SPATIALLY MATCHED *IN VIVO* AND *EX VIVO* MR METABOLIC PROFILES OF PROSTATE CANCER – INVESTIGATION OF A CORRELATION WITH GLEASON SCORE

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Purpose: Prostate cancer is characterized by altered metabolite levels, specifically increased levels of choline and decreased levels of citrate[1]. Magnetic resonance (MR) metabolic profiling of the prostate is promising as an additional diagnostic approach to separate indolent from aggressive prostate cancer. Metabolite profiles can be obtained non-invasively from patients *in vivo* by magnetic resonance spectroscopic imaging (MRSI) or from tissue samples *ex vivo* by high resolution magic angle spinning (HR-MAS) MR spectroscopy (MRS). The objective of this study was to assess the relationship between Gleason score and the metabolic biomarker (choline+creatine+spermine)/citrate (CCS/C) measured *ex vivo* by HR-MAS MRS and *in vivo* by MRSI, and to evaluate the correlation between *in vivo* and *ex vivo* measured metabolite ratios from spatially matched prostate regions.

Methods: Patients (n=13) underwent *in vivo* MRSI prior to radical prostatectomy. Tissue samples (n=40) for *ex vivo* analyses were excised from a 2 mm transversal prostate slice according to a new harvesting method[2]. The location of the excised tissue samples were matched to *in vivo* MRSI voxels (Fig. 1). *In vivo* MRSI was performed on a 3T clinical MR system (Magnetom Trio, Siemens, Erlangen, Germany) and *ex vivo* HR-MAS on a 14.1T spectrometer (Bruker BioSpin GmbH, Germany). Relative metabolite concentrations were calculated by LCModel[3] fitting of *in vivo* spectra and by peak integration of *ex vivo* spectra. Spearman's rank correlations (ρ) between CCS/C from *in vivo* and *ex vivo* MR spectra and between metabolite ratios and their corresponding Gleason score were calculated.

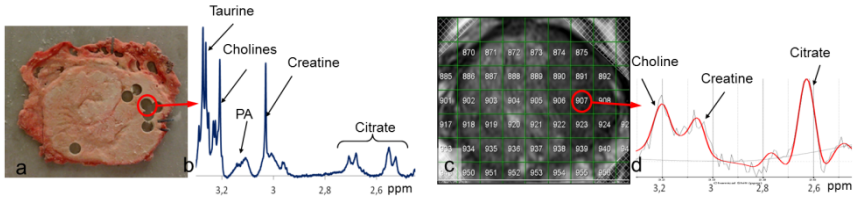

Figure 1: Frozen prostate tissue slice with marked tissue excision areas (a) and the corresponding MRSI voxel grid (c). Metabolite ratios derived from HR-MAS pules-acquire spectra of tissue samples (b) is compare to metabolite ratios derived from *in vivo* spectra (d)

Results: There was a strong positive correlation between Gleason score and CCS/C measured both in vivo and ex vivo (ρ=0.77 and ρ=0.69, respectively, $p<0.001$), and between in vivo and ex vivo metabolite ratios from spatially matched regions (ρ=0.67, $p<0.001$) (Fig. 2).

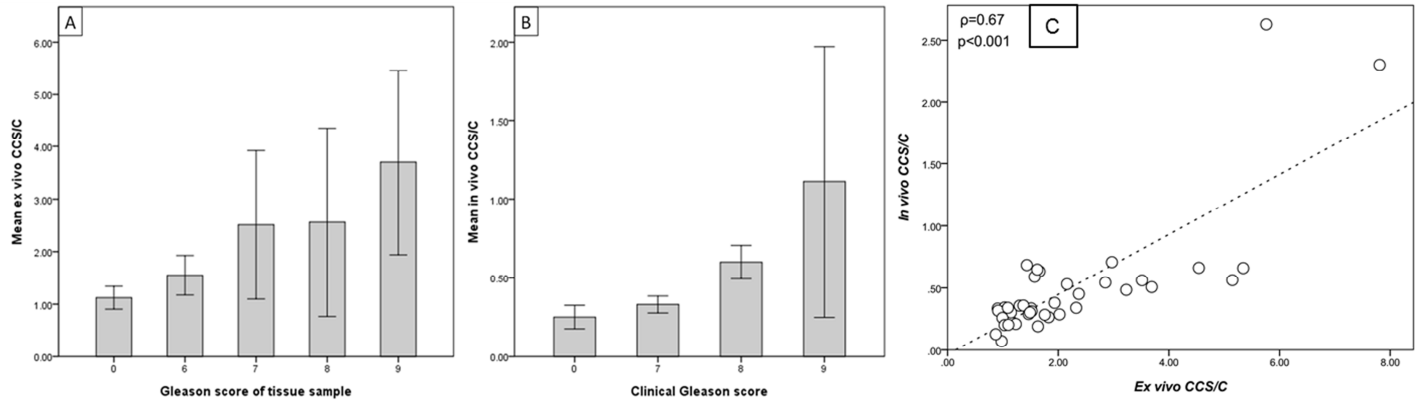

Figure 2: A) Relationship between CCS/C ratio determined by *ex vivo* HR-MAS MRS and Gleason score B) Relationship between CCS/C ratios determined *in vivo* by MRSI and Gleason score C) Correlation between spatially matched *in vivo* measured CCS/C ratios and *ex vivo* measured CCS/C ratios.

Conclusions: Our data indicates that MR metabolic profiling is a potential useful tool for the assessment of cancer aggressiveness. Moreover, the good correlation between *in vivo* and *ex vivo* measured CCS/C demonstrates that our method is able to bridge imaging information and molecular analysis.

References: 1) Swanson et al, MRM, 2006; 2) Bertilsson et al, Prostate, 2011; 3) Provencher; Magn Reson Med (1993)