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# SINGLE CENTRE RETROSPECTIVE STUDY COMPARING MAGNETIC RESONANCE-TRANSRECTAL ULTRASOUND (TRUS) FUSION TARGETED AND SYSTEMATIC BIOPSY VERSUS CONVENTIONAL TRUS SYSTEMATIC BIOPSY FOR DETECTING PROSTATE CANCER

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| **Dr. Houssein EL Hajj** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Oliveira E Silva Tania** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Dalati Mohamad Fadi** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Biaou Ibrahim** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Entezari Cedric** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Thibeau Jean-François** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Tollet Valentine** | M.D, Department Of Urology, UMC Saint-pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium |
| **Sirtaine Nicolas** | M.D, Department Of Pathology, Jules-Bordet Institute, Université Libre De Bruxelles (ULB), Brussels, Belgium |
| **Gutu Razvan** | M.D, Department of Radiology, UMC Saint-Pierre, Univeristé Libre de Bruxelles (ULB), Brussels, Belgium |
| **Entezari Kim** | M.D, Department Of Urology, UMC Saint-Pierre, Univeristé Libre De Bruxelles (ULB), Brussels, Belgium. |

**ABSTRACT** **Purpose:** The aim of this retrospective study is to compare the results of MRI-TRUS fusion targeted and systematic prostate biopsy (TSPB) versus conventional systematic prostate biopsy (SPB), in biopsy naïve patients with available MRI results at time of biopsy. **Materials And Methods:** Between January 1, 2018, and May 31, 2022, patients with clinical suspicion of prostate cancer based on abnormal PSA level and/or abnormal Digital Rectal Exam (DRE) who were scheduled for prostate biopsy, were included. All patients had undergone multiparametric (mp) MRI before biopsy, and the results of this scan were known to the urologist performing the biopsy. Patients were classified according to whether they had undergone MRI-TRUS fusion targeted + systematic biopsies (TSPB, group 1) or standard TRUS systematic biopsies (SPB, group 2). We compared cancer detection rate (CDR), clinically significant cancer (ISUP≥2) detection rate, rate of upgrading or downgrading in radical prostatectomy treatment group and prostate biopsy complications. **Results:** There was no statistically significant difference in global CDR between group 1 (TSPB) and group 2 (SPB), CDR 59.7% (43/72) and 54.8% (102/186), (p< 0.48), respectively. Prostate cancer prevalence was 56.2% (145/258). There was 3 times higher risk of PCa detection in patients with MRI-visible lesions comparable to those with no MRI-visible lesions, CDR 66% (110/166 patients), and 38% (35/92 patients), OR 3.2 CI [1.9-5.4], (p<0.001), respectively. Rates of upgrading and downgrading on whole-mount histopathological analysis were 23.5% and 17.6% respectively. There was no increased risk of complications rates post prostate biopsy in both groups. **Conclusion:** In this single centre retrospective study we found no differences in CDR across combined MRI-TRUS fusion + systematic prostate biopsies versus systematic prostate biopsies in men having undergone mpMRI. Knowledge of the anatomical location of the index lesion may benefit CDR in patients undergoing standard systematic biopsies. **Patient summary:** Our study investigated the results of prostate biopsy strategy in patients suspected of having prostate cancer based on their abnormal PSA level and/or DRE. The results showed that there was no significant difference between the prostate biopsies done systematically or those done using MRI-TRUS fusion (targeted and systematic) even when there is MRI-visible lesion.

**KEYWORDS :** Prostate, multiparametric MRI, Systematic prostate biopsy, MRI-TRUS fusion Targeted prostate biopsy, PI-RADS, Prostate cancer detection rate.

## INTRODUCTION

Prostate cancer is still the second most common cancer in men [1,2]. The disease manifestations ranges from indolent to highly lethal. Inaccurate diagnosis is a longstanding obstacle in prostate cancer care. Until recently, the biopsy method most used was transrectal ultrasound guided 12-cores systematic prostate biopsy, without knowledge of the tumour location within the gland [3].

It has been shown that this technique leads to frequent missed diagnoses, grade misclassification, overtreatment, undertreatment or complications in a considerable rate [4-8].

Over the last decade, multiple high-quality studies have showed that multiparametric prostate magnetic resonance imaging (mpMRI) followed by MRI-targeted biopsy resulted in better detection of clinically significant cancer and less detection of clinically insignificant cancer compared to systematic biopsy [9-13]. Most of studies are performed in high volume academic institutions with experienced Radiologists and Urologists.

The introduction of MRI-targeted prostate biopsy combined with the conventional 12- cores TRUS systematic biopsy in the EAU guidelines in patients with visible MRI lesion (i.e., PI-RADS ≥ 3), has led urologists to adopt this method in their daily practice in prostate cancer diagnosis. One of the methods used in targeting the MRI-visible lesion is the MRI-TRUS fusion technique. This novel biopsy technique needs special training in reading MRI, labelling of the lesions and fusion of the images. It is time consuming and adds to the cost of prostate cancer

care.

Our department introduced this method in June 2020, we conducted this retrospective study to evaluate the prostate biopsy results before and after implementation of the image guided MRI-TRUS fusion targeted technique to study whether this would improve prostate cancer diagnosis, classification and therefore treatment, while also examining the accuracy of MRI results and the complications rates associated with each modality in our institution.

## PATIENTS AND METHODS

We retrospectively reviewed patients suspected of having prostate cancer based on abnormal PSA level (≥2.5ng/ml) and/or abnormal DRE, patients with suspected TRUS or prostate mpMRI findings, aged between 40 and 90 years, who have had prostate biopsy in our institution between January 1, 2018, and May 31, 2022. We excluded patients with PSA level more than 100 ng/ml, patients who were in active surveillance protocols, patients who had targeted prostate biopsy only, patients with no mpMRI done prior to biopsy and those with repeated biopsy. Targeted and systematic prostate biopsy (TSPB) were done by two Urologists trained in targeted biopsy. Systematic prostate biopsies (SPB) were done by all Urologists in the department, who were not blinded to the MRI results. Pathologic examination and biopsy features were determined by two pathologists using consensual definitions.

The risk groups were obtained according to the 2022 EAU guidelines (Low risk, Intermediate risk, High risk, locally advanced and metastatic prostate cancer patients), and the 2022 National Comprehensive Cancer Network (NCCN) guidelines (Very low risk, Low risk, Favourable intermediate risk, Unfavourable intermediate risk, High risk and Very high-risk prostate cancer).

Ethical committee of our institution approved the Study. This study was conducted in accordance with the declaration of Helsinki. No external funding was received.

**Prostate Biopsy Protocol:** All patients received prophylactic per os (PO) antibiotic started 24 hours before the date of biopsy for 3 days. Patients were positioned on left lateral decubitus, Rectal preparation with Povidone-Iodine solution cleansing enema was performed, local anaesthesia with periprostatic injection of 10 ml of Xylocaine 2% was done. For TSPB patients, mean four cores [min.2-max.10] were taken from each visible lesion using the BK® Fusion MRI/Ultrasound biopsy workflow which uses rigid registration. Thereafter 16 cores (mean) [min.8-max.21] random systematic biopsies were performed according to the department's protocol, with the use of standard segmentation to acquire medial and lateral cores from each sextant prostate region [14], (2 cores per segment (base, middle, apex) of the right and left peripheral zone and transitional zone of the prostate). For SPB patients, sixteen cores (mean) [min.6- max.26] were taken randomly if there was no identified lesion on MRI, and randomly and cognitively targeted ones if mpMRI shows visible lesions.

**MRI Protocol:** Multiparametric MRI, 1.5T with surface antenna, of the prostate was performed, T2-weighted (Axial, coronal and sagittal), contrast-enhanced, diffusion-weighted (b400, b1000, b2000) and T1 axial series were obtained. MRI lesions were given a Prostate Imaging Reporting and Data System (PI-RADS v2 and v2.1) score of 1 to 5 (with higher scores indicating more clinically suspicious lesions) to stratify the risk of prostate cancer. Three Radiologists interpreted the images in our institution, and they reviewed the mpMRI done outside our institution. Lesions that had been identified were labelled by urologists performing the targeted biopsy in agreement with the same reference radiologists.

**Prostatectomy Cohort:** Among patients in whom prostate cancer was diagnosed, various treatment options were offered. These options included active surveillance, radical prostatectomy, external-beam radiation with or without androgen deprivation therapy. For the patients who underwent radical prostatectomy, we correlated the ISUP (International Society of Urological Pathology 2014) grade group as determined on whole-mount histopathological analysis with the biopsy findings.

**Statistical Analysis:**

The analysed parameters were: age, PSA, PSAD, DRE, prostate volume measured by MRI, the detected lesions on mpMRI of the prostate, the size of primary or index lesion, and their PI-RADS classification, the highest Gleason score according to International Society of Urological Pathology 2014 (ISUP 2014), number of cores at prostate biopsy, percentage of cores invaded by cancer calculated by dividing number of positive cores by total number of prostate biopsy cores and the 2017 TNM classification.

For quantitative variables, a Mann–Whitney test was used, and for qualitative variables, a chi-square test was used. Statistical analyses were performed using 95% confidence intervals (CI) and the statistical significance level was established at 5%. SPSS IBM® was used as statistical software program (version 28).

## RESULTS:

Between January 1st, 2018, and May 31, 2022, 471 patients underwent prostate biopsy in our institution. 258 patients were eligible for analysis, 72 (28%) patients had undergone MRI-TRUS fusion targeted + systematic prostate biopsy (TSPB) and 186 (72%) patients had TRUS systematic prostate biopsy (SPB) in whom 92(49.5%) patients had no MRI-visible lesions, and 94 (50.5%) had one or more MRI-visible lesions (PI-RADS≥3), Fig.1. The global prostate cancer prevalence in our population was 56.2% (145/258). Table 1 summarizes baseline patients characteristics. There were no statistically significant differences in PSA level (10.5±11.3 vs 11.3±10.2), DRE findings (30.8% vs 22.5%), PSA Density, and PSAD if patients were classified in various categories (PSAD < 0.15, PSAD ≥0.15 and PSAD < 0.1, PSAD ≥ 0.1) between SPB and TSPB, respectively. There were statistically significant differences in age (63.7±8.6 vs 66.4±9.3) (p<0.04) between SPB and TSPB respectively, and prostate volume. Larger mean prostate volumes were found in TSPB group compared to SPB group, 59.8 cc and 48.3 cc (p<0.011) respectively.

Larger primary index lesions (L1) (16.2±8.2 VS 12.6±5, p<0.005) were visible on mpMRI in SPB compared to TSPB patients. In contrast, there was no statistically significant difference in PI-RADS classification of lesions between the two groups. Table 2 supplementary materials shows the mean number of total biopsy cores (16 cores in SPB and 20.6 cores in TSPB), targeted biopsy cores, positive cores and mean length and percentage of cancer in positive cores in both groups.

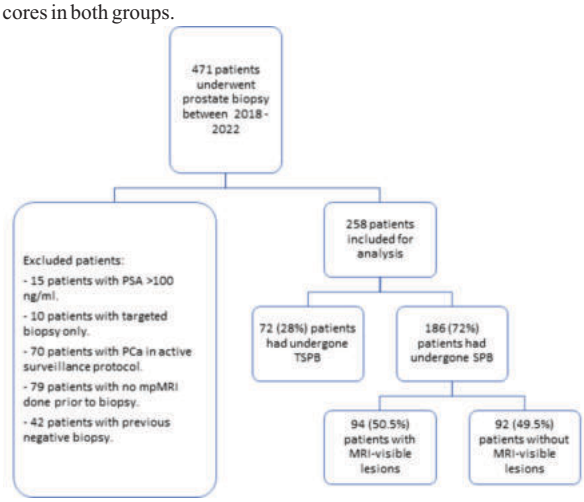


**Fig.1 Flow chart of enrolment of study subjects.**

**Table 1: Patient demographic and clinical characteristics at baseline. Larger primary lesions (L1) on MRI are visible in group 2 patients (SPB) compared to group 1 (TSPB), (p<0.005) respectively. DRE: digital rectal exam, PSA: prostate specific antigen, PSAD: PSA density, Sd (Standard deviation). *P value statistically significant.**

| | Systematic prostate biopsy SPB | Targeted & systematic prostate biopsy TSPB | All patients | P value, OR 5% CI |
|---|---|---|---|---|
| Number of patients, (%) | 186 (72%) | 72 (28%) | 258 | - |
| Mean age, y ± (Sd) | 63.7 ± 8.6 | 66.4 ± 9.3 | 64.4 ± 8.9 | 0.04* |
| Mean PSA level, ng/ml ± Sd | 10.5 ± 11.3 | 11.3 ± 10.2 | 10.7 ± 11 | 0.33 |

| | | | | |
|---|---|---|---|---|
| Maximum PSA level | 87 | 63 | - | - |
| Mean prostate volume, cc ±Sd | 48.3 ± 22.3 | 9.8 ± 32.2 | 51.5 ± 26 | 0.011* |
| Maximum prostate volume, cc | 120 | 160 | - | |
| Mean PSA density, ±Sd ng/ml/cc | 0.23 ± 0.24 | 0.23 ± 0.21 | 0.23 ± 0.24 | 0.37 |
| PSAD, N of patients (%) | | | | |
| <0.1 ng/ml/cc | 32 (17.4%) | 17 (23.6%) | 49 (19.1%) | 0.26 |
| ≥0.1 ng/ml/cc | 152 (82.6%) | 55 (76.4%) | 207 (80.9%) | |
| <0.15 ng/ml/cc | 81 (44%) | 35 (48.6%) | 116 (45.3%) | 0.5 |
| ≥0.15 ng/ml/cc | 103 (56%) | 37 (51.4%) | 140 (54.7%) | |
| DRE | | | | |
| Non-suspicious DRE | 128 (69.2%) | 55 (77.5%) | 183 (71.5%) | 0.2 |
| Suspicious or abnormal DRE | 57 (30.8%) | 16 (22.5%) | 73 (28.5%) | |
| MRI no visible lesion | 92 (49.5%) | - | 92 (35.6%) | |
| MRI single lesion L1 | 79 (41.3%) | 61 (84.7%) | 140 (54.3%) | - |
| MRI 2 or more lesions | 15 (8.1%) | 11 (15.3%) | 26 (10.1%) | |
| Primary lesion L1 | | | | |
| PI-RADS 3 | 18 (19.6%) | 9 (12.5%) | 27 (16.5%) | 0.067 |
| PI-RADS 4 | 46 (50%) | 49 (68.1%) | 95 (57.9%) | |
| PI-RADS 5 | 28 (30.4%) | 14 (19.4%) | 42 (25.6%) | |
| Mean size of index lesion L1 in mm ± Sd | 16.2 ± 8.2 | 12.6 ± 5 | 14.5 ± 7 | 0.005* |
| Index lesion: | | | | 0.3 |
| <10mm | 18 (23.4%) | 22 (31%) | 40 (27%) | |
| ≥10mm | 59 (76.6%) | 49 (69%) | 108 (73%) | |
| Mean size of L2 in mm ± Sd | 11.5 ± 5.6 | 11.5 ± 3.4 | 11.5 ± 4.5 | 0.9 |

**CDR between the 2 groups:** There was no statistically significant difference in global CDR between group 1 (TSPB) and group 2 (SPB), CDR 59.7% (43/72) and 54.8% (102/186) respectively, (p<0.48). In TSPB group, systematic biopsy alone detected 54% (39/72) of prostate cancer and targeted biopsy alone detected 42% (30/72), 9% (4/43 patients) would be missed if only systematic biopsies were done, and 30% (13/43 patients) would be missed if targeted biopsies only were done. The absolute added value of targeted biopsy is 5% (4/72). The CDR of clinically significant (cs) PCa (ISUP ≥2) for SPB and TSPB were 28% and 36% (p<0.007), respectively. The global CDR of cs PCa in our population was 30% (78/258). The CDR of clinically insignificant prostate cancer was 26% (62/258). There were no statistically significant differences between the two groups regarding clinical T staging, EAU and NCCN risk group classifications. (Table 2).

**Table 2: Shows global CDR, ISUP grade, clinical T staging, EAU and NCCN risk group between the two groups, SPB and TSPB. ISUP International Society of Urological Pathology, PCa prostate cancer. PTEN: human phosphatase and tensin homolog (tumour suppressor protein). *P value statistically significant.**

| | Systematic prostate biopsy (SPB) | MRI-TRUS targeted + systematic prostate biopsy (TSPB) | Total | P value |
|---|---|---|---|---|
| Global prostate CDR | 54.8% (102/186) | 59.7% (43/72) | 56.2% (145/258) | 0.48 |
| CDR by ISUP grade groups | | | | 0.007* |
| ISUP 1 | 49% (50/102) | 39.5% (17/43) | 46.2% (67/145) | |
| ISUP 2 | 20.6% (21/102) | 48.8% (21/43) | 29% (42/145) | |
| ISUP 3 | 19.6% (20/102) | 4.7% (2/43) | 15.2% (22/145) | |
| ISUP 4 | 4.9% (5/102) | 2.3% (1/43) | 4.1% (6/145) | |
| ISUP 5 | 5.9% (6/102) | 4.7% (2/43) | 5.5% (8/145) | |
| Clinical T staging | | | | 0.66 |
| cT1c | 62.4% (63/101) | 73.8% (31/42) | 65.7% (94/143) | |
| cT2a | 16.8% (17/101) | 9.5% (4/42) | 14.7% (21/143) | |
| cT2b | 11.9 % (12/101) | 7.1% (3/42) | 10.5% (15/143) | |
| cT2c | 5.9% (6/101) | 7.1% (3/42) | 6.3% (9/143) | |
| cT3a | 3% (3/101) | 2.4% (1/42) | 2.8% (4/143) | |
| cT3b | 0.0% (0/101) | 0.0% (0/42) | 0.0% (0/143) | |
| EAU risk groups | | | | 0.22 |
| Low risk | 35% (35/100) | 23.8% (10/42) | 31.7% (45/142) | |
| Intermediate risk | 40% (40/100) | 45.2% (19/42) | 41.5% (59/142) | |
| High risk | 14% (14/100) | 26.2% (11/42) | 17.6% (25/142) | |
| Locally advanced | 9% (9/100) | 2.4% (1/42) | 7% (10/142) | |
| Metastatic PCa | 2% (2/100) | 2.4% (1/42) | 2.1% (3/142) | |
| NCCN risk groups | | | | 0.72 |
| Very low risk | 9.8% (10/102) | 4.8% (2/42) | 8.3% (12/144) | |
| Low risk | 21.6% (22/102) | 16.7% (7/42) | 20.1% (29/144) | |
| Favourable intermediate risk | 21.6% (22/102) | 23.8% (10/42) | 22.2% (32/144) | |
| Unfavourable intermediate risk | 28.4% (29/102) | 28.6% (12/42) | 28.5% (41/144) | |
| High risk | 12.7% (13/102) | 21.4% (9/42) | 15.3% (22/144) | |
| Very high risk | 5.9% (6/102) | 4.8% (2/42) | 5.6% (8/144) | |
| PTEN status | | | | 0.25 |
| Not reported | 70.6% (72/102) | 9.3% (4/43) | 52.4% (76/145) | |
| Reported | 29.4% (30/102) | 90.7% (39/43) | 47.6% (69/145) | |
| Expression of PTEN | 83.3% (25/30) | 92.3% (36/39) | 88.5% (61/69) | |
| Loss of expression of PTEN | 16.7% (5/30) | 7.6% (3/39) | 11.5% (8/69) | |

**CDR in patients with MRI-visible lesion:** In subgroup analysis of patients who had MRI-visible lesions (PI-RADS≥3), global CDR in the SPB subgroup (94 patients with MRI-visible lesion) and TSPB group (72 patients), was in favour of the systematic biopsy but it does not reach statistical significance, 71.3% (67/94) and 59.7% (43/72), (p<0.2) respectively. However, in this subgroup there were statistically significant differences in abnormal DRE findings (44.1% vs 22.5%, p<0.004, OR 0.4, CI [0.2-0.7], prostate volume (45.8 vs 59.8 cc, p<0.004) and size of the index lesion (16.2 vs 12.6 mm, p<0.005) between SPB and TSPB groups, respectively. Clinically significant PCa detection rate was higher in SPB subgroup (patients with MRI-visible lesion) versus TSPB group, 44.7% vs 36%, (p<0.009) respectively. (Table 4, supplementary material).

**Correlation With Whole Mount Histopathological Analysis:** fifty-one patients (35%) underwent radical prostatectomy. Upgrading on histopathological analysis occurred in 12 of 51 patients (23.5%). 6/14 patients (43%) of ISUP grade 1 upgraded to ISUP grade 2. 5/22 patients (22.5%) of ISUP grade 2 upgraded to ISUP grade 3 (4/22 patients (18%)) and ISUP grade 4 (1/22 patients (4.5%)). No patients from ISUP grade 3 upgraded to higher ISUP grade. Downgrading on

whole-mount histopathological analysis occurred in 9 of 51 patients (17.6%). 2/22 patients (9%) of ISUP grade 2 downgraded to ISUP grade 1. 5/10 patients (50%) from ISUP grade 3 downgraded to ISUP grade 2 (4/10 patients (40%)), and ISUP grade 1 (1/10 patient (10%)). 1/3 patients (33.3%) from ISUP grade 4 downgraded to ISUP grade 2. (Table 3).

**Table 3: Cross-tabulations showing upgrading and downgrading of ISUP grade between prostate biopsy histopathological analysis (TSPB and SPB) and whole-mount radical prostatectomy histopathological analysis.**

| ISUP Radical prostatectomy / ISUP prostate Biopsy | ISUP 1 | ISUP 2 | ISUP 3 | ISUP 4 | ISUP 5 | Total |
|---|---|---|---|---|---|---|
| ISUP 1 | 8 (57%) | 6 (43%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 14 (27.5%) |
| ISUP 2 | 2 (9%) | 15 (68%) | 4 (18%) | 1 (4.5%) | 0 (0.0%) | 22 (43.1%) |
| ISUP 3 | 1 (10%) | 4 (40%) | 5 (50%) | 0 (0.0%) | 0 (0.0%) | 10 (19.6%) |
| ISUP 4 | 0 (0.0%) | 1 (33.3%) | 0 (0.0%) | 1 (33.3%) | 1 (33.3%) | 3 (5.9%) |
| ISUP 5 | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (50%) | 1 (50%) | 2 (3.9%) |
| Total | 11 (21.6%) | 26 (51%) | 9 (17.6%) | 3 (5.9%) | 2 (3.9%) | 51 patients |

**MRI Results:** The rates of MRI-visible lesions (PIRADS≥3) and No MRI-visible lesions in our population were 64.3% (166/258) and 35.7% (92/258) respectively. The global prostate CDR is 66.3% (110/166 patients) for the former group compared to 38% (35/92 patients) for the latter, OR 3.2, CI [1.9-5.4], (p<0.001). The prostate biopsy in patients with MRI-visible lesions detected more cs PCa (ISUP≥2) compared to patients with no MRI-visible lesions. There were no ISUP grade 4 or 5 detected in patients with no MRI-visible lesion. (Table 4).

Calculated global sensitivity, specificity, PPV and NPV of mpMRI for detecting prostate cancer, were: 76%, 50%, 66% and 62%. While rates for cs PCa (ISUP≥2) detection were: 87%, 50%, 55% and 85%, respectively.

**Table 4: Shows the CDR in patients with MRI visible lesion (66.3%) and those with No MRI visible lesion (38%), OR=3.2 [1.9-5.4], p<0.001. Also are showed ISUP grade group results, no ISUP grade 4 or 5 were detected in patients with No MRI visible lesions, p<0.009. CDR: cancer detection rate. *P value statistically significant.**

| | MRI visible lesions | No MRI visible lesions | P value |
|---|---|---|---|
| Positive prostate biopsy | 110 patients | 35patients | - |
| Negative prostate biopsy | 56 patients | 57 patients | - |
| Total | 166 | 92 | - |
| CDR | 110/166 (66.3%) | 35/92 (38%) | 0.001* |
| Clinical ISUP<br>ISUP 1<br>ISUP 2<br>ISUP 3<br>ISUP 4<br>ISUP 5 | <br>42/110 (38.2%)<br>36/110 (32.7%)<br>18/110 (16.4%)<br>6/110 (5.5%)<br>8/110 (7.3%) | <br>25/35 (71.4%)<br>6/35 (17.1%)<br>4/35 (11.4%)<br>0/35 (0.0%)<br>0/35 (0.0%) | 0.009* |

In our population CDR increased from 49.2% in patients with non-suspicious DRE into 72.6% in those with suspicious DRE, OR: 2.7 CI [1.5-4.9] (p<0.001). Calculated sensitivity, specificity, PPV and NPV for DRE were: 37%, 82%, 72% and 51%, respectively. (Table 3 supplementary materials)

Rates of prostate biopsy complications are shown in the table 1 supplementary materials. A total of 14 (5.4%) patients developed complications: 1/257 (0.4%) fever, 4/257 (1.6%) sepsis, 6/257 (2.3%) UTI (prostatitis and epididymitis) and 3/257 (1.2%) developed haematuria for more than 48 hours. No statistically significant differences in complications rates were found between the two groups. There was no reported death due to prostate biopsy.

## DISCUSSION

This retrospective study has shown that there was no difference in CDR between targeted + systematic prostate biopsies versus systematic biopsies. Several factors may explain our results including, larger index lesion, smaller prostate volume, and cognitive targeting of visible lesions, when present, in the SPB group. Other explanation may be the inaccuracy in targeted biopsy technique, which could be the result of inadequate interpretation of the MRI and labelling of the lesions and of poor targeting experience, as shown in the relatively high percentage of patients (30%) with PCa who would be missed if only targeted biopsies were performed. However, the relatively high number of biopsy cores in both groups compensated for potential targeting and labelling errors as shown in the relatively low rates of upgrading and downgrading on whole mount radical prostatectomy pathology results.

The trials demonstrating a benefit from MRI targeted biopsy applied the strategy to selected patients, which may affect the generalizability of the results when transferred to men referred for biopsies in the general population. The PRECISION trial [26], which demonstrated superiority of MRI targeted biopsy over TRUS systematic biopsy, included men with PSA ≤ 20 ng/ml and < cT3 and most men (85%) had normal DRE. Our cohort included men with higher PSA value, (up to 87 ng/ml), and higher percentage of men with suspected DRE (30.8% in SPB group vs 22.5% in TSBP group). This may explain the high likelihood of diagnosing clinically significant prostate cancer on systematic TRUS biopsies (44.7%) and why the benefit of adding MRI targeted biopsy could not be demonstrated in our study. The high likelihood of diagnosing cs PCa on systematic TRUS biopsies in population-based setting was also reported in a retrospective study by Kawa et al (40.8%) [27]. It is possible to suggest that patients selected to undergo targeted and systematic or systematic prostate biopsy should be based on their risk profile. This may reduce the cost and the time in prostate cancer care.

In the ERSPC trial, Gosselaar, C., et al reported that an abnormal DRE in conjunction with an elevated PSA more than doubled the risk of a positive biopsy (48.6% vs. 22.4%) [15]. Herrera-Caceres, J.O., et al. reported that abnormal DRE is associated with an increased risk of higher ISUP grade [16]. Current literature including systematic reviews and meta-analyses do not show clear superiority of one image-guided technique over another (in bore MRI, MRI-TRUS fusion or cognitive) in targeting MRI visible lesions [17,18,19]. In our study, the presence of larger index lesion L1 (16.6±8mm vs 12.4±5, p<0.001) in SPB vs TSPB respectively, the smaller prostate volume and the cognitive targeting of the lesions in the SPB group when MRI shows visible lesions, all may explain the comparable CDR between the 2 groups, and the increased detection rate of cs PCa (ISUP≥2), 44.7% vs 36% in SPB subgroup (with MRI-visible lesions), compared to Targeted + systematic biopsy group, respectively.

In their prospective study on biopsy naïve patients, Van der Leest et al reported CDR of csPCa of 30% and clinically insignificant PCa of 23% in the combined pathway (12 cores systematic biopsy with in bore-MRI targeted biopsy) [20]. In the Assessment of Prostate MRI Before Prostate Biopsies (MRI-FIRST) trial, 251 biopsy-naive patients underwent TRUS-guided systematic biopsy by an operator who was blinded to MRI findings, and MRI-targeted biopsy by another operator. Magnetic resonance Imaging-targeted biopsy detected ISUP grade ≥ 2 cancers in a higher percentage of patients, but the difference was not significant (32.3% vs. 29.9%, p<0.38; detection ratio: 1.08), [21]. Herein we reported comparable CDR of csPCa and insignificant PCa (30% and 26%). However, the rate of csPCa (30%) in our cohort is lower compared with contemporary cohorts (38-47%), [22,23], an explanation could be the higher rate of MRI-visible lesions reported in these cohorts (64-73% vs 64% in our cohort).

Ahdoot et al, in the secondary analysis of the TRIO study using PI-RADS scores to select an optimal prostate biopsy method in biopsy naïve and prior biopsy patients, reported a global CDR of 69.7%, [24], which is slightly higher than our CDR in patient with MRI-visible lesion (66%). An important explanation for this is their higher reported rate of PI-RADS 5 lesions (PI-RADS 2 and 3, 4 and 5: 7.1% and 12%, 47.9% and 33.1% vs 16.4%, 57.9% and 25.6% in our cohort respectively).

In a Cochrane meta-analysis which compared MRI to template biopsies (> 20 cores) in biopsy-naive and repeat-biopsy settings, MRI had a pooled sensitivity of 0.91 (95% CI: 0.83–0.95) and a pooled specificity of 0.37 (95% CI: 0.29–0.46) for ISUP grade ≥ 2 cancers,

[25]. In our study, calculated sensitivity, specificity, PPV and NPV of mpMRI were: 87%, 50%, 55% and 85% respectively. The reported discrete lower rate of MRI sensitivity deserves better standardisation of interpretation and quality check of acquisition of MRI images in our institution.

Van der Leest et al also reported an upgrading between 21-25% and downgrading between 35-38%, on whole mount prostatectomy specimen histopathological analysis, [20]. In our prostatectomy cohort rates of upgrading (23.5%) and downgrading (17.6%) are relatively lower, which maybe resulted from the relatively high number of biopsy cores (16-20 cores) taken in both groups, better cancer mapping and more consistent histopathological analyses. The major drawback of whole mount histopathological analysis is that not all diagnosed patients undergo radical prostatectomy.

Finally, Rates of infectious complications post biopsy were comparable in both groups irrespective of the number of biopsy cores taken and were in line with those reported by Van der Leest et al (6%), [20] and Ahmed HU et al (5.9%), [28].

Strengths and limitations: The limitations of the study are multiple and include: retrospective nature of the project, heterogenous population, evolving expertise in targeted prostate biopsy of urologists. However, this study reflects the daily living reality in prostate cancer diagnosis, as the interpretation of prostate MRI, and subsequent biopsy are performed by specialists with different level of experience. As strengths, the ISUP grade of prostate biopsies were correlated to the whole mount histopathological analysis of radical prostatectomy. This article may reflect the reality among institutions that are starting to adopt image guided (MRI-TRUS fusion) prostate biopsy technique, showing again the reason this technique was not consensual as first biopsy strategy, and that image guided fusion versus cognitive targeting could have the same results. Therefore, the impact of image guided MRI fusion prostate biopsy should not be overestimated and should be applied to selected patients based on their risk profile.

## CONCLUSION

This retrospective study evaluated cancer detection rate in patients undergoing combined MRI-TRUS fusion targeted + systematic prostate biopsies (TSPB) versus systematic prostate biopsies (SPB). It showed the same CDR in both groups. It underlines, once again, the impact of mpMRI in detecting clinically significant prostate cancer.

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**Supplementary materials:**

**Table 1: Prostate biopsy complications rate in the two groups. UTI: urinary tract infection (prostatitis, Epididymitis), Haematuria is reported if it persists for more than 2 days.**

| Prostate biopsy complications | SPB | TSPB | Total | P value |
|---|---|---|---|---|
| None | 173/185 (93.5%) | 70/72 (97.2%) | 243/257 (94.6%) | 0.73 |
| Fever | 1/185 (0.5%) | 0/72 (0.0%) | 1/257 (0.4%) | |
| Sepsis | 3/185 (1.6%) | 1/72 (1.4%) | 4/257 (1.6%) | |
| UTI | 5/185 (2.7%) | 1/72 (1.4%) | 6/257 (2.3%) | |
| Haematuria | 3/185 (1.6%) | 0/72 (0.0%) | 3/257 (1.2%) | |

**Table 2: Shows the mean number of total biopsy cores, targeted biopsy cores, positive cores and Mean length and percentage of cancer in positive cores, in both groups (TSPB and SPB). Sd= Standard deviation.**

| | SPB | TSPB | P value |
|---|---|---|---|
| Mean number of total cores ±Sd | 16 ± 2.7 | 20.6± 2 | 0.00 |
| Mean number of total positive cores ± Sd | 3.2 ± 4.4 | 4.7 ± 6.5 | 0.2 |
| Mean number of Targeted biopsy cores ± Sd | - | 4.6 ± 1.6 | - |
| Mean number of positive targeted biopsy cores ± Sd | - | 1.4 ± 2 | - |
| Mean percentage of positive cores ± Sd | 21.2 ± 29.6 % | 22.6 ± 30.6% | 0.6 |
| Mean total length of cancer ± Sd in positive cores TC, in mm | 20.5± 23.6 | 26.2 ± 24.2 | 0.11 |
| Mean total length of positive cores (TLC) in mm | 62.3 ± 44.4 | 71.8 ± 48.3 | 0.37 |
| Mean percentage TC/TLC % | 38.7 ±29.5 % | 44.2 ± 30.7 % | 0.27 |

**Table 3: Shows CDR between patients with suspicious DRE and those with non-suspicious DRE, OR: 2.7, CI [1.5-4.9], * P value statistically significant.**

| | Positive prostate biopsy result | Negative prostate biopsy result | P value |
|---|---|---|---|
| Non-suspicious DRE | 49.2% (90/183) | 50.8% (93/183) | <0.001* |
| Suspicious DRE | 72.6% (53/73) | 27.4% (20/73) | |

**Table 4: Demographic and clinical baseline characteristics of patients with visible-MRI lesions subgroup analysis. More patients with abnormal DRE findings, smaller prostate volume and larger index lesion L1, were found in systematic biopsy group compared to targeted and systematic biopsy group. * P value statistically significant.**

| | SPB subgroup | TSPB | Total | P value, Or, 5% CI |
|---|---|---|---|---|
| Nb of patients | 94 | 72 | 166 | - |
| Mean age, (year) | 64.6 ± 8.9 | 66.4 ± 9.3 | 65.3 ± 9 | 0.2 |
| Mean prostate volume, (cc) | 45.8 ± 20.2 | 59.8 ± 32.2 | 51.9 ± 27 | 0.004* |
| Mean PSA level (ng/ml) | 11.8 ± 13.2 | 11.3 ± 10.2 | 11.6 ± 12 | 0.8 |
| PSA density, PSAD (ng/ml/cc) | 0.28 ± 0.3 | 0.23 ± 0.21 | 0.26 ± 0.27 | 0.064 |
| Mean size of index lesion (L1), (mm) | 16.2 ± 8.2 | 12.6 ± 5 | 14.5 ± 7 | 0.005* |
| PI-RADS of L1 | | | | 0.067 |
| PI-RADS 3 | 18/92 (19.6%) | 9/72 (5.5%) | 27/164 (16.5%) | |
| PI-RADS 4 | 46/92 (50%) | 49/72 (68.1%) | 95/164 (57.9%) | |
| PI-RADS 5 | 28/92 (30.4%) | 14/72 (19.4%) | 42/164 (25.6%) | |
| DRE results | | | | 0.004* |
| Suspicious DRE | 41/93 (44.1%) | 16/71 (22.5%) | 57/164 (34.8%) | OR 0.4, CI [0.2-0.7] |
| Non-suspicious DRE | 52/93 (55.9%) | 55/71 (77.5%) | 107/164 (65.2%) | |
| PSAD <0.1 ng/ml/cc | 13/92 (14%) | 17/72 (23.6%) | 30/164 (18.3%) | 0.2 |
| PSAD ≥0.1 ng/ml/cc | 79/92 (86%) | 55/72 (76.4%) | 134/164 (81.7%) | |
| PSAD <0.15 ng/ml/cc | 34/92 (37%) | 35/72 (49%) | 69/164 (42%) | 0.13 |
| PSAD ≥ 0.15 ng/ml/cc | 58/92 (63%) | 37/92 (51%) | 95/164 (58%) | |
| Biopsy results | | | | |
| CDR | 67/94 (71.3%) | 43/72 (59.7%) | 110/166 (66.3%) | 0.2 |
| ISUP grade groups | | | | 0.009* |
| ISUP 1 | 25/67 (37.3%) | 17/43 (39.5%) | 42/110 (38.2%) | |
| ISUP 2 | 15/67 (22.4%) | 21/43 (48.8%) | 36/110 (32.7%) | |
| ISUP 3 | 16/67 (23.9%) | 2/43 (4.7%) | 18/110 (16.4%) | |
| ISUP 4 | 5/67 (7.5%) | 1/43 (2.3%) | 6/110 (5.5%) | |
| ISUP 5 | 6/67 (9%) | 2/43 (4.7%) | 8/110 (7.3%) | |

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