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

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Introduction and Purpose

Active surveillance is a promising option to reduce overtreatment in patients with organ-confined prostate cancer (PCa) [1]. The current gold standard for disease monitoring–annual transrectal ultrasound-guided biopsy–however, has a substantial sampling error that may result in undergrading for up to 40% of the lesions [2]. Morphological and functional data from multiparametric magnetic resonance imaging (mpMRI) are increasingly considered as a means to determine tumor aggressiveness [3,4]. The purpose of this study was to assess the value of diffusion-weighted MR imaging (DWI), MR spectroscopic (MRS) imaging and their combination for the prediction of PCa aggressiveness.

Materials and Methods

Thirty-nine patients with histopathologically confirmed PCa have undergone endorectal mpMRI at 3 T (Magnetom Tim Trio, Siemens). 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 following an established prostate protocol (PRESS volume localization, 8 slices covering the whole prostate) [5].

The standard of reference was provided by histopathological analysis of whole-mount step sections (n=32) or of biopsy material obtained under MRI guidance (n=6). An experienced pathologist marked the dedifferentiated lesions and defined the corresponding Gleason Score (GS). Tumors were classified as low, intermediate or high grade corresponding to GS ≤6, 7, and ≥8 [6]. After correlation with morphologic MR images, apparent diffusion coefficient (ADC), normalized ADC (tumor ADC over ADC in healthy mirror region, nADC), choline/citrate (CC) and (choline+creatine)/citrate (CCC) ratios were measured and correlated with GS (Fig. 1). Accuracies of these parameters in differentiating low ("indolent") from combined intermediate and high-grade ("aggressive") tumors were evaluated by calculating the areas under (AUC) the receiver operating characteristic (ROC) curves. An experienced radiologist who was blinded to all clinical data prospectively reviewed all MR images and used the determined threshold values to distinguish between indolent and aggressive PCa.

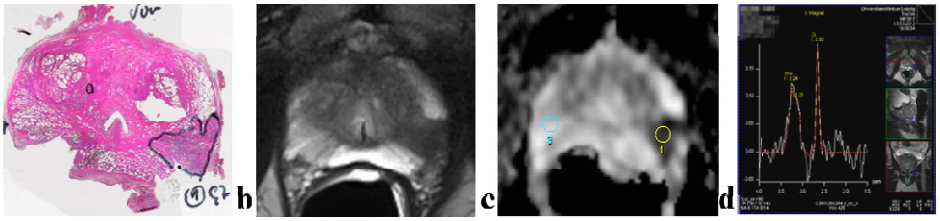

Figure 1: Example of a 68 y.o. patient with a preoperative PSA level of 4.8 ng/mL. (a) The dedifferentiated tumor component (GS 4+3) was highlighted in the whole-mount step section and matched to the corresponding T2-weighted image (b). Regions of interest of the tumor (yellow) and of the mirror location (blue) in the corresponding ADC map (c) were used to calculate the normalized ADC. (d) shows the MR spectrum of the nearest CSI voxel.

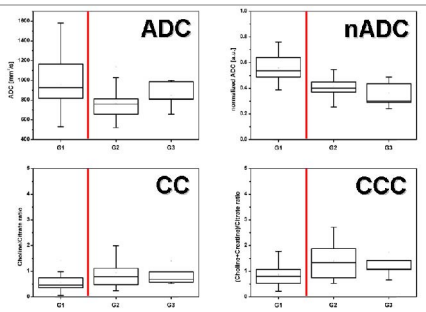

Figure 2: Box plot diagrams showing ADC, nADC, CC and CCCratio as a function of qualitative grade groups. nADC demonstrated the best correlation (Pearson ρ=-0.65, P<0.001) with tumor dedifferentiation.

Results and Discussion

A total of 80 lesions (1×GS=5, 43×GS=6, 29×GS=7, 6×GS=8) were included for ROC analysis. The nADC showed a higher discriminatory power than the tumor ADC (AUC: 0.88 vs. 0.72). AUC for CC and CCC ratios were 0.72 and 0.78, respectively (Figs. 2 and 3). Using nADC<0.46 and CCC>1.3 as thresholds for aggressive PCa, the reader correctly identified aggressive and indolent tumors in 31 (79%) and 28 (72%) of 39 patients, respectively. By combining both criteria, 33 of 39 patients (85%) were correctly assigned.

Conclusion

The combination of the highly sensitive normalized ADC with the highly specific CCC ratio was found to be well suited to estimate tumor aggressiveness. Combined diffusion-weighted and MRS imaging is a promising option for the noninvasive assessment of PCa aggressiveness and may have a role, for example, for patients undergoing active surveillance.

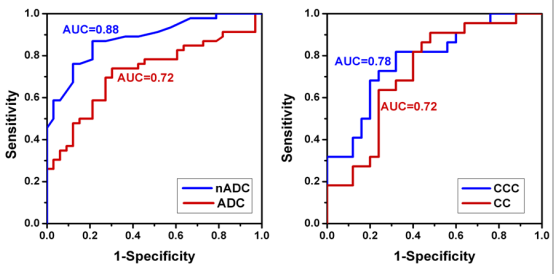

Figure 3: ROC curves of tumor ADC and nADC values as well as CC and CCC ratios used to differentiate between low and combined intermediate- and high-grade lesions. The highest discriminatory power was achieved by the nADC (0.88±0.03), followed by the CCC ratio (0.78±0.06).

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