

## **Transperineal MRI-targeted biopsy versus transperineal template prostate mapping biopsy in the detection of localised radio-recurrent prostate cancer**

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## **Abstract**

**Purpose:** Multi-parametric MRI (mpMRI) may identify radio-recurrent intra-prostatic cancer accurately. We aimed to compare visually directed MRI-targeted biopsies (MRI-TB) to an accurate reference standard – Transperineal Prostate Mapping (TPM) biopsies with 5mm sampling - in the detection of clinically significant cancer in men with biochemical failure after radiotherapy.

**Methods:** A retrospective registry analysis between 2006-2014 identified 77 men who had undergone mpMRI followed by MRI-TB and TPM. Clinical significance was set at two definitions of disease. Definition 1 was Gleason  $\geq 4+3$  and/or maximum cancer core length  $\geq 6$ mm. Definition 2 was Gleason  $\geq 3+4$  and/or maximum cancer core length  $\geq 4$ mm.

**Results:** Of the 77 patients included, mean age was 70 years (range 61-82; SD 5.03). Median PSA at time of EBRT was 14ng/ml (IQR 7.83-32.50). The most frequent EBRT dose given was 74Gy over 37 fractions. Eight patients had iodine-seed implant brachytherapy or high-dose rate brachytherapy. Neo-adjuvant/adjuvant hormonal therapy use was reported in 38. Time from EBRT to biochemical recurrence was a median 60 months (IQR 36.75-85.00). Median PSA at time of mpMRI was 4.68ng/ml (IQR 2.68-7.60). The median time between mpMRI and biopsy was 2.76 months (IQR 1.58-4.34). Total of 2,392 TPM and 381 MRI-TB cores were taken with 18% and 50% cancer detection, respectively. Detection rates of definition 1 clinically significant cancer were 52/77 (68%) vs. 55/77 (71%) for MRI-TB and TPM, respectively. MRI-TB was more efficient requiring 1 core vs. 2.8 cores to detect definition 2 cancer.

**Conclusion:** MRI-TB seems to have encouraging detection rates for clinically significant cancer with fewer cores compared to TPM, although TPM had higher detection rates for smaller lower grade lesions.

**Key Words:** Radio-recurrent Prostate Cancer, Multi-parametric MRI, Template Biopsy, Cognitive Target Biopsy

## **Introduction**

Radiotherapy is effective in treating localised prostate cancer. However, biochemical failure between 7 years can occur in approximately one-third of men.<sup>1</sup> Without additional therapy time for distant spread has been found to be approximately 5 years<sup>2</sup>, so there may be a potential window of opportunity for further curative local salvage therapy. Despite this potential for delivering local curative therapy, most men who fail radiotherapy are placed on expectant management with delayed androgen deprivation therapy (ADT)<sup>3</sup>. This may be because the existing therapies target the whole prostate using salvage radical prostatectomy, cryosurgery, high intensity focused ultrasound or brachytherapy – and confer significant risk of incontinence and rectal injury.<sup>4</sup>

For local salvage therapy to be delivered appropriately, an accurate determination of the presence or absence of localised recurrence in this group of patients is important. This may also aid the delivery of a focal tissue-preserving approach to salvage local therapy in order to mitigate the harms currently seen with whole-gland salvage<sup>4</sup>. Whilst transrectal ultrasound systematic 10-12 core (TRUS)<sup>1</sup> guided biopsies can be used to detect or rule-out local disease, they have inherent

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## **Abbreviations**

TRUS - Transrectal ultrasound

EBRT- External Beam Radiotherapy

mpMRI - Multiparametric MRI

T2W - T2-weighted

DCE-MRI - Dynamic Contrast Enhanced

DWI - Diffusion Weighting Imaging

TPM -Transperineal prostate mapping

MRI-TB – MRI Target Biopsies

MRI-US Fusion TB – MRI-US Fusion Target Biopsies

inaccuracies as a diagnostic strategy and may lead to inappropriate therapeutic decisions. First, TRUS-guided biopsies can miss clinically significant disease. Second, they can misclassify significant disease as insignificant. These two errors may lead to a patient undergoing improper expectant management and ADT rather than potentially curative local therapy. Third, TRUS-guided biopsies detect small volume clinically insignificant disease that may inappropriately be attributed as the cause of biochemical failure, when actually micro-metastatic disease may be the cause of a rising PSA.<sup>5 6</sup> This could lead to unnecessary local salvage therapy with the presumption that metastases are not present especially if staging scans – with their own inherent inaccuracies – are negative.

If imaging could be used to identify recurrent intra-prostatic cancer more accurately, this might help in the selection of patients for local salvage therapies.<sup>7</sup> Multi-parametric MRI (mpMRI) using T2-weighted (T2W), Dynamic Contrast Enhanced (DCE-MRI) and Diffusion Weighting Imaging (DWI), has gained much interest in the diagnosis of prostate cancer in the primary setting.<sup>8 9</sup> A limited number of studies have shown that mpMRI may have encouragingly high performance characteristics in the radiorecurrent setting.<sup>10 11 12 13 14</sup>

We compared the cancer detection rates of biopsies targeted to an mpMRI-detected lesion (MRI-Target Biopsy – MRI-TB) against Transperineal Prostate Mapping (TPM) using a 5mm sampling frame - in men with rising PSA after prior radiotherapy. The use of TPM in this setting allowed us to compare the performance of targeted biopsies in all men who underwent mpMRI due to biochemical failure without selection bias. This study is START and STARD compliant.<sup>15</sup>

## **Materials and Methods**

Research ethics committee exemption was granted for this study by the institutional research office. A retrospective analysis identified 147 consecutive men, between July 2006 and May 2014 referred with suspicion of radio-recurrent prostate cancer due to rising PSA post-EBRT or brachytherapy, a lesion suspicious for cancer on mpMRI and who subsequently underwent transperineal biopsies. We contacted all referring physicians and sent reminders in order to collate all pre-radiotherapy

baseline disease characteristics. All men had no evidence of distant disease based on a combination of radioisotope bone-scan and CT/PET scans (FDG initially and later 18F-choline). This is the standard of care for such patients referred to our institution for consideration of local salvage therapy. Our cohort comprised of 77 men who underwent an MRI-TB at the same time as TPM biopsies. MRI-TB was taken first followed by TPM. Eight men were referred having been started on ADT and underwent imaging whilst on hormones. Eleven men underwent biopsy whilst on hormonal treatment, which had been started post-imaging in 3. The mean time for hormonal treatment in these 11 was 8 months. Complications were assessed on review of subsequent clinic appointments.

### ***MR-Imaging***

The MRI scans were prospectively reported (blind to all histology). Reports were conducted by several expert uro-radiologists. Radiologists had access to all baseline clinical data including pre-radiotherapy disease characteristics and post-radiotherapy PSA kinetics, where available. Due to the nature of the aims of our study – to determine the clinical validity of MRI-targeting – there was no need for double reporting as the targeting was based on the report issued at the time.

As discussed in our previous paper <sup>14</sup>, each prostate was divided into four sectors in 3 sections (base, mid-gland, apex) with the urethra as the anatomical dividing point between right and left and anterior and posterior. Each of the 12 resulting sectors and seminal vesicles were scored using the 5-point Likert scale (1 – highly likely no tumour and 5 – highly likely tumour).<sup>16</sup>

As a retrospective study, from the period 2007-2014, scans were reported prior to the European Consensus report on prostate MRI and the ESUR guidelines on reporting of prostate MRI.<sup>16 17</sup> However, our three senior uro-radiologists were formally involved in both of the guidelines and much of how we reported the scans in this series is currently incorporated into the ESUR and British Society of Uro-Radiology guidelines<sup>18</sup>. Patients were scanned on the 1.5T scanner (Symphony or Avanto, Siemens AG, Munich, Germany) using a pelvic phased-array coil. The sequences were evaluated in the following manner. First, the T2 sequences were used to provide morphology and anatomical localisation. DCE played a greater role

for the peripheral zone with the additional reference of the DWI scans. A score of 1 or 2 was given if there was no enhancement; a score of 3 given if symmetrical diffuse enhancement was seen; if there was focal or asymmetrical enhancement  $\geq 3$  mm and no abnormality seen on DWI, a score of 4 was given; if there was focal or asymmetrical enhancement  $\geq 3$  mm and/or corresponding DWI abnormality in the same anatomical location, a score of 5 was recorded.

A similar technique was used to report for lesions in the transition zone, with DWI sequences given greater weighting compared to DCE. DCE shows more enhancement of adenomas in this zone, especially after radiotherapy. However, an equivocal score of 3 based on DWI could be upgraded to 4 or 5 if there was an associated obvious DCE abnormality in the same anatomical location.<sup>14</sup>

### ***Biopsy strategies***

MRI-TB were carried out with cognitive targeting or as has been deemed more accurately, visual estimation.<sup>19</sup> Individual lesions that scored 3-5 were first transperineally targeted using a 5mm-brachytherapy template grid with 2-4 cores taken per target. This was followed by TPM biopsies from the remainder of the prostate which included the targeted biopsy area. We have previously reported the details of how the full sampling of the prostate was conducted <sup>14</sup>, in brief; a 5mm transperineal brachytherapy grid was used to take biopsies transperineally under general anaesthetic using TRUS guidance. If the prostate apex-base length was greater than the core length, two biopsies were taken at the same grid coordinate and labelled separately. Biopsies were taken in 20 sectors with 1-2 cores per sector according to the size of the prostate. (Figure 1)<sup>19</sup>

Biopsy cores were analysed and reported by two dedicated expert uro-pathologists with over 10 years of experience in the diagnosis of prostate malignancy. Biopsy results were grouped into four ROIs per prostate, reflecting the mp-MRI reporting. Pathologists were aware of clinical details and MRI findings.

### ***Statistics***

Analysis was performed at the whole prostate level. Two-by-two and three-by-three tables of agreement were drawn up comparing the detection of clinically significant,

clinically insignificant and no cancer by each of the two-biopsy techniques. The primary outcome was the detection rate of clinically significant prostate cancer (defined using UCL/Ahmed definition 2 - Gleason  $\geq 3+4=7$  and/or maximum cancer core length (MCCL)  $\geq 4\text{mm}$ )<sup>20</sup>. Secondary outcomes were set for a target definition of UCL/Ahmed definition 1 cancer only (Gleason  $\geq 4+3=7$  and/or MCCL  $\geq 6\text{mm}$  only, excluding those that met criteria of UCL/Ahmed Definition 2), any Gleason pattern 4 or greater and 'all cancer'. The UCL definitions were used as they were developed specifically and validated for the presence of 0.2cc and 0.5cc lesion on a transperineal sampling strategy.<sup>20</sup> For each target condition the difference between the biopsy techniques was compared using McNemar's test. Data was analysed using SPSS version 22 (IBM Corp 1989, 2013 Release 22.0.0.0). A p value  $< 0.05$  was chosen for indicating a statistically significant difference.

## Results

Of 77 patients included, mean age was 70 years (range 61-82; SD 5.03). Median PSA at time of radiotherapy was 14ng/ml (range 4.5-143 IQR 7.83-32.50). Information on pre-radiotherapy stage and risk was available for 63 patients. Further baseline information is available in Table 1.

Adverse event data was available in all 77; one reported haematospermia (1.3%), 3 (3.9%) reported dysuria with no associated infection/sepsis and 1 (1.3%) had fever and bowel disturbance treated with oral antibiotics for presumed gastrointestinal infection.

### **Primary Outcome:**

*Detection of Clinically Significant Cancer:* Using UCL/Ahmed Definition 2, (Gleason  $\geq 3+4$  and/or MCCL  $\geq 4\text{mm}$ ), 60 (77.9%) on MRI-TB compared to 66 (85.7%) on TPM (Table 2).

In terms of agreement, 3 (3.9%) classified as clinically insignificant or no cancer on TPM were found to have clinically significant cancer on MRI-TB (Figures 2-4). Nine (11.7%) reported as having no cancer or clinically insignificant cancer on MRI-TB

were found to have clinically significant cancer on TPM ( $p=0.15$ ) (Table 4). Eight of these cases were of cancer in the targeted area (targeting error) and one had cancer outside of the targeted area (mpMRI detection error). This patient had an overall mpMRI score of 3/5 in all areas of the prostate, the left posterior on TPM biopsy was found to be positive for Gleason 4+3 MCCL 1mm. The posterior midline was targeted in this patient, but this did not reveal any cancer.

On a per core analysis, 190/381 (50%) of MRI-TB cores were positive for clinically significant cancer compared to 425/2392 (17.8%) of TPM cores. (Table 5) For the detection of clinically significant prostate cancer, 2.0 MRI-TB cores had to be taken vs. 5.6 cores on TPM biopsy (Table 5).

### ***Secondary outcomes:***

First, MRI-TB had a similar rate of detection of UCL/Ahmed Definition 1 disease compared to TPM (52 patients [68%] vs. 55 patients [71%]). For the detection of clinically significant prostate cancer 2.2 MRI-TB cores had to be taken vs. 6.3 cores on TPM biopsy.

Second, TPM had a higher detection rate of Gleason  $\geq 3+4$  cancer compared with MRI-TB (65 patients [84.4%] vs. 58 patients [75.3%]). For the detection of cancer Gleason  $\geq 3+4$  2.1 MRI-TB cores had to be taken vs. 6.3 cores on TPM biopsy.

Third, TPM had a higher all cancer detection rate 69 patients (89.6%) compared to 63 patients (81.8%) for MRI-TB. TPM misclassified 1 patient (1.3%) as no cancer but found to have cancer on MRI-TB. However MRI-TB misclassified 7 patients (9.1%) as no cancer that were found to have cancer on TPM biopsy. These cases were of cancer in the targeted area (targeting error) in 7 cases. ( $p=0.07$ ) (Table 3).

Fourth, based on MRI score, 67/77 patients (87.0%) scored  $\geq 4$  (Table 6) of which 60/67 patients (90.0%) were found to have clinically significant cancer on TPM and 57/67 patients (85.1%) on MRI-TB (Table 7). 10/77 had an mpMRI Score of  $\leq 3/5$  Of



these 6/10 (60%) had clinically significant cancer on TPM (all had Gleason Score  $\geq 7$ ). On MRI-TB 3/10 (30%) had clinically significant cancer (with 2 of these having Gleason Score  $\geq 7$ ).

## **Discussions**

To our knowledge, this is the first study to compare cancer detection rates of transperineal MRI-targeted biopsies and transperineal template mapping biopsies in the radio-recurrent prostate cancer setting. We found that MRI-TB has an encouraging and acceptable detection rate for clinically significant prostate cancer using any number of definitions (68.0-77.9%). Although TPM biopsies had 10% higher detection rates for a more conservative definition of clinically significant cancer, the performance was similar for a higher threshold of disease burden. MRI-TB was also consistently more efficient with fewer biopsies required compared with TPM; 1 core vs. 2.8 cores for the detection of clinically significant disease; 1.00 core vs. 2.9 cores for UCL/Ahmed Definition 1 disease, respectively.

## **Limitations**

Prior to discussing the clinical implications of our findings, our study does have some limitations. First, the retrospective design and small sample size limits the external validity of our findings. We are currently recruiting to a large prospective multicentre study in this setting using MRI-TB versus TPM biopsies. The FORECAST (FOCaL RECURRENT Assessment and Salvage Treatment) study will incorporate the use of image-fusion targeted biopsies [clinicaltrials.gov number: NCT01883128]. Second, as nearly all of our patients were referred from external centres, there was incomplete information on radiotherapy doses, initial PSA and initial Gleason scores. Third, whilst the notion of clinically important disease is gaining acceptance in primary prostate cancer, such a notion has not been adequately explored in radio-recurrent disease. To mitigate this, we evaluated outcomes using a number of histological target definitions. It has been reported that delayed tumour regression and eventual conversion to negative biopsies occurs at a mean time of 30 months.<sup>21</sup> However within our study only one patient was sampled within 30 months (at 15 months) of completion of radiotherapy. The average time post EBRT for biopsy was 86 months. Thus any cancer detected is likely to be a true recurrence and not a

continuing change in prostate tissue morphology from radiation.

### ***Comparison to existing studies***

Sensitivity and specificity of mpMRI have been reported as high as 86-100%<sup>12 13 22</sup>. However, these studies used TRUS biopsy as the reference standard so the mpMRI detection error may have been under reported. There is limited data available about the use of targeted biopsy in the radiorecurrent setting. Rud et al.<sup>23</sup> examined the detection rate of DWI and MRI-US fusion targeted biopsy (MRI-US fusion TB) in men with radiorecurrent prostate cancer. MRI-US fusion TB had a higher rate of detection of cancer compared with random TRUS-guided biopsies - 83% vs 21%, respectively. However, poor reference standard used in this study and random biopsies were not performed in the area where a targeted biopsy had been undertaken. Instead random TRUS-guided biopsies were taken in the contralateral lobe.

In order to further place our data in context of targeted biopsy series, we have to turn to the primary setting. There are several studies that report on the improved detection of cognitive MRI targeted biopsy and now MRI-US fusion targeted biopsy (MRI-US fusion TB) compared with whole-gland sampling in the primary setting. One study showed similar detection rates of MRI-TB versus TPM in primary prostate cancer of 57% versus 62% ( $p=0.174$ ). This study also showed a higher proportion of cores positive for cancer with MRI-TB (38%) than with TPM (14%).<sup>24</sup> MR-US fusion biopsies have reported higher cancer detection rates compared to standard sampling. One study compared MRI-US fusion TB with transperineal biopsy in the primary setting and found 46.0% of MRI-US fusion TB vs 7.5% of systematic TPM detected Gleason  $\geq 7$  cancers. TPM biopsy missed 20.9% Gleason  $\geq 7$  cancers compared to 12.8% for MRI-US fusion TB.<sup>25</sup> A more recent study also showed that MRI-US fusion TB resulted in 22% and 67% additional cases of Gleason  $\geq 3+4$  and Gleason  $\geq 4+3$  prostate cancer than 12 core systematic biopsy, respectively.<sup>26</sup>

Two recent systematic reviews have shown MRI-TB to be superior when compared to whole-gland transrectal systematic sampling. Moore et al <sup>27</sup> examined MRI-TB compared with whole-gland sampling in the primary setting. Core-based analysis showed that just 7% of systematic cores were positive for any cancer compared to

30% on MRI-TB. On a per patient basis, MRI-TB had a higher cancer detection rate of 48% vs. 36% for standard biopsy. Both targeted and standard biopsy detected clinically significant cancer in 43% with similar rates of missing cancer (23.4% vs 21.6%, respectively). Another systematic review<sup>28</sup> reported on cancer detection rates of MRI-US fusion targeted biopsies in comparison to systematic biopsy. Clinically significant cancer was detected in 33.3% vs. 23.6%, respectively. MRI-US fusion biopsy was again reported to be more efficient with four times the number of cores needed in systematic sampling compared with an MR-US fusion TB approach. MRI-US fusion biopsies also detected a median of 9.1% additional clinically significant cancers that were missed by standard biopsy alone. Conversely, standard biopsies detected a median of 2.1% additional clinically significant cancers that were missed by MRI-US fusion TB. It is important to note that these systematic reviews predominantly examined targeted biopsy in the primary setting.

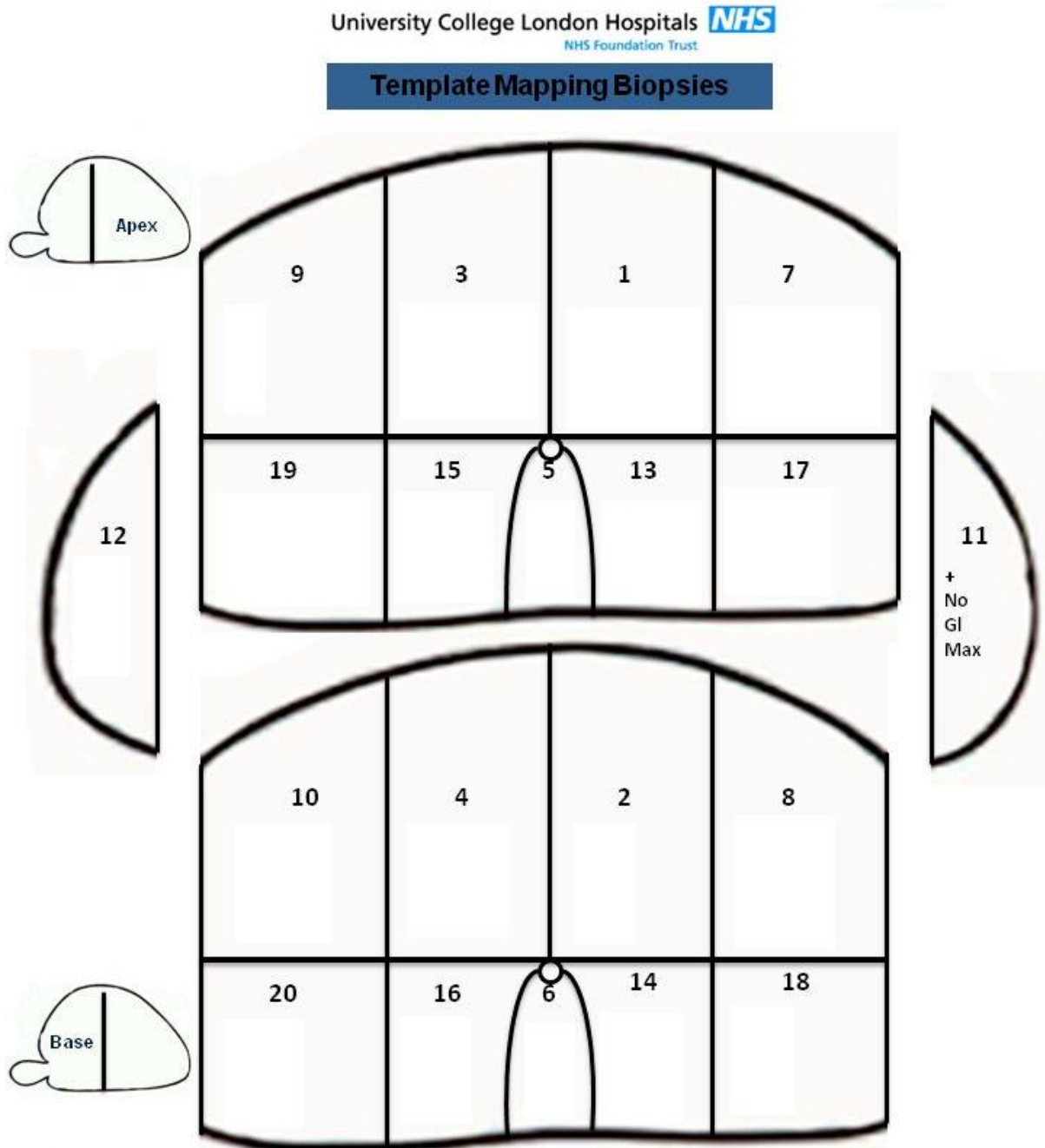
If our results are reproducible in further studies and larger numbers across multiple sites, it is possible that in future, men who fail radiation therapy and who wish to consider local salvage therapy should undergo a mpMRI with targeted biopsies to suspicious areas to confirm histological local recurrence. As with all diagnostic tests and strategies, a balance between accuracy and burden of the test(s) needs to be evaluated. The additional number of biopsy cores that are taken from TPM do lead to a 10% higher detection rate but in themselves are not perfect either as misclassification does occur. Patients and their physicians need to make an individualised decision weighing up the additional detection rate with the requirement for TPM to be carried out under general anaesthetic with high number of cores and side-effects that these cause.

Future research needs to focus on whether image-fusion targeting has any clinical utility in this setting or whether mpMRI cognitive, visually directed biopsies, as we have carried out in our study, is sufficient. Further, mpMRI with targeted biopsy confirmation may facilitate greater acceptance or delivery of local salvage therapies such as radical prostatectomy or minimally invasive approaches such as tissue preserving focal salvage therapy.<sup>4</sup>

## **Conclusions**

Mp-MRI targeted transperineal biopsies shows some promise in the diagnosis of clinically significant radiorecurrent prostate cancer when compared to a systematic biopsy approach using transperineal template biopsies. Further prospective multi-centre trials are needed to determine if these results are stable and reliable across a larger number of men.

**Figure 1 – Template Mapping Histopathology Report – Modified 20 Barzell zones**



**Modified Barzell Zones**

- |                                    |                                      |
|------------------------------------|--------------------------------------|
| 1 Left Parasagittal Anterior Apex  | 11 Left Lateral                      |
| 2 Left Parasagittal Anterior Base  | 12 Right Lateral                     |
| 3 Right Parasagittal Anterior Apex | 13 Left Parasagittal Posterior Apex  |
| 4 Right Parasagittal Anterior Base | 14 Left Parasagittal Posterior Base  |
| 5 Midline Apex                     | 15 Right Parasagittal Posterior Apex |
| 6 Midline Base                     | 16 Right Parasagittal Posterior Base |
| 7 Left Medial Anterior Apex        | 17 Left Medial Posterior Apex        |
| 8 Left Medial Anterior Base        | 18 Left Medial Posterior Base        |
| 9 Right Medial Anterior Apex       | 19 Right Medial Posterior Apex       |
| 10 Right Medial Anterior Base      | 20 Right Medial Posterior Base       |

- |   |
|---|
| <span style="display: inline-block; width: 15px; height: 15px; background-color: green; border: 1px solid black;"></span> Clinically insignificant disease              |
| <span style="display: inline-block; width: 15px; height: 15px; background-color: yellow; border: 1px solid black;"></span> Gleason = 3+4 AND/OR Max Cancer length 4-5mm |
| <span style="display: inline-block; width: 15px; height: 15px; background-color: red; border: 1px solid black;"></span> Gleason >= 4+3 AND/OR Max cancer length >=6mm   |

**Table 1 - Patient baseline demographics of patients undergoing transperineal biopsies for suspicion of radiorecurrent prostate cancer**

Total No of Patients	77
Mean age (range) years (SD)	70.48 (61-82) (5.03)
Median PSA (ng/ml at) EBRT (range) (IQR)	14 (4.5-143 IQR 7.83-32.5)
D'Amico Risk Score at time of EBRT, N (%)	
Risk information known	63 (100)
1 - High-risk: PSA >20, G >8, T2c-3a.	33 (52.4)
2 - Intermediate risk: PSA 10 - 20, G7, or T2b	19 (30.2)
3 - Low risk: PSA <10, G <6, T1-2a	11 (17.5)
Time between EBRT and biochemical failure (months), median (range) (IQR)	60 (5-156 IQR 36.75-85.00)
PSA at time of MRI (ng/ml), median (range) (IQR)	4.68 (0.54-20 IQR 2.68-7.60)
Time between EBRT and TPM (months), median (range) (IQR)	78 (15-199 IQR 61.5-110)
Time between mpMRI and TPM (months), median (IQR)	2.76 (1.58-4.34)

**Table 2 - Cancer Detection rates using TPM and MRI-TB biopsies in patients with radiorecurrent prostate cancer**

	TPM N (%)	MRI- TB N (%)
Total	77 (100.0)	77 (100.0)
No Cancer	8 (10.4)	14 (18.2)
Clinical insignificant (Gleason 3+3 and <math>\leq 3\text{mm}</math>)	3 (3.9)	3 (3.9)
UCL/Ahmed Definition 2 (Gleason $\geq 3+4$ and/or MCCL $\geq 4\text{mm}$ )	11 (14.3)	8 (10.4)
UCL/Ahmed Definition 1 (Gleason $\geq 4+3$ and/or MCCL $\geq 6\text{mm}$ )	55 (71.4)	52 (67.5)

**Table 3 – Comparison of cancer detection between TPM and MRI-TB cognitive, visual-estimation method in patients with radiorecurrent prostate cancer**

		TPM		
		No Cancer	Any cancer	Total
MRI-TB	No cancer	7	7	14
	Any cancer	1	62	63
	Total	8	69	77

**Table 4 – Comparison of clinically significant cancer detection between TPM and MRI-TB cognitive, visual-estimation method in patients with radiorecurrent prostate cancer**

		TPM		
		No Cancer/ Clinical insignificant cancer	UCL/Ahmed Defn 2 OR UCL/Ahmed Defn 1	Total
MRI-TB	No Cancer/ Clinical insignificant cancer	8	9	17
	UCL/Ahmed Defn 2 OR UCL/Ahmed Defn 1	3	57	60
	Total	11	66	77

**Table 5 - Core based comparison of detection of any cancer, clinically significant cancer and cancer Gleason  $\geq 7$  between TPM and MRI-TB cognitive, visual-estimation method in patients with radiorecurrent prostate cancer**

	TPM (%)	MRI-TB (%)
Total No of Cores	2392 (100)	380 (100)
Any Cancer	428 (17.9)	203 (53.4)
UCL/Ahmed Defn 2 OR UCL/Ahmed Defn 1	425 (17.8)	190 (50.0)
Gleason Score $\geq 7$	419 (17.5)	181 (47.6)
UCL/Ahmed Definition 1	379 (15.8)	177 (46.6)

**Table 6 - MRI Score and detection of any cancer, clinically significant cancer and Gleason  $\geq 7$  by TPM in patients with radiorecurrent prostate cancer**

MRI Score	N (%)	ANY CANCER, N (%)	UCL/Ahmed Defn 2 OR UCL/Ahmed Defn 1, N (%)	GLEASON $\geq 7$ , N (%)	UCL/Ahmed Defn 1, N (%)
1. Clinically significant disease is highly unlikely to be present	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
2. Clinically significant cancer is unlikely to be present	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
3. Clinically significant cancer is equivocal	9 (11.7)	6 (66.7)	6 (66.7)	6 (66.7)	2 (22.2)
4. Clinically significant cancer is likely to be present	25 (32.5)	22 (88.0)	20 (80.0)	19 (76.0)	17 (68.0)
5. Clinically significant cancer is highly likely to be present.	42 (54.5)	41 (97.6)	40 (95.2)	40 (95.2)	36 (85.7)
Total	77	69 (89.6)	66 (85.7)	65 (84.4)	55 (71.4)



**Table 7 – MRI Score and detection of any cancer, clinically significant cancer and Gleason  $\geq 7$  by MRI-TB cognitive, visual-estimation method in patients with radiorecurrent prostate cancer**

MRI Score	N (%)	ANY CANCER, N (%)	UCL/Ahmed Defn 2 OR UCL/Ahmed Defn 1, N (%)	GLEASON $\geq 7$ , N (%)	UCL/Ahmed Defn 1, N (%)
1. Clinically significant disease is highly unlikely to be present	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
2. Clinically significant cancer is unlikely to be present	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)
3. Clinically significant cancer is equivocal	9 (11.7)	3 (33.3)	3 (33.3)	2 (22.2)	2 (22.2)
4. Clinically significant cancer is likely to be present	25 (32.5)	21 (84.0)	19 (76.0)	19 (76.0)	17 (68.0)
5. Clinically significant cancer is highly likely to be present.	42 (54.5)	39 (92.9)	38 (90.5)	37 (88.1)	33 (78.6)
Total	77 (100)	63 (81.8)	60 (77.9)	58 (75.3)	52 (67.5)

## Case Study

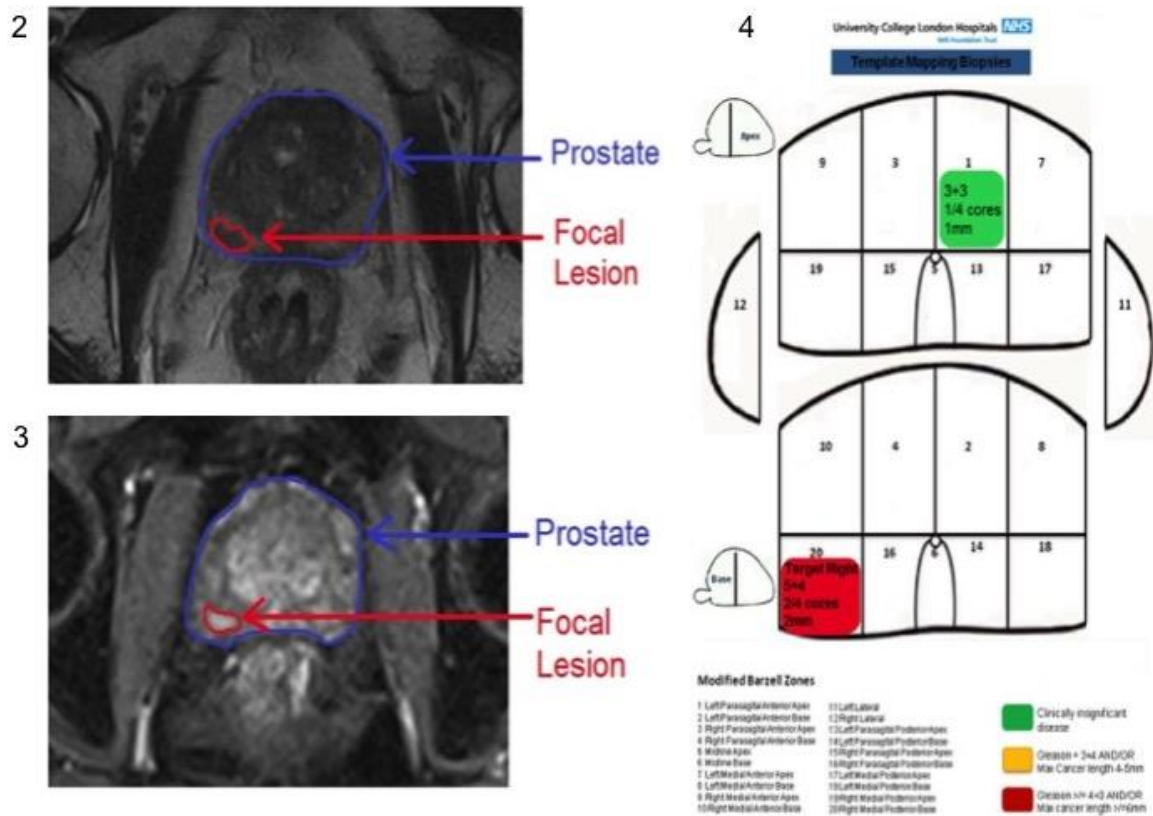


Figure 2 – T2Weighted sequence MpMRI - Patient A

Figure 3 –Dynamic Contrast Enhanced sequence MpMRI - Patient A

Figure 4 - Histopathology Outcome – Patient A

### Figures 2-4

Patient A - 72 year old patient who EBRT in 2007 for a T2c Gleason 3+3 prostate cancer with a presenting PSA of 16ng/ml. PSA nadir was 0.1. PSA then rising to 2.41. MpMRI showed prostate volume 40ml and 0.4ml of likely recurrent tumour within the mid/basal right PZ abutting the capsule at 7 o'clock position. There is small volume T2 low signal associated with restricted diffusion and focal enhancement - score 4/5. Patient underwent TPM and targeted biopsy. Targeted right PZ showed Gleason 5+4 overall in 2 of 4 cores, 2mm (15%) and 2mm (20%). TPM showed Gleason 3+3 in left anterior apex only.

## References

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- <sup>1</sup> Spratt DE1, Pei X, Yamada J, et al. Long-term survival and toxicity in patients treated with high-dose intensity modulated radiation therapy for localized prostate cancer. Int J Radiat Oncol Biol Phys. 2013 Mar 1;85(3):686-92.
- <sup>2</sup> Zumsteg ZS, Spratt DE, Romesser PB, et al. The natural history and predictors of outcome following biochemical relapse in the dose escalation era for prostate cancer patients undergoing definitive external beam radiotherapy. *Eur Urol* 2014 Oct 9. pii: S0302-2838(14)00965-8.
- <sup>3</sup> Grossfeld GD, Li YP, Lubeck DP et al (2002) Predictors of secondary cancer treatment in patients receiving local therapy for prostate cancer: data from cancer of the prostate strategic urologic research endeavor. *J Urol* 168:530–535
- <sup>4</sup> Kanthabalan A, Arya M, Punwani S et al. Role of focal salvage ablative therapy in localised radiorecurrent prostate cancer. World J Urol. 2013 Dec;31(6):1361-8.
- <sup>5</sup> Merrick GS, Gutman S, Andreini H et al. Prostate cancer distribution in patients diagnosed by transperineal template-guided saturation biopsy. *Eur Urol* 2007 Sep;52(3):715-23.
- <sup>6</sup> Morgan PB<sup>1</sup>, Hanlon AL, Horwitz EM et al. Timing of biochemical failure and distant metastatic disease for low-, intermediate-, and high-risk prostate cancer after radiotherapy. Cancer. 2007 Jul 1;110(1):68-80.
- <sup>7</sup> Haider MA, Chung P, Sweet J *et al.* Dynamic contrast enhanced magnetic resonance imaging for localisation of recurrent prostate cancer after external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 2008; 70: 425–30
- <sup>8</sup> Tanimoto A, Nakashima J, et al. Prostate cancer screening: the clinical value of diffusion-weighted imaging and dynamic MR imaging in combination with T2-weighted imaging. *J Magn Reson Imaging.* 2007 Jan;25(1):146-52.

---

9 van Dorsten FA, van der Graaf M et al. Combined quantitative dynamic contrast-enhanced MR imaging and (1)H MR spectroscopic imaging of human prostate cancer. *J Magn Reson Imaging*. 2004 Aug;20(2):279-87

<sup>10</sup> Abd-Alazeez M, Ramachandran N, Dikaios N et al. Multiparametric MRI for detection of radiorecurrent prostate cancer: added value of apparent diffusion coefficient maps and dynamic contrast-enhanced images. *Prostate Cancer Prostatic Dis*. 2015 Jun;18(2):128-36. doi: 10.1038/pcan.2014.55. Epub 2015 Feb 3.

<sup>11</sup> Donati OF, Jung SI, Vargas HA et al. Multiparametric prostate MR imaging with T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences: are all pulse sequences necessary to detect locally recurrent prostate cancer after radiation therapy? *Radiology*. 2013 Aug;268(2):440-50. doi: 10.1148/radiol.13122149. Epub 2013 Mar 12. PMID: 23481164

12 Kara T, Akata D, Akyol F et al (2011) The values of dynamic contrast-enhanced MRI in the detection of recurrent prostate cancer after external beam radiotherapy: correlation with transrectal ultrasound and pathological findings. *Diagn Interv Radiol* 17(1):38–43.

13 Haider MA, Chung P, Sweet J et al (2008) Dynamic contrast enhanced magnetic resonance imaging for localization of recurrent prostate cancer after external beam radiotherapy. *Int J Radiat Oncol Biol Phys* 70(2):425–430

14 Arumainayagam N, Kumar S, Ahmed HU et al (2010) Accuracy of multiparametric magnetic resonance imaging in detecting recurrent prostate cancer after radiotherapy. *Br J Urol Int*

15 Moore CM, Kasivisvanathan V, Eggener S et al. START Consortium. Standards of reporting for MRI-targeted biopsy studies (START) of the prostate: recommendations from an International Working Group. *Eur Urol*. 2013 Oct;64(4):544-52.

16 Dickinson L, Ahmed HU, Allen C, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. *Eur Urol*. 2011 Apr;59(4):477-94

17 J.O. Barentsz, J. Richenberg, R. Clements, *et al.* ESUR prostate MR guidelines 2012  
*Eur Radiol*, 22 (2012), pp. 746–757

18 Kirkham AP1, Haslam P, Keanie JY Prostate MRI: who, when, and how? Report from a UK consensus meeting. *Clin Radiol*. 2013 Oct;68(10):1016-23. doi: 10.1016/j.crad.2013.03.030. Epub 2013 Jul 1.

19 Onik G, Barzell W. Transperineal 3D mapping biopsy of the prostate: an essential tool in selecting patients for focal prostate cancer therapy. *Urol Oncol* 2008; 26: 506–10

20 Ahmed HU1, Hu Y, Carter T, Characterizing clinically significant prostate cancer using template prostate mapping biopsy. *J Urol*. 2011 Aug;186(2):458-64. doi: 10.1016/j.juro.2011.03.147. Epub 2011 Jun 15.

21 Crook JM, Perry GA, Robertson S Routine prostate biopsies following radiotherapy for prostate cancer: results for 226 patients. *Urology*. 1995 Apr;45(4):624-31; discussion 631-2.

---

<sup>22</sup> Morgan VA<sup>1</sup>, Riches SF, Giles S, et al. Diffusion-weighted MRI for locally recurrent prostate cancer after external beam radiotherapy. *AJR Am J Roentgenol*. 2012 Mar;198(3):596-602. doi: 10.2214/AJR.11.7162.

<sup>23</sup> Rud E<sup>1</sup>, Baco E, Lien D et al. Detection of radiorecurrent prostate cancer using diffusion-weighted imaging and targeted biopsies. *AJR Am J Roentgenol*. 2014 Mar;202(3):W241-6. doi: 10.2214/AJR.12.10483.

<sup>24</sup> Kasivisvanathan V, Dufour R, Moore CM et al. Transperineal magnetic resonance image-targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. *J Urol*. 2012 Oct 10

<sup>25</sup> Radtke JP<sup>1</sup>, Kuru TH<sup>2</sup>, Boxler S<sup>3</sup>, et al. *J Urol*. Comparative analysis of transperineal template saturation prostate biopsy versus magnetic resonance imaging targeted biopsy with magnetic resonance imaging-ultrasound fusion guidance. 2015 Jan;193(1):87-94. doi: 10.1016/j.juro.2014.07.098. Epub 2014 Jul 28.

<sup>26</sup> Siddiqui MM et al. Magnetic Resonance Imaging/Ultrasound–Fusion Biopsy Significantly Upgrades Prostate Cancer Versus Systematic 12-core Transrectal Ultrasound Biopsy *European Urology* Volume 64, Issue 5, November 2013, Pages 713–719

<sup>27</sup> Moore CM<sup>1</sup>, Robertson NL, Arsanious Net al. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. *Eur Urol*. 2013 Jan;63(1):125-40.

<sup>28</sup> Valerio M1, Donaldson I2, Emberton M2 et al. Detection of Clinically Significant Prostate Cancer Using Magnetic Resonance Imaging-Ultrasound Fusion Targeted Biopsy: A Systematic Review.

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Eur Urol. 2014 Nov 1. pii: S0302-2838(14)01040-9. doi:  
10.1016/j.eururo.2014.10.026