CORRELATION BETWEEN *IN VIVO* ^{1}H MRSI AND *EX VIVO* ^{1}H HR MAS IN SPATIALLY MATCHED REGIONS IN PROSTATE CANCER PATIENTS

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Purpose: The decrease in citrate and the elevation of choline-containing components in prostate cancer has been well documented both by *in vivo* ^{1}H magnetic resonance spectroscopy imaging (^{1}H MRSI) and by *ex vivo* ^{1}H High resolution magic angle spinning spectroscopy (^{1}H HR MAS) [1,2]. However, no studies have investigated how accurately these methods relate to each other in matched regions of the same prostate cancer patient. The purpose of this study was to validate the interpretation of the lower resolution *in vivo* ^{1}H MRS spectra by correlating high resolution *ex vivo* ^{1}H HR MAS spectra in spatially matched regions in the same prostate cancer patient.

Methods: Thirty-nine ^{1}H HR MAS spectra were correlated to 39 corresponding *in vivo* 3D ^{1}H MRSI voxels from 13 different patients (mean age: 62 years old). *Ex vivo* cylinder tissue samples (3mm in diameter, 13.3±4.3mg, mean cancer content: 64±17.3%) were carefully extracted from a 2mm-transversal prostate slice dedicated for research after prostatectomy by using a new harvesting method as described in Bertilsson et al. [3] (Fig. 1a). Tissue extraction is based on image fusion with the two HES stained histopathology slides closest to the research slice, and the Gleason score is verified by a cryosection (4µm) of each tissue sample before HR MAS analysis. HR MAS spectra (Fig. 1b) were acquired using a spin echo CPMG sequence (effective TE=60ms) on a 14.1T Bruker Avance spectrometer (Bruker Biospin, Germany), and 3D MRSI were performed using a 3D PRESS sequence (TR/TE=750/145 ms) on a 3T system without an endorectal coil (Trio, Siemens, Germany). After correlating magnetic resonance imaging (MRI) data to histopathology and thereby finding the MRSI slice that most closely correspond to the image of the prostate tissue slice with marked extraction areas (Fig. 1a), each tissue sample was matched to an MRSI voxel by comparing the image of the prostate slice (Fig. 1a) to the MRSI voxel grid (Fig. 1c). The matching was guided by benign anatomical landmarks such as the urethra, ejaculatory ducts and size and shape of the peripheral zone. The choline+creatine/citrate (CC/C) ratios were calculated by integration in the *ex vivo* spectra and by using a LC Model fitting routine [4] on the *in vivo* ^{1}H MRSI data (Fig. 1d). Pearson's correlation coefficients were calculated for the *in vivo* and *ex vivo* CC/C ratios and for the CC/C ratios correlated to Gleason score (low risk = Gleason 6, medium risk = Gleason 7, high risk = Gleason > 7). Due to very low citrate levels both *in vivo* and *ex vivo* in 5 samples/voxels giving unreliable high CC/C ratios, and due to failure in the LC model fitting routine for two spectra, seven spectra were excluded from the correlation analysis, giving 32 samples from 11 different patients (9 normal, 8 low risk, 6 medium risk and 9 high risk samples).

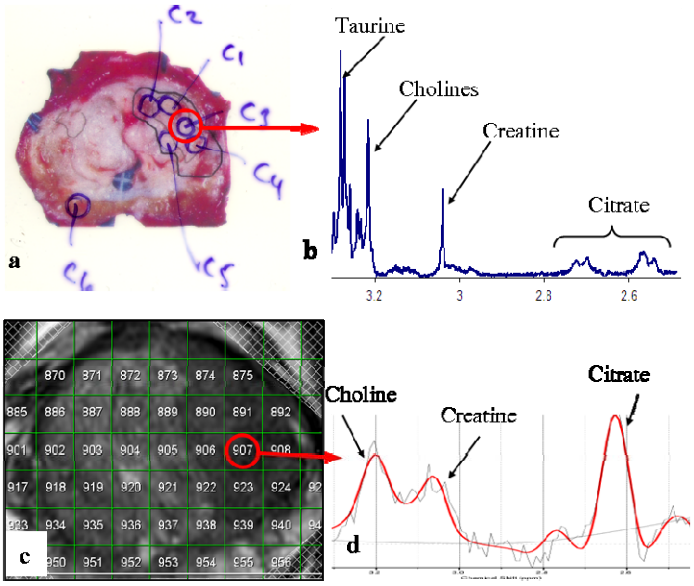

Figure 1: a) A prostate tissue slice from a 61 year old patient with a pT2b prostate cancer with marked tissue extraction areas and **c)** the corresponding MRSI voxel grid. **b)** HR MAS spectrum from tissue sample C3 is compared to **d)** LC model fitted in vivo spectrum from the same location as the tissue extraction.

Results: The CC/C ratios from *in vivo* ^{1}H MRSI and *ex vivo* ^{1}H HR MAS in spatially matched regions in the same prostate cancer patient were significantly correlated with a Pearson's coefficient of 0.63 ($p<0.001$) (Fig. 2a). Both *ex vivo* and *in vivo* CC/C ratios were also correlated to Gleason score ($r = 0.65$, $p<0.001$ and $r = 0.62$, $p<0.001$, respectively) (Fig. 2b and 2c).

Conclusions: This study demonstrates that the CC/C ratios in prostate cancer tissue from *ex vivo* ^{1}H HR MAS spectra are correlated to *in vivo* ^{1}H MRSI measured ratios, despite the partial volume effect *in vivo* and the fact that we did not correct for T1 and T2 relaxation in this material. The *ex vivo* samples are based on tissues with a very high cancer content (mean: 64±17.3%) and both *ex vivo* and *in vivo* CC/C ratios verifies the relation to Gleason score. *Ex vivo* ^{1}H HR MAS provides a detailed characterization of an individual's prostate tumor which adequately represent the original *in vivo* tumor and can therefore be an important tool for investigating cancer types and malignancy provided that the material is obtained from viable tumor tissue.

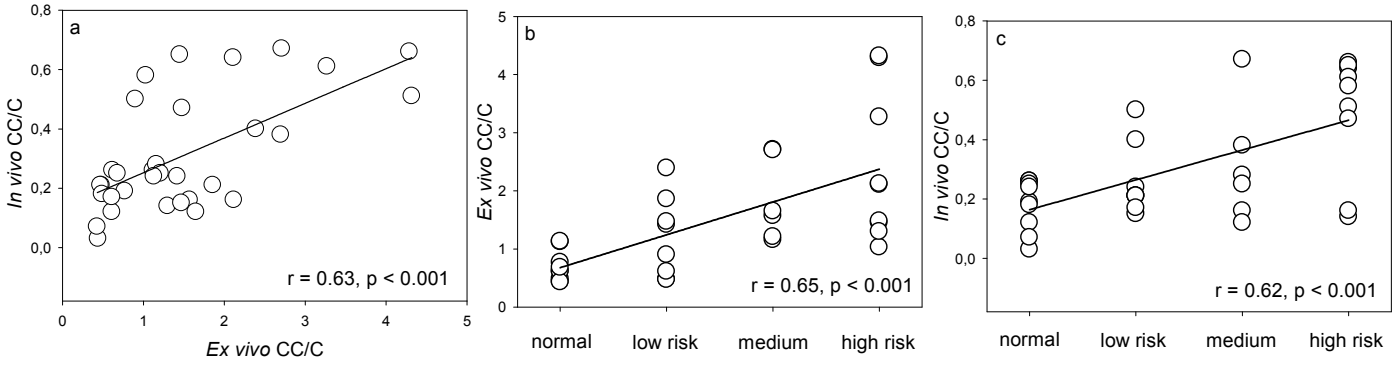

Figure 2: a) Correlation between *in vivo* and *ex vivo* CC/C ratios. **b)** Correlation between *ex vivo* CC/C and Gleason score. **c)** Correlation between *in vivo* CC/C and Gleason score. **c)** Classifications: normal, low risk = Gleason score 6, medium risk = Gleason score 7, high risk = Gleason score > 7.

References: **1**.Scheenen et al. Radiology, 2007;245(2). **2**. Swanson et al. NMR Biomed, 2006;19(2). **3.** Bertilsson et al. The Prostate, 2010;21. **4**. Provencher, S.W., Magn Reson Med, 1993. 30(6).