Combination of MR spectroscopic and diffusion weighted imaging of the prostate for the prediction of tumor aggressiveness

Gregor Thörmer[1], Josephin Otto[1], Christian Schröder[1], Nikita Garnov[1], Martin Reiss-Zimmermann[1], Lars-Christian Horn[2], Minh Do[3], Jens-Uwe Stolzenburg[3], Michael Moche[1], Thomas Kahn[1], and Harald Busse[1]

[1]Dept. of Diagnostic and Interventional Radiology, Leipzig University Hospital, Leipzig, Saxony, Germany, [2]Institute of Pathology, Division of Breast, Urogenital and Perinatal Pathology, University of Leipzig, Leipzig, [3]Dept. of Urology, Leipzig University Hospital, Leipzig, Saxony, Germany

Introduction/Purpose

For early stages of localized prostate cancer (PCa), active surveillance is an alternative option to radical treatment assuming that these tumors progress relatively slowly [1]. Such an approach requires an accurate identification of low-risk cancers and a reproducible, non-invasive technique to follow up patients. Transrectal ultrasound-guided biopsies (TRUS bx) are the current gold standard but also have a substantial sampling error that results in an undergrading in 40% of the lesions. Therefore, tissue parameters derived from diffusion-weighted MR imaging (DWI) and MR spectroscopy (MRS) have been considered to refine the information from TRUS bx. The purpose of this study was to identify the most appropriate set of functional MR parameters to differentiate indolent from aggressive cancer.

Materials and Methods

Thirteen patients with histopathologically confirmed PCa have yet undergone multiparametric, endorectal MRI diagnostics at 3 T (Magnetom Tim Trio, Siemens) prior to radical prostatectomy. The protocol included DWI in transverse planes (in-plane resolution: 1.0×1.0 mm^2, TR/TE: 3000/85 ms, slice thickness: 3 mm, FOV: 250×250 mm^2) using b-values of 50, 500, 800 and 1,500 sec/mm^2 as well as spectroscopic chemical-shift imaging (CSI) following an established prostate protocol (PRESS volume localization, 8 slices covering the whole prostate) [2]. Tumors were classified as low, intermediate or high grade (corresponding to Gleason scores GS of ≤ 6, 7, and ≥ 8, respectively) and the least differentiated areas were highlighted in whole-mount step sections by the pathologist. Apparent diffusion coefficient (ADC), normalized ADC (tumor ADC over ADC in healthy mirror region), choline/citrate (CC) and (choline+creatine)/citrate (CCC) ratios were measured in corresponding regions of the MR acquisitions. Accuracies of these parameters in differentiating low from combined intermediate and high-grade tumors were evaluated by calculating the areas under (AUC) the receiver operating characteristic (ROC) curves. An experienced radiologist who was blinded to all information then prospectively reviewed all image data and used the determined threshold values to distinguish between low and higher risk patients.
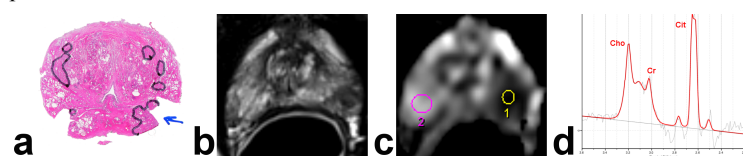
Figure 1: Example of a 50 y.o. patient with a preoperative PSA level of 4.1 ng/ml. **(a)** The least differentiated tumor component (GS 3+3) was highlighted (arrow) in the whole mount step section and matched to the corresponding T2w finding **(b)**. Regions of interest of the tumor (1) and of the mirror location (2) in the corresponding ADC image **(c)** were used to calculate the normalized ADC. **(d)** shows the individual spectrum of the nearest CSI voxel.
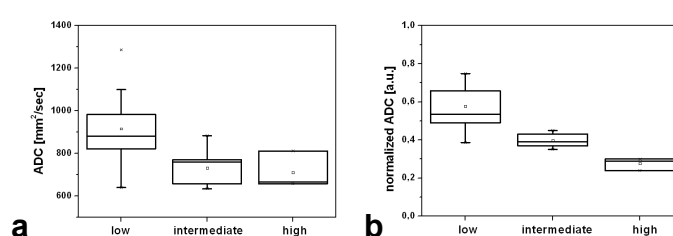
Figure 2: The box plots show tumor ADC (a) and normalized ADC values (b) as a function of qualitative grade groups. The normalized ADC showed a better correlation with cancer aggressiveness (Pearson ρ=-0.83, P<0.001) than the absolute tumor ADC (Pearson ρ=-0.57, P<0.05).
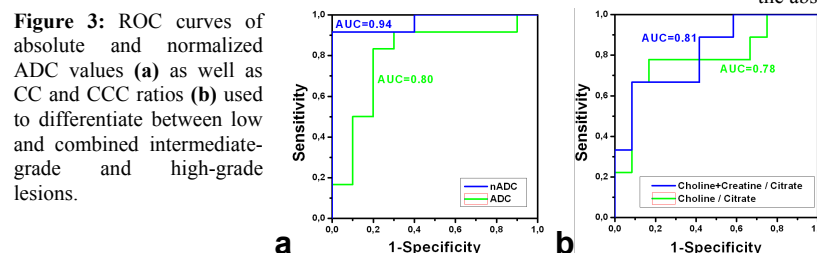
Figure 3: ROC curves of absolute and normalized ADC values **(a)** as well as CC and CCC ratios **(b)** used to differentiate between low and combined intermediate-grade and high-grade lesions.

Prostatectomy	TRUS bx		MRI (DWI+CSI)	
	low	intermed. and high	low	intermed. and high
low	7	0	5	2
intermed. and high	2	4	0	6

Table 1: Tumor grades predicted from TRUS bx and multiparametric MR imaging versus histopathological standard after radical prostatectomy.

Results and Discussion

A total of 22 lesions with primary and secondary Gleason grades of 2+3 in 1 case, 3+3 in 11 cases, 3+4 in 7 cases and 4+4 in 3 cases were included for ROC analysis. The resulting AUC values were 0.80 for absolute tumor ADC, 0.94 for normalized ADC, 0.78 for CC ratio and 0.81 for CCC ratio. A normalized ADC below 0.45 and/or a CCC ratio above 1.3 were chosen as thresholds for the prospective discrimination of aggressive cancers. Using the combination of both MRI criteria, 11 out of 13 patients were correctly assigned to low and intermediate/high risk groups; one patient with a GS of 5 and one with a GS of 6 were overgraded. In comparison, the use of TRUS bx findings resulted in the undergrading of two patients with intermediate aggressive cancers.

Conclusion

These preliminary results suggest that a combination of two functional MR parameters is well suited to discriminate low-grade from higher-grade prostate cancers.

Acknowledgements

References [1] Freedland SJ, et al. J Urol 2006; 175:1298–1302. [2] Verma S, et al. AJR 2010;194:1414-1426.