Original Paper

Should PI-RADS 3 be Subclassified According to ADC Values in the Transition Zone?

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ABSTRACT: The premise of this paper starts from the fact that a more precise definition related to the intensity of the lesions on the ADC sequence can lead to a new subclassification of PI-RADS 3 lesions in the transitional zone and to an improvement of the specificity of the PI-RADS classification. The study was retrospective and included only patients who, based on prostate MRI examinations, contained exclusively PI-RADS 3 lesions, without other PI-RADS 4 or 5 lesions. The number of cases that meet all these conditions was reduced to 18, where a series of characteristics were noted for each one: PI-RADS 3 lesion area on the ADC sequence, the minimum and average ADC value of the lesion, the average ADC value of the transitional zone outside the lesion, PSA, prostatic volume, PSA density and biopsy result. The average ADC value of the negative lesions was 865(±165) µm2/sec, and of the positive ones was 869(±118) µm2/sec, which denies the hypothesis that there could be a value limit ADC to delimit PI-RADS 3 from PI-RADS 2 or 4 in this sample of patients. Furthermore, we reported the average ADC value of each such lesion to the adjacent unchanged transitional zone and obtained a greater difference of 432(±163) µm2/sec between the negative lesions and their adjacent transitional zone, compared to the difference of 399(±127) µm2/sec between the positive lesions and their adjacent ones.

KEYWORDS: *Prostate, MRI, PIRADS 3, ADC.*

Introduction

Prostate cancer remains the most frequent cancer in men worldwide [1,2].

The Prostate Imaging Reporting and Data System (PI-RADS) is the structured reporting system for the assessment of magnetic resonance imaging (MRI) of the prostate.

It is divided into PI-RADS 1, 2 for low risk, 3 for medium risk, and 4.5 for high risk.

A lesion marked PI-RADS 1, 2, 4 or 5 is considered useful for the attending physician because the biopsy decision can be easily made in these cases, but PI-RADS 3 often brings ambiguity to this decision [3].

In the peripheral zone, a PI-RADS 3 lesion is characterized primarily on the diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences, and secondarily on the DCE sequence where it has the possibility of being upgraded to PI-RADS 4, while in the transitional zone they are characterized primarily on the T2 weighted image (T2WI) sequence and then secondarily on the DWI and ADC sequences, without being influenced in any way by the dynamic contrast-enhanced (DCE) sequence, so the use of gadolinium does not bring benefits [4].

Although all sequences are exposed to signal noise in prostate MRI without an endorectal coil [5], it damages more the evaluation of the transition zone, where the reporting is done on the T2WI sequence and boils down to a greater number of characteristics (intensity, homogeneity, shape, edges, size) unlike the peripheral area where the ADC sequence complements DWI and the lesions are limited only to size and intensity.

In Figure 1 we can see how these artifacts look, but it is also a good example of the interpretation of the lesions because the peripheral lesion (blue arrow) looks similar to the transitional lesion (orange arrow) on the DWI sequence, but according to the PI-RADS 2.1 guide the peripheral lesion represents a very high risk (exceeds 15mm) and the transitional lesion represents an equivocal risk (if it does not exceed 15mm) because on the T2WI sequence that area shows no changes compared to the rest of the transitional area.

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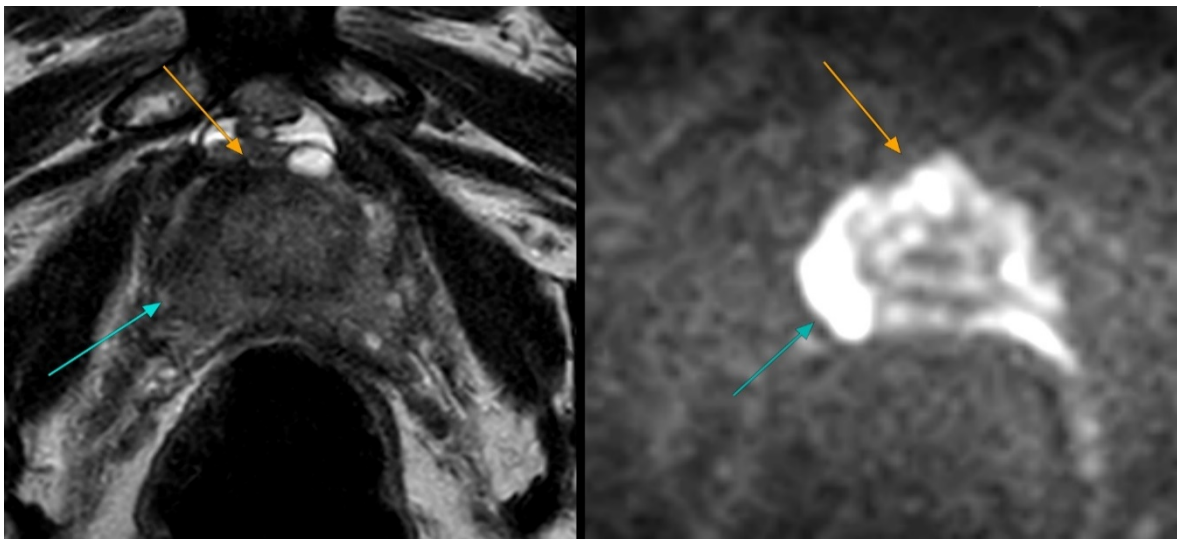

Figure 1. Prostate MRI examination showing motion artifacts due to rectal contents. The anxious patient could no longer resist inside the MRI, so these are the only T2WI (left) and DWI (right) sequences obtained. The T2WI sequence shows a prostate with relatively homogeneous changes, but the DWI sequence (confirmed by the ADC sequence, not included in the figure) clarifies the report by the presence of two suspicious areas present both in the peripheral area on the right side (blue arrow) and in the area previous transitions (orange arrow), although both sequences were artifactual.

Also, according to the PI-RADS 2.1 guide, a lesion with equivocal risk in the transitional zone can also be described as a high or very high-risk lesion according to the DWI and ADC sequences, while it is of low risk on the T2WI sequence (Figure 2).

T2W	DWI	DCE	PI-RADS
1	Any*	Any	1
2	≤3	Any	2
	≥4	Any	3
3	≤4	Any	3
	5	Any	4
4	Any	Any	4
5	Any	Any	5

Figure 2. Classification of PI-RADS lesions in the transitional area [4].

In the transitional area, the number of PI-RADS 3 lesions is more than that of PI-RADS 4 and 5 combined [6,7] so the problem of risk stratification arises because less than 20% of them are proven in studies on a large group of patients to be clinically significant cancer [6,8-10].

The DWI sequence analyzes the property of water molecules to be in Brownian motion in normal fluids, and to be restricted in areas where there are cell membranes, due to their hydrophobic nature.

In areas that contain more cells, such as cancer, the water diffusion restriction will be increased compared to that of adjacent normal tissues of the same type.

The ADC sequence calculates the net displacement of water molecules on a timescale that reflects diffusion sensitization, and the hyposignal of an area confirms the diffusion restriction visualized in the hypersignal on the DWI sequence (Figure 3).

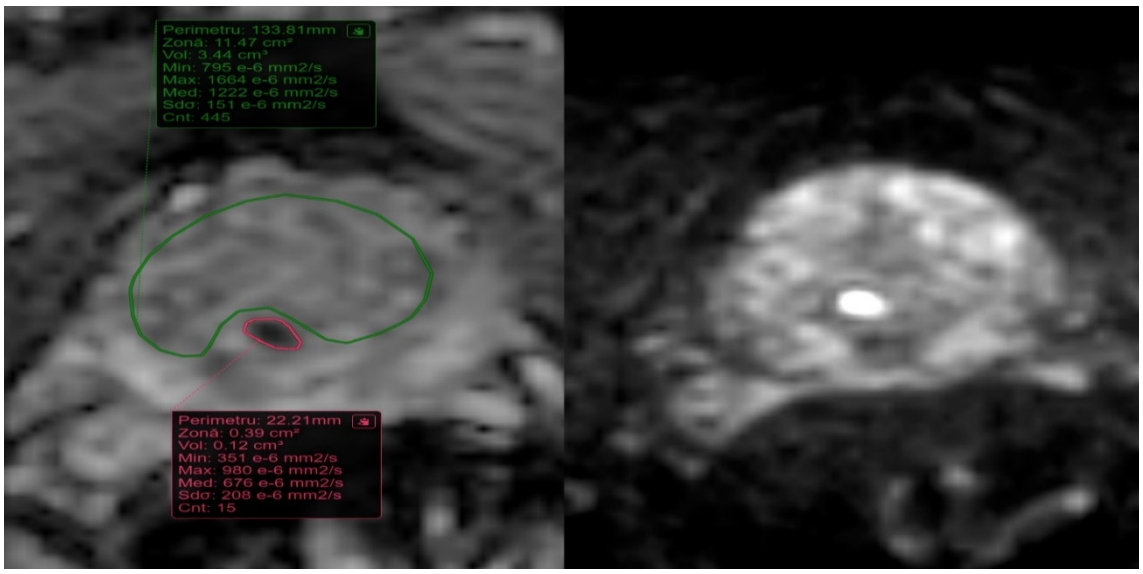

Figure 3. Method of measurement of the suspicious lesion (red, left) and of the transitional zone without changes (green, left) in the 3DnetTM platform and the confirmation of diffusion restriction at the level of the suspicious zone on the DWI sequence (right). Despite the fact that there is an important diffusion restriction at the level of this PI-RADS 3 lesion, the histopathological result was negative.

The premise of this paper starts from the fact that a more precise definition related to the intensity of the lesions on the ADC sequence can lead to a new subclassification of PI-RADS 3 lesions in the transitional zone and to an improvement of the specificity of the PI-RADS classification.

Methods

The study was retrospective and included MRIs performed between March 2020 and July 2023 in the Medical Imaging Department of the University of Medicine and Pharmacy of Craiova using a Philips Ingenia 3.0T MRI scanner, selecting only patients who, based on prostate MRI examinations, contained exclusively PI-RADS 3 lesions, visible on DWI and ADC sequences, without other lesions of the same prostatic half that are PI-RADS 4 or 5 at the level of the transitional zone or PI-RADS 3,4,5 lesions or with the appearance of prostatitis at the level of the peripheral zone.

These were filtered from a database, by three radiologists, who analyzed and re-evaluated the examinations with a prostate image quality score (PI-QUAL) of 5 or 4, which corresponded to the PI-RADS V2.1 criteria;

A final filtering was done at the end, where only the examinations where the histo-pathological examination was found were kept.

The number of cases that meet all these conditions was reduced to 18, where a series of characteristics were noted for each one: PI-RADS 3 lesion area on the ADC sequence, the minimum and average ADC value of the lesion, the average ADC value of the transitional zone outside the lesion, prostate-specific antigen (PSA), prostatic volume, PSA density and biopsy result.

The characteristics of the described lesion were calculated using the software integrated into the 3Dnet™ platform provided by ©Biotronics3D (Figure 3), and the serological results were obtained from laboratories accredited by the Romanian accreditation association.

The cognitive-targeted biopsy was performed in the Craiova county emergency clinical hospital and we do not know the local protocol by which the biopsy of a patient with a PI-RADS 3 lesion is decided, which is why we left the search for the histopathological result at the very end of the data search.

Results

The final number of examinations that met all the conditions of the study was 18.

Of these, 4 (22%) were negative, 3 (16%) proved to be prostatitis, 7 (39%) were Gleason 6 (3+3), and the remaining 4 (22%) had clinically significant cancer (Figure 4).

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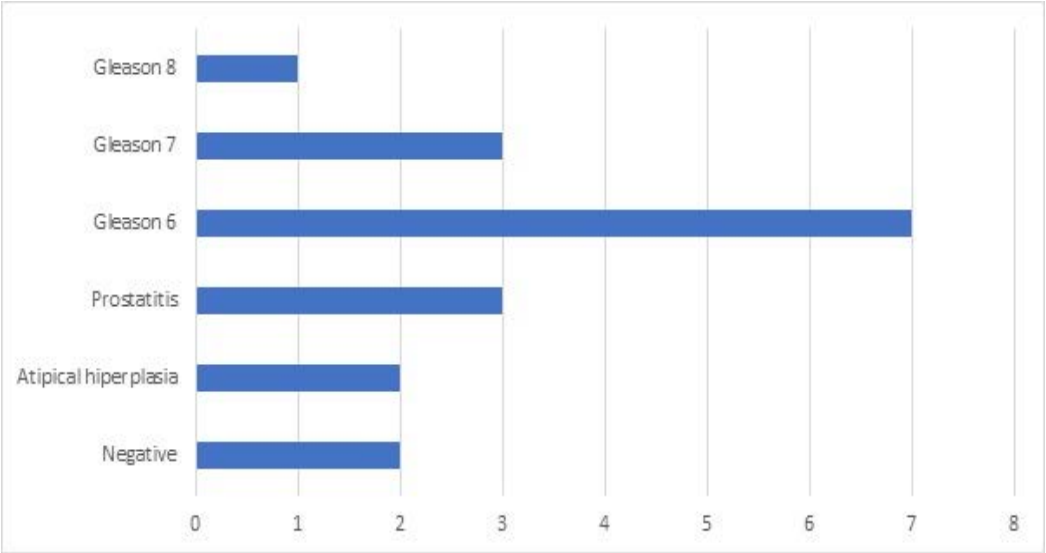

Figure 4. Histopathological results of the 18 biopsies performed on PI-RADS 3 lesions

The average ADC value of the negative lesions was 865 (±165) µm2/sec, and of the positive ones (including Gleason 6) was 869 (±118) µm2/sec, which denies the hypothesis that there could be a value limit ADC to delimit PI-RADS 3 from PI-RADS 2 or 4 in this sample of patients.

Furthermore, we reported the average ADC value of each such lesion to the adjacent unchanged transitional zone and obtained a greater difference of 432 (±163) µm2/sec between the negative lesions and their adjacent transitional zone, compared to the difference of 399 (±127) µm2/sec between the positive lesions and their adjacent ones (Figure 5).

The fact that positive and negative lesions not only had similar values but even had a slight negative correlation denotes the lack of metric specificity of the ADC sequence in PI-RADS 3 lesions in the transitional zone.

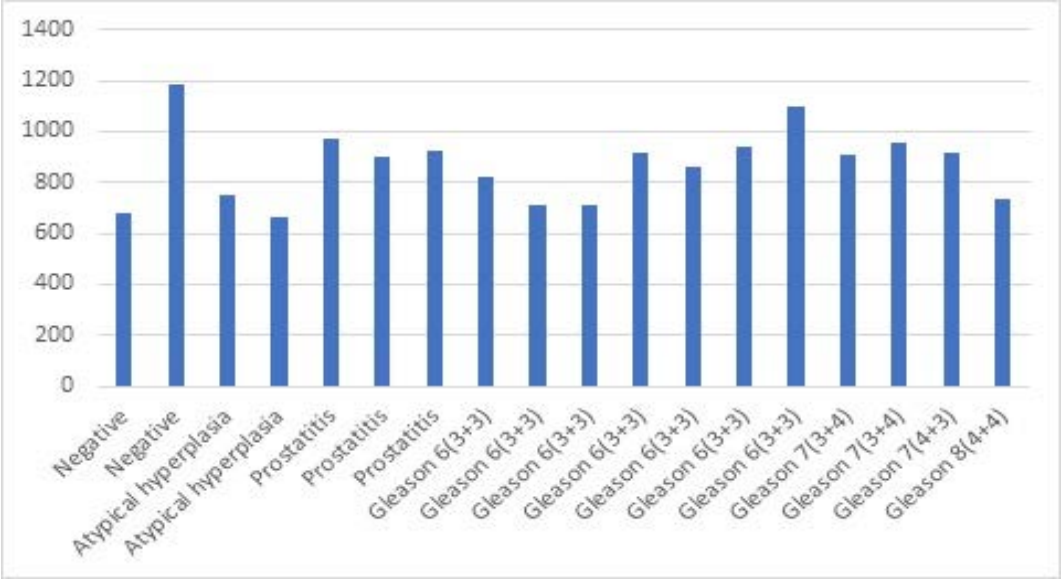

Figure 5. Average ADC values of the biopsied lesions sorted according to the histopathological result.

The average PSA value of negative lesions was 5.23 (±1.31) ng/ml, of positive lesions 8.72 (±3.58) ng/ml and of cases with prostatitis 13.57 (±3, 53) ng/ml, which says more about PI-RADS 3 lesions than the ADC value (Figure 6).

Two of the three total positive lesions that had a PSA greater than 10 were the only ones from the entire group of patients that had positive lesions diagnosed at the same histopathological examination in the contralateral half.

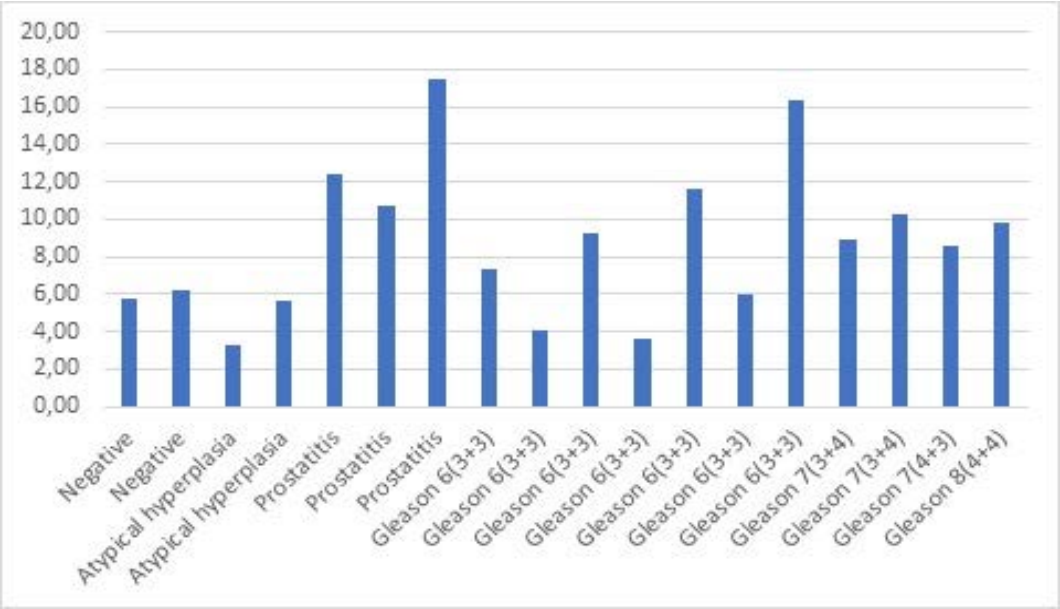

Figure 6. PSA values of the biopsied lesions sorted according to the histopathological result.

PSA density, calculated by the ratio between PSA and prostate volume can be seen in Figure 7, where all 4 negative, non-prostatitis cases had PSA density below 0.1 and the 4 positive, clinically significant cases had PSA density above 0.1.

It should be noted that the two cases with the highest PSA densities are at the same time the only ones that showed positive lesions in the other half of the prostate as well.

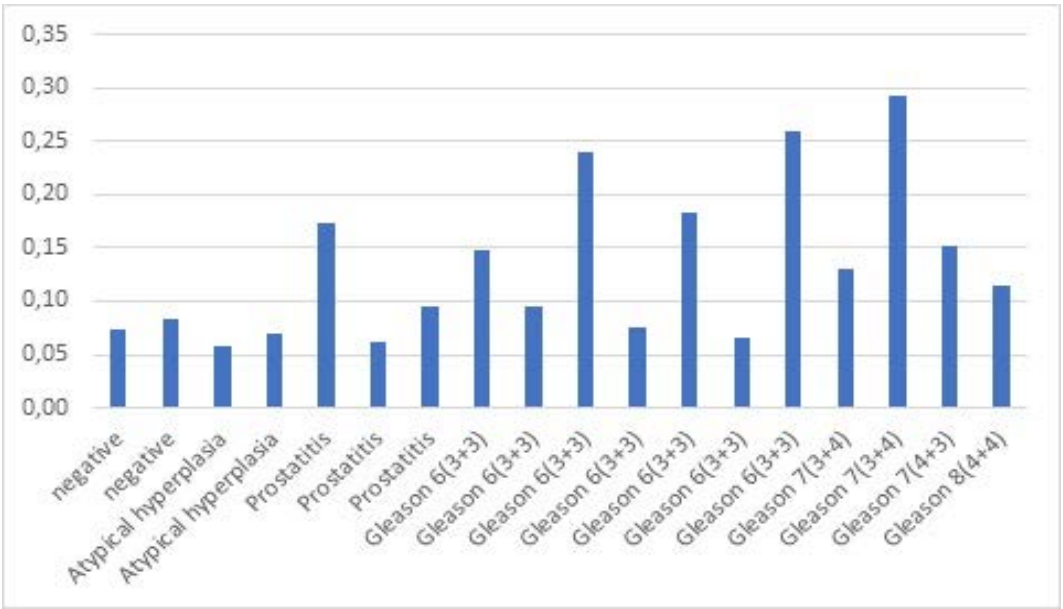

Figure 7. The PSA density values of the prostates from which the lesions were biopsied, sorted according to the histopathological result.

The age of the patients and the calculation of the minimum ADC value from each lesion did not correlate significantly with the histopathological results, but were added to the final data table (Table 1).

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Table 1. All data obtained, sorted according to the histopathological result.

AGE	PSA (ng/ml)	LESION DIAGNOSTIC	CONTRALATERAL DIAGNOSIS	LESION AREA	LESION MIN ADC	LESION AVG ADC	NON-SUSPECT AREA AVG ADC	PROSTATE VOLUME
67	5,73	Negative	-	0,39 cm^2	351	676	1222	78,83 cm^3
51	6,23	Negative	-	2,11 cm^2	897	1181	1312	74,99 cm^3
74	3,30	Atyp. hyperplasia	-	0,19 cm^2	577	747	1297	56,33 cm^3
70	5,65	Atyp. hyperplasia	-	0,73 cm^2	450	661	1284	82,01 cm^3
67	12,44	Prostatitis	-	0,44 cm^2	771	969	1343	71,67 cm^3
69	10,74	Prostatitis	-	0,46 cm^2	680	899	1330	171,34 cm^3
79	17,52	Prostatitis	-	1,16 cm^2	784	927	1302	184,52 cm^3
67	7,38	Gleason 6(3+3)	-	0,4 cm^2	707	818	1063	49,94 cm^3
63	4,02	Gleason 6(3+3)	-	0,67 cm^2	566	711	1050	42,10 cm^3
71	9,21	Gleason 6(3+3)	-	0,57 cm^2	488	714	1175	38,36 cm^3
70	3,65	Gleason 6(3+3)	-	0,75 cm^2	745	915	1252	48,32 cm^3
73	11,60	Gleason 6(3+3)	-	0,83 cm^2	570	857	1303	63,23 cm^3
76	6,02	Gleason 6(3+3)	-	0,93 cm^2	783	942	1233	91,06 cm^3
68	16,40	Gleason 6(3+3)	7(3+4)	1,69 cm^2	893	1096	1350	63,10 cm^3
64	8,97	Gleason 7(3+4)	-	0,8 cm^2	771	905	1385	69,04 cm^3
77	10,32	Gleason 7(3+4)	7(4+3)	0,9 cm^2	625	957	1513	35,20 cm^3
75	8,57	Gleason 7(4+3)	-	0,81 cm^2	691	919	1261	56,59 cm^3
75	9,83	Gleason 8(4+4)	-	0,43 cm^2	204	732	1374	85,53 cm^3

Discussions

We chose to look for a method of subclassifying PI-RADS 3 lesions according to the ADC value, and for this we looked for a very specific patient profile: with exclusively PI-RADS 3 lesions in the transitional zone and without other lesions at least the same half of the prostate, this is mainly because the biopsies to which we had access were cognitive-guided and sorted in the histopathology report as lesions in the left half, respectively in the right half.

This specific profile led to a small number of subjects but increased confidence in the results obtained.

PSA value and PSA density proved specific, reconfirming the conclusions of Schoots et al. [11] according to which unnecessary biopsies can be avoided by applying a PSA density threshold of 0.1 in PI-RADS 3 lesions.

This threshold is also motivated by the report of patient #13 from Table 1, with PSA values of 6.02 and PSA density of 0.07, initially his PSA was monitored over a 6-month interval and it increased slightly during this period, which is why it was subsequently biopsied and confirmed with Gleason 6 (3+3).

The main purpose of this paper still remains the correlation between the ADC value of PI-RADS 3 lesions in the transitional zone and the risk of cancer, including the clinically insignificant one, and in our small group of patients we are dealing with an even slightly negative correlation, so that we expect that even in larger groups of patients there will not be a threshold between biopsiable and non-biopsiable PI-RADS 3 lesions.

Abreu-Gomez et al. [12] concluded in another context that the size of visible lesions on the ADC sequence was associated with the pathological stage, while the ADC metrics were not, while Zhang et al. [13] argue that applying an ADC threshold of 900µm2/sec to all PI-RADS 3 lesions proved to be useful only when correlated with PSA density.

Since the threshold we are looking for in the ADC value seems to be found in the PSA density rather than in other imaging aspects, future work will include studies on several biopsied PI-RADS 3 lesions, preferably under ultrasound guidance, in which we will look for ways to associate serological results with imaging ones in search of more effective risk stratifications between cancer and inflammatory changes.

Conclusions

PI-RADS 3 lesions did not prove to be subclassifiable according to ADC values, because in our sample they alone or compared to other measurements did not prove relevant for risk stratification, while PSA value and PSA density proved useful.

Conflict of Interests

None to declare

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