

# Utility of Transrectal Ultrasound Guided Transperineal Prostate Sector Biopsy in the Detection of Missed Prostate Cancer After a Previous Negative Transrectal Ultrasound Guided Systematic Extended Biopsy: An Observational Study

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A substantial number of patients will present with persistently elevated serum prostate specific antigen (PSA) after a previous negative Transrectal ultrasound guided prostate needle biopsy (TRUSPNB) suggesting potentially missed cancers during the initial biopsy. Transperineal prostate sector biopsy (TPSB), with its increased access to the undersampled anterior region, has been utilized to improve cancer detection rate.

**Objectives:** The study aims to look into the ability of the TPSB to better detect potentially missed cancers in a population of patients with previous negative TRUSPNB

**Materials and Methods:** This is an observational study based on a review of the biopsy database of the senior author. A total of 26 patients underwent a repeat prostate biopsy due to persistently elevated PSA ( $>4.0$  ng/ml) after an initial negative TRUSPNB biopsy were included. All patients underwent both the TPSB followed by TRUSPNB at the same setting. Their overall cancer detection rates were reported and compared.

**Results:** Among the 26 patients who underwent repeat prostate biopsy, TPSB was able to detect 14 cancers while the TRUSPNB detected only 3 cancers. The 54% (14/26) overall cancer detection rate using TPSB is significantly higher than the 12% (3/26) overall cancer detection rate of TRUSPNB. Subset analysis of the 15 cancers identified showed that the TPSB was able to detect 14 out of the 15 (93.3%) cancers while the TRUSPNB detected only 3 out of the 15 (20.0%) cancers.

**Conclusion:** The TPSB technique increases the prostate cancer detection rates in the subset of men who undergo repeat biopsy after a previous negative TRUSPNB but still highly suspicious for malignancy. Majority of the cancers in the repeat biopsy setting originated from the anterior zone which may be quite difficult to be detected with the transrectal approach.

**Key words:** transrectal ultrasound guided prostate needle biopsy (TRUSPNB), transperineal prostate sector biopsy (TPSB), prostate cancer

## Introduction

Transrectal ultrasound guided prostate needle biopsy (TRUSPNB) is presently the gold standard for early detection of prostate cancer.<sup>1,2</sup> This

technique primarily samples the peripheral zone of the prostate, from which 75% of cancers would arise. Through the years, several modifications on the procedure, mainly focused on increased number of biopsy cores as well as more laterally

directed biopsy cores still showed an overall cancer detection rate of 35 to 40% at best.<sup>3,4,5,6</sup>

A substantial number of patients will present with persistently elevated serum prostate specific antigen (PSA) after a previous negative prostate biopsy. There is still a further 20% cancer detection rate in repeat biopsies in this group of patients, suggesting potentially missed cancers during the initial biopsy.<sup>7,8,9</sup>

Furthermore, radical prostatectomy specimen have shown that as high as 30% of prostate cancers arise from the anterior region of the prostate. These tumors would not have been detectable using the transrectal ultrasound-guided approach due to their high anterior location.<sup>10,11,12</sup>

Transperineal prostate sector biopsy (TPSB), with its increased access to the undersampled anterior region, has been utilized to improve the detection rate.<sup>13,14,15,16</sup> In fact, current evidences strongly show an increased diagnostic yield of this technique in patients suspected to have prostate cancer who had a previous negative biopsy.<sup>17</sup> However, there is, at present, no reported local data regarding this procedure, more so, in a repeat biopsy setting. This study aims to report on the first Philippine experience on transperineal prostate sector biopsy.

This study aimed to look into the ability of the TPSB to better detect potentially missed cancers in a population of patients with previous negative TRUSPNB.

## **Materials and Methods**

This is an observational study based on a review of the biopsy database of the senior author. From December 2014 to September 2015, a total of 26 patients who underwent a repeat prostate biopsy due to persistently elevated PSA (>4.0 ng/ml) after an initial negative TRUSPNB biopsy were included.

Informed written consents were obtained from all patients before the procedures. As preparation, patients were advised to hold intake of anti-coagulants for at least 7 days. Oral broad-spectrum antibiotics (fluoroquinolones) were given 3 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. An Intravenous antibiotic (3rd generation Cephalosporin) was also given 30 minutes prior to the procedure. After the biopsy, the fluoroquinolones were continued for 5 more days and metronidazole for 2 more days.

All procedures were done in a single tertiary institution by a single urologist (senior author) using the BK Falcon Ultrasound unit utilizing the 8808 brachytherapy probe. The biopsies were performed under total intravenous sedation anesthesia. All patients underwent the TPSB and the TRUSPNB at same setting. All the specimen were interpreted by a single group of pathologists.

Patients were initially placed in the lithotomy position for the TPSB. A Fr 16 Foley catheter was inserted to facilitate identification of urethra and prostatic-vesical junction. (Figure 1)

Ten (10) anteriorly directed biopsy cores based on the template grid were taken to sample both the right and the left anterior and middle sector of the prostate for a total of 20 cores (Figure 2). These were collectively labeled as TPSB Specimen.

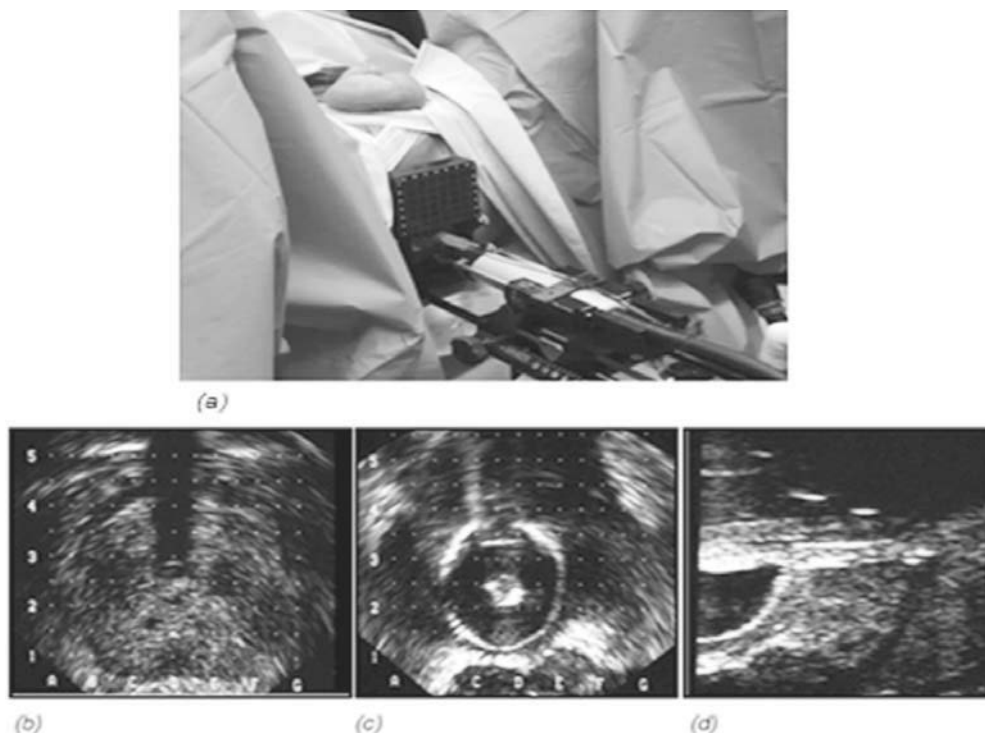
Immediately after the TPSB, the patients were then placed in the right lateral decubitus position and subsequently underwent the standard TRUSPNB through 6 peripherally directed biopsy cores to sample both the right and left peripheral zones of the prostate for a total of 12 biopsy cores. These were collectively labeled as TRUSPNB specimen .

## **Statistical Analysis**

The overall cancer detection rate was reported. Furthermore, the detection rates of the 2 groups (TPSB AND TRUSPNB) were analyzed and compared using the McNemar's test with a p-value of <0.05 considered statistically significant. The statistical data analysis was done using the VassarStats Online.

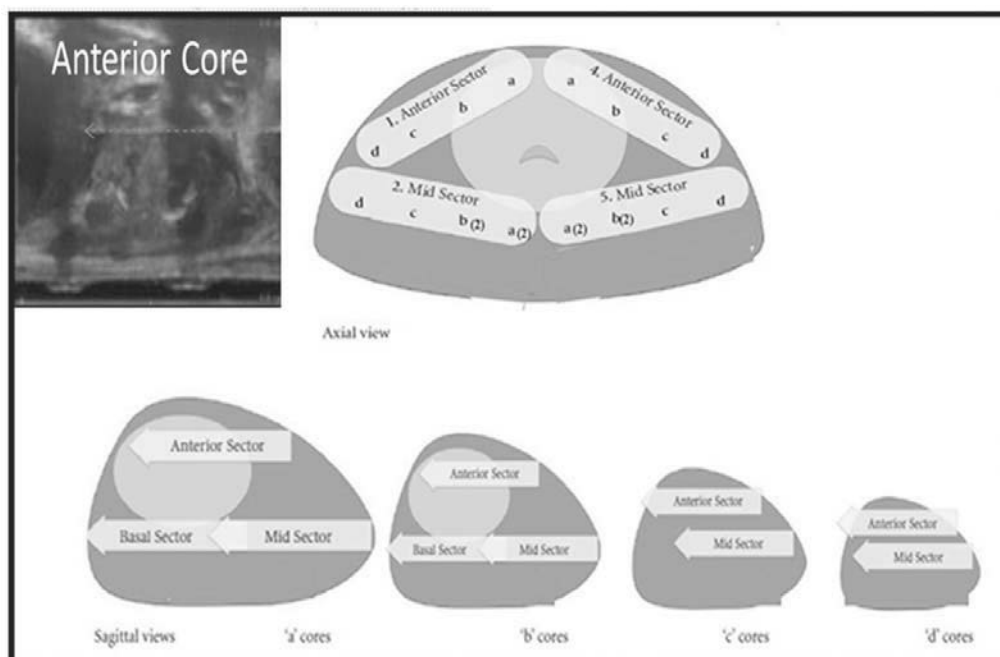
## **Results**

The data of the 26 patients were analyzed in this observational study. The mean age is 66.7 years (range: 52-86). The mean serum PSA is 8.84



**Figure 1.** Patient Positioning for TPSB

Patient is placed in lithotomy position and draped. (Figure 2a) Sonographic images showing the urethra at the center of the grid (Figure 2b) as well as images of the prostatic urethra (Figures 2c and 2d)



**Figure 2.** Axial and sagittal views of the prostate and the corresponding areas sampled by the senior author using the transperineal approach.

Sixteen areas were sampled with 2 cores being obtained from the from regions a and b of the right and left mid sectors for a total of 20 cores. Inset is a sonographic image of the sagittal view demonstrating the direction of the biopsy needle as it traverses the anterior sector of the gland. (Illustration based on (Kuru, Timur H., et al. "Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg Study Group for Enhanced Prostate Diagnostics." *BJU international* 112.5(2013):568-577)

ng/ml (range:4.2-15.33 ng/ml). The mean gland volume is 47.56 grams (range: 24 - 141). The mean total procedural time is 31 minutes, 22 minutes for the TPSB part and 9 minutes for the TRUSPNB part including the repositioning of the patient. (Table 1)

**Table 1.** Patient demographics.

n=26	Mean	Range
Age	66.7 years	52-86 years
Serum PSA	8.84 ng/ml	4.2-15.33 ng/ml
Prostate Gland Volume	47.56grams	24-141 grams
Procedure Time (TPSB +TRUSPNB)	31 minutes	27-38 minutes
Procedure Time (TPSB)	22 minutes	18-28 minutes
Procedure Time (TRUSPNB)	9 minutes	7-12 minutes

### Prostate Cancer Detection

Among the 26 patients who underwent repeat prostate biopsy, TPSB was able to detect 14 patients with cancer. The TRUSPNB, on the other hand, detected only 3 patients with cancer. The 54% (14/26) overall cancer detection rate using TPSB is significantly different to the 12% (3/26) overall cancer detection rate of TRUSPNB in this sample population. The statistic used for this computation was McNemar's Test. The value for the two-tailed computation was used with an alpha of 0.05. (Table 2)

**Table 2.** Overall cancer detection.

		TPSB		Total	p-value (two-tailed)	Odds ratio	Confidence Interval
		Cancer (+)	Cancer (-)				
n=26					0.0017	12	(1.56 - 92.29)
TRUSPNB	Cancer (+)	2	1	3 (12%)			
	Cancer (-)	12	11	23			
Total		14 (54%)	12	26			

A total of 15 out of the 26 (57.7 %) patients were identified to have prostate cancer. In the subset analysis of patients detected to have prostate cancer, the transperineal technique (TPSB specimen) was able to detect 14 out of the 15 (93.3%) overall cancers identified. All of which were identified either on the anterior or the mid sector. Only 1 out of the 15 cancers detected was missed by the TPSB technique. The transrectal technique (TRUSPNB specimen), on the other hand, missed 12 and detected only 3 out of the 15 (20.0%) total cancers identified. (Table 3).

**Table 3.** Subset Analysis of 15 patients who were identified to have cancer comparing TPSB and TRUSPNB.

n=15	Patients detected to have cancer	
TPSB	14/15	93.3%
TRUSPNB	3/15	20%

### Post Biopsy Complications

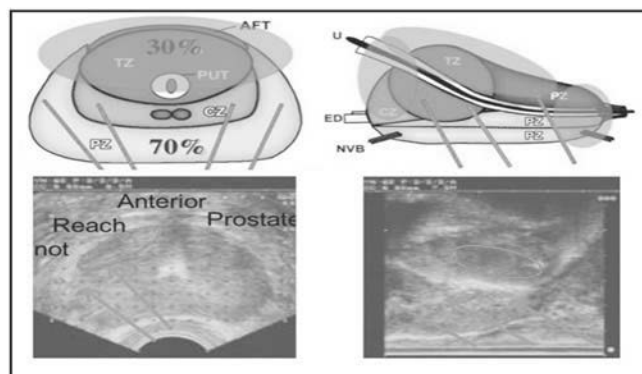
One patient developed acute urinary retention which was addressed by reinsertion of an indwelling urethral catheter which resolved in 5 days. There was no patient who developed sepsis nor excessive bleeding that required hospital readmission. There were, however, 2 patients who developed mild perineal bruising, without any pain nor discomfort, which eventually resolved spontaneously.

## Discussion

Since its introduction in the 1980s, transrectal ultrasound guided systematic biopsy of the prostate has consistently showed a low cancer detection rate. As this procedure is done through a transrectal approach, the biopsy needle has to pierce through the rectum via a slot built in the ultrasound probe. This serves as a fulcrum at which the biopsies were to be obtained as the punctures have to originate from a common point located well below the prostate gland. This places severe constraints in its ability to sample certain areas of the prostate, particularly the anterior zone (Figure 3).

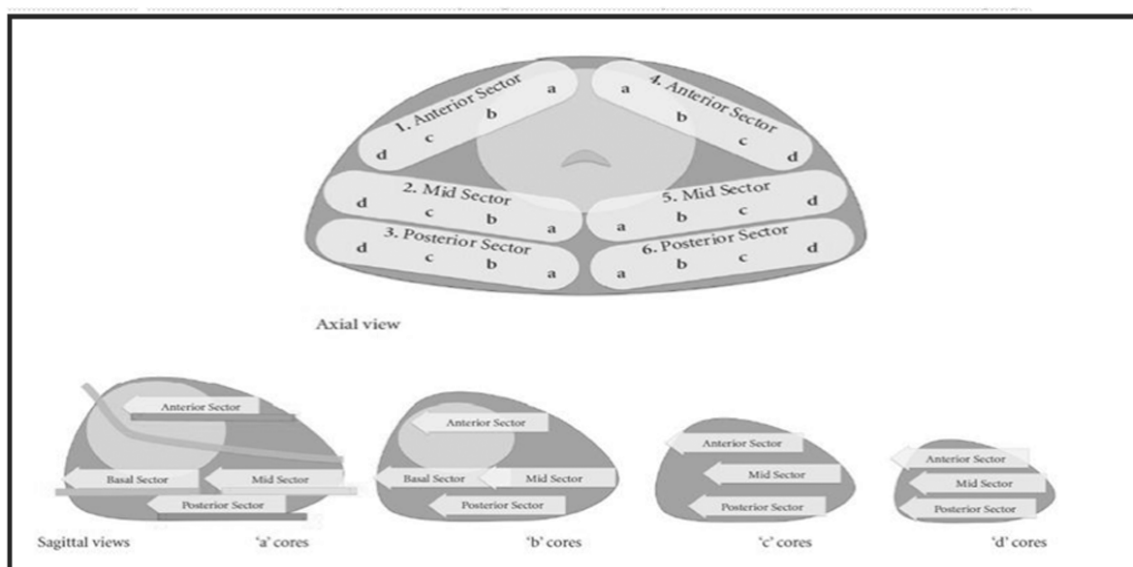
One can argue that a deeper penetration of the biopsy device can be done before firing the needle to reach the anterior location. However, in addition to the already mentioned limitation, it would be more traumatic, considering that the needle has to traverse and pierce deeply through the rectum. Furthermore this can potentially increase the risk of infection when the needle is introduced more deeply into the prostate as it increases the area of exposure of the sterile gland to the unsterile rectal environment.

The TPSB was developed and have shown its potential to replace the standard TRUS biopsy



**Figure 3.** Axial and sagittal views of the prostate gland while performing transrectal ultrasound guided prostate biopsy. The areas marked by the red lines correspond to the areas that are readily sampled. Whereas the areas highlighted in orange are the regions that are potentially missed. KOTECHA, ISHA. et. al "3T MRI in prostate cancer evaluation with DWI, ADC and MR spectroscopy." European Congress of Radiology 2012

technique. This procedure allows for a more accurate sampling of the prostate gland based on a preplanned map and template to sample areas of interests. (Figure 4). The biopsy needle can be inserted at the exact coordinates provided by the template based on the pre-procedural plan. This allows for a potentially more accurate and thorough sampling of the prostate.



**Figure 4.** Standard technique of sampling in the Transperineal Prostate Sector Biopsy. (Kuru, Timur H., et al. "Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg Study Group for Enhanced Prostate Diagnostics." BJU international 112.5 (2013): 568-577)

Furthermore, tumors in the anterior third of the prostate gland are more easily sampled using the transperineal approach. As much as 60% of cancers may be found uniquely in the anterior zone of the prostate.<sup>18</sup>

This prompted the senior author to adopt the TPSB procedure in a repeat biopsy setting. The transperineal prostate biopsy targeting the anterior aspect (20 cores) was initially performed. This was followed immediately by the transrectal technique in the usual standard manner (12 cores).

The specimen obtained were separately labeled so that the yield of the two techniques can be compared. The observed cancer detection rates and location of cancers in the repeat biopsies have definitely revealed the superiority of the TPSB over the traditional TRUSPNB technique.

In this study, a total of 15 out of the 26 (57.7%) patients who underwent a repeat prostate biopsy were identified indeed to have cancer. This overall cancer detection would be the highest thus far based on local Philippine statistics.<sup>19,20</sup>

The TPSB technique was able to detect 14 out of the 15 (93.3%) overall cancers identified. The TRUS guided technique, on the other hand, was only able to detect 3 out of the 15 (20.0%) total cancers identified. Needless to say, not having done the transperineal technique could have resulted in to a significant number (12 out of 15 or 80.0%) of undetected cancers and therefore miss the window of opportunity for cure.

Our observation regarding the higher proportion of cancers detected in the anterior zones in the setting of a missed biopsy is in congruence with international data including the treatment guidelines as proposed by National Institute for Health and Clinical Excellence.<sup>17,21,22</sup>

In addition to the increased yield, the transperineal technique avoids the rectal route of needle insertion, thus, virtually eliminating the risk of infection and eventual sepsis. This is the other accepted advantage proposed by advocates of this procedure. Furthermore, it could potentially lower the risk of rectal bleeding after the procedure as there is virtually no puncture of the rectum. Minor complications such as hematuria, not different from the transrectal approach, and perineal discomfort or bruising may occur in some cases

but are usually self limiting. Available data suggests no statistically significant difference between the incidence of these complications on both techniques.<sup>23</sup>

The standard transperineal prostate sector biopsy technique is obtained by transperineal puncture to sample the entire prostate gland from the anterior aspect (anterior and middle sector) and the peripheral zone (posterior sector) for a total that can reach as many as 38 biopsy cores. (Figure 4) The total number of cores obtained from patients in this study is 32 cores, which is not more than a standard TPSB.

As the peripheral zone of the prostate corresponds to the posterior sector in the transperineal technique, sampling the posterior sector through the transperineal route can replace the transrectal approach. Repeat prostate biopsies therefore, can be performed using an entirely transperineal approach which obviates entirely the rectal puncture of biopsy needles as well as the change in patient positioning, further facilitating and shortening the biopsy time, without compromising the detection rate.

## **Conclusion**

The TPSB technique increases the prostate cancer detection rates in the subset of men who undergo repeat biopsy after a previous negative TRUSPNB but still highly suspicious for malignancy. Majority of the cancers in the repeat biopsy setting originated from the anterior zone which may be quite difficult to be detected with the transrectal approach.

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