (Fig 4a). The polyamines resonance at 3.1 ppm obtained *in vivo* demonstrates the possibility to detect spermine at 7T as a possible additional biomarker in prostate cancer (Fig 4b).

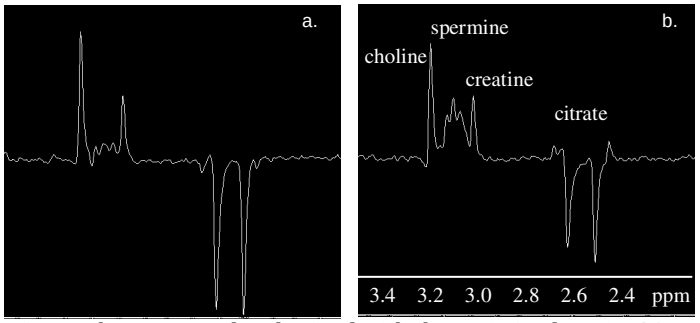

Fig 2: Phantom results obtained with the optimized semi LASER sequence at TE=56ms either without (a) or with (b) selective refocusing pulses. Note the enhanced spermine resonance.

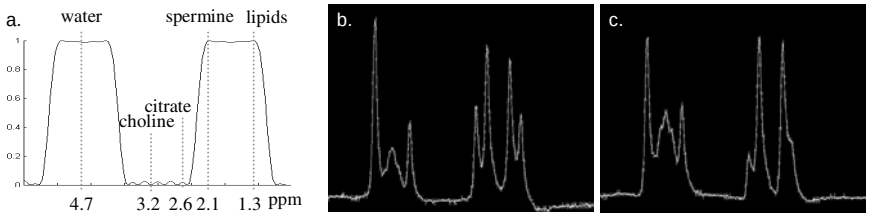

Fig 3: Frequency profile (a) of the 16ms chemical shift selective refocusing pulse (MEGA) added into the semi LASER sequence at the next optimum TE of 118ms. Phantom results obtained either without (b) or with (c) these MEGA pulses demonstrate improved spermine detection without affecting the main citrate resonance.

Conclusion

The large chemical shift dispersion at 7T can be used to selectively refocus J-coupling effects for the enhancements of spermine resonances without effecting the choline and citrate resonances.

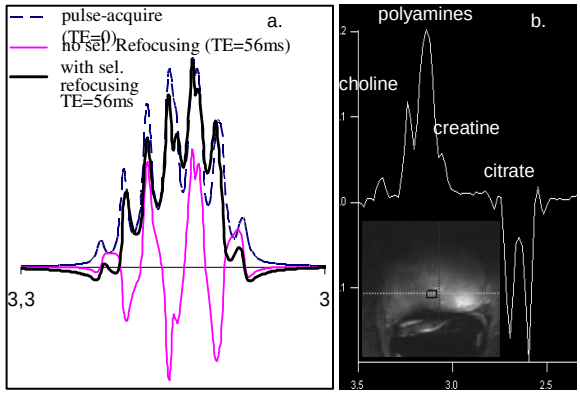

Fig 4: Both quantum mechanical simulations (a) as in vivo results (b) show signal enhancement of spermine (major compound of polyamines). The in vivo results were obtained using an endorectal transceiver at the optimum TE of 56ms.

References

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