Characterization of the human prostate by *in vivo* ^{31}P MR spectroscopic imaging at 7 Tesla

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Introduction:
The metabolism of the human prostate gland is an important subject of study in the determination of pathologies as benign hyperplasia and prostate cancer. Choline compounds involved in phospholipid metabolism may be specific biomarkers for tumor presence and malignancy and can be studied by ^{31}P MR spectroscopy (1). At a magnetic field strength of 7 Tesla the spectral resolution of *in vivo* ^{31}P spectra is expected to be high enough to distinguish the various compounds in the phoshpomonoester (PME) and phosphodiester (PDE) regions. These compounds are major buildup and breakdown products of cell membrane phospholipids.
The aim of this study was to characterize the phosphorus metabolites present in and around the prostate of a healthy volunteer and study their distribution by ^{31}P magnetic resonance spectroscopic imaging at 7T.

Methods:
All measurements on a 36-year-old volunteer were performed on a 7T whole body MR system (Magnetom, Siemens, Erlangen). A ^{31}P T_X/R_X endorectal coil tuned to 120.3 MHz in combination with a ^{1}H T_X/R_X 8-channel body array coil was used for ^{31}P spectroscopic imaging and ^{1}H imaging respectively. Transversal T_2-weighted images (TR=3s, TE=71ms) were recorded to provide an anatomical background for 3D ^{31}P spectroscopic imaging. 3D phasemap shimming was used to optimize the B0 homogeneity in the prostate. ^{31}P MRSI was run with a pulse acquire sequence with an 8ms adiabatic excitation RF pulse (BIR-4) with a flip angle of 45°, allowing for a relatively short TR of 1500ms. The carrier frequency of the adiabatic pulse was positioned at the frequency of phosphocreatine (PCr). In 11 minutes high-quality ^{31}P spectra of 5.8 cc voxels were acquired from the prostate, the bladder, seminal vesicles and muscles. All measurements were performed within SAR safety limits.

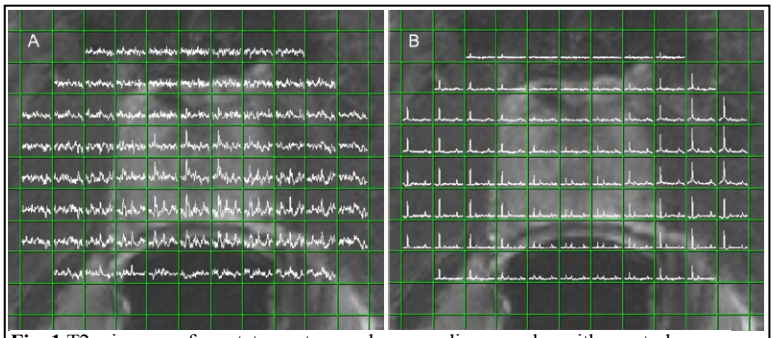

Fig. 1 T2w images of prostate, rectum and surrounding muscles with spectral maps of (**A**) phosphorylated compounds in phospholipid metabolism (8 - 2ppm) and (**B**) high energy phosphates (2- -20ppm) showing good performance of localization: high PME and low PCr inside the prostate, the reverse in muscle and absence of signals in the rectum.

Results and discussion:
^{31}P MR spectra with clearly distinguishable peaks from phosphorylated metabolites involved in phospholipid metabolism and from high-energy phosphates were obtained throughout the whole prostate with minimal voxel bleed from the surrounding muscle tissue (Fig. 1). The PCr signal in the prostate has approximately the same intensity as the ATP signals, contrary to surrounding muscles with the PCr intensity 5 times higher than ATP, illustrating a low level of fast energy demand in the organ. The β-ATP signal was attenuated by sub-optimal excitation at the limit of the bandwidth of the excitation pulse. In the PDE region, possible signals from glycerophosphocholine (GPC) and glycerophosphoethanolamine (GPE) were distinguishable from noise only in a few voxels in the center of the prostate (Fig. 2). This low concentration of PDE's is in accordance with in vitro measurements of normal prostate tissue (2). Unlocalized *in vivo* ^{31}P spectroscopy of the prostate at 2T revealed a larger peak in this area (3), probably due to signals of large phospholipid molecules that obtain a short T_2 at higher field. In the midgland and apex of the prostate the PME phosphoethanolamine (PE) signal is up to about twice as large as the PME phosphocholine (PC) signal (Fig. 2A), contrary to the ratio of PE to PC of about 4 as reported in vitro (2). In the base of the prostate the reverse is visible (Fig. 2B), likely due to signal bleed from voxels of the seminal vesicles which gave rise to high PC signals. In many voxels in the prostate, double or triple resonances could be observed between 5.4 and 4.8 ppm (Fig. 2AB). As suggested before (4), a double inorganic phosphate (Pi) resonance could reflect two separate phosphate pools with different pH. A third resonance might represent the 2-P' of 2,3-diphosphoglycerate (2,3-DPG) in the well perfused prostate, a metabolite present in human red blood cells. This would require either a local high prostatic blood volume or a substantial extravascular or intracellular 2,3-DPG pool in the prostate. Both options need further investigation. Since the 3-P' of 2,3-DPG would resonate at approximately the same frequency as PC, the signal of PC should be interpreted with caution. Both Pi and 2,3-DPG resonances are highly pH dependent in physiological pH range (4), making it difficult to assign the peaks with certainty to the right compounds. The resonance at 5.4ppm may correspond with Pi in a surprisingly alkaline environment of pH ~7.7 or with 2-P' of 2,3-DPG at pH ~7.4 (pH derived from distance to PCr resonance). The peak at 4.9 ppm is most likely originating from Pi in an environment of pH ~7.1 and the peak at 5.1 ppm may be from 2-P' of 2,3-DPG at pH ~7.1 or from Pi at pH ~7.3. It is likely that a pH difference exists between the main tissue constituents of the prostate, stroma and luminal space, as the luminal space contains high concentrations of citrate, which probably decreases the pH in this compartment. In the base of the prostate, close to the bladder, voxel bleed from Pi in urine is observed by elevation of the peak at 5.4ppm (Fig. 2C). To study phospholipid metabolism alone, it might be helpful to apply the sRINEPT polarization transfer technique which improved the sensitivity for ^{31}P nuclei coupled to protons, specifically PE, PC, GPE and GPC and suppressed signals from uncoupled ^{31}P nuclei (5). Especially this editing property can be very useful to assign resonances in the Pi region.

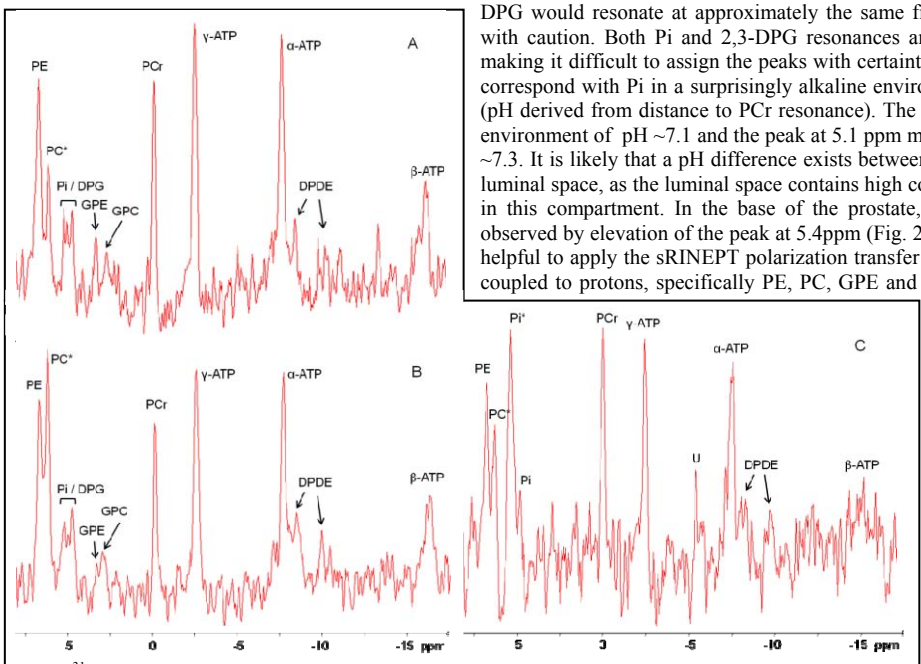

Fig. 2 ^{31}P spectra of three voxels of a 3D MRSI dataset of the prostate of a healthy volunteer.
Peak assignments: PE (6.7 ppm), PC* (6.3 ppm), Pi*/2,3-DPG (5.3, 5.1 and 4.8 ppm), GPE (3.6 ppm), GPC (3.0 ppm), PCr (0 ppm), ATP's (-2.6, -7.6 and -16.2 ppm), diphosphodiesters (DPDE, -8.4 and -9.9ppm), unknown compound (U, -5.4ppm). *: possible contribution from 2,3-DPG.
A: Midgland, peripheral zone, PE>PC. **B**: Base, central zone and transition zone, possible contamination of PC from seminal vesicles. **C**: Base, transition zone, increased Pi at 5.4ppm.

Conclusion:
High resolution *in vivo* ^{31}P spectra contain valuable information about the distribution of phosphorus metabolites throughout the prostate and surrounding tissues. The spectra show ratios of resonances different from in vitro work, and possibly identifies new resonances not observed in vitro.

References:
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