^{1}H MRSI of prostate cancer incorporating spermine in the quantification, a 7 tesla patient study

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Introduction: Magnetic resonance spectroscopic imaging (MRSI) is useful for detection and staging of prostate cancer. Metabolites such as choline (cho), citrate (cit) and creatine (cr) reflect the presence or absence of tumor, while polyamines (pa) predominated by spermine (spm) may be indicative of tumor aggressiveness [1]. Previous studies have shown the importance of incorporating the polyamines signal for detection of prostate cancer [2].
At 1.5 and 3T the ratio of choline and creatine over citrate is taken as a marker for tumor presence commonly calculated by signal integration. However because of the overlap of polyamines on these metabolites, the obtained ratio might be over- or underestimated. . This results in a hampered detection of prostate cancer and tumor aggressiveness. The increased spectral resolution offered by high magnetic field strengths e.g. 7T, makes it possible to detect the metabolites individually and separate them during fitting.
In this study at 7T, we show the influence of polyamines in the variability of the ratio by using spectral fitting with simulated basissets at 7T instead of the commonly used signal integration when including more than 200 MR spectra acquired in six patients diagnosed with prostate cancer.
Materials and Methods: 2D MRSI (nsLASER [3],TE/TR=56/2000 ms, 30x10 or 24x8 matrix, 5x5x5 mm^3 voxel, acquisition time=7.46 min) was acquired with a 7T MR system (Philips, Best, the Netherlands) using a 2-elements endorectal coil [4] tuned and matched at 298 MHz and filled with fluorinated fluid (Galden, Solvay Solexis, Milan, Italy).
6 patients with biopsy-proven prostate cancer were scanned, after informed consent was obtained (Table 1). The 2D MRSI was placed in the area suspected for prostate cancer.
Spectral fitting was performed using the LCModel fitting routine [5]. A basisset was created by simulations of citrate, creatine, spermine and choline using published values of chemical shifts and scalar couplings [5]. Peaks of choline (3.2 ppm), spermine (3.1 ppm), creatine (3.0 ppm) and citrate (2.6 ppm) were fitted by the basisset using a varying phase and linewidth and a variable, but limited frequency (±4Hz). The following ratios were calculated: (cho+pa+cr)/cit and (cho+cr)/cit. In case of a division by zero (no citrate present) a -1 was assigned to the voxel. All voxels within the prostate were selected for each patient. At this point, no distinction was made between healthy and tumor tissue.

Patient	PSA (ng/mL)	Gleason score	Age	Voxels
#1	9.8	7	68	31
#2	8.6	6	73	26
#3	8.7	6	70	48
#4	5.1	7	70	35
#5	4.8	6	63	25
#6	7.1	6	68	46

Table 1: *Patient characteristics*

Results and discussion: In all patients the resonances of polyamines, creatine and citrate were observed in the prostate. The fit results for patient #4 (Fig. 1B) show an almost absence of polyamine signals, while for patient #6 the polyamines signals predominate the spectra (Fig. 1A). The difference between ratios incorporating (+) or excluding (-) the fitted polyamine resonances show a clear trend towards less spread over the voxels when excluding polyamines from the ratio (Fig. 2). These results demonstrate the importance of incorporating the polyamines in fitting the metabolites in the prostate, also illustrated by the intra subject variability in fitted spermine amplitudes (Fig. 3). In fact, considering the reduced spread while including substantial data from tumor areas, it may be questionable whether choline and creatine over citrate would be the most sensitive marker of prostate cancer.
Conclusion: Spectral fitting with simulated basissets of ^{1}H prostate MR spectra acquired at 7T allows to distinguish the substantial polyamines signals from choline and creatine. As shown, using only the signals of choline, creatine and citrate leads to smaller differences between the voxels (tumor as well as healthy). Noticeable is that the intra subject variability of the ratio of all the detected metabolites is mainly determined by the inclusion of the polyamines signal.

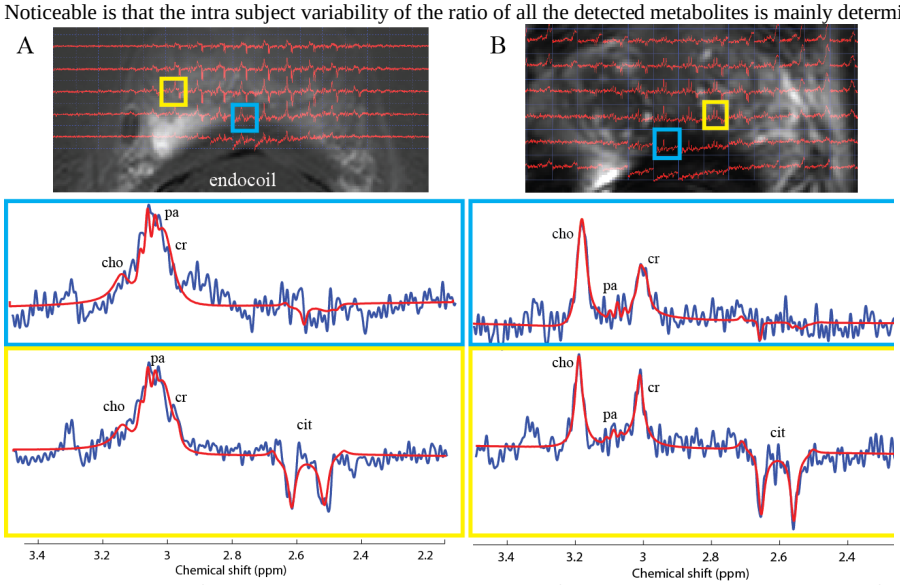

Figure 1: *Fit results for patient #4 (B) and #6 (A). Spectra of patient #4 show a clear absence of polyamines, while in the spectra of patient #6 the polyamines predominate the spectrum.*

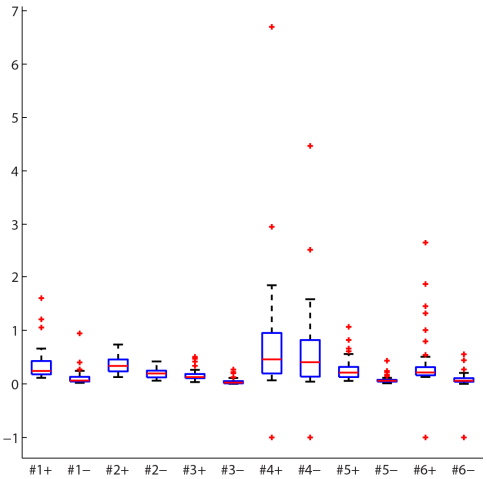

Figure 2: *The ratios incorporating (+) polyamines or excluding (-) the fitted polyamines resonances are shown for all six patients. The difference in spread for including or excluding polyamines in the ratio over citrate can be clearly noticed. The outlier voxels (shown in red) are suspected to be located in the tumor area as these are voxels with either no citrate (-1) or a high ratio because of low levels of citrate. In the case of patient #4 the difference in spread between incorporating (+) polyamines or excluding (-)in the ratio is smaller, due to the fact that the voxels of this patient only contain small levels of polyamines*

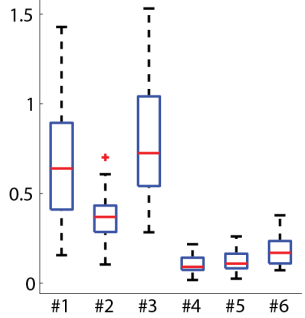

Figure 3: *The amplitudes of the fitted polyamines resonances are shown for all six patients. Noticeable is the substantial intra- and inter subject variability in spread.*

References: [1] Dunzendorfer U., et al. Cancer Res. 1978 [2] Shukla-Dave, A., et al. Radiol. 2007.[3] Arteaga de Castro, C. S., at al. NMR Biomed. 2012 [4] Arteaga de Castro, C.S. et al. Magn Res Med 2012 [5] R. A. de Graaf, et al., Anal. Chem. 2011