Relationship between MR visible metabolites, MR imaging parameters and quantitative histopathology in prostate cancer

Kirsten Margrete Selnæs1,2, Riyas Vettukattil1, May-Britt Tessem1,2, Helena Bertilsson3,4, Alan Wright5, Arend Heerschap1,3, Anders Angelsten1,3, and Tone Frost Bathen1
1Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway, 2St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, 3Department of Urology, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, 4Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway, 5Department of Radiology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands

Introduction: Metabolic and morphologic changes due to prostate cancer (PCa) lead to changes in MR imaging (MRI) and MR spectroscopic (MRS) parameters. These cancer related changes may be caused by both increased cellularity and reduced luminal space. Attempts have been made to elucidate the relationship between MR visible metabolites and MR imaging parameters such as apparent diffusion coefficient (ADC) [1]. However, due to low spectral resolution in vivo, correlation between MRI parameters and individual metabolites (choline-containing compounds and citrate) has not yet been investigated. The objective of this study was to assess the relationship between MRI parameters (T2 intensity and ADC) measured on patients in vivo, individual metabolites measured on prostatectomy tissue ex vivo and quantitative histopathological features (percentage nuclei and luminal space).

Methods: Fresh frozen tissue samples (n=53 from 15 patients) were extracted from transversal prostate slices and linked to in vivo MR parameters as previously described [2,3]. A cryosection was taken from one end of each sample and stained with Hematoxylin, Erythrosine and Saffron (HES). These HES stained slides were digitized with 4× magnification and color-based segmentation (Positive Pixel Count algorithm in ImageScope v.11, Aperio Technologies) was used to identify luminal space and nuclei as described by Langer et al [4]. High resolution magic angle spinning 1H MR spectra were obtained using a 14.1T spectrometer (Bruker Biospin) and post-processed as previously described [5]. Quantification of metabolites was performed by LC Model. T2 weighted images and ADC maps from preoperative MR examinations (3T, Siemens Trio) were used to calculate minimum T2 intensity and maximum ADC in regions of interest corresponding to tissue resection areas (Fig. 1a-c). Spearman’s rank correlation (ρ) was calculated between in vivo MR parameters, ex vivo metabolite concentrations and morphological features. One sample was removed due to poor HES slide quality.

Results and discussion: There is a positive correlation between total choline and the amount of nuclei (ρ=0.38, p<0.01) and between citrate and the amount of lumen (ρ=0.37, p<0.01) (Table 1). The latter may indicate that the reduction of citrate seen in cancer is partly due to morphological changes. ADC is positively correlated to lumen and negatively correlated to amount of nuclei (ρ = 0.54 and -0.36 respectively, p<0.01), confirming dependency to both cellularity and free diffusion in regions of luminal space. T2 was also positively correlated to amount of lumen (ρ=0.49, p<0.01), consistent with T2 being sensitive to extracellular water. However, no significant correlation between T2 and amount of nuclei was observed (p=-0.06, p=0.68).

Conclusion: This study shows that tumor microstructures observed by quantitative histopathology are linked to MR characteristics in prostate cancer.