

## Supplementary Appendix 2: Detailed PRIME Biopsy Plans

To be pragmatic and allow results to be generalisable to biopsy practice around the world, biopsies can be performed transperineally (**Figures 1 and 2**) or transrectally (**Figures 3 and 4**) as per local practice. We split this Appendix into these sections, respectively.

If there is an MRI lesion (scores 3, 4 or 5 on *either* Likert or PI-RADS v2.1 scoring systems), then MRI-targeted biopsy and some limited contralateral systematic biopsy should be performed. MRI-targeted biopsy should be performed **first**, with 4 cores per suspicious area. Then the systematic biopsy cores should be taken but avoid taking biopsies from the same side of the prostate that targeted biopsies were taken from.

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## Systematic Transperineal Biopsy Schema

**Figures 1** and **2A-F** depict examples of how to perform the systematic biopsy in the **absence** of an MRI lesion and in the **presence** of MRI lesions, respectively.

### Non-suspicious MRI but a PSA Density of $\geq 0.15\text{ng/mL/mL}$ scenario

In patients with a **non-suspicious MRI but a PSA Density of  $\geq 0.15\text{ng/mL/mL}$** , 12-core systematic biopsy should be performed (**Figure 1**).

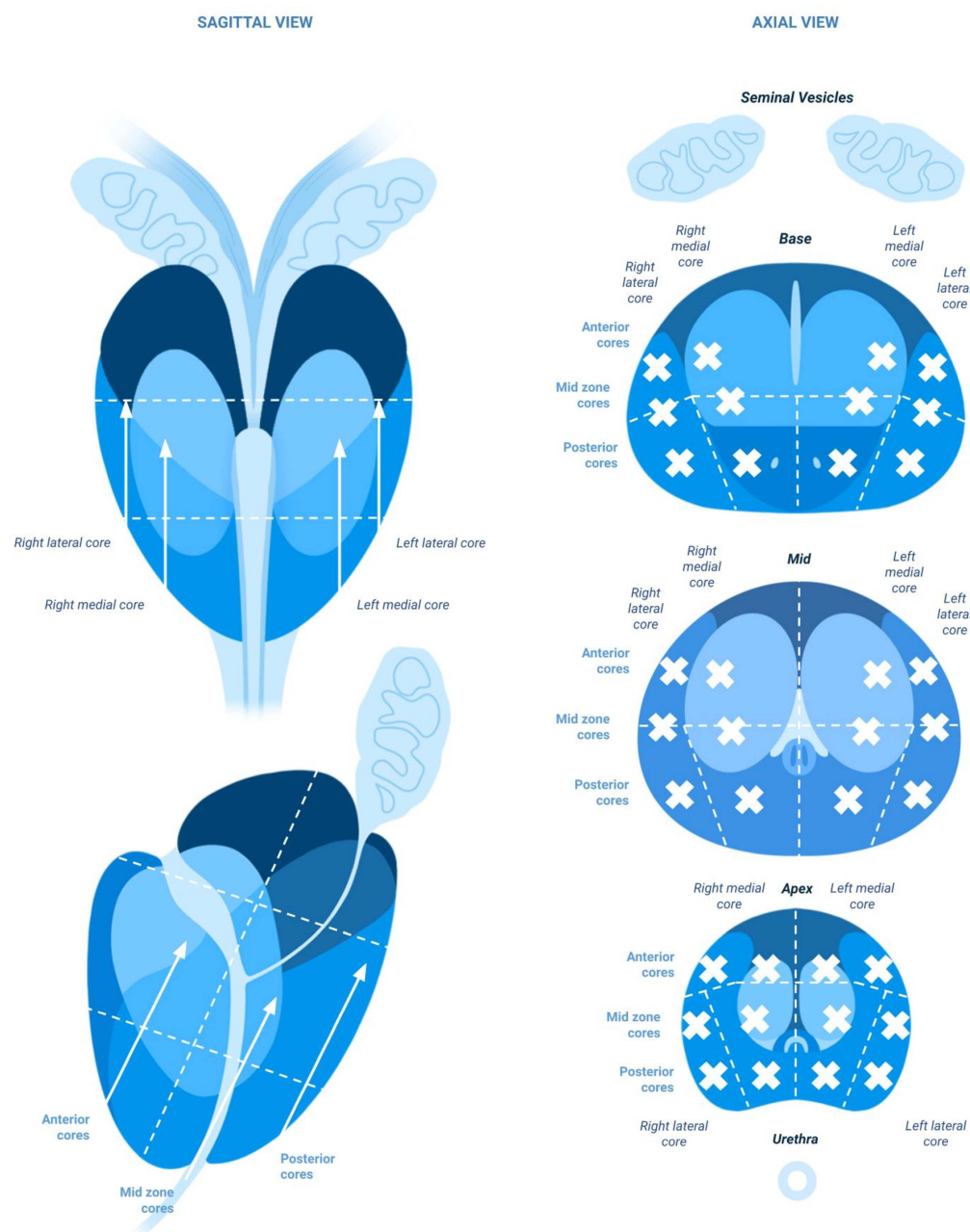
The number of systematic cores that should be taken per patient is **12**.

Systematic biopsy cores are taken from:

- Right anterior zone (2 cores)
- Right mid zone (2 cores)
- Right posterior zone (2 cores)
- Left anterior zone (2 cores)
- Left mid zone (2 cores)
- Left posterior zone (2 cores)

Systematic biopsy cores should be stored and labelled in a way that their **location** can be identified when the pathologist reports the result.

**Figure 1.** The transperineal biopsy schema for men with a **non-suspicious MRI** (scores 1 or 2 on both Likert and PI-RADS v2.1 scoring systems) *but* a PSA Density of  $\geq 0.15\text{ng/mL/mL}$ , undergoing 12-core systematic biopsy.

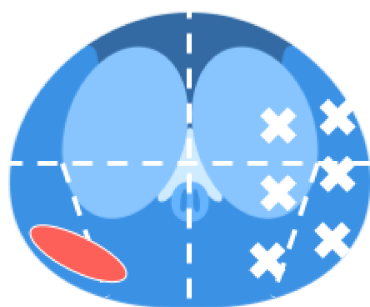


For each pair of biopsies – one core is more lateral, one core is more medial. From anterior—posterior, there are 3 planned rows of biopsies – anterior, mid zone, posterior. Avoid biopsy around the urethra.

### Suspicious MRI lesion scenarios

**Figure 2.** Examples of how to perform transperineal biopsies in patients with an MRI Target (scores 3, 4 or 5 on *either* Likert or PI-RADS v2.1 scoring systems).

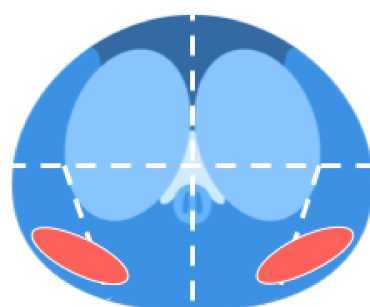
#### 2A. Single lesion example.



This is a single lesion in the right mid-gland peripheral zone posteromedially (PZ pm) and posterolaterally (PZ pl).

- Take **4 targeted biopsies** from the Target.
- Then take **6 peripheral zone focused biopsies** from the **contralateral** side.
- Do **not** resample the targeted biopsy side.

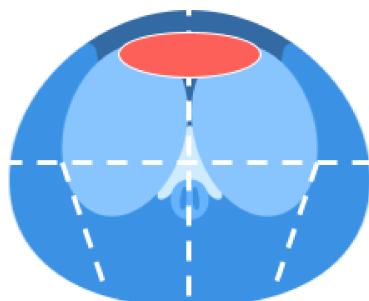
#### 2B. Bilateral peripheral zone lesions example.



There are **two lesions**: one in right mid-gland, peripheral zone posteromedially and posterolaterally (PZ pm and PZ pl); one in left mid-gland, peripheral zone posteromedially and posterolaterally (PZ pm and PZ pl).

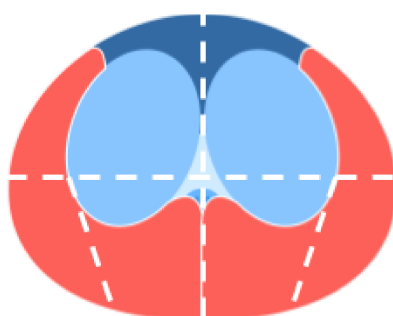
- Take **4 targeted biopsies** from **each** Target – *i.e.* **8 targeted biopsies** in **total**.
- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.



**2C.** Lesion crossing midline example.

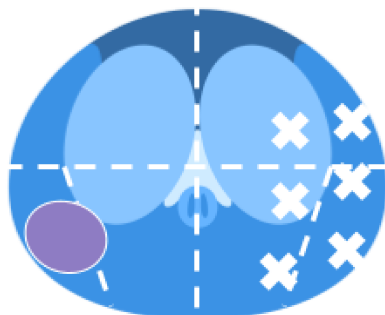
This is one lesion crossing the midline in the mid-gland, anterior fibromuscular stroma.

- Take **4 targeted biopsies** from the Target.
- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.

**2D.** Bilateral diffuse change on Likert scoring example.

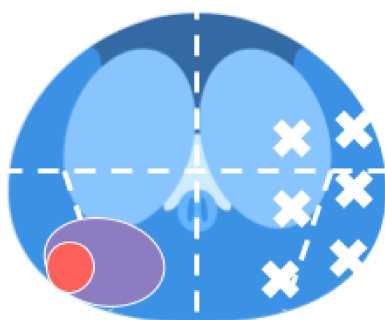
In the circumstance where on Likert scoring, the peripheral zone gives diffuse change, scoring 3 out of 5, arbitrarily **treat each peripheral zone** as a **different Target**.

- Take **4 targeted biopsies** from *each half* of the peripheral zone – *i.e. 8 biopsies* in total.
- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.

**2E.** A new lesion is revealed on DCE sequence example.

This is one lesion in the right mid-gland, peripheral zone posterolaterally. This **new Target** was specifically *not* suspicious (scored 1 or 2 on both Likert and PI-RADS v2.1) on bpMRI sequences (T2W and DWI). However, when the contrast sequence is revealed, the lesion appears to be suspicious (scored 3, 4 or 5 on Likert) on the dynamic contrast-enhanced (DCE) sequence than on the bpMRI.

- Thus, label the **new lesion** as a **DCE-Target**.
- Take **4 targeted biopsies** from **DCE-Target-1**.
- Then take **6 peripheral zone focused biopsies** from the **contralateral** side of the prostate.
- Do **not** resample the targeted biopsy side.

**2F.** A new **part** of an *existing* lesion is revealed on DCE sequence example.

There are two lesions in this example. **Target 1 (red)** was suspicious on **both** bpMRI and mpMRI. It is in the right mid-gland, peripheral zone, posterolaterally (PZ pl). It scores Likert 4 and PI-RADS v2.1 4.

However, when the contrast sequence is revealed, this lesion appears to be larger on the DCE sequence than on bpMRI. The part of the lesion that is **non-overlapping** would **not** have been

target biopsied if bpMRI alone was used. Thus, the second lesion (the non-overlapping part, **purple**) is called **DCE Target 1**. It is in the right mid-gland, peripheral zone, posteromedially (PZ pm).

Thus, the instructions are as follows in this instance:

- Take **4 targeted biopsies** from **Target 1**.
- Take **4 targeted biopsies** from **DCE Target 1**.
- Take **6 peripheral zone focused biopsies** from the **contralateral** side of the prostate.
- Do **not** resample the targeted biopsy side.

## Systematic Transrectal Biopsy Schema

**Figures 3** and **4** depict examples of how to perform the systematic biopsy in the **absence** of an MRI lesion and in the **presence** of MRI lesions, respectively.

### Non-suspicious MRI but a PSA Density of $\geq 0.15\text{ng/mL/mL}$ scenario

In patients with a **non-suspicious MRI but a PSA Density of  $\geq 0.15\text{ng/mL/mL}$** , 12-core systematic biopsy should be performed (**Figure 3**).

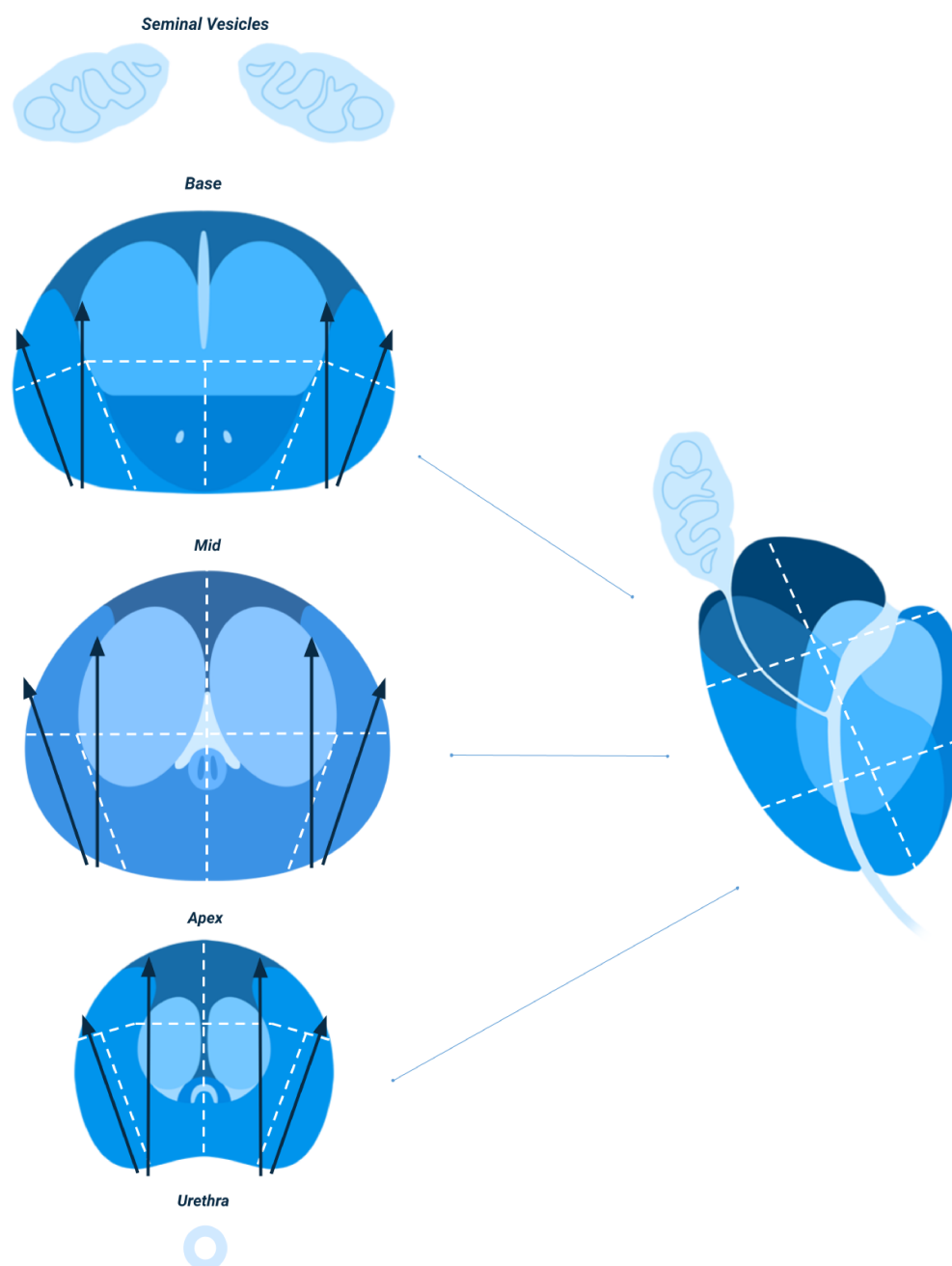
If performing biopsies transrectally, systematic biopsy cores should be taken from:

- Right base (2 cores)
- Right mid gland (2 cores)
- Right apex (2 cores)
- Left base (2 cores)
- Left mid gland (2 cores)
- Left apex (2 cores)

Systematic biopsy cores should be stored and labelled in a way that their location can be identified when the pathologist reports the result.

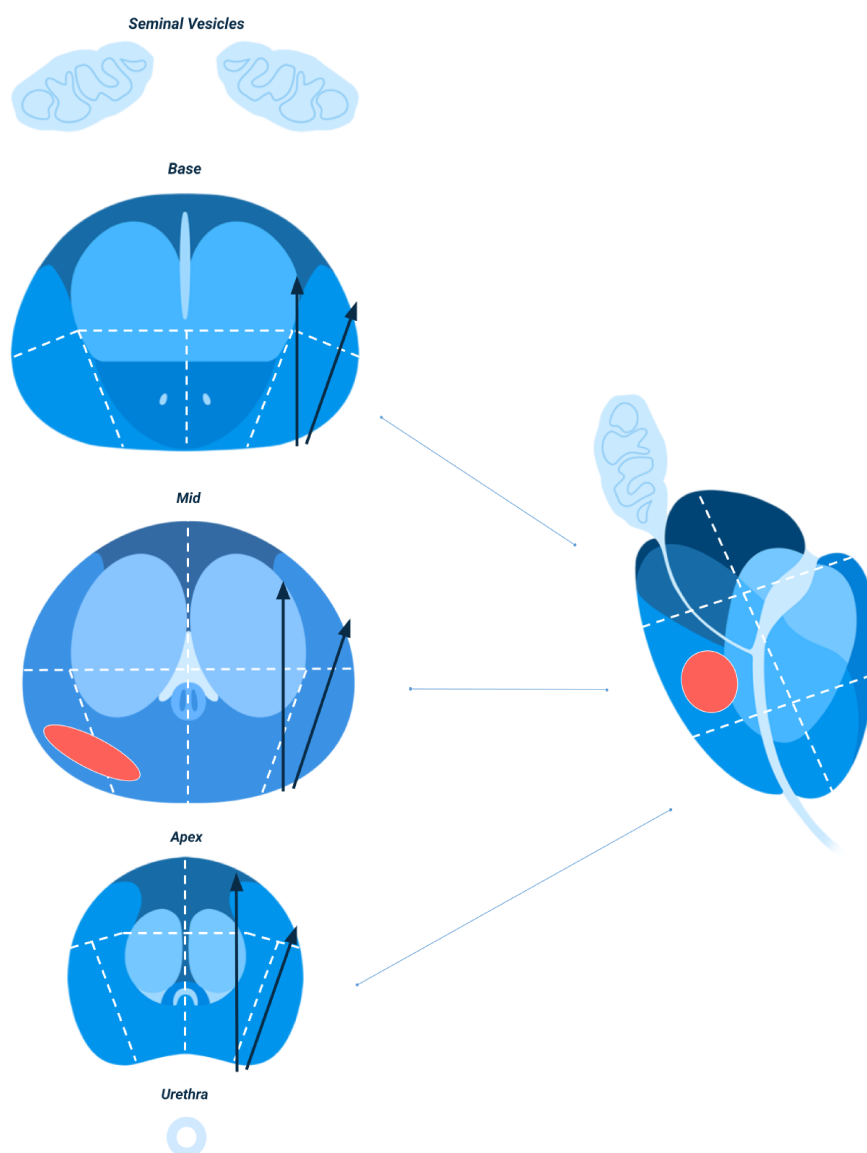
The 12 systematic biopsies **should be focused on the peripheral zone**. The urethra should be avoided.

**Figure 3.** The transrectal biopsy schema for men with a **non-suspicious MRI** (scores 1 or 2 on both Likert and PI-RADS v2.1 scoring systems) *but* a PSA Density of  $\geq 0.15\text{ng/mL/mL}$ , undergoing 12-core systematic biopsy.



## Suspicious MRI lesion scenarios

**Figure 4.** Examples of how to perform transrectal biopsies in patients with an MRI Target (scores 3, 4 or 5 on *either* Likert or PI-RADS v2.1 scoring systems).

**4A.** Single lesion example.

This is a single lesion in the right mid-gland peripheral zone posteromedially (PZ pm) and posterolaterally (PZ pl).

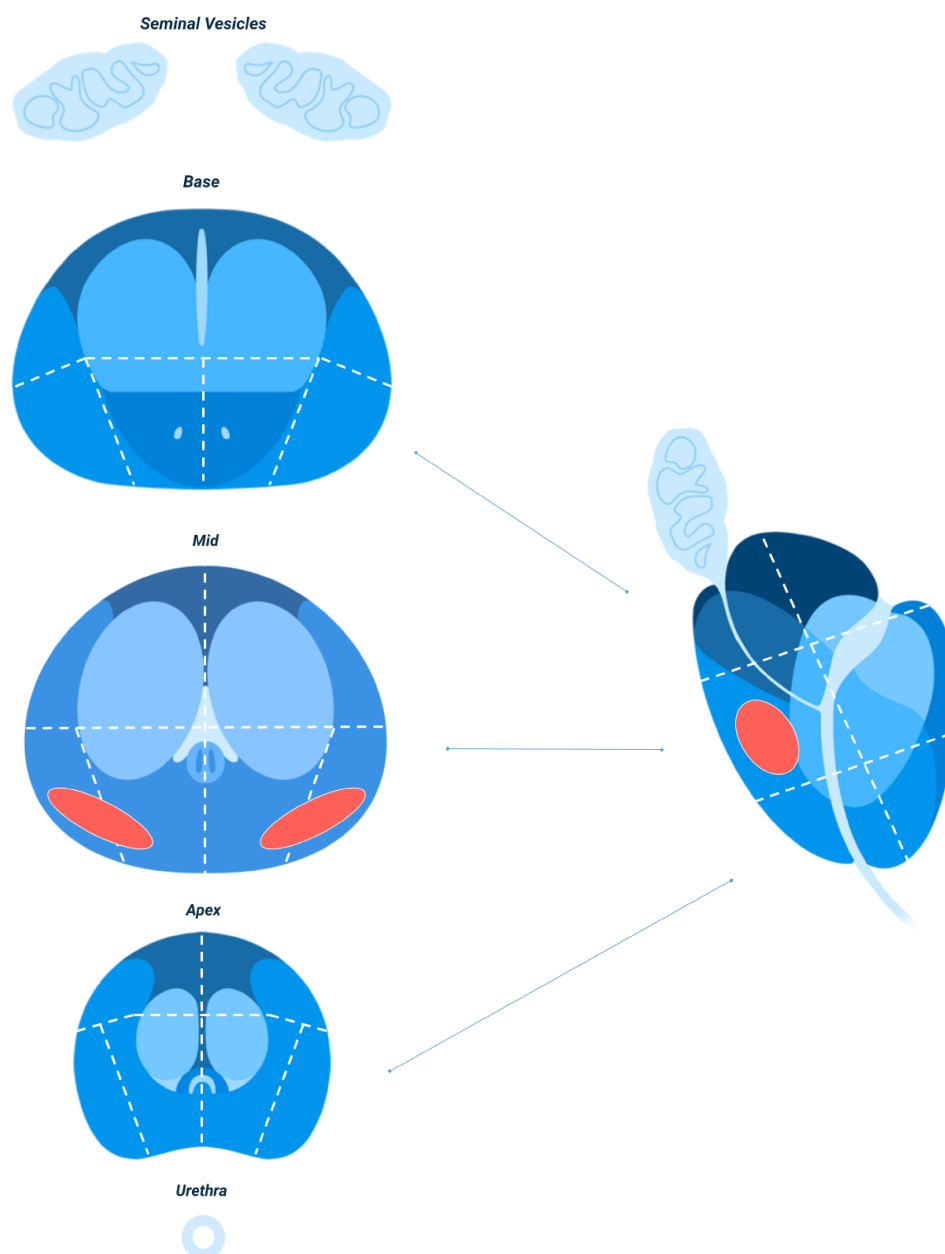
- Take **4 targeted biopsies** from the Target.
- Then take **6 peripheral zone focused biopsies** from the **contralateral** side.

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- Do **not** resample the targeted biopsy side.

#### 4B. Bilateral peripheral zone lesions example.

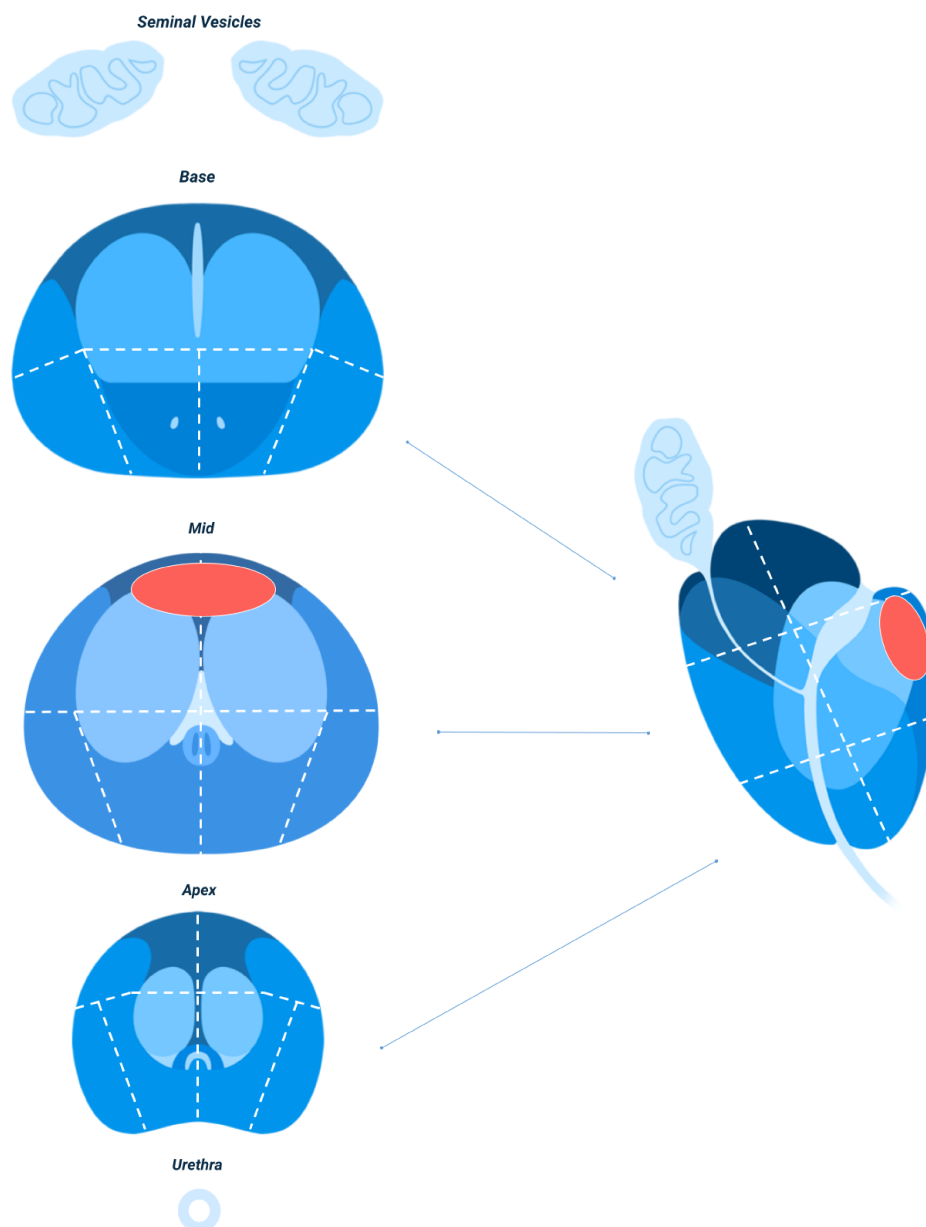


There are **two lesions**: one in right mid-gland, peripheral zone posteromedially and posterolaterally (PZ pm and PZ pl); one in left mid-gland, peripheral zone posteromedially and posterolaterally (PZ pm and PZ pl).

- Take **4 targeted biopsies** from **each** Target – *i.e.* **8 targeted biopsies** in **total**.

- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.

**4C.** Lesion crossing midline example.

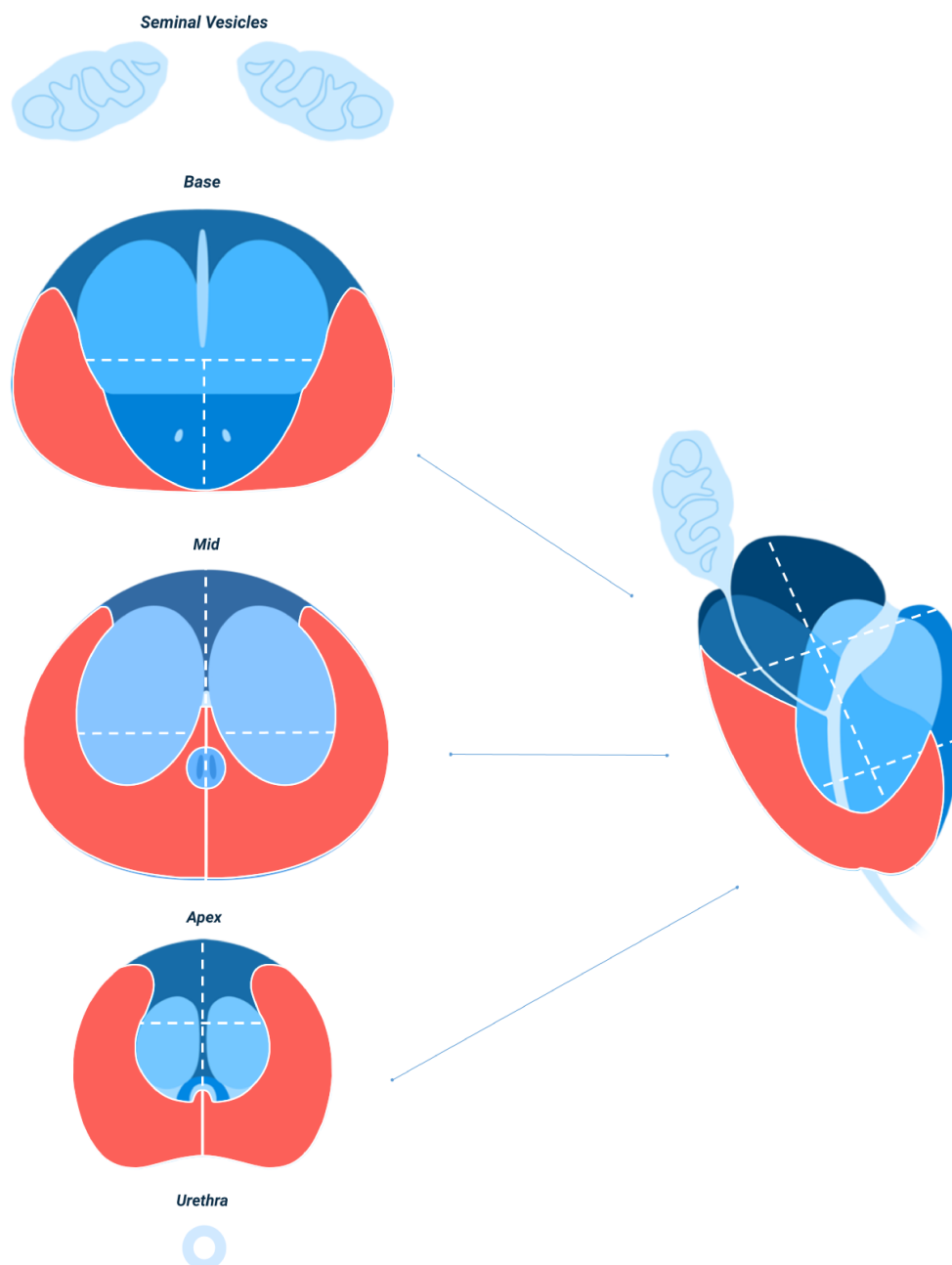


This is one lesion crossing the midline in the mid-gland, anterior fibromuscular stroma.

- Take **4 targeted biopsies** from the Target.

- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.

**4D.** Bilateral diffuse change on Likert scoring example.

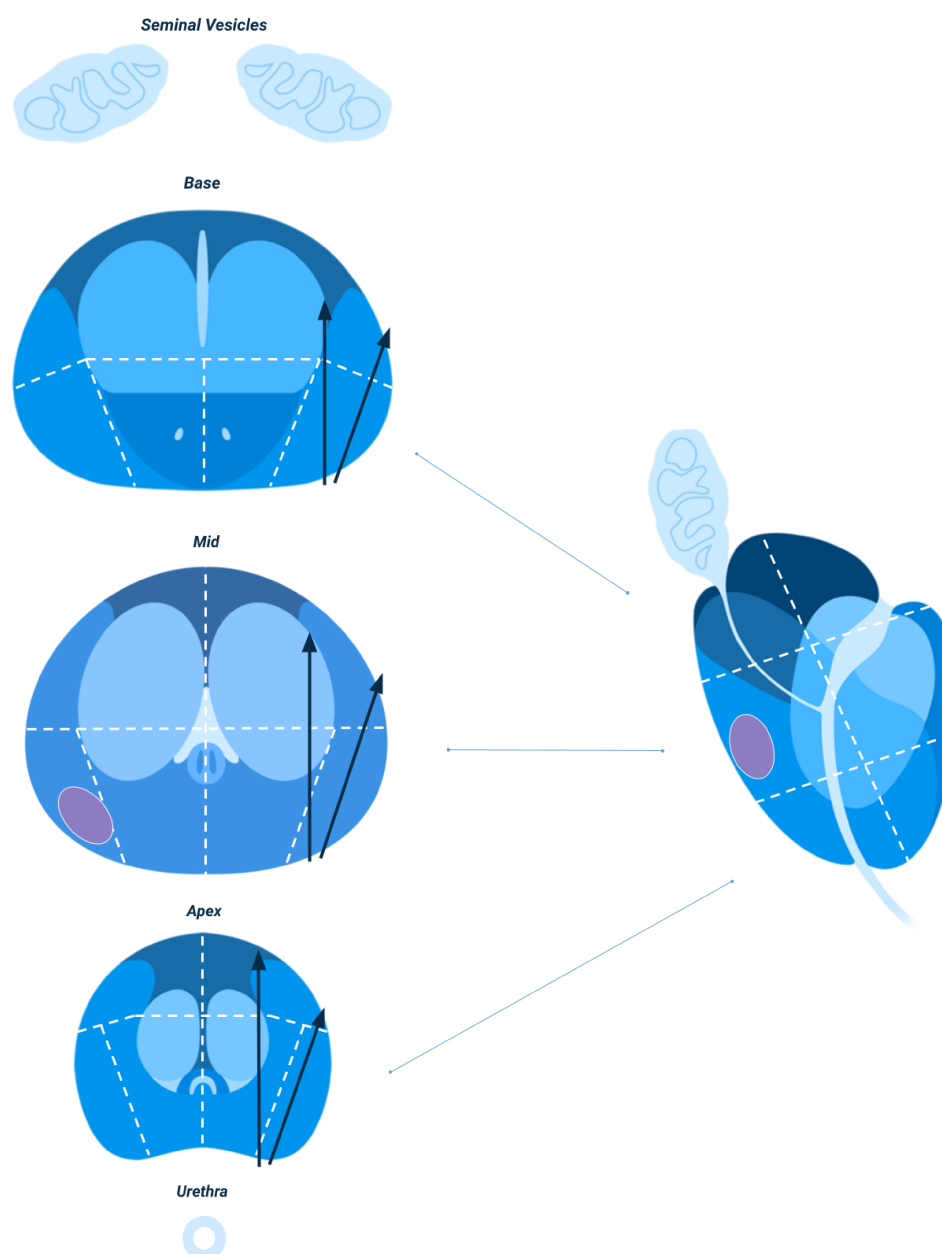


In the circumstance where on Likert scoring, the peripheral zone gives diffuse change, scoring 3 out of 5, arbitrarily **treat each peripheral zone as a different Target.**



- Take **4 targeted biopsies** from *each half* of the peripheral zone – *i.e.* **8 biopsies** in total.
- **Do not take any systematic biopsies** as targeted biopsies are taken from both sides of the prostate.

**4E.** A new lesion is revealed on DCE sequence example.



This is one lesion in the right mid-gland, peripheral zone posterolaterally. This **new Target** was specifically *not* suspicious (scored 1 or 2 on both Likert and PI-RADS v2.1) on bpMRI sequences (T2W and DWI). However, when the contrast sequence is revealed, the lesion

appears to be suspicious (scored 3, 4 or 5 on Likert) on the dynamic contrast-enhanced (DCE) sequence than on the bpMRI.

- Thus, label the **new lesion** as a **DCE-Target**.
- Take **4 targeted biopsies** from **DCE-Target-1**.
- Then take **6 peripheral zone focused biopsies** from the **contralateral** side of the prostate.
- Do **not** resample the targeted biopsy side.

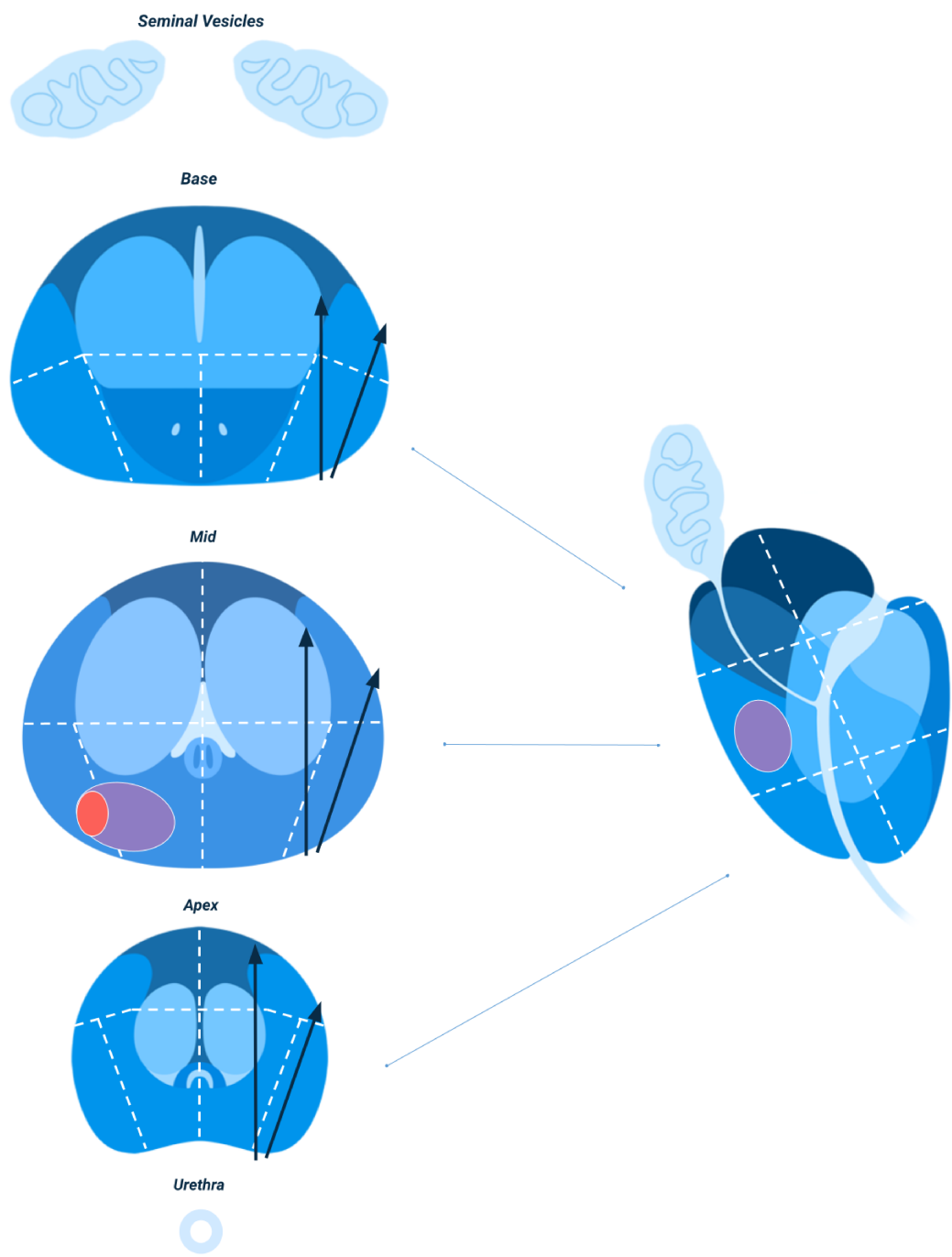
**4F.** A new **part** of an *existing* lesion is revealed on DCE sequence example.

There are two lesions in this example. **Target 1 (red)** was suspicious on **both** bpMRI and mpMRI. It is in the right mid-gland, peripheral zone, posterolaterally (PZ pl). It scores Likert 4 and PI-RADS v2.1 4.

However, when the contrast sequence is revealed, this lesion appears to be larger on the DCE sequence than on bpMRI. The part of the lesion that is **non-overlapping** would **not** have been target biopsied if bpMRI alone was used. Thus, the second lesion (the non-overlapping part, **purple**) is called **DCE Target 1**. It is in the right mid-gland, peripheral zone, posteromedially (PZ pm).

Thus, the instructions are as follows in this instance:

- Take **4 targeted biopsies** from **Target 1**.
- Take **4 targeted biopsies** from **DCE Target 1**.
- Take **6 peripheral zone focused biopsies** from the **contralateral** side of the prostate.
- Do **not** resample the targeted biopsy side.



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## Summary Biopsy Guidelines

Number of MRI targets	Location of MRI targets in prostate	Number of MRI-targeted biopsy cores	Number of contralateral systematic cores	Total number of biopsy cores
0	If PSA Density is < 0.15ng/ml/ml			0
0	If PSA Density is $\geq$ 0.15ng/ml/ml, then 12 systematic biopsy cores are taken (6 from each side)			12
1	Unilateral	4	6	10
2	Unilateral	8	6	14
3	Unilateral	12	6	18
4–8	Unilateral	16–32	6	22–38
1	Bilateral (e.g. crossing midline)	4	0	4
2	Bilateral	8	0	8
3	Bilateral	12	0	12
4–8	Bilateral	16–32	0	16–32