# A RETROSPECTIVE AUDIT OF BIOJET® PROSTATE FUSION BIOPSIES AMONGST PATIENTS SEEN IN A HIGH-VOLUME PRIVATE REFERRAL CENTRE IN CAPE TOWN BETWEEN JANUARY 2017 AND APRIL 2020


## Abstract

**Introduction:** The field of prostate cancer has seen a dramatic change in its approach to diagnosis, from the advent of PSA in the 1980s to the transrectal ultrasound guided 12 core biopsies with a false negative rate of approximately 30%. Recent advances in this field involve fusing MRI images with real-time ultrasound images to guide the surgeon. The aim of the study was to evaluate the performance of Biojet® prostate fusion biopsy system in a high-volume private referral centre.

**Methods:** Retrospective observational audit of men who presented to a private urology practice in Cape Town for Biojet® prostate fusion biopsy based on clinical suspicion for prostate cancer. Data were collected as per the recommendations of the Standards of Reporting for MRI-targeted Biopsy Studies (START) of the Prostate group and anonymously entered onto a Redcap database.

**Results:** The median age of the patient population was 64 (SD 9.124) years. The median PSA level was 6.5 ng/ml (IQR- 4.7). Most patients (78/135) had a clinical stage of T1c (57%). In the biopsy naïve group, a total of 103 PIRADS lesions were identified. Amongst the PIRADS 3 lesions 15/28 lesions (53%) had a positive cancer diagnosis. Of the PIRADS 4 lesions 37/60 lesions (62%) had a positive cancer diagnosis and in the PIRADS 5 group 13/15 lesions (87%) had a positive cancer diagnosis. 21 of the 42 men (50%) with a previous negative prostate biopsy had a positive cancer diagnosis using the Biojet® prostate fusion biopsy.

**Conclusion:** In this study the Biojet® prostate fusion biopsy performed similar to other international studies however the pickup rate of cancer in those who had a previous negative biopsy was higher than those seen in the other global studies.



Keywords: prostate, biopsy, MRI/Ultrasound fusion, Biojet

## INTRODUCTION

With an estimated 1,276,106 new cases of prostate cancer reported in 2018, prostate cancer remains the second highest newly diagnosed cancer in men and ranks fifth amongst the leading causes of death worldwide according to GLOBOCAN 2018 estimates[1]. The age standardised incidence rates of prostate cancer are highly variable worldwide. The incidence rate of 64.1 per 100,000 reported in the Southern African region is lower than the incidence rate in Australia and New Zealand which is 85.4 per 100,000. Some of the reasons postulated for such variability include different screening strategies for prostate cancer, underdiagnosis, and inequalities in healthcare access. It is suggested that Africa will have the highest incidence of prostate cancer worldwide by the year 2040, which represents an increase exceeding 120% [1].

South Africa is classified as an upper middle income country. Although the private healthcare sector plays an important role in the health system, it covers only about 16% of the population. There are major discrepancies in access to surgical services between the public and private health sectors in South Africa[2].

The discovery of prostate specific antigen (PSA) in blood by Papsidero in 1980 revolutionised the diagnosis and management of benign and malignant conditions of the prostate. Though PSA is not an ideal tumor marker it remains the most widely used cancer diagnosis and follow-up marker [3]. An ideal prostate cancer test should be minimally invasive with a low complication rate.It should also detect a high proportion of clinically significant disease and avoid the diagnosis of clinically insignificant disease. The traditional diagnostic pathway for prostate cancer has been by prostate biopsy after an abnormal digital rectal exam (DRE) and/or an elevated PSA is detected in the investigation of symptomatic men;or during screening for prostate cancer in an asymptomatic men.The diagnostic pathway of prostate cancer has evolved to include PSA isoforms [4] and nomograms[5]) ; alternative prostate sampling approaches (number of cores, saturation biopsies); alternative prostate sampling routes (transperineal prostate biopsy), and fusion biopsy techniques (in-bore MRI fusion biopsy, MRI-TRUS fusion biopsy, cognitive fusion biopsy) [6],[7]. The traditional diagnostic pathway has significant limitations that have been exemplified by large studies such as: **European Randomised Study of Screening for Prostate Cancer (ERSPC), CAP randomised clinical trial**, and PIVot trial. The **European Randomised Study of Screening for Prostate Cancer (ERSPC)** showed that PSA-based screening reduced the rate of death from prostate cancer by 20% but was associated with a high risk of overdiagnosis. The **CAP**

**randomised clinical trial** showed that a single PSA-screening intervention detected more prostate cancer but had no significant impact on prostate cancer mortality after a median follow up of 10 years. The **PIVOT trial** – showed that radical prostatectomy did not reduce all-cause or prostate cancer specific mortality amongst men with localised prostate cancer detected during the early era of PSA testing. These studies suggest that the traditional pathway of prostate cancer diagnosis had a high detection rate of clinically insignificant disease.

The role of prostate MRI in optimising the diagnostic pathway for prostate cancer is supported by the following landmark studies:

**PROMIS** study [8]**(** reported that -incorporating MRI as an initial test in unscreened men referred for prostate biopsy was likely to reduce the proportion of unnecessary biopsies , miss fewer men with clinically significant prostate cancer, and enhance cost effectiveness.

**PRECISION study** [9] compared targeted biopsy in patients with a positive MRI with PI-RADS v2 (Prostate Image- Reporting and Data Systems version 2) lesion 3 or greater and no biopsy in patients with a negative MRI. The results showed that fewer men required a biopsy, fewer biopsy cores were required, more clinically significant cancers were detected, and fewer clinically insignificant cancers were detected.

Similarly, other studies by Preisser et al. and Maxeiner et al.[10] [11] have demonstrated the increased cancer detection rates using the MRI pathway in patients who are biopsy naïve and those who have had a previous biopsy. They have also demonstrated that the risk of harbouring prostate cancer increases with a higher PIRADS score.

MRI-FIRST study [12] –showed that combining systematic and targeted prostate biopsy based on MP-MRI findings improved the detection of clinically significant (ISUP grade group2 or greater) prostate cancer in biopsy-naïve patients.

Studies done by **Kasivisvanathan**[9] and **Schoots**[13] have illustrated the important role which the MRI diagnostic pathway plays in avoiding the diagnosis of insignificant cancer, wherein approximately 25% -33% of the patients avoided a prostate biopsy based on a negative MRI. The criteria used to qualify prostate biopsy histopathology results as significant cancer varies from study to study and no global consensus exists on this matter.[14]By extrapolating from active surveillance data, some studies[15] use the "Epstein criteria" (defined as cancer Gleason score 3+3= 6 (GrG1), involving one or two cores, with no core involved with >50% of cancer, and a PSA density of <0.15ng/ml per $cm^3$ to define insignificant cancer. The Ahmed

criteria uses a more complex definition**,** borrowed from transperineal mapping biopsy results.[16] It classifies insignificant cancer as: Gleason 3+3 =6, total cancer core length of ≤ 5mm, and maximum cancer core lenth of ≤ 3mm. In the PRECISION study [9]insignificant cancer was based on the highest Gleason score being ≤3+3 =6.

In the studies done by **Kasivisvanathan et al.[9]**, **Porpiglia et al.[17]**, **Baboudjian et al.[18]**, **and Ahdoot et al.[19]**, the patients had a mean age of 63-70 years, median PSA level of 5.9-9.2ng/ml, and a normal rectal examination finding varied from 35% of patients **(Ahdoot [19])** to 86% **(Kasivisvanathan [9])**.

The field of prostate cancer diagnosis is evolving with MRI assuming a pivotal role in contemporary diagnosis paradigms.

There are no local/ African studies reporting on the role of MRI in the diagnosis of prostate cancer. It is therefore unclear whether MRI will have similar effects on prostate cancer detection in a local cohort as has been reported in European and American populations. We aimed to report the positive prostate biopsy rate by a single operator using the Biojet® prostate fusion biopsy system in a privately funded urology practise in Cape Town, South Africa.

## MATERIALS AND METHODS

### Study population

This was a retrospective, audit of prospectively collected data. Men who visited a private urology practice in Cape Town and underwent Biojet® MRI fusion prostate biopsies between January 2, 2017, and April 30, 2020, were considered for inclusion in this study. Specifically, in this practice all men who had both a clinical suspicion of prostate cancer and a positive MRI result were offered a Biojet® MRI fusion prostate biopsy conducted by the operator at the centre during the mentioned timeframe. One hundred and thirty-six patient folders were audited. None of the 136 cases eligible for inclusion were excluded. The Epstein criteria were used to define clinically significant disease. The data was collected on a data collection sheet as per the START [20]recommendations. This data was anonymised and captured onto a REDCap database. The protocol was reviewed by UCT human research ethics committee (HREC 564/2020).

### Data analysis

IBM SPSS ™version 29 was used for data analysis. Continuous variables were reported with the appropriate measures of central tendency. Frequency tables were produced for categorical data. Statistical significance for inferential statistics was accepted at $p \leq 0.05$.

## RESULTS

The median age of the patient population was 64 (SD 9.124) years. The median PSA level was 6.5 ng/ml (IQR- 4.7). Most patients (78/135) had a clinical stage of T1c (57%), followed by T2a (34/135) (25%), T2b (19/135) (14%) and T2c (3/135) (2.2%). The most common clinical presentation was for lower urinary tract symptoms 64/138 (47%), the second most common presentation was for prostate cancer screening 55/138 (40%), (Table 1).

A total of 60/136 patients (44%) had a previous biopsy, (Table 1). Of those that had a previous biopsy, the TRUS method was the most common 54/60 (90%). A total of 16/18 (12%) had a previous positive biopsy of Grade Group (GG) 1 (one had GG2and one had > GG3).

Most patients 121/136 (89%) had no benign prostatic obstruction directed prostate treatment prior to biopsy. Of the 15/136 patients who had surgical prostate treatment prior to biopsy, eight patients had functional reasons while for two patients the reason was not clearly stated. 25% (15/60) of patients who had a previous biopsy were on active surveillance.

A 3-Tesla MRI was used in 55% (75/136) of the cases. It is not known what the details of the MRI scanner were for the rest of the group (42% [57/13]). An endorectal coil was used in 4 /136 patients. In 99% (134/136) of the patients, all 3 sequences of a multi-parametric MRI were used for reporting. All the MRI reports were in prose, 19% (38/136) of the reports included drawings, and 11% (22/136) had snapshots of the lesions with the prose report.

**Table 1:** Patient demographic characteristics and multiparametric MRI findings

| **Men included in analysis,** *n* | **136** |
|---|---|
| Age, median (SD), years | 64 (9.124) |
| PSA, median (IQR), ng/ml | 6.5 (4.7) |
| Clinical stage, *n* (%) | |
| T1a/b | 1 (0.7) |
| T1c | 78 (57.4) |
| T2a | 34 (25.0) |
| T2b | 19 (14.0) |
| T2c | 3 (2.2) |
| Presentation, *n* (%) | |
| LUTS | 64 (47.1) |
| Screening | 55 (40.4) |
| Other | 18 (13.2) |
| Unknown | 1 (0.7) |
| Prostate volume, median (IQR), ml | 44 (33) |
| Previous biopsy, *n* (%) | |
| Yes | 60 (44) |
| No | 76 (56) |
| On Active Surveillance, *n* (%) | 15 (11) |
| mpMRI findings | |
| Total number of lesions, *n* | 272 |
| PIRADS score, *n* (%) | |
| PIRADS 3 | 61 (22) |
| PIRADS 4 | 151 (56) |
| PIRADS 5 | 40 (15) |
| Biopsy Naïve group, *n* of lesions | 103 |
| PIRADS 3 | 28 |
| PIRADS 4 | 60 |
| PIRADS 5 | 15 |

The median prostate size was 44mls (IQR- 33) with a minimum of 14cc and a maximum of 148cc, (Table 1). Amongst the 136 patients there was a total of 272 lesions, with a mean of 1,99 ± 1,10 (SD) lesions per patient. The mean lesion size was 9,68mm ± 5,98 (SD). Most lesions were on the right (47%) (128/272), the rest were on the left (43%) (117/272). Most lesions (77%) (208/269) were in the peripheral zone (PZ), the transitional zone (21%) (57/269) and anterior fibromuscular stroma (1.5%) (4/269) accounted for the rest. Most (63%) (86/135) of the MRI studies were done at radiology firm A, and (21%) (28/135) at firm B. The remaining 21 MRIs were done by 7 different radiology firms, each of which had less than 5 MRI reports per firm over the study period.

Most lesions had a PIRADS of 4 (56%), followed by PIRADS 3 (22%). Forty lesions (15%) had a PIRADS of 5. (Table 1)

In the biopsy naïve group, a total of 103 PIRADS lesions were identified. Amongst the PIRADS 3 lesions 15/28 lesions (53%) had a positive cancer diagnosis. Of the PIRADS 4 lesions 37/60 lesions (62%) had a positive cancer diagnosis and in the PIRADS 5 group 13/15 lesions (87%) had a positive cancer diagnosis. (Figure 1)

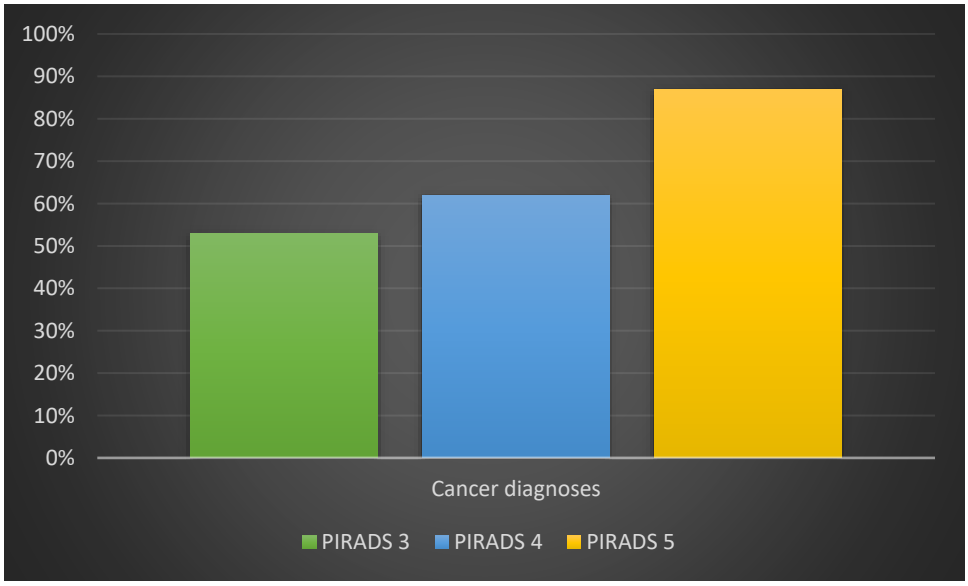


FIGURE 1: Positive pick-up rates for the corresponding PIRADS amongst the biopsy naïve patients' group.

A chi-square test of independence was conducted between PIRADS and cancer diagnosis. All expected cell frequencies were greater than five. There was a statistically significant association between PIRADS and cancer diagnosis, $\chi 2$ (2) = 10,38, p = 0,006. The association was moderately strong , Cramer's V = 0,203[21].

A total of 2046 targeted cores were taken for the 272 lesions identified, with a median of 7 cores. A total of 62/136 (46%) patients had cores positive for clinically significant disease from targeted biopsies and 23/136 (17%) patients had cores positive for clinically insignificant disease. 95 patients had accompanying systematic biopsy of which a total of 1268 cores were sampled. A total of 28/95 (29%) patients had cores positive for clinically significant disease from non-targeted biopsies while 11/95 (12%) patients had cores positive for insignificant disease.

18/136 patients (13%) had a radical prostatectomy (17 of which had Robotic Assisted Laparoscopic Prostatectomy (RALP). 70% of the patients who underwent radical prostatectomy had a PIRADS 4 lesion, 20% PIRADS 5 and 10% PIRADS 3 lesion. Most had a Gleason score of 3+3 for both right and left reports. The mean involvement was 23,43% (SD- 24,46) on the right side and 27,99% (27,21SD) on the left. The biopsy diagnosis was accurate (biopsy grade was similar to the final histopathology specimen) for 61% of patients who underwent a radical prostatectomy. In those whom it was inaccurate- 6 were upstaged and 2 were down staged.

21 of 42 patients (50%) with a previous negative biopsy had a positive cancer diagnosis with the Biojet® MRI fusion targeted prostate biopsy. (Figure 3) 17 of the 21 patients (81%) with a previous negative biopsy had a clinically significant cancer.

FIGURE 3: Infographic from our study showing that of the 50% who had a previous negative TRUS guided biopsy had a positive diagnosis for cancer using the Biojet® MRI fusion targeted prostate biopsy (Key: Blue- positive for cancer, Black- negative for cancer)

## DISCUSSION

The study reflects a real-life scenario outside of an academic hospital setting and the only study reporting on the matter from sub-Saharan Africa.

The patient demography in this study was similar to international studies.[9, 17-19] The cohort included in this study is from a private healthcare service which, according to Dell et al.[2] , forms about 16% of the South African health care system. This group has much better access to healthcare services than most of the South African population who use government-funded

healthcare services. These findings may therefore not be generalisable to a wider South African population.

The distribution of PIRADS scores was like those in the studies reported by **Preisseret al.[10] and Maxeiner et al. [11]**, where majority of the lesions were PIRADS 4 lesions. In the biopsy naïve cohort, the cancer detection rates for PIRADS 3, 4 and 5 were 53%, 62% and 87% respectively. This is comparable to other studies where the PIRADS 3, 4 and 5 cancer detection rates were: 31%,63% and 89% **(Preisser 2019[10] )**; 38%, 78% and 95% **(Maxeiner 2018 [11])**; and 57%, 82% and 95% **(Donato, 2019 [22])**. Biopsy detection rates with this system seem similar in this South African cohort to those reported in international studies. The fusion biopsies reported in this study were performed by a high-volume, expert single operator. It is uncertan whether less experienced operators will obtain equivalent ouctomes.

The cancer detection rate in the cohort with a previous negative biopsy was slightly higher than that reported by (**Preisser 2019 )**, 50% in the cohort reported in this study versus 38% in the (**Preisser 2019)** study[10]. We cannot account for this difference.

## CONCLUSION

As fusion biopsy becomes more widely accessible in South Africa in the future, pooled results from multiple operators on multiple fusion biopsy systems may elucidate whether MRI-fusion biopsy outcomes are indeed equivalent locally to those reported abroad. These outcomes may also assist in defining the role of MRI-fusion biopsy in the prostate cancer diagnosis paradigm in the local context.

## LIMITATIONS

In this retrospective audit, some data may not have been captured due to variations in patient treatment choices, with not all patients undergoing prostatectomy and some seeking treatment at external facilities. Consequently, the final prostatectomy results for these individuals were unavailable for analysis.

Numerous confounding factors, such as variations in the expertise of reporting MRI studies and histopathological specimens, as well as the accuracy of fusion during the procedure, remain unaccounted for and have the potential to impact the study outcomes.

## FURTHER RESEARCH

A prospective study that has addressed the confounders would perhaps yield a more accurate results on the positive pick-up rate of Biojet® prostate fusion biopsy system in a South African population.

## REFERENCES


1. Rawla P. Epidemiology of Prostate Cancer. World J Oncol. 2019;10(2):63-89.
2. Dell AJ, Kahn D. Where are general surgeons located in South Africa? S Afr J Surg. 2018;56(1):12-8.
3. Rao AR, Motiwala HG, Karim OM. The discovery of prostate-specific antigen. BJU Int. 2008;101(1):5-10.
4. Lepor A, Catalona WJ, Loeb S. The Prostate Health Index: Its Utility in Prostate Cancer Detection. Urol Clin North Am. 2016;43(1):1-6.
5. Salagierski M, Sosnowski M, Schalken JA. How accurate is our prediction of biopsy outcome? PCA3-based nomograms in personalized diagnosis of prostate cancer. Cent European J Urol. 2012;65(3):110-2.
6. Descotes JL. Diagnosis of prostate cancer. Asian J Urol. 2019;6(2):129-36.
7. Sathianathen NJ, Christidis D, Konety BR, Lawrentschuk NL. Magnetic resonance imaging cognitive fusion biopsy - is near enough good enough? BJU Int. 2018;121(3):324-6.
8. Brown LC, Ahmed HU, Faria R, El-Shater Bosaily A, Gabe R, Kaplan RS, et al. Multiparametric MRI to improve detection of prostate cancer compared with transrectal ultrasound-guided prostate biopsy alone: the PROMIS study. Health Technol Assess. 2018;22(39):1-176.
9. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018;378(19):1767-77.
10. Preisser F, Theissen L, Wenzel M, Humke C, Bodelle B, Köllermann J, et al. Performance of Combined Magnetic Resonance Imaging/Ultrasound Fusion-guided and Systematic Biopsy of the Prostate in Biopsy-naïve Patients and Patients with Prior Biopsies. Eur Urol Focus. 2021;7(1):39-46.

11. Maxeiner A, Kittner B, Blobel C, Wiemer L, Hofbauer SL, Fischer T, et al. Primary magnetic resonance imaging/ultrasonography fusion-guided biopsy of the prostate. BJU Int. 2018;122(2):211-8.

12. Rouvière O, Puech P, Renard-Penna R, Claudon M, Roy C, Mège-Lechevallier F, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. Lancet Oncol. 2019;20(1):100-9.

13. Schoots IG, Padhani AR, Rouvière O, Barentsz JO, Richenberg J. Analysis of Magnetic Resonance Imaging-directed Biopsy Strategies for Changing the Paradigm of Prostate Cancer Diagnosis. Eur Urol Oncol. 2020;3(1):32-41.

14. Haffner J, Lemaitre L, Puech P, Haber GP, Leroy X, Jones JS, et al. Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging-targeted and systematic biopsy for significant prostate cancer detection. BJU Int. 2011;108(8 Pt 2):E171-8.

15. Matoso A, Epstein JI. Defining clinically significant prostate cancer on the basis of pathological findings. Histopathology. 2019;74(1):135-45.

16. Ahmed HU, Hu Y, Carter T, Arumainayagam N, Lecornet E, Freeman A, et al. Characterizing clinically significant prostate cancer using template prostate mapping biopsy. J Urol. 2011;186(2):458-64.

17. Porpiglia F, Manfredi M, Mele F, Cossu M, Bollito E, Veltri A, et al. Diagnostic Pathway with Multiparametric Magnetic Resonance Imaging Versus Standard Pathway: Results from a Randomized Prospective Study in Biopsy-naïve Patients with Suspected Prostate Cancer. Eur Urol. 2017;72(2):282-8.

18. Baboudjian M, Bandelier Q, Gondran-Tellier B, Abdallah R, Michel F, Sichez PC, et al. MRI-targeted biopsy for detecting prostate cancer: have the guidelines changed our practices and our prostate cancer detection rate? Int Urol Nephrol. 2020;52(4):611-8.

19. Ahdoot M, Wilbur AR, Reese SE, Lebastchi AH, Mehralivand S, Gomella PT, et al. MRI-Targeted, Systematic, and Combined Biopsy for Prostate Cancer Diagnosis. N Engl J Med. 2020;382(10):917-28.

20. Moore CM, Kasivisvanathan V, Eggener S, Emberton M, Fütterer JJ, Gill IS, et al. Standards of reporting for MRI-targeted biopsy studies (START) of the prostate: recommendations from an International Working Group. Eur Urol. 2013;64(4):544-52.

21. Cohen J. Statistical Power Analysis for the Behavioral Sciences: Lawrence Erlbaum Associates; 1988.

22. Donato P, Morton A, Yaxley J, Teloken PE, Coughlin G, Esler R, et al. Improved detection and reduced biopsies: the effect of a multiparametric magnetic resonance imaging-based triage prostate cancer pathway in a public teaching hospital. World J Urol. 2020;38(2):371-9.