Quantification of T_1 relaxation times and nuclear Overhauser effect of ^{31}P metabolites in the human prostate at 7T

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Introduction – ^{31}P MR spectroscopic imaging (MRSI) may be a useful tool to study prostate cancer in vivo. At a field strength of 7T, it is possible to obtain well-resolved ^{31}P spectra of the human prostate [1], with resonances from phospholipid- and energy-related metabolites. To perform 3D ^{31}P MRSI with relevant spatial resolution in a clinically acceptable measurement time, the SNR per unit time of the ^{31}P MRSI sequence should be optimized. We therefore assessed T_1 relaxation times of ^{31}P metabolite spins in the human prostate and evaluated the nuclear Overhauser effect (NOE) as signal enhancement strategy for ^{31}P MRSI of the prostate at 7T.

Methods – Data of 12 patients with prostate cancer (age: 66.1±3.4y, median PSA=9.7) and 1 healthy volunteer (34y) were acquired on a 7T whole body MR system (Magnetom, Siemens, Erlangen). A ^{31}P T_X/R_X endorectal coil tuned to 120.3 MHz was used in combination with an 8-channel ^{1}H T_X/R_X body array coil. The B_0 homogeneity in the prostate was optimized using 3D phasemap shimming. B_1^+-phase shimming maximized ^{1}H phase coherence in the prostate to allow efficient continuous wave (CW) irradiation for NOE. T_2-weighted TSE images (TR=3s, TE=71ms) were recorded to provide an anatomical background for the ^{31}P measurements. Progressive saturation T_1 measurements with variable TR (range: 2-16 s) were performed in 6 patients using an adiabatic 2D localization sequence (non-slice selective adiabatic half passage 90° excitation pulse and two pairs of adiabatic full passage slice selective refocusing pulses, TE = 30 ms). The coil sensitivity profile provided localization in the 3rd (A-P) direction (fig. 1). In 8 subjects, 3D ^{31}P pulse-acquire MRSI with 8ms BIR-4 45° RF pulses (γB_1=960Hz) was performed twice, with a nominal voxel size of 12x12x12mm^3 (TR=1500ms, TA=10minutes): once without, and once with NOE using low-power CW ^{1}H irradiation (γB_1=20Hz) during the 1.5s TR (except during 204ms signal acquisition). All measurements were performed within SAR safety limits. Metabolite Report (Siemens Healthcare) was used to fit the ^{31}P spectra to quantify the NOE in 2 non-neighbouring prostate voxels per subject. T_1 relaxation times were determined by fitting the function $M = M0\ (1 - e^{-TR/T1})$ to the progressive saturation data using a least squares fit.

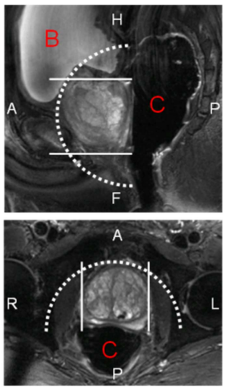

Fig. 1 2D localization of T_1 measurements. Coil profile in AP direction for localization. B: bladder. C: endorectal coil.

Results and discussion – Example spectra of the progressive saturation experiment and their fits are shown in fig. 2. Resonances of phosphoethanolamine (PE), phosphocholine (PC), inorganic phosphate (Pi), phosphocreatine (PCr), γATP and αATP were present and well resolved in most prostate ^{31}P data, although the limited excitation bandwidth in the T_1 measurement prevented T_1 determination of αATP. Glycerophosphocholine (GPC) and glycerophosphoethanolamine (GPE) signals were very low or not present in most spectra, even with NOE, which is in accordance with in vitro measurements of prostatic tissue [2]. Figure 3 shows example metabolite maps of PE with and without NOE of 1 subject, not corrected for B1 profile. The results of all T_1 and NOE measurements are listed in table 1.

All ^{31}P T_1 times measured at 7T were longer compared to reported values for prostate at 1.5T [3]. The T_1 relaxation times of PE, GPE, GPC and γATP in prostate at 7T were also longer than those reported for human brain and muscle at the same field strength [4,5]. T_1 values of Pi in prostate were comparable to muscle, but longer than in brain. Only PCr showed comparable values in these 3 different tissues at 7T. T_1 values for PC at 7T have not been reported before for other tissues. The Ernst angle corresponding to the calculated T_1 values of PCr, PE and PC at a TR of 1.5s were 46°, 35° and 39° respectively. With the current settings of the MRSI (45° flip angle, TR=1.5s), partial saturation of all metabolites was induced, but the optimal SNR per unit time was nearly reached. A lower flip angle should be considered for protocol optimization.

A positive NOE effect was observed for all metabolites in the prostate except the ATPs (table 1). This is in line with previously published NOE data from ^{31}P metabolites in brain at 7T [4]; however, our NOE values showed larger variation. This may have resulted from the limited bandwidth of CW irradiation used to saturate water, which makes NOE saturation efficiency vulnerable to B_0 inhomogeneities. Different approaches to saturate water with a larger bandwidth, such as WALTZ pulses, may reduce the variation in NOE values in the prostate.

In many prostate spectra, two peaks resonate in the chemical shift range of Pi. These peaks may represent Pi in two compartments with different pH. 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, possibly giving rise to lower pH. The differences in T_1 times and NOE values for the two peaks assigned to Pi may also reflect separate surroundings. However, the presence of other metabolites instead of Pi cannot be ruled out. Editing techniques such as polarization transfer, which suppresses signals from uncoupled ^{31}P nuclei (e.g. Pi), should be explored to improve assignment of resonances in in vivo prostate ^{31}P spectra.

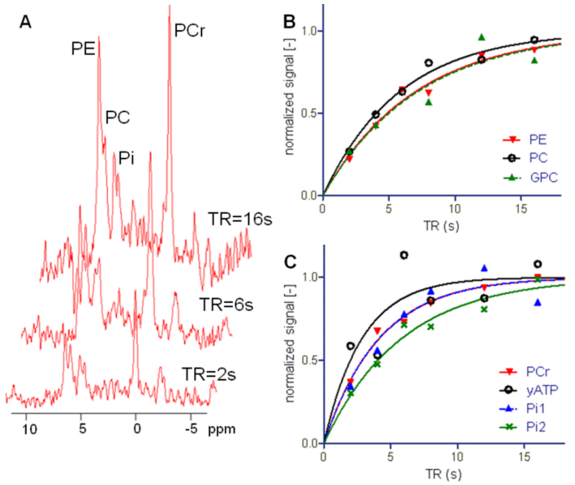

Fig. 2 (A) Example spectra of T_1 progressive saturation measurement, (B,C) Example of fitting T_1 ^{31}P relaxation curves in 1 subject.

	PE	PC	GPE	GPC	PCr	γATP	αATP	Pi (1, high pH)	Pi (2, low pH)
T_1 (s)	7.6 ± 1.5 (6)	5.9 ± 1.3 (6)	8.3 (1)	5.9 ± 1.7 (4)	4.1 ± 0.4 (6)	3.0 ± 0.9 (4)		4.56 ± 1.9 (5)	6.5 ± 2.4 (5)
NOE (%)	42 ± 20 (8)	15 ± 36 (8)	8 ± 21 (1)	20 ± 31 (4)	20 ± 15 (8)	-4 ± 20 (8)	-9 ± 31 (8)	49 ± 54 (8)	11 ± 38 (7)

Table 1 Apparent T_1 relaxation time (s) and NOE (%) of ^{31}P metabolites in prostate tissue at 7T. (n): number of subjects included in analysis.

Conclusion – T_1 relaxation times for ^{31}P in human prostate at 7T were found to be relatively long compared to other human tissues. To obtain a 3D ^{31}P MRSI dataset within a clinically acceptable measurement time (TR ≤ 1.5s) with optimal SNR per unit time, a strongly reduced flip angle (≤ 45°) is required. Signal enhancement by irradiating the water resonance to obtain NOE was successful, yielding up to 42% more signal for PE.

References [1] Kobus et al, MRM 2012 Feb 14 (Epub ahead of print), [2] Cornel et al. J Urol. 150(6):2019-2024(1993), [3] Thomas et al, JMR 99:377-386(1992), [4] Lei et al, MRM 49:199-205(2003) [5] Bogner et al, MRM 62:574-582(2009) **Acknowledgement** ERC Grant agreement n° [243115]

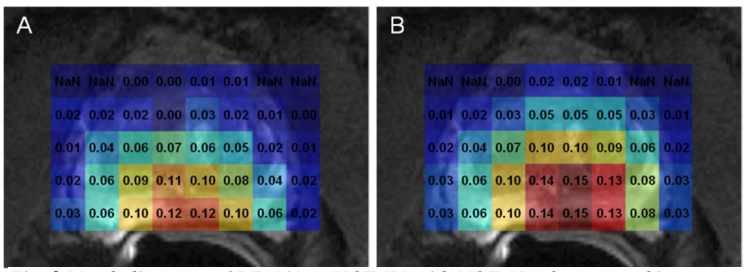

Fig. 3 Metabolite maps of PE: (A) no NOE (B) with NOE. Numbers are arbitrary representations of the signal intensity.