

## Frequency of Incidental Prostatic Carcinoma in Transurethral Resection Biopsies

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### ABSTRACT

**Background:** Incidental prostate malignancy can be detected in men who are undergoing transurethral resection of the prostate for nodular hyperplasia. Consequently, it is crucial to thoroughly assess the transurethral resection specimen for precise diagnosis, grading, and staging.

**Objectives:** To investigate the frequency of prostate cancer incidentally discovered in transurethral resection specimens and to ascertain its correlation with some clinicopathological factors.

**Methods:** This study included 200 patients who had undergone transurethral resection of the prostate for the treatment of nodular prostatic hyperplasia between January 2020 and January 2023. Patients' age, prostate-specific antigen serum levels, and the resected prostate weight were assessed. Additionally, tumor stage, Gleason grade group, perineural invasion, and lymphovascular status were evaluated in the prostate cancer group. Statistical analysis was done to investigate the relationship between these parameters and the detection of prostate cancer.

**Results:** The study revealed an incidental detection rate of prostate cancer at 11.5%. This group exhibited notably higher average ages and prostate-specific antigen levels than the nodular prostatic hyperplasia group. Furthermore, the weight of the removed specimen influenced the detection rate of incidental prostate cancer. Out of the 23 identified cases of incidental prostate cancer, 17 (73.9%) were categorized as stage T1b. Statistically significant disparities were observed among the T1 stages concerning prostate-specific antigen levels and the weight of the excised specimen.

**Conclusions:** This study demonstrates a rise in the frequency of unsuspected prostate cancer following transurethral resection of presumed nodular prostatic enlargement in Nineveh province. Most of these neoplasms were of the high-grade group, indicating a higher likelihood of clinical significance. Precise histopathological assessment of all transurethral resection of prostate specimens might enhance the possibility of detecting incidental cancer in nodular prostate hyperplasia.

**Keywords:** Transurethral resection, nodular prostatic hyperplasia, Prostate-specific antigen, Unsuspected prostate cancer.

### تواتر سرطان البروستات العرضي في خزعات الاستئصال عبر الإحليل

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### الخلاصة

**الخلفية:** يمكن العثور على ورم خبيث في البروستات لدى الرجال الذين يخضعون لاستئصال البروستات عبر الإحليل بسبب تضخم حميد. وبالتالي، فمن الأهمية بمكان إجراء تقييم شامل لعينة استئصال عبر الإحليل.

**الأهداف:** دراسة مدى الإصابة بسرطان البروستات المكتشف بالصدفة في عينات الاستئصال عبر الإحليل، والتأكد من ارتباطه بالعوامل المرضية الإكلينيكية.

**الطرق:** شملت هذه الدراسة ٢٠٠ مريض خضعوا لاستئصال البروستات عبر الإحليل لعلاج تضخم البروستات الحميد بين يناير ٢٠٢٠ ويناير ٢٠٢٣. قمنا بتقييم عمر المرضى ومستويات مصل مستضد البروستات النوعي (PSA) ووزن البروستات المستأصلة. بالإضافة إلى ذلك، قمنا بتقييم مرحلة الورم، ومجموعة غليسون، والغزو حول العصب، وحالة الأوعية الدموية للمفاوية في مجموعة سرطان البروستات. أجرينا تحليلاً لاستقصاء العلاقة بين هذه المعلمات والكشف عن سرطان البروستات.

**النتائج:** كشفت الدراسة عن معدل اكتشاف عرضي لسرطان البروستاتا بنسبة ١١.٥%. أظهرت هذه المجموعة متوسط أعمار ومستويات PSA أعلى بشكل ملحوظ من مجموعة تضخم البروستاتا الحميد. وعلاوة على ذلك، فإن وزن العينة التي تمت إزالتها أثر على معدل اكتشاف سرطان البروستاتا العرضي. من بين ٢٣ حالة تم تحديدها لسرطان البروستاتا العرضي، تم تصنيف ١٧ (٧٣.٩%) على أنها المرحلة T1b. وقد لوحظت فروق ذات دلالة إحصائية بين مراحل T1 فيما يتعلق بمستويات PSA ووزن العينة المستأصلة.

**الاستنتاجات:** توضح هذه الدراسة ارتفاع معدل الإصابة بسرطان البروستاتا غير المتوقع بعد استئصال تضخم البروستاتا الحميد عبر الإحليل في محافظة نينوى. وكانت معظم هذه الأورام من المجموعة العالية، مما يشير إلى احتمال أكبر للأهمية السريرية. قد يؤدي تقييم جميع عينات البروستاتا عبر الإحليل إلى تعزيز إمكانية اكتشاف السرطان العرضي في تضخم البروستاتا الحميد.

**الكلمات المفتاحية:** استئصال عبر الإحليل، تضخم البروستاتا الحميد، مستضد البروستات النوعي، سرطان البروستات الغير مشتبه به.

## INTRODUCTION

Prostatic cancer is the second most common neoplasm in men, with a frequency of 7.3%<sup>1</sup>. It stands as one of the most important causes of morbidity and the fifth leading cause of death in males, responsible for 3.8% of cancer-related mortality worldwide<sup>1</sup>. In Iraq, the incidence of prostate cancer is increasing. It ranks as the fourth most commonly diagnosed cancer in men, with an 8.46% incidence rate during the year 2021, compared to its previous rank of seventh, with an incidence of 4.53% in 2012<sup>2</sup>. Prostate cancer is incidentally detected in a significant number of transurethral resection of prostate (TURP) specimens for nodular prostatic hyperplasia, ranging from 5.5% to 21%<sup>3</sup>.

Incidental prostate cancer (IPC) is defined as a clinically unapparent tumor that is incidentally diagnosed after surgery for nodular prostatic lesions<sup>4</sup>. Unsuspected prostate cancer is neither palpable nor visible by imaging and incidentally detected, for example, after radical cystoprostatectomy for patients with bladder cancer or at the time of TURP<sup>5</sup>. Most IPCs are considered clinically insignificant, but recent suggestions suggest that their clinical course becomes more unfavorable<sup>6</sup>. Depending on the percentage of the resected cancerous tissue, it can be classified into clinical stages T1a or T1b. Some IPCs have been shown to be clinically relevant, specifically tumors with a higher Gleason score and stage T1b<sup>7</sup>.

According to the European Association of Urology Guidelines, active surveillance or watchful waiting is recommended for IPC if the Gleason score is six or less and the patient's life expectancy is less than 10 years<sup>8</sup>. While radical prostatectomy is recommended for those with T1b stage and a life expectancy of more than 10 years<sup>8</sup>.

The role of prostatic biopsy is established for the detection of cancer and follow-up of the patient, and the common way to obtain a biopsy is TURP followed by open prostatectomy, where these procedures are considered safe<sup>9</sup>.

According to our knowledge, no previous studies were reported from Nineveh province regarding the frequency and prognostic factors for incidental prostate cancer in males who underwent TURP.

This study aimed to focus on the prostatic cancer incidentally identified on biopsies for benign prostatic hyperplasia, the frequency of these incidental tumors, and ascertain its correlation with some clinicopathological factors.

## PATIENTS AND METHODS

This case series study was conducted in Nineveh province after approval of the institutional ethics review committee. A total of 200 patients, ranging between 43-99 years, who had transurethral resection of the prostate (TUR-P) for the treatment of nodular prostatic hyperplasia (NPH) were included.

The study utilized a multi-center database that was collected both prospectively and retrospectively for analysis, and the materials, including paraffinized blocks and slides, were sampled from the histopathology department of AL-Jamhuri Teaching Hospital and some private laboratories in Mosul City between January 2020 and January 2023. From the surgeon's phone call, patients with no signs of cancer through direct rectal examination and imaging studies were included, while those with a history of adenocarcinoma were excluded. Furthermore, we excluded cases when the specimen was not all submitted for processing.

Demographic information and preoperative prostate-specific antigen (PSA) serum levels. All cases were obtained from patient medical files when accessible. Histopathological findings were obtained from reviewing pathology slides and reports.

## Specimen Evaluation and Handling

According to a standard protocol outlined by the College of American Pathologists (CAP), specimens weighing 12 grams or less would be submitted in their entirety. In comparison, in the case of specimens weighing more than 12 grams, the initial 12 grams would be submitted, and for every additional 12 grams of the remaining specimen, an extra cassette was included, along with an additional 2 grams for every 12 grams of resected tissue.

In this study design, we submitted the specimens in their entirety regardless of the weight of the specimen.

The specimens were fixed in 10% neutral buffered formalin with overnight processing.

A single hematoxylin and eosin-stained section was cut from each block and examined histologically.

The reporting of incidental prostate cancer detected during TURP followed the guidelines and recommendations of the CAP<sup>10</sup>. In this context, pT1a disease was categorized as an incidental tumor discovered in 5% or less of TURP biopsies. Conversely, pT1b disease was classified when more than 5% of TURP specimens revealed an incidental tumor.

## Statistical Analysis

Data was analyzed using SPSS version 20 (SPSS Inc, Chicago, IL, USA). The chi-square test and t-test were employed to evaluate categorical data whenever applicable. Statistical significance was determined by a two-sided P-value of equal or less than 0.05.

## RESULTS

The study involved 200 cases of transurethral resection of the prostate (TURP), with 23 cases being incidental prostate carcinoma (IPC) and 177 cases being nodular prostatic hyperplasia (NPH). The average age of patients who underwent transurethral resection of the prostate and were diagnosed with incidental prostate carcinoma was 76.26 years, with a standard deviation (SD) of 11.58 years. The seventh and eighth decades of life were the most common age groups for all patients with incidental prostatic carcinomas. The incidental finding of prostate cancer was determined to be 11.5%.

The majority of patients (73.9%) diagnosed with incidental carcinoma were pathologically staged as T1b. Table 1 reveals the frequency of prostatic carcinoma during the specimen collection period.

Table 1: Year-wise frequency of unsuspected prostate carcinoma in the transurethral resection of the prostate.

Year	Total Biopsy Specimens (n) [NPH + PC]	PC commonest decade	PC Incidence% [%[No. of PC cases/No. of Biopsies]
2020	31	7	19.4% (6/31)
2021	79	8	11.4% (9/79)
2022	62	8	9.7% (6/62)
2023	28	7	7.1% (2/28)

NPH: Benign prostate hyperplasia; PC: prostate carcinoma.

The baseline characteristics of the studied patients are presented in Table 2. In summary, there was a highly statistically significant difference between incidental prostatic cancer and nodular prostatic hyperplasia in terms of age, PSA, and specimen weight, with a p-value of (0.001). The IPC group exhibited a higher average age (76.26 years) and PSA level (5.83ng/ml) when compared to the NPH group, which had an average age of 70.10 years and a PSA level of 3.09ng/ml, respectively. On the other hand, the mean value for specimen weight was higher in the second group (14.44gm) compared to the first group (13.43gm).

Table 2: Clinicopathological characteristics of the studied TURP samples.

Variables	IPC (23) Mean $\pm$ SD	NPH (177) Mean $\pm$ SD	Total Mean $\pm$ SD	P-value
Age (years)	76.26 $\pm$ 11.58	70.10 $\pm$ 10.341	73.18 $\pm$ 10.99	*0.001
PSA (ng/ml)	5.83 $\pm$ 3.05	3.09 $\pm$ 3.38	3.29 $\pm$ 4.38	*0.001
Specimen weight (gm)	13.43 $\pm$ 2.78	13.93 $\pm$ 2.45	13.68 $\pm$ 2.62	*0.001

\*Independent t-test was used. p-value <0.05 significant; IPC: Incidental prostate carcinoma; NPH: Nodular prostate hyperplasia; PSA: Prostate specific antigen.

In comparing various variables between the incidental prostatic cancer and nodular prostatic hyperplasia groups, the age group analysis indicated that the most frequently observed age range among individuals diagnosed with incidental prostatic cancer was between 70 and 79 years, which was approximately a decade higher compared to the NPH group.

Notably, 47.8% of individuals with IPC had PSA levels above 10ng/ml, while only 6.8% of those with nodular prostatic hyperplasia had these levels.

In terms of the specimen weight, 14 (60.8%) of individuals with incidental prostatic cancer had specimens weighing more than 10 grams, whereas 124 (71.1%) from NPH revealed specimens weighing less than 10 grams.

The baseline characteristics of incidental prostate cancer stage T1a and stage T1b are presented in Table 3. In summary, there was no significant difference in age, perineural invasion, and lymphovascular invasion between both stages. However, PSA levels and specimen weight showed significant differences between both stages, with p-values of 0.001 and 0.050, respectively. Notably, 33.3% of T1a cases were classified as grade group 3 (Table 4), while 47.0% of T1b cases belonged to grade group 5; Table 4 represents these findings. Figure 1 demonstrates incidental prostate carcinoma in transurethral resection of the prostate for nodular prostatic hyperplasia, while the perineural invasion was identified in stage T1b, as shown in Figure 2.

Table 3: Clinicopathological characterization of incidental prostatic cancer stage T1 specimens.

Variables	T1a ( 6 )	T1b (17)	Total (23)	P- value
Age (years) mean± SD	69.5±9.25	70.35± 8.54	69.93± 8.89	0.223
PSA (ng/mL) mean± SD	3.87±1.35	7.04±2.12	5.83± 3.05	*<0.00 1
Specime n weight (gm) mean± SD	10.33±2.4 5	14.52±3.1 2	13.43±2.7 8	*0.050
Peri-neural invasion				
Present	0	9	9	0.063
Absent	6	8	14	
Lymphovascular invasion				
Present	0	7	7	0.460
Absent	6	10	16	

**\*\*Independent t-test was used..** p-value <0.05 significant; PSA: Prostate specific antigen.

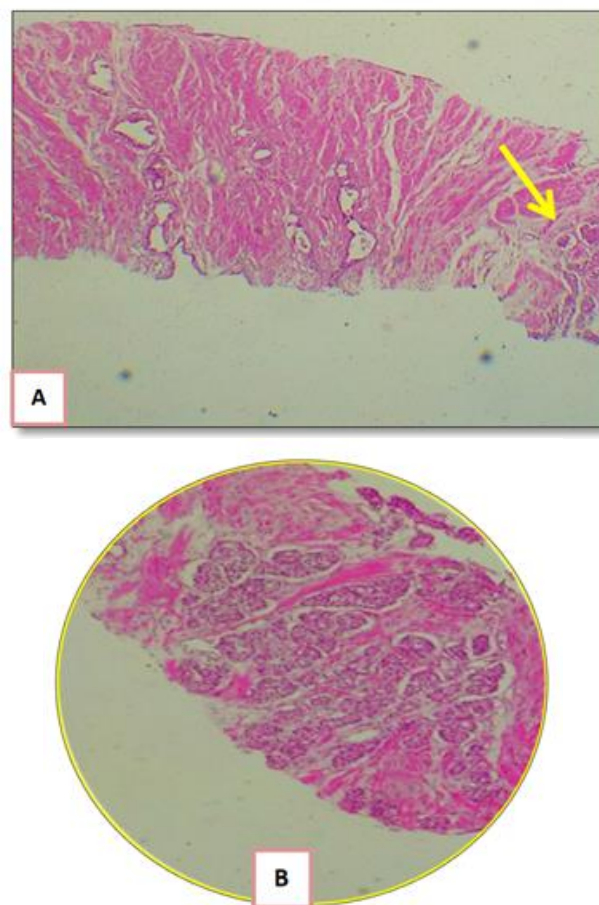


Figure 1: Incidental prostate carcinoma in transurethral resection of the prostate for nodular prostatic hyperplasia. A: Infiltrative glands (yellow arrow)(HE, magnified at 100x). B: Close-up view reveals a high-power focus of the encircled infiltrative glands (HE, magnified at 400x).

Table 4: Gleason Scores and Grade groups distribution for incidental prostate cancer stage T1 specimens.

Gleason score	Grade Group	StageT1a	Stage T1b
Gleason score 6 (3+3=6)	1	2(33.3%)	0(0.0%)
Gleason score 7 (3+4=7)	2	2(33.3%)	0(0.0%)
Gleason score 7 (4+3=7)	3	2(33.3%)	5(29.4%)
Gleason score 8 (4+4=8)	4	0(0.0%)	4( 23.6%)
Gleason score 9 and 10 (4+5=9, 5+4=9 , and 5+5=10)	5	0(0.0%)	8(47.0%)
<b>Total (23 cases)</b>	-	6(100.0%)	17(100.0%)

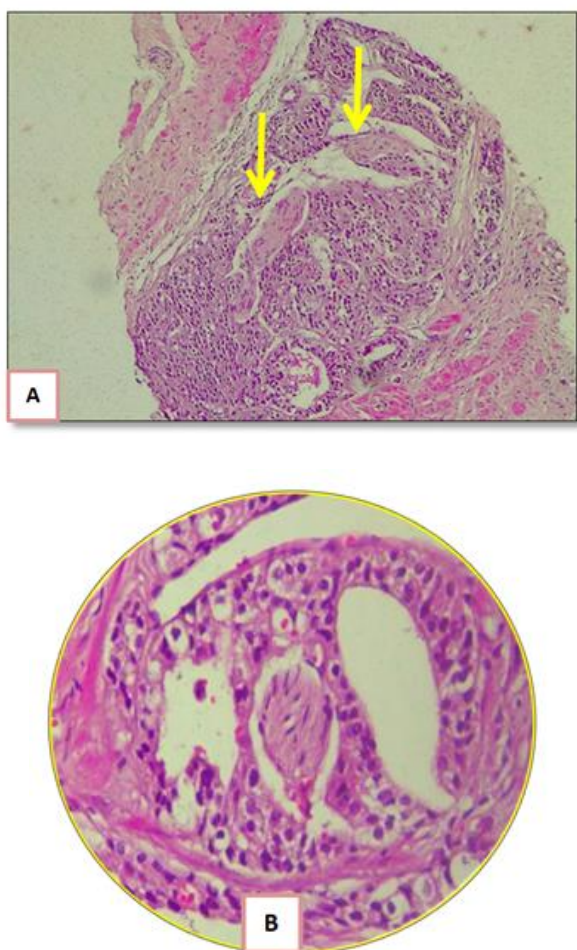


Figure 2: Perineural invasion by incidentally identified prostate carcinoma (yellow arrows) (HE, magnified at 100x), with a high-power focus on the infiltrative glands (HE, magnified at 400x).

## DISCUSSION

The current study reveals that 11.5% of patients were incidentally found to have unsuspected prostatic cancer within their transurethral resection specimens. Among them, 73.9% exhibited stage T1b. This percentage is higher than a prior study conducted by Hussein SA and Al-Khafaji in Baghdad City, Iraq<sup>11</sup>.

This frequency closely resembles findings from Pakistan, as reported by Janjua TK et al.<sup>12</sup>, where they discovered that 10.7% of patients were diagnosed with prostate cancer. Additionally, Matanhelia DM et al., from Ireland, revealed that 10.3% of patients discovered an incidental diagnosis of prostate carcinoma following TURP. Among them, 51.4% had pT1a disease, while the remaining 48.6% had pT1b disease<sup>13</sup>.

According to a systemic review conducted by Cheng et al., in the TURP procedure, the historical frequency of unsuspected prostate cancer ranged from 1.4% in some studies to 16.7% in others<sup>14</sup>.

In holmium laser enucleation of the prostate studies, the incidence of IPC was also quite variable, ranging from 2.5% to 32%<sup>15</sup>.

These geographic differences may be attributed to the disparity in diagnostic guidelines clinically used to diagnose prostate cancer. Since the diagnostic value of digital rectal examination alone is low, there is a chance of missing neoplasm when PSA testing is not used, besides the variable life expectancy of elderly men, coupled with enhanced access to medication<sup>16</sup>.

Indeed, the method employed for collecting prostate tissue can influence the detection rate of incidental prostate cancer (IPC).

In their study, He G and colleagues found that the overall detection rate of prostate cancer in the HoLEP (Holmium Laser Enucleation of the Prostate) group was greater than that in the TURP (Transurethral Resection of the Prostate) group, with percentages of 6.24% versus 3.94%, respectively<sup>17</sup>.

However, there was no significant difference in the detection rate of prostate cancer between the two groups when the PSA level exceeded 10 ng/ml<sup>17</sup>.

Our results and those from previous studies prove a positive correlation between prostate cancer and advancing age, particularly in the later decades of life<sup>18</sup>. Thus, advanced age can account for greater cases of nodular prostate hyperplasia and resulting unexpected cancers in the prostate gland<sup>19</sup>. It is crucial to note that we identified 17.3% of unsuspected prostate cancer cases in men aged ≤59 years.

Therefore, we recommend that TURP specimens of patients in this age group should be thoroughly examined. Failure to submit the entire TURP specimen for pathological examination may lead to the under-identification of cancer due to the loss of tissue.

Throughout the years of this research, we observed a consistent decrease in the detection rate of incidental prostate cancer during transurethral resection of the prostate. This decline may be attributed to the PSA screening. This finding was compatible with that conducted by Andr  n OL et al., who observed a decrease in the frequency of incidental neoplasm after the introduction of PSA screening<sup>20</sup>.

The study results illustrate that PSA is a valuable parameter for distinguishing between stage T1 cancer and nodular prostatic hyperplasia, especially within the PSA range of 7.0 to 10.0 ng/ml. This finding aligns with the observations made by Amir-Reza AB et al. and colleagues in their study, where they reported a PSA cut-off point of 3.8 ng/mL for detecting incidental prostate cancer<sup>21</sup>.

A study by Hiros M et al.<sup>22</sup> mentioned a significant decrease in the frequency of incidental cancer following TURP when comparing the pre-prostate-specific Antigen era and the PSA era. Specifically, they observed a decline from 27% to 9% in the detection rates of incidental cancer. Notably, this decrease was more pronounced in T1b lesions, dropping from 15% to 2%. Several studies have suggested that PSA screening plays a role in the detection rates of incidental cancer, particularly in the case of T1b lesions<sup>23</sup>.

Additional factors contributing to the decrease in unsuspected prostate cancer cases involve the reduced frequency of surgical treatment for NPH, attributed to the rising utilization of medical therapy and the increased adoption of ablative therapies<sup>18</sup>.

In terms of specimen weight, all specimens submitted for histological evaluation revealed that more than half of the incidental prostate cancer cases involve specimens that weigh over 10 grams. Regrettably, there is a lack of consensus when it comes to the pathological assessment of TURP specimens. Typically, the standard procedure involves embedding and analyzing only a portion of the larger specimen. According to the guidelines provided by the College of American Pathologists (CAP), a full examination is recommended for specimens weighing less than 12 grams. For specimens weighing more than 12 grams, the initial 12 grams are examined, and an additional 2 grams of tissue are included for every 10 grams of specimen beyond that weight threshold<sup>24</sup>.

Common sense would suggest that histological examination of the entire TURP specimen would likely result in a higher rate of prostate cancer detection. The methodology in tissue processing was responsible for the high IPC detection rate in the current study. Our results suggest that a comprehensive assessment can detect up to 100% of incidental cancer in TURP specimens.

This finding aligns with the results of Marlon Perera et al.<sup>25</sup>, who conducted a study involving TURP specimens from males aged less than 65 years to quantify the incidence of incidental prostate cancer by subjecting the entire specimen to histological evaluation. In contrast, for men aged over 65 years, the TURP specimens were sampled following standard guidelines<sup>24</sup>.

In terms of Gleason grade group distribution, this study revealed that grade group 5 was more prevalent in stage T1b when compared to T1a, where grade groups 1, 2, and 3 are predominantly observed. This discovery was also reported by Hiros M et al., who recorded that a T1b lesion is associated with a higher Gleason score and a higher risk of progression<sup>22</sup>. A similar observation was made by Amir-Reza Abedi et al.<sup>21</sup>.

The current study has some limitations that need to be acknowledged. Firstly, the microscopical examination was conducted by a single pathologist, which may have contributed to a potential overdiagnosis of prostate malignancy. To address this concern, all small foci were validated by blind review by other pathologists.

Furthermore, the study primarily consists of patients from a single institution practice, which could introduce selection bias and might have led to exposure to a more aggressive treatment approach.

This makes it essential to recognize that the findings may not fully represent the broader population.

While the primary observation of the study emphasizes that prostate cancer is a relatively common finding in TURP specimens, it is essential to highlight the necessity for a larger and more extensive study that can determine the frequency in the general population and evaluate its clinical significance.

Additionally, the study underscores the importance of submitting all TURP specimens for pathological examination, especially for older patients undergoing surgical management for NPH.

## CONCLUSIONS

This study demonstrates a rise in the frequency of unsuspected prostate cancer following transurethral resection of presumed nodular prostatic enlargement in Nineveh province. Most of these neoplasms were of the high-grade group, indicating a higher likelihood of clinical significance.

The assessment of all transurethral resection of prostate specimens might enhance the possibility of detecting incidental cancer in benign prostate hyperplasia.

## Source(s) of Support

Nil.

## Presentation at a Meeting

Nil.

## Conflicting Interest

No conflicts of interest to report.

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