MEGA-editing of Spermine/Spermidine in Healthy Human Prostates using External Phased-Array Coil Assembly

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Introduction: Due to their specific role in cell proliferation and differentiation in cancer, there is a significant interest in detecting the polyamines, such as spermidine (Spd) and spermine (Spm) (1). The prostate has the highest level of polyamine biosynthesis of any tissue, and it is the only tissue in which polyamines are purposely synthesized for export. An additional rationale for targeting polyamines in prostate cancer derives from the fact that polyamine metabolism was the most systematically affected of all biochemical and signaling pathways as evidenced from the gene expression analysis of benign and malignant prostate samples (2). Several groups have initiated developing methodology for detection of these polyamines in prostate cancer (3). Both Spm and Spd signals co-resonate and cannot be separated. Recently, subtraction-based editing approaches such as MEGA have been implemented for selectively editing GABA (4) and glutathione (GSH) (5) in human brain. In this study we have implemented a single-voxel localized MEGA-editing sequence on a whole body 3T MRI scanner and evaluated the feasibility of detecting the polyamine resonances (spermine/spermidine) in healthy prostate using an external phased-array "receive" matrix coil assembly.

Methods: MEGA editing was integrated into a PRESS sequence (4, 5). A Siemens 3T whole body Trio-Tim MRI/MRS scanner currently running on the VB15 platform equipped with a quadrature body MRI coil for "transmit" and a body phased array matrix coil. The resonances of spermine and spermidine co-resonate at 3.1 ppm and 1.8ppm and they are J-coupled. Hence, the sequence was programmed for placing the frequency of MEGA rf pulses at an arbitrary location compared to the central carrier frequency set on water resonance. Two acquisitions were targeted, one with the MEGA rf pulse on one of the multiplets of Spm and another with 700Hz away from water. Even though a minimum TE of 30ms was possible for the PRESS sequence, a longer TE (68ms) was necessary for the MEGA-editing sequence due to the presence of MEGA train on both sides of the last 180^0 rf pulse. The method was validated using simulations and phantom experiments using a prostate phantom containing several metabolites at physiological concentrations and the pH value was set to 7.4. The prostate phantom consisted of the following: 50mM citric acid (Cit), 10mM creatine (Cr), 2mM choline chloride (Cho), 3mM phosphocholine (PCh), 3mM phosphoethanolamine (PE), 5mM myo-inositol (mI), 2mM taurine (Tau) and 7.3mM Spm. Six healthy human volunteers have been investigated so far.

Results: Figure 1a shows the conventional PRESS spectrum (TR=2s, 6ml voxel, TE=30ms and 128 averages) recorded predominantly in the peripheral/central zone of a 34 years old healthy prostate. The dominant multiplet due to Cit was identified at 2.6ppm and the multiplets of Spm, one centered at 1.8ppm and the other at 3.1ppm. Other resonances from Cho/PCh, Cr, mI, etc. were severely overlapping between 1 and 4ppm. Figure 1b shows the edited spectrum recorded in the same healthy prostate after subtracting two sets of acquisition (one with MEGA pulse set at 3.1ppm and the other at approximately 6ppm away from water) each one using 128 averages. The multiplets of (spermine and spermidine) in the high field region were clearly visible. At 3T, the center of Cit multiplet was less than 60Hz away, hence the leakage of Cit resonances was unavoidable as shown in Fig.1b. of Both the phantom and in vivo spectra clearly demonstrate the separation of spermine / spermidine from other overlapping signals.

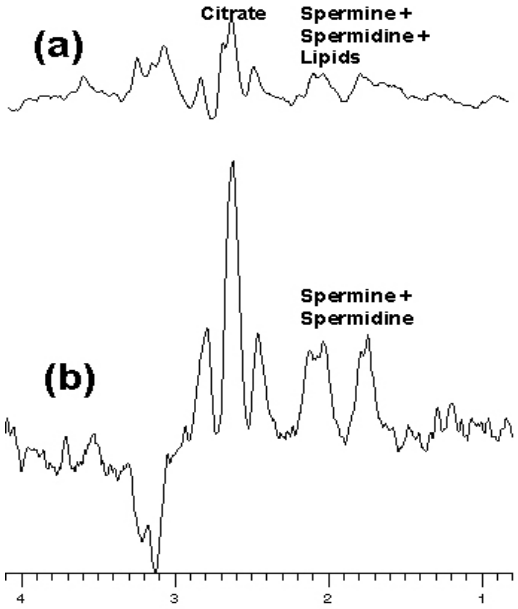

Figure 1(a): PRESS-localized 1D MR spectrum (6ml) recorded in a 34 yo healthy prostate. (**b**) A MEGA-edited spectrum from the same subject.

Discussion: A MEGA-based editing technique was implemented for selecting the signals of (spermine+spermidine) from other overlapping resonances including lipids. Due to the proximity of other multiplets such as Cit, leakage of these resonances was unavoidable even at 3T. Due to the absence of an endorectal coil, this technique can be easily implemented. The efficiency of detecting polyamines has been validated using theoretical simulations, phantom experiments and tested in six healthy prostates. Detection and quantification of polyamines with reference to radiation or chemotherapy might serve as a potential biomarker in evaluating the response of the therapy in prostate cancer.

Conclusion: We have implemented the MEGA-based editing approach on a 3T MRI/MRS scanner for editing the combined signals from spermine and spermidine and to our knowledge, this is the first demonstration of MEGA-editing in human prostate without using an endorectal coil.

References:

1. Casero Jr RA, Marton LJ., Nat Rev Drug Discov 2007;6: 373.
2. Rhodes DR, Barrette TR, Rubin MA, et al., Cancer Res 2002;62: 4427.
3. Yue K, Marumoto A, Binesh N and Thomas MA. Magn Reson Med 2002; 47:1059–1064.
4. Mescher M, Merkle H, Kirsch J, et al. NMR Biomed 1998;11:266
5. Terpstra M, Henry PG, Gruetter R., Magn Reson Med 2003;50:19.