Prediction of prostate cancer aggressiveness using Diffusion MRI: correlation of ADC values with Gleason score on TRUS Biopsy

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Introduction: Selecting the appropriate treatment strategy for patients detected to have prostate cancer (PCa) is one of the foremost challenges for clinicians caring for these men. Serum prostate specific antigen (PSA) may result in overdiagnosis of indolent tumors and transrectal ultrasound (TRUS) guided biopsy has limited sensitivity and also suffers from sampling errors leading to underestimation of PCa aggressiveness (1). It is well known that only some of the PCa detected through biopsy are aggressive and others may only require active surveillance. Hence, it is essential to find a non-invasive tool which could determine tumor aggressiveness and possibly guide decision making on the therapeutic approaches. Apparent diffusion coefficient (ADC), the quantitative parameter obtained using diffusion weighted imaging (DWI), seems to be a promising imaging method to evaluate tumor aggressiveness. The present study demonstrates the potential of ADC values in the prediction of PCa aggressiveness on TRUS biopsy in men with PSA 4-10 ng/ml.

Materials and methods:

In an IRB approved prospective study, men (mean age 64.33 ± 7.41 yrs, range 42-85 yrs) with an abnormal digital rectal examination (DRE) or elevated PSA (mean PSA 7.23 ± 1.83 ng/ml) between 4-10ng/ml, presenting to the urology clinic of our institution were scheduled to undergo a standard 12 core TRUS-guided biopsy for detecting PCa were recruited for this study. Patients with known causes for PSA increase like retention, prostatitis, urinary tract infection and any contraindication for MRI were excluded. The MR investigations were carried out at 1.5 T using a whole-body MR scanner (Avanto, Siemens, Erlangen, Germany). MR images were acquired using the endorectal surface coil (Medrad Inc., Pittsburgh, PA) in combination with the pelvic phased array coil. After acquisition of scout images in three orthogonal planes, the position of the endorectal coil was checked on sagittal images. Following this, T2-weighted images in the transverse and sagittal planes were acquired, using the turbo spin-echo sequence (TR=5000 ms, TE=98 ms, matrix size=256x256, slice thickness=4 or 5 mm, without an interslice gap). DW images were acquired using single-shot DWI-EPI in the transverse plane with the same slice locations as the transverse T2-weighted images, using the following imaging parameters: TR = 3000 ms, TE = 96 ms, matrix = 128X128, 4-5 mm slice thickness without an interslice gap. Five different b values, namely 0, 250, 500, 750 and 1000 s/mm^2, were used to acquire different diffusion weightings for the calculation of ADC. Circular regions of interest (ROIs) of uniform size (5 pixels) were drawn consecutively to cover the whole prostate irrespective of the T2-weighted image findings. The number of ROIs varied from patient to patient (range 20–75) depending on the size of the prostate. A cut-off value of ADC less than 1.17x10^{-3} mm^2/s was used to predict malignancy of peripheral zone (PZ) and 1.09 x10^{-3} mm^2/s was used to predict malignancy of central gland from our earlier study (2). Further, ADC values were correlated with the biopsy findings. One-way analysis of variance (ANOVA) was used to determine whether there were any significant differences between the means of three GS groups and to observe the dependency of ADC values on GS. A p value of < 0.05 was considered as a significant level. All the statistical analysis was carried out using statistical software SPSS 16.

Results: Of 103 patients, two patients with motion or susceptible artefacts were excluded from the analysis. Hence, analysis was performed on 101 patients. Out of 101 patients, 21 patients were positive for malignancy on TRUS biopsy (histopathology). Out of 21 patients, two patients had a GS of 4 with a mean ADC value of 1.00 ± 0.04 x10^{-3} mm^2/s and six patients with GS of 6 with a mean ADC value of 1.11 ± 0.25 x 10^{-3} mm^2/s. These two groups of patients were pooled together as low grade tumors. In nine patients with intermediate grade tumors had a GS of 7, with a mean ADC value of 0.9 ± 0.06 x10^{-3} mm^2/s. In four patients with high grade tumors (GS = 8), the obtained ADC value was 0.73 ± 0.06 x10^{-3} mm^2/s. Post hoc analysis revealed that the ADC value for three different grades of tumors was statistically significant ($p < 0.01$). An inverse correlation was observed between ADC and different GS (r = -0.69), (Figure 1). Figure 2 shows the trend among the values of ADC for different GS groups as box plot. A statistical significant difference was observed between patients with GS = 6 and GS = 7 ($p = 0.05$) as well as a significant difference was observed between patients with GS = 6 and GS = 8 ($p < 0.01$). However, for patients with GS = 7 and GS = 8, the difference was not statistical significant despite reduction of ADC value ($p = 0.156$), which may turn out to be significant if sample size could be increased.

Discussion: Highly aggressive tumors can metastasize quickly and require precise treatment regimen as compare to indolent tumors. Reduction of ADC may be attributed to the altered tissue structure attributed to the cell proliferation associated with malignancy. ADC values and GS have been found to correlate inversely with the cellularity of tumors (3, 4). We chose the clinically challenging gray zone of PSA (4-10 ng/ml) as our study group since it poses the largest clinical challenge in decision making. Further, we chose this group since there is no general consensus on whether ADC can vary with the PSA level (2, 3) . In our dataset, we observed four patients with GS = 8, in contrary to general agreement that this group has less likelihood of aggressive tumors. In one patient with GS = 6, the calculated ADC value was 1.59 x 10^{-3} mm^2/s, which was false negative. However in this patient, the pathology findings revealed that majority of tissues have high grade prostatic intraepithelial neoplasia. Our study had some limitations. First we could not compare our data of GS with final histopathology obtained from radical prostatectomy specimens, and hence the outcome of Gleason grading of TRUS biopsy and radical prostatectomy specimen could slightly differ (5). Another limitation was that we could not match MR images slice positions with histopathology sections, because TRUS biopsy may miss the cancer due to limited number of cores. Also necrosis, fibrosis can be confounding factors in the estimation of ADC.

Conclusion: The present study showed that the ADC values provided reliable and noninvasive method to assess the PCa aggressiveness on TRUS biopsy.

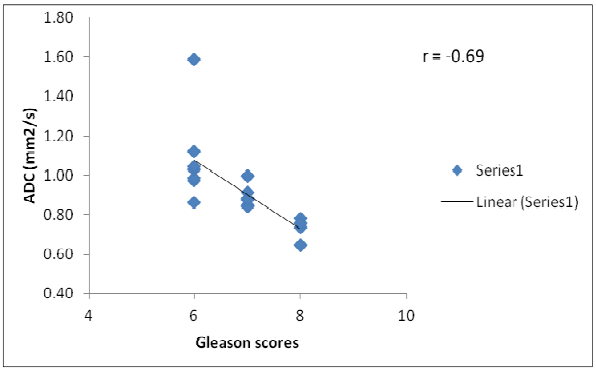

Figure 1. Correlation plot of the ADC values versus Gleason scores

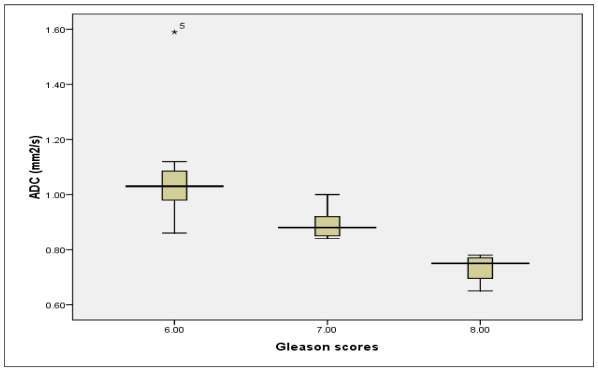

Figure 2. Box plots of ADC values of different Gleason scores groups ($p < 0.001$)

References: (1) Schröder FH et al. NEJM. 2009; 360: 1320 (2) Kumar V et al. NMR Biomed. 2007; 20: 505 (3) Itou Y et al. JMRI 2011; 33: 167 (4) Gleason DF et al. J Urol 1974; 111:58 (5) Kvåle R et al. BJUI 2009; 103: 1647.