PICTORIAL ESSAY | Urogenital imaging

Prostate cancer imaging and diagnosis: A pictorial review with common and uncommon findings

George Agrotis[1], Katerina Vassiou[1], Ioannis Tsougos[2], Anastasios Karatzas[3], Vasilis Tzortzis[3], Marianna Vlychou[1]

[1]*Department of Radiology, University Hospital of Larissa, Greece*
[2]*Department of Medical Physics, University Hospital of Larissa, Greece*
[3]*Department of Urology, University Hospital of Larissa, Greece*

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ABSTRACT

The implementation of multiparametric magnetic resonance imaging (mpMRI) is considered the standard of reference for the diagnosis, staging, and surveillance of prostate cancer. There has been an increase in the number of studies performed, and it is becoming more common for normal and incidental findings to be detected. Also, an inadequate description of cancerous findings may not prompt appropriate patient management, whereas over-reporting of normal findings comes with risks for the patient. This review article aims to improve awareness, and present key imaging features seen on prostate MRI, ranging from common to rare and from benign to cancer, also presenting the latest biopsy strategies for prostate cancer diagnosis.

KEY WORDS | multiparametric magnetic resonance imaging, prostate, cancer

CORRESPONDING AUTHOR, GUARANTOR | Marianna Vlychou, e-mail: mvlychou@med.uth.gr
Department of Radiology, School of Health Sciences, Faculty of Medicine, University of Thessaly, Biopolis, 41110, Larissa, Greece

Introduction

Prostate cancer is considered the leading cancer type in men in European Union. Around 450,000 European men are diagnosed with prostate cancer yearly, and 107,000 European men die of prostate cancer. Recent data shows that it has overtaken colorectal cancer [1], and its mortality is higher than breast cancer in women. However, both cancers have shown an overall decline in their mortality rates over the past decades [2]. Epidemiologic data from Greece in particular, indicate a rising 17.1% (6217) new cases for 2020, comprising 13.2% of all cancers with a mortality rate of 8.7-12 per 100,000 males. It is now well established, that the main problem with prostate cancer is overdiagnosing and overtreating indolent adenocarcinomas, with no benefit whatsoever for the patient.

Although prostate imaging can be performed by various modalities, multiparametric magnetic resonance imaging has been proven to be the most effective method for locoregional detection and staging prostate pathology. Therefore, mpMRI is performed prior to prostate biopsy, with high sensitivity and negative predictive values of up to 95% for the exclusion of prostate cancer [3]. However, many false positive exams still undergo unnecessary biopsies.

Diffusion-weighted imaging (DWI) and quantitative apparent diffusion coefficient (ADC) maps are essential parts of mpMRI for identifying imaging characteristics of prostate cancer. Aggressive lesions with restricted diffusion and low ADC values correspond to highly cellular lesions with higher histologic Gleason Score (GS). Diffusion method is based upon the random motion of water molecules (Brownian motion) in biological tissues and is dependent on restricted motion caused by cellularity or fibrosis. Quantification of this restriction is measured by the Apparent Diffusion Coefficient (ADC) factor in order to classify suspicious lesions [4].

The aim of this pictorial essay is to review typical findings of prostate mpMRI imaging and fusion biopsy diagnosis, along with incidental findings encountered within our institution's experience.

MRI Imaging Protocol and Pathology grading

Our institution's imaging protocol is consistent with international recommendations, given in the Prostate Imaging-Reporting and Data System (PI-RADS) v2.1 document published by the American College of Radiology (ACR), European Society of Urogenital Radiology (ESUR), AdMeTech Foundation and is specially curated with the help of our Medical Physicists. It is performed on a 3T scanner with a 16-channel external body phase array coil. Pulse sequences include both large and small field of view axial, sagittal, coronal T2-weighted, axial diffusion-weighted (b0, b500, 800, 1000 and 1600s/mm2), ADC calculated maps and axial dynamic contrast-enhanced T1-weighted imaging. Endorectal coils and antispasmodics are not routinely used and are not featured in the examples presented in this article.

Table 1. Clinical sequelae of BPH [7]
Increased frequency of urination at night (nocturia)
Urgent need to urinate
Difficulty starting urination
Weak stream – dribbling at the end of urination
UTI infections
Haematuria

Regarding pathology, prostate cancer grades are described according to the Gleason Score**,** a system named for the pathologist who developed it in the 1960s. It has been accepted that cancerous cells from prostate gland fall into 5 distinct patterns as they change from normal cells to tumor cells. Cells grading corresponds to cancerous transformation from normal to high grade; therefore the higher the grade the more aggressive the pathology diagnosis.

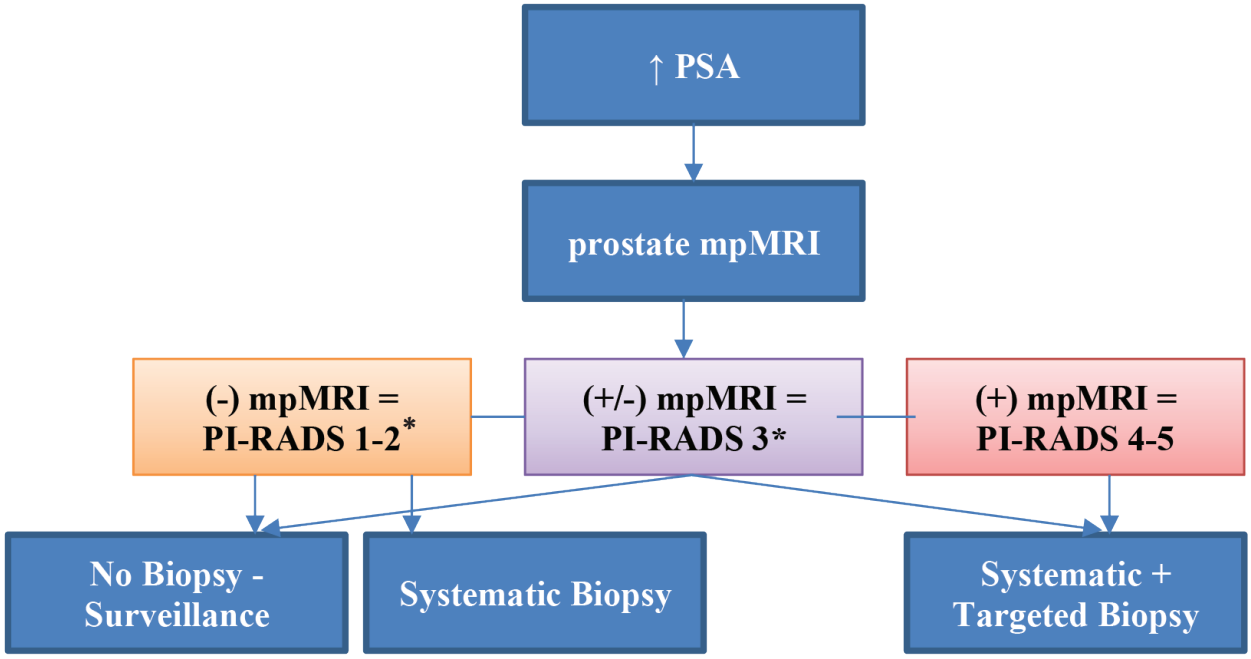
The standard pathology procedure for prostate cancer is formed in the following template: the biopsy sample will assign one Gleason grade to the most predominant pattern and a second Gleason grade to the second most predominant pattern. For example: 3 + 4. The two grades will then be added together to determine the final Gleason score. Based on pathology, Gleason scores range from 2 to 10. However, clinically insignificant prostate cancer is given a score of 6 and clinically significant cancer is given a score between 7 to 10. Subsequently, a Gleason score of 6 is low grade, 7 is intermediate grade, and a score of 8 to 10 is high grade prostate cancer.

Normal Findings – Anatomy

All following mpMRI images are from our pool data of patients.

Table 2. Imaging differentiation of Prostatitis and Prostate Cancer[9]		
	Prostatitis	PCa
Morphology	Triangular- wedge shape	Round
Contour	Sharp borders	Ill defined
DWI	Normal /mild restriction	Higher restriction
ADC	Normal/ mild hypointense	Marked hypointense
ADC Value	Intermediate low value	Low value
DCE	Uptake of contrast media	Uptake of contrast media

Table 3. Diagram of proposed biopsy protocol



*High/intermediate risk of PCa [14]
PSA density ≥ 0.15 ng/mL
Abnormal DRE
Family history of csPCa

The prostate gland is commonly referred to as a chestnut, due to its conical shape. It consists of a base (just below the urinary bladder), the midgland and the apex. There are four distinct histological zones that can be identified on mpMRI of the normal prostate; the peripheral zone (PZ), transition zone (TZ), central zone (CZ) and the anterior fibromuscular stroma (AFM). Glandular tissue mainly exists in the peripheral zone, thus 75% of prostate cancer originates here, and only 25% in the other zones (Fig. 1). As age increases benign prostate hyperplasia (BPH) occurs and transition zone is expanded, causing the central and peripheral zone to compress [5], with clinical symptoms and sometimes severe impact on the quality of life on men (Table 1).

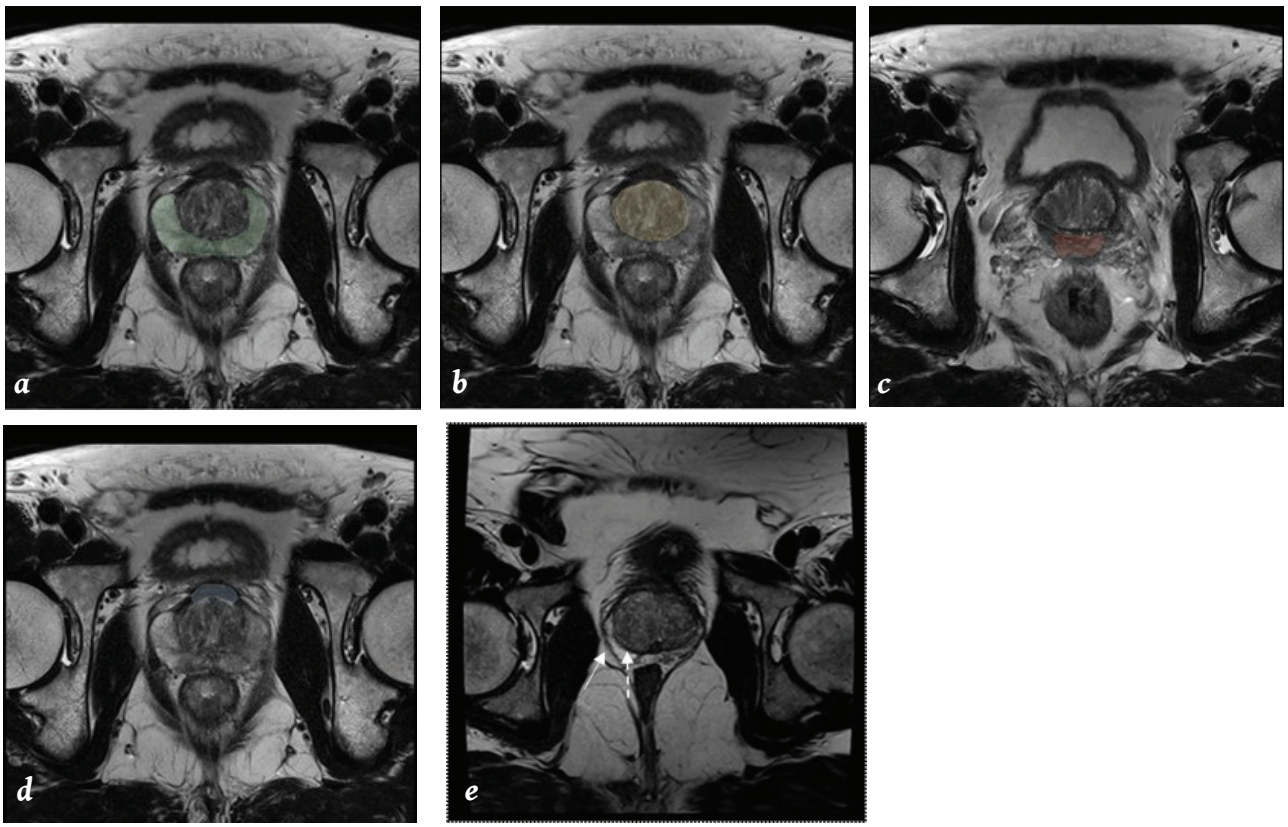


FIGURE 1 (a-e)
a) Peripheral Zone: 75% of cancers
b) Transition Zone: 20% of cancers
c) Central Zone: 5% of cancers
d) Anterior Fibromuscular stroma: can be secondarily infiltrated
e) Delineation of prostate gland by a thin line of fibrous tissue is shown as low T2 signal (arrow). A thin, low-intensity rim separates the peripheral zone from the transition zone, which is compressed prostate tissue (dotted arrow)

The prostate gland is surrounded by a thin layer of fibrous tissue that is identified as low signal on T2 images and is important for accessing extraprostatic extension of cancer

Prostate volume calculation is based on the ellipsoid formula. The ellipsoid formula is obtained by multiplying the height (anterior-posterior), width (medio-lateral) and length (cranio-caudal) values of the prostate by 0.52 (W×H×L×0.52). It is a reliable method for the assessment of prostate volume, with excellent intra- and interobserver agreement [6] .Caution should be given to accurate measure the volume by MRI to correlate with PSA level and calculation of the PSA density (PSA/prostate volume). Based on PIRADS v2.1 measurements should be taken as shown in the following images **(Fig. 1, Fig.2)** [5].

Common findings

Benign nodules – Benign Prostatic Hyperplasia (BPH)

Benign prostate hyperplasia is found in the transition zone due to response to testosterone levels. It is a mixture of stromal and glandular hyperplasia and can be found as "band-like" areas and/or "encapsulated round nodules with circumscribed or encapsulated margins". They can have variable signal in T2 images and can be easily distinguished by their signal intensity and borders. Some BPH can be highly vascular on after contrast media enhancement with various signal intensities on DWI. Dense nodules can show restriction of diffusion, finding that is not always considered malicious **(Fig. 3)**.

Some nodules can be contained inside other nodules

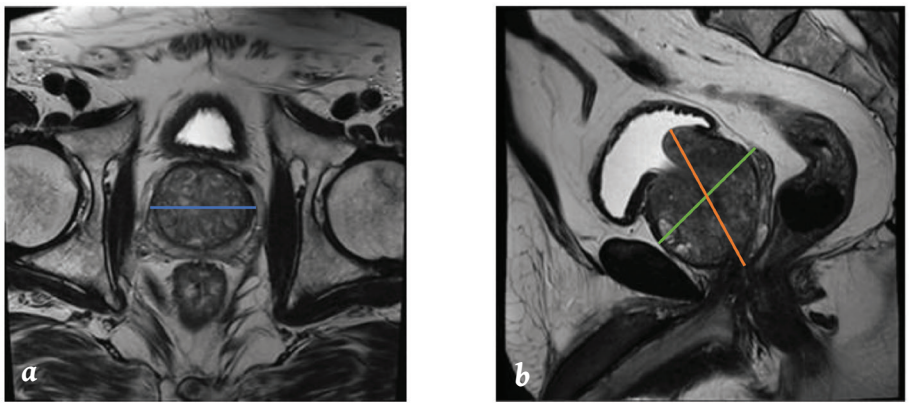


FIGURE 2 (a,b)
a) T2W mid axial image with maximum transverse diameter
b) T2W mid sagittal image with maximum anterior - posterior and craniocaudal diameter

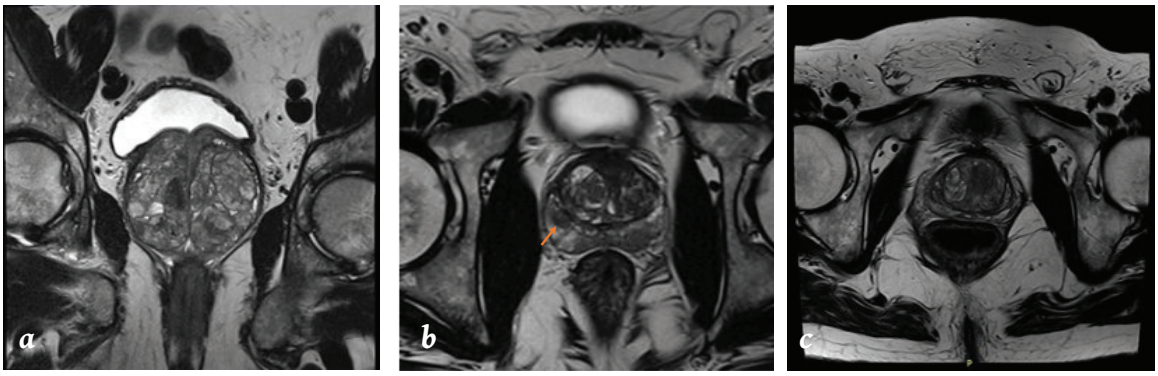


FIGURE 3 (a,b,c)
a) Most common findings of the transitional zone are encapsulated stromal nodules
b) Ectopic nodule in the peripheral zone (arrow).
c) Organized chaos – multiple benign nodules

(nodule in nodule). Typical appearance of TZ zone of what is called "organised chaos" with many stromal and glandular nodules, some contained in larger nodules (arrow). However, not all nodules exist in the TZ. Some can be ectopic and can be found in the peripheral zone. This entity shouldn't be confused with prostate cancer.

Haemorrhage

Low signal lesions in T2 images can represent blood products. These findings may adversely affect the interpretation of prostate MRI for staging and diagnosis. The presence of hemosiderin with well-established MR signal changes during time requires consideration regarding MR interpretation; therefore, an interval of at least 4-6 weeks or longer should suffice between biopsy and MRI for haemorrhaging artefacts to dissolve[8]. These findings can appear as focal or diffuse hyperintensities on T1W images and isointense or even hypointense signal on T2W images. Due to haemoglobin transitions, chronic blood can appear hypointense both in T1 and T2 images (**Fig.4**).

Cysts

Another common finding in the prostate gland are various types of cysts. Simple cysts contain clear fluid and are typically hyperintense on T2W images and hypointense on T1 images (**Fig.5**). Complicated or proteinaceous cysts can be of various signal intensity in T1 images.

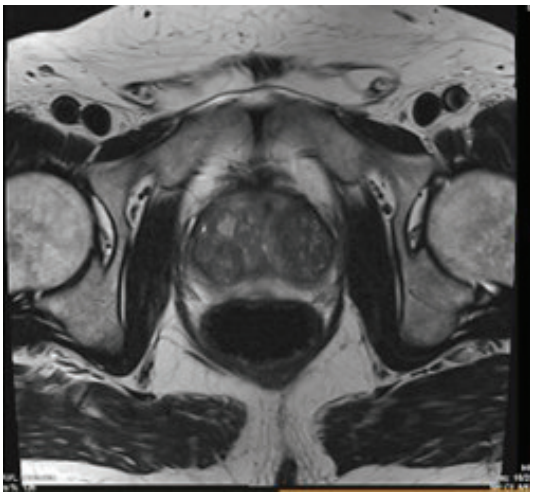


FIGURE 4
Focal hyperintensity on T1 image representing post biopsy blood product.

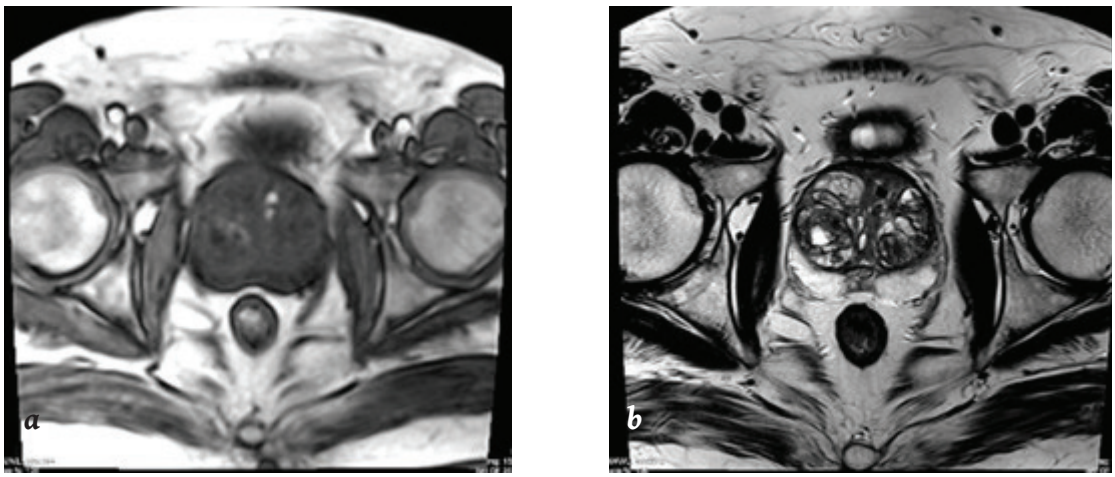


FIGURE 5
Prostate gland with multiple cystic changes, typically returning low signal on T1-w (a) and high signal on T2-w images (b)

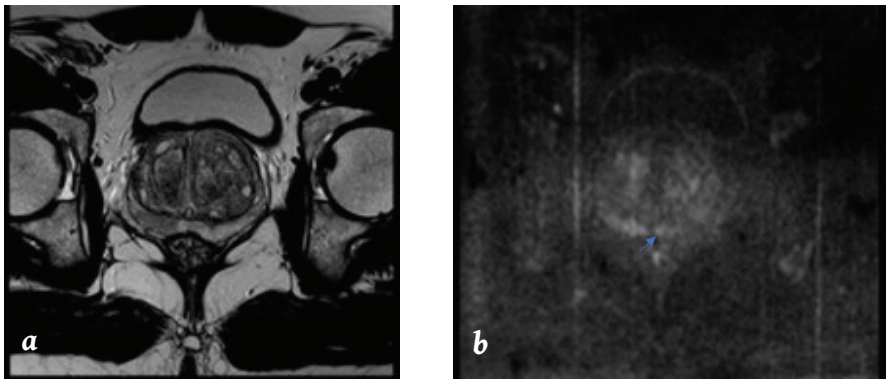


FIGURE 6
a)T2-w image shows a low intensity triangular lesion with b) mildly restricted diffusion in DWI. Fusion guided biopsy revealed an area of inflammation.

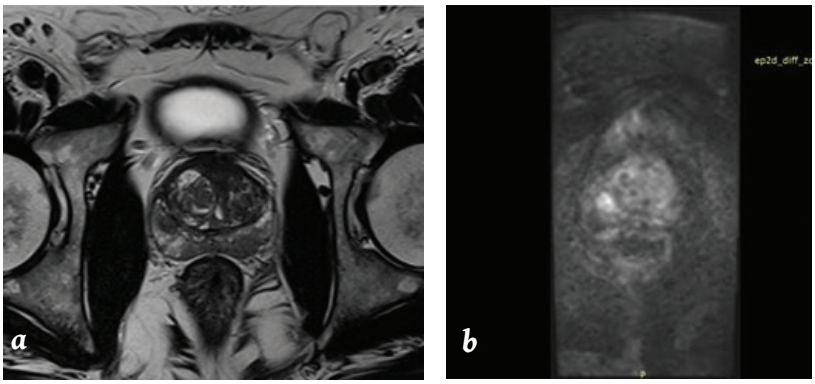


FIGURE 7

a) T2-w image shows a low intensity lesion with

b) highly restricted diffusion in DWI. Fusion guided biopsy revealed an abscess.

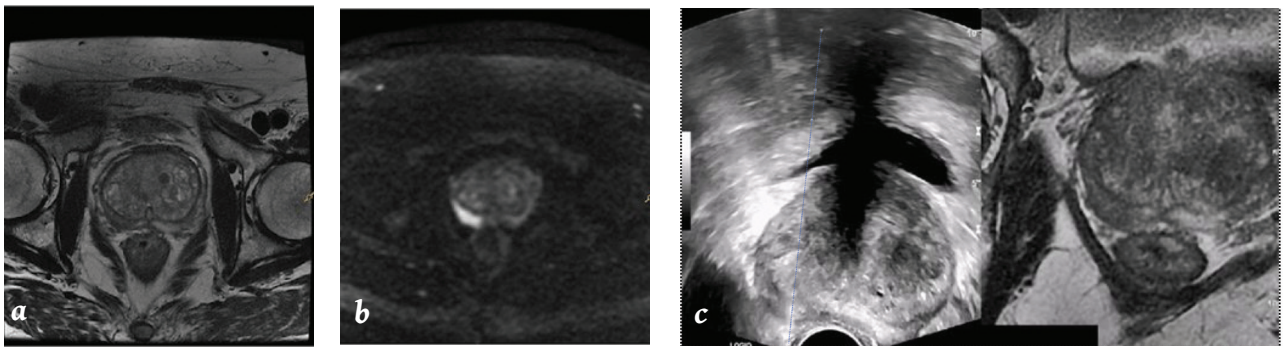


FIGURE 8a,b,c

a) T2W image with low-intensity lesion, b) DWI with highly restricted diffusion,

c) Fusion-guided biopsy revealed an area of adenocarcinoma Gleason 7 (4+3) Dotted blue line represents the track of the biopsy needle.

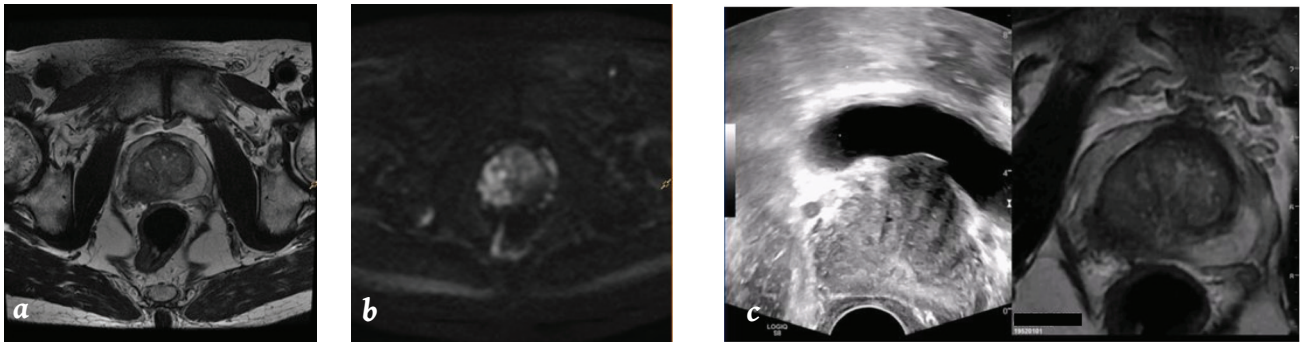


FIGURE 9

a) T2W image with low intensity lesion, b) DWI with highly restricted diffusion, c) Fusion guided biopsy revealed an area of adenocarcinoma Gleason 8 (4+4) with extraprostatic extension.

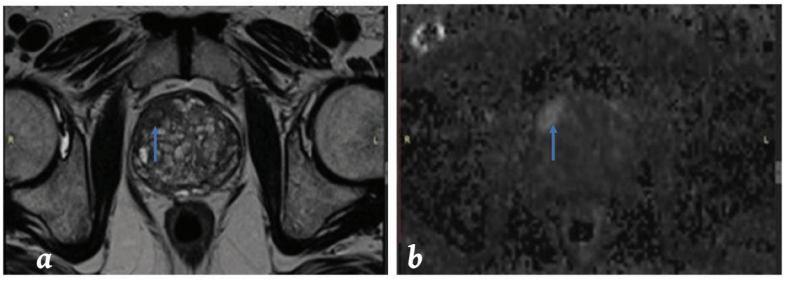


FIGURE 10

a) T2W image with low intensity lesion (arrow) b) DWI with highly restricted diffusion (arrow). Fusion guided biopsy revealed an area of high grade prostatic intraepithelial neoplasia.

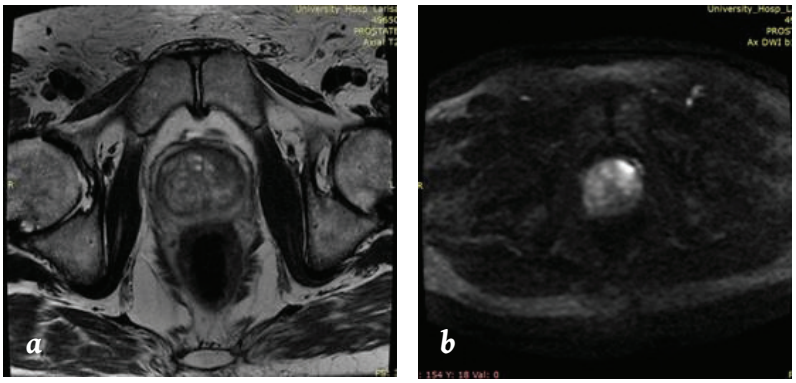


FIGURE 11

a) T2W with low intensity lesion, b) DWI with highly restricted diffusion, Targeted fusion guided biopsy revealed an area of adenocarcinoma Gleason 8 (4+4) whereas systematic biopsies showed Gleason 7 (3+4).

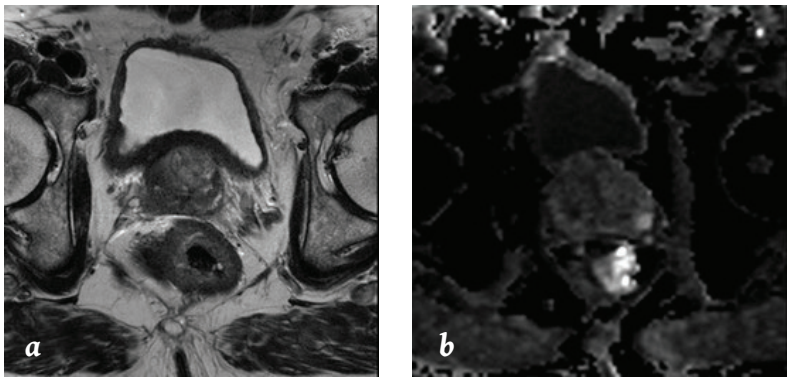


FIGURE 12

a) T2W image, on the left peripheral zone in the midgland a low-intensity lesion was found with DWI image with restriction of diffusion. This was an adenocarcinoma of Gleason 8 (4+4). b) Incidentally a lobulated polypoid mass was found on the rectum.

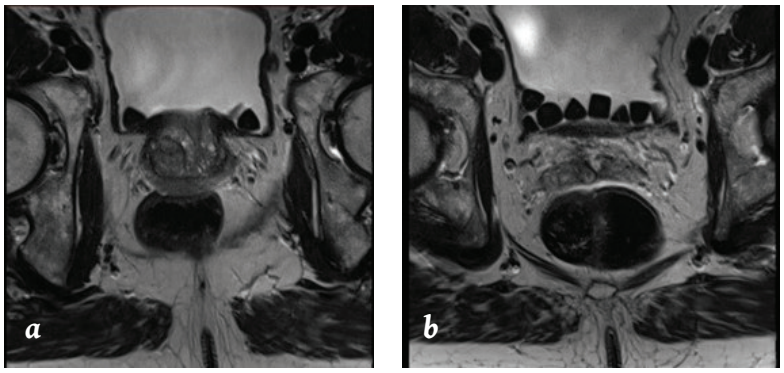


FIGURE 13

a) T2W images showing adenocarcinoma of Gleason 8(4+4) b) Incidental finding of urinary bladder stones.

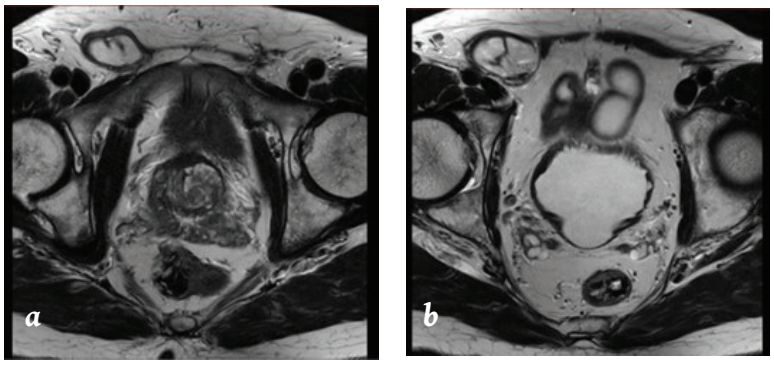


FIGURE 14

a) hypertrophicic anterior fibromuscular zone can be confused with a suspicious lesion. This is a normal finding. b) inguinal hernias, containing fat and intestines.

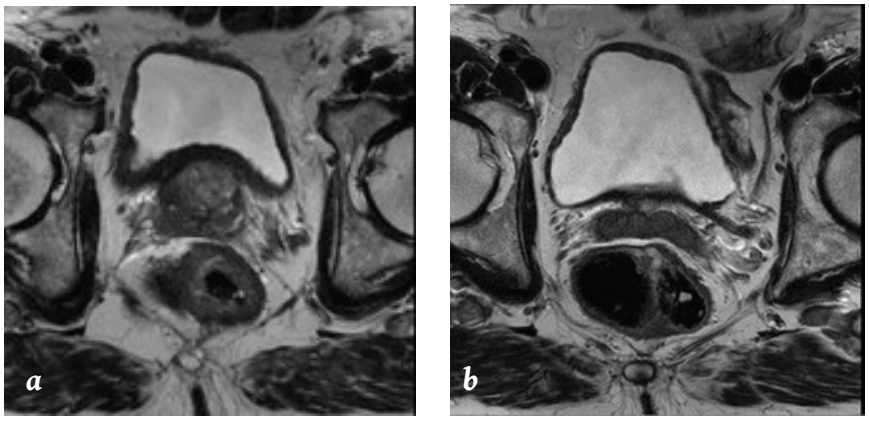


FIGURE 15

a) T2W axial images showing adenocarcinoma of Gleason 9 (4+5) on the right peripheral zone with EPE. b) There is also infiltration of the seminal vesicles, which are shown with diffuse low signal.

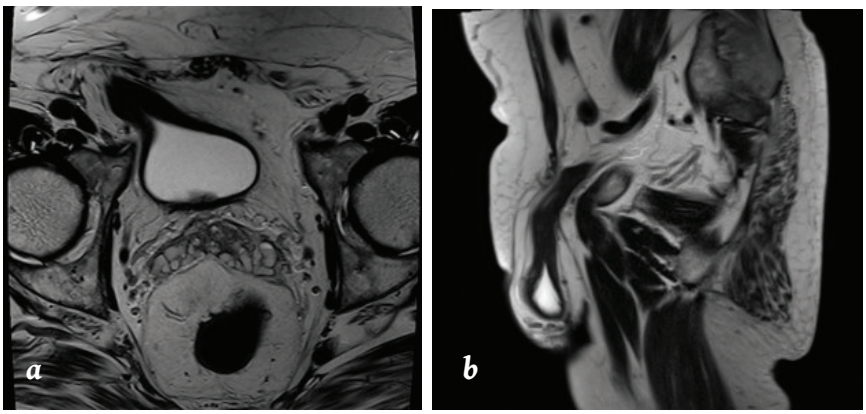


FIGURE 16

a) T2W axial and b) sagittal image from a prostate mpMRI with no suspicious findings of the prostate. b) a urinary bladder hernia was detected and reported.

Inflammation – Prostatitis

The biggest challenge for the radiologist is to differentiate inflammation of the prostate from prostate cancer, based on imaging characteristics. It is reported that prostatitis can appear with decreased signal on T2W images, show increased diffusion and low ADC values and show DCE uptake, creating many false positive results (Table 2). Based on PI-RADS terminology inflammation is presented with "morphology commonly band-like, wedge-shaped, or diffuse rather than focal, round, oval, or irregular". Corresponding changes; namely signal drop on the ADC map is generally not as pronounced nor as focal as in malignancy".

Case 1

From our series of biopsies, a patient aged 57 years old was referred to our department due to a raised PSA 9ng/ml, PSA density 0.07 and a score of PIRADS 5 due to a low intensity area in the right peripheral zone at the midgland, with restriction of diffusion and DCE enhancement. Diameter of the lesion was reported as 1.7cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method. Histopathology results showed chronic inflammation of the prostate and no cancer present. Careful re-examination of the imaging characteristics confirmed that the suspicious lesion was triangular and was consistent with an inflammatory lesion (**Fig.6**).

Case 2

A patient aged 70 years old, was referred to our department due to a raised PSA of 9ng/ml, PSA density 0.10 and a score of PI-RADS 5 was given, due to a low intensity area in the right peripheral zone at the midgland, with restriction of diffusion and DCE enhancement which showed vivid and peripheral enhancement of the lesion. Diameter of the lesion was 1.7cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method. Histopathology results showed abscess formations. Peripheral enhancement is typical imaging finding of an abscess (**Fig.7**).

Institutions Biopsy Protocol

There are a lot of proposed methods in the literature regarding the biopsy of a suspicious prostate lesion. The European Association of Urology stated in proposed guidelines that both targeted, MRI guided and systematic prostate biopsies should be performed [10]. Similarly, the American Urological Association recommends personification of the method based on the patient [11]. UK's National Institute for Health and Care Excellence guidelines recommend biopsy only of the suspicious lesion. The PI-RADS v2 Steering Committee recommends biopsy of the ROI and surrounding perilesional tissue when evaluating PI-RADS 4 and 5 lesions, but addition of systematic biopsy when evaluating PI-RADS 3 lesions [12].

The diagnostic protocol followed by our radiology department, is consistent with the latest recommendations from European Association of Urology guidelines and Risk-based MRI-directed diagnostic pathway (Table 3). In case of an increased PSA value, men always undergo prostate mpMRI. Based on the results e.g. PIRADS 1,2 do not undergo biopsy, PIRADS 4,5 undergo both systematic and targeted biopsies whereas PIRADS 3 studies are discussed and clinically evaluated whether they should undergo a biopsy or be actively surveyed. Also, PIRADS cases 1,2 with high risk and high suspicion of PCa could undergo systematic biopsies [13 ,14].

Case 3

A patient aged 71 years old was referred to our department due to a raised PSA of 39ng/ml, PSA density 0.20 and a score of PI-RADS 5 was given due to a low intensity area in the right peripheral zone at the midgland, with restriction of diffusion and DCE enhancement. Diameter of the lesion was 1.8cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method. Histopathology results showed adenocarcinoma of Gleason 7 (4+3) **(Fig. 8)**.

Case 4

A patient aged 69 years old was referred to our department due to a raised PSA of 13.3ng/ml, PSA density 0.16 and a score of PI-RADS 5 was given due to a low intensity area in the right peripheral zone at the midgland with characteristics of extraprostatic extension There is distinct restriction of diffusion, DCE enhancement and the diameter of the lesion was 1.7cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method. Histopathology results showed adenocarcinoma of Gleason 8 (4+4) with extraprostatic extension **(Fig. 9)**.

Case 5

A patient aged 79 years old was referred to our department due to a raised PSA of 6.4ng/ml, PSA density 0.05 and a score of PI-RADS 4 was given due to a low intensity area in the right anterior TZ zone at the midgland. There is restriction of diffusion, DCE enhancement, diameter of the lesion was 1.2cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method.

Histopathology results showed of high grade prostatic intraepithelial neoplasia (HPIN) **(Fig 10)**. It should be noted that a repeat biopsy was performed after six months due to increased concern that clinical significant prostate cancer (csPCa) is present. Second biopsy also confirmed a HPIN lesion. Not all lesions scored based on PI-RADS criteria of >4, contain adenocarcinomas.

Based on recent meta-analyses the true positive predictive value of PIRADS 3 is 12%, PIRADS 4 is 48% and PIRADS 5 is 72% [15], whereas the negative predictive value of mpMRI is 95% [16]. In simple language, this means that a negative mpMRI can safely exclude csPCa, whereas caution should be given in positive mpMRIs due to heterogeneity in reporting and protocols.

Case 6

A patient aged 70 years old was referred to our department due to a raised PSA of 6.4ng/ml, PSA density 0.16 and a score of PI-RADS 4 was given due to a low intensity area in the left anterior TZ zone at the midgland. There is restriction of diffusion, DCE enhancement, diameter of the lesion was 1cm. Biopsy was followed in our department with the fusion guided software assisted mpMRI – TRUS method **(Fig 11)**.

In Case 6, systematic biopsy missed the more aggressive area of the adenocarcinoma, probably due to the difficult anterior location of the lesion. It is now well accepted that targeted biopsies can provide more to the diagnostic yield for the patient, identifying the "core" of the cancerous lesion. Performing systematic biopsies,

the needle could miss the area of cancer, or even detect an insignificant adenocarcinoma [17]. A recent study shows that overall of 90% of csPCa cores are found in a radius of 10mm from the region of interest, which is called the penumbra area [18]. This is a step forward towards the perilesional biopsies replacing the systematic method and becoming eventually the new standard of method combined with targeted biopsies, for performing prostate biopsies.

The main problems we came across trying to identify and biopsy prostate lesions, were mainly due to the learning curve of the procedure [19]. Also, limitations such as targeting problems/ software-registration problems, deviation of the needle, anterior lesions difficult to reach, large prostate volumes and the number of biopsy cores were also limiting factors. Also, it should be noted that not all prostate cancers are visible on MRI, especially mucinous subtypes [20,21].

Incidental findings in mpMRI

Case 7

Patient with a family history of prostate cancer, aged 69 years old and PSA value of 5.9ng/ml and PSA density of 0.15. On the left peripheral zone in the midgland a low intensity lesion was found with restriction of diffusion and low ADC values on the ADC map. This was an adenocarcinoma of Gleason 8 (4+4). Incidentally a lobulated polypoid mass was found on the rectum. These findings should always be reported (**Fig 12**).

Other incidental findings are shown in cases 8,9,10,11 (**Figs 13,14,15,16**).

Conclusions

The fundamental objective of prostate mpMRI is to detect clinically significant cancer in a standardized and repeatable manner. There are numerous potential applications that require extensive development and evaluation, including dynamic contrast media sequences and artificial intelligence. In the meantime, it is essential to enhance our existing standards by accurately utilizing PI-RADS criteria and up to date biopsy procedures, while also being mindful of potential challenges and limitations. This review provides a solid foundation for future upgrades, improve diagnostic outcomes, and ultimately increase patient and clinical acceptance.

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