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COMPARISON BETWEEN TRUS AND FINGER-GUIDED PROSTATE BIOPSY: A 5-YEAR AUDIT AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL



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To be submitted in partial fulfilment for the degree of Master of Medicine (Urology), Division of Urology, Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand

31st August 2022

Declaration

I Kadima Tshimanga declare that this research report is my own, unaided work. It is being submitted for the Degree of Master of Medicine (Urology), Division of Urology, Department of Surgery, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



……

Kadima Tshimanga

31st day of August 2022 in Johannesburg.

Dedication

I dedicate this MMed to my wife Laetitia Tshiani for her hard work and unwavering love for me and our children. That enabled me to pursue my research and complete this important research project. To my daughters, Maëlys Nseya, Roïs Bambi, and the twins Solen Ngasa and Enor Disanka: I hope you find inspiration in this work to help you achieve your highest goals!

Acknowledgments

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Presentations

1. Annual Bert Myburgh Research Day, November 2021, Johannesburg,
2. Charlotte Maxeke Johannesburg Academic Hospital, March 2022, Johannesburg.
3. 49th Surgical Research Society of Southern Africa Congress, July 2022, Johannesburg.

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List of Abbreviations

ASAP	Atypical Small Acinar Proliferation
CHBAH	Chris Hani Baragwanath Academic Hospital
DRE	Digital Rectal Examination
FG	Finger-Guided
HGPIN	High Grade Prostatic Intra-Epithelial Neoplasia
MRI	Magnetic Resonance Imaging
NHLS	National Health Laboratory Service
PSA	Prostate Specific Antigen
TRUS	Trans-Rectal Ultra-Sound

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Submissible Format

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Comparison Between TRUS and Finger Guided Prostate Biopsy: A 5-Year Audit at Chris Hani Baragwanath Academic Hospital.

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Conflict of Interest: All the authors have no conflict of interest to declare.

Abstract

Background: Although trans-rectal ultrasound guided prostate biopsy is the gold standard diagnostic tool for prostate cancer, finger-guided prostate biopsy is still used in low- and middle-income settings. This study was conducted to determine if finger-guided prostate biopsy is still an appropriate diagnostic technique for suspected prostate cancer.

Methods: An audit of records of patients who underwent a prostate biopsy was conducted. Data collected included demographic information, findings on digital rectal examination, level of prostate specific antigen, type of biopsy and histology results. Data were summarised using the mean with standard deviation for continuous variables or percentages for categorical data. Pearson's Chi square test, Fisher's exact test or Student's t-test was used to compare findings where it was appropriate. A p-value below 0.05 was considered significant. The data were analysed statistically using Stata software version 15.

Results: A total of 3115 records were found of which 62% (1933/3115) were of patients who had trans-rectal ultrasound guided prostate biopsy. Sixty-seven percent of patients in the finger-guided biopsy group had a normal digital rectal examination compared with 58% in the trans-

rectal ultrasound group. The mean prostate specific antigen level was 15 (8-56) ng/ml for the finger-guided group and 19 (9-84) ng/ml for the transrectal ultrasound group, respectively. Prostate cancer was confirmed in 53% in the finger-biopsy guided group compared to 62% following trans-rectal ultrasound guided biopsy. Repeat biopsy showed prostate cancer in 39% of the finger-guided biopsy and 42% in the transrectal ultrasound-guided biopsy group.

Conclusion: Both transrectal ultrasound- and finger-guided prostate biopsy had higher cancer yield above 50%. Transrectal ultrasound-guided biopsy had superior cancer pick-up rate overall. Finger-guided biopsy led to marginal increase in cancer diagnosis in patients with normal prostate on DRE but level of PSA equal or greater than 10ng/ml. And, in patients with palpable nodule, the two techniques had comparable outcomes. Therefore, finger-guided biopsy remains appropriate for use in low- and middle-income settings where patients present at an advanced stage of prostate cancer.

Key words: Biopsy, Finger-guided, Prostate, TRUS-guided.

Background

Cancer of the prostate is the commonest cancer in men between the sixth and seventh decade of life (1,2). Digital rectal examination (DRE) and prostate specific antigen (PSA) are used for screening of men for prostate cancer (3). About 20% of prostate cancer in diagnosed in patients who have normal DRE and/or PSA below 4ng/ml (3-5). Prostate biopsy is the only accepted method for the diagnosis of prostate cancer and a 10 to 12-core trans-rectal ultrasound (TRUS) guided prostate biopsy is recommended when cancer is suspected (6). The TRUS allows for assessment of the prostate, seminal vesicles, urinary bladder and surrounding structures. Trans-rectal ultrasound also assists in the work-up and management of some of the conditions of the prostate such as aspiration of cysts and abscesses as well as high-intensity focussed ultrasound insertion of radiation seeds for brachytherapy and for cryotherapy (7,8).

Prostate cancer is often asymptomatic in early stage and is diagnosed on screening. Signs and symptoms of prostate cancer develop when the cancer is advanced. Among the signs and symptoms of advanced prostate cancer is obstructive features, bone pains, spinal cord compression, anaemia and renal dysfunction (9,10). In low- and middle-income settings where PSA screening protocols are not applied most patients present with either locally advanced or metastatic prostate cancer (11).

The diagnostic yield of TRUS-guided biopsy in cases of suspected prostate cancer is 40–50% (12-16). Historically, the cancer pick-up rates were 17 to 47% on finger-guided trans-rectal (FG) sextant biopsy (17). The 10-12 core biopsy is currently recommended if cancer of the prostate is suspected, regardless of the method of biopsy (18). In our setting, 10-12 core biopsy was applied for both FG and TRUS guided biopsy.

Before the introduction of TRUS-guided biopsy, FG trans-rectal biopsy was solely used and is still relied on in low- and middle-income settings. The FG biopsy technique has got a higher diagnostic yield when there a palpable nodule on DRE (19,20).

This study was conducted to determine if FG biopsy is still appropriate for use in the diagnostic evaluation of patients suspected to be having prostate cancer.

Methods

The study was based on an audit of histopathology records of patients who were seen in the Academic Department of Urology and had a biopsy for suspected cancer of the prostate. The records were retrieved from the National Health Laboratory Service (NHLS) Labtrak database using the words “Prostate Histology Baragwanath Hospital” from 1st January 2013 to 31st December 2017 (a 5-year period). Labtrak is an electronic web-based database that keeps record of all laboratory study results in South Africa. All consecutive histology reports following biopsy of the prostate were retrieved and entered on a data collection sheet. The FG

biopsy group were patients seen from 1st January 2013 to 31st April 2015 and the TRUS-guided biopsy group from the 1st May 2015 to 31st December 2017.

Data extracted included demographic information, PSA levels, findings on DRE, biopsy type, histology results and the need for a repeat biopsy. Data was analysed using the Stata software version 15. Categorical findings were reported as frequencies and percentages. The Pearson's Chi-square test or the Fisher's exact test was used for comparison of categorical data. The mean with standard deviation or median and interquartile range was used to compare continuous data. The Student t-test or the Mann-Whitney U test was used for comparing continuous data. A p-value below 0.05 was considered statistically significant. Permission to conduct the study was received from the local ethics committee (M200162) and the CEO of the hospital.

Results

A total of 3115 records were found and 1182 (38%) were of patients who underwent FG biopsy (Group 1) and 1933 (62%) had a TRUS-guided biopsy (Group 2). Sixty-two (1.7%) cases comprising of 29 (2.39%) from Group 1 and 33 (1.67%) from Group 2 were excluded due to biopsy samples being unsuitable for examination or missing mandatory data such as PSA and/or DRE findings. The median age of all the patients who had prostate biopsy was 65 years (range: 30-94 years). The mean age for patients in Group 1 was 65±7.5 years and 67.5±8.6 years for Group 2. Five hundred and forty-eight (50%) patients in Group 1 and 838 (44%) patients in Group 2 were in the 60-69 years age range. The difference in the age distribution of patients in Group 1 and Group 2 was statistically significant (p-value < 0.0001) (Table 1).

Table 1: Comparison of age categories of patients in Group 1 (FG) and Group 2 (TRUS).

Variable	Number (%)	FG n (%)	TRUS n (%)	p-value
Age category				
<40 years	7(1)	1(0)	6(0)	
40-49 years	59(2)	35(3)	24(1)	
50-59 years	468(16)	191(17)	277(15)	<0.001
60-69 years	1386(46)	548(50)	838(44)	
70-79 years	914(30)	307(28)	607(32)	
80+ years	169(5)	17(2)	152(8)	

Seven hundred and eighty-one (67%) patients in Group 1 had a normal DRE compared to 1121 (58%) in Group 2, with the difference that was statistically significant (p-value < 0.001). The mean value of PSA was 15 (8-56) ng/ml for Group 1 and 19 (9-84) ng/ml for Group 2. Prostate cancer was diagnosed following initial biopsy in 621 (53%) patients in Group 1 and 1187 (62%) in Group 2, and the difference was statistically significant (p-value = 0.001) (Table 2).

Two hundred and seventy-six (44%) prostate cancers were confirmed in the 60-69-year-old patients in Group 1 and 517 (44%) cases in Group 2. For this study population, three (0.2%) patients who had prostate cancer were younger than 40 years and two (0.1%) patients had a normal DRE with a PSA of less than 4ng/ml. Three hundred and fifteen (51%) patients who had prostate cancer in Group 1 had a normal DRE. Abnormal DRE were recorded in 643 (54%) of patients in Group 2.

Table 2: Comparison of histological findings following FG biopsy (Group 1) and TRUS-guided biopsy (Group 2).

Variable	Number (%)	FG n (%)	TRUS n (%)	p-value
Histology results				<0.001
Ca prostate	1808(58)	621(53)	1187(62)	0.001
BPH*	217(7)	116(10)	101(5)	0.001
Prostatitis	830(27)	342(29)	488(25)	<0.0001
Normal	47(2)	26(2)	21(1)	0.059
Others	200(6)	75(6)	125(7)	0.338

*BPH = Benign prostatic hyperplasia.

A Gleason score of 8-10 was reported in 333 (53%) cases in Group 1 and 594 (50%) cases in Group 2. A Gleason score less than 7 was reported in 101 (16%) of the cases in Group 1 and 109 (9%) cases in Group 2. The difference in the reported Gleason score between Group 1 and Group 2 was statistically significant, with a p-value below 0.0001 (Table 3).

Table 3: Comparison of prostate cancer Gleason score between Group 1 (FG) and Group 2 (TRUS).

Variable	Number (%)	FG n (%)	TRUS n (%)	p-value
Gleason Score category				
<7	210(12)	101(16)	109(9)	
7	675(37)	191(31)	484(41)	<0.001
8-10	927(51)	333(53)	594(50)	

The mean volume of the tumour as a percentage of the sample was 42.5% (40-44.9%) in Group 1 and 43% (41.7-45%) in Group 2. The mean tumour volume below 20% accounted for 204 (32%) of cases in Group 1 and 395 (31%) cases in Group 2 (Table 4).

Table 4: Comparison of tumour volume between Group 1(FG) and Group 2 (TRUS).

Variable	Number (%)	FG n (%)	TRUS n (%)	p-value
Percentage category				
<10	264(15)	102(16)	162(14)	
10-19	299(17)	102(16)	197(17)	
20-29	174(10)	66(11)	108(9)	
30-39	122(7)	30(5)	92(8)	0.277
40-49	113(6)	34(5)	79(7)	
50-59	88(5)	33(5)	55(5)	
60-69	175(10)	58(9)	117(10)	
70-79	185(10)	58(9)	127(11)	
80-89	210(12)	77(12)	133(12)	
90+	176(10)	62(10)	114(10)	

For the subgroup of patients with a normal DRE and PSA below 10ng/ml, the categories of tumour percentages of 1-9% and 10-19% had highest proportion with 35% of cases for Group

1 and for Group 2 the category of tumour percentage 1-9% had the highest proportion with 52% of cases. And for combined PSA categories from 20+ng/ml, the highest proportions were found in categories of tumour percentages 80-89% and 90+% with 100% of cases each for Group 1; for Group 2, the category of tumour percentages 90+% had the highest proportion with 84% of cases. For the PSA category 10-19ng/ml, the category of tumour percentages with the highest fraction was 30-39% with 46% of cases for Group 1 and the category 10-19% with 37% of cases for Group 2; but did not demonstrate a specific pattern.

For the subgroup of patients with an abnormal DRE, the tumour percentages did not demonstrate a clear trend in relation to PSA categories. And the difference was not statistically significant (Table 5).

Table 5: Comparison of tumour volume for the specific technique in relation to PSA and DRE findings.

		Normal DRE						**Abnormal DRE**					
	PSA	<4	4-9	10-19	20-99	100+	p-value	<4	4-9	10-19	20-99	100+	p-value
%													
1-9	FG	0	35	44	21	0	0.118	5	24	29	33	9	0.499
	TRUS	0	52	33	15	0		5	32	35	14	14	
10-19	FG	2	33	41	21	3	0.888	0	13	17	35	35	0.790
	TRUS	1	33	37	26	3		0	22	20	29	29	
20-29	FG	0	28	36	26	10	0.388	0	4	4	44	48	0.227
	TRUS	0	26	29	40	5		0	16	16	29	39	
30-39	FG	0	8	46	46	0	0.554	0	9	9	55	27	0.870
	TRUS	0	19	30	46	5		2	4	17	45	32	
40-49	FG	0	6	35	59	0	0.134	0	0	0	18	82	0.635
	TRUS	0	27	30	35	8		0	2	2	34	62	
50-59	FG	0	17	17	58	8	0.749	0	0	23	31	46	0.223
	TRUS	0	14	36	43	7		0	5	5	30	60	
60-69	FG	0	15	15	50	20	0.728	4	4	4	22	66	0.848
	TRUS	0	15	12	38	35		1	2	4	29	64	
70-79	FG	0	8	30	54	8	0.951	0	0	3	12	85	0.068
	TRUS	0	7	25	56	12		0	1	8	31	60	
80-89	FG	0	0	0	71	29	0.125	0	0	5	22	73	0.217
	TRUS	0	10	20	40	30		0	0	2	13	85	
90+	FG	0	0	0	63	37	0.677	0	0	0	23	77	0.480
	TRUS	0	11	5	58	26		0	0	3	19	78	

The cancer detection rate related to PSA categories in patients with a normal DRE demonstrated left skewed distributions, with a sharp rise from PSA category 4-9ng/ml and drop

at PSA category 100+ng/ml. For Group 1 the highest number of prostate cancers was in PSA category 20-99ng/ml with 107 (34%) cases and the lowest in PSA category below 4ng/ml with only one case. For Group 2, the peak in number of cases was observed in the PSA category 20-99ng/ml with 176 (33%) cases and the least in the PSA category less than 4ng/ml with one case. And the difference between the 2 groups was not statistically significant (Figure 1).

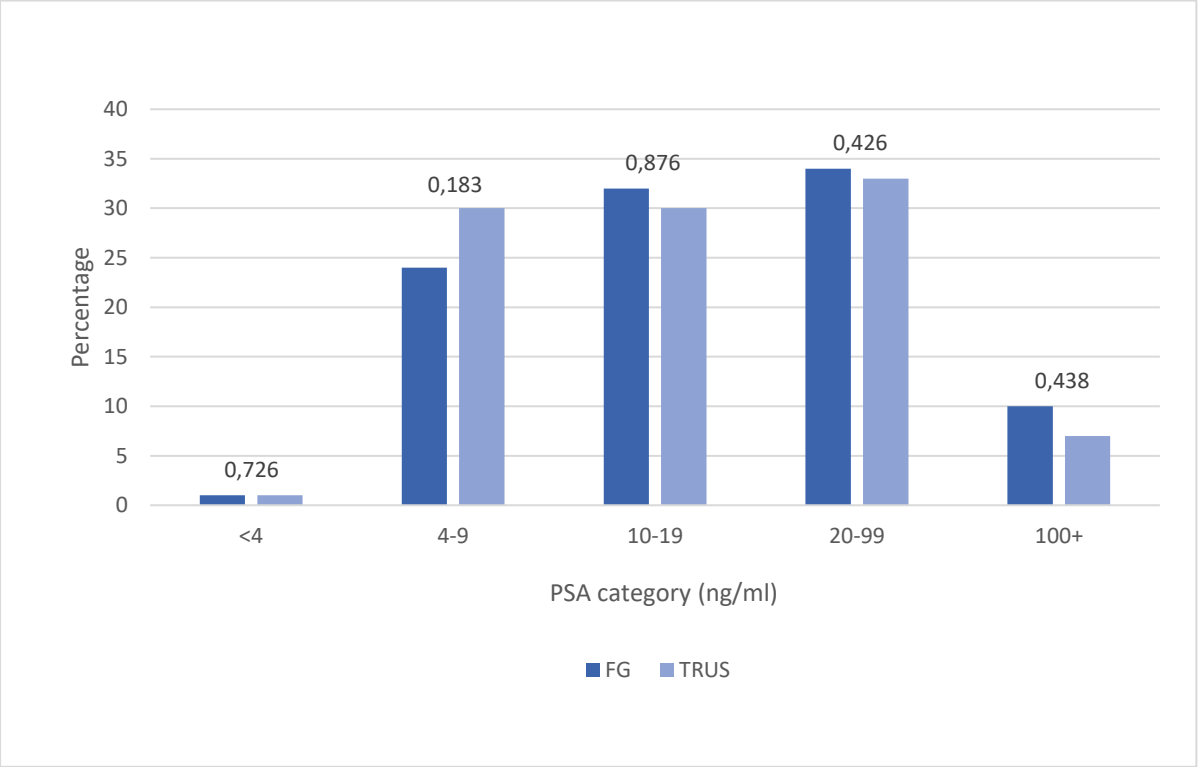

Figure 1: Comparison of prostate cancer detection rate between FG and TRUS-guided biopsy in patients with normal DRE findings.

In patients with an abnormal DRE, cancer detection rate followed ascending patterns related to the increase in PSA values. For Group 1, the maximum detection rate in the PSA category ≥100ng/ml with 176 (58%) cases and the minimum in the PSA category below 4ng/ml with three cases. For Group 2, the greatest number of cancers was observed in the PSA category ≥100ng/ml with 378 (59%) cases and the least in the PSA category <4ng/ml with five cases. And the difference between the two groups was not statistically significant (Figure 2).

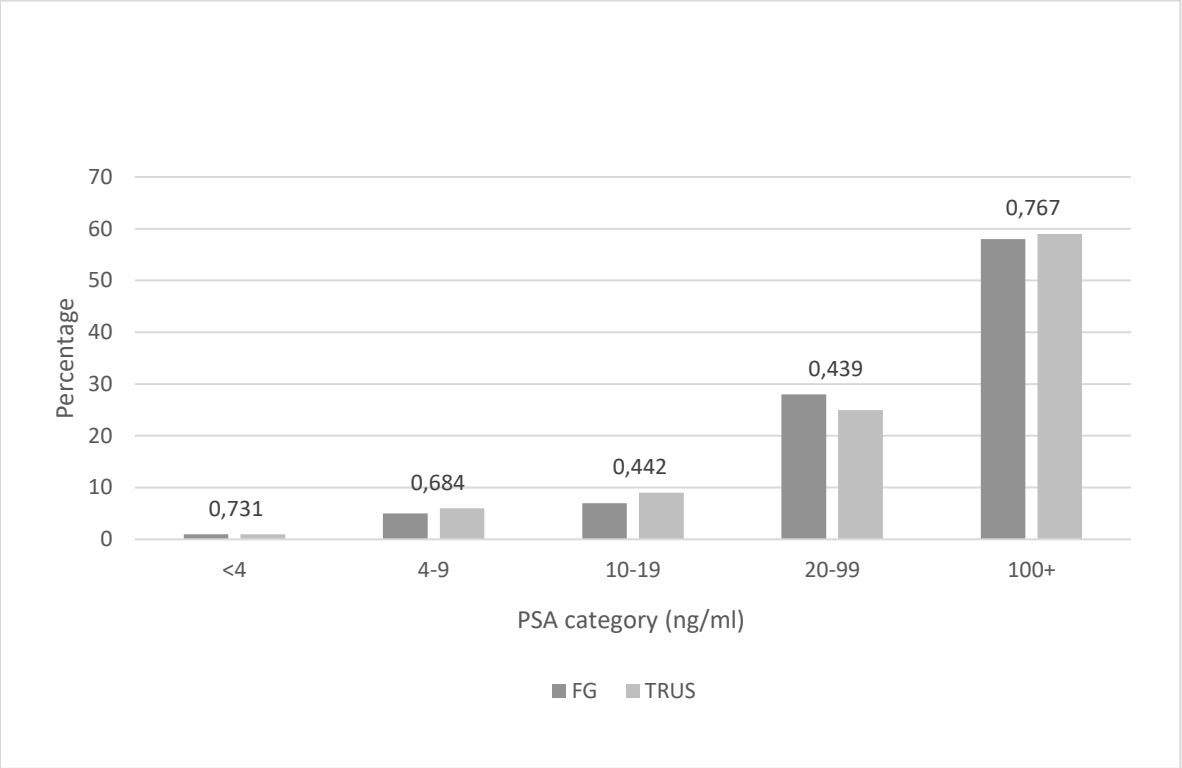

Figure 2: Comparison of prostate cancer detection rate between FG and TRUS-guided biopsy in patients with abnormal DRE findings.

One hundred (8%) patients had repeat biopsy in the Group 1 and 162 (8%) in Group 2 and prostate cancer was confirmed in 39 (39%) and 69 (42%), respectively. The difference in cancer confirmation following repeat biopsy between the two groups was not statistically significant (p-value = 0.691).

Discussion

Prostate cancer may be suspected clinically or following screening using serum PSA and DRE. Some patients present and are diagnosed when the prostate cancer is locally advanced and causing obstructive symptoms or when the disease is metastatic. Prostate biopsy is almost solely done to rule out cancer. The specimen obtained following prostate biopsy should be of

enough volume to allow for confirmation of cancer and subsequently, tumour grading. This study was conducted to determine if FG biopsy of the prostate is still appropriate in era of TRUS guided biopsy. Key findings from the study include that prostate cancer is rare in men below the age of 40 years, some patients who had prostate cancer had normal DRE and/or serum PSA, and the diagnostic yield of FG is not inferior to TRUS guided when there is a palpable nodule.

Majority of patients who had prostate cancer were above 60 years old, with the highest number in patients between 60 and 69 years of age and the lowest number in patients younger than 40 years, which is similar to what is written in the literature (1,2). Nevertheless, we observed an increase in incidence of prostate cancer for the category of patients older than 80 years amongst those who had a TRUS-guided biopsy. The increase of prostate cancer in patients older than 80 years might have been due to a shift to a more aggressive approach in the work up of the elderly patients which was implemented by our department in 2015. The proportion of patients who had a normal or an abnormal DRE were comparable amongst confirmed prostate cancers between the FG and TRUS-guided biopsy groups. And for the study population, only a few patients (0.2%) younger than 40 years have been found with prostate cancer. Also, a very small proportion of patients (0.1%) with prostate cancer presented with a PSA less than 4ng/ml together with a normal finding on DRE. This highlight the high positive predictive value of the combination of an abnormal DRE and PSA of 4ng/ml or more (21).

The DRE findings and PSA values in the FG and TRUS group demonstrated similar trends, making these two groups comparable. The high number of abnormal DRE and high PSA values is likely due to patients only presenting on occurrence of symptoms of advanced prostate cancer, to our health service providers. Infection, urinary retention, bladder catheterisation and transurethral instrumentation are other variables responsible for raised PSA but were not included in our study.

The difference in the diagnosis of prostate cancer is noticeable with a higher yield from the TRUS-guided biopsy technique of 62% compared to 53% for the FG technique. These rates surpassed the widely reported prostate cancer diagnostic yield of 40-50% on TRUS-guided biopsy (12,16). Because our patients present with symptoms rather than being chosen based on a screening criterion, they frequently have locally advanced prostate cancer. This would explain the high diagnostic yield on prostate biopsy observed in this study.

The relative advantage of the TRUS-guided technique over the FG technique was shown in the subgroup of patients with a normal DRE and a PSA level of 4 to 9ng/ml where the difference in detection rate was the greatest, but not statistically significant. For patients with a PSA of 10ng/ml or more in the subgroup of patients with a normal DRE, the FG technique marginally outperformed the TRUS in cancer detection rate. In patients with PSA of less than 4ng/ml and a normal DRE, the cancer pick-up rates were similar and in keeping with findings from a recent study (20).

For those with an abnormal DRE, the patterns of prostate cancer detection rate were similar either using FG or TRUS-guided prostate biopsy which is in accordance with some researchers who found the diagnosis of prostate cancer much easier by targeting the prostatic nodule on palpation during an FG biopsy (22-24). The need for repeat prostate biopsy was the same following FG and TRUS-guide biopsy with a slightly higher cancer detection rate following TRUS-guided at 42% versus 39% for FG biopsy. The prostate cancer confirmation rates in the current study were higher than the 18% to 32% reported for repeat TRUS-guided biopsy (25,26). Around 30% of prostate cancers are missed by TRUS-guided biopsy due to difficult access to the apical and anterior regions of the prostate (27). However, the good results following repeat biopsy in this study might have been due either a tighter selection of patients with ongoing suspicion of prostate cancer after an initial negative biopsy or a greater number of undiagnosed cancers on the initial biopsy.

When compared with the TRUS technique, the FG technique detected a higher incidence of prostate cancer with a Gleason category score below 7, which include low-grade and clinically insignificant cancers based on PSA value, DRE finding and tumour volume. Sixteen percent for FG and 9% for TRUS-guided technique, these numbers are lower than 17% to 30% reporter internationally. This would be explained by the lack of routine PSA screenings in our setting (28). The study found that the tumour volume was closely related to PSA values but appeared dissociated from DRE findings for both TRUS and FG groups. Tumour volume percentages were higher as the PSA values increased. These findings were like those of previously reported series (29). Although the estimation of tumour volume is prone to calculation errors and depend on the technique utilised, tumour volume remains an important parameter in the selection of patient for active surveillance and in the prognostication of prostate cancer.

Limitation of the study

The study was retrospective; therefore, some data were missing. Additional information such as presenting signs and symptoms, presence of infection, urinary retention, bladder catheterisation, transurethral instrumentation, other comorbidities and/or medication were not included in the study. However, this would not have contributed to information on how the two techniques compare in our setting, and thus would not add to the conclusion. Because the two techniques were not used on the same patients and were not compared to specimen from prostatectomy, the study did not allow for the calculation of sensitivity and specificity. As a result, we were unable to include the sensitivity and specificity of the two techniques in our research.

Conclusion

Men in their sixth and seventh decade of life bear the heaviest burden of prostate cancer, but this diagnosis can still be made in patients younger than 40 years. And patients with PSA value of less than 4ng/ml and normal DRE finding are less likely to have prostate cancer. Both

transrectal ultrasound- and finger-guided prostate biopsy had higher cancer yield above 50%. Transrectal ultrasound-guided biopsy had superior cancer pick-up rate overall. Finger-guided biopsy diagnosed more prostate cancers in patients with normal prostate on DRE but level of PSA equal or greater than 10ng/ml compared to the FG-biopsy technique. In patients with palpable nodule, the two techniques had comparable outcomes. Therefore, finger-guided biopsy remains appropriate for use in low- and middle-income settings where patients present at an advanced stage of prostate cancer.

Recommendation

Healthcare facilities irrespective of the income status should still be encouraged to acquire resources to enable the performance of TRUS guided biopsy of the prostate as it would improve the diagnosis and management of prostate cancer.

References

1. Kaestner LA. Is ethnicity a risk for high-grade prostate cancer (MMed (Urology) thesis)? University of cape Town, Cape Town, South Africa. 2010.

2. Heyns CF, Lecouna AJ, Trollip GS. Prostate cancer: prevalence and treatment in African men. JMHG. 2005;2(4):400-5.

3. Cary KC, Cooperberg MR. Biomarkers in prostate cancer surveillance and screening: past, present, and future. Ther Adv Urol. 2013;5(6):318-29.

4. Catalona WJ, Smith DS, Ornstein DK. prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0 ng/ml and benign prostate examination: Enhancement of specificity with free psa measurements. JAMA. 1997;277(18):1452–1455.

5. Teoh JY, Yuen SK, Tsu JH, et al. Prostate cancer detection upon transrectal ultrasound-guided biopsy in relation to digital rectal examination and prostate-specific antigen level: what to expect in the Chinese population? Asian J Androl. 2015;17(5):821-825.

6. Carter HB. American Urological Association (AUA) guideline on prostate cancer detection: Process and rationale. BJU Int. 2013;112(543-547).

7. Ludwig M, Schroeder-Printzen I, Schiefer HC, Weidner W. Diagnosis and therapeutic management of 18 patients with prostatic abscess. Urology 1999;53(340-5).

8. Beerlage HP. Alternative therapies for localized prostate cancer. Curr Urol Rep.4:216-20.

9. Wang G, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. Genes Dev. 2018 Sep 01;32(17-18):1105-1140.

10. Suzman DL, Boikos SA, Carducci MA. Bone-targeting agents in prostate cancer. Cancer Metastasis Rev. 2014 Sep;33(2-3):619-28.

11. Kingham TP, Alatise O, Vanderpuye V, Casper C, Abantanga FA, et al. Treatment of cancer in sub-Saharan Africa. Lancet Oncol. 2013;4:158-167.

12. Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. J Urol. 1997;157:199-202.

13. Naughton CK, Miller DC, Mager DE, Ornstein DK, Catalona WJ. A prospective randomized trial comparing 6 versus 12 prostate biopsy cores: impact on cancer detection. J Urol. 2000;164:388-92.

14. Presti JC, Chang JJ, Bhargava V, Shinohara A. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. J Urol. 2000;163:163-7.

15. Babaian RJ, Toi A, Kamoi K, Troncoso P, Sweet J, Evans R, et al. A comparative analysis of sextant and an extended 11-core multisite directed biopsy strategy. J Urol. 2000;163:152-7.

16. Serag H, Banerjee S, Saeb-Parsy K, Irving S, Wright K, Stearn S, et al. Risk profiles of prostate cancers identified from UK primary care using national referral guidelines. Br J Cancer. 2012;106:436-9.

17. Weaver RP, Noble MJ, Weigel JW. Correlation of ultrasound guided and digital directed transrectal biopsies of palpable prostatic abnormalities. J Urol. 1991;145:516-8.

18. Heidenreich A, Bastian PJ, Bellmunt J, Bolla M, Joniau S, et al. EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent—update 2013. Eur Urol. 65(1):124–137.

19. Temi AP, Gbenga OJ. Prevalence of Voiding Dysfunction After Finger-Guided Prostate Needle Biopsy in Nigerian Men. Sur Urol. 2017;6.

20. Jehle KS, Lazarus JM, Barnes RD. A review of transrectal ultrasound guidedprostate biopsies: Is there still a role for finger guided prostate biopsies? Afr J Urol. 2015;21:62-6.

21. Catalona WJ, Richie J P, Ahmann FR, Hudson MA, Scardino PT, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol. 2017;197(2):S200-S207.

22. Resnick MI. Transrectal ultrasound guided versus digitally directed prostatic biopsy: a comparative study. J Urol. 1988;139(4):754-7.

23. Van Emery MJ, Rooney B. Comparison of ultrasound-guided and digitally directed transrectal biopsy of palpable prostate lesions. Urology. 1993;42:677-9.

24. Figueiredo AJC, Seen K, Anson KM, Furtuado AJL, Miller RA. Are transrectal guided biopsies required for the accurate diagnosis of carcinoma of the prostate? Can digitally guided systematic biopsies offer an acceptable alternative? Br J Urol. 1995;76:187-91.

25. Yuasa T, Tsuchiya N, Kumazawa T, Inoue T, Narita S, Saito M, et al. Characterization of prostate cancer detected at repeat biopsy. BMC Urol. 2008;8.

26. Aganovic D, Prcic A, Kulovac B, Hadziosmanovic O. Prostate cancer detection rate and the importance of premalignant lesion in rebiopsy. Med Arh. 2011;65:109-12.

27. Scattoni V, Zlotta A, Montironi R, Schulman C, Rigatti P, Montorsi F. Extended and saturation prostatic biopsy in the diagnosis and characterisation of prostate cancer: a critical analysis of the literature. Eur Urol.52:1309-1322.

28. Fleshner K, Carlsson SV, Roobol MJ. The effect of the USPSTF PSA screening recommendation on prostate cancer incidence patterns in the USA. Nat Rev Urol. 2017 Jan;14(1):26-37.

29. Carvalhal GF, Daudi SN, Kan D, Mondo D, Roehl KA, Loeb S, Catalona WJ. Correlation between serum prostate-specific antigen and cancer volume in prostate glands of different sizes. Urology. 2010 Nov;76(5):1072-6.

Appendix A: Letter to the Editor of the African Journal of Urology.

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Johannesburg, 31st March 2022

To: The Editor

African Journal of Urology

Dear Sir/Madam

Re: Submission of manuscript for consideration

We hereby submit a research article for consideration by your journal. The title of the manuscript is: "Comparison Between TRUS and Finger Guided Prostate Biopsy: A 5-Year Audit at Chris Hani Baragwanath Academic Hospital". All the authors made significant contribution to the research and have authorized the submission. There is no conflict of interest.

Thank you very much for considering our manuscript.

Yours sincerely,

Dr K. Tshimanga
Urology Registrar
University of the Witwatersrand

Appendix B: Research Proposal.

COMPARISON BETWEEN TRUS AND FINGER GUIDED PROSTATE BIOPSY: A 5-YEAR AUDIT AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL.

Introduction

Cancer of the prostate is the commonest cancer in the male population between the sixth and seventh decade of life (1, 2). Prostate biopsy remains the only accepted tool in the diagnosis of prostate cancer in the face of widely used prostate specific antigen, digital rectal examination, trans-rectal ultra-sound and magnetic resonance imaging in the evaluation of most prostatic diseases (3).

The European Association of Urology recommends, as the rest of first world countries do, a 10 to 12-core Trans-Rectal Ultra-Sound (TRUS) guided prostate biopsy if cancer is suspected. This provides a systematic and extended core biopsy, in reference to the original sextant protocol proposed by Hodge in 1989, when TRUS assisted prostate biopsy was introduced in Urology. TRUS can be used to assess the prostate, seminal vesicles and urinary bladder including and surroundings structures. It also assists in the diagnostic work-up and management of other conditions of the prostate such as aspiration of cysts (4) and abscesses (4); in high-intensity focussed ultrasound, insertion of radiation seeds for brachytherapy and for cryotherapy (5).

At Chris Hani Baragwanath Academic Hospital (CHBAH) the finger guided (FG) trans-rectal 12-core prostate biopsy has been routine for more than 10 years. It is also a common practice in low-income settings which include most parts of Africa (6). The finger-guided technique is preferred because of limited access to resources such as trans-rectal ultra-sound facilities (7). The FG is feasible and reliable if there is a palpable nodule on digital rectal examination. Its reliability, however, is low in cases with a non-palpable nodule. Being a tertiary hospital, the

bulk of our patients come from satellite hospital and clinics, also private practitioners and are mostly symptomatic.

From Mai 2015 we saw a shift in the daily practice with the upgrade of ultra-sound equipment including in the Department of Urology at CHBAH. Currently the department has access to a state-of-the-art ultrasound machine which is fitted with a trans-rectal probe and biopsy needle guide. The urology team has since then been encouraged and opted to perform TRUS guided prostate biopsy instead, except for one staff member. However, in certain instances FG biopsies still happen, often in patients bedridden or difficult to mobilise lying in outside wards. Although previous studies have compared TRUS to FG guided biopsy of the prostate, very few of the studies are from middle to low-income settings. I will therefore review and compare the effectiveness between TRUS and FG prostate biopsy at CHBAH.

Relevant Literature Review

Literature focused on the comparison between TRUS and FG prostate biopsy is scarce. The large majority of publications are of retrospective studies comprising small numbers. In the late nineties, in what was then considered ground-breaking studies; Hodge et al compared TRUS to FG prostate biopsy and found that the accuracy of TRUS biopsy was 94% of cancers previously diagnosed on FG biopsies (8). Furthermore, TRUS was able to confirm the diagnosis of cancer in 23 of 43 cases which were previously negative following FG biopsy (9, 10). On the strength of these findings, TRUS was introduced to Urology and TRUS prostate biopsy is now considered the gold standard procedure for prostate biopsy.

Weaver et al (11), compared FG biopsies of abnormal prostate on DRE with simultaneous TRUS biopsies in 51 patients and found that 45.1% were malignant following TRUS while whereas FG biopsies were diagnostic in 17.6%. They concluded that TRUS was superior to FG biopsy even for cases which have a palpable nodule. Türkeri et al (12) also compared FG

to TRUS guided biopsy and found TRUS superior. They concluded that FG biopsy is archaic and should abandoned.

Huynh et al did a similar study comparing TRUS and FG biopsy. They studied 240 patients who had palpable prostate nodules and found that only 7.5% of the cancers were detected in the FG biopsies, with an increased yield of cancer from 47.9% to 55.4% using TRUS (13). Elsewhere Resnick et al (14) also compared FG with TRUS guided biopsies in 45 men with an overall cancer yield of 31% and found no difference between the two techniques in patients with an abnormal DRE. Similarly, Van Emery et al (15) and Figueiredo et al (16) found that TRUS guidance was comparable to FG biopsies.

Recently, in a study at Groote Schuur Hospital in Cape Town in South Africa; Jehle demonstrated no superiority of TRUS over FG biopsy (8). The above was true except for patients who had PSA below 10 ng/dl and a normal DRE. Their study included 454 cases of which 192 had TRUS biopsy using 12-core protocol. The remaining 262 had FG biopsy using 6-core protocol (8). The TRUS is easy to perform and to learn, and is cost effective. A novice would require five supervised cases before being fully independent and confident in performing TRUS biopsy (17, 18).

The ultrasound guided trans-perineal approach to prostate biopsy, a variant of TRUS; is being practiced in some centres in parts of the world (19). In this case the biopsy needle is passed through the skin of the perineal area instead of advancing it from inside the rectum. It has been described in the literature as time consuming, requiring training time, posing financial constraints and necessitating high-grade anaesthesia which makes it less popular among urologists (19). Some studies have shown it to have better diagnostic yield especially for lesions located in the peripheral apical regions of the prostate where prostate cancer is more prevalent (20). Its cancer detection rate is similar to trans-rectal approach more so when extended core

biopsy is applied (21, 22). It is however associated with higher complications rate as compared with the TRUS biopsy (23).

The introduction of TRUS in the late nineties has revolutionised prostate biopsy techniques and prostate cancer management (9, 10). Since its introduction the number of prostate biopsies using this technique have increased exponentially. Current consensus is that 10 to 12 core biopsies should be taken during TRUS biopsy (24, 25). More than 12 biopsies have not proven to be significantly more conclusive and increase the likelihood of complications (24, 25).

Table 6: Prostate cancer detection rates with extended core biopsy protocols.

Study	***No. of patients***	***No. of Cores***	***Cancer Detection Rate***
Eskew et al, 1997 (26)	119	6	26.1%
		13	40.3%
Naughton et al, 2000 (27)	160	6	26%
		12	27%
Presti et al, 2000 (28)	483	6	33.5%
		8	39.7%
		10	40.2%
Babaian et al, 2000 (29)	362	6	20%
		11	30%

In South-African males, prostate cancer is the most common non-skin cancer, accounting for 19.18% of all cancers in 2014 (30)**.** It is the third leading cause of death in men in Europe and the USA (31, 32). Its risk factors include amongst others genetic predisposition (33, 34). Factors such as diet, sexual behaviour, alcohol consumption, exposure to ultraviolet radiation, chronic inflammation and occupational exposure have all been discussed as being aetiologically important (35, 36). Exogenous factors also affect the risk of progression from latent to clinical prostate cancer.

Significance of Research

Cancer of the prostate gland is the commonest cancer in men in South Africa. Although TRUS biopsy is the preferred method for prostate biopsy, resources that are required to perform it are not always available. The above applies more in rural parts of South Africa and predictably in other low- and middle-income countries. The FG biopsy technique is cheaper and feasible.

Research Question

Is FG prostate biopsy still appropriate for use in the diagnostic evaluation of patients suspected to have prostate cancer?

Aim

To determine if FG prostate biopsy is still appropriate for use in the diagnostic evaluation of patients suspected to be having prostate cancer?

Objectives

1. To determine demographic, clinical and histological findings in patients who had prostate biopsy at CHBAH.
2. To determine sensitivity, specificity and accuracy of FG and TRUS biopsy techniques.
3. To compare the outcome of prostate biopsy using FG and TRUS.

Methods

The data will be retrieved from the National Health Laboratory Service (NHLS) Labtrak using the words “Prostate Histology Baragwanath Hospital” from January 2013 to December 2017. Labtrak is an electronic web-based database, it keeps record of all laboratory studies results in South Africa.

Nature of the study

Retrospective audit.

Setting

The Department of Urology at Chris Hani Baragwanath Academic Hospital.

Period

From 1st January 2013 to 31st December 2017.

Population inclusion criteria

Records of all patients who had prostate biopsy at CHBAH during the study period.

Population exclusion criteria

a. Samples from prostatectomy,

b. Transurethral resection of the prostate (TURP) chips biopsy.

Sample Size Determination

15 to 25 biopsies of prostate are performed per week on the average.

Data Collection

All prostatic histology reports will be retrieved from the National Health Laboratory Service (NHLS) from Chris Hani Baragwanath Academic Hospital during our study period, and entered in a data collection sheet using theses parameters: case number, Age, PSA, DRE findings, prostate biopsy type, histology results and repeat biopsy.

Data Analysis

Data will be summarised using frequencies and percentages. Comparison of categorical data will be done using Pearson's Chi squared test and Fisher's exact test where appropriate. Mean and standard deviation will be used for continuous data. And Student's T test and Mann-

Whitney U test will be relied on for comparison of continuous data. A p-value of less than 0.05 will be considered significant. Data will be analysed using the recent version of Stata software.

Ethics

Ethical approval will be sought from the Human Research Ethics Committee of the University of the University of the Witwatersrand and from the Chris Hani Baragwanath Academic Hospital Review Board.

Confidentiality

All personal information relating to the patient will be kept confidential.

Informed consent

Not required.

Cost Analysis and Budget

Cost will be borne by the researcher and not the Hospital, nor the University.

References

1. Kaestner LA. Is ethnicity a risk for high-grade prostate cancer (MMed (Urology) thesis)? University of Cape Town, Cape Town, South Africa. 2010.

2. Heyns CF, Lecouna AJ, Trollip GS. Prostate cancer: prevalence and treatment in African men. JMHG. 2005;2(4):400-5.

3. Carter HB. American Urological Association (AUA) guideline on prostate cancer detection: Process and rationale. BJU Int 2013;112(543-547).

4. Ludwig M, Schroeder-Printzen I, Schiefer HC, Weidner W. Diagnosis and therapeutic management of 18 patients with prostatic abscess. Urology 1999;53(340-5).

5. Beerlage HP. Alternative therapies for localized prostate cancer. Curr Urol Rep.4:216-20.

6. Director general. World Health Report: Fighting disease, fostering development. Geneva: World Health Organisation. WHO; 1996.

7. Temi AP, Gbenga OJ. Prevalence of Voiding Dysfunction After Finger-Guided Prostate Needle Biopsy in Nigerian Men. Sur Urol 2017;6.

8. Jehle KS, Lazarus JM, Barnes RD. A review of transrectal ultrasound guidedprostate biopsies: Is there still a role for finger guided prostate biopsies? Afr J Urol. 2015;21:62-6.

9. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol. 1989;142:71-5.

10. Hodge KK, McNeal JE, Stamey TA. Ultrasound guided transrectal core biopsies of the palpably abnormal prostate J Urol. 1989; 142(1):66-70.

11. Weaver RP, Noble MJ, Weigel JW. Correlation of ultrasound guided and digital directed transrectal biopsies of palpable prostatic abnormalities. J Urol 1991;145:516-8.

12. Türkeri L, Tarcan T, Biren T, Küllü S, Akdaş A. Transrectal ultrasonography versus digitally guided prostate biopsies in patients with palpable leions on digital rectal examination. Br J Urol. 1995;76:184-6.

13. Huynh CC, Awad N, Fulton M. The advantage of finger guided prostate biopsies in addition to transrectal ultrasound guided prostate biopsies in patients with palpable disease. BJU Int 2006;97 (S1):19.

14. Resnick MI. Transrectal ultrasound guided versus digitally directed prostatic biopsy: a comparative study. J Urol. 1988;139(4):754-7.

15. Van Emery MJ, Rooney B. Comparison of ultrasound-guided and digitally directed transrectal biopsy of palpable prostate lesions. Urology. 1993;42:677-9.

16. Figueiredo AJC, Seen K, Anson KM, Furtuado AJL, Miller RA. Are transrectal guided biopsies required for the accurate diagnosis of carcinoma of the prostate? Can digitally guided systematic biopsies offer an acceptable alternative? Br J Urol. 1995;76:187-91.

17. Karam JA, Shulman MJ, Benaim EA. Impact of training level of urology residents on the detection of prostate cancer on TRUS biopsy. Pros Cancer Prost Dis. 2004;7:38-40.

18. Lawrentschuk N, Toi A, Lockwood GA, Evans A, Finelli A, O'Malley M, et al. Operator is an Independent Predictor of Detecting Prostate Cancer at Transrectal Ultrasound Guided Prostate Biopsy. J Urol. 2009;182:2659-63.

19. Chang DT, Challacombe B, Lawrentschuk N. Transperineal biopsy of the prostate–is this the future. Nat Rev Urol. 2013;10:690-702.

20. Kawakami S, Okuno T, YoneseJ, IgariT, Arai G, Fujii Y, et al. Optimal sampling sites for repeat prostate biopsy: a recursive partitioning analysis of three-dimensional 26 core systematic biopsy. Eur Urol 2007;51:675-82.

21. Takenaka A, Hara R, Ishimura T, Fujii T, Jo Y, Nagai A, et al. A prospective randomized comparison of diagnostic efficacy between transperineal and transrectal 12-core prostate biopsy. Prostate Cancer Prostatic Dis. 2008;11:134-8.

22. Hara R, Jo Y, Fujii T, Kondo N, Yokoyoma, T MY, et al. Optimal approach for prostate cancer detection as initial biopsy: prospective randomized study comparing transperineal versus transrectal systematic 12-core biopsy. Urology. 2008;71:191-5.

23. Kakehi Y, Naito S. Complication rates of ultrasound-guided prostate biopsy: a nation-wide survey in Japan. Int J Urol. 2008;15:319-21.

24. Van den Bergh RC, Roemeling S, Roobol MJ, Aus G, Hugosson J, Rannikko AS, et al. Outcomes of men with screen-detected prostate cancer eligible for active surveillance who were managed expectantly. Eur Urol 2009;55(1):1-8.

25. Van As NJ, Norman AR, Thomas K, Khoo VS, Thompson A, Huddart RA, et al. Predicting the probability of deferred radical treatment for localised prostate cancer managed by active surveillance. Eur Urol 2008;54(6):1297-305.

26. Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. J Urol. 1997;157:199-202.

27. Naughton CK, Miller DC, Mager DE, Ornstein DK, Catalona WJ. A prospective randomized trial comparing 6 versus 12 prostate biopsy cores: impact on cancer detection. J Urol 2000;164:388-92.

28. Presti JC, Chang JJ, Bhargava V, Shinohara A. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. J Urol 2000;163:163-7.

29. Babaian RJ, Toi A, Kamoi K, Troncoso P, Sweet J, Evans R, et al. A comparative analysis of sextant and an extended 11-core multisite directed biopsy strategy. J Urol. 2000;163:152-7.

30. National cancer registry. Cancer in South Africa full report. National institute for communicable diseases; 2014.

31. Siegel R, Naishadham D, Jemal A. Cancer statistics. CA Cancer J Clin 2013;2013(63):11-30.

32. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, Rosso S, Coebergh JWW, Comber H, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 49:1374-403.

33. Jansson KF, Akre O, Garmo H, Bill-Axelson A, AdolfssonJ, Stattin P, et al. Concordance of tumor differentiation among brothers with prostate cancer. Eur Urol. 2012;62.

34. Hemminki K. Familial risk and familial survival in prostate cancer. World J Urol. 2012;30.

35. Nelson WG, De Marzo AM, Isaacs WB. Prostate cancer. N Engl J Med. 2003;349.

36. Leitzmann MF, Rohrmann S. Risk factors for the onset of prostatic cancer: age, location, and behavioral correlates. Clin Epidemiol 2012;4:1.

Appendix C: Data Collection Sheet.

COMPARISON BETWEEN TRANS-RECTAL ULTRASOUND-GUIDED AND FINGER-GUIDED PROSTATE BIOPSY: A 5-YEAR AUDIT AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL.

DATA COLLECTION SHEET

1. Patient study number: ☐
2. Age: ☐ years
3. PSA: ☐ ug/L
4. DRE findings:

Normal	Abnormal

5. Prostate biopsy type:

TRUS	FG

6. Histology report:

Ca Prostate	BPH	Prostatitis	Normal tissue	Others

7. Gleason score:

	N/A

8. Tumour percentage ☐
9. Repeat biopsies

YES	NO

Appendix D: Turn-it-in Digital Receipt.

08901071:Tshimanga_MMed_FINAL_for_Turn-it-in_02_April_2022.docx

ORIGINALITY REPORT

11%	8%	7%	2%
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20	Fawzi T. Abul, Narayanaswamy Arun, Mona A. Abu-Assi, Akram M. Asbeutah. "Transrectal ultrasound guided biopsy for detecting prostate cancer: can random biopsies be reduced using the 4-dimensional technique?", International Urology and Nephrology, 2007 Publication	<1 %
21	Giacomo Novara. "Detection rate and factors predictive the presence of prostate cancer in patients undergoing ultrasonography-guided transperineal saturation biopsies of the prostate", BJU International, 05/2010 Publication	<1 %
22	Mahul Amin, Liliane Boccon-Gibod, Lars Egevad, Jonathan I. Epstein et al. "Prognostic and predictive factors and reporting of prostate carcinoma in prostate needle biopsy specimens", Scandinavian Journal of Urology and Nephrology, 2009 Publication	<1 %

Appendix E: Ethics Clearance Certificate.

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr K Tshimanga

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200162

NAME: (Principal Investigator)	Dr K Tshimanga
DEPARTMENT:	School of Clinical Medicine Department of Surgery Division of Urology Medical School University
PROJECT TITLE:	Comparison between TRUS and finger-guided prostate biopsy: a five year audit at Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	2020/01/31
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor T Luvhengo
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/07/28

This clearance certificate is valid for 5 years from the date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **«Missing mail merge field»** and will therefore reports and re-certification will be due early in the month of **«Missing mail merge field»** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

30/07/2020
Date

Appendix F: Hospital Approval.

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 10th December 2018

TITLE OF PROJECT:

Comparison Between TRUS and Finger Guided Prostrate Biopsy: A 5-Year Audit at Chris Hani Baragwanath Academic Hospital.

UNIVERSITY: Witwatersrand

Principal Investigator: Dr K Tshimanga

Department: Urology

Supervisor : Prof T Luvhengo

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

.....
Recommended
(On behalf of the MAC)
Date: 10/12/2018

.....
Approved/Not Approved
Hospital Management
Date: 13 12 2018

Appendix G: Post-Graduate Approval.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PROTOCOL ASSESSORS MEETING

Candidate Full Name: **Kadima TSHIMANGA**. . . . . (Supervisors: Luvhengo/Doherty/?)

Student Number: . . . 2300865 . . . . . Date: . . . 13th November 2019. . . . . .

School / Department / Division: . Department of Surgery, Division of Urology. . . . . .

Degree: ...MMed.....Title: *Comparison between thrus and finger guided prostate biopsy: A 5-year audit at Chris Hani Baragwanath Hospital.*

1. **Type of study** *(tick all that apply)*:

- ✓ Quantitative
- o Qualitative
- o Mixed Methods
- o Laboratory
- o Clinical
- o Other, please specify..... Retrospective .....

2. **Is title of the study appropriate** (*preferably fewer than 20 words*)? ✓ Yes / No

Comments: _____

3. **Are the study objectives clear and linked to the research aim and title?** ✓ Yes / No

Comments: _____

4. **Is the design of the study appropriate to meet the study objectives?** Yes / ✓ No

Comments: Specify how you would determine if TRUS or FG was used & how uncertainties would be dealt with.

Page **1** of **3** Student: Kadima **TSHIMANGA**

5. **Are the proposed methods and tools appropriate to meet the research objectives?** Yes / No

Comments: Statistical methodology not appropriately phrased or suitable for sens/spec analysis.
How will the study be conducted? Elaborate. Less on the procedure.

6. **Is the study feasible within the resources of:**

a) The applicant? Yes / No

b) The department? Yes / No

c) The time frame? Yes / No

7. ~~**If this is a PhD protocol assessment:**~~

a) Is the content original? Yes / No

b) Does the content show the scope and depth of a PhD? Yes / No

Comments:

Do you recommend:

i. Additional revision/amendment of the protocol? Please be specific on the recommendations being made:
Add SA or SSA specific statistics for prostate Ca. (National Cancer Registry). Add non-screened population.
9 patients were symptomatic.
Table 1: add no. of pts.

ii. The appointment of a Co-Supervisor? Yes / No

Nominee/s: Dr M. Nel.

Overall recommendation regarding the protocol:

i. Revision of the protocol to the satisfaction of the Supervisor (**NB: if HoD approval is also required, please specify**): [Yes ✓] [No]
*(**Candidate**: one copy, list of corrections with page numbers and Supervisor approval letter – submit to PG Office).*

ii. Revision of the protocol to the satisfaction of the Assessor Group/Chair: [Yes] [No]
*(**Candidate**: one copy, list of corrections with page numbers, Supervisor approval letter – submit to PG Office and PG Office to forward to the Assessor Group Chair).*

iii. Revision of the protocol and resubmission of the revised protocol to the next Assessor Group Meeting: [Yes] [No]
*(**Candidate**: six copies, list of corrections with page numbers, Supervisor approval letter – submit one copy to PG Office / 5 to school assessor group administrator / for PhD, all six copies to be submitted to the PG Office).*

iv. Candidate goes ahead (*no revision required*): [Yes] [No]

Details of Assessors:

Name:	Email:	Sign:
Prof Geoff Candy	Geoffrey.Candy@wits.ac.za	
Prof Clem Penny	Clement.Penny@wits.ac.za	
Dr Sarah Nietz	sarah.nietz@gmx.de	

Details of Assessor Group Chair:

Name:	Email:	Sign:
Prof Geoff Candy	Geoffrey.Candy@wits.ac.za	

Date:____13th November 2019_____

Appendix H: NHLS Approval.

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SCHOOL OF PATHOLOGY
Division of Anatomical Pathology

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Dr Y Perner MBBCh (Witwatersrand) FCPath (SA); MMed (Witwatersrand)

Human Research Ethics Committee (Medical)
University of the Witwatersrand
Johannesburg
20000

August 26, 2019

Re: Consent for access to NHLS database

This letter serves to confirm that the Department of Anatomical Pathology at the University of the Witwatersrand and NHLS is happy to assist Dr Kadima Tshimanga with his research entitled "Comparison between TRUS and finger guided prostate biopsy: A 5-year audit at Chris Hani Baragwanath Academic Hospital".

Publication of such work is encouraged and in the event that the information used comprises the diagnosis only then joint authorship from a member of staff in the Department of Anatomical Pathology would not be expected. However, should additional information be extracted from the report for purposes of further interpretation such as morphological details and immunohistochemical profiles, it would be expected that this would be done in conjunction with a member of staff in the Department of Anatomical Pathology and that joint authorship would follow in resulting publications. Dr Tshimanga will be in contact with the Department of Anatomical Pathology in respect of this.

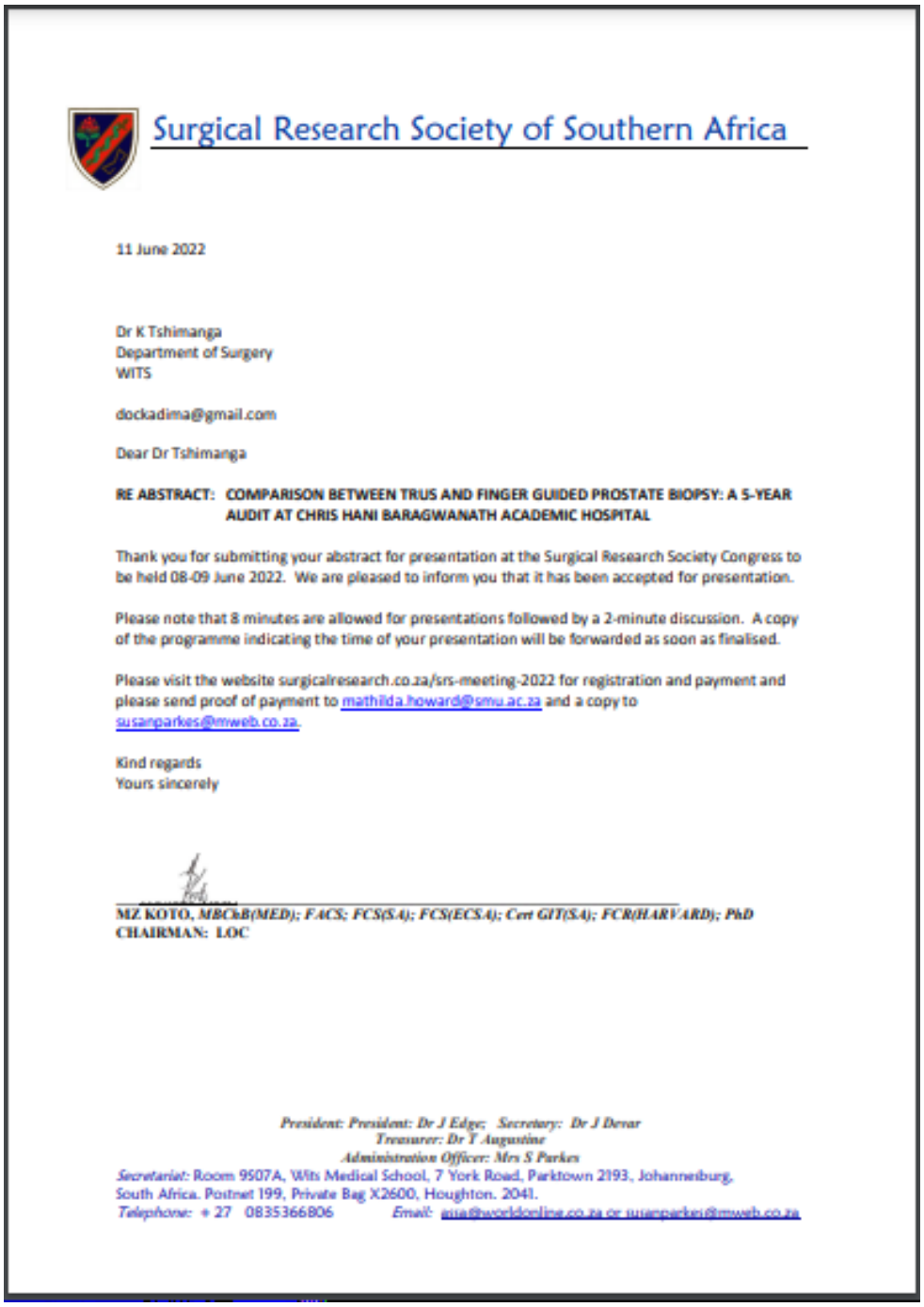
Assuring you of the Department of Anatomical Pathology's co-operation in this and future research projects.

With best wishes.

Yours sincerely,

Dr Yvonne Perner
Head: Department of Anatomical Pathology

Appendix I: Abstract Acceptance Letter From Surgical Research Society Of Southern Africa Congress.



Surgical Research Society of Southern Africa

11 June 2022

Dr K Tshimanga
Department of Surgery
WITS

dockadima@gmail.com

Dear Dr Tshimanga

RE ABSTRACT: COMPARISON BETWEEN TRUS AND FINGER GUIDED PROSTATE BIOPSY: A 5-YEAR AUDIT AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

Thank you for submitting your abstract for presentation at the Surgical Research Society Congress to be held 08-09 June 2022. We are pleased to inform you that it has been accepted for presentation.

Please note that 8 minutes are allowed for presentations followed by a 2-minute discussion. A copy of the programme indicating the time of your presentation will be forwarded as soon as finalised.

Please visit the website surgicalresearch.co.za/srs-meeting-2022 for registration and payment and please send proof of payment to mathilda.howard@smu.ac.za and a copy to susanparkes@mweb.co.za.

Kind regards
Yours sincerely

MZ KOTO, *MBChB(MED); FACS; FCS(SA); FCS(ECSA); Cert GIT(SA); FCR(HARVARD); PhD*
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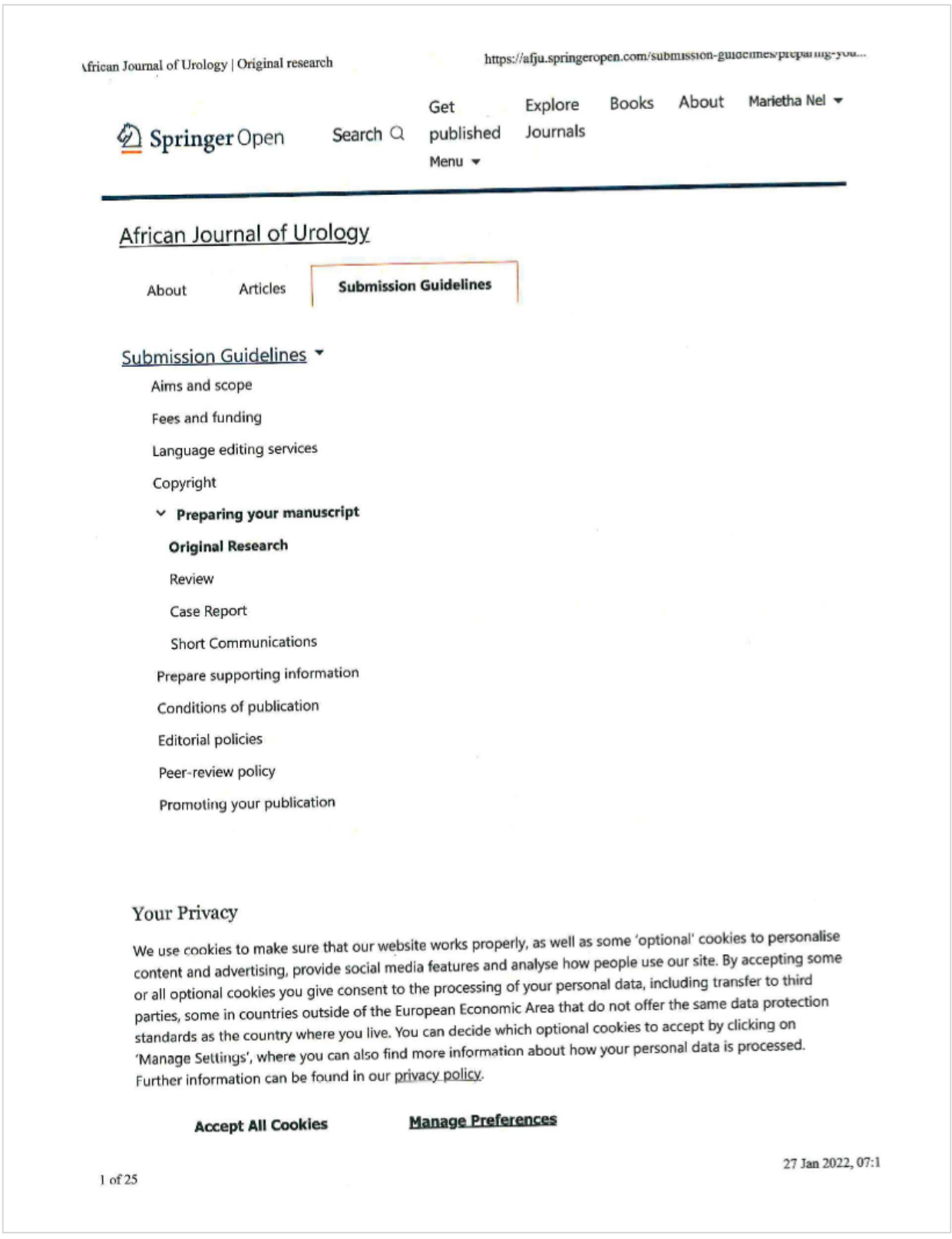
Appendix J: Instructions to Authors.



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All data generated or analysed during this study are included in this published article [and its supplementary information files].

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