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Project 1: Prostate Cancer at 7T – Metabolomic Imaging for human prostate cancer Detection

The project included building a prostate shaped phantom, which contains three metabolic solutions in three spherical globes of different concentrations of approxemately 30 common biological metabolites playing a major role in prostate cancer. These metabolites have been tested before at 14T in order to evaluate their consistency. It also included building a single loop surface coil and a Transmission-Receive-Switch that was placed around the phantom at mid level, through which localized Multi Voxel MR spectra were acquired for three axial prostate cross-section planes. I developed a scan protocol and arranged the sequences adjusted to the *Siemens Syngo Software*.

At 7T we collected T2 weighted images of 1mm slice thickness by using a Turbo Spin Echo(TSE) sequence, to get an accurate MRS voxel placement. From these T2 slices, a center plane, approximately at the coil level, and two side planes, each 6 mm above and below the center-plane, were chosen for two-dimensional proton 16 x 16 voxel-MRS followed by a multivoxel 3D-CSI-Sequence. The subsequent scan protocol for the prostate specimens follows the identical algorithm as the phantom protocol does.

After surgery the prostate gland including the seminal vesicles was placed in a sample holder, which was floated with Deuterium water in order to create a proton-free environment for the measurement. The integrity of the prostate tissue was also tested in a previous experiment.

According to the mentioned protocol I scanned 15 prostate samples and phantoms. The obtained metabolomic spectra from the prostate phantom and surgical prostate tissue, respectively, underwent an automatic shim routine followed by final manual shimming and were processed by *JMRUI*, *MATLAB* and *NUTS*. For curve fitting *NUTS* was used and led to admissible spectra and the final relative concentrations followed by an evaluation of the spectral quality and further statistical analysis via JMP.

The quantification of alterations in prostate metabolomic profiles may result in identification of PCa chemical signatures, which permits disease detection and classification according to precise biochemical criteria and leads to improved diagnostic accuracy.

Project 2: Retrospective analysis of prostate cancer recurrence potential with tissue metabolomic profiles.

BACKGROUND: In clinical care of prostate cancer patients, an improved method to assess the risk of recurrence after surgical treatment is urgently needed. We aim to retrospectively evaluate the ability of ex vivo tissue magnetic-resonance-spectroscopy-based metabolomic profiles to estimate the risk of recurrence.

METHODS: PCa recurrence is defined biochemically as the detection of serum PSA after radical prostatectomy. Sixteen consecutive PCa-recurrent cases, those with an initial PSA increase of 0.69 +/- 0.26 ng/ml monitored 47.7 +/- 2.6 months after prostatectomy were paired by age and Gleason score with cases without recurrence of the same pathological and clinical stages (n = 16/each). We analyzed ex vivo intact-tissue spectroscopy results from these 48 individuals at the time of prostatectomy at 14T. From these spectra, we identified the 27 most common and intense spectral metabolic

regions for statistical analyses.
RESULTS: Principal component analysis (PCA) on these spectral regions from cases of clinical-stage-matched groups with and without recurrence identified four pathology-related principal components. Canonical analysis of these four and the first nine principal components for cases in the two groups defined metabolomic profiles as the canonical score that can differentiate the two groups with statistical significance. By applying the coefficients from PCA and canonical analysis to the pathological-stage-matched groups, recurrence was predicted with an accuracy of 78%.
CONCLUSIONS: Results indicate the potential of tissue metabolomic profiles measured with ex vivo spectroscopy to identify PCa aggressiveness in terms of cancer recurrence. With further study, this may greatly contribute to the future design of clinical strategy for personalized treatment of PCa patients.

Project 3: The evaluation of metabolomic profiles of human prostate cancer biopsy
tissue by using different T2-Filters at 14T.
BACKGROUND: The indispensability of radiology in disease detection and diagnosis is increasingly recognized. Based on the hypothesis that cellular metabolic status at the time of tissue excision is preserved within intact tissues, results of human PCa metabolomics have been analyzed using ex vivo tissue MRS under high-resolution magic angle spinning (1H HRMAS) conditions. We therefore hypothesize that instead of using prefixed MRprotocols the use of different T2-Filters can improve the ability of diagnostic radiology to visualize malignancy in
prostate cancer tissue based on PCa metabolomics.
METHODS: We used two T2-Filters: Time Echo(TE) 35ms for short TE and 135ms for long TE. Fifty-three consecutive PCa-Biopsy cases have been analyzed. All 53 prostate specimens underwent high resolution magic angle spinning (1H HRMAS) magnetic resonance spectroscopy (MRS) at 14 Tesla. We analyzed ex vivo intacttissue spectroscopy results from these 53 individuals at the time after transrectal ultrasound guided prostate biopsy. These spectra have been processed by *Acorn NUTS in order* to identify the 36 most common and intense spectral metabolic regions. In further statistical analyses a principal component analysis was applied on the relative intensities of the regions of interest within the measured spectra. We also included the coefficients we were able to report with significance in earlier publication. (Cheng et al., Cancer Res. 2005 Apr 15;65(8):3030-4.) In order to demonstrate the power of PCa Metabolomic profiles to separate malignant from benign tissue.
RESULTS: *Expected soon together with Franziska; she is using the short-TE-Data for her correlation*.

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Retrospective analysis of prostate cancer recurrence potential with tissue metabolomic profiles. Maxeiner A, Adkins CB, Zhang Y, Taupitz M, Halpern EF, McDougal WS, Wu CL, Cheng LL. Prostate. 2010 May 15;70(7):710-7.