**Apparent Diffusion Coefficient (ADC) Values as a Complementary Tool in the Prostate Gland Disease: A Prospective Evaluation of Apparent Diffusion Coefficient (ADC) Values with Pathological Data**

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**Conflict of interest:**The authors declare that they have  no conflict of interest.

**Compliance with Ethical Standards:**All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval obtained from a local commitee of Health Sciences University, Bozyaka Training and Research Hospital. Consent form obtained from each patient.

**Abstract**

**Background:**This prospective study aims to reveal whether the lesion is a benign pathological process or malignant by measuring ADC values under PI-RADSv2.1 guidance on MpMRI examinations. Additionally, the paper evaluates whether there is a correlation between malignant lesions’ pathological grade and ADC values, and whether ADC values provide noninvasive information about prostate cancer aggressiveness.

**Purpose**:To determine the cut-off ADC values that may exist to identify and distinguish between benign and malignant lesions and also identify cancers with an ISUP score≥2 and cancers with an ISUP score1 defined as silent disease.

**Methods:**This study includes 243 patients and they were diagnosed with TRUS-guided cognitive MRI fusion as tissue diagnosis. MpMRI images were evaluated before biopsy according to PI-RADSv2.1 guideline by a radiologist. Three groups which are benign prostatic tissue, prostatitis, prostate cancer, were obtained according to the histopathological results.

**Results:** When the cut-off value for ADC is 780 x10-3, sensitivity was 80%. When the cut-off value was taken as 668 x10-3, the sensitivity was found to be 72% and specificity 62%. When the cut-off ADC value was taken as 647 x10-3, the sensitivity was 83% and the specificity was 48.5%. ADC values varied significantly according to ISUP groups [p= 0.003]. It was determined that ISUP 1 group was significantly higher than each of the other groups. ADC group mean values did not show a statistically significant difference between Group 2,3,4 and 5.

**Conclusion:**ADC value shows significant potential, and may it improve the diagnostic accuracy.

**Keywords:** Prostate Cancer Aggressiveness, Magnetic Resonance Imaging, Apparent Diffusion Coefficient Value, PI-RADSv2.1

**What is Known?**

In PI-RADSv2, a range between 750–900 mm2/s is suggestive for PCa. However, in the literature; there is no consensus on the cut-off ADC value in distinguishing between PCa and healthy parenchyma.

Several previous studies have shown that ADC values are inversely correlated with GS and can therefore be considered a marker of PCa aggressiveness. Also, there are no agreed ADC values that corresponds to ISUP grades.

Wu et al. revealed that higher ADC values [0.830×10–3 mm2/s] were significantly associated with low-risk prostate cancer [GS 6 disease]. Alessandrino et al. found that quantitative values obtained from ADC [median ADC, and ADC ratio] are inversely correlated with ISUP score.

Threshold values are enabling us to distinguish between prostatitis and benign lesions, and those values can be obtained with ADC mapping since it reflects the internal architecture and localization of the pathological process within the prostate.

Esen et al. reported that ADC values are highly effective in differentiating PCa from prostatitis, but there was no significant difference between normal prostate parenchyma and prostatitis.

Also, in distinguishing prostate cancer from normal prostate parenchyma and prostatitis; ADC value shows significant potential, and may it improve the diagnostic accuracy.

**What is New?**

In our study, the mean ADC value of the malignant lesions included was 629.97±151.77 for the PZ and 614.75±152.23 for the TZ. When PCa and non-cancerous lesions were compared, it was seen that ADC values were significantly different. DWI and ADC mapping demonstrated that the tissue cellularity of prostate parenchyma are basic sequences that can provide important information.

Our study shows that ADC values are successful in distinguishing cancers with an ISUP-1, which are defined as silent diseases, from cancers with a clinically important[ISUP≥2]. Thus, in elderly patients where radical prostatectomy will not change the 5-year survival rate, with a simple measurement of ADC value, we can predict clinically insignificant[ISUP-1] PCa before surgery. And we can protect these patients’ groups from the possible morbidity of radical prostatectomy, such as incontinence, by choosing a more conservative treatment plan.

No significant difference was found between benign prostatic tissue and prostatitis group ADC values, but a significant difference was observed between normal prostate tissue and benign prostate disease ADC values as well as between normal prostate tissue and PCa.

We think that the ADC values we found in our study will contribute to the literature in distinguishing between prostatitis and similar benign processes, clinically insignificant low-grade cancers and high-grade cancers.

The importance of ADC values has been shown in the latest version of PI-RADS and we believe that ADC values should be used in the new version of the PI-RADS to be created.

**Apparent Diffusion Coefficient (ADC) Values as a Complementary Tool in the Prostate Gland Disease: A Prospective Evaluation of Apparent Diffusion Coefficient (ADC) Values with Pathological Data**

**Introduction:**

Prostate cancer [PCa] is the most common cancer in men and is the second most common reason for cancer-related deaths1. There is a broad spectrum, ranging from low-grade organ-confined tumors to aggressive tumors that can metastasize and lead to death. Therefore, proper diagnosis and staging are essential2. Most of the cases diagnosed with PCa are asymptomatic or cancers that do not decrease life expectancy and therefore have no clinical significance3. There are several treatment options for PCa; vary between emergency radical surgery, hormonotherapy, and active surveillance4. However, radical treatment decreases the quality of life with the risks of incontinence and impotence. The difficulty of managing localized PCa is to distinguish clinically significant cancers that should receive a radical treatment from clinically insignificant5. Recently, researches in the literature focused on distinguishing well-differentiated lesions expressed as “silent disease” with almost no fatality describing as clinically insignificant PCa [tumors with Gleason score[GS] of 6] from high-grade and aggressive cancers6.

Multiparametric Magnetic resonance imaging[MpMRI] has become the basic noninvasive examination for the evaluation of the prostate gland3,7,8. Diffusion-weighted imaging[DWI] is the basic functional sequence used in prostate MRI protocols in addition to conventional sequences, as it has advantages such as short exposure time, rapid acquisition, creation of qualitative and quantitative parametric image maps based on apparent diffusion coefficient[ADC] and using standard software. DWI is the main sequence in the evaluation of peripheral zone[PZ] lesions and its contribution to the final PI-RADS score in the transitional zone[TZ] has increased with the updated Prostate Imaging Reporting and Data System version 2.1[PI-RADSv2.1] guide published in 20199. To evaluate MpMRI data more accurately and objectively, determining ADC values in addition to the visual signal assessment, suggested in the PI-RADSv2.1, can contribute to reporting standardization. ADC cut-off values can be used as a diagnostic tool showing malignancy risk and tumor aggressiveness of focal lesions. To establish such a model, the histopathological diagnosis of the lesion determined in the MpMRI and if the lesion is malignant, its grade should be known10,11.

This prospective study aims to reveal whether the lesion is a benign pathological process or malignant by measuring ADC values under PI-RADSv2.1 guidance on MpMRI examinations and transrectal ultrasound(TRUS) guided cognitive fusion biopsy(CF-Bx). Additionally, the study evaluates whether there is a correlation between malignant lesions’ pathological grade[ISUP score] and ADC values and whether ADC values provide noninvasive information about PCa aggressiveness. We tried to determine the cut-off ADC values that may exist to identify and distinguish between benign and malignant lesions and also identify cancers with an ISUP score≥2 and cancers with an ISUP score 1(Gleason Score 3+3) defined as silent disease.

**Material and methods:**

This prospective study includes consecutive 243 patients, who were referred to the Radiology Clinic because of the elevated PSA values during the follow-up or positive digital rectal examination, or family history of PCa, underwent MpMRI for PCa diagnosis and screening between April 2019 and April 2020. 1.5T Siemens Magnetom Aera device was used in this study. Oral and written consents were obtained from all patients who participated in our study and ethics committee approval was obtained from the scientific research ethics committee. All images were evaluated on the SYNGO.VIA workstation. The inclusion criteria were to have a PI-RADS v2.1 score≥3 lesion and after mpMRI, to examine by MRI-TRUS cognitive fusion biopsy. Fifty-three patients who had PI-RADS<3 lesions, 15 patients with unsuitable image quality due to persistent rectal gas distension, 30 patients with bx performed previously, without cognitive fusion biopsy in our hospital and with prostate cancer treatment before testing, 10 patients with no tissue diagnosis due to refusing biopsy were excluded from the study. Finally, a total of 135 patients and 152 lesions with a PI-RADSv2.1 score≥3 were found eligible for our study, and they were diagnosed with TRUS-guided cognitive MRI fusion as tissue diagnosis in our urology clinic.

***MRI Protocol***

Prostate MpMRI images examined in the study were performed with a 1.5T Siemens Magnetom Aera [Siemens Healthcare, Erlangen, Germany] MRI device with 18 channels [body 18 A 1.5T Tim Coil] pelvic coil according to the protocols shown in Table-1. DWI was obtained in the axial plane using 4 different b-values before contrast administration [b: 50-800-1200-1800 sec/mm2]. The b-2000 value was calculated and generated by the device itself, and the ADC values were calculated with a monoexponential model on a pixel-pixel basis using all b values. ADC values were obtained quantitatively from ADC maps. Different b‐value distributions were applied which is vary between 50 and 1800 sec/mm2.

***Evaluation of Images and Histopathological Correlation***

MpMRI images were evaluated before biopsy according to PI-RADSv2.1 guideline by a radiologist with 5 years of experience in MpMRI evaluation. Patient age, serum prostate-specific antigen [PSA] value, PSA density [PSAd], prostate volume were recorded. The lesions in the TZ and PZ were scored from 1 to 5 according to the PI-RADSv2.1 guideline by specifying their appearance and size. All lesions with a PI-RADSv2.1 score ≥3 were included in this study. Localization, largest diameter, and PI-RADS score of the tumors were recorded. The assessing radiologist chose the best suited ADC map image for each lesion with a PI-RADSv2.1 score≥3 and measured the ADC values of the lesions. Measurements were made prospectively using an elliptical or circular ROI tool available on the SYNGO.VIA workstation using a field of view[FOV] adjusted to prostate imaging from lesions and for comparison, measurements were taken avoiding borders in the parenchyma areas that appear homogeneous in all sequences without lesions in the PZ and TZ. The measured ROI area was chosen between 10 mm2[6 pixels] and 22 mm2[13 pixels], with an average ROI area of 15 mm2[8 pixels]. Measurements were performed twice for both PZ and TZ and each lesions, and a lower ADC value was used for the evaluation. In the radiology report, ADC values were defined as millimeter2×10-3 per second. Relationships between patient age, serum PSA level, tumor ADC value, and GS were investigated. Lesions with pathologically Gleason GS≥6 were accepted as positive. In our hospital, MpMRI cognitive fusion TRUS-bx,18G automatic tru-cut biopsy needle, and hypoechogenic-hyperechogenic foci were also taken into consideration and correlated with the foci identified in the MpMRI obtained before biopsy and marked on the sector map, and two samples were made from each lesion by 15 years experienced urologist. The radiologist and urologist made a consensus then decided on the localization of the lesion together during the biopsy. Histopathological analysis of prostate specimens was performed by 20 years experienced urological pathologist. Three groups which are benign prostatic tissue, prostatitis, prostate cancer, were obtained according to the histopathological results. The malignant lesions were grouped according to the International Association of Urological Pathology[ISUP] criteria[ISUP1, GS3+3; ISUP2, GS3+4; ISUP3, GS4+3; ISUP4, GS4+4; ISUP5, GS≥9]12.

***Statistical analysis***

In the descriptive analysis, continuous variables are presented as mean ± standard deviation or median [25-75th percentile], and categorical variables as a percentage[%]. The compliance of the data to the normal distribution was evaluated using the Shapiro-Wilk test. When the distribution of the data was normal, the t-test was used in the comparison of the two groups, and the Mann-Whitney-U test was used under non-parametric conditions. One-way ANOVA or non-parametric Kruskal-Wallis test was used to compare continuous variables between three and more categories. The strength of the correlation between two continuous variables was evaluated using Spearman correlation analysis. Accordingly, the correlation coefficient [r] values <0.2 show very weak or no correlation, values from 0.2-0.4 show weak correlation, from 0.4-0.6 show moderate correlation, 0.6-0.8 show a high correlation, and values>0.8 are interpreted as very high correlation. ROC analysis was used to evaluate the success of the obtained variables in diagnosing prostate cancer and to determine the cut-off values, and the area under the curve [AUC], sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV] were calculated. After confirming that the data were normally distributed, unpaired t-tests were used to determine significant differences in mean ADC value between normal and cancer regions in the prostate gland according to zones. The relationships between ADC values and tumor Gleason score in both PZ and TZ cancers were evaluated using the Spearman rank correlation coefficient["].

SPSS 22.0 and MEDCALC programs were used for statistical analysis. p<0.05 was considered statistically significant. Data are shown as mean ± 95% confidence interval[CI].

**Results:**

A total of 135 patients and 152 lesions were included in this study. The mean age of the patients was 63.7±7.12. The mean PSA, prostate volume, and PSAd of the individuals are 9.78±14, 65.83±35.07, 0.24±0.39, respectively. In the PI-RADS groups 3, 4, and 5, there were 84, 39, and 29 lesions identified respectively, and the PCA prevalence of them was 24.2%, 60%, and 93.4% respectively. Forty[26.3%] of 152 lesions obtained from individuals were diagnosed as benign prostatic tissue, 55[36.2%] prostatitis, and 57[37.5%] of them were diagnosed with PCa[Table 2]. 16 lesions were identified as ISUP1 and 41 of the lesions had higher ISUP grades.

When PCa-nonPCa lesions and PCa-prostatitis lesions were evaluated according to age, PSA, prostate volume, and PSAd; the mean PSA values were not statistically different [p: 0.051 and p: 0.256]. Mean age and PSAd were higher in the PCa group, and prostate volume was lower [Table 2]. Age showed a low level positive correlation [r= 0.308, p= 0.004] with the mean PSA. While there was a weak positive correlation between PSA and prostate volume [r= 0.275, p= 0.011]; a moderate positive correlation [r= 0.617, p<0.001] was observed with the PSAd. A moderate negative correlation was found between prostate volume and PSAd [r= -0.502, p <0.001] [Table 3].

The mean ADC value for the normal PZ was 1174.22±178.19x10-3 [min-max: 739.0-1537.0x10-3], the mean ADC value for the normal TZ was 920.27±158.27x10-3 [min-max: 312.4-1521.0x10-3]. While there was a weak negative correlation between PZ ADC value and PSAd [r=-0.236, p=0.036], a weak positive correlation was observed between TZ ADC and PSAd [r=0.326, p=0.003] [Table 3].

           When cancer lesions and non-cancerous lesions were compared ADC values were found to be significantly different[Table 4]. When the mean ADC value of the malignant lesions according to the zones is evaluated, it is 629.97±151.77 for the PZ and 614.75±152.23 for the TZ, and the difference between them is not statistically significant[p= 0.830] [Table 5]. ADC values of benign prostatic tissue, prostatitis, and prostate cancer groups showed a statistically significant difference [p= 0.001].

To determine the group in which the difference originated, paired comparisons were made, no significant difference was found between the benign prostatic tissue and prostatitis group ADC values[p= 0.076].

# The ADC values of the PCa lesions [598.82±145.35 x10-3] were found to be significantly lower than the prostatitis group [790.51±148.15 x10-3][p=0.011] and the benign prostatic tissue group [707.34±131.04 x10-3][p ≤0.005]. AUC is 0.796 [0.702-0.890] for the ADC value in diagnosing PCa, [p<0.001]. When the cut-off value for ADC is 780 x10-3, sensitivity was 80% and specificity was 45.5%. When the cut-off value was taken as 668x10-3, the sensitivity was found to be 72% and specificity 62%. AUC is 0.775 [0.686-0.864], p<0.001 for ADC value in diagnosing prostatitis. When the cut-off ADC value was taken as 647x10-3, the sensitivity was 83% and the specificity was 48.5%. When the cut-off value for ADC was 773x10-3, sensitivity was 53% and specificity was 75.0% (CI was 95%). ADC values varied significantly according to ISUP groups [p= 0.003]. In paired comparisons, it was determined that ISUP 1 group was significantly higher than each of the other groups. ADC group mean values did not show a statistically significant difference between Group 2,3,4 and 5 [Table 6, Figure-1,2].

**Discussion:**

PCa itself is a disease with a very heterogeneous clinical course, 5-year survival ranging from 100% to 29% for the localized disease13–15. ISUP score is a widely accepted histopathological grading system for PCa, it reveals a 5-year survival rate of patients after radical prostatectomy12. Differentiating a low-grade [ISUP-1] tumor from significant [ISUP 2–5] PCa, which is not expected to have a significant effect on 5-year survival, may decrease prebiopsy and pretreatment risk stratification of the patient16. It will save the patient from the morbidities of radical prostatectomy that decrease the quality of life e.g. incontinence, especially in very elderly patients, and may lead the clinician to prefer more conservative treatments. It is a delicate balance to be able to distinguish between PCa cases that do not require any intervention and patients who will undergo radical treatment, and it can only be established by using the correct auxiliary modalities. Advances in the MpMRI technique increase the diagnostic accuracy in detecting prostate cancer17.

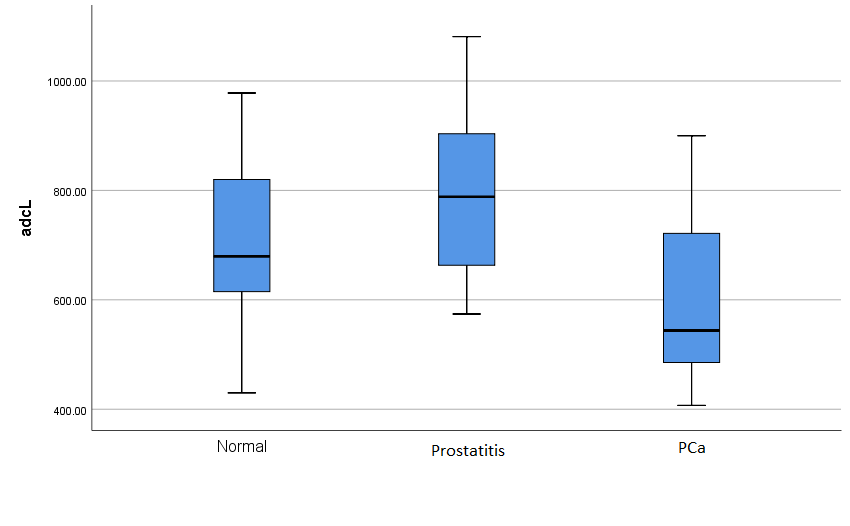
DWI and ADC are two important milestones in PI-RADSv2.1 for evaluating the PZ, where PCa is most common, and TZ 18. It is a known fact that highly cellular cancers have smaller interstitial space and lower ADC values19. Healthy prostate tissue observed in the PZ of the prostate contains rich tubules and allows the diffusion of water. ADC value is high in this area. On ADC maps, lower ADC values are detected since PCa destructs the normal tissue and invades the ducts of the gland20. In PCa detection and localization; ADC maps obtained from DWI are recommended by the American College of Radiology as part of standardized MpMRI protocol and increases the diagnostic accuracy15. Several previous studies have shown that ADC values are inversely correlated with GS and can therefore be considered a marker of PCa aggressiveness21,22. However, absolute ADC values vary considerably depending on individual factors such as b values selected and patient demographics23. There is no consensus on the cut-off ADC value in distinguishing PCa from healthy parenchyma. Also, no agreed ADC values are corresponding to the ISUP grades. However, a range between 750–900 mm2/s is suggestive for PCa in PI-RADSv224. The mean ADC value of the lesions included in our study was 629.97±151.77 for the PZ and 614.75±152.23 for the TZ. Currin et al. reported that malign cells within the aggressive PCa produce duct and acini then displacing normal prostatic secretions and have marked nucleomegaly, this may cause ISUP 2 or 3 tumors to resemble high-risk PCa at MRI25. Wu et al. revealed that higher ADC values [0.830×10–3 mm2/s] were significantly associated with low-risk prostate cancer [GS 6 disease]26. Alessandrino et al. found that quantitative values obtained from ADC [median ADC, and ADC ratio] are inversely correlated with ISUP score 15. In another study, ADC values can distinguish GS 6, 7 PCa from 8–10, but there was no statistical difference between GS 3+4 and 4+3 PCa27. Hambrock et al. found that ADC values can perfectly differentiate low- vs. intermediate vs. high-grade PCa from each other28. In another study, ADC values reduce the false-negative rate of MpMRI [PI-RADS<3] for clinically significant PCa29. In a meta-analysis in which Shaish et al evaluated the studies about ADC values recently published in the literature; 13 studies were included, providing 1107 tumor foci in 705 patients. They reported that ADC values demonstrate moderate accuracy in distinguishing clinically significant PCa from insignificant. They reported that significant bias may occur in these studies, therefore the performance of ADC values in distinguishing high-grade cancers from low-grade cancers may have been exaggerated, and that there was substantial heterogeneity in the results 30. In fact, the results of our study also supported this broad meta-analysis. In paired comparisons, it was determined that ISUP-1 group was significantly higher than each of the other groups. Mean ADC values did not show a statistically significant difference between Group 2,3,4,5. Our study shows that ADC values are successful in distinguishing cancers with an ISUP-1, which are defined as silent diseases, from cancers with a clinically important[ISUP≥2]. Thus, in elderly patients where radical prostatectomy will not change the 5-year survival rate, with a simple measurement of ADC value, we can predict clinically insignificant[ISUP-1] PCa before surgery. And we can protect these patients’ groups from the possible morbidity of radical prostatectomy, such as incontinence, by choosing a more conservative treatment plan.

The effectiveness of ADC values in differentiating PCa from benign processes is a known fact. In our study, when PCa and non-cancerous lesions were compared, it was seen that ADC values were significantly different. DWI and ADC mapping demonstrated the tissue cellularity of prostate parenchyma are basic sequences that can provide important information. Threshold values are enabling us to distinguish between prostatitis and benign lesions, and those values can be obtained with ADC mapping since it reflects the internal architecture and localization of the pathological process within the prostate31. PCa and chronic prostatitis are associated with variable clinical manifestations and clinical presentation may interfere. Unfortunately, there are no specific diagnostic laboratory tests to distinguish them from each other31. In another study, the accuracy of MR imaging was observed in the differentiation of PCa from other prostatic disorders, such as benign prostatic hyperplasia, acute bacterial prostatitis, and chronic bacterial prostatitis. The sensitivity to differentiate PCa from benign disorders was high, but they found that the accuracy of detecting bacterial prostatitis was low compared to other prostatitis groups32. Prostatitis has two forms known as acute and chronic prostatitis. Low signal intensity on T2-weighted images and early enhancement on dynamic MRI is both seen in PCa and prostatitis. Esen et al. reported that ADC values are highly effective in differentiating PCa from prostatitis, but there was no significant difference between normal prostate parenchyma and prostatitis33. Similarly, in our study, no significant difference was found between benign prostatic tissue and prostatitis group ADC values, but a significant difference was observed between normal prostate tissue and benign prostate disease ADC values as well as between normal prostate tissue and PCa.

Our study had some limitations; first, the reference ADC values did not investigate different b-values. In our study, only the most preferred b-values in the routine were used and normal ADC reference values were not compared according to the b-value used. It is left for further studies to investigate its effect. The significant disadvantages of TRUS-guided cognitive fusion biopsy are that success rates are highly dependent on the operator’s experience and lack of standardization14. In our study, the false-negative rate of TRUS-guided CF-Bx, especially in clinically insignificant tumors, was not taken into consideration. The present study was performed with one type and a 1,5T MRI. Other manufacturers’ devices should be investigated and compared. Also, interobserver variability was not evaluated in our study, we suggest a larger scale of a prospective study to be conducted.

In conclusion, ADC value is a potent and noninvasive imaging method that can provide useful information about tissue structure in prostate parenchyma. Creating a reference range for pathological ADC values accepted by all radiologists in the differentiation of prostate cancer from normal prostate parenchyma and prostatitis is also promising and has become a necessity. ADC values can be used as a complementary imaging method for clinically distinguishing insignificant PCa from significant tumors. Considering the presence of operator-dependent false-negative results in TRUS-guided biopsy and CF-Bx; especially in the elderly patient group, demonstrating clinically insignificant PCa before surgery with accuracy may protect this patient group from possible complications of radical prostatectomy. Also, in distinguishing prostate cancer from normal prostate parenchyma and prostatitis; ADC value shows significant potential, and may it improve the diagnostic accuracy. Similar to our study, the importance of ADC values has been shown in the latest version of PI-RADS and we believe that ADC values should be used in the new version of the PI-RADS to be created.

***Graphic 1. Distribution of ADC values of Patholojical Results in the Peripheral and Transitional Zone***



The mean ADC value for the normal peripheral zone is 1174.22 ± 178.19 x10-3 (min-max: 739.0-1537.0 x10-3), the mean ADC value for the normal transitional zone is 920.27 ± 158.27 x10-3 (min-max: 312.4-1521.0 x10-3).

***Tables:***

***Table 1. Prostate MRI Protocol***

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Prostate MRI Protocol (1.5T Siemens Magnetom Aera)** | | | | | | | | | | |
|  | **Sequence** | **Slice Thickness (mm)** | **Number of Slice** | **Voxel Dimensions (mm3)** | **Imaging Area (mm)** | **TE  (ms)** | **TR (ms)** | **Space (mm)** | **b value\*** | **Flip Angle** |
| **T2W coronal** | haste | 5 mm | 30 | 1,4x1,4x5 | 360x360 | 92 | 1400 | 1 mm |  | 180 |
| **T2A axial** | haste | 6 mm | 30 | 1,5x1,5x6 | 380x380 | 91 | 1400 | 1.2 mm |  | 180 |
| **T2W sagittal** | haste | 5 mm | 30 | 1,2x1,2x5 | 300x300 | 92 | 1400 | 0 mm |  | 180 |
| **T2W coronal** | TSE | 3 mm | 20 | 0,7x0,7x3 | 224x224 | 96 | 5490 | 0 mm |  | 160 |
| **T2A axial** | TSE | 3 mm | 24 | 0,6x0,6x3 | 200x200 | 101 | 6620 | 0 mm |  | 160 |
| **DWI** |  | 3 mm | 20 | 0,8x0,8x3 | 200x200 | 80 | 5000 | 0 mm | 50 800 1200 1800 2000\*\* | - |
| **T1W axial Lymph node** | TSE | 4 mm | 26 | 0,9x0,9x4 | 300x300 | 20 | 552 | 0.8 mm |  | 167 |
| **T1 Map axial** | Vibe tra | 3,5 mm | 20 | 1,4x1,4x3,5 | 260x260 | 1,9 | 4,11 | 0 mm |  | 2 15 |
| **T1W DCE-MRI\*\*\*** | vibe tra | 3,5 mm | 20 | 1,4x1,4x3,5 | 260x260 | 1,58 | 4,46 | 0 mm |  | 12 |
| **Post-contrast T1W axial** | TSE | 4 mm | 34 | 0,6x0,6x4 | 360x360 | 11 | 606 | 0.8 mm |  | 180 |
| **HASTE:Half-fourier acquisition single shot turbo spin echo TSE:Turbo Spin Echo TE:Time of Echo TR:Time of Repetition VIBE TRA:Volumetric interpolated breath-hold examination T1W: T1-Weighted T2W: T2-Weighted DWI: Diffusion-Weighted Imaging \*\*:Calculated B value** | | | | | | | | | | |

\*There is no currently widely accepted optimal “high b-value” beyond the requirement for a DW image set with a b-value ≥1,400 sec/mm2.18

\*\*\*In dynamic contrast enhancement imaging (DCE-MRI), a gadolinium-based contrast agent with an automatic injector at 0.1-0.2 mmol/kg concentration and 2-4 mL/s injection rate via IV were used and T1 axial sections were obtained over 240-300 sc. duration with one every 7 sc. before, during, and after administration including the entire prostate.

***Table 2. Descriptive statistics of patients who have PCa or nonPCa or Prostatitis***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variables | **PCa positive n:51** | **nonPCa n:84** | **Prostatitis n:59** | **p value** | **p value\*** |
| mean±SD | mean±SD | mean±SD |  |  |
| Age | 65.23±7.8 | 62.06±6.90 | 61.41±7.04 | 0.051 | 0.048 |
| PSA | 16.24±24.12 | 8.70±7.52 | 9.64±9.13 | 0.250 | 0.256 |
| Prostat volume | 45.71±29.21 | 76.54±39.51 | 76.49±42.68 | **<0.001** | **0.003** |
| PSA density | 0.42±0.55 | 0.128±0.121 | 0.13±0.12 | **<0.001** | **0.012** |
| p value refers to comparison in between PCa and nonPCa, p value\* refers to comparison in between PCa and Prostatitis. | | | | | |

PCa: Prostat cancer, n: number of lesions, SD: standart deviation PSA: prostate spesific anjigen PSAd: PSA density

Prostate Volume and PSAd values are statistically significant for PCa and prostatitis lesion differentation.

***Table 3. The correlation analysis between patient age, serum PSA value, prostate volume, PSAd and ADC values***

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Age** | **PSA** | **Prostate**  **volume** | **Prostate density** | **Peripheral**  **zone ADC** | **Transitional**  **zone ADC** |
| **Age** | r | 1 | **0.308\*\*** | 0.125 | 0.155 | -0.170 | 0.016 |
| p value |  | 0.004 | 0.259 | 0.160 | 0.134 | 0.888 |
| **PSA** | r | **0.308\*\*** | 1 | **0.275\*** | **0.617\*\*** | -0.18 | 0.026 |
| p value | 0.004 | . | 0.011 | <0.001 | 0.112 | 0.822 |
| **Prostate volume** | r | 0.125 | 0.275\* | 1 | **-0.502\*\*** | 0.052 | 0.019 |
| p value | 0.259 | 0.011 | . | <0.001 | 0.651 | 0.866 |
| **Prostate density** | r | 0.155 | **0.617\*\*** | **-0.502\*\*** | 1 | **-0.236\*** | 0.015 |
| p value | 0.160 | <0.001 | <0.001 | . | 0.036 | 0.897 |
| **Peripheral zone ADC** | r | -0.170 | -0.180 | 0.052 | **-0.236\*** | 1 | **0.326\*\*** |
| p value | 0.134 | 0.112 | 0.651 | 0.036 | . | 0.003 |
| **Transitional zone ADC** | r | 0.016 | 0.026 | 0.019 | 0.015 | **0.326\*\*** | 1 |
| p value | 0.888 | 0.822 | 0.866 | 0.897 | 0.003 |  |

PSA: Prostate spesific antigen, n: number of lesions, SD: standart deviation, p value less than 0,05 considered as statistically significant.

***Table 4. The comparation of ADC values between cancer lesions and non-cancerous lesions***

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **PCa (n:57)** | **nonPCa (n:95)** | **p value** |
| **ADC** | 598.8233±145.3503 x10-3 | 758.9636±146.49521 x10-3 | <0.001 |

PCa: Prostate cancer, n: number of lesions, SD: standart deviation

***Table 5. Mean ADC values according to the pathological diagnosis***

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pathological definitive diagnosis** | | | | | |
| **Variables** | | **Benign prostatic tissue (n:40)** | **Prostatitis (n:55)** | **PCa(n:57)** | **p values** |
| **ADC** | **Mean±SD** | 707.34±131.04 x10-3 | 790.51±148.15 x10-3 | 598.82±145.35 x10-3 | <0.001 |
| **Median**  **(25p-75p)** | 679.48 x10-3 (608.00-820.76) | 788.39 x10-3 (663.05-905.25) | 544.50 x10-3 (485.0-727.83) |

PCa: Prostate cancer, n: number of lesions, SD: standart deviation, p value less than 0,05 considered as statistically significant.

***Table 6. The Asssociation between ADC values and ISUP grades***

|  |  |  |  |
| --- | --- | --- | --- |
| **ADC** | **ISUP** | **mean±SD** | **p value** |
| 1 (n:16) | 726.71±143.08 x10-3 | 0.003 |
| 2 (n:9) | 558.03±132.98 x10-3 |  |
| 3 (n:10) | 496.21±73.69 x10-3 |  |
| 4 (n:12) | 508.67±27.94 x10-3 |  |
| 5 (n:10) | 527.16±63.48 x10-3 |  |

SD: standart deviation, p value less than 0.05 considered as statistically significant.

***Image Legends:***

***Figure 1:***

A 68-year-old male patient whose serum PSA level was 6.7 ng/mL. a.) On the T2W axial view; a prominent hypointense lesion (17x12x10 mm in size) located in the right middle part of the peripheral zone is seen. b.) on DWI axial image (b = 1800 s/mm2); lesion is markedly hyperintense, c.) ADC map shows markedly hypointens lesion and ADC value measured as 471,90x10-3mm2/s. d.) on DWI axial image (b = 2000 s/mm2); lesion is markedly hyperintense. Lesion evaluated as PI-RADS score:5 and histopathologically confirmed as ISUP Grade 5 PCa.

***Figure 2:***

A 55-year-old male patient whose serum PSA level was 5.6 ng/mL. a.) On the T2W axial view; a prominent hypointense lesion (7x8x10mm in size) located in the left middle part of the peripheral zone is seen. b.) on DWI axial image (b = 1800 s/mm2); lesion is mildly hyperintense, c.) ADC map shows markedly hypointens lesion and ADC value measured as 710,94x10-3mm2/s. d.) on DWI axial image (b = 2000 s/mm2); there is no abnormal signal. Lesion evaluated as PI-RADS score:3 and histopathologically confirmed as ISUP Grade 1 PCa.

**Acknowledgments:**

Professor Doctor Enver Vardar, working in the department of pathology, helped us to evaluate the pathology preparations of our patients.

**Funding:**

This study was not funded by any organization.

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