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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Designed by Aqua Asif
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 $\geq0.15\text{ng/mL/mL}$, 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.

![Single lesion example](image_url)

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.

![Bilateral lesion example](image_url)

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 ≥ 0.15ng/mL/mL scenario**

In patients with a _non-suspicious MRI but a PSA Density of ≥ 0.15ng/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 ≥0.15ng/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.
- 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.
## Summary Biopsy Guidelines

<table>
<thead>
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<th>Number of MRI targets</th>
<th>Location of MRI targets in prostate</th>
<th>Number of MRI-targeted biopsy cores</th>
<th>Number of contralateral systematic cores</th>
<th>Total number of biopsy cores</th>
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<td>If PSA Density is ≥ 0.15ng/ml/ml, then 12 systematic biopsy cores are taken (6 from each side)</td>
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<td>22–38</td>
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