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An Analysis of MRI-Fusion Prostate Biopsy Results in PI-RADS 3 MRI Findings in a Cohort of Men in a Community Hospital Setting

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Abstract

Introduction: With the advent of multiparametric MRI (mpMRI), clinicians added an important tool for helping to decide whether a man should undergo a prostate biopsy. The MRI PI-RADS system stratifies the risk of finding cancer on prostate biopsy. PI-RADS 3 lesions often prove to be a diagnostic challenge, and many men are advised not to proceed with a biopsy based on this finding. The goal of our paper was to evaluate the likelihood of finding cancer of clinical significance in this group. Methods: A retrospective 4-year data and quality analysis was performed of 312 evaluable men undergoing prostate MRI. Of the subset with scores of PI-RADS 3 who underwent biopsy (N = 32), 100 percent were biopsied using an MRI-guided fusion technique, greatly raising the likelihood that the MRI lesion was, in fact, the area sampled. Results: A total of 34% of the men with PI-RADS 3 lesions were found to have Grade Group ≥ 1, with 15.6 % demonstrating Grade Group ≥ 2. In the men with cancer, we analyzed and report the relationship to age, ethnicity, PSA density, and the presence or absence of cribriform findings. Conclusions: We found that many men with PI-RADS 3 findings on multiparametric MRI do, in fact, have clinically significant prostate cancer. We suggest that many factors (such as rate of rise of PSA over time, family history, and rectal examination findings) be considered in addition to the MRI PI-RADS score to advise whether or not to proceed with a biopsy of the prostate. Our findings, from a single, large, community hospital with a diverse ethnic makeup, parallel the findings of large trials done at academic centers of excellence. This de-

monstrates that comparable diagnostic mpMRI/biopsy quality may be found in the community setting.

Keywords

MeSH Headings: Prostate, Neoplasms, Diagnosis, Magnetic Resonance Imaging

1. Introduction

Urologists face a difficult challenge in deciding who should undergo a biopsy to evaluate for prostate cancer. Multiple strategies have evolved to help decide when a biopsy of the prostate should be performed. These must be balanced against the risks of a biopsy including sepsis, cost, the possibility of false positive or negative results, and discomfort. As MRI has become more frequently used as a diagnostic adjunct, our group decided to examine more closely the characteristics of patients who underwent a prostate biopsy with mpMRI findings of PI-RADS 3. Management of this intermediate risk group has proved challenging to many clinicians.

MRI has become an important adjunct in the decision-making process. Advances including 3 Tesla magnets and improved software have increased the sensitivity and specificity of locating likely sites of prostate cancer. The first version of the Prostate Imaging-Reporting and Data System (PI-RADS v1) was published in 2012. Further refinements have improved accuracy and decreased inter-observer variation since. These advances have helped increase the likelihood of tumor detection and staging [1]. The specific definition of the various PI-RADS findings are as follows:

PI-RADS 1: Clinically significant disease is highly unlikely to be present;

Pi-RADS 2: Clinically significant disease is unlikely to be present;

PI-RADS 3: Clinically significant Cancer is equivocal (intermediate risk);

PI-RADS 4: Clinically significant cancer is likely to be present;

PI-RADS 5: Clinically significant cancer is highly likely to be present.

The mpMRI can be used to help target a suspicious MRI lesion, maximizing the likelihood of the biopsy obtaining tissue from the area of interest [2] [3] [4].

2. Materials and Methods

Exempt status was granted on August 2, 2021, by the Clinical Research Review Committee of Lowell General Hospital [5]. After de-identification, a retrospective analysis was performed of all MRI-fusion guided biopsies performed between October 16, 2017, and November 15, 2021, numbering 320 in total. Patients were excluded unless the maximal PI-RADS score was 3 or higher, and appropriate follow-up information and demographic data were complete. A total of 312 evaluable patients were ultimately included. Data were obtained regarding

age, ethnicity, pre-biopsy serum PSA level (ng/ml), maximum PI-RADS score obtained on a multiparametric MRI, and calculated PSA density (PSAD) expressed as ng/ml/cc), and the final pathology results. PSA was determined using a Qualigen Therapeutics FastPack PSA system (Qualigen, Carlsbad, CA). If the initial PSA at the time of referral came from another institution, it was generally repeated using the Qualigen system for consistency. A decision to proceed with an mpMRI, and/or ultimately to an MRI-guided prostate fusion biopsy, was made by the patient and their Urologist after a discussion of the risks and benefits. All Urologists were in the same single specialty department at the hospital. Many patients with a PI-RADS 3 finding ultimately elected to not undergo biopsy. This report focuses only on the patients who were biopsied.

MpMRI studies were performed on a Siemens Magnetom Skyra (3 Tesla) device (Siemens USA, Washington DC), utilizing multiplanar T2W sequences with diffusion-weighted imaging and dynamic contrast-enhanced sequences prior to and following the intravenous administration of Dotarem without the use of an endorectal coil. All studies were read by Radiologists with subspecialty training in abdominal imaging. If the decision was made to proceed with an MRI-guided fusion biopsy, three-dimensional segmentation of the prostate gland with mapping of any prostatic lesions was performed on a separate workstation. All prostate fusion biopsies were performed in a trans-rectal fashion using an ARTEMIS 3D Semi-Robotic Prostate Fusion Biopsy System (InnoMedicus, Ltd, Switzerland) under either general anesthesia or deep sedation by an experienced Urologist. All specimens were reviewed by several Pathologists. Pathologic findings included Gleason score, presence, or absence of perineural invasion, concurrent prostatitis, atypical small acinar cell proliferation and presence or absence of Gleason 4 pattern cribriform morphology (which suggests a poorer prognosis). As the description of cribriform pathology was developed during the study period, our Pathologists re-reviewed all the PI-RADS 3 patients whose biopsies contained Gleason 4 areas for the presence or absence of cribriform change, allowing a more contemporary comparison between studies obtained early in the observation period to later specimens.

3. Results

A total of 312 evaluable patients were identified with PI-RADS scores of 3, 4 or 5, (32 patients with PI-RADS 3, 197 with PI-RADS 4 and 83 with PI-RADS 5). Only maximal PI-RADS score were used for analysis. If prostate cancer was identified, the highest Gleason score was reported. Many patients had a component of benign hyperplasia (BPH) in the transitional zone (not separately reported). Significant BPH is recognized as a possible factor accounting for a higher PSA score, as is the presence of prostatitis. In **Figure 1**, the overall characteristics of the entire study group are summarized. Note the associated trend towards higher average PSA values, higher age, higher PSA density and higher likelihood of identifying cancer as the maximal PI-RADS scores increase.

We then further analyzed the specific subgroup of patients with a maximal MRI finding of PI-RADS 3 as shown in Figure 2 and Figure 3.

A total of 34% of the patients with PI-RADS 3 were found to have prostate cancer ≥ Gleason score 3 + 3) with 15.6% demonstrating Grade Group 2 (Gleason grade 3 + 4) or higher on MRI-guided fusion biopsy. Patients having a prior diagnosis of prostate cancer in the past on active surveillance and not found to have cancer currently (n = 2) were excluded. Twelve out of the 32 patients had new findings of cancer: one patient demonstrated Gleason 4 + 4 adenocarcinoma, two patients demonstrated Gleason 4 + 3 adenocarcinoma, two patients demonstrated Gleason 3 + 4 adenocarcinoma, and seven patients demonstrated Gleason 3 + 3 adenocarcinoma (one in active surveillance). Of patients who eventually underwent surgical treatment, concordance of the final pathology with the preoperative biopsy results was high, although one patient with initial Gleason 3 + 3 was upgraded to Gleason 3 + 4. Six patients identified with cancer

Maximal PI-RADS Score	Average PSA (ng/ml)	Average Age (years)	PSAD*	Percent Cancer Identified
3 (n = 32)	8.16	64.6	0.167	34%
4 (n = 199)	9.55	66.8	0.30	68%
5 (n = 73)	9.74	78.6	0.55	89%

* PSAD = PSA/volume of prostate, expressed as ng/ml/cc

Figure 1. Overall characteristics of study group.

PSA	AGE	PI-RADS VERSION	RACE	FAMILY HISTORY?	PRIOR BIOPSY?	PSAD	IN AS?	+Bx MATCHES MRI?	BIOPSY PATHOLOGY
9	75	2.0	White	Yes (prostate)	Yes (negative)	0.15	N/A	N/A	Prostatitis
9.8	68	2.0	Hispanic	No	Yes (negative)	0.18	N/A	N/A	Prostatitis
12	74	2.0	Asian	No	Yes (negative)	0.17	N/A	N/A	prostatitis
8.7	65	2.0	White	No	Yes (Prostate Cancer)	0.36	Yes	Yes	Extensive Gleason 3 + 3, + PNI
12.6	66	2.0	White	Yes (prostate)	Yes (ASAP)	0.13	Yes	Yes	Gleason 3 + 3, - (PNI) ASAP
5.0	69	2.0	White	No	Yes (negative)	0.14	N/A	N/A	High Grade PIN, prostatits
13.6	56	2.0	Asian	No	No	0.32	N/A	Yes	ASAP ("worrisome" for Cancer)
6.7	69	2.1	Hispanic	Yes (female breast)	Yes (negative)	0.17	N/A	Yes	Gleason 4 + 3, - PNI, prostatatitis
20.8	67	2.1	White	Yes (prostate)	Yes (negagive)	0.29	N/A	N/A	ASAP, High Grade PIN
11.9	62	2.1	White	No	Yes (negative)	0.2	N/A	NO	Gleason 3 + 4, - PNI, ASAP
13.8	62	2.1	White	Yes (female breast)	No	0.25	N/A	A/S	prostatitis
9.7	67	2.1	White	No	Yes (negative)	0.11	N/A	N/A	ASAP
7.6	60	2.1	Hispanic	Yes (prostate)	Yes (negative)	0.1	N/A	Yes	Gleason 4 + 3, - PNI, High grade PIN
2.5	63	2.1	White	Yes (prostate)	No	0.06	N/A	Yes	Gleason 3 + 3, - PNI, prostatitis
8.7	73	2.1	White	No	No	0.16	N/A	N/A	prostatitis
6.9	61	2.1	Asian	No	No	0.19	N/A	N/A	prostatitis
3.5	65	2.1	White	No	Yes (prostate cancer)	0.15	Yes	N/A	New biopsy: ASAP only
5.1	62	2.1	Hispanic	No	Yes (negative)	0.8	N/A	NO	Gleason 3 + 4, - PNI, prostatitis
13.5	76	2.1	White	No	Yes (negative)	0.13	N/A	N/A	prostatitis
4.4	62	2.1	White	No	No	0.09	N/A	N/A	prostatitis
5.7	67	2.1	White	No	No	0.09	N/A	N/A	prostatitis
5.7	60	2.1	Hispanic	No	No	0.08	N/A	N/A	High Grade PIN
20.2	76	2.1	Asian	No	Yes (negative)	0.24	N/A	N/A	prostatitis
5.1	71	2.1	White	No	No	0.08	N/A	Yes	Gleason 3 + 3, - PNI, ASAP
5.0	63	2.1	White	No	Yes (negative)	0.1	N/A	N/A	ASAP
0.86	54	2.1	White	Yes (female uterine)	No	0.02	N/A	N/A	Benign
2.9	37	2.1	White	No	No	0.16	N/A	N/A	Benign
6.2	54	2.1	White	No	No	0.11	N/A	N/A	prostatitis
6.8	63	2.1	White	Yes (female breast)	Yes (prostate cancer)	0.09	Yes	Yes	Gleason 3 + 3, - PNI, prostatitis
6.8	67	2.1	White	No	No	0.11	N/A	N/A	prostatitis
5.0	57	2.1	White	Yes (prostate)	No	0.08	N/A	Yes	Gleason 3 + 3, - PNI, prostatitis
10.6	75	2.1	White	No	No	0.06	N/A	Yes	Gleason 4 + 4, - PNI, cribriform pattern, prostatitis

PSAD=PSA/prostate volume (ng/ml/cc), PNI = perineural invasion, PIN=prostatic intraepithelial neoplasia, ASAP=atypical small acinar cell proliferation, AS=active surveillance

Figure 2. Characteristics of maximum score PI-RADS 3 patients.

Age	PSA	Family History	PSAD*	MRI fusion Bx Pathology	Additional Pathology Comments	Treatment
63	6.8	Yes (female breast)	0.09	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
71	5.1	No	0.08	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
57	5.0	Yes	0.08	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
62	5.1	No	0.8	Adenocarcinoma	Gleason 3 + 4, - Cribriform pattern	Radiation Therapy
65	8.7	No	0.36	Adenocarcinoma	Extensive Gleason 3 + 3, + perineural invasion, upgraded to 3 + 4 on	radical prostatectomy
66	12.6	Yes	0.13	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
69	6.7	Yes (female breast)	0.17	Adenocarcinoma	Gleason 4 + 3, - cribriform pattern	Radiation Therapy
65	3.5	No	0.15	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
60	7.6	Yes	0.1	Adenocarcinoma	Gleason 4 + 3 (60% 4), + cribriform pattern, + perineural invasion	Radical Prostatectomy
75	10.6	Yes	0.08	Adenocarcinoma	Gleason 4 + 4	Active Surveillance
63	11.9	No	0.2	Adenocarcinoma	Gleason 3 + 3	Active Surveillance
62	11.9	No	0.2	Adenocarcinoma	Gleason 3 + 4, -perineural invasion, ASAP	Radiation Therapy

* PSAD = PSA/volume of prostate, expressed in ng/ml/cc,

ASAP = Atypical Small Acinar Cell Proliferation

Figure 3. Management decision as of 2022 for PI-RADS 3 Patients with cancer.

had concurrent findings of prostatitis (see **Figure 2**), yet their average PSA was lower than the group, suggesting that this alone did not prompt the biopsy. Patients with cancer in the PI-RADS 3 group had a lower PSAD average than those without cancer (0.137 (ng/ml/cc) vs 0.21). Four of the twelve cancer patients had a family history of prostate cancer, whereas an additional two patients had a family history of female breast cancer. Gleason 4 with cribriform morphology was not initially reported during the early years of this study but was included in the results after pathologic re-review, as it generally conveys a poorer prognosis [6]. As regards treatment, as of this writing in 2022 six patients are in active surveillance protocols, three elected to be treated with external beam radiation therapy, and three proceeded with robotic assisted laparoscopic prostatectomy. As seen in **Figure 2**, we noted a high correlation with positive biopsy findings in the areas identified as PI-RADS 3 (10 of 12).

4. Discussion

This project demonstrates our experience in a large community hospital with the management of patients with a maximal mpMRI PI-RADS score of 3. This is a common finding on MRI, and often presents a challenge for the treating physician and patient as to whether to proceed with a biopsy. Although our sample size is relatively small, we believe that this is the result of progressive stratification during the workup process for PSA elevation using mpMRI. Our group of 7 Urologists in a single large community hospital required 4 years to find 32 cases of PI-RADS 3 patients that were biopsied. In many communities based on prior studies, the finding of a PI-RADS 3 result typically reduces the likelihood of the offer of a biopsy. We believe that this study had to be done in a retrospective fa-

shion. We did not feel that it would be ethical to perform a prospective study where a group of men with PI-RADS 3 would receive a biopsy and then be compared to a group that did not. As expected, there appeared to be a significant likelihood of finding cancer in patients with mpMRI PI-RADS 4 or 5, and almost no patients were reported as PI-RADS 1 or 2. We noted a positive correlation of an increased pre-biopsy average PSA of patients with a finding of cancer. Of the remaining far smaller group that were found to have PI-RADS 3, and elected to proceed with biopsy, we identified a 34% chance of finding any prostate cancer in this group, with 5 of the 12 biopsies containing elements of Gleason grade 4 (Grade Group 2 or higher) (including one with Gleason pattern 4 cribriform morphology). Radiologists occasionally report a "predicted PSA" on mpMRI reports, based on the measured volume of the prostate, assuming that larger glands will likely produce more PSA. (A PSA density (PSAD = PSA/prostate volume) of 0.12 ng/ml/cc is used to predict the expected PSA score). PSAD has been studied as an independent predictor of the likelihood of finding cancer on biopsy, with higher values conferring a higher chance of cancer [7] [8] [9]. We noted the average PSAD in PI-RADS categories 3, 4 and 5 were higher than the "predicted" PSA, confirming this association. Increasing age also predicted a higher chance of finding cancer.

In the interpretation of prostate MRI, the possibility of inter-observer variation between Radiologists must also be considered. A recent meta-analysis attempted to address this issue, finding good inter-observer agreement in interpretation of PI-RADS scores of 4 or 5, as compared to lesser, but still generally acceptable agreement in the interpretation of PI-RADS 3 [10]. We noted a strong correlation of positive cancer findings in PI-RADS 3 lesions, suggesting that our experience parallels that of centers of excellence.

The racial composition of our cohort paralleled the surrounding towns. An ethnic estimation of the overall geographic study area consists of 54.3% White (non-Hispanic), 25.6% Asian, and 18.1% Hispanic. Black or African Americans make up a relatively small percentage. In our PI-RADS 3 group, there were 23 White patients (72%, of whom 9 had cancer), 5 Hispanic men (16%, of whom 3 had cancer), and 4 Asian men, of whom none had cancer. No Black men in the entire study group had a PI-RADS 3 score: however, all 7 Black men in the PI-RADS 4 group were found to have cancer, and the average PSA was 11.7, which was higher than the overall study population for PI-RADS 4 patients. It is unclear whether this suggests a selection bias for Black men being referred for Urologic consultation until their average PSA is higher than the rest of the population or other unidentified factors. One Black man had a PIRADS score of 5 and was also found to have cancer on biopsy.

For clinicians, several challenges exist. While many organizations advocate some form of screening for prostate cancer (at least with a PSA test) for patients between the approximate ages of 50 and 70 - 75, the best methods for this are debated. Another challenge is deciding which cancers are "clinically insignificant" (*i.e.* unlikely to cause harm to the individual during their lifespan) and

which are "clinically significant" (*i.e.* likely to progress and produce morbidity or mortality during their lifetime). It is this latter group that should be offered treatment for cancer. Many men are now in active surveillance protocols, in which definitive treatment for the prostate cancer is not immediately undertaken unless evidence of clinical progression is noted. Routine follow up biopsies or follow up pelvic MRI) are frequently used to evaluate for the possibility of progression, in which case definitive treatment may be started. Prior studies have suggested that cancers identified on biopsies done for patients with a maximum score of PI-RADS 3 are associated with a low likelihood of clinically significant prostate cancer, defined as Gleason score 3 + 3 (Grade Group 1) [11]. Recently, however, several groups have questioned this, suggesting that clinically important prostate cancers may be missed with such an approach, particularly if other risk factors are present (older age, smaller median prostate size (which would correlate with a higher PSAD, such as found in our study) [12] [13]. These studies suggest that the size of the MRI-identified lesion did not have a positive correlation with the likelihood of finding cancer. These authors have called into question the frequent practice of not performing a biopsy for PI-RADS 3 lesions, finding that a higher than previously reported incidence of clinically significant prostate cancer may in fact be present. Findings of clinically significant prostate cancer (defined here as Grade group ≥ 2) may range as high as 27% for a first biopsy [10] [11]. Our data finds a significant percentage of all-grade prostate cancers (34%) in this group, with 5 of the 12 positive biopsies in the PI-RADS 3 group demonstrating a Gleason score of ≥6 (*i.e.* ≥Grade Group 2). This equates to the finding of "clinically significant" prostate cancer in 15.6% of all PI-RADS 3 findings on MRI.

The use of MRI will likely continue to increase, both at academic and community hospitals. This will lead to more findings of PI-RADS 3 cases, challenging Urologists who need to educate patients on the implications.

The newer literature has begun to suggest that the widespread practice of not offering a biopsy to a man with a PI-RADS 3 lesion may be short sighted, and that there are patients in this group that harbor clinically significant prostate cancer-thus excluding them from diagnosis simply based on an "equivocal" PI-RADS score. This may be an incorrect approach without including other factors that may favor a biopsy—PSA density is one such example [14]. We believe that our study is the only one of its kind that employed MRI-fusion guided biopsies for 100% of the study group, increasing the likelihood that the significant lesions identified on imaging were in fact the tissue that was sampled.

Finally, we note that most of the Urology practiced around the world is performed by community Urologists, and our large community hospital experience should add to the world's experience with this challenging diagnosis and management.

5. Conclusion

Our findings, as well as the evolving literature, suggest that only performing a

prostate biopsy on an MRI PI-RADS finding of 4 or 5 may miss some men who have clinically significant (*i.e.* Grade Group 2 or higher) prostate cancer. An individualized approach is highly advised, utilizing as many additional decision making factors as possible.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] PI-RADS—Prostate Imaging-Reporting and Data System (2019) Version 2.1. The American College of Radiology, the European Society for Urologic Radiology and the AdMeTech Foundation. https://www.acr.org/-/media/ACR/Files/RADS/Pi-RADS/PIRADS-V2-1.pdf

[2] Kasivasvanathan, V., Rannikko, A.S., Borghi, M., *et al.* (2018) MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. *The New England Journal of Medicine*, **378**, 1767-1777.

[3] Eklund, M., Jaderling, F., Discacciati, A., *et al.* (2021) MRI-Targeted or Standard Biopsy in Prostate Cancer Screening. *The New England Journal of Medicine*, **385**, 908-920. https://doi.org/10.1056/NEJMoa2100852

[4] Lee, A.Y.M., Chen, K., Law, Y.M., *et al.* (2021) Robot-Assisted Magnetic Resonance Imaging-Ultrasound Fusion Transperineal Targeted Biopsy. *Urology*, **155**, 46.

[5] Clinical Research Review Committee, Lowell General Hospital, a Member of Tufts Medicine, Lowell, MA.

[6] Chen, Z., Pham, H., Abreu, A., *et al.* (2021) Prognostic Value of Cribriform Size, Percentage, and Intraductal Carcinoma in Gleason Score 7 Prostate Cancer with Cribriform Gleason Pattern 4. *Human Pathology*, **118**, 18-29. https://doi.org/10.1016/j.humpath.2021.09.005

[7] Bruno, S., Falagario, U., D'Altilia, N., *et al.* (2021) PSA Density Help to Identify Patients with Elevated PSA due to Prostate Cancer Rather Than Intraprostatic Inflammation: A Prospective Single Center Study. *Frontiers in Oncology*, **11**, Article 693684. https://doi.org/10.3389/fonc.2021.693684

[8] Yanai, Y., Kosaka, T., Hongo, H., *et al.* (2018) Evaluation of Prostate-Specific Antigen Density in the Diagnosis of Prostate Cancer Combined with Magnetic Resonance Imaging before Biopsy in Men Aged 70 Years and Older with Elevated PSA. *Molecular and Clinical Oncology*, **9**, 656-660. https://doi.org/10.3892/mco.2018.1725

[9] Osses, D.F., Arsov, C., Schimmoller, L., Schoots, I.G., Van Lenders, G.J.L.H., Esposito, I., Remmers S., *et al.* (2020) Equivocal PI-RADS Three Lesions on Prostate Magnetic Resonance Imaging: Risk Statification Strategies to Avoid MRI-Targeted Biopsies. *Journal of Personalized Medicine*, **10**, Article 270. https://doi.org/10.3390/jpm10040270

[10] Park, K.J., Choi, S.H., Lee, J.S., *et al.* (2020) Interreader Agreement with Prostate Imaging Reporting and Data System Version 2 for Prostate Cancer Detection: A Systematic Review and Meta-Analysis. *Journal of Urology*, **204**, 661-670. https://doi.org/10.1097/JU.0000000000001200

[11] Liddell, H., Jyoti, R. and Haxhimolla, H.Z. (2014) mpMRI Prostate Characterized PIRADS 3 Lesions Are Associated with a Low Risk of Clinically Significant Prostate Cancer-A Retrospective Review of 92 Biopsied PIRADS 3 Lesions. *Current Urology*, **8**, 96-100. https://doi.org/10.1159/000365697

[12] Sheridan, A.D., Nath, S.K., Syed, J.S., *et al.* (2018) Risk of Clinically Significant Prostate Cancer Associated with Prostate Imaging Reporting and Data System Category 3 (Equivocal) Lesions Identified on Multiparametric Prostate MRI. *American Journal of Roentgenology*, **210**, 347-357. https://doi.org/10.2214/AJR.17.18516

[13] Schoots, I.G. (2018) MRI in Early Prostate Cancer Detection: How to Manage Indeterminate or Equivocal PI-RADS 3 Lesions? *Translational Andrology and Urology*, **7**, 70-82. https://doi.org/10.21037/tau.2017.12.31

[14] Tapia, M.F., Labra, A., Adlerstein, I., Olivares, J.P., Schultz, M., Silva, C., *et al.* (2019) Densidad de APE en pacientes PI-RADS 3. Un parámetro clínico útil para su manejo. *Revista Chilena de Radiología*, **25**, 119-127. https://doi.org/10.4067/S0717-93082019000400119