AN EVALUATION OF THE CONCORDANCE BETWEEN MAMMOGRAPHY AND HISTOPATHOLOGY FINDINGS IN WOMEN WITH BREAST LESIONS AT MANKWENG HOSPITAL, LIMPOPO PROVINCE

by

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DEDICATION

To my parents Masekela and Kgabo Magoro, who enabled me to be where I am today.

My wife Moitoi S Magoro for her consistent encouragement throughout my registrar training.

My children Makgomo, Maletsatsi and Masekela Magoro.

Thank you.

DECLARATION

I Machuene Stephen Magoro declare that AN EVALUATION OF THE CONCORDANCE BETWEEN MAMMOGRAPHY AND HISTOPATHOLOGY FINDINGS IN WOMEN WITH BREAST LESIONS AT MANKWENG HOSPITAL, LIMPOPO PROVINCE hereby submitted to the University of Limpopo, for the degree of Master of Medicine in Diagnostic Radiology, has not previously been submitted by me for a degree at this or any other university, that it is my work in design and in execution, and that all material contained herein has been acknowledged.

Magoro, MS (Dr) 17 April 2023

Surname, Initials (title)

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ABSTRACT

BACKGROUND: Breast lesions in women can be caused by any disease process or physical injury occurring at any age. The lesions may be benign (non-cancerous) or malignant (cancerous) with the cancerous lesions having a more ominous implication when diagnosed. Mammography is usually performed as the initial investigation for breast cancer followed by histopathology as the confirmatory investigation. Therefore, the agreement between mammography and histopathology findings is critical in determining the correct management of patients with breast lesions.

PURPOSE: To evaluate the concordance between mammography and histopathology findings in women with breast lesions at Mankweng Hospital.

METHOD: Data was collected at Mankweng Hospital from the records of patients who underwent mammography and subsequent histopathological diagnosis. The qualifying data was entered onto Microsoft Excel and data analyses were conducted in STATA version 15. Continuous variables such as age, were summarised by means and standard deviations. Categorical variables were described with frequencies and percentages. Agreement between mammography and histological diagnoses were assessed by Kappa statistics. Performance of mammograph as a screening test for malignant breast disease using histology as the gold standard was evaluated by computing sensitivity, specificity, negative and positive predictive values. A p-value of ≤0.05 was considered as statistically significant**.**

RESULTS: Total of 41 patient records were part of the study. Findings indicated a high degree of concordance between mammogram findings and histology report when using a BIRADS cut-off of 5. A lower but still statistically significant concordance was realised when using BIRADS cut-off of 4.

CONCLUSION: The study demonstrated agreement between mammography and histopathologic diagnosis of breast lesions categorised as BIRADS 4 and 5. The PPV findings are comparable with those of ACR BIRADS guidelines. The result demonstrates that reporting of mammography findings of breast lesions according to BIRADS lexicon in Mankweng Hospital is in keeping with standardised BIRADS reporting guidelines.

KEY CONCEPTS: Breast lesions**,** Mammography, Histopathology, Image guided Biopsy, Concordance, Positive Predictive Value

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DEFINITION OF CONCEPTS

Benign is a tumour that does not invade and destroy the tissue in which it originates or spread to distant sites in the body, i.e. a tumour that is not cancerous (Law and Martin 2020). In this study it was defined as the absence of malignant cells in the breast tissue specimen.

Biopsy is the removal of a specimen of tissue for microscopic analysis to aid the process of diagnosis (Ireland and Chuen 2020). In this study, Biopsy means the removal of a small piece of living tissue from the breast by a radiology doctor.

Concordance is an agreement between individuals or point of view (Law and Martin 2020). In the study the concordance will mean the agreement between mammography findings and the histopathological report in a setting of breast lesions.

Digital tomosynthesis is a type of limited angle tomography that allows reconstruction of multiple image planes from a set of projection data acquired over a limited range of an X-ray tube movement. In this setting digital breast tomosynthesis is a mammography technique that gives multi-layered images of the breast (Mazzei, Gentili, Tini, Pirtoli and Volterrani, 2019)

Immunohistochemistry a form of histochemistry in which appropriately labelled antibody preparations are used to detect specific structures in tissues (Cammack 2006). In this study the focus was on the proteins in breast cancer cells which assist in; hormone receptor testing; assessing the presence of human epidermal growth factor receptor 2 (HER2); and assessing Ki67 proliferative index.

Histopathology is the study of the structure of diseased or abnormal tissues at a cellular level (Ireland and Chuen 2020). In this study histopathology means the microscopic appearance of the abnormal cells in the breast together with its characteristics.

Lesion is a zone of tissue with impaired function because of damage by disease or wounding (Law and Martin 2020). In this study lesions are pathology within the breast which present as lumps, nipple discharge and skin changes.

Malignant describes a mutant cell or group of cells that proliferates at a faster rate than normal cells and has the capacity to spread to other sites in the body (Hine 2019).

In this study malignant means the presence of malignant cells from breast tissue biopsy specimen.

Mammography is the study of the breast by imaging techniques, most commonly by X-ray examination (Martin and McFerran 2017). In this setting mammography is a study using an X-ray machine to image breast to assist in early detection of breast lesions.

LIST OF ABBREVIATIONS

ASR: Age Standardised Rates

CNB: Core Needle Biopsy

BIRADS: Breast Imaging Reporting and Data System

HER2: Human epidermal growth factor receptor 2

NHLS: National Health Laboratory Services

NPV: Negative Predictive Value

PPV: Positive Predictive Value

CHAPTER ONE

1. INTRODUCTION AND BACKGROUND

1.1 Introduction

Breast lesions in women can be caused by any disease process or physical injury occurring at any age. The lesions may be benign (non-cancerous) or malignant (cancerous) with the cancerous lesions having a more ominous implication when diagnosed. Breast cancer has been reported over a decade ago as one of the most common cancers affecting women worldwide with a rapidly rising incidence in developing countries (Tfayli, Temraz, Abou Mrad, & Shamseddine, 2010). An estimated 19.3 million new cancer cases were reported worldwide in 2020, and of those 2.3 million were as result of breast cancer (Sung *et al*., 2021; Tfayli *et al*., 2010). Breast cancer was the commonest cancer reported in 2020, surpassing colorectal cancer (Sung *et al*., 2021). It was the 5th most common cause of cancer related death in 2020 (Sung *et al*., 2021).

In 2020, Sub-Saharan Africa had an estimated 801 392 new cancer cases (Bray & Parkin, 2022). Of the reported cases in 2020, breast cancer was the commonest, and together with cervical cancer accounted for two thirds of the new cancer cases (Bray & Parkin, 2022).

In South Africa, according to National Institute of Communicable Disease, National Cancer Registry: Cancer in South Africa (National Institute of Communicable Disease, 2019), breast cancer was the most frequent histologically diagnosed cancer in women in 2019, accounting for 23.22 of all cancer diagnosis, with an Age Standardized Incident Rates (ASR) of 33.95 per 100 000.

Limpopo province had the lowest overall age standardised cancer mortality rate in South Africa (Made, Wilson, Jina, Tlotleng, Jack, Ntlebi & Kootbodien, 2017). The top causes of cancer mortality amongst women in Limpopo were cervical cancer followed by breast cancer (Made *et al*., 2017).

The above statistics indicate that breast cancer is of both local and global concern. The need for active management of breast lesions is of vital importance in our country. With that said, the optimal management decision and favourable treatment outcomes of breast lesions depend on early diagnosis by meticulous clinical assessment, mammography, and tissue biopsy (Buccimazza, 2011). Mammography is a non-invasive procedure which is critical for early diagnosis, timeous treatment, and favourable outcome in a setting of breast cancer, thus, leading to increased survival rates and a reduction in patient mortality (Chetlen, Mack, & Chan, 2016; Tfayli *et al.*, 2010)). Mammography is used to characterise and determine the size of a lump and to evaluate the rest of the breast for lesions that are not clinically detectable. Each breast is imaged separately in three different views thus craniocaudal, mediolateral oblique, and mediolateral (Buccimazza, 2011).

The current breast mammography screening guidelines recommend that the procedure begin at age 40 in women of average risk of developing breast cancer (Monticciolo *et al*., 2018). Mammography findings are reported according to the Breast Imaging Reporting and Data System (BIRADS). BIRADS, a tool developed by the American College of Radiology, is used worldwide to minimise variability in reporting amongst radiologists (Balleyguier *et al*., 2007). According to the BIRADS classification, lesions are categorised from 0 to 6 (Balleyguier *et al*., 2007). The use of BIRADS classification has proved to be useful in the characterisation and analysis of mammographic images (Balleyguier *et al*., 2007). The sensitivity and specificity of mammography in characterising breast lesions is approximately 90% and 88% respectively, with known false negative rates of between 8 to 10 percent (Buccimazza, 2011). However, a negative mammography report in a clinically evident breast lesion, or a breast lesion visualised on mammography may need further characterisation by tissue biopsy and histopathological analysis.

Breast tissue is usually harvested via a process known as core needle biopsy (CNB). It is usually performed via a needle inserted into the area of interest obtaining enough breast tissue for histopathology and immunohistochemistry analysis. CNB is associated with a specificity of between 85-100% and sensitivity of 80-95%

(Buccimazza, 2011). The sensitivity of CNB can be improved by performing the procedure under image guidance. Image guided biopsy of the breast is the mainstay investigation of breast lesion which uses ultrasound, stereotactic, or magnetic resonance imaging (MRI) guidance (O'Flynn, Wilson, & Michell, 2010). Ultrasound guided biopsy is more cost effective and readily available (O'Flynn *et al*., 2010). Stereotactic biopsy is commonly used when lesions are not visualised on ultrasound, especially in a setting of breast microcalcifications (O'Flynn *et al*., 2010). Core needle biopsy is an essential component in diagnosing breast cancer as a means of harvesting the affected breast tissue for an accurate and definitive histopathological analysis.

Histopathological analysis of biopsy tissue in conjunction with immunohistochemistry gives vital information on the correct therapeutic approach to breast lesions. For example, if findings are benign, immediate surgical excision may be indicated or the patient may be suitable for follow-up only. On the other hand, surgery with or without systemic therapy such as cytotoxic chemotherapy, targeted therapy, or endocrine therapy is indicated if the findings are of a malignant lesion.

Understanding mammographic imaging requires an accurate application of the BIRADS system. BIRADS is a useful and widely used tool for the standardisation of mammography interpretation and quantitative analysis (Joy, Penhoet, and Diana, 2005). The current study sought to understand the significance of achieving a high level of accuracy in mammography reporting in the diagnosis of breast lesions. The selected site for this study was Mankweng Hospital located in Limpopo Province, South Africa. Analysis of the Mankweng Hospital mammography and histopathological reports is suitable for this study as it a central referral site for all women diagnosed with breast cancer in the public sector in Limpopo province for further management. This research evaluated the extent to which the accuracy of diagnosis of breast lesions is achieved by the current methods of conducting and reporting mammography, and histopathology tests. The findings in this research will further provide a guidance on the interpretation of mammographic imaging, which in turn will allow the radiology department at the hospital to evaluate its current standard of practice. The findings will

also serve as a baseline for improvement strategies related to mammographic imaging and interpretation.

1.2 Research problem

1.2.1. Source and background of the research problem

Breast cancer being a common malignancy amongst women, early and accurate diagnosis of breast cancer can improve the treatment outcome of affected individuals. Mammography is usually performed as the initial investigation for breast cancer followed by histopathology as the confirmatory investigation.

However, not all patients who have undergone mammography are eligible for an urgent biopsy and histopathological analysis as urgent biopsy and histopathological analysis is recommended for lesions reported as BIRADS 4 and 5 (Balleyguier *et al*., 2007). Therefore, the agreement between mammography and histopathology findings is critical in determining the correct management of patients with breast lesions. False negative results are particularly significant because an appropriate therapeutic approach is either delayed or missed altogether with severe adverse consequences to the patient. Similarly, false positive results also have adverse consequences when a lesion is diagnosed as suspicious on imaging but turns out to be non-malignant on histology because a patient may undergo an unnecessary treatment regimen.

In the Mankweng Hospital Radiology Department, one of the duties of the radiology doctor is to report mammograms according to BIRADS classification system. Lesions classified as BIRADS 4 and 5 need immediate biopsy due to the high suspicion for malignancy (Balleyguier *et al*., 2007). The doctor in radiology is then required to perform a biopsy and harvest a portion of the lesion which is then sent off for histopathological analysis. Hence, accurate mammography interpretation is critical when assigning the BIRADS category since the decision to take a urgent biopsy depends on the category assigned. Therefore, investigating the concordance between imaging and histopathological findings in Mankweng Hospital is critical as a way of evaluating the accuracy of the mammographic reporting.

1.2.2 Problem statement

Mammography is performed on patient with breast lesion to assess the likelihood of the lesion being malignant. Mammogram alone is not a definitive diagnostic investigation for breast neoplasm. Histopathological diagnosis in needed for a definitive diagnosis and to plan the treatment. Therefore, the suspicion of breast malignancy raised from the mammographic image interpretation by the radiology doctor needs to be confirmed by histopathological diagnosis.

1.2.3 Hypothesis

Concordance exists between the mammographic findings according to BIRADS classification and histopathology report amongst women with breast lesions at Mankweng Hospital

1.2.4 Rational and motivation for research

Mammography is a non-invasive procedure which is critical for early diagnosis, timeous treatment, and favourable outcome in a setting of breast cancer, resulting in a better chance of survival and a reduction in patient mortality (Chetlen *et al.*, 2016; Tfayli *et al*., 2010). Therefore, accurate interpretation of the mammograms is paramount in ensuring early diagnosis of breast cancer.

1.3 Purpose of study

1.3.1 Aim of the study

To evaluate the concordance between mammography and histopathology findings in women with breast lesions at Mankweng Hospital.

1.3.2 Objectives

- To determine the prevalence of women undergoing mammography with subsequent histopathological diagnosis at Mankweng Hospital.
- To assess the BIRADS classification of breast lesions in women who underwent mammography, biopsy and histopathological diagnosis at Mankweng Hospital.
- To assess the histopathological diagnosis of breast lesions in women who underwent mammographic studies followed by biopsy and histological analysis at Mankweng Hospital.
- To determine the statistical agreement between the mammographic and histopathological findings in women with breast lesions who have undergone both mammography and histopathological investigations at Mankweng Hospital.

1.4 Research question

What is the concordance between the mammographic and histopathology findings amongst women with breast lesions at Mankweng Hospital?

1.5 Research methods

1.5.1 Research Design

A quantitative, descriptive study was conducted in this research.

1.5.2 Sampling

A census type sampling technique was used in this research.

1.5.3 Data collection

Data was collected in Mankweng Hospital radiology department in June 2022 and collated onto a data collection sheet prepared for this study. Radiology attendance registers for the study period were used to retrieve mammography reports and histopathological reports were retrieved from the National Hospital Laboratory Service (NHLS) laboratory.

1.5.4. Data analysis

The data collected was entered onto Microsoft excel and data analysis were conducted in STATA 15. Continuous variables such as age, were summarised by means and standard deviations. Categorical variables were described with frequencies and percentages. Agreement between mammography and histological diagnoses were assessed by Kappa statistics. Performance of mammograph as a screening test for malignant breast disease using histology as the gold standard was evaluated by computing sensitivity, specificity, negative and positive predictive values. A p-value of ≤ 0.05 was considered as statistically significant.

1.5.5 Reliability, validity and objectivity

To account for reliability this study has a clear methodology that has been described with a clear data collection process. The use of a specified data collection tool ensures that the study can replicated by another researcher to collect a similar data.

To account for validity, the equipment used for performing mammograms and analyse biopsy specimen at NHLS underwent regular quality assurance checks performed by qualified personnel. The registrars and medical officers who reported the mammography images were under supervision of a qualified Diagnostic Radiologist.

To account for objectivity in the study secondary (hospital) data was utilised with no alterations. The participants' identity is anonymised, and the results are reported without alterations.

1.5.6 Bias

In this study even though the use of a census can introduce selection bias mainly due to the set study period the data collection process was performed without alteration and reported as found.

1.6 Ethical Considerations

The ethical clearance to perform this research was obtained from the Turfloop Research Ethics Committee (TREC) with the research project number TREC/66/22: PG (Annexure 5). Permission to perform the research was granted by the Limpopo Department of Health and recorded in the National Health Research Database with reference number LP_2021_04_022 (Annexure 6). The Clinical Executive Director of Mankweng Hospital also granted permission to perform the study within the Hospital premises (Annexure 7).

1.7 Significance of the Study

The findings in this research will provide a guidance on the interpretation of mammographic imaging, which in turn will allow the radiology department at the hospital to evaluate its current standard of practice. The findings will also serve as a baseline for improvement strategies for mammographic imaging and interpretation.

1.8 Outline of the dissertation

The dissertation is comprised of literature review, research data results and analysis. The research results are further discussed and compared to reports found in the literature. The research contributions and recommendations are given.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Introduction

In this chapter, the relevant of work of different authors with respect to the topic at hand is reviewed. One of the advantages of the using BIRADS system is that it is a well-established lexicon which produces dependable results with regard to mammography, and as such eliminates ambiguity in the interpretation and reporting of results of studies on breast examination (D'Orsi *et al*., 2003; Sickles, D'Orsi, & Bassett, 2012). However, it is crucial to note that consistent use of BIRADS descriptors is essential for global reliance on the interpretation and reporting of mammography data. The BIRADS lexicon is updated and refined regularly (Spak, Plaxco, Santiago, Dryden, & Dogan, 2017). The ultimate significance of the consistent use of the BIRADS lexicon is the accurate determination of breast pathology.

2.2 Local and international Breast cancer demographics

Breast cancer was the commonest cancer reported in the world in 2020, surpassing colorectal cancer (Sung *et al*., 2021). It was the 5th most common global cause of cancer related death in 2020 (Sung *et al*., 2021) Breast cancer accounts for 28.2% of cancers amongst females, with a mortality rate of 18.2% in Europe (Ferlay, Colombet, Soerjomataram, Dyba, Randi, Bettio, Gavin, Visser, and Bray 2018). This study further indicates that breast cancer is an ongoing dilemma, early diagnosis and management is significant in reducing mortality(Ferlay *et al*., 2018).

In 2020 Sub-Saharan Africa had an estimated 801 392 new cancer (Bray & Parkin, 2022). Of the reported cases in 2020, breast cancer was the commonest, and together with cervical cancer accounted for two thirds of the new cancer cases (Bray & Parkin, 2022).

In South Africa according to the National Institute of Communicable Disease, National Cancer Registry: Cancer in South Africa (National Institute of Communicable Disease, 2019), breast cancer was the most frequent histologically diagnosed cancer in women in 2019, accounting for 23.22 of all cancer diagnosis, with an Age Standardized Incident Rates (ASR) of 33.95 per 100 000 (National Institute of Communicable Disease, 2019). The overall cancer related mortality for 2020 was 56802 and breast cancer accounted for 8.2%, just below lung and cervical cancer accounting for 12.9 and 11.1% respectively (Sung *et al*., 2021).

Limpopo province had the lowest overall age standardised cancer mortality rate in South Africa (Made *et al*., 2017). The top causes of cancer mortality amongst women in Limpopo were cervical cancer followed by breast cancer (Made *et al*., 2017).

2.3 Background of the BIRADS Classification

The BIRADS classification was proposed and later published by the American College of Radiology (ACR), the initial edition of BIRADS was released in 1993 (D'Orsi, Sickles, Mendelson, Morris, Creech, and Butler, 2013). The second, third, and fourth editions were released in 1995, 1998, and 2003 respectively (Burnside, Sickles, Bassett, Rubin, Lee, Ikeda, Mendelson, Wilcox, Butler, & D'Orsi, 2009). The first edition was only devoted to mammography reporting up until 2003, when the 4th edition was released, which included ultrasound and MRI. Currently the ACR BIRADS is in its 5th edition. The BIRADS Classification of breast lesions are classified from zero to 6 (D'Orsi *et al.,* 2013). The BIRADS zero classification is allocated to a lesion that needs further imaging to prior to allocating a suitable BIRADS category (D'Orsi *et al.,* 2013). BIRADS classification 1 and 2 are allocated to negative normal breast findings and benign breast findings respectively (D'Orsi *et al.,* 2013). BIRADS 3 classification is allocated to probably benign breast findings which means that the individual will need short interval follow-up (D'Orsi *et al.,* 2013). BIRADS 4 classification is allocated to lesions suspicious for malignancy, these lesions are further subcategorised into 4a, 4b and 4c which indicate low, moderate, and high suspicion for malignancy (D'Orsi *et al.,* 2013). BIRADS 5 classification is allocated to lesions that are suggestive of malignancy (D'Orsi *et al.,* 2013). BIRADS 6 classification is allocated to biopsy proven

breast malignancy (D'Orsi *et al.,* 2013). BIRADS Classification is a quality assurance system intended to homogenize the data collection and quality of mammographic reports. The correct use of the BIRADS classification also assures standardisation of reports amongst radiologists which in turn improves communication of results as well as provide for outcome monitoring resulting in improve patient care (Burnside *et al.,* 2009*)*.

2.4 Mammography screening and BIRADS classification

Breast cancer screening is currently recommended to commence at the age of 40 in women of average risk of developing breast cancer (Monticciolo *et al*., 2018). Even though the recommended breast cancer screening age is 40, there are individuals as young as 30 years with breast cancer and the incidence increases more with age (Ferlay *et al*., 2018). Due to the presence of breast cancer amongst younger individuals, there are clear recommendations that indicate that women need to be evaluated for breast cancer risk no later than the age of 30 (Monticciolo *et al.*, 2018).

Breast cancer screening with mammography has resulted in a statistically significant reduction in breast cancer mortality (Chetlen *et al*., 2016). Furthermore, addition of digital breast tomosynthesis (DBT) was found to improve the detection rate in mammography screening (Chetlen *et al*., 2016). The number of false-positive findings with DBT was lower than that with digital mammography due to fewer asymmetric densities, except in extremely dense breasts, The superiority of DBT to conventional digital mammography owes to the fact that DBT acquires images from multiple planes (Mazzei, Gentili, Tini, Pirtoli, & Volterrani, 2019).

The use of the BIRADS classification by the clinician reporting mammographs has proven to be useful in the characterisation and analysis of mammographic (Balleyguier *et al*., 2007). Currently tissue biopsy is indicated for BIRADS categories 4 and 5 (Balleyguier *et al.*, 2007). Image guided biopsy is performed by the clinician to acquire a tissue sample for histopathological diagnosis.

2.5 Relationship between mammographic and histopathological diagnosis

In the available data there is a consensus in the results that indicate that as PPV increases as the BIRADS category increases (Gülsün, Demirkazık, & Arıyürek, 2003; Lacquement, Mitchell, & Hollingsworth, 1999; Lazarus, Mainiero, Schepps, Koelliker, & Livingston, 2006; Sickles *et al.*, 2012). The BIRADS atlas 5th edition under the mammography section shows the probability of malignancy for BIRADS 1, 2, 3, 4 and 5 to be 0, 0, 0-2, 2-95 and >95% respectively (Sickles *et al*., 2012). Positive predictive value (PPV) is the proportion of positive test results that are true positives and its reported in percentages (Montano, 2014). PPV is frequently used to assess the relationship between radiological mammographic findings and histopathological diagnosis (Chotiyano, Srinakarin, Triamwittayanont, Wongsiri, & Koonmee, 2013; Cupido, Vawda, Sabri, & Sikwila, 2013; Gülsün *et al*., 2003; Lacquement *et al*., 1999). The PPV represents the probability that a patient's biopsy will return positive for malignancy depending on the BIRADS category assigned.

Looking at individual results (Lacquement *et al.*, 1999) shows PPVs per BIRADS category as follows: Category 1 (0.0), category 2 (0.04), category 3 (0.03), category 4 (0.23), category 5 (0.92). The study further concludes that BIRADS classification improves the quality of the risk assessment information by making the PPV more specific to a patient's mammogram rather than simply relating it to an overall PPV (Lacquement et al., 1999).

BIRADS is further subcategorised into 4a, 4b and 4c with each subcategory having its individual PPV These Subcategories were found useful in predicting the likelihood of malignancy (Lazarus *et al*., 2006). The PPVs of BIRADS 4 subcategories attained good interobserver agreement reported as follows: category 4a, six (6%) of 102; category 4b, 17 (15%) of 110; category 4c, 48 (53%) of 91; and category 5, 71 (91%) of 78 as reported previously (Lazarus *et al*., 2006).

In another study the researchers report PPV ranging from 17 to 25% for BIRADS 4 and PPV of 44% to 64% for BIRADS 5 lesions (Gülsün *et al*., 2003). The PPV for BIRADS 5 appears lower in this study compared to the findings in the Lacquement *et al*. (1999) study discussed above possibly because it focuses only on suspicious

breast calcifications (Gülsün *et al*., 2003). In was concluded that BIRADS does not always succeed as expected in reducing ambiguity in the assessment of breast calcifications but is useful in the standardisation of mammography reports (Gülsün *et al.*, 2003).

Nevertheless, a South African study conducted Addington Hospital in which breast tissue specimen was acquired through stereotactic core needle biopsy reports a combined PPV of 20.9% for suspicious lesions (Cupido *et al*., 2013). Even though BIRADS classification is not specified in this study, “suspicious lesions” fall under BIRADS category 4 and 5. As a way forward, they emphasise that BIRADS allows better organisation, consistency and clarity in breast imaging reporting, as well as accurate data comparison between centres facing limitations similar to their own (Cupido *et al.*, 2013).

2.6 Histopathological diagnosis of Breast Cancer

After mammography with or without image-guided biopsy, histopathological analysis of breast tissue is performed to confirm the characteristics of the lesion which is critical for a tailored approach to treatment. Histopathological analysis is necessary because breast cancer is a heterogeneous disease featuring distinct histopathological, molecular and clinical phenotypes that require distinctly different types of treatment approach (Rakha & Green, 2017). The histopathology report includes hormone receptor testing, human epidermal growth factor receptor 2 (HER2) and Ki67 proliferative index levels (Rakha & Green, 2017).

The hormone receptor testing looks at tumour expression of progesterone and oestrogen receptors. Patients with breast cancer showing any nuclear expression of hormone receptor in invasive tumour cells above the cut-off are likely to respond to hormonal manipulation and therefore are potential candidates for hormone therapy such as tamoxifen, anastrozole, and goserelin (Rakha and Green 2017).

Human epidermal growth factor receptor 2 (HER2) is a growth-promoting protein on the outside of all breast cells. Breast cancer cells with higher-than-normal levels of

HER2 are called HER2-positive. HER-2 positive cancers tend to grow and spread faster than other breast cancers (Rakha & Green, 2017). Addition of anti-HER-2 such as trastuzumab to the treatment regimen of a HER-2 positive cancer is often needed for a better outcome. Ki-67 proliferation index is used to assess the rate of new cell formation. Cancers with high Ki-67 index (>15%) tend to respond better to systemic cancer therapy such as chemotherapy.

2.7 Imaging – histologic concordance and discordance in breast lesions

Mammography is considered an accurate imaging method for the diagnosis of breast lesions. However, false negative or false positive findings may occur due to diverse reasons such as operator factors (e.g. contributory search, perception and decision making behaviors), technical, patient and lesion factors (e.g. positioning including depth, size, breast density, presence of implants, and breast compression), nature and type of the cancer, and architectural distortion (Ekpo, Alakhras, & Brennan, 2018; McGuinness *et al*., 2018). The sensitivity of mammography is approximately 90%, with specificity up to 88%. False negative rate of between 8% and 10% have been reported. Approximately 1-3% of women with a clinically suspicious abnormality and negative imaging may have breast cancer (Buccimazza, 2011). Therefore, in the case of a negative mammogram further investigation is necessary if a lump is detected on clinical examination.

Imaging-histopathological correlation is critical in evaluating the accuracy of mammographic reporting. Concordance between imaging and histopathological findings is said to occur when histopathology findings confirm the mammography report, and discordance is when these do not correspond. There are categories of imaging-histopathology concordance which includes concordant malignancy, discordant malignancy, concordant benign, discordant benign and borderline or high-risk (Park, Kim, Moon, Yoon, & Kim, 2018). Considering that most cases that are biopsied are BIRADS 4 and 5, our concordance category of interest will be concordance malignancy. In this category, a lesion shows imaging features suspicious for malignancy (e.g. BIRADS 4 or 5 lesion) and is latter diagnosed as malignancy on histopathology (Park *et al*., 2018). The other important category in this study is that of

discordant malignant, in this category the lesion shows benign imaging features but is diagnosed as malignancy on histopathological grounds (Park *et al*., 2018).

There is a reported imaging-histopathological discordance rate of 3.1% in corresponding mammography and histopathology reports of 1785 consecutive breast lesions which were classified as BI-RADS 3, 4 and 5 (Liberman *et al*., 2000) In this series, the frequency of carcinoma was highest among discordant BI-RADS 5 than 4, and decreased significantly with increased operator experience (Liberman *et al*., 2000). False negative results are particularly significant because an appropriate therapeutic approach is either delayed or missed altogether with severe adverse consequences to the patient. Optimisation of techniques, imaging-histopathological correlation, and post mammographic follow-up protocols are recommended in order to reduce the incidences of false negative diagnosis (Youk, Kim, Kim, Lee, & Oh, 2007).

False positive results also occur with adverse consequences when a lesion is diagnosed as suspicious on imaging but turns out to be non-malignant on the histopathology report. In mammography, false positive results may necessitate recall imaging or repeat biopsy. The consequences of false-positive results are the severe psychological distress it causes to the women, in addition to the unnecessary cost to the healthcare system and the patient for imaging and procedures (McGuinness *et al*., 2018). In an analysis of screening mammography results of 2361 women performed in a USA hospital over a 1-year period, McGuiness found that about 53% had at least one false positive result, 52% had at least one recall breast imaging and 12% of them had at least one biopsy that did not result in breast cancer. Factors associated with having a false positive result were age, frequency of screening, and breast density (McGuinness *et al.*, 2018).

2.8 Conclusion

The consistent use of BIRADS lexicon is at the core of the discussions by various authors who have investigated its accuracy in the diagnosis of breast lesions. Consistent use of BIRADS descriptors is essential for reliable interpretation and reporting of mammography data. Some authors believe that BIRADS does not always

succeed as expected in reducing the ambiguity in the assessment of breast calcifications but is useful in the standardisation of mammography reports (Gülsün *et al*., 2003). The use of PPV can give a good indication of how well the use of BIRADS classification can predict the probability of breast cancer as the BIRADS category increases as already described. But the use of concordance between mammography and histopathology assists in affirming the radiologist that their reporting is in line with those of the histopathologist.

CHAPTER 3

3. RESEARCH METHODOLOGY

3.1 Introduction

Chapter three describes the research methods including research design, study setting, study population, sampling, and sample size. The process of data collection, data analysis, measures taken to ensure validity and reliability, and ways of minimizing bias are discussed. Ethical considerations are also presented.

3.2 Research Design

The research design used in this study was a quantitative, descriptive involving a retrospective review of the medical records of patients with breast lesions who underwent mammography screening followed by tissue biopsy and histopathological analyses from the 1st of January 2019 to the 31st of December 2019. Descriptive study design analyses findings in a population in terms of distribution of the variables, and frequency of outcomes of interest (Awaisu, Mukhalalati, & Mohamed Ibrahim, 2019). A descriptive study design was appropriate for this research because it describes findings of breast lesions in women investigated at Mankweng Hospital whose mammogram and histopathology results were captured without any interventions or alterations.

3.3 Study Setting

The study was conducted at the radiology department in Mankweng hospital situated in the Turfloop region.

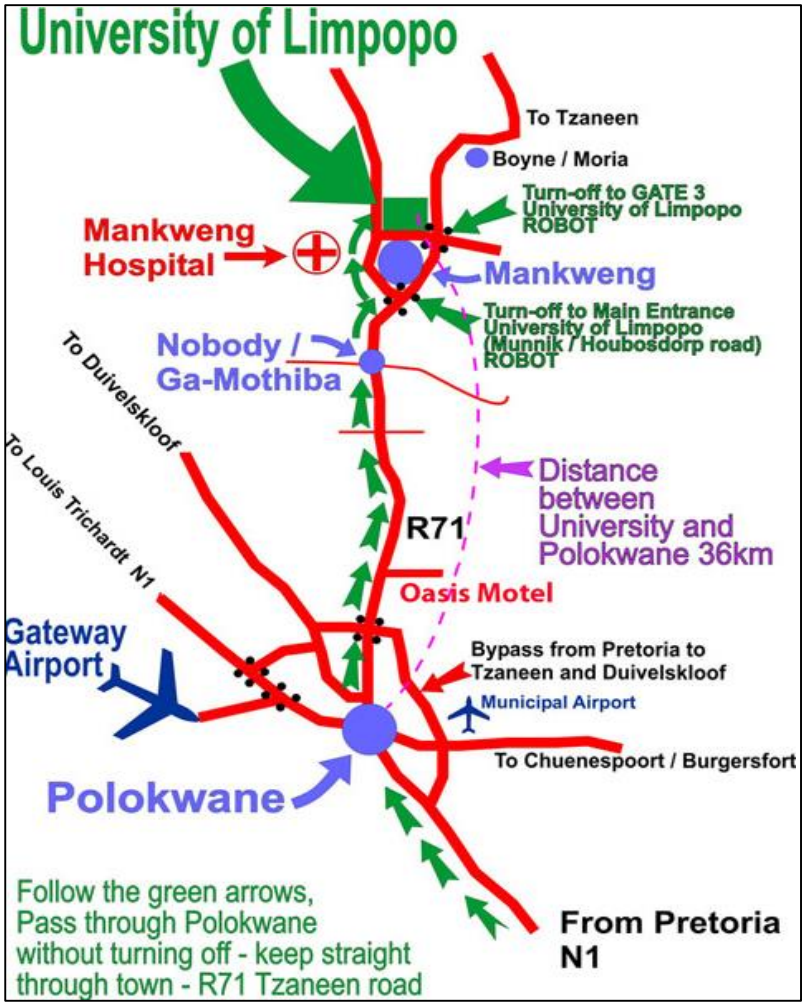

Figure 1: Study site location: Mankweng Hospital, (Source: *https://www.ul.ac.za/application/text_images/turfloop/get_here_map.jpg)*

3.4. Sampling

3.4.1 Study population

The study focussed on women with breast lesions who had mammography done at Mankweng Hospital with subsequent histopathological diagnosis.

3.4.2 Inclusion criteria

The study included females with breast lesions, seen at Mankweng hospital with any BIRADS category lesion that have a histopathological and mammography

examinations report available falling within the study period from 1 January 2019 to 31 December 2019.

3.4.3 Exclusion Criteria

The researcher excluded individuals younger than 18 years, males, patients outside study period and patients with incomplete information (e.g. missing demographics, missing histopathology reports and mammogram reports with no BIRADS allocation).

3.4.4 Sample Size

According to the mammogram register found in Mankweng Hospital radiology department 880 mammograms were performed from 1 January 2019 to 31 December 2019. Using the Mammogram register as a guide, mammogram reports were retrieved from the radiology department archived and the reports scrutinised. To access accurate corresponding histology reports the specimen biopsy number which were available in the departmental biopsy book, and the patients file numbers recorded on the mammogram report and register, were used to access histopathological report from the NHLS website. A total of 41 reports met the inclusion criteria and whilst 839 were excluded. The exclusion of the reports was mainly from unavailability of the histopathological reports associated with the available mammograms and missing data in general.

3.4.5 Sampling method

Sampling is the selection of small groups of entities to represent a large number of entities in statistics (Law & Martin, 2020). In this study, a census method was used. Consecutive patients seen in the mammography unit that satisfy the inclusion criteria are included in the study.

The census method was used in this study because the population size was small, and it was feasible to include all the qualifying participants in the study. The study

sample comprised of 41 medical records of female with breast lesions who had mammography done in Mankweng hospital with subsequent histopathology report.

3.5 Data Collection

3.5.1 Data collection tool

Relevant data was extracted from the patient files and recorded on the data sheet designed for this study (refer to Annexure 2). The data collection sheet included information available on the records. There were no alterations made to the available data.

3.5.2 Characterisation of the data collection tool

The data collection tool captured the following data from the records:

- Age of patient;
- Mammographic report (with BIRADS category);
- Histopathological report (histological type, hormonal receptor status, and Human Epidermal Growth Factor 2 – HER 2).

3.5.3 Data Collection process

The researcher retrieved mammography report files from the Mankweng Hospital radiology department records during the month of June 2022. The patients who had biopsy done were entered onto the data collection sheet and their Histopathology reports were retrieved from the NHLS track care website.

3.6 Data analysis

The collected data was entered onto Microsoft excel. Descriptive statistics such as mean, proportions and frequency were used to analyse the variables. Kappa statistics

were used to assess the agreement (concordance). Subgroup analysis were done where appropriate.

Continuous variables such as age were summarised by means and standard deviations. Categorical variables were described with frequencies and percentages. Agreement between mammography and histological diagnoses were assessed using Kappa statistics. Performance of mammograph as a screening test for malignant breast disease using histology as the gold standard was evaluated by computing sensitivity, specificity, negative and positive predictive values. All analysis were conducted in STATA 15 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA). A p-value of < or equal to 0.05 was considered to be statistically significant.

3.7 Quality criteria

3.7.1 Reliability

The reliability of a study is defined as “the consistency of the analytical procedures, including accounting for personal and research method biases that may have influenced the findings”(Noble & Smith, 2015). Meaning the study produces similar results under same conditions at different times. This study has a clear methodology that has been described with a clear data collection process. And the use of unaltered secondary data in this study further confirms that the study can replicated by the next researcher. The Mammographers and the Doctors in radiology followed standardised departmental imaging and reporting protocols. The NHLS has trained histopathologist who reported on the biopsy specimens.

3.7.2 Validity

Validity refers to how effective an instrument is at measuring what is claims to measure. Internal validity refers to the extent to which the observed effects can be attributed to the independent variable, whereas external validity is the extent to which the findings of the research can be generalized from the sample to the population

(Frambach, van der Vleuten, & Durning, 2013). Validity was ensured for the immunohistochemistry data as daily quality assurance measures were done by the laboratory personnel according to the protocols of the company (National Hospital Laboratory Service). External tissue controls were also used to standardize and optimize immunohistochemistry.

Validity of data collection was ensured as initial tissue samples were harvested by qualified clinicians for purpose of providing accurate medical care to breast cancer patients. It is taken that the laboratory staff extracted appropriate samples and ran the tests accurately since this information was used to treat the patients. The immunohistochemical tests were performed on the breast cancer pathological tissue sample obtained from the initial biopsy sample and /or from subsequent lumpectomy/mastectomy specimens in patients deemed to be operable. Leica bond III machine was used for the immunohistochemical tests. Antibodies for ER, PR, and HER2 were also from Leica bond and were used according to the manufacturer's recommendations. Automation of the process guaranteed the uniformity of immunohistochemistry and avoided variations among the laboratory staff. The information was collected and analysed as found without any alterations. The researcher who has experience in oncology and is familiar with the relevant information to include for accurate study findings captured data.

3.7.3. Objectivity

Objectivity is the extent to which personal biases are removed and value free information is gathered (Frambach *et al*., 2013). In the study secondary (hospital) data was utilised with no altercations. The participants' identity is anonymised, and the results are be reported without alterations.

3.8. Bias

Bias is systematic deviation of results from the truth (Martin & McFerran, 2008). Understanding bias in research is essential because bias impact on validity and reliability of study findings. Even though bias exists in all study designs, in quantitative

studies having a well-designed research protocol explicitly outlining data collection and analysis can assist in reducing bias. The data collection process is not free of bias because a random sampling type was not used, but to minimise sampling bias all data which met the inclusion criteria was included in the study without alterations.

3.9. Ethical Considerations

3.9.1 Ethical clearance

The ethical clearance to perform this research was obtained from the Turfloop Research Ethics Committee (TREC) with the research project number TREC/66/22:PG (Annexure 6). Further permission to perform the research was granted by the Limpopo department of health (Annexure 7) through the National Health Research Database with reference number LP_2021_04_022. The Clinical Executive Director of Mankweng Hospital also granted permission to perform the study within the Hospital Premises (Annexure 8).

3.9.2 Anonymity and confidentiality

The research participants' identity was kept confidential. Coded Identifiers were used instead of patients' names. The copies of the data sheets were be kept in a password protected computer. The mammography reports and histology reports were handled only by the researcher. All the data collection process was done within the hospital premise and no patient file or report left the hospital premises. The publication of the study results will not include identifiers that can link back to the patient's identity this includes patients' names, reports, pictures or file numbers.

3.9.3 Non-maleficence

In this study the researcher dealt with the participants' radiological and histopathological reports, no direct physical harm was inflicted on the individuals. To

avoid sensitive patient information being released to the public, the reports with patients' information remain within the hospital.

CHAPTER FOUR

4. RESULTS

4.1 Introduction

In this chapter, the findings of the research are presented as follows.

- Description of data collection process.
- Data analysis which includes:
    - Description of the study population demographics
    - Statistical analysis of Agreement between mammography report and histological report using cut-off of BIRADS score of 5.
    - Statistical analysis of Agreement between mammography report and histological report using cut-off of BIRADS score of 4.
    - Description of histopathological diagnosis in relation to BIRADS score

This study incorporates the description of variables related to its objectives as found in women with breast lesions investigated at Mankweng Hospital. The researcher utilised records of patients as explained in the research methodology section in the previous chapter. Variables examined in this study are those related to BIRADS lexicon and histopathological findings of a benign or malignant breast lesion.

4.2 Description of the data collection process

The main aim of the research was to determine the concordance between mammographic and histopathological findings in women with breast lesions who underwent both mammography and histopathological investigations.

The research focused on the following objectives to achieve the aim:

- To determine the prevalence of women undergoing mammography with subsequent histopathological diagnosis at Mankweng Hospital.
- To assess the BIRADS classification of breast lesions in women who underwent mammography, biopsy, and histopathological diagnosis at Mankweng Hospital.

- To assess the histopathological diagnosis of breast lesions in women who underwent mammographic studies followed by biopsy and histological analysis at Mankweng Hospital.
- To determine the statistical agreement between the mammographic and histopathological findings in women with breast lesions who has undergone both mammography and histopathological investigations at Mankweng Hospital.

4.3 Findings

4.3.1 Description of the study population demographics.

The records of 880 patients who underwent mammography between 1st January 2019 and 31st December 2019 were reviewed. From the 880, 839 were excluded from the study for not meeting the inclusion criteria. Forty-one (41) patients met the inclusion criteria and are included in the final analysis.

Patient characteristics are described in Table 1. Of the 41 patients 38 patients were over the age of 40 and 3 fell between the ages of 18 and 39. The youngest patient was 28 and the oldest was 99 with a mean age of 60.4 and a standard deviation of 16.5 (Table 1). Most of the patients in the research had a BIRADS score of 5 (n = 32) with the second highest number being BIRADS 4 (n= 5), followed by BIRADS 2 and 3, having 1 and 2 patients respectively.

Table 1: Characteristics of patients (N=41)

Description	**n (%) or mean (sd) or median (range)**
Age	60.4 (16.5) or 58 (28-99)
Age category	
18-39	3 (7.3)
40+	38 (92.7)
BIRADS score	
2	1 (2.4)
3	2 (4.9)

4	6 (14.6)
5	32 (78.1)
Histopathology diagnosis	
Malignant	32 (78.1)
Benign	9 (21.9)
Oestrogen receptor (n=30)	
Positive	24 (80.0)
Negative	6 (20.0)
Progesterone receptor (n = 29)	
Positive	17 (58.6)
Negative	12 (41.4)
HER- 2 (n=28)	
Positive	8 (28.6)
Negative	12 (42.8)
Equivocal	8 (28.6)
Ki67 in percentage (n=27)	
0-20	12 (44.4)
21-40	9 (33.3)
41-60	4 (14.8)
61-80	2 (7.4)

4.3.2 Agreement between mammography and histological reports (cut-off BIRADS score of 5)

The histopathological diagnosis was malignant in 32 patients and benign in 9 patients. The BIRADS category with the highest number of malignancies was BIRADS 5 with a total of 31 malignant cases and only 1 benign case (Table 2). There was 95.2% concordance between mammography and histopathological diagnosis with a kappa value of 0.86 and p-value of < 0.05 (Table 4). The positive predictive value of BIRADS 5 was 96.9%.

Table 2: Performance of mammograph as a screening test for malignant breast disease (cut off BIRADS score of 5)

		Histological diagnosis						
		Negative (Benign lesion)	**Positive (Malignant lesion)**	**Totals**	**Sensitivity (95% CI)**	**Specificity**	**Negative Predictive Value**	**Positive Predictive Value**
Mammograph diagnosis	**Negative (BIRADS score < 5)**	8	1	9	96.9% (83.8-99.9)	90.0% (55.5-99.7)	90.0% (55.5-99.7)	96.9% (83.8-99.9)
	Positive (BIRAD score =5)	1	31	32				
Number		10	32	42				

Table 3: Kappa agreement statistics between mammography and histological reports (cut off BIRADS score of 5)

Description	Agreement	Expected agreement	Kappa	Z	Prob>z
Value	95.2%	63.7%	0.86	5.63	0.0001

4.3.3 Agreement statistics between mammography and histological report using cut off of BIRADS score of 4

BIRADS 4 category had the second highest number of malignant cases with 1 out 6 cases malignant. There was 85.7% concordance between mammography and histological diagnoses when using BIRADS 4 as a cut-off, with a kappa value of 0.52 and p value <0.05 (Tables 5 and 6).

Table 5: Performance of mammograph as a screening test for malignant breast disease (cut off BIRADS score of 4)

		Histological diagnosis						
		Negative (Benign lesion)	**Positive (Malignant lesion)**	**Totals**	**Sensitivity (95% CI)**	**Specificity**	**Negative Predictive Value**	**Positive Predictive Value**
Mammograph diagnosis	**Negative (BIRADS score < 4)**	3	0	3	100% (89.1-100)	40% (12.2-73.8)	100% (39.8-100)	84.2% (68.7-100)
	Positive (BIRADS score 4+)	6	32	38				
		9	32	41				

Table 6: Agreement statistics between mammography report and histological report (cut off of BIRADS score of 4)

Description	Agreement	Expected agreement	Kappa	Z	Prob>z
Value	85.7%	71.2%	0.52	3.76	0.0001

4.3.4 Description of histopathological diagnoses with relation to BIRADS score

The commonest histological findings were that of invasive or infiltrative carcinoma accounting for 30 of the 32 malignant cases. Of the 30 invasive or infiltrating carcinoma cases, 29 were found in the BIRADS 5 score. Carcinoma in situ only accounted for 2 of the 32 malignant cases. Abscess formation was the only non-malignant finding in BIRADS 5 category No malignant cases were found in BIRADS 2 and 3 category. Only 1 of the 32 malignant case was found in BIRADS 4 category. The rest of the BIRADS 4 of the 5 category findings were benign (Table 7).

Table 7: histopathological diagnoses with relation to BIRADS score

BIRADS SCORE	INVASIVE OR INFITRATING CARCINOMA (Malignant)	CARCINOMA IN SITU (Malignant)	FIBROADENOMA (Benign)	ABSCESS FORMATION (Benign)	CHRONIC INFLAMATORY CELLS (Benign)	BENIGN BREAST TISSUE, NO INSITU OR INVASIVE MALIGNANCY, BENIGN FIBROADIPOSE TISSUE (Benign)	INTRADUCTAL PAPILOMA (benign)	TOTAL
2	0	0	1	0	0	0	0	1
3	0	0	1	0	0	1	0	2
4	1	0	1	0	1	2	1	6
5	29	2	0	1	0	0	0	32
TOTAL	30	2	3	1	1	3	1	41

4.3.5 Summary

Findings indicate perfect concordance between mammogram findings and histopathology report when using a BIRADS cut-off of 5 and less but still statistically significant concordance when using BIRADS cut-off of 4 or more.

CHAPTER FIVE

5. DISCUSSION

5.1 Introduction

The layout of this chapter is as follows:

- Discussion and interpretation of research results
- Contributions and recommendations
- Study limitations
- Conclusion

5.2 Discussion and interpretation of study results

5.2.1 Prevalence of women undergoing mammography and histopathological diagnosis

The data shows that out of 880 women imaged in 2019 only 41 had histopathology results, accounting for only 4.9% of the imaged patients. The reason for the relatively low number owes to the fact that biopsy is recommended for patients with BIRADS 4 and 5 (Balleyguier *et al.*, 2007). And the 880 reported mammograms included all BIRADS categories ranging from 0 to 6. The 839 excluded patients did not meet the inclusion and exclusion criteria.

The current national mammography screening guidelines recommend annual mammography screening for women 40 years or older with the exclusion of the identified at risk patients who should start screening earlier (Monticciolo *et al*., 2018) . In the current study malignant findings were encountered from 36-years of age. This implies that a detailed clinical history is needed to ascertain if the patient is an at-risk patient or not. The information on risk factors is vital to determine a suitable patient specific breast cancer screening program.

5.2.2 BIRADS classification in women undergoing mammography and histopathological diagnosis.

Of the 32 malignant cases, the commonest histological subtype was invasive or infiltrating carcinomas with few carcinomas in situ. A majority of invasive or infiltrating carcinoma were found in the BIRADS 5 category. And within BIRADS 5 category the only benign finding was that of Abscess formation. Abscess formation is one of the described mimickers of malignancy (Guirguis, Adrada, Santiago, Candelaria, & Arribas, 2021). The other mimickers of malignancy include other inflammatory breast, proliferative breast conditions and benign tumours as depicted in the flow chart below (Guirguis *et al.*, 2021).

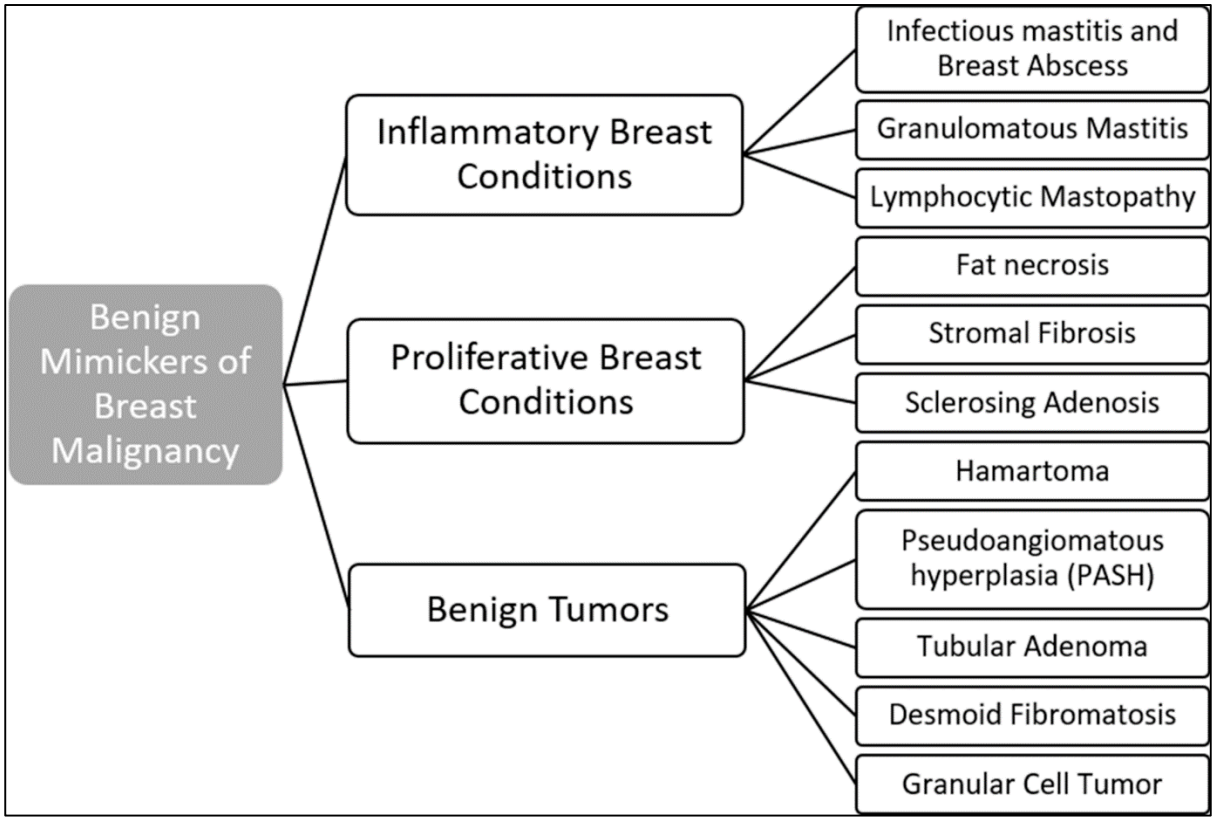

Figure 2**:** Differential diagnoses of breast malignancy *[Source (Guirguis et al., 2021)]*

5.*2.3 Histopathological diagnosis of women undergoing mammography and histological analysis.*

Defining breast lesions according to cellular morphology on histopathology was outside the scope of this study, hence is not discussed. However, majority of malignant lesions were hormone receptor positive (oestrogen=80% and progesterone=57%). Human epidermal growth factor receptor 2 (HER 2) was positive in 27% of the malignant tumours. The reported ER, PR and HER2 where higher than those reported previously (Mahmoud & Mahmoud, 2014; Nabi, Ahangar, & Kaneez, 2016). Their ER, PR and Her-2/neu expression was seen positive 50.7, 47.8 and 41.3%; as well as 49.6% cases were ER+, 49.6% cases were PR+, and HER-2/neu was positive (3+) in 15.8% cases respectively (Mahmoud & Mahmoud, 2014; Nabi *et al*., 2016). And as described breast cancers with positive ER and PR expression are amenable to hormonal manipulation and those with HER2 expression grow and breast faster. Therefore, our patients having higher ER and PR as well as low HER2 indicates that their breast cancer is more likely to respond to hormonal manipulation and less likely to grow and spread faster.

5.2.4 Concordance between the mammographic and histopathologic findings at Mankweng Hospital.

- Positive Predictive Values (PPVs)

The positive predictive value of BIRADS 5 was also 96.9% compared to the PPV of available studies tabulated in the table below:

Author(s)	BIRADS 1	BIRADS 2	BIRADS 3	BIRADS 4	BIRADS 5
Sickles *et al*., (2013) As per ACR BIRADS	0%	0%	0 – 2%	2 – 95%	>95%

Atlas guidelines					
Orel *et al.,* (1999)		0%	2%	30%	97%
Lacquement *et al.* (1999) (PPV is decimal)	0.0	0.04	0.03	0.23	0.92
Lazarus *et al.* (2006) PPV in percentages	-	-	-	4a – 6% 4b – 15% 4c – 53%	91%
Gülsün *et al*. (2003) (PPV in Percentage)	-	-	-	17 – 25%	44 – 64%
Chotiyano *et al* (2013)	-	-	-	-	85%

The BIRADS 5 category in our study has a PPV of 96.9% which is well within the recommendations laid out by the ACR BIRADS atlas 5th edition. The PPV is higher than most of the PPVs tabulated above, and just 0.1% lower than that reported by Orel and colleagues (Orel, Kay, Carol, & Sullivan, 1999). Therefore, the result of the current study is comparable to the available data, suggesting that the mammogram reporting standards at Mankweng Hospital Radiology Department are on par with available data.

In this study BIRADS 4 sub-categories were aggregated into a single entity rather than analyse them individually as 4a, 4b and 4c. BIRADS 4 category had the second highest number of malignant cases with 1 out 6 cases malignant. Within BIRADS 4 category in our study 16,7% of the cases where positive for malignancy, and the percentage falls within the cut-off set out by the BIRADS atlas for category 4. No subcategory PPV was calculated due to the low numbers within the individual BIRADS 4 subcategories.

- Kappa Cohen Statistics, Concordance and Discordance

The measure of concordance between mammography is of utmost importance to ascertain that the involved individuals receive the appropriate care. Significant discordance between the mammography and histopathological report from a percutaneous breast biopsy can be an indication for Surgical excision of breast lesion for repeat histopathological analysis(Liberman *et al.*, 2000). There was high-rate concordant malignancy found in BIRADS 5 category of 31 out of 32. But there was discordant benign in BIRADS 5 of 1 out of 32. A Discordant benign lesion is described as a lesion shows suspicious imaging features with subsequent benign histopathological features (Park *et al.*, 2018). In this setting, it is recommended that the findings be communicated between the radiologist, the histopathologist and the surgeon in order to decide if surgical excision is necessary (Park *et al.*, 2018).

The current study found 95.2% concordance between mammography and histopathological diagnosis when using BIRADS 5 as a cut-off. The kappa value was 0.86 which implies almost perfect agreement between the two methods. The p-value of < 0.05 shows that this is a statistically significant agreement (Table 4).

The concordance of 85.7% concordance between mammography and histopathological diagnosis achieved when using BIRADS 4 or more as a cut-off together with the kappa value of 0.52 and the p-value of < 0.05 implies moderate agreement between the two methods. However, even though the results demonstrate less specificity and PPV with BIRADS 4 cut-off point compared to BIRADS 5, there is higher sensitivity and the negative predictive value (NPV) compared to BIRADS 5 cut-off.

5.3 Conclusion

The study demonstrated agreement between mammography and histopathological diagnosis of breast lesions categorised as BIRADS 4 and 5. The PPV findings are comparable with those of ACR BIRADS guidelines. The result also demonstrates that the reporting of breast lesions detected on mammography according to BIRADS

lexicon in Mankweng Hospital is in keeping with standardised BIRADS reporting guidelines.

5.4 Contributions and recommendations of the study

- The study recommends expansion of the mammography screening project to reach patients earlier.
- We recommend that further research be done within the Mankweng Hospital to assess risk factors and characterise breast lesions in women younger than 40 at Mankweng hospital.
- We recommend a fully digital medical records system, for ease of data access.
- We recommend a study focusing on BIRADS 4 lesions to further assess the subcategory concordance and positive predictive values.
- We recommend a study focusing on imaging and histopathology concordance in lesions categorised as BIRADS 2 and 3.

5.5 Limitations of the study

The relatively small number (n=41) with histopathology was a limitation in the study considering that 880 mammograms were performed in the study period. The lack of histopathological reports for BIRADS 1 to 3 lead to those categories not being included in the study thus contributing to the small number.

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ANNEXURE 1

2022 Research Timeline

	Jan '22	Feb '22	Mar '22	Apr '22	May '22	Jun '22	Jul '22	Aug '22	Sep '22	Oct '22
TREC SUBMISSION										
DATA COLLECTION										
DATA ANALYSIS AND WRITEUP										
SUBMISSION AND CORRECTIONS										

ANNEXURE 2

Data collection tool

STUDY NUMBER:

DEMOGRAPHICS:

AGE RANGE:

1. 18 – 39 years □
2. 40+ □

MAMMOGRAPHY REPORT:

DATE OF STUDY:

a) What is the BIRADS Score? (Tick appropriate box)

1. BIRADS 1 □
2. BIRADS 2 □
3. BIRADS 3 □
4. BIRADS 4 □
5. BIRADS 5 □
6. BIRADS 6 □

HISTOPATHOLOGICAL FINDINGS:

DATE SPECIMEN TAKEN:

a) Is the histopathological diagnosis malignant? (Tick appropriate box)

1. YES □
2. NO □

b) Immunohistochemistry

a. Oestrogen receptor (ER)

1. Positive □
2. Negative □
3. Not available □

b. Progesterone Receptor (PR)

1. Positive □
2. Negative □
3. Not available □

c. HER2

1. Positive □
2. Negative □
3. Not available □

d. and Ki67.

1. 0-15 □
2. >15 □
3. Not available □

ANNEXURE 3

University of Limpopo School Senior Degrees Committee research proposal approval letter

University of Limpopo
Faculty of Health Sciences
School of Medicine

To: **Prof SM Risenga**
Director: School of Medicine

From: **Prof CJ Sutton**
Chairperson: School Senior Degrees Committee

Date: **10 August 2021**

Subject: **Submission of Master of Medicine in Diagnostic Radiology Proposal**

A research proposal of Dr MS Magoro for Master of Medicine in Diagnostic Radiology is hereby submitted for consideration by Faculty Higher Degrees Committee. The proposal was approved by the School Senior Degrees Committee on 15th July 2021.

Title: "An Evaluation of the Concordance between Mammography and Histopathology findings in Women with Breast Lesions at Mankweng Hospital, Limpopo Province"

Kind regards,

Prof CJ Sutton
Chairperson: School Senior Degrees Committee.

Finding solutions for Africa

ANNEXURE 4

University of Limpopo Faculty of Health Sciences research proposal approval letter

University of Limpopo
Faculty of Health Sciences
Executive Dean
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 2149, Fax: (015) 268 2685, Email: tebogo.mothiba@ul.ac.za

DATE: 28 NOVEMBER 2021

NAME OF STUDENT: DR MAGORO MS
STUDENT NUMBER: 201735865
DEPARTMENT: DIAGNOSTIC RADIOLOGY
SCHOOL: MEDICINE
QUALIFICATION: MMED

Dear Student

FACULTY APPROVAL OF PROPOSAL (PROPOSAL NO. FHDC2021/7)

I have pleasure in informing you that your MMED proposal served at the Faculty Higher Degrees Meeting on the 13 OCTOBER 2021 and your title was approved as follows:

Approved Title: "An Evaluation of the Concordance between Mammography and Histopathology findings in Women with Breast Lesions at Mankweng Hospital, Limpopo Province".

Note the following:

Ethical Clearance	Tick One
Requires no ethical clearance Proceed with the study	
Requires ethical clearance (TREC) (apply online) Proceed with the study only after receipt of ethical clearance certificate	√

Yours faithfully

Prof T.M Mothiba
Chairperson

CC: **Supervisor: Dr F Ooko**

Finding solutions for Africa

ANNEXURE 5

Turfloop Research Ethics Committee Ethics Clearance Certificate

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email: anastasia.ngobe@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: **19 April 2022**

PROJECT NUMBER: **TREC/66/2022: PG**

PROJECT:

Title:	An Evaluation of the Concordance between Mammography and Histopathology Findings in Women with Breast Lesions at Mankweng Hospital, Limpopo Province.
Researcher:	MS Magoro
Supervisor:	Dr. F Ooko
Co-Supervisor/s:	N/A
School:	Medicine
Degree:	Master of Medicine in Diagnostic Radiology

PROF D MAPOSA
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

Finding solutions for Africa

ANNEXURE 6

Limpopo Department of Health permission to conduct research in departmental facilities

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Department of Health

Ref : LP_2022-04-022
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

Machuene Magoro

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

An evaluation of the concordance between mammography and Histopathology findings in women with breast lesions at Mankweng hospital, Limpopo province

1. Permission to conduct research study as per your research proposal is hereby Granted
2. Kindly note the following:
   a. Present this letter of permission to the office of District Executive Manager a week before the study is conducted.
   b. The approval is **ONLY** for **Mankweng Hospital.**
   c. In the course of your study, there should be no action that disrupts the routine services, or incur any cost on the Department.
   d. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   e. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   f. The approval is only valid for a 1-year period.
   g. If the proposal has been amended, a new approval should be sought from the Department of Health
   h. Kindly note that, the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated

_____ 11/05/2022

Head of Department **Date**

pp

Private Bag X9302 Polokwane
Fidel Castro Ruz House, 18 College Street. Polokwane 0700. Tel: 015 293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

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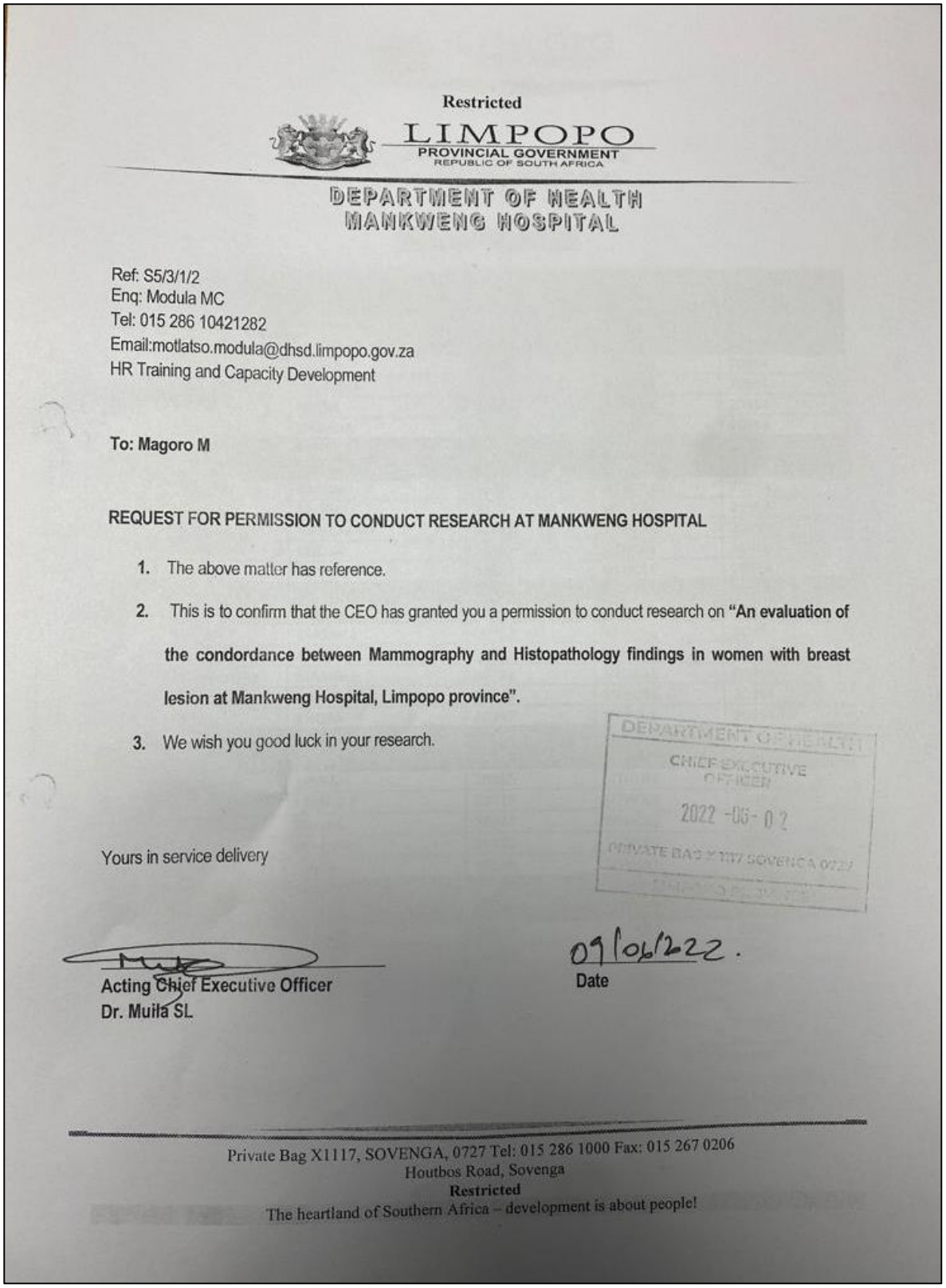
ANNEXURE 7

Permission letter to conduct research in Mankweng Hospital



Restricted

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH
MANKWENG HOSPITAL

Ref: S5/3/1/2
Enq: Modula MC
Tel: 015 286 10421282
Email:motlatso.modula@dhsd.limpopo.gov.za
HR Training and Capacity Development

To: Magoro M

REQUEST FOR PERMISSION TO CONDUCT RESEARCH AT MANKWENG HOSPITAL

1. The above matter has reference.
2. This is to confirm that the CEO has granted you a permission to conduct research on **"An evaluation of the condordance between Mammography and Histopathology findings in women with breast lesion at Mankweng Hospital, Limpopo province".**
3. We wish you good luck in your research.

DEPARTMENT OF HEALTH
CHIEF EXECUTIVE OFFICER
2022 -06- 07
PRIVATE BAG X1117 SOVENGA 0727

Yours in service delivery

09/06/2022.

Acting Chief Executive Officer
Dr. Muila SL

Date

Private Bag X1117, SOVENGA, 0727 Tel: 015 286 1000 Fax: 015 267 0206
Houtbos Road, Sovenga
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ANNEXURE 8
Language editor certificate

Arowana Health and Research Consulting

18 Touws Road

Ext 3

Norkem Park

Kempton Park

1618

011

10 October 2022

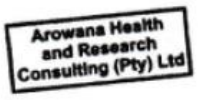
Ref: Certificate of editing

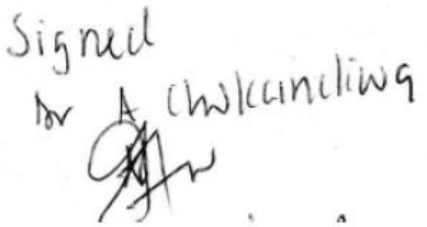
This serves to confirm that I have language edited and formatted the mini-dissertation of

Dr Machuenne Stephen Magoro

Student number: **201735865**

Entitled **AN EVALUATION OF THE CONCORDANCE BETWEEN MAMMOGRAPHY AND HISTOPATHOLOGY FINDINGS IN WOMEN WITH BREAST LESIONS AT MANKWENG HOSPITAL, LIMPOPO PROVINCE**





Dr A.T Chikandiwa *(MBChB, MPH, PhD)*

Senior Researcher: University of the Witwatersrand

Technical Head: Arowana Health and Research Consultants

Email: ahrcsa@gmail.com

Landline: 011 391 2507