

## Introduction

## Dear Participant,

With this Casebook for beginning readers, you will be able to test your skills in detecting "clinically significant" prostate cancer using PI-RADS version 2.1.

Ten cases are presented here.

This syllabus presents the clinical data and representative images: T2WI, DCE (T1WI with Wash-in overlay), ADC and calculated b-1400. Based on these you are invited to use the workstation and to make your diagnosis.

Please make your scoring for each modality separately: T2WI (5-point scale), DWI (5-point scale) and DCE (+ or -), and your final PI-RADS version 2.1 category assessment.
Please mention also if you see extraprostatic extension or seminal vesicle involvement.

At the end of each case, you will find a hyperlink, which will lead you to the "expert score" and the findings at pathology of MRI-guided biopsies, MR-US-fusion guided biopsies and/or TRUS biopsies and sometimes radical prostatectomy. In all cases, the offered therapy is presented.
Often an educational "message" will be presented too.

We hope that after these 10 cases you will be better able to recognize a clinically significant prostate cancer, and that you have improved your PI-RADS version 2.1 category assessment.

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The Radboud Prostate MR Expert (Reference) Center (PMRC) fights prostate cancer by optimizing diagnosis throughout the world. This center's expertise is in multi-parametric MRI of the prostate. Through research, innovation and education it develops and shares knowledge worldwide. The PMRC has built a Prostate MRI Network of more than 15 Centers of Excellence (CoE) worldwide. All CoE's have been educated to apply multi-parametric MRI of the prostate according to the highest quality guidelines that are set by the PMRC. The PMRC will continue to further expand and strengthen the Prostate MRI Network, while simultaneously continuing to develop the knowledge on MRI of the Prostate through scientific research and innovation.
For more information on the PMRC and Prostate MRI Network you can contact:
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## Radboudumc

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| Case Number Clinical history | 1.01 |
| :---: | :---: |
|  | 58-year-old male |
|  | Possible prostate cancer |
|  | PSA: $21 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 67 ml |
|  | PSAD: 0.31 (normal < 0.20) |
|  | Clinical stage: cT0 |
|  | No previous biopsies |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $>15 \mathrm{~mm}$ | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images



## Radboudumc

## Findings

T2WI: circumscribed, homogeneous, hypo-intense lesion in the left lateral peripheral zone midprostate to apex.
On the coronal T2WI the lesion can be seen to reach from mid-prostate into the apical region.
There is an elongated area of close contact with the overlying prostate capsule, with bulging and probably breaching.
On the sagittal T2WI you can find an enlarged pre-sacral lymph node, $10 \times 6 \mathrm{~mm}$.
DWI: the lesion is markedly hypo-intense on ADC (= 474; normal with our center's Siemens 3T Skyra and sequence is > 950) and markedly hyper-intense on high $b$-value DWI (b-1400).
In fact, the lesion remains bright too on the calculated b-1600, b-2000 and b-5000 images!

b1600

b2000

b5000

DCE: positive "focal enhancement".
The size of the lesion is: $12 \times 31 \times 15 \mathrm{~mm}$.

Link to answer Case 1.01

| Case Number Clinical history | 1.02 |
| :---: | :---: |
|  | 68-year-old male |
|  | Possible prostate cancer |
|  | PSA: $9.1 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 57 ml |
|  | PSAD: 0.16 (normal < 0.20) |
|  | Clinical stage: cT0 |
|  | No previous biopsies |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $>15 \mathrm{~mm}$ | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images



## Radboudumc

## Findings

T2WI: the left lateral peripheral zone mid-prostate has a diffused lower signal intensity. No real lesion visible. Slight bulging laterally on the left side.

DWI: strong diffusion restriction (minimal ADC = value: 346, normal >950), very bright on b-1400.

DCE: positive.

The size of the lesion, as measured on the ADC images, is $11 \times 9 \times 9 \mathrm{~mm}$.

Broad contact with the capsule (length 10 mm ), bulging, probably still intraprostatic, but minimal extraprostatic extension (EPE) is possible.
No signs of invasion into the neurovascular bundle.
No invasion of the seminal vesicles.

Link to answer Case 1.02

| Case Number | $\mathbf{1 . 0 3}$ |
| :--- | :--- |
| Clinical history | 57-year-old male <br> Significant lesion? |
|  | PSA: $5.4 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 47 ml |
|  | PSAD: 0.11 (normal $<0.20$ ) |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | >15 mm | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images



## Radboudumc

## Findings

T2WI: in nearly the whole peripheral zone of the prostate, an elongated area is found adjacent to the capsule, more on the right side than on the left.
This area has low signal intensity, the borders are mostly ill defined.

DWI: there is some diffusion restriction ( $A D C=902$, normal $>950$ ), not really bright areas on b-1400. There are some other dark areas in the vicinity on $A D C$, but these seem to be veins.

DCE: some enhancement, but not focal: negative.

No signs of extraprostatic extension (EPE).
No signs of invasion into the neurovascular bundle.
The seminal vesicles appear normal.

| Case Number Clinical history | 1.05 |
| :---: | :---: |
|  | 64-year-old male |
|  | Suspect digital rectal examination (DRE) |
|  | PSA: $4.6 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 28 ml |
|  | PSAD: 0.18 (normal < 0.20) |
|  | No previous (TRUS) biopsy sessions |


| Pl-RADS |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | T2WI | $\emptyset$ | DWI | ADC | $\emptyset$ | DCE | >15 mm | EPE | Overall |
| Lesion 1 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |
| Lesion 2 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |
| Lesion 3 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images

Lesion 1.


## Radboudumc

Lesion 2.


Lesion 3.


## Radboudumc

## Findings

## Lesion 1:

T2WI: ill-defined lesion in the right peripheral zone, from apex to base.

DWI: there is a bright signal on the $b-1400$ and a strong diffusion restriction (ADC $=600$, normal > 950).

DCE: positive.

The lesion measures $22 \times 10 \times 20 \mathrm{~mm}$.
There is a long contact with the prostate capsule and some bulging, especially laterally.
Broad contact with the base of the seminal vesicles, but no visible invasion.
b-1400 overlay:


Coronal
Sagittal
Axial

## Lesion 2:

T2WI: ill-defined lesion in the anterior horn of the left peripheral zone, at the apex of the prostate.

DWI: there is a bright signal on the $b-1400$ and a diffusion restriction (ADC $=799$, normal $>950$, at one slice lower a small area with a value of 753 can be found).

DCE: positive.

The lesion measures $13 \times 6 \times 9 \mathrm{~mm}$.
There is contact with the prostatic capsule over the entire length of the lesion and some suspicion of a breach on the anterior-lateral side:

## Radboudumc


b-1400 overlay:


## Lesion 3:

T2WI: ill-defined, streaky lesion in the left lateral dorsal basal peripheral zone.
This could be tumor, but also fibrosis.

DWI: small area with diffusion restriction ( $A D C=719$, normal $>950$ ), bright on $b-1400$ images.

DCE: positive.

The lesion measures $13 \times 6 \times 6 \mathrm{~mm}$.
There is contact with the left dorsolateral capsule at the level of the left neurovascular bundle, extraprostatic extension (EPE) thus cannot be excluded.

The seminal vesicles seem uninvolved.
b-1400 overlay:


Link to answer Case 1.05

## Radboudumc

| Case Number | 1.08 |
| :--- | :--- | :--- |
| Clinical history | 58-year-old male <br> Significant cancer? |
|  | PSA: $9 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 65 ml |
|  | PSAD: 0.14 (normal < 0.20 ) |
|  | Clinical stage: cT1 |
|  | No previous biopsy sessions |



## Images

Lesion 1.


## Radboudumc

Lesion 2.


Lesion 3.


## Findings

## Lesion 1:

T2WI: circumscribed, hypointense mass right peripheral zone mid-prostate at 8 o'clock and < 15 mm in greatest dimension, broad contact with surface, bulging, thickening of the neurovascular bundle on the right.
No invasion in the seminal vesicles.

DWI: restricted diffusion (minimal $A D C=459$, normal $>950$ ), high signal on high b-value images.

DCE: positive.

## Lesion 2:

T2W: small hypointense focus with indistinct margins right peripheral zone at 8 o'clock, at the junction of apex and mid-prostate.

DWI: restricted diffusion (minimal $A D C=663$, normal $>950$ ), bright on high b-value image.

DCE: negative.

The size of the lesion, measured on the DWI lesion: $6 \times 7 \times 8 \mathrm{~mm}$.

## Lesion 3:

T2WI: wedge shape area left peripheral zone at 4 o'clock.

DWI: somewhat low signal on ADC image (minimal ADC = 941, normal >950), not really markedly bright on b-1400.

DCE: some enhancement.

Link to answer Case 1.08

## Radboudumc

| Case Number | 1.09 |
| :--- | :--- | :--- |
| Clinical history | 62-year-old male <br> Significant cancer? |
|  | PSA: $5 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 42 ml |
|  | PSAD: 0.12 (normal $<0.20$ ) |
|  | Clinical stage: cT0 |
|  | No previous biopsies |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $\mathbf{> 1 5} \mathbf{~ m m}$ | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images



## Findings

T2WI: focal low signal intensity with ill-defined margins in the medial left peripheral zone, midprostate at 5 o'clock.

DWI: low signal on ADC-image (minimal ADC $=864$, normal $>950$ ), high signal on b-1400.

DCE: focal early enhancement: positive.

The size of the lesion is $8 \times 7 \times 12 \mathrm{~mm}$.
Normal neurovascular bundles.
No signs of extraprostatic extension (EPE).
Normal seminal vesicles.

## Radboudumc

| Case Number | $\underline{1.17}$ |
| :--- | :--- |
| Clinical history | 68-year-old male <br> Significant prostate cancer? <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br>  <br> PSA: $6.6 \mathrm{ng} / \mathrm{ml}$ <br> PSAD: 0.18 (normal $<0.20$ ) |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $>15 \mathrm{~mm}$ | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |



## Findings

T2WI: in the anterior transition zone, in the midline, there is a lesion with an erased charcoal aspect.

DWI: there is a bright signal here on the $b-1400$ and diffusion restriction (ADC $=585$, normal $>950$ ).

DCE: positive.

The size of the lesion as measured on the ADC images, is: $8 \times 9 \times 10 \mathrm{~mm}$.
No signs of extraprostatic extension (EPE).
As far as can be seen on these images:
No signs of lymph node metastases or bone metastases.
Link to answer Case 1.17

## Radboudumc

| Case Number | $\underline{1.21}$ |
| :--- | :--- |
| Clinical history | 64-year-old male <br> Significant prostate cancer? |
|  | PSA $10 \mathrm{ng} / \mathrm{ml}$ <br> Prostate volume: 65 ml <br>  <br>  <br>  <br>  <br>  <br> PSAD: 0.15 (normal $<0.20$ ) <br> Clinical stage: cT0 |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $\mathbf{> 1 5} \mathbf{~ m m}$ | EPE | Overall |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images



## Findings

T2WI: enlargement of the transition zone with protrusion into the bladder. The transition zone has the aspect of "organized chaos".
The peripheral zone is compressed.

DWI: No diffusion restriction on ADC, no focal high signal intensities on the b-1400 images.

DCE: No focal enhancing lesions.

The seminal vesicles are normal.
Normal aspect of the neurovascular bundles.

Link to answer Case 1.21

## Radboudumc

| Case Number Clinical history | 1.22 |
| :---: | :---: |
|  | 77-year-old male |
|  | 3 years previously: Gleason $3+3=6$ prostate cancer (MRI guided biopsy) |
|  | iPSA: $4.5 \mathrm{ng} / \mathrm{ml}$ |
|  | Active surveillance |
|  | PSA now: $6 \mathrm{ng} / \mathrm{ml}$ |
|  | Significant cancer? |
|  | Prostate volume: 44 ml |
|  | PSAD: 0.14 (normal <0.20) |


| Pl-RADS |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | T2WI | $\emptyset$ | DWI | ADC | $\emptyset$ | DCE | >15 mm | EPE | Overall |
| Lesion 1 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |
| Lesion 2 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images

Lesion 1.


## Radboudumc

Lesion 1 two years ago:


Lesion 2.



## Findings

## Lesion 1:

T2WI: in the left transition zone / AFS, prostate base, a lenticular lesion is seen, 11-1 o'clock.
The size of this lesion is $14 \times 17 \times 23 \mathrm{~mm}$. Two and three years ago this was $9 \times 15 \times 21 \mathrm{~mm}$. The lesion has thus grown in size.

DWI: the lesion shows progressive diffusion restriction (ADC $=660$ [previously 885, normal > 950]) and is bright on b-1400 images. The lesion thus seems more aggressive now.

DCE: positive.

## Lesion 2:

T2WI: in the right peripheral zone at 7 o'clock a focal lesion is now seen, previously this was diffuse, resembling prostatitis.

DWI: the lesion shows diffusion restriction ( $A D C=885$, normal $>950$ ) and is bright on b-1400.

DCE: positive.
The size of the lesion tumor (measured on the ADC images) is: $7 \times 14 \times 16 \mathrm{~mm}$.

## Radboudumc

There are no signs of EPE.
The seminal vesicles appear to be normal. Normal neurovascular bundles.

Link to answer Case 1.22

## Radboudumc

| Case Number Clinical history | 1.26 |
| :---: | :---: |
|  | 46-year-old male |
|  | Urinary tract infection and enlarged prostate on rectal examination |
|  | PSA: $18 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 47 ml |
|  | PSAD: 0.38 (normal < 0.20) |
|  | No previous biopsies |
|  | Clinical stage: cT3a (left) |


| PI-RADS |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | >15 mm | EPE | Overall |
| Lesion 1 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |
| Lesion 2 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images

Lesion 1.


Lesion 2.


## Findings

T2WI: nearly the whole left peripheral zone, most of the left transition zone and part of the bilateral AFS and anterior right transition zone is occupied by a diffuse hypo-intense lesion.

DWI: the lesion shows strong diffusion restriction (minimal $\operatorname{ADC}$ value $=430$, normal $>950$ ) and is bright on b-1400 images.

DCE: positive.
The size of this lesion $30 \times 39 \times 30 \mathrm{~mm}$.
There is definite extraprostatic extension (EPE).
The neurovascular bundle on the left is possibly involved, the seminal vesicles seem to be spared.

There is an enlarged lymph node with diffusion restriction (ADC = 478) anterior to the prostate on the left (Lesion 2), and a few enlarged lymph nodes in the right and left pelvis:

## Radboudumc



Link to answer Case 1.26

| Case Number | 2.07 |
| :---: | :---: |
| Clinical history | 75-year-old male |
|  | Significant pathology? |
|  | PSA: $14 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: 34 ml |
|  | PSAD: 0.41 (normal < 0.20) |
|  | No previous biopsies |


| Pl-RADS | T2WI | $\varnothing$ | DWI | ADC | $\varnothing$ | DCE | $\mathbf{> 1 5}$ <br> $\mathbf{m m}$ | EPE | Overall |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Lesion 1 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

Images


## Radboudumc

## Findings

T2WI: in the AFS / anterior transition zone base to mid-prostate, in the midline, an ill-defined hypo-intense lesion is seen.

DWI: there is a bright signal on the $\mathrm{b}-1400$ and on the ADC images diffusion restriction is found
(minimal ADC = 799, normal > 950).
DCE: positive.
The size of the lesion, as measured on the ADC images, is: $14 \times 13 \mathrm{~mm}$ as measured on the axial
plane.
There is probably no extraprostatic extension (EPE).
Normal neurovascular bundles.
Normal seminal vesicles.
Link to answer 2.07

| Case Number | $\underline{3.13}$ |
| :--- | :--- | :--- |
| Clinical history | 62-year-old male |
|  | PSA: $4.4 \mathrm{ng} / \mathrm{ml}$ |
|  | Prostate volume: $\mathbf{4 4} \mathrm{ml}$ |
|  | PSAD: $\mathbf{0 . 0 9}$ (normal $<\mathbf{0 . 2 0}$ ) |
|  | Significant lesions? |


| Pl-RADS |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | T2WI | $\emptyset$ | DWI | ADC | $\emptyset$ | DCE | >15 mm | EPE | Overall |
| Lesion 1 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |
| Lesion 2 |  |  |  |  |  |  |  |  |  |
| PZ |  |  |  |  |  |  |  |  |  |
| TZ |  |  |  |  |  |  |  |  |  |

## Images

Lesion 1.


## Radboudumc

Lesion 1a.


Sagittal T2WI

Lesion 2.


Lesion 2a.


Coronal T2WI

## Findings

## Lesion 1:

T2WI: caudal in the apex there is a slightly low signal area on the right side. Is this peripheral zone or transition zone?

DWI: the lesion is very bright on b-1400 and shows diffusion restriction (ADC $=648$, normal $>950$ ).

DCE: positive.

The size of the lesion (measured on the ADC images) is: $8 \times 5 \times 10 \mathrm{~mm}$. No signs of an EPE.
b-1400 overlay over the T2WI:


Coronal
Sagittal
Axial

## Radboudumc

## Lesion 2:

T2WI: there is an area of low signal intensity in the left dorsolateral peripheral zone or the left central zone.

DWI: this area is not very bright on $\mathrm{b}-1400$, but shows a diffusion restriction with a minimal ADC value of 669 (normal > 950).

DCE: negative.
The size of this lesion (as measured on the axial ADC images) is: $15 \times 11 \mathrm{~mm}$. No signs of an EPE.
Normal seminal vesicles.

## Radboudumc

## ANSWERS TO THE CASES

## Case 1.01:

## Diagnosis

Large significant prostate cancer in the left peripheral zone, probably with extraprostatic extension (EPE) and a suspect pre-sacral lymph node (PI-RADS 5).
Pl-RADS

|  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |

## Discussion / evaluation / histology

The findings fit best with a high grade, significant prostate cancer in the peripheral zone (PI-RADS 5, because the lesion measures $\geq 15 \mathrm{~mm}$ ).
When searching for prostate cancers, especially in the transition zone, DWI with low ADC / high signal on high and ultra-high b-value images, can be quite helpful.

## MRI-US Fusion guided biopsy:

In all 3 biopsies in the left PZ mid-prostate, 3 o'clock: PCa Gleason $5+4=9,60$ volume $\%$.
Epstein Prognostic Grading Group: 5.

## PET-CT F18 PSMA scan:

1. Prostate carcinoma left and right, especially on the left, with possible extraprostatic extension.
2. Lymph node metastasis pre-sacral. No signs of nodal metastases elsewhere.


No signs of distant metastases in bones or other organs.

## Therapy:

Curative intent:
Radiotherapy in combination with hormonal therapy.

## Radboudumc

## Teaching Point

Sometimes, when having to decide if a lesion is carcinoma or not, especially in the transition zone where differentiation between a stromal rich BPH nodule and a carcinoma can be very difficult, even higher b-values than the b-1400 can be of help. In this case, the lesion remains bright and is easily detected, even on the b-5000 images.

## Return

Case 1.02:

## Diagnosis

Intermediate to high-grade prostate cancer (PI-RADS 4).
PI-RADS

|  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 3 | DWI | 4 | DCE | + | Overall | 4 |

## Discussion / evaluation / histology

In the rest of the peripheral zone there is no suspicion of a significant cancer.
Mild BPH in the transition zone.

Spread out in the right seminal vesicle more than in the left, there are discreet areas of low signal intensity, most probably small calcifications.


## MRI guided biopsy:

I-III: prostate biopsies left lateral peripheral zone:
In 2/3 biopsies: adenocancer, Gleason score $4+4=8$, total length 9 mm .

Epstein Prognostic Grading Group: 4.

## TRUS biopsy:

I-VI left: no malignancy.
VII-XII right: no malignancy.
In the biopsies: focal atrophy and slight chronic inflammation.

## Radboudumc

## MRI Prostate Bone and Nodes:

No signs of bone metastases.
A few slightly enlarged lymph nodes in the left iliac region, metastases cannot be ruled out here.

## Therapy:

Radical prostatectomy with resection of the seminal vesicles:
Tumor I: (acinar) adenocancer, left lateral: Gleason score: $4+4=8$.
Size of the tumor: 12 mm
Extraprostatic extension (EPE): an area of 1 mm left dorsolateral mid-prostate.

Tumor II: (acinar) adenocancer, left dorsal and apex: Gleason score: 3+3=6.
Size of the tumor: 8 mm .

Tumor III: (acinar) adenocancer; left lateral: Gleason score: $3+3=6$.
Size of the tumor: 4 mm

Extraprostatic extension (EPE): present: an area of 1 mm left dorsal-lateral mid-prostate.
Seminal vesicles: no signs of a malignancy.
Invasion in bordering structures other than the seminal vesicles: none.
Resection margins: no tumor.

Regional lymph nodes on the right: no metastases.
Regional lymph nodes on the left: no metastases.
TNM classification (7e edition):
pT3aNORO

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## Radboudumc

## Case 1.03:

## Diagnosis

The findings strongly suggest a prostatitis.
Because of the minimal ADC value of 902 (normal in our center: $>950$ ) a minimal intermediate grade carcinoma cannot be excluded. (PI-RADS 3).

| PI-RADS |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 2 | DWI | 3 | DCE | - | Overall | 3 |

## Discussion / evaluation / histology

## MRI guided biopsy:

I-II: medial right peripheral zone mid-prostate: no signs of a malignancy.
III: lateral right peripheral zone mid-prostate: no signs of a malignancy.

## TRUS biopsy:

I-VI left: no malignancy.
VII-XII right: no malignancy.
In samples II, IV and XI a minimal, active inflammation is found.

## Follow-up:

PSA yearly, new MRI if PSA rises.

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## Case 1.05:

## Diagnosis

## Lesion 1:

Significant prostate cancer (PI-RADS 5) right peripheral zone, with possible minimal EPE.

## Lesion 2:

Significant prostate cancer (PI-RADS 4) left peripheral zone, with possible minimal EPE.

## Lesion 3:

Significant prostate cancer (PI-RADS 4) left peripheral zone, with possible minimal EPE.

## PI-RADS



## Discussion / evaluation / histology

## Lesion 1:

The findings are consistent with a significant, intermediate- or high-grade prostate cancer. The size of the lesion as measured on the ADC images, is: $22 \times 10 \times 20 \mathrm{~mm}$.
The lesion thus has to be classified as PI-RADS 5.
The lesion shows a broad contact with the capsule and some bulging, especially laterally.
There is therefore a suspicion of minimal extraprostatic extension.
Broad contact with the right seminal vesicle, without visible infiltration.

## Lesion 2:

The findings are consistent with a significant, intermediary- or high-grade prostate cancer.
The size of the lesion as measured on the ADC images, is: $13 \times 6 \times 9 \mathrm{~mm}$.
The lesion thus has to be classified as PI-RADS 4.
The lesion shows a broad contact with the anterolateral capsule, with some lateral bulging. Extraprostatic extension therefore cannot be excluded.

## Lesion 3:

The findings are consistent with a significant, intermediary- or high-grade prostate cancer. DWI is dominant in the PZ, so the lesion has to be classified as PI-RADS 4.
The lesion shows a broad contact with the dorsolateral capsule and the margin is irregular. Extraprostatic extension therefore cannot be excluded.

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## MRI-US Fusion guided biopsy:

## Lesion 1:

Peripheral zone right side mid prostate:
2 biopsies, both prostate cancer, Gleason score $3+4=7$, 95 volume\%.
Lesion 2:
Anterior horn peripheral zone apex left:
1 biopsy: prostate cancer, Gleason score $3+3=6,70$ volume\%.

Lesion 3:
Lateral peripheral zone left:
2 biopsies: both prostate cancer, Gleason score $3+3=6$, length $4 \mathrm{~mm}, 20$ volume\%.

Epstein Prognostic Grading Group: 2.

## Therapy:

Patient preferred radiotherapy to prostatectomy.
Treatment with radiotherapy on the prostate and proximal seminal vesicles with the VMATtechnique ( 10 MV ) up to a dose of $28 \times 2.5=70 \mathrm{~Gy}, 4 \times /$ week, biologically equivalent to 78 Gy in fractions of 2 Gy .

Three years later his PSA is down to 0.3 , no adverse effects.

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## Case 1.08:

## Diagnosis

## Lesion 1:

Significant cancer right lateral-dorsal peripheral zone with extraprostatic extension (EPE): PI-RADS 5.

## Lesion 2:

Small probably significant cancer, PI-RADS 4, right dorsal peripheral zone.

## Lesion 3:

Fibrosis/post inflammatory changes: PI-RADS 2.

## PI-RADS

| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 2 | DWI | 4 | DCE | + | Overall | 4 |
| T2WI | 2 | DWI | 2 | DCE | - | Overall | 2 |

## Discussion / evaluation / histology

## MRI-guided biopsy:

Lesion 1: Adenocancer Gleason $4+4=8$. Length $10 \mathrm{~mm}, 60$ volume\%.

Lesion 2: Gleason $3+3=6$ (with high cell density). Length $2 \mathrm{~mm}, 10$ volume\%.
Lesion 3: Fibrosis.
Epstein Prognostic Grading Group: 4.

## Therapy:

Unknown. The patient was treated elsewhere.


## Teaching Point

The size of lesion 1 should make it a PI-RADS 4 lesion, but because of the definite extraprostatic extension (EPE) this should now be scored as a PI-RADS 5 lesion.

Some low-grade Gleason $3+3=6$ lesions (e.g. lesion 2 ) have high cell density and thus have low ADC result in a PI-RADS 4 diagnosis, which is false positive for significant cancer.

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## Radboudumc

## Case 1.09

## Diagnosis

Significant prostate cancer (PI-RADS 4) lesion left peripheral zone.

| Pl-RADS |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 4 | DWI | 4 | DCE | + | Overall | 4 |

## Discussion / evaluation / histology

MR-US fusion guided biopsy:
Adenocancer Gleason score: $3+5=8$.

Epstein Prognostic Grading Group: 4.

## Therapy:

Unknown, patient was treated elsewhere.

## Return

Case 1.17:

## Diagnosis

Significant prostate cancer, PI-RADS 4.

| PI-RADS |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :---: |
| T2WI | 4 | DWI | 4 | DCE | + | Overall | 4 |  |

## Discussion / evaluation / histology

The findings fit well with a significant cancer in the anterior transition zone.
Lesions in the midline here are especially suspicious, as BPH nodules usually do not cross the midline, and if they do, their origin is usually easily distinguished.

## MRI guided biopsy:

In 2 of 3 biopsies: adenocancer, Gleason score $4+3=7,50$ volume $\%$.
In 1 of 3 biopsies: adenocancer, Gleason score $4+4=8$, 50 volume $\%$.
There is cribriforme growth.
No extracapsular extension.
Epstein Prognostic Grade Group: 4.

## MRI Prostate Bone and Nodes:

Aortic aneurism, 3.5 cm in diameter.
No signs of skeletal metastases.
No signs of nodal metastases.

## Therapy:

Radical prostatectomie, nerve sparing, with bilateral lymph node resection.
Tumor in the anterior transition zone, Gleason score $4+4=8$.
Residual tumor (R): RO: none.
Seminal vesicles: no tumor.
Regional lymph nodes on the right: 8 nodes, no metastases.
Regional lymph nodes on the left: 4 nodes, no metastases

Epstein Prognostic Grade Group: 4.
TNM classification ( $8^{\text {th }}$ edition UICC):
pT2NO.

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## Case 1.21:

## Diagnosis

Benign prostate hypertrophy (PI-RADS 1).

| PI-RADS |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 1 | DWI | 1 | DCE | - | Overall | 1 |

## Discussion / evaluation / histology

The findings fit best with extensive BPH in the transition zone.
In PI-RADS version 2, this was scored as PI-RADS 2.
In the new update, PI-RADS version 2.1, this is now scored as follows:
Since MRI findings of age-related BPH are present in the transition zone in almost all men undergoing prostate mpMRI for the assessment of clinically significant prostate cancer (csPCa), and typical BPH nodules are highly unlikely to harbor csPCa, findings of BPH alone are considered a normal variant in PI-RADS V2.1 and should be assigned a T2WI score of 1. These types of nodules do not have to be reported separately. Since every MRI examination should be assigned a PI-RADS assessment category of 1-5, when there are no findings with a PI-RADS assessment category of >1, the overall PI-RADS assessment category for the MRI examination should be reported as PI-RADS 1: clinically significant cancer is highly unlikely.

Turkbey B, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. Eur Urol (2019), https://doi.org/10.1016/j.eururo.2019.02.033

## TRUS biopsy:

I-VI on the left: no tumor.
VII-XII on the right: no tumor.
In the biopsies a chronic active inflammation with atrophy is found.

## Therapy:

Yearly follow-up PSA.

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## Case 1.22:

## Diagnosis

The findings fit with progressive size and aggression of the mass in the anterior transition zone/AFS at $11-01$ o'clock and of the mass in the peripheral zone at 7 o'clock, both mid-prostate (both PI-RADS 5).
Pl-RADS

| Lesion 1 |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |
| Lesion 2 |  |  |  |  |  |  |  |
| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |

## Discussion / evaluation / histology

## MRI- guided biopsy:

I. Prostate biopsies target (1) transition zone/AFS:

In 2/2 biopsies: (acinar) adenocancer, Gleason score $3+4=7 ; 80$ volume\%, total length 14.5 mm . No signs of cribriforme growth or of intraductal cancer (IDC-P).
II. Prostate biopsies target (2) right peripheral zone mid-prostate/apex:

In 1/2 biopsies: (acinar) adenocancer, Gleason score $3+4=7 ; 5$ volume\%, total length 1.0 mm .
No signs of cribriforme growth or of intraductal cancer (IDC-P).
Extra prostatic extension (EPE): not found.

Epstein Prognostic Grading Group: 2.

## MRI Prostate Bone and Nodes:

No bone metastases.
No enlarged lymph nodes.
Diverticulosis of the sigmoid

## Clinical stage:

cT1cN0M0

## Therapy:

Radiotherapy of prostate and proximal seminal vesicles with a VMAT-technique ( 10 MV ) up to a dose of $20 \times 3=60 \mathrm{~Gy}, 4 \mathrm{x} /$ week, biologically equivalent to 78 Gy in fractions of 2 Gy .
Prior to this treatment: implantation of gold markers for positive verification and -correction of the prostate during treatment; in addition, the use of an endorectal balloon to spare the anal-rectum region.

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## Case 1.26:

## Diagnosis

The findings fit best with very large, aggressive, prostate carcinoma (PI-RADS 5), with extra prostatic extension and possible lymph nodes metastases.


## Pl-RADS

| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

## Discussion / evaluation / histology

## MRI-US Fusion guided biopsy:

I- III: prostate biopsies left peripheral zone:
Extensive chronic active inflammation.
Histiocytic component present.
The findings are consistent with an incipient granulomatous prostatitis.
No signs of a malignancy.

## SelectMDX:

84\% chance of prostate cancer in biopsy,
$57 \%$ chance of a prostate cancer with a Gleason score $\geq 7$ in biopsy.

## Treatment:

The SelectMDX result was considered to be suspicious, so a follow-up of PSA and MRI was advised for after 6 months. In the meanwhile, he received antibiotics.
Patient came back 10 months later.
He had stopped the antibiotics early, because they didn't seem to help.
There was a regression of the lower urinary tract symptoms (LUTS) complaints. PSA was down from 18 to 5.3.

MRI after 10 months:

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## MRI Prostate nr. 2, 10 months after nr. 1:



The extensive lesion has resolved completely.

## Advice:

Yearly PSA check by General Practitioner.
If the PSA rises > 25 \% (to / over 6.6): referral to Urologist.

## Return

Case 2.07:

## Diagnosis

The findings initially seem to fit well with a significant prostate cancer, PI-RADS 4.
The size of the tumor (as measured on the ADC images) is $14 \times 13 \mathrm{~mm}$.
However, in one considers the cranial-caudal diameter of the tumor too, the largest diameter turns out to be 16 mm .


Sagittal T2WI with b1400 overlay
The tumor is thus upgraded from PI-RADS 4 to PI-RADS 5.

## Teaching Point

In mpMRI, the lesion should be measured in 3 dimensions, to avoid undergrading.

| PI-RADS |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| T2WI | 5 | DWI | 5 | DCE | + | Overall | 5 |

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## Discussion / evaluation / histology

MRI guided biopsy:
I-II: prostate biopsies AFS mid-prostate:
In 2/2 biopsies: adenocancer, Gleason score $3+4=7$, total length approximately 14 mm , 45 volume\%.
No perineural growth.
No signs of extraprostatic extension.
Epstein Prognostic Grading Group: 2.

MRI Prostate Nodes and Bone:
No nodal metastases.
No bone metastases.

Classification:
cT1cNOM0 Gleason $3+4=7$.

Therapy:
Advice: external radiotherapy or brachytherapy.
Patient chose brachytherapy.

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## Case 3.13:

## Diagnosis

## Lesion 1:

The findings fit best with a possible intermediate grade prostate cancer in the peripheral zone.
The differential diagnosis would be a protruding nodule from the apical transitional zone, but after examination of the sagittal images (see image Lesion 1a), it seems clear that this lesion does lie in the peripheral zone.
Hence the diagnosis is: probably significant PCa in the peripheral zone, PI-RADS 4.

## Lesion 2:

Again, one should look at this area from another anatomical point of view, in this case the coronal view (see Lesion 2a). Now this area looks quite well delineated. The images are somewhat asymmetrically taken, which makes a decision sometimes difficult. It is very important that images are symmetric!!
The findings best with a BPH in the central zone, the differential diagnosis can be a low-grade cancer (PI-RADS 2).

| Pl-RADS |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| T2WI | 3 | DWI | 4 | DCE | + | Overall | 4 |
| T2WI | 2 | DWI | 4 | DCE | - | Overall | 2 |

## Discussion / evaluation / histology

## MR guided biopsy:

I-II: right anterior horn apex: in 2/2 biopsies adenocancer, Gleason score $3+3=6$, total length 10 mm .


III: base peripheral zone/central zone left: no malignancy.

Epstein Prognostic Grading Group: 1.

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## TRUS biopsy:

1 biopsy in the left peripheral zone, mid-prostate: adenocancer, Gleason score $3+3=6,1 \mathrm{~mm}$.
The other 11 biopsies showed no signs of cancer.
Epstein Prognostic Grading Group: 1.

Patient complained of bone pains and insisted on further evaluation:

## MRI Prostate Bone and Nodes:

No bone metastases.
No enlarged lymph nodes.

## Therapy:

Patients choice: Radical prostatectomy, no active surveillance.
Radical prostatectomy, including the seminal vesicles:
Bilateral (acinar) adenocancer, Gleason score 3+4=7.
Extraprostatic extension (EPE): absent.
Seminal vesicles: no malignancy.
Resection margins: not free: apex right: 8 mm .

Epstein Prognostic Grading Group: 2.

TNM Classification ( $7^{\text {th }}$ Edition):
pT2cR+(8mm) NX.

3 years post-RALP:
PSA stable, < $0.1 \mathrm{ng} / \mathrm{ml}$.

## Teaching Point

1. It is important always to localize a lesion, is it in the peripheral zone, transition zone or is it the central zone? To do that one should examine a suspect lesion in different planes of the T2WI: (axial, coronal, sagittal).
In our protocol a coronal and sagittal series is made too and they should be studied carefully to decide where a lesion is in the peripheral zone or the transitional zone / central zone.
2. TRUS biopsy does find more cancers than MRI of the prostate would predict: in this case a cancer of the left dorsal peripheral zone, invisible on MRI. Usually, however, these additional tumors are not significant, low-grade cancers, and may result in patients' anxiety and/or overtreatment.

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## APPENDIX 2



Fig. 1 - PI-RADS version 2.1 assessment for the peripheral and transition zone.

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## APPENDIX 3:

## PI-RADS version 2.1: Assessment

In the technical part a few minor modifications were made:
In DWI it is, in order to decrease the vascular effect, now recommended not to use b-0.
The use of high b-value images (>1400) is mandatory. These images can either be acquired or calculated.
For the interpretation: DCE-MRI is a 2-point scale: "-" or "+" instead of a 5-point scale:

## PIRADS vs 2.1: DCE (both TZ \& PZ)

(-) No early enhancement, or diffuse enhancement not corresponding to a focal finding on T2 and/or DWI, or focal enhancement corresponding to a lesion demonstrating features of BPH on T2WI
(+) Focal, and earlier than or contemporaneously with enhancement of adjacent normal prostatic tissues, and corresponds to suspicious finding on T2 and/or DWI

## PIRADS vs 2.1: T2W: PZ

1 Uniformly hyperintense signal intensity (normal)

2 Linear, wedge-shaped, or diffuse mild hypointensity, usually indistinct margin

3 Heterogeneous signal intensity or non-circumscribed, rounded, moderate hypointensity

4 Circumscribed, homogenous moderate hypointense focus/mass confined to prostate and $<1.5 \mathrm{~cm}$ in greatest dimension

5 Same as 4 but $\geq 1.5 \mathrm{~cm}$ in greatest dimension or definite extraprostatic extension/invasive behavior

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## PIRADS vs 2.1: T2W: TZ

1 Homogeneous intermediate signal intensity or containing fully encapsulated heterogenous BPH-nodules
2 Circumscribed hypo-intense nodules or partially encapsulated heterogenous BPH nodules

3 Non-circumscribed non-encapsulated hypo-intense or heterogeneous nodules, or others than 1, 2, 4 or 5

4 Non-circumscribed, homogenous moderate hypointense, and $<1.5 \mathrm{~cm}$ in greatest dimension

5 Same as 4 but $\geq 1.5 \mathrm{~cm}$ in greatest dimension or definite extraprostatic extension/invasive behavior

## PIRADS vs 2.1: DWI (both TZ \& PZ)

1 No abnormality (i.e. normal) on ADC and high b-value DWI

2 Non-focal hypo-intense on ADC and/or non-focal hyper-intense on high b-value DWI

3 Focal mildly/moderately hypo-intense on ADC and isointense/mildly hyper-intense on high b-value DWI
4. Focal markedly hypo-intense on ADC and markedly hyperintense on high b-value DWI; <1.5cm on axial
5 Same as $\mathbf{4}$ but $\geq 1.5 \mathrm{~cm}$ in greatest dimension or definite extra-prostatic extension/invasive behavior

For the PI-RADS overall assessment one should use:

- for the Peripheral Zone the DWI sequence is dominant, and
- for the Transition Zone the T2W sequences are dominant (see tables on next page).


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## PI-RADS version 2.1 Assessment

Peripheral Zone (PZ)


For scoring, recommendations are provided concerning description of number of lesions, measurement of lesion (a-p x l-r x c-c $\times 0.53$ ) and lesion location.

The use of a 39 -sector scheme is recommended.
In this scheme the peri-urethral tissue and the Central Zone (CZ) are added compared to the PI-RADS version 1 scheme.

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## APPENDIX 4:

PI-RADS 3 Score settled: what's next?

## PI-RADS 3: <br> What do I recommend?

1. Very low no biopsy, no follow-up
2. Low no biopsy, repeat MRI if PSA 个

3 ) Intermediate PSAD < 0.12: f.u.; PSAD >0.15: MR-biopsy (20\%)
4 High MR-guided biopsy (40-80\%)
5 Very high MR-guided biopsy (70-95\%)
PI-RADS 3:

Also take into account clinical risk! High suspicion:

1. Venderink, Eur Urol 2017

- $\quad$ PSAD $>0.12^{1}$
- Free/Total PSA ratio <25\%
- Hereditary (incl. BRCA positive)
- Positive DRE

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