# A Comparative Study on the Diagnostic Efficacy and Safety of Ultrasound-Guided Transperineal and Transrectal Prostate Needle Biopsy

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***Objective***: To compare the diagnostic efficacy between the transperineal and the transrectal prostate needle biopsy as the initial biopsy strategy for detection of prostate cancer.
***Methods***: A total of 179 patients with PSA of 2.5 - 20 ng/mL who underwent initial prostate needle biopsy were included. One hundred eight (108) patients underwent transrectal prostate needle biopsy (TRUS-BX) from March to December 2014, while 71 patients underwent transperineal prostate needle biopsy (TP-BX) from January 2015 - August 2016. Descriptive statistics including mean, median and percentage were used for the patient demographics. Student's t-test was used to compare continuous variables between the two groups. $X^2$ or Fisher's exact probability tests were used for categorical variables.
**Results**: The mean age of the patients who underwent the TP-BX and TRUS-BX were 66.10 years and 62 years respectively (p = 0.0003). The mean prostate volumes were 44.10 mL and 42.39 mL (p=0.5405), while the mean PSA were 9.51 ng/mL and 9.21 ng/ml (p = 0.6096) for the TP-BX and TRUS-BX, respectively. The TP-BX provided a greater overall cancer detection rate of 63.38% (45/71) compared to 35.19% (38/108) obtained from the TRUS-BX (p <0.0001). Detection of clinically significant cancer, defined as Gleason score of 7 or higher was likewise greater in the TP-BX compared to the TRUS-BX (77.78% vs 55.26%; p = 0.029). Among patients with PSA values of 2.5 ng/mL - 10 ng/mL, cancer detection was significantly higher in the TP-BX group (59.09% vs 31.11% p value = 0.002). Cancer detection rates in patients with PSA 10 ng/mL - 20 ng/mL were comparable in between the two groups (70.37% vs 55.56% p value = 0.309). Of the patients who had cancer in the TP-BX group, 77.77% (35/45) involved the anterior sector, 60% (27/45) the middle sector and 48.89% (22/45) the posterior sector. Thirteen out of the 35 cancers (37.14%) detected in the TP-BX group involved exclusively the anterior sector. The most common complication was hematuria at 35.21% for TP-BX and 50% for TRUS-BX. Complications that occurred exclusively for TRUS-BX included fever (2.78%) and 1 case (0.93%) of septicemia requiring hospitalization and parenteral antibiotics. Minor perineal bruising occurred exclusively in 8.45% of the patients who underwent TP-BX.
**Conclusion**: The transperineal prostate needle biopsy should be considered as the initial biopsy strategy for detection of prostate cancer. The manifested advantages are the following: a) The overall cancer detection rate is significantly higher, b) The detection rate of clinically significant cancer is significantly greater, c) It provides a far more superior detection of exclusive anterior zone cancers which are often under detected or undetected with the current standard TRUS-BX and d) Complications are comparable, if not fewer than the current standard TRUS-BX.

***Key words***: transperineal, transrectal, prostate neddle biopsy

## Introduction

Since its introduction in the 1980's, transrectal ultrasound guided prostate needle biopsy (TRUS-BX) has been the standard method for early detection of prostate cancer (PCa).[1] This simple procedure can be performed under local anesthesia in an outpatient, non-operating room setup. In general, the indication for a prostate biopsy is an abnormality in the serum prostate specific antigen (PSA) or an abnormality in the digital rectal examination (DRE).[2]

This technique involves taking at least 12 systematic cores of the peripheral zone of the prostate using a biopsy needle traversing through the rectum, utilizing transrectal ultrasound guidance. However, the diagnostic yield ranges only from 30%-35%[3-4], despite numerous modifications through the years, from increasing the number of cores, to laterally directed cores and even saturation biopsy.[5-10]

The transperineal prostate needle biopsy (TP-BX) provides excellent sampling of the anterior and apical regions of the prostate, which are frequently under sampled using the transrectal approach.[11] However, this technique is still not widely utilized yet due to its requirement for anesthesia and the need of an operating room setup, making it potentially more cumbersome, especially in inexperienced hands. The most common indication for the TP-BX would be in men with prior negative biopsies, but nevertheless, were still suspected of having PCA, due to persistently elevated or rising PSA and / or a suspicious DRE. The detection rate ranges from 22% - 83.3% in the anterior sector after at least two negative previous TRUS-BX.[12-15] A local study comparing the yield of TP-BX performed in a group of patients with a previous negative TRUS-BX revealed a 54% detection rate. Most important of note is that more than 90% of the cancers detected on the repeat TP-BX are located in the anterior sectors.[14] These data suggest that a considerable number of potentially missed cancers during the initial TRUS-BX.

Utilizing the TP-BX approach as the initial biopsy procedure could potentially avoid missing these anteriorly located cancers that could not have been sampled using the TRUS-BX.

Active surveillance had gained grounds due to the increasing detection of the so called "clinically insignificant cancers". A pathology report of Gleason score 6 is considered indolent in nature and generally need not be treated aggressively. However, the challenge is the considerable under grading of current biopsies in sampling the true picture of the prostate gland. Recent data indeed suggest that the TP-BX can give a better picture of the true pathology of the prostate gland by virtue of its ability to detect a higher proportion of Gleason 7 and above cancers or the so called "clinically significant" cancers.

It was therefore the objective of this study to compare the diagnostic efficacy be-tween TP-BX and TRUS-BX as the initial biopsy strategy for detection of prostate cancer, not only in the ability to detect cancers but also in the ability to detect clinically significant cancer that warrants a potentially more aggressive management approach.

### *Significance of the Study*

The peripheral zone of the prostate has always been regarded as the most common site of PCA.[2] However, recent evidences showed that 47%-83%[12] of PCA may involve the anterior sector of the prostate gland and as high as 22% involve exclusively the anterior sector.[13] These carcinomas may be clinically significant and these could have been missed by TRUS-BX due to its anatomic location.

The incidence of post biopsy sepsis is increasing due to widespread misuse of antibiotics that led to development of resistant strains of microorganisms causing potential septic complications in a supposedly simple, safe and outpatient procedure.[16]

There is a need for a more efficient and safer technique of prostate biopsy. Utilizing the transperineal approach as the initial strategy for prostate biopsy may potentially increase the likelihood of detecting clinically significant anteriorly located cancer while minimizing potential septic complications.

This study would be timely because this is the first local study to compare the diagnostic efficacy of the two techniques in the initial biopsy setting.

## Materials and Methods

This is a retrospective cohort study. Participants were patients who underwent an initial prostate biopsy using TRUS-BX from March to December 2014 and TP-BX from January 2015 - August 2016.

Only patients with PSA between 2.5 to 20 ng/mL were included in the study. Excluded were patients with palpable prostatic nodule/s by DRE, those who underwent previous prostate biopsy, patients with known bleeding disorders, with hypercoagulable states, peripheral arterial occlusive disease and deep vein thrombosis.

All demographic data, detection rates, percentage of clinically significant cancers defined as Gleason score of 7 and above, anatomical location of detected cancers, as well as complications were obtained from the prostate biopsy database of the senior author. This study was approved by the hospital's Ethics Review Committee.

*Transperineal Prostate Biopsy Technique*

All procedures were performed at the UST Hospital by a single urologist using the BK Falcon flex focus 800 Ultrasound unit utilizing SA8848 bi plane transducer. The biopsies were performed under total intravenous sedation anesthesia in the operating room. Written and informed consent was obtained prior to the procedure.

Oral broad-spectrum antibiotics (fluoroquinolones) were given 2 days prior to the procedure. Bowel preparation, in the form of bisacodyl was given the night before the procedure. On the day of the procedure, patient was given Ceftriaxone 1g/IV. For the procedure, patients were placed in the lithotomy position. A Fr 18 3-way Foley catheter was inserted to facilitate identification of urethra and prostatovesical junction (Figure 1). Operative time was recorded starting from the insertion of the ultrasound probe into the rectum and ending with removal of the ultrasound probe.

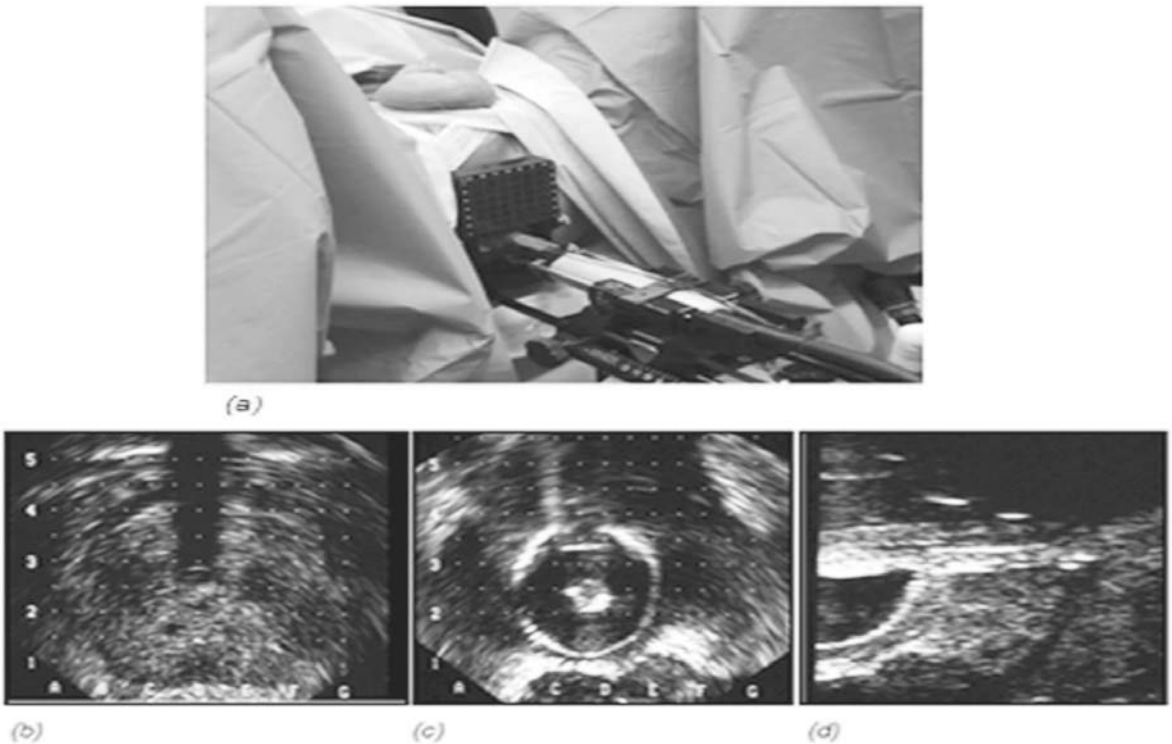


**Figure 1.** Patient is placed an lithotomy position and draped.(Figure 1a) Sonographic images showing the urethra at the center of the grid (Figure 1b) as well as images of the prostatoveiscal junction (Figure 1c & 1d)

The sites and the number of biopsy cores were taken following the standard 'Victorian Transperineal Template" as seen in figure 2.[17] The number of biopsy cores taken was based on the prostate volume with additional cores upon the discretion of the senior author. Samples were obtained in such a way as to cover the anterior, mid gland and posterior sectors of both the right and the left side of the prostate gland. Twenty-four (24) cores were taken for prostate size less than 30 mL, 32 cores for prostate size 31 mL - 60 mL, and 38 cores for greater than 60 mL (Table 1). After the biopsy, the oral fluoroquinolones were continued for 5 more days.

**Table 1**. TP-BX template-guided biopsy cores according to prostate size.

| Prostate Size (in mL) | Number of Biopsy Cores |
|---|---|
| Less than 30 mL | 24 |
| 31 mL - 60 mL | 32 |
| Greater than 60 mL | 38 |

All specimen were placed in formalin solution, properly labeled and sent for histopathologic processing to be interpreted by a single group of pathologists dedicated to interpret prostate biopsy specimen.

As a matter of policy, patients were advised an overnight stay in the hospital and the catheter was maintained for 24 hours. This was by no means compulsory but the preference of the attending urologist.

*Transrectal Prostate Biopsy Technique*

All procedures were performed at UST Hospital by a single urologist using the BK Falcon flex focus 800 Ultrasound unit utilizing SA8848 bi plane transducer.

The biopsies were performed under total intravenous sedation anesthesia in the operating room. Written and informed consent was obtained from the patients prior to the procedure.

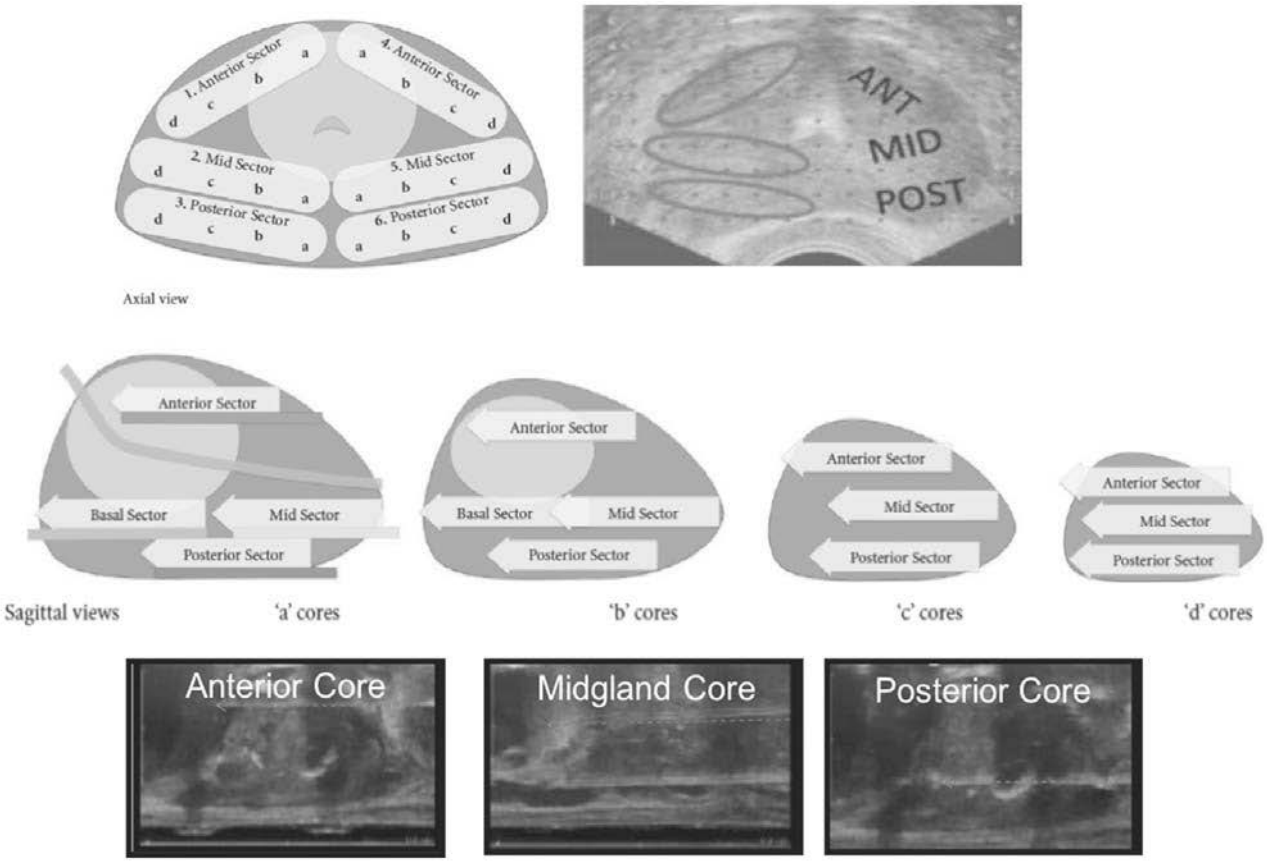


**Figure 2.** Standard technique of sampling in the transperineal prostate sector biopsy.[17]

Oral broad-spectrum antibiotics (fluoroquinolones) were given 2 days prior to the procedure and an oral anaerobic antimicrobial (metronidazole) was given one day prior to the procedure. Bowel preparation, in the form of bisacodyl was given the night before the procedure. Operative time was recorded starting from the insertion of ultrasound probe into the rectum and ending with removal of ultrasound probe into the rectum. The number of cores taken was 24, with at least 4 cores each to sample the apex, mid and base of both the right and the left side of the prostate gland. Additional cores usually at the suspicious lesions on ultrasound were taken upon the discretion oft the senior author. A parenteral antibiotic (Ceftriaxone, 1g/IV) was given 30 minutes prior to the procedure. After the biopsy, the fluoroquinolones were continued for 5 more days and metronidazole for 2 more days.

Patients were initially placed in the right lateral decubitus position. Twelve peripherally directed biopsy cores to sample both the right and left peripheral zones of the prostate for a total of 24 biopsy cores were obtained. These were labeled as TRUS-BX specimen.

**Complications**

Complications associated with biopsy were grouped as major or minor according to need for subsequent inpatient intervention.

A. Major Complications
   1. Septicemia - blood culture positive requiring parenteral antibiotics,
   2. Major Perineal bleeding (PR) - requiring intervention
   3. Major Rectal bleeding - requiring intervention
   4. Major hematuria - more than 3 days or requiring intervention
   5. Major Perineal bruising - presence of butterfly hematoma

B. Minor Complications - side effects that are routinely expected from biopsy
   1. Minor hematuria - of less than 3 days duration
   2. Pain at post-biopsy site
   3. Vasovagal syncope
   4. Dysuria
   5. Rectal bleeding
   6. Infection/fever greater than 38.5°C - controlled by oral antibiotics with negative blood culture
   7. Perineal bruising - minor discoloration of the perineal area

Complications were managed in the standard manner.

**Statistical Analysis**

The PASS 2008 software was used to calculate the minimum sample size for the study. A total of 71 TP-BX patients and 108 TRUS-BX patients were needed to achieve 80% power with a confidence level of 95%. Data were tabulated in Microsoft Excel version 15.11.2. Data processing and analysis were done using Stat SE version 12. Descriptive statistics such as mean, median and percentage were presented. Student's t-test was used to compare continuous variables between the two groups. $X^2$ or Fisher's exact probability tests were used for categorical variables. Statistical significance was accepted in the present study when P-value was below 0.05.

## Results

The study population consisted of 71 men who underwent TP-BX and 108 men who underwent TRUS-BX. Table 2 shows the characteristics of the patients in each group. The patients in the TP-BX group had a higher mean age of 66.10 years compared to the 62 years for the TRUS-BX group ($p = 0.0003$). The mean prostatic volumes as well as the mean PSA values were not significantly different at 44.10 mL compared to 42.39 mL ($p= 0.5405$) and 9.51 ng/mL compared to 9.21 ng/mL ($p= 0.6096$) for the TP-BX and TRUS-BX groups respectively.

The overall cancer detection rate (Table 3) was significantly higher in TP-BX compared to TRUS-BX (63.38% vs 35.19%; $p<0.0001$). Detection of clinically significant cancer was likewise higher in TP-BX compared to TRUS-BX (77.78% vs

55.26%; p =0.016). On the other hand, the detection of clinically insignificant cancers was lower in the TP-BX group compared to the TRUS-BX group (22.22% vs 44.74%; p =0.016).

One hundred thirty-four patients in the series had PSA range of 2.5 ng/mL to 10 ng/mL (Table 3). Among patients with PSA level between 2.5 ng/mL to 10 ng/mL, TP-BX showed a higher cancer detection rate (59.09% vs 31.11%; p value = 0.002). Subsequently, patients with PSA level between 10 ng/mL to 20 ng/mL, TP-BX had a numerically higher detection rate compared to TRUS-BX although not statistically significant (70.37% vs 55.56% p value = 0.309).

Further sub-analysis (Table 3) showed that, among patients with PSA range 2.5 ng/mL to 10 ng/mL, detection rate of TP-BX and TRUS-BX was comparable for clinically significant cancer (30.77% vs 46.43%; p value = 0.238) and for clinically insignificant cancer as well (69.23% vs 60%; p value = 0.238). For PSA range 10 ng/mL to 20 ng/mL, detection rate of TP-BX and TRUS-BX was also comparable for clinically significant cancer (10.53% vs 40% p value = 0.063) and for clinically insignificant cancer (89.47% vs 60%; p value = 0.063).

A total of 45 cancers were detected out of 71 patients (63.38%) in the TP-BX group. The thirty-five patients (77.77%) involved the anterior sector, 27 (60%) involved the middle sector and 22 (48.89%) involved the posterior sector. Of note is that 13 (37.14%) out of the 45 cancers detected involve exclusively the anterior sector (Table 4).

Of the patients who had cancer involving exclusively the anterior sector, 53.84% were clinically significant (Table 5).

**Table 2**. Characteristics of patients assigned to TP-BX and TRUS-BX groups and operative time of both procedures.

| | TP-BX (n=71) | TRUS-BX (n=108) | p-value |
|---|---|---|---|
| Age (in years), mean | 66.10 ± 7.48 | 62 ± 7.28 | 0.0003*[a] |
| Prostate volume (in ml), mean | 44.10 ± 22.65 | 42.39 ± 14.54 | 0.540[a] |
| PSA (in ng/ml), mean | 9.51 ± 4.84 | 9.21 ± 3.04 | 0.609[a] |
| Operative time (in minutes), mean | 15.73 + 3.72 | 8.14 + 0.91 | < 0.00001*[a] |

*statistically significant (p<.0.05)
[a]independent t-test was used for analysis

**Table 3**. Cancer detection rate of TP-BX vs TRUS-BX.

| | TP-BX (n=71) | TRUS-BX (n=108) | p-value |
|---|---|---|---|
| Overall | 45/71 (63.38%) | 38/108 (35.19%) | <0.0001* |
| Clinically insignificant cancer | 10/45 (22.22%) | 17/38 (44.74%) | 0.016*[a] |
| Clinically significant cancer | 35/45 (77.78%) | 21/38 (55.26%) | |
| PSA | | | |
| PSA 2.5 ng/mL - 10 ng/mL | 26/44 (59.09%) | 28/90 (31.11%) | 0.002* |
| Clinically significant cancer | 8/26 (30.77%) | 13/28 (46.43%) | 0.238 |
| Clinically insignificant cancer | 18/26 (69.23%) | 15/28 (60%) | |
| PSA > 10 ng/mL - 20 ng/mL | 19/27 (70.37%) | 10/18 (55.56%) | 0.309 |
| Clinically significant cancer | 2/19 (10.53%) | 4/10 (40%) | 0.063 |
| Clinically insignificant cancer | 17/19 (89.47%) | 6/10 (60%) | |

*statistically significant (p<.0.05)
[a]chi square test was used for analysis

**Table 4**. Anatomic distribution of cancer (TP-BX).

| | TP-BX |
|---|---|
| Anterior Sector | 35/45 (77.77%) |
| Anterior Only | 13/35 (37.14%) |
| Anterior + Other sectors | 22/35 (62.85%) |
| Middle Sector | 27/45 (60%) |
| Middle Only | 3/27 (11.11%) |
| Middle + Other sectors | 24/27 (88.89%) |
| Posterior Sector | 22/45 (48.89%) |
| Posterior Only | 3/22 (13.63%) |
| Posterior + Other Sectors | 19/22 (86.36%) |

**Table 5**. Clinically significant cancers positive cores based on location.

| | TP-BX | |
|---|---|---|
| | Clinically Significant (n) | Clinically Insignificant (n) |
| All patients | | |
| Anterior sector only | 7/13 (53.84%) | 6/13 (46.15%) |
| Mid sector only | 3/4 (75%) | 1/4 (25%) |
| Posterior sector only | 3/4 (75%) | 1/4 (25%) |

Of note (Table 6), patients with PSA range of 2.5 ng/mL to 10 ng/mL, 38.64% (17/44) involved the anterior sector and 15.91% (7/44) involved the anterior sector only. Consequently, patients with PSA range from 10 ng/mL to 20 ng/mL, 66.67% (18/27) involved the anterior sector and 22.22% (6/27) involved the anterior sector only.

Hematuria was reported in 35.21% (25/71) of TP-BX patients and 50% (54/108) of TRUS-BX patients (Table 7). Three (2.78%) TRUS-BX patients had minor infection which were managed with oral antibiotics. One (0.93%) TRUS-BX patient had septicemia which resolved with administration of appropriate culture-guided parenteral antibiotic. There were no infections noted in the TP-BX. Four (5.63%) TP-BX patients complained of dysuria after removal of catheter which resolved spontaneously. Two (1.85%) TRUS-BX patients noted dysuria which resolved spontaneously. Minor perineal bruising was noted in 6 (8.45%) of the TP-BX patients. There were no reported pain at post-op site, vasovagal syncope, rectal bleeding and mortality in both TP-BX and TRUS-BX. Complication rates were not statistically significant in both groups except for minor perineal bruising present in TP-BX group.

**Table 6**. PSA range of anterior sector cancers.

| | Anterior Sector (n) | Anterior Sector Only (n) |
|---|---|---|
| PSA 2.5 ng/mL - 10 ng/mL | 17/44 (38.64%) | 7/44 (15.91%) |
| PSA 10 ng/mL - 20 ng/mL | 18/27 (66.67%) | 6/27 (22.22%) |

## Discussion

This study reported the comparison of TP-BX and TRUS-BX as an initial biopsy strategy for prostate cancer detection. The increased overall cancer detection rate of the TP-BX group over the TRUS-BX group in this study was consistent with current literature particularly with that of Symons' (64.4%)[18] and that of Ong's (53%)[13] series.

In this study, 77.78% of the cancers detected with the TP-BX involved the anterior sector, 37.14% of which were located in the anterior sector exclusively, wherein more than half of which (53.84%) were clinically significant. This is contrary to the existing data that majority of cancers involved the peripheral zone.[2]

The increased detection of clinically significant cancers in the TP-BX group over the TRUS-BX group is in congruence to contemporary series particularly with the 77.8% detection of anterior sector cancers by Hossack[11] and 63% by Ong's series.[13] These anterior sector tumors could have been missed by the TRUS-BX.

In this study, TP-BX had a significantly higher detection rates compared to TRUS-BX (59.09% vs 31.11%; p value = 0.002) in patients with PSA level between 2.5 ng/mL to 10 ng/mL. This is contrary to Takenaka's series wherein there was no significant difference in both TP-BX and TRUS-BX groups at any PSA levels.[19] However, this series showed comparable detection rates between TP-BX and TRUS-BX groups in patients with PSA

**Table 7**. Comparison of complication rates between TP-BX and TRUS-BX.

| Complication | Number of Patients | | |
|---|---|---|---|
| | TP-BX | TRUS-BX | p-value |
| Pain at post-op site needing pain medications | 0 | 0 | - |
| Hematuria | | | |
| Minor | 25 (35.21%) | 54 (50%) | 0.155 |
| Major | 0 | 0 | - |
| Vasovagal syncope | 0 | 0 | - |
| Infection/fever | | | |
| Minor | 0 | 3 (2.78%) | 0.066 |
| Septicemia | 0 | 1 (0.93%) | 0.416 |
| Dysuria | 4 (5.63%) | 2 (1.85%) | 0.346 |
| Perineal bruising | | | |
| Minor | 6 (8.45%) | 0 | 0.031* |
| Major | 0 | 0 | - |
| Major Perineal Bleeding | 0 | 0 | - |
| Rectal Bleeding | | | |
| Minor | 0 | 0 | - |
| Major | 0 | 0 | - |
| Mortality | 0 | 0 | - |

*statistically significant (p<.0.05)

levels between 10 ng/mL to 20 ng/mL similar to those of Takenaka's series. Therefore, in patients with 'gray-zone' PSA values, TP-BX is an ideal initial prostate biopsy strategy. Some reports showed that the 'gray-zone' PSA values had cancers in the transition zone in 18% - 27% of cases.[19-20] In this series, patients with 'gray-zone' PSA involved the anterior sector in 38.64% of cases and 15.91% involved the anterior sector only.

One of the most devastating complications of a prostate biopsy is infection, which could lead to septicemia. The reported incidence of infection after TRUS-BX reached 6.3%, as high as 4.1% of these infections required hospital admission and parenteral antibiotics.[25,27,29,30] The infectious complication of TRUS-BX was attributed to the passage of the biopsy needle through the rectum. In the present study, one (0.93%) of the TRUS-BX patients developed septicemia due to ESBL positive *Escherichia coli* and 3 (2.78%) developed fever while none occurred in the TP-BX group, although this had not reached statistical significance. This may be due to the fact that TP-BX avoids the rectum and thus avoids the source of the infections.[31]

Gross hematuria, hematospermia and rectal bleeding commonly occurs after a prostate biopsy.[23] Majority of the reported 10%-84% incidence of gross hematuria in modern series were minor, though 0.4%-1.4% were severe requiring catheterization and hospitalization.[24-27] In this series, the TRUS-BX was associated with a numerically higher incidence of minor hematuria which resolved spontaneously within 3 days compared to TP-BX (50% vs 35.21%), though not statistically significant. The present study showed that mild perineal bruising occurs in 8% of the TP-BX which is in agreement with the 1%-6% incidence in published data.[28] The incidence of urinary retention is 4.2%-11%[18-19], however, none of the patients from either group developed such.

## Conclusion

In conclusion, transperineal prostate needle biopsy should be considered as the initial biopsy strategy for detection of prostate cancer. The manifested advantages are the following:

a. The overall cancer detection rate is significantly higher.
b. The detection rate of clinically significant cancer is significantly greater.
c. It provides a far more superior detection of exclusive anterior zone cancers which are often underdetected or undetected with the current standard TRUS-BX.
d. Complications are comparable, if not fewer than the current standard TRUS-BX.

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