Transperineal Prostate Biopsies Using Local Anesthesia: Experience with 1,287 Patients. Prostate Cancer Detection Rate, Complications and Patient Tolerability

Veselina Stefanova, Roger Buckley,* Stanley Flax, Les Spevack, David Hajek, Adam Tunis, Enoch Lai and Andrew Loblaw

From the Western University (VS), London and Division of Urology (VS, RB, SF, LS, DH, AL) and Department of Diagnostic Imaging (AT, EL), North York General Hospital, Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre (AL) and Department of Health Policy, Measurement and Evaluation, University of Toronto (AL), Toronto, Ontario, Canada

Purpose: We report our experience with transperineal prostate biopsy as well as the cancer diagnosis rate, complications and patient tolerability in 1,287 consecutive patients at risk for prostate cancer.

Materials and Methods: Beginning in October 2016 transperineal prostate biopsy was performed using local anesthesia in all patients undergoing prostate biopsy. Data on prebiopsy characteristics and results, including the cancer detection rate, complications and patient tolerability scores, were collected retrospectively from patient records.

Results: The cancer detection rate of transperineal prostate biopsy was 49.8% (641 of 1,287 patients). Clinically significant prostate cancer was detected in 385 patients and 62 (9.7%) had exclusively anterior zone pathology findings. Urinary retention developed in 20 patients (1.6%) following transperineal prostate biopsy, requiring temporary catheterization. In 4 patients (0.3%) lower urinary tract symptoms were suggestive of infection but only 1 had a positive urine culture. The only hospital admission was for a patient with persistent hypotension after biopsy. Patients tolerated transperineal prostate biopsy reasonably well and generally reported only mild levels of discomfort on a pain visual analogue scale. Infiltration of the anesthesia was rated more painful than the biopsy.

Conclusions: Transperineal prostate biopsy with the patient under local anesthesia is a feasible alternative to transrectal biopsy in the detection of prostate cancer. Transperineal prostate biopsy has an acceptable cancer detection rate with additional detection of anterior zone cancers. It is a safer alternative in patients due to the low risk of complications, in particular urosepsis, and it is well tolerated. Transperineal prostate biopsy using local anesthesia could be considered a standard modality for the initial diagnosis of prostate cancer.

Key Words: prostatic neoplasms; biopsy; anesthesia, local; pain; diagnosis

Abbreviations and Acronyms

AUA = American Urological Association
CDR = cancer detection rate
ER = emergency room
IV = intravenous
NYGH = North York General Hospital
PCa = prostate cancer
TPBx = transperineal prostate biopsy
TRUSBx = transrectal ultrasound guided biopsy
VAS = visual analogue scale
WPC = Wright Prostate Center

Accepted for publication January 17, 2019.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.

* Correspondence: 222-1333 Sheppard Ave. East, Toronto, Ontario, M2J1V1, Canada (telephone: 416-499-1333; e-mail: officeofrogerbuckley@gmail.com).

PROSTATE cancer is the most commonly diagnosed noncutaneous cancer among North American men with approximately 1 of 7 men diagnosed with this disease in a lifetime. In fact, currently PCa is the second leading cause of cancer death in men.[1]

TRUSBx is the most frequently performed technique to diagnose prostate cancer. However, the AUA White Paper[2] and others[3,4] estimated that the risk of infection after TRUSBx is between 5% and 7% with hospital admission rates ranging from 2% to

0022-5347/19/2016-1121/0
THE JOURNAL OF UROLOGY®

https://doi.org/10.1097/JU.0000000000000156
Vol. 201, 1121-1126, June 2019
Printed in U.S.A.

4% despite preventive measures. These estimates reflect our hospital experience. An internal audit at NYGH of 711 TRUSBx procedures performed between March 2015 and May 2016 revealed 38 ER visits (5.3%) and 18 patients (2.2%) admitted to the hospital.

Many published studies on TPBx have yielded a significantly lower infection rate compared to TRUSBx.[5–12] However, most TPBx series in the literature often involved general or spinal anesthesia because of the use of the perineal template. This creates a logistic barrier to widespread use of this technique in the urological community. Based on the differences between the reported rates of infection due to TRUSBx and TPBx our group unanimously decided to convert to the exclusive use of TPBx using local anesthesia at the WPC as of October 2016. The aim was to improve patient related health outcomes and safety.

In the current study we report our experience with TPBx performed using local anesthesia as the primary diagnostic strategy to detect PCa. The primary goal was to reduce the rate of infectious complications while preserving diagnostic sensitivity. Patient reported pain tolerability scores were recorded to more accurately assess the level of discomfort during the procedure.

METHODS

The NYGH Research Ethics Board reviewed and approved this study in July 2017 and July 2018 (IRB No. NYGH REB 17-0026). Beginning on October 12, 2016, we converted to TPBx from TRUSBx in all patients undergoing prostate biopsy at the WPC.

We retrospectively reviewed the electronic and/or paper charts of 1,287 consecutive patients who underwent TPBx at NYGH from October 12, 2016 to July 26, 2018. Data were collected on patient characteristics, pathological results, complications and patient tolerability scores. A nurse specialist from the WPC prospectively contacted each patient who underwent biopsy within 30 days to assess whether a complication had required a visit to a primary care physician or an ER, or hospital admission.

Beginning in November 2017 we began to assess patient reported tolerability scores in real time using the VAS.[13] Patients ranked the pain level on a scale of 0 to 10 for ultrasound probe insertion, skin infiltration, periprostatic infiltration of local anesthesia and prostate biopsy.

In regard to the biopsy technique the clinic work flow is identical to performing TRUSBx. After a 4 to 6-week learning curve the average time to perform standard TPBx was 10 to 12 minutes. Antibiotic prophylaxis in virtually all patients was a single oral dose of cefuroxime 500 mg or cephalexin 500 mg given 2 hours prior to biopsy. In accord with the recommendations of our infectious disease team the patients with a cardiac valve replacement received a single dose of ampicillin 2 gm IV and gentamicin 120 mg 2 hours before biopsy. Sulfamethoxazole was given to patients with severe penicillin drug allergies. Quinolones were not administered.

Patients were placed in the dorsal lithotomy position and prepared with iodine. Transrectal ultrasound was done with a Pro Focus 2202 Ultrasound Scanner (BK Medical, Herlev, Denmark). TPBx was performed with a 12 to 4 MHz endocavitary transducer (BK Medical), which is a biplanar ultrasound probe. Figure 1 shows the biopsy technique. A minimum of 10 cores were obtained, including the anterior apex, anterior base, posterior apex, posterior base and mid lateral on the right and left sides. Biopsy was performed with a freehand technique.

RESULTS

During the study period 1,287 TPBx procedures were performed. Two patients did not undergo TPBx because they could not be placed in the dorsal lithotomy position. Instead TRUSBx was performed and these 2 men were excluded from study. The table shows details of the demographics of the study population. Median patient age was 66 years (range 38 to 92) and the median AUA score was 7.1 (range 0 to 35). Median prostate volume was 40 ml and median prostate specific antigen was 7.05 ng/ml.

Prostate cancer was detected in 641 of the 1,287 patients (49.8%). The table lists positive pathological findings according to the Gleason Grade Group and score systems. Of the 641 patients diagnosed with prostate cancer low grade disease (Grade Group 1) was reported in 256 (39.9%). Clinically significant prostate cancer (Grade Group 2 or greater) was detected in 385 patients (60.1%).

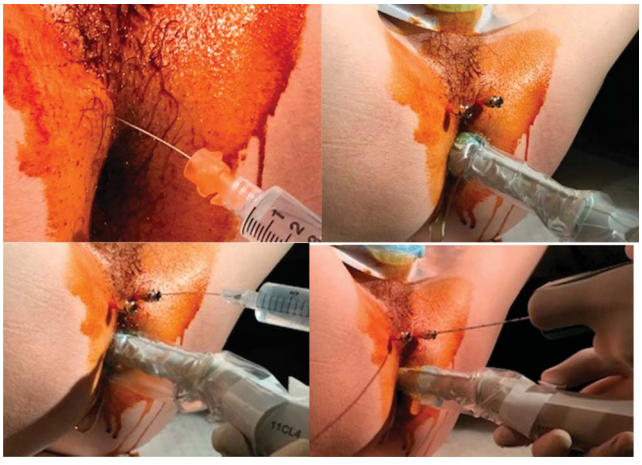

Figure 1. Patient is placed in dorsal lithotomy position and transrectal ultrasound probe is introduced. Using 25 gauge $1\frac{1}{2}$-inch needle 1% lidocaine is administered to anesthetize perineum and subcutaneous tissues. Bilaterally 14 gauge $1\frac{1}{4}$-inch cannula is inserted in perineum at about midpoint of each prostate side. To anesthetize periprostatic tissue 22 gauge 5-inch spinal needle is used to administer total of 25 cc 1% lidocaine. Biopsies are done through 14 gauge IV cannula with Bard® Magnum® gun and 18 gauge 20 cm Bard biopsy needles.

Characteristics of patients who underwent TPBx, patients diagnosed by TPBx and patients diagnosed with PCa with positive anterior zone pathology

	Overall
Underwent TPBx	
No. pts	1,287
Median age	66
No. race (%):	
Asian	203 (15.8)
African American	70 (5.4)
Caucasian	610 (47.4)
Other	61 (4.7)
Not available or reported	343 (26.7)
Median prostate specific antigen (ng/ml)	7.05
Median AUA Symptom Score	7.0
Median prostate vol (ml)	40
Diagnosed by TPBx	
No. pos pathology	641
% Prostate Ca detection	49.8
No. Gleason Grade Group/score (%):	
1/3 + 3	256 (39.9)
2/3 + 4	232 (36.2)
3/4 + 3	96 (15.0)
4/3 + 5	2 (0.3)
4/4 + 4	21 (3.3)
5/4 + 5	32 (5.0)
5/5 + 4	2 (0.3)
Clinically significant prostate Ca*	385 (60.1)
Diagnosed with PCa + pos anterior zone pathology	
Anterior zone involvement†	338 (52.7)
Exclusively anterior prostate Ca:	62 (9.7)
Grade Group 1	32 (5.0)
Clinically significant*	30 (4.7)

* Grade Group 2 or greater.
† One or more cores positive for prostate cancer.

Of the patients diagnosed with PCa 338 (52.7%) had anterior involvement, which was exclusive to the anterior zone in 62 (9.7%). Of these 62 patients 32 had Grade Group 1 (5.0%) and 30 (4.7%) had Grade Group 2 or higher (clinically significant) prostate cancer (see table).

There was a low rate of minor complications and no major complications following TPBx. Urinary retention developed in 20 of the 1,287 men (1.6%). Four patients (0.3%) received oral antibiotics after TPBx for symptoms suggestive of infection. The family physician prescribed antibiotics in 3 of these 4 men but urine cultures were negative. In the remaining patient a urine culture was positive for Enterococcus. This patient attended the ER for a febrile urinary infection and was treated with a single dose of IV ceftriaxone but was ultimately discharged home. One man attended the ER and was admitted to the hospital for persistent symptomatic hypotension following TPBx. However, in this patient urine and blood cultures were negative and it was thought that hypotension was likely cardiac in nature. More importantly, there were no cases of urosepsis requiring hospital admission and no mortality following TPBx.

We assessed 4 aspects of biopsy in 511 patients in real time using the VAS. Skin infiltration of local anesthesia was rated as the most uncomfortable at a score of 3.1. The periprostatic infiltration of local anesthesia, the biopsy itself and insertion of the ultrasound probe were rated 3.0, 2.5 and 2.4, respectively (fig. 2). We also surveyed 70 patients who had undergone a previous TRUSBx and a current TPBx regarding any perceived difference in the discomfort between the 2 approaches. Comparable discomfort was reported by 49 patients while 13 considered TPBx and 8 considered TRUSBx more painful. No patient requested that the physician stop during biopsy.

DISCUSSION

To our knowledge this is one of the largest reported series of TPBx performed using local anesthesia as the primary diagnostic strategy in a clinical setting. Our single center experience with prostate biopsy reflects one of the first adoptions of an exclusively transperineal approach in a urological practice. This initiative was done in an attempt to minimize the increasingly elevated rates of infectious complications associated with traditional TRUSBx.

The primary intents of our study were to evaluate the feasibility, diagnostic value and tolerability of the transperineal approach in a population of men at risk for PCa. Our findings support the growing body of literature on the reasonable performance of TPBx to diagnose prostate cancer with a low risk of post-biopsy complications.[5–7,9,10,12]

Previous studies have mentioned the similar CDRs of these 2 prostate biopsy techniques, providing support for the comparable diagnostic efficacy of TPBx and TRUSBx.[5,8,11,12] In the current study prostate cancer was diagnosed in 49.8% of patients, a rate higher than our previously published CDR of 42% using TRUSBx in a similar patient population.[14] In that analysis a total of 1,358 biopsies (42.0%) positive for PCa were detected among 3,231 patients who

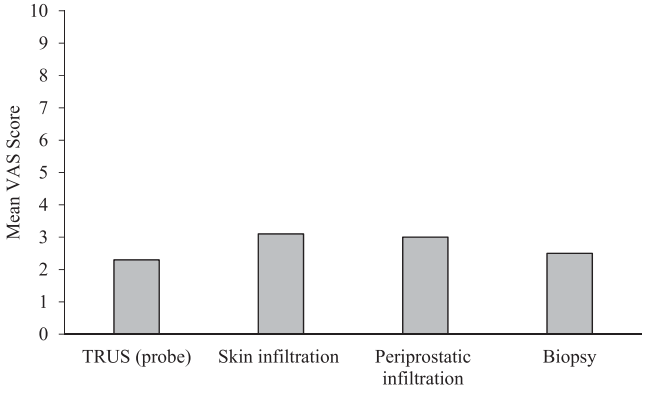

Figure 2. Pain scores were rated 0—no pain to 10—worst pain imaginable in 511 patients who underwent TPBx under local anesthesia.

underwent TRUSBx. While this is statistically significant ($p < 0.005$), only multivariate analysis would determine whether this represents a true increase in pathological detection. However, we hypothesize that the higher CDR in our current series of TPBx compared to TRUSBx might reflect the increased detection of anterior zone cancer by TPBx.

An estimated 20% to 30% of men with prostate cancer have some disease located in the anterior zone.[15] In the current study we found that 52.7% of patients with positive histology had some anterior zone involvement. Importantly in 62 of all men (9.7%) diagnosed with PCa the anterior zone was exclusively involved. In this group 30 patients (4.7%) had clinically significant cancer (Grade Group 2 or greater) and 32 (5.0%) had Grade Group 1 disease. This potentially implies a better CDR for anterior zone tumors than for TRUSBx.

Most importantly, our series revealed a low rate of minor post-biopsy complications and no major complications. Acute urinary retention developed in 20 patients (1.6%), which resolved in all without the need for surgical intervention. There was a low 0.3% rate of post-biopsy infection with infection developing in only 4 patients. Although 1 patient presented to the ER with a febrile urinary infection, 3 had a negative urine culture and were treated empirically with antibiotics by the family physician. Importantly, there was no case of urosepsis following TPBx which required hospital admission. Only 1 patient was admitted to the hospital, although this was for hypotension believed to be secondary to cardiac issues.

Our findings echo those in other TPBx studies which have consistently reported that the transperineal approach is associated with an almost zero rate of post-biopsy sepsis.[5–7,9,10,12] There are obvious health care savings associated with a negligible post-biopsy sepsis rate. The cost of admission for TRUSBx related urosepsis has been estimated to be US$6,844 in Australia and US$4,129 in New York State.[16,17] However, these are likely conservative estimates as additional costs were not quantified, including direct fees associated with ER and primary care physician visits, and time off work as well as the disutility of the complication. This is particularly relevant considering that approximately 1 million men undergo prostate biopsy each year in the United States.[3] The recent AUA White Paper estimated that 2% of hospital admissions are due to complications following TRUSBx.[2] According to this finding replacing TRUSBx with TPBx could represent up to 20,000 preventable hospital admissions annually in the United States.

In the majority of patients in this study a single dose of cephalexin or cefuroxime was given orally 2 hours prior to prostate biopsy as antibiotic prophylaxis. Patients with a cardiac valve replacement were administered intravenous antibiotics according to infectious disease recommendations while oral sulfamethoxazole was used for severe penicillin allergies. No quinolones were given in this study. A growing body of evidence suggests that quinolones have disutility and might even cause more harm as a prophylactic antibiotic for all prostate biopsy techniques. The FDA (Food and Drug Administration) recommended avoiding quinolones when possible due to its rare but permanently disabling side effects.[18] Roberts et al also suggested that decreasing unnecessary quinolone use may help reduce the development of quinolone resistant bacteria.[19] Our data support that quinolones are not necessary as a prophylactic agent for TPBx.

Our study differs from similar investigations in the field because it represents a relatively large sample of consecutive TPBx procedures performed uniquely with the patient under local anesthesia. There are few cost implications to switching from TRUSBx to TPBx. The only additional capital cost of the transperineal technique is the purchase of a biplanar ultrasound probe. The transperineal approach has been described using general or spinal anesthesia, which has been a limiting factor that has deterred urologists from embracing this technique. Performing TPBx with the patient under local anesthesia eliminates the cost associated with general or spinal anesthesia.

After a learning curve the time needed to perform TPBx is approximately 10 to 12 minutes. In addition, integrating novel technologies such as the FDA approved PrecisionPoint™ can help physicians by ensuring the reproducibility of this technique.[12]

Previous studies have shown that TPBx performed using local anesthesia is reasonably tolerated by patients.[20,21] The current study addressed the concern of pain tolerability associated with a transperineal approach. The most uncomfortable part of the procedure was infiltration of the skin and the periprostatic tissue with local anesthesia rather than the biopsy itself (fig. 2). The VAS score of the ultrasound probe, which is identical in the transrectal and transperineal approaches, allowed for comparison between the discomfort levels related to each technique. It is also worth mentioning that the patients who underwent TRUSBx as well as TPBx were equivocal in rating the tolerability of one approach as superior to the other.

We acknowledge that our data collection by chart review represents a study limitation due to the lack of randomization and control. Also, the lack of a direct comparison between the transperineal and transrectal approaches with regard to histological outcomes and resource consumption represents an additional shortcoming of the current study. Ideally a randomized controlled study of the 2 approaches performed using local anesthesia might address this issue.

CONCLUSIONS

TPBx using local anesthesia is well tolerated by patients and it has a quick learning curve, making it feasible to integrate into a busy urological practice. The transperineal approach significantly reduces post-biopsy complications without quinolone antibiotics, especially urosepsis, while achieving an acceptable CDR which preserves diagnostic sensitivity compared to TRUSBx. TPBx considerably improves patient safety and health related outcomes. Therefore, it could be offered to patients for the initial detection of PCa.

ACKNOWLEDGEMENTS

Collaborators: Jeff Noakes, Nicole Golda, Beverly Persaud and Kimberly Spevack, Division of Urology; Joseph Peltz, Hassan Deif, Irving Jacobs and Ryan Margau, Department of Diagnostic Imaging; and Simon Raphael, Department of Laboratory Medicine, North York General Hospital; and Gerard Morton, Patrick Cheung and Hans Chung, Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada. Lucia Blair assisted with the manuscript and with editing.

REFERENCES

1. Canadian Cancer Society Advisory Committee on Cancer Statistics: Canadian Cancer Statistics 2017. Toronto: Canadian Cancer Society 2017.
2. Liss MA, Ehdaie B, Loeb S et al: An update of the American Urological Association White Paper on the prevention and treatment of the more common complications related to prostate biopsy. J Urol 2017; **198:** 329.
3. Loeb S, Carter HB, Berndt SI et al: Complications after prostate biopsy: data from SEER-Medicare. J Urol 2011; **186:** 1830.
4. Nam RK, Saskin R, Lee Y et al: Rising hospital admission rates for urologic complications after transrectal ultrasound-guided prostate biopsy. J Urol 2010; **183:** 963.
5. Grummet J, Pepdjonovic L, Huang S et al: Transperineal vs. transrectal biopsy in MRI targeting. Transl Androl Urol 2017; **6:** 368.
6. Grummet J, Pepdjonovic L and Moon D: Re: Marco Borghesi, Hashim Ahmed, Robert Nam, et al. Complications after systematic, random, and image-guided prostate biopsy. Eur Urol 2017; 71: 353-65. Eur Urol 2017; **71:** e143.
7. Grummet JP, Weerakoon M, Huang S et al: Sepsis and "superbugs": should we favour the transperineal over the transrectal approach for prostate biopsy? BJU Int 2014; **114:** 384.
8. Guo LH, Wu R, Xu HX et al: Comparison between ultrasound guided transperineal and transrectal prostate biopsy: a prospective, randomized, and controlled trial. Sci Rep 2015; **5:** 16089.
9. Pepdjonovic L, Tan GH, Huang S et al: Zero hospital admissions for infection after 577 transperineal prostate biopsies using single-dose cephazolin prophylaxis. World J Urol 2017; **35:** 1199.
10. Symons JL, Huo A, Yuen CL et al: Outcomes of transperineal template-guided prostate biopsy in 409 patients. BJU Int 2013; **112:** 585.
11. Xue J, Qin Z, Cai H et al: Comparison between transrectal and transperineal prostate biopsy for detection of prostate cancer: a meta-analysis and trial sequential analysis. Oncotarget 2017; **8:** 23322.
12. Di Bianco JM, Mullins JK and Allaway M: Ultrasound guided freehand transperineal prostate biopsy: an alternative to the transrectal approach. Urol Pract 2016; **3:** 134.
13. Breivik H, Borchgrevink PC, Allen SM et al: Assessment of pain. Br J Anaesth 2008; **101:** 17.
14. Guy D, Ghanem G, Loblaw A et al: Diagnosis, referral, and primary treatment decisions in newly diagnosed prostate cancer patients in a multidisciplinary diagnostic assessment program. CUAJ 2016; **10:** 120.
15. Sahu M, Wijesekera N and Donohue JF: Anterior prostate cancer: current perspectives and diagnostic dilemmas. J Clin Urol 2017; **10:** 49.
16. Roth H, Millar JL, Cheng AC et al: The state of TRUS biopsy sepsis: readmissions to Victorian hospitals with TRUS biopsy-related infection over 5 years. BJU Int, suppl., 2015; **116:** 49.
17. Halpern JA, Sedrakyan A, Dinerman B et al: Indications, utilization and complications following prostate biopsy: New York State analysis. J Urol 2017; **197:** 1020.
18. FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects: U.S. Food and Drug Administration. May 12, 2016. Available at http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm. Accessed January 14, 2019.
19. Roberts MJ, Bennett HY, Harris PN et al: Prostate biopsy-related infection: a systematic review of risk factors, prevention strategies, and management approaches. Urology 2017; **104:** 11.
20. Merrick GS, Irvin S, Fiano R et al: Pathology and quality of life outcomes following office-based transperineal prostate biopsy. Urology 2016; **94:** 24.
21. Smith JB, Popert R, Nuttall MC et al: Transperineal sector prostate biopsies: a local anesthetic outpatient technique. Urology 2014; **83:** 1344.

EDITORIAL COMMENTS

The authors assessed the usefulness of the transperineal approach for prostate biopsies. They report an acceptable prostate cancer detection rate of approximately 50%, a low 0.3% rate of infectious complications and the absence of septic events. While currently it is seldom used, this report confirms the findings of previous studies concluding that the transperineal approach is accurate and carries less risk of serious infection events than the transrectal approach.

Although the cancer detection rates of the 2 prostate biopsy techniques were previously found to be comparable, transperineal biopsy was more burdensome than transrectal biopsy due to the need for additional anesthesia and longer procedural time so that it is usually underused.[1] In the current

study only 2 perineal cannulas were used to access the prostate instead of a grid guided biopsy template. This seemed to provide high tolerability and prevented subjecting men to spinal or general anesthesia. Achieving optimal access through 2 perineal cannulas might require additional training with a steeper learning curve to gain proficiency with this approach.

In addition to preventing biopsy complications, better selection of men who will benefit from biopsy should be the highest priority. Magnetic resonance imaging was shown to reduce unnecessary biopsies by a quarter while increasing the detection of clinically significant cancer using fusion technology.[2] These 2 technical advances in conjunction with newer molecular tests will definitely improve the safer detection of clinically significant prostate cancer.

Ahmet M. Aydin and Julio M. Pow-Sang
Department of Genitourinary Oncology
H. Lee Moffitt Cancer Center and Research Institute
Tampa, Florida

REFERENCES

1. Hara R, Jo Y, Fujii T et al: Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology 2008; **71:** 191.

2. Ahmed HU, El-Shater Bosaily A, Brown LC et al: Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017; **389:** 815.

This is a simple but highly impactful and practice changing study. It is the first large series of transperineal biopsy performed with the patient under local anaesthesia and so it overcomes the most challenging impediment to widespread uptake of this approach, which is logistics. Importantly, data on all 3 patient centered aspects of biopsy are covered, namely the cancer detection rate, the complication rate and patient tolerance of the procedure, with excellent results.

This study further supports the major advantage of transperineal biopsy of near zero sepsis,[1] a clear benefit for individual patients. Importantly, it also shows that neither quinolone nor multidrug prophylaxis is necessary when avoiding rectal flora via the transperineal approach, which may also confer a public health benefit by preventing the further promotion of quinolone resistant bacteria.[2]

Now that transperineal prostate biopsy has been shown to be just as feasible in daily clinical practice as transrectal biopsy, given the major advantage to patient safety of this approach, it will be increasingly difficult to justify the ongoing use of transrectal biopsy.

This pioneering work is likely to help change how we diagnose prostate cancer and benefit the millions of patients around the world who experience that process every year.

Jeremy Grummet
Department of Surgery
Central Clinical School
Monash University
Melbourne, Victoria, Australia

REFERENCES

1. Grummet J: How to biopsy: transperineal versus transrectal, saturation versus targeted, what's the evidence? Urol Clin North Am 2017; **44:** 525.

2. Centers for Disease Control and Prevention, United States Department of Health and Human Services: Antibiotic Resistance Threats in the United States, 2013. Available at http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf. Accessed January 30, 2019.