Retrospective review: Diagnostic performance of Prostate- Imaging and Data Scoring System version 2.1 (PI-RADS v2.1) categories 4 and 5 in predicting clinically significant prostate cancer in patients presenting to Groote Schuur Hospital, South Africa

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DECLARATION

I, BRETT WEGNER, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.
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Date: 23/04/2024…….

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List of abbreviations

GSH- Groote Schuur Hospital
SA- South Africa
csPCa- Clinically significant prostate cancer
PI-RADS- Prostate Imaging and Reporting and Data System
PI-RADS v2.1- Prostate Imaging and Reporting and Data System version 2.1
PACS- Picture achieving and Communication system.
NHLS- National Health and Laboratory System
ACR- American College of Radiology
ESUR- European Society of Urogenital Radiology
mpMRI- multiparametric Magnetic Resonance Imaging
DRE- Digital rectal examination
T2W- T2 weighted.
DWI- Diffusion weighted image
DCE- Dynamic contrast enhancement
PSA- Prostate specific antigen
TRUS- Transrectal ultrasound
PPV- Positive predictive value
HREC- Human research ethics committee

Abstract

Title: Retrospective review: Diagnostic performance of Prostate- Imaging and Data Scoring System version 2.1 (PI-RADS v2.1) categories 4 and 5 in predicting clinically significant prostate cancer in patients presenting to Groote Schuur Hospital, South Africa.

Background:

Multiparametric MRI (mpMRI) prostate has become a fundamental part of prostate cancer primary diagnosis, active surveillance, and lesion localization.
PI-RADS reporting lexicon is used to report mpMRI prostate examinations and is a risk-adjusted reporting structure designed by the European Society of Urogenital Radiology in combination with the American College of Radiology with the main aim to internationally standardized mpMRI prostate reporting into five risk categories, of which a higher PI-RADS category represents an increasing probability that the prostate pathology represents clinically significant cancer.
Groote Schuur Hospital (GSH) radiology division has been reporting prostate mpMRI according to the updated PI-RADS v2.1 since its introduction in 2019, however no studies have been performed to assess the reliability of PI-RADS v2.1 at GSH for detecting clinically significant prostate cancer.
This study aims to assess and validate the accurate use of PI-RADS v2.1 category 4 and 5 against internationally recognized standards of performance.
The PI-RADS lexicon should be a reliable predictor of significant prostate cancer to promote confidence in its continued use and to justify the expenditure on mpMRI prostate examinations in the diagnostic pathway of prostate cancer at GSH.

Objectives:

The primary objective: To assess the diagnostic performance of PI-RADS v2.1 category 4 and 5 in predicting clinically significant prostate cancer confirmed on biopsy with appropriate histopathology.
Secondary objective:

- Correlate and validate the diagnostic performance of PI-RADS v2.1 category 4 and 5 lesions at GSH by comparing the outcomes with accepted international performance standards.
- Identify problems with the use of PI-RADS v2.1 at GSH to improve prostate reporting with the ultimately goal of improving patient outcomes.

Methods:

Single institution retrospective study assessing mpMRI prostate PI-RADS (v2.1) category 4 and 5 reports performed at GSH between the dates of 01 June 2021 to 12 January 2024.
Prostate reports categorised as PIRADS (v2.1) 4 or 5 are evaluated on PACS and correlated with the histological diagnosis on National Health Laboratory Service (NHLS).
Prostate histology will be categorised into clinically significant prostate cancer or insignificant depending on the Gleason score.
These outcomes will be measured against high powered international studies to assess the overall performance of the GSH radiology division when reporting PI-RADS 4 and 5 lesions.

Results:

This study incorporates a retrospective design structure and analysis where a grand total of 215 mpMRI prostate studies were considered for the period dated 01 June 2021 and 12 January 2024.
From the 215 mpMRI prostate scans performed 89 studies met the strict inclusion and exclusion criteria: n=89.
The sample size of 89 represented 37 PI-RADS category 4 and 52 PI-RADS category 5.
The measures of sensitivity and specificity for the PI-RADS 4 and PI-RADS 5 categories in detecting clinically significant prostate cancer proven on biopsy are as follows:

For **PI-RADS 4:**
Sensitivity: 19.4, 95% CI: [5.4, 33.3]
Specificity: 53.4, 95% CI: [40.6, 66.3]
PPV : 16.2 95% CI:4.3-28.1
NPV: 51.9 95% CI:38.3-65.5

For **PI-RADS 5**:
Sensitivity: 80.6, 95% CI: [66.7, 94.6]
Specificity: 46.6, 95% CI: [33.7, 59.4]
PPV: 48.1 95% CI:34.5- 61.7
NPV: 83.8 95% CI:71.9- 95.7

Conclusions:

The findings in this study validates the accurate and reliable use of PI-RADS (v2.1) category 5 at GSH when measured against the expected cancer detection rates reported in large high powered international studies.
PI-RADS (v2.1) category 4 revealed a lower-than-expected correlation to international performance standards and is proposed to be the result of multiple interplaying factors such as reporting inexperience, inter-rater variability, suboptimal image acquisition and patient preparation and misrepresentative prostate biopsy.
The Urology department, GSH management and patients can draw reserved confidence in the performance of the GSH radiology division reporting mpMRI prostate examinations according to PI-RADS v2.1 lexicon with a higher confidence in PI-RADS (v2.1) category 5 reports than PI-RADS (v2.1) category 4 reports.

This study is not extrapolating to PI-RADS 1, 2 and 3 category lesions without further research.

Keywords:
PI-RADS v2.1, PI-RADS 4, PI-RADS 5, Clinically significant prostate cancer, mpMRI prostate.

CHAPTER 1: LITRATURE REVIEW

Rationale:

Multiparametric MRI (mpMRI) prostate has become a fundamental part of prostate cancer primary diagnosis, active surveillance, and lesion localization (1).
PI-RADS reporting lexicon is a form of structed reporting and has been around since 2012, continually improving with subsequent versions affording more accurate delineation of prostate pathology, specifically significant prostate cancer (2).
PI-RADS lexicon is an important concept in mpMRI prostate reporting as it risks stratifies prostate pathology into 5 categories that have direct implications of patient management and the potential diagnosis of clinically significant prostate cancer.
A concerted effort by the GSH radiology division towards the strict adherence to PI-RADS reporting lexicon followed the most recent PI-RADS v2.1 update in 2019 (3).
Since the strict implementation of PI-RADS v2.1 lexicon for mpMRI prostates research has been required to assess and validate the accurate use of PI-RADS v2.1 at GSH against international recognized standards of PI-RADS performance.
The PI-RADS lexicon should be a reliable predictor of significant prostate cancer to promote confidence in its use by the urology department and to justify the expenditure for a complex investigation in the diagnostic pathway of prostate cancer at GSH.

Prostate Cancer and mpMRI:
Prostate cancer is a significant disease entity and is the most common cancer diagnosis in males with the second highest cause of cancer related morbidity (4).
In South Africa prostate cancer is the most common cancer diagnosis amongst men countrywide, reported by the National Cancer Registry (NCR), with a documented incidence of 61.8 per 100 000(5). Over a 10-year period the incidence of prostate cancer has increased steadily from 29.4 per 100 000 in 2007 to 49.4 per 100 000 in 2017(5).
Southern Africa has the highest incidence in Africa at 64.1 per 100 000, followed by Northern Africa with a rate of 35.9 per 100 000(5). Western and Eastern Africa reported the lowest incidence rates at 23.9 per 100 00 and 13.2 per 100 000, respectively(5).
The reported incidence of prostate cancer in Africa is said to be underestimated and a direct result of inadequate screening programs, lack of expertise and failing infrastructure(5).
Historically the assessment of prostate cancer hinged on a combination of factors which includes correctly identifying clinically at-risk individuals followed by clinical, pathological, and imaging assessment in the form of digital rectal examination (DRE), Prostate Specific Antigen (PSA) and low resolution transrectal ultrasound imaging to crudely diagnose prostate cancer and often leading to inappropriate overdiagnosis and unnecessary treatment of patients (6).
The introduction of Magnetic resonance imaging (MRI) in the 1980's heralded a new era in the management and assessment of prostate cancer leading to improved assessment and management of patients suspected of prostate cancer (7).
In the early years, MRI evaluation of the prostate gland was poorly utilised for prostate cancer owing to a limited understanding of mpMRI prostate interpretation and a lack of standardised international guidelines for prostate imaging technique and lesion characterisation (8).
Overtime this barrier to mpMRI prostate utilization has been addressed by introducing standardised reporting in the form of the PI-RADS lexicon, increased knowledge on prostate

cancer pathophysiology, and rapid advancements in MRI technology all leading to superior imaging sequences and better image acquisition (6)(9).

Introduction of PI-RADS:

Early prostate mpMRI reporting was plagued by interpretation inconsistency hindering widescale acceptance of mpMRI for characterisation of prostate pathology.
The European Society of Urogenital Radiology (ESUR) addressed this problem in 2012 with the development of a standardized set of imaging guidelines, known as PI-RADS version 1.0, which characterised imaging parameters and interpretation criteria into definable categories according to the percentage risk of representing clinically significant prostate cancer (10).
Since 2012, several updated versions have existed with version 2.1 being the most recent and up to date guideline, published in March 2019(3).
PI-RADS is a standardised reporting lexicon and considered a living document which is continually updated and adapted in line with the latest evidence and new mpMRI sequences available (1).
Version 2.1 entertains minor alteration to the previous guidelines with slight changes to MRI sequence protocols, imaging techniques and a more simplified approach to reporting and assessment of prostate lesions to address and reduce the inter-reader variability (3).
PI-RADS utilises and combines different MRI sequences to accurately evaluate and characterise the anatomical and physiological details of the prostate gland, thus allowing the reporting radiologist to easily and more consistently identify and classify abnormal regions within the prostate gland (2).
T1- weighted (T1W) and T2-weighted (T2W) sequences allows accurate assessment of the glandular anatomy whilst diffusion-weighted imaging (DWI) with the derivative apparent diffusion co-efficient (ADC) and dynamic contrast enhancement (DCE) allowing for assessment of the functional physiology of the prostate gland(10).
T2W imaging is important for assessing the transition zone, whilst T2W imaging in combination with DWI/ ADC is important to assess the peripheral zone of the prostate gland (11).
Abnormal findings in the prostate gland can either represent a benign process such as chronic prostatitis with scarring or a more sinister malignant process such as clinically significant prostate cancer(12).
PI-RADS v 2.1 utilises a risk-adjusted scoring system to categorise these prostate lesions into 5 categories (2),of which the higher the PI-RADS category the higher the likelihood the prostate pathology represents clinically significant prostate cancer (1).
PI-RADS category 4 and 5 is considered to have a high and very high respective risk of representing clinically significant prostate cancer. PI-RADS 3 is deemed an intermediate risk, whilst PI-RADS 1 and 2 have a very low and low respective risk(13).
A recent systemic review and meta-analysis by Oerther et la, (1) determined that the PI-RADS v2.1 detection of clinically significant prostate cancer for category 4 and 5 lesions is 52% and 89% respectively(1).

Clinically significant prostate cancer:

No universal agreement to define clinically significant prostate cancer exists, however, the consensus and accepted histopathological definition in the literature regards histopathology Gleason score (GS) greater or equal to 7, extra-prostatic extension (EPE) and tumour volume greater than 0.5 cc as determinants of clinically significant prostate cancer (14).

GS is based on the distribution and architecture of malignant cells within the tumour as well as degree of tumour cell differentiation, and these findings represent the predominant pattern which is subsequently graded 1-5, with 5 representing completely abnormal glandular prostate tissue (15).
A significant GS is based on the likelihood that the detected prostate lesion will negatively impact the patient's lifetime years and is directly associated with the histological aggressiveness of the tumour (11).
The two most predominant histological patterns are determined, and the grades are then summed up to create the total GS(15). A Gleason score greater than or equal to 7 is regarded as representing clinically significant prostate cancer.

PI-RADS v2.1 does not provide management recommendations for PI-RADS category 4 and 5 reports (1), however, in clinical practice the diagnostic pathway requires tissue sampling with histopathological assessment to confirm the presence of prostate cancer and to determine clinically significant prostate cancer (16).
Prostate biopsy and histopathological assessment is regarded as the gold standard to confirm prostate cancer (17).

PI-RADS category 4 and 5 and the South African context:

PI-RADS category 4 and 5 is considered the most significant categories owing to the high predicted risk for representing clinically significant prostate cancer and thus the requirement for invasive histopathological confirmation or exclusion of prostate cancer (1).
Patients scored as PI-RADS category 4 and 5 are led down a predetermined diagnostic pathway which has far-reaching impact on the patient physically, psychologically, and social well-being, in addition to consequences on the local, regional, and national health systems (18,19).
Psychologically patients are given a diagnosis which is pre-terminal which leads to varying degrees and stages of mental illness and impact on social functioning (20).
Physically patients are destined for invasive prostate biopsies with risks such as bleeding, sepsis, urinary retention and very rarely death(21).
From a health economics perspective PI-RADS category 4 and 5 lesions impacts the health budget with costs related to both inpatient and outpatient care and costly investigations (22).
GSH is one of two specialty referral pathways for managing prostate cancer in the Western Cape public sector catering for just over two million males(23). Accurate reporting of mpMRI examination can assist with decreasing the already burdened urology and pathology services.

The purpose and aim of this research is to assess the diagnostic performance of PI-RADS (v2.1) 4 and 5 category at Groote Schuur Hospital against international performance standards.
Lastly this research hopes to identify any problems with the use of PI-RADS v2.1 at GSH and to address these problem areas with the end goal of benefiting the radiology division, urology department and patients' management.

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CHAPTER 2: FULL TEXT JOURNAL ARTICLE FOR SUBMISSION

Abstract

Title: Retrospective review: Diagnostic performance of Prostate- Imaging and Data Scoring System version 2.1 (PI-RADS v2.1) categories 4 and 5 in predicting clinically significant prostate cancer in patients presenting to Groote Schuur Hospital, South Africa.

Background:

In South Africa prostate cancer is the most common cancer diagnosis amongst men countrywide, reported by the National Cancer Registry (NCR), with a documented incidence of 61.8 per 100 000(5). Over a 10-year period the incidence of prostate cancer has increased steadily from 29.4 per 100 000 in 2007 to 49.4 per 100 000 in 2017(5).
The reported incidence of prostate cancer in Africa is said to be underestimated and a direct result of inadequate screening programs, lack of expertise and failing infrastructure(5).
Multiparametric MRI (mpMRI) prostate has become a fundamental part of prostate cancer primary diagnosis, active surveillance, and lesion localization.
PI-RADS reporting lexicon is used to report mpMRI prostate examinations and is a risk-adjusted reporting structure designed by the European Society of Urogenital Radiology in combination with the American College of Radiology with the main aim to internationally standardized mpMRI prostate reporting into five risk categories, of which a higher PI-RADS category represents an increasing probability that the prostate pathology represents clinically significant cancer.
Groote Schuur Hospital (GSH) radiology division has been reporting prostate mpMRI according to the updated PI-RADS v2.1 since its introduction in 2019, however no studies have been performed to assess the reliability of PI-RADS v2.1 at GSH for detecting clinically significant prostate cancer.
This study aims to assess and validate the accurate use of PI-RADS v2.1 category 4 and 5 against internationally recognized standards of performance.
The PI-RADS lexicon should be a reliable predictor of significant prostate cancer to promote confidence in its continued use and to justify the expenditure on mpMRI prostate examinations in the diagnostic pathway of prostate cancer at GSH.

Objectives:

The primary objective:

To assess the diagnostic performance of PI-RADS v2.1 category 4 and 5 in predicting clinically significant prostate cancer confirmed on biopsy with appropriate histopathology.

Secondary objective:

- Correlate and validate the diagnostic performance of PI-RADS v2.1 category 4 and 5 lesions at GSH by comparing the outcomes with accepted international performance standards.
- Identify problems with the use of PI-RADS v2.1 at GSH to improve prostate reporting with the ultimately goal of improving patient outcomes.

Methods:

Single institution retrospective study assessing mpMRI prostate PI-RADS (v2.1) category 4 and 5 reports performed at GSH between the dates of 01 June 2021 to 12 January 2024.
Prostate reports categorised as PIRADS (v2.1) 4 or 5 are evaluated on PACS and correlated with the histological diagnosis on National Health Laboratory Service (NHLS).
Prostate histology will be categorised into clinically significant prostate cancer or insignificant depending on the Gleason score.
These outcomes will be measured against high powered international studies to assess the overall performance of the GSH radiology division when reporting PI-RADS 4 and 5 lesions.

Results:

This study incorporates a retrospective design structure and analysis where a grand total of 215 mpMRI prostate studies were considered for the period dated 01 June 2021 and 12 January 2024.
From the 215 mpMRI prostate scans performed 89 studies met the strict inclusion and exclusion criteria: n=89.
The sample size of 89 represented 37 PI-RADS category 4 and 52 PI-RADS category 5.
The measures of sensitivity and specificity for the PI-RADS 4 and PI-RADS 5 categories in detecting clinically significant prostate cancer proven on biopsy are as follows:
For **PI-RADS 4:**
Sensitivity:: 19.4, 95% CI: [5.4, 33.3]
Specificity:: 53.4, 95% CI: [40.6, 66.3]
PPV:16.2 95% CI:4.3-28.1
NPV:51.9 95% CI:38.3-65.5
For **PI-RADS 5**:
Sensitivity: 80.6, 95% CI: [66.7, 94.6]
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Conclusions:

The findings in this study validates the accurate and reliable use of PI-RADS (v2.1) category 5 at GSH when measured against the expected cancer detection rates reported in large high powered international studies.

PI-RADS (v2.1) category 4 revealed a lower-than-expected correlation to international performance standards and is proposed to be the result of multiple interplaying factors such as reporting inexperience, inter-rater variability, suboptimal image acquisition and patient preparation and misrepresentative prostate biopsy.

The Urology department, GSH management and patients can draw reserved confidence in the performance of the GSH radiology division reporting mpMRI prostate examinations according to PI-RADS v2.1 lexicon with a higher confidence in PI-RADS (v2.1) category 5 reports than PI-RADS (v2.1) category 4 reports.

This study is not extrapolating to PI-RADS 1, 2 and 3 category lesions without further research.

Keywords:

PI-RADS v2.1, PI-RADS 4, PI-RADS 5, Clinically significant prostate cancer, mpMRI prostate.

Introduction

Multiparametric MRI (mpMRI) prostate has become a fundamental part of prostate cancer primary diagnosis, active surveillance, and lesion localization (1).
PI-RADS reporting lexicon is a form of structed reporting and has been around since 2012 and is continually improving with subsequent versions affording more accurate delineation of prostate pathology, specifically significant prostate cancer (2).
PI-RADS lexicon is an important concept in mpMRI prostate reporting as it risk stratifies prostate pathology into 5 categories that have direct implications of patient management and the potential diagnosis of clinically significant prostate cancer.
A concerted effort by the GSH radiology division towards the strict adherence to PI-RADS reporting lexicon followed most recent PI-RADS v2.1 update in 2019 (3).
Since the strict implementation of PI-RADS v2.1 lexicon for mpMRI prostates research has been required to assess and validate the accurate use of PI-RADS v2.1 at GSH against internationally recognized standards for PI-RADS performance.
The PI-RADS lexicon should be a reliable predictor of significant prostate cancer to promote confidence in its continued use and to justify the expenditure on mpMRI prostate examinations in the diagnostic pathway of prostate cancer at GSH.

Prostate cancer is a significant disease entity and is the most common cancer diagnosis in males with the second highest cause of cancer related morbidity (4).
In South Africa prostate cancer is the most common cancer diagnosis amongst men countrywide, reported by the National Cancer Registry (NCR), with a documented incidence of 61.8 per 100 000(5). Over a 10-year period the incidence of prostate cancer has increased steadily from 29.4 per 100 000 in 2007 to 49.4 per 100 000 in 2017(5).
Southern Africa has the highest incidence in Africa at 64.1 per 100 000, followed by Northern Africa with a rate of 35.9 per 100 000(5). Western and Eastern Africa reported the lowest incidence rates at 23.9 per 100 00 and 13.2 per 100 000, respectively(5).
The reported incidence of prostate cancer in Africa is said to be underestimated and a direct result of inadequate screening programs, lack of expertise and failing infrastructure(5).
MRI has become the non- invasive investigation of choice for further characterisation of prostate pathology and is directly correlated to rapid advancements in MRI technology and software, better imaging sequences and image acquisition with improved understanding of prostate cancer and its pathophysiology (9).
PI-RADS reporting lexicon is designed by the ESUR in consultation with ACR and aims to standardise prostate mpMRI reporting into defined risk categories by accurately evaluating and characterising abnormal regions in the prostate gland, specifically looking for abnormal regions likely to represent prostate cancer (2).
PI-RADS v2.1 is the most up to date lexicon, released in 2019, has 5 categories into which prostate lesions are classified. A higher PI-RADS category represents an increased likelihood of clinically significant prostate cancer in the prostate (2)(1).
PI-RADS 4 and 5 category lesions are considered to have a high and very high respective risk of representing clinically significant prostate cancers. PI-RADS 3 is deemed an intermediate risk, whilst PI-RADS 1 and 2 have a very low and low risk respectively(13).
A recent systemic review and meta-analysis by Oerther et la, (1) determined that the PI-RADS v2.1 detection of clinically significant prostate cancer for category 4 and 5 lesions is 52% and 89% respectively(1).

GSH is one of two specialty referral pathways for managing prostate cancer in the Western Cape public sector catering for just over two million males(23).
Accurate reporting of mpMRI prostate examination will assist in decreasing the burdened urology and pathology services and improve health equality for all-in the region.
This retrospective study will assess all mpMRI prostate MRI designated PI-RADS category 4 and 5 against a recent prostate biopsy histology result from the period 1 June 2021 to 12 January 2024.

The objective and aims of this research is to assess the diagnostic performance of PI-RADS (v2.1) category 4 and 5 at Groote Schuur Hospital against international performance outcomes.
Lastly this research hopes to identify any problems with the use of PI-RADS v2.1 at GSH and to address these problem areas with the end goal of benefiting the radiology department, urology department, patients' management, and health system.

Research Methods and design

Study design:

Single institution retrospective study will be performed.
Patients who have received mpMRI prostate and reported as PI-RADS category 4 or 5 will be evaluated, and corresponding prostate biopsy and retrospective radical prostatectomy histology reviewed to determine clinically significant or insignificant prostate cancer between the period 01 June 2021 to 12 January 2024.

Inclusion and exclusion criteria:

Male patients of all ethnicities and racial demographics known to Groote Schuur Hospital Urology department, aged between 18 years to 90 years, and having received 3T mpMRI prostate for further investigation of suspected prostate cancer.

A list of prostate mpMRI patients was provided by accessing the register at the 3 Tesla Cubic MRI scanner GSH.
mpMRI prostate images and reports stored in the Picture Achieving and Communications System (PACS) database were reviewed and PI-RADS category 4 and 5 reports were selected and stored.
Only mpMRI prostate studies primary reported by a qualified consultant radiologist or primary reported by a radiology registrar and signed out by a qualified radiology consultant will be included in the study.
Detailed search was performed, using query builder (Philips, xiris 8.3.16) database search tool to access all 3 Tesla mpMRI prostate studies on the PACS system for the period 1 June 2021 to 12 January 2024.
The search results were filtered by making use of the search parameters: "MR prostate and specified date".
The mpMRI prostate reports were cross referenced with the NHLS data system Labtrak for a detailed histological diagnosis of the corresponding prostate biopsy or retrospective radical prostatectomy histology.

The histology result determined if the patient has clinically significant prostate cancer or not and was dependent on the Gleason score.
A gleason score of greater than 7 is considered significant and comprised of minimum scores of 3+4 and 4+3.

Setting:

GSH is a tertiary hospital institute providing specialty prostate imaging and for the Western Cape public sector.

Characteristics of the study population:

Sample size:

A meta-analysis estimated a sensitivity of 0.89 and sensitivity 0.73 using PI-RADSv1 and PI-RADSv2 (10). A single study showed a specificity of 0.93 for peripheral PCa(24). Therefore, we estimate the sensitivity and specific of 0.9 each can be demonstrated. The estimated prevalence PCa was 0.4 of those referred for imaging in a Chinese study(25). It is hypothesized that PCa prevalence is higher in South African tertiary hospitals, and for the purposes of this calculation, conservatively estimated at 0.5. We wish to have performance metrics with a 95% confidence interval and precision of 0.1. Resulting in 95% Confidence intervals +-0.1 the point estimate.
The minimal sample size is n=69. Since this is retrospective record review, no attrition rate need be applied, and the principal investigator can collect data until the sample minimal sample size is saturated.

Data Collection:

Data was collected in the form of categorical variables and captured on an Excel spreadsheet designed for data entry.

Fields captured were:

Demographics:

- Age of the patient.

Imaging result:

- PI-RADS designation either PI-RADS 4; PI-RADS 5 or both.

Pathology result:

- Histology result either clinically significant prostate cancer or clinically insignificant prostate cancer.
- Gleason Score.

Data analysis:

Analysis was conducted using Rstudio.
Patients were considered positive if they had clinically significant biopsy positive prostate cancer.
Descriptive table of the median (IQR) age of patients was calculated and compared between Biopsy positive and negative using Wilcoxon ranksum test.
Diagnostic performance will be determined using sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with associated 95% confidence intervals.

Diagnostic performance using biopsy positive clinically significant prostate cancer as the gold standard diagnostic will be determined for two endpoints, PI-RADS 4 and PI-RADS 5.

Ethical considerations:

This retrospective study was approved by the local institutional review board and Human Research Ethics Committee (HREC).
HREC REF: 130/2023

Results

This study incorporated a retrospective design structure and analysis where a total of 215 mpMRI prostate studies were considered for inclusion in this study for the period 01 June 2021 and 12 January 2024.
From the 215 mpMRI prostate scans performed 89 studies met the strict inclusion and exclusion criteria.
There was n=89 patients included in the analysis and made up the total sample size.
122 mpMRI studies (57 %) of the initial 215 sample studies were excluded.
The 122 studies were excluded for the following reasons:

- 95 studies were designated PI-RADS 1: 2 or 3 categories (78 %).
- 2 studies were excluded owing to interpretable image quality (1.5 %).
- 12 studies were excluded because patients with PI-RADS 4 or 5 category reports were not biopsied (10 %).
- 2 mpMRI studies did not have imaging on PACS or official GSH reports (1.5 %).
- 11 studies had inconclusive biopsy results (9 %).
- 0 studies failed to use the PI-RADS v2.1 reporting lexicon.

The median (IQR) age of included patients was 63 (61-67).
The youngest participant was 52 and the oldest was 74 years old.

Characteristic	**Overall**, N = 89[1]
Age	63.0 (61.0, 67.0)

[1]Median (IQR)

From the total of 89 participants, 37 were reported as PI-RADS category 4 and 52 studies were reported as PI-RADS category 5.
The prevalence of biopsy positive (gold standard) for clinically significant prostate cancer in this setting is 34.8 % (n/N = 31/89), CI [24.9;44.7 %].

Cross tabulation of PI-RADS 5 and PI-RADS 4 with biopsy results

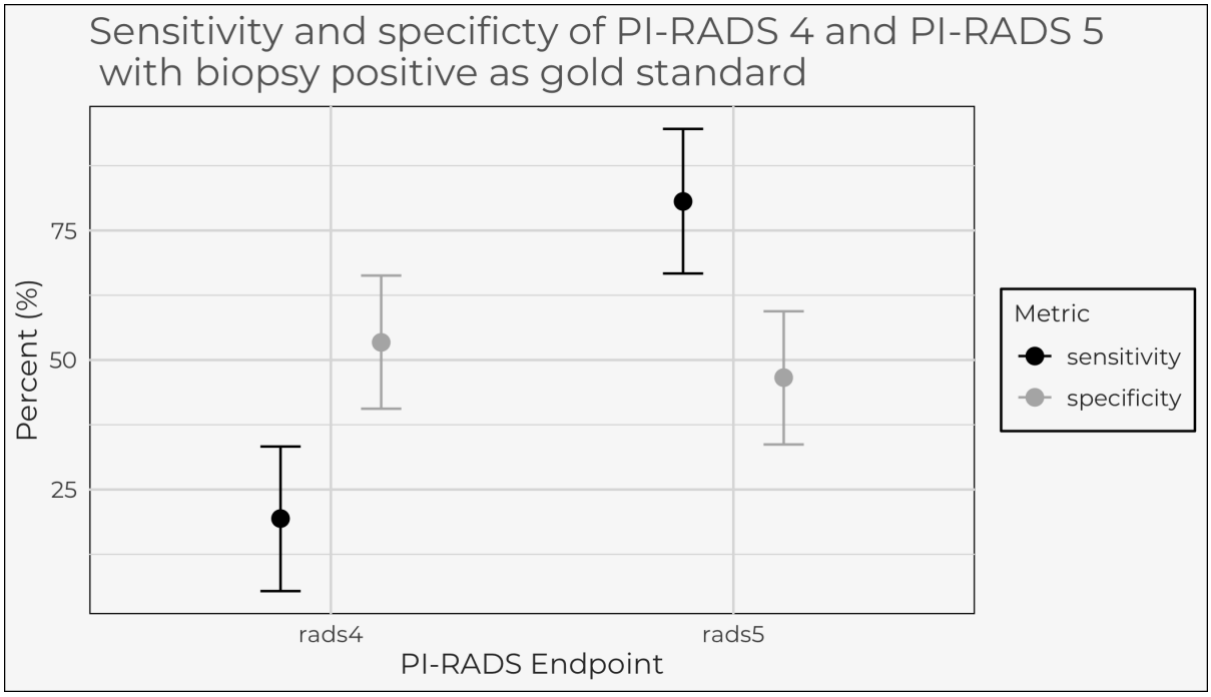
	BIOPSY		
	Negative	Positive	**Total**
PI-RADS 5			
Negative	31	6	37
Positive	27	25	52
PI-RADS 4			
Negative	27	25	52
Positive	31	6	37
Total	58	31	89

The measures of sensitivity and specificity for the different PI-RADS measures are as follows:
For **PI-RADS 4:**
Sensitivity: 19.4, 95% CI: [5.4, 33.3]
Specificity: 53.4, 95% CI: [40.6, 66.3]
PPV : 16.2 95% CI:4.3-28.1
NPV: 51.9 95% CI:38.3-65.5

For **PI-RADS 5**:
Sensitivity: 80.6, 95% CI: [66.7, 94.6]
Specificity: 46.6, 95% CI: [33.7, 59.4]
PPV: 48.1 95% CI:34.5- 61.7
NPV: 83.8 95% CI:71.9- 95.7

Performance Metrics for PI-RADS 4 and PI-RADS 5

PI_RADS	Sensitivity	Specificity	PPV	NPV
4	19.4 (5.4, 33.3)	53.4 (40.6, 66.3)	16.2 (4.3, 28.1)	51.9 (38.3, 65.5)
5	80.6 (66.7, 94.6)	46.6 (33.7, 59.4)	16.2 (4.3, 28.1)	51.9 (38.3, 65.5)



Discussion

Multiparametric MRI prostate is increasingly being utilized for prostate cancer primary diagnosis, active surveillance, and lesion localization(1), and should be a reliable predictor of significant prostate cancer to promote continued confidence in its use at GSH by both Urology and GSH management.
The prevalence of PI-RADS 4 and 5 reports which correlated to significant prostate cancer on histology was 35% (25- 45%).
Control comparisons are made with several high-powered international studies showing a wide variation in the cancer detection rate for PI-RADS 4 and PI-RADS 5 ranging from 39% to 52% for PI-RADS 4 and 72% to 89% for PI-RADS 5 (1) (26) (27) (28) (29).
A south African study by Patel et al, utilized a similar research strategy showed PI-RADS 4 designation correlating to a 62% pickup rate of clinically significant prostate cancer and a PI-RADS 5 designation correlating to 87% pick-up rate (30).

From the data analysis we report that the use of PI-RADS v2.1 category 5 at GSH is aligned with internationally and local reported accuracy for representing clinically significant prostate cancer, having with a sensitivity of 81% (CI 67-95%).
PI-RADS category 4 reports reveals a lower-than-expected correlation to international and local performance standards with a sensitivity of 19% (CI 5- 33%).

The result of this study validates the reliable use of PI-RADS v2.1 category 5 at GSH radiology when the sensitivity is measured against the expected cancer detection rates reported in large high powered international studies.
PI-RADS 4 is universally known to have a lower detection rate for clinically significant cancer, however the sensitivity in this study is much lower than expected (28).
The reported sensitivity value of 19% nor the wide confidence interval does not approach any referenced sensitivity point value of several international studies or local study used as a control comparison in this review.
The 35 % prevalence of PI-RADS category 4 and 5 for representing significant prostate cancer is largely impacted by the low sensitivity of the PI-RADS 4 category reports and well below the prevalence of 49% reported in a similar study by Westphalen et al(27).
The reported poor sensitivity of the PI-RADS category 4 for representing significant cancer is concerning as these patients still require invasive workup to exclude significant prostate cancer which associated with increased patient morbidity and costs.
We propose that the reduced performance of PI-RADS category 4 at GSH is multifactorial and is largely related to a relatively new and inexperienced mpMRI prostate service at GSH, Interrater reliability challenges, technical factors related to patient preparation and image acquisition and lastly misrepresentative prostate biopsies are recognized as establish limitations to this study.

Relatively new and inexperienced mpMRI prostate service at GSH and inter-rater variability challenges:
Accurate reporting of mpMRI prostate exams is highly dependent of the experience and training of the radiology reporting team and acquisition of the images by the radiographers performing the studies and we believe that these factors had a huge influence on the outcome of the study.

At GSH the prostate mpMRI studies are pooled with the general MRI examinations and is reported by general radiologists and registrars with minimal advanced training in reading and interpreting mpMRI prostate scans.
The accuracy of prostate mpMRI reporting by the general radiologists and registrar at GSH is highly dependent on the individuals past exposure to prostate mpMRI and self-learning which is widely variable across the range of reporting radiologists and registrars.

Inter- rater reliability (IRR) is well documented shortfall to standardized reporting of prostate lesions according to the PI-RADS v2.1 lexicon, despite several updates to the PI-RADS lexicon since 2012 this bias continues to impact the reproducibility of prostate mpMRI reporting and ultimately decreases the sensitivity and specificity of prostate reporting (31).
The study by Patel et al (31) notes varied inter-rater reliability (IRR) when characterizing transition zone and peripheral zone lesions according to the PI-RADS v2.1 lexicon. The study revealed a high to moderate IRR with regards to T2W assessment of transition zone lesions and no agreement with regards to DWI signal abnormality characterization in both the peripheral zone and transition zone.
A further study by Rosenkrantz et al (16) looked at 6 experienced radiologist and concluded that a moderate degree of reproducibility amongst experience radiologists with regards to PI-RADS v2.0 lexicon. There was higher agreement with regards to peripheral zone lesions than transition zone lesions.
The IRR variation at GSH is thought to be higher than international statistics and is proposed to be the result of the PI-RADS reporting lexicon being a relatively new concept to GSH in addition to a relatively inexperienced team of radiologists and registrars reporting mpMRI prostates.
This variation in IRR affects the accurate allotment of PI-RADS v2.1 lexicon and directly impacts correct reporting PI-RADS 4 and 5 lesions and subsequent histological detection of clinically significant prostate cancer.

mpMRI prostate acquisition and patient preparation:
An additional impact on accurate mpMRI prostate reporting is related to the acquisition of T1W axial, T2W multiplanar, T2W axial small field of view, DWI/ ADC, and dynamic contrast enhancement sequences.
At GSH the standard imaging sequences and acquisition planes follows the recommendations by the American college of Radiology in the white paper, “PI-RADS v2.1 Prostate Imaging- Reporting and Data System 2019” (2).
Despite utilizing a standardized and internationally accepted mpMRI prostate protocol the acquisition of data sets remains dependent on patient preparation and radiographer skill.
The 3T MRI scanner where prostate MRIs are performed is staffed by three qualified radiographers who have different degrees of training when it comes to mpMRI prostate studies. This results in non-uniform data set acquisitions mostly related to the planes of acquisition and patient preparation.
The American journal of Radiology performed a critical review on PI-RADS v2.1 reporting (32), noting that variations in the planes of T2W axial, sagittal and coronal acquisition can lead to a source of confusion in characterizing and localizing the lesions to a particular sector of the prostate.
This has a direct consequence on the quality and accurate reporting of prostate cancer and lesion localization for confirmatory targeted prostate biopsies.

There is no consensus with regards to patient preparation according to the American college of Radiology white paper, “PI-RADS v2.1 Prostate Imaging- Reporting and Data System 2019”(2), however the paper does recommend administrating antispasmodics to limit motion artefact and emptying the rectum in order improve DWI acquisition.
Both motion artefact and poor DWI acquisition can lead to gross misinterpretation of prostate pathology utilizing the PI-RADS v2.1 lexicon (32).
At GSH patient preparation is minimal owing to limited radiographer expertise, patient understanding and limited time to perform a mpMRI prostate examination.
A recent paper by Giganti et al (33) , concluded that there were fewer and less significant artifacts on DWI acquisition and motion artefact in patients who received preprocedural enema and rectal evacuation leading to improved image interpretation and accuracy.
Ullrich et al (34) published study confirming that administration of antiperistalsis agents reduced motion- related artifact and improved prostate lesion characterization, anatomic details of the prostate and surrounding structures on T2W multiparametric sequences.
At GSH patients do not receive antiperistalsis agents prior to the examination and often the scan is distorted by motion artefact and the DWI sequence is unreadable.
In the GSH setting where there is limited experience in reporting mpMRI prostate reducing ambiguity by optimizing DWI data and reducing motion artefact is important in improving PI-RADS v2.1 reporting accuracy.

Misrepresentative prostate biopsy and prostatectomy histology:
Lastly, prostate biopsy is the gold standard to the diagnosis of clinically significant prostate cancer but can be misrepresentative of the reported PI-RADS category 4 or 5 lesion if the biopsy does not correctly target the pathological area in the prostate leading to diagnostic uncertainty (35).
Prostate biopsies are performed by the GSH Urology department, and most biopsies are trans-rectal ultrasonography (TRUS) guided systematic 12- core biopsies which are not MRI fusion targeted biopsies or cognitive biopsies which would allow for more accurate sampling of an area of concern in the prostate.
In cases where there is a high clinical and radiological suspicion of prostate cancer and negative TRUS biopsy an MRI guided fusion biopsy is acquired.
Furthermore, many patients have had previous biopsies or prostate interventions prior to an MRI which can result in hemorrhage or fibrosis which leads to misinterpretation and incorrect lesion localization for directed biopsy of the prostate.
Research conducted by Kawa et al (36) assessed the detection rate of significant prostate cancer utilizing TRUS prostate biopsy techniques and concluded that diagnostic accuracy for TRUS biopsy was high for men with either a high PSA (>20), T2 stage disease or palpable tumors approached 75%. In men with non-palpable tumors, PSA < 20 and T1 stage prostate cancer the accuracy of TRUS biopsy decreased to 58%.
Thus, it is evident that TRUS biopsy accuracy is not 100% representative and is largely determined by important variables such as palpable cancer, PSA level and stage of disease.
No doubt TRUS biopsies are reliant on the operator technique and experience which will be a big factor in the outcome and accuracy of the biopsies performed.
The combination of TRUS biopsy and MRI fusion shows an improved detection rate of clinically significant prostate cancer (37).

The histology obtained following a radical prostatectomy is thought to result in negligible histological reporting bias as the whole prostate is assessed at the time of analysis.

How does it impact the use of PI-RADS at GSH:
We believe that this research answers the fundamental question with regards to the appropriate use of mpMRI and PI-RADS (v2.1) category 4 and 5 at GSH for the primary diagnosis of clinically significant prostate cancer and for further management of prostate cancer patients.
The Urology department at GSH can draw confidence utilizing mpMRI prostate PI-RADS 5 reports when deciding on further patient management or for additional prostate biopsies in patients with a previously negative biopsy.
PI-RADS category 4 lesions need to be interpreted with caution and correlated with other patient and clinical parameters such as age, performance status, digital rectal examination, and previous biopsy results.
The GSH management can use these results, particularly pertaining to PI-RADS 5 reports to justify the use and funding for mpMRI prostate imaging as a primary diagnostic pathway in the management of patients suspected of having prostate cancer.
This research primarily looked at PI-RADS category 4 and 5 lesions and the rate of detecting significant prostate cancer, thus we suggest that further research should be conducted before extrapolated these findings to PI-RADS 1, 2 and 3 categories.

Strength of this study
Strength of this study lies in its regional and international reproducibility in terms of the strict adherence to PI-RADS v2.1 lexicon and that the standardized technical parameters with regards to acquisition of mpMRI prostate exams which aligned with the recommendations in the PI-RADS v2.1 white paper (2).

Limitations of this study
There were a few limitations to this study and largely related to the small sample sized after the strict inclusion and exclusion criteria was applied. A small sample size impacts data analysis with higher sampling error leading to a decreased accuracy of the data reflecting the true relationship between the variables measured and therefore reducing the statistical power of the study as is seen with our wide confidence intervals.
Furthermore, the generalizability of a small sample size is limited as it may not reflect the true values that a larger study would demonstrate.
We still believe that the study design, data obtained, and data interpretation is robust and can be used a framework to assess other large academic hospitals in South Africa where mpMRI prostate studies are performed.
Lastly, this study did not evaluate PI-RADS 1, 2 and 3 lesions.

Conclusion:

The result of this study validates the reliable use of PI-RADS v2.1 category 5 at GSH radiology when measured against the expected cancer detection rates reported in large high powered international studies.
PI-RADS v2.1 category 4 revealed lower than expected correlation to international performance standards and should not be utilized alone to inform further patient management or treatment.
The Urology department, GSH management and prostate cancer patients can draw confidence in the performance mpMRI prostate examinations with a PI-RADS category 5 designation reported by GSH radiology division.

The strengths and limitations of this study should be carefully considered and extrapolating these findings to PI-RADS 1, 2 and 3 category lesions or to hospitals outside of GSH is not recommended.
We hope that the recommendations made in this study is fulfilled as this will promote continued improvement in mpMRI prostate reporting service and patient management at GSH.

Recommendations:
We offer the following recommendations based on the findings in this research:

- The radiology division at GSH should focus on implementing a dedicated curriculum with measured performance outcomes designed to enhance the skills and knowledge of mpMRI prostate reporting according to the PI-RADS v2.1 lexicon.
- Repeat research on the performance of PI-RADS category 4 and 5 at GSH should be conducted after instituting the curriculum and training changes.
- Within the GSH radiology division a small team dedicated to mpMRI prostate examinations and reporting should be created. This will ensure continued reproducibility and progressive accuracy of the prostate mpMRI reports. This dedicated team can lead the drive for further education and training on mpMRI prostate interpretation and understanding as well as continually assess the outcomes of the PI-RADS reports.
- Further research on this topic looking at PI-RADS 1, 2 and 3 lesions is required to further assess the performance of the PI-RADS v2.1 at GSH.
- Adequate patient preparation in the form of pre-procedure enema and rectal evacuation, in addition to antispasmodic agent administration to enhance the quality of the mpMRI acquisition should be included in the pre-mpMRI checklist.
- Lastly, further research into the accuracy of the prostate biopsies performed by the Urology department should be conducted to assess the impact a misrepresentative biopsy has on the measured outcomes of PI-RADS category 4 and 5 reports.

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Competing Interests

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced the writing of this article.

Author contribution

B. Wegner was the lead author, gathered the data and prepared the manuscript.
Dr G. Human primary supervised and Prof. Sulaiman Moosa secondary supervised the project, edited, and approved the final manuscript for submission.

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Data Availability

Data is available from the authors upon reasonable request.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy of our institution.

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Appendix A- South African Journal of Radiology Instructions to Authors

Title: The article's full title should contain a maximum of 95 characters (including spaces).

Abstract: The abstract, written in English, should be no longer than 250 words and must be written in the past tense. The abstract should give a succinct account of the objectives, methods, results and significance of the matter. The structured abstract for an Original Research article should consist of six paragraphs labelled Background, Objectives, Method, Results, Conclusion and Contribution.

- Background: *Why do we care about the problem?* State the context and purpose of the study. (What practical, scientific or theoretical gap is your research filling?)
- Objectives: *What problem are you trying to solve*? What is the scope of your work (e.g. is it a generalised approach or for a specific situation)? Be careful not to use too much jargon.
- Method: *How did you go about solving or making progress on the problem*? State how the study was performed and which statistical tests were used. (What did you actually do to get the results?) Clearly express the basic design of the study; name or briefly describe the basic methodology used without going into excessive detail. Be sure to indicate the key techniques used.
- Results: *What is the answer*? Present the main findings (that is, as a result of completing the procedure or study, state what you have learnt, invented or created). Identify trends, relative changes or differences in answers to questions.
- Conclusion: *What are the implications of your answer*? Briefly summarise any potential implications. (What are the larger implications of your findings, especially for the problem or gap identified in your motivation?)
- Contribution: What key insights into the research results and its future function are revealed? How do these insights link to the focus and scope of the journal? It should be a concise statement of the primary contribution of the manuscript; and how it fits within the scope of the journal.

Do not cite references and do not use abbreviations excessively in the abstract.

Introduction: The introduction must contain your argument for the social and scientific value of the study, as well as the aim and objectives:

- Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by the use of evidence from the literature.
- Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic and should clarify the knowledge gap that this study will address. Your argument should be supported by the use of evidence from the literature.

- Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.
- Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.

Research methods and design: This must address the following:

- Study design: An outline of the type of study design.
- Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.
- Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.
- Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.
- Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected and any key issues involved, e.g. language barriers.
- Data analysis: Describe how data were captured, checked and cleaned. Describe the analysis process, for example, the statistical tests used or steps followed in qualitative data analysis.
- Ethical considerations: Approval must have been obtained for all studies from the author's institution or other relevant ethics committee and the institution's name and permit numbers should be stated here.

Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish your interpretation of qualitative data. All units should conform to the **SI convention** and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

Discussion: The discussion section should address the following four elements:

- Key findings: Summarise the key findings without reiterating details of the results.
- Discussion of key findings: Explain how the key findings relate to previous research or to existing knowledge, practice or policy.
- Strengths and limitations: Describe the strengths and limitations of your methods and what the reader should take into account when interpreting your results.

- Implications or recommendations: State the implications of your study or recommendations for future research (questions that remain unanswered), policy or practice. Make sure that the recommendations flow directly from your findings.

Conclusion: Provide a brief conclusion that summarises the results and their meaning or significance in relation to each objective of the study.

Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Refer to the acknowledgement structure guide on our *Formatting Requirements* page.

Also provide the following, each under their own heading:

- Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: *The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.* Read our **policy on competing interests**.
- Author contributions: All authors must meet the criteria for authorship as outlined in the **authorship** policy and **author contribution** statement policies.
- Funding: Provide information on funding if relevant
- Data availability: All research articles are encouraged to have a data availability statement.
- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

References: Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Refer to the journal referencing style downloadable on our *Formatting Requirements* page.

Appendix B- Ethical Approval

UNIVERSITY OF CAPE TOWN
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07 March 2023

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Dr G Human
Division of Diagnostic Radiology
Email: gercois@gmail.com
Student:Brett.n.wegner@gmail.com

Dear Dr Human

PROJECT TITLE: RETROSPECTIVE REVIEW: DIAGNOSTIC PERFORMANCE OF PROSTATE-IMAGING AND DATA SCORING SYSTEM VERSION 2.1 (PI-RADS V2.1) 4 AND 5 IN PREDICTING CLINICALLY SIGNIFICANT PROSTATE CANCER IN PATIENTS PRESENTING TO GROOTE SCHUUR HOSPITAL, SOUTH AFRICA-
(MMED CANDIDATE-DR BRETT WEGNER)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 March 2024.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Brett Wegner will also be involved in this study.

Please quote the HREC REF 130/2023 in all your correspondence.

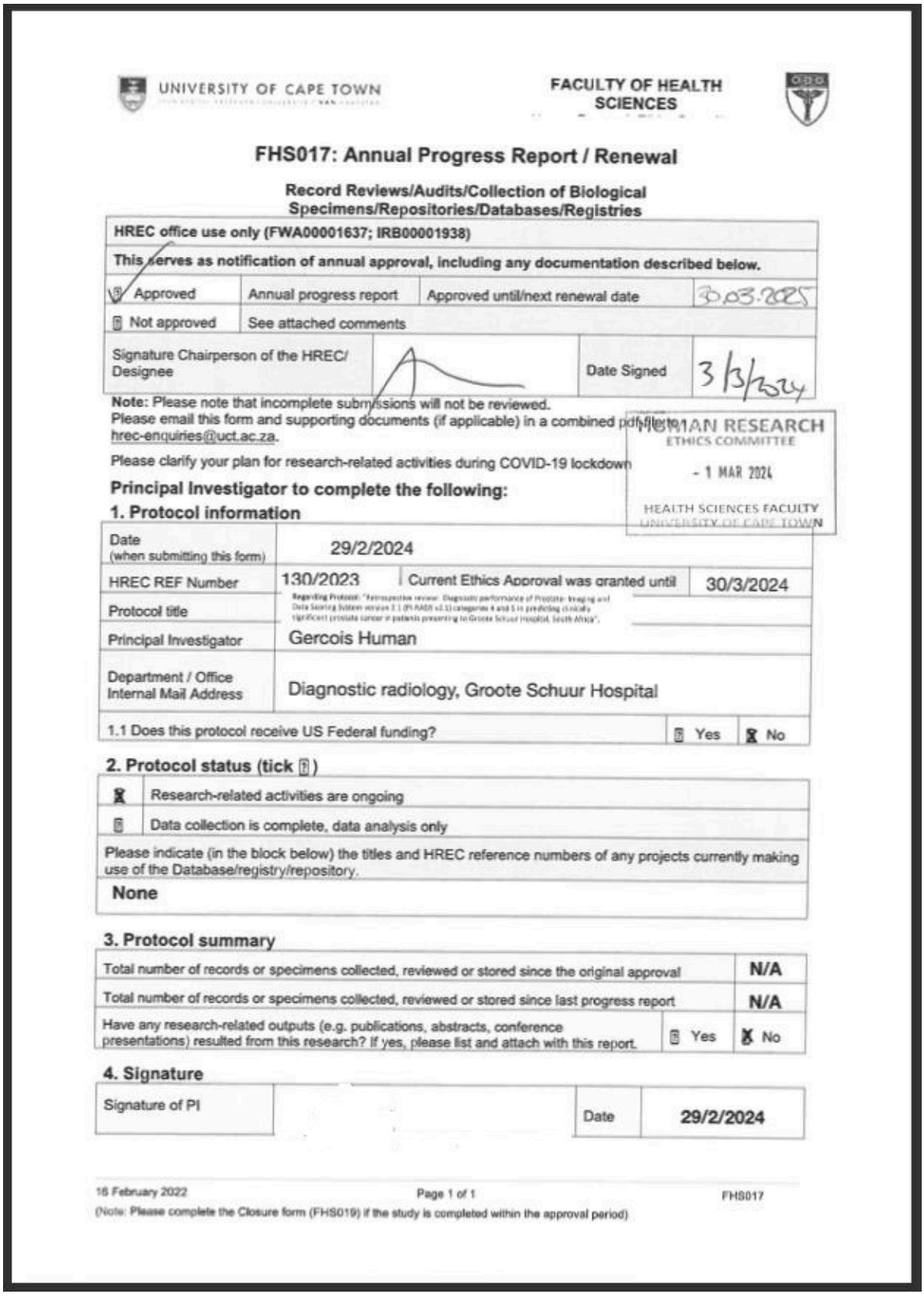
Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Appendix C- Ethics approval renewal



UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.03.2025
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	3/3/2024

Note: Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf file to hrec-enquiries@uct.ac.za.

Please clarify your plan for research-related activities during COVID-19 lockdown

HUMAN RESEARCH ETHICS COMMITTEE
- 1 MAR 2024
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	29/2/2024		
HREC REF Number	130/2023	Current Ethics Approval was granted until	30/3/2024
Protocol title	Regarding Protocol: "Retrospective review: Diagnostic performance of Prostate Imaging and Data Scoring System version 2.1 (PI-RADS v2.1) categories 4 and 5 in predicting clinically significant prostate cancer in patients presenting to Groote Schuur Hospital, South Africa".		
Principal Investigator	Gercois Human		
Department / Office Internal Mail Address	Diagnostic radiology, Groote Schuur Hospital		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☒ No

2. Protocol status (tick ☐)

☒	Research-related activities are ongoing
☐	Data collection is complete, data analysis only

Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.

None

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		**N/A**
Total number of records or specimens collected, reviewed or stored since last progress report		**N/A**
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	☒ No

4. Signature

Signature of PI		Date	**29/2/2024**

(Note: Please complete the Closure form (FHS019) if the study is completed within the approval period)

Appendix D- Institutional approval

Western Cape Government

GROOTE SCHUUR HOSPITAL
Enquiries: Mr Lionel Naidoo
e-mail: GSHResearch.Request@westerncape.gov.za

Dr G. Human
Division of Diagnostic Radiology

E-mail: gercois@gmail.com

Dear Dr G. Human

RESEARCH PROJECT: Retrospective Review: Diagnostic Performance of Prostate – Imaging and Data Scoring System Version 2.1 (PI-RADS V2.1) Categories 4 and 5 in Predicting Clinically Significant Prostate Cancer in Patients Presenting to Groote Schuur Hospital, South Africa.

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 March 2024**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) Confidentiality must always be maintained.
d) No additional costs to the hospital should be incurred as indicated in your Annexure 2 i.e. Lab, consumables or stationery. **If access to TRACK Care/NHLS is required, kindly attach our letter of approval to the application form and approach Information Management to assist with data.**
e) **No patient folders may be removed from the premises or be inaccessible.**
f) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) If the researcher is not GSH staff member, a supernumerary contract is required before commencement of the research.
m) Please contact Michelle Riley (Patient Fees) at ext. 2276 to ascertain if there will be charges for conducting the Research and to obtain a quote or to discuss charges
n) Kindly submit a copy of the publication or report to this office on completion of the research.
o) At no time should any posters encouraging patients to partake in research, be displayed within a clinical area.
p) Please adhere to ALL COVID-19 regulations and Groote Schuur Hospital policies.
q) All Clinical Trials to be registered on Clinicom with Michelle Riley.
michelle.riley@westerncape.gov.za

I would like to wish you every success with the project.

Yours sincerely

LIONEL NAIDOO
HEAD: ALLIED HEALTH
Date: 28 March 2024
C.C. Mr. L. Naidoo, Mr. A. Mohamed, Dr N. Khumalo, Professor N. Ntusi

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