Cape Peninsula
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BI-RADS FINAL ASSESSMENT CATEGORIES IN BREAST CANCER PATIENTS

by

TASNEEM DANIELS **Student number: 206094574**

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Supervisors: Ms F. Isaacs & Mr A. Speelman

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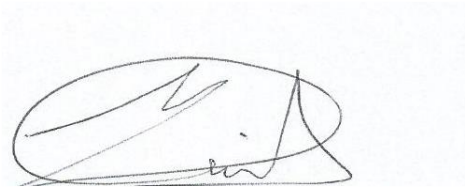
DECLARATION

I, **Tasneem Daniels**, declare that the contents of this thesis represent my own unaided work, and that the thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology.



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Signed **Date**

ABSTRACT

INTRODUCTION: The Breast Imaging Reporting and Data System (BI-RADS) was developed by the American College of Radiology (ACR). The BI-RADS is an internationally accepted method of assessing and reporting on mammograms and breast ultrasound images. The BI-RADS consists of a lexicon (descriptors) and assessment categories. The ACR aimed to standardise mammography reporting and placing the findings in the appropriate assessment category. The aim of this study was to establish the accuracy of the BI-RADS assessment categories for mammography and breast ultrasound images in women diagnosed with breast cancer.

METHOD: Data were retrieved from 77 patients who were diagnosed with breast cancer from 1 January 2013 to 31 December 2014. Seven did not meet the inclusion criteria and were excluded. The study sample size was 70 (*n*=70) patients.

All mammography reports included a BI-RADS assessment category of all patients diagnosed with breast cancer within the study period. These reports were analysed and compared with histopathology results.

The BI-RADS assessment category and descriptors were collected from the mammogram reports; the histopathology report indicated the type of breast cancer. All reports were obtained from the patients' folders at the research site. In addition, questionnaires were distributed among radiologists to assess whether their experience and training had an influence on the accuracy of reporting in the BI-RADS assessment categories. Descriptive and inferential statistical analysis was used for data analysis.

RESULTS: The most common malignancy diagnosed was invasive ductal carcinoma with a total of 70% (*n*=54), followed by ductal carcinoma in situ with 10.4% (*n*=8) and invasive lobular carcinoma with 9.1% (*n*=7).

The histology results confirmed breast cancer for all BI-RADS 4 and 5 assessment categories. The mammogram was able to detect 93.5% of abnormalities and breast ultrasound 84.4% of abnormalities in this study sample. Breast ultrasound was used as an adjunct to mammography and hence an overall combined diagnostic rate was 100%.

Mammography descriptors: The more common malignancy findings were spiculated mass margin, 35.1% (*n*=27). Ultrasound descriptors: The more common malignancy findings were

hypoechoic echo pattern, 55.8% (*n*=43). There was no significant association (*p*=0.152) between the radiologists' years of experience and BI-RADS 3, 4 and 5 assessment category reporting. Of the 15 responses, 67% agreed that the BI-RADS standardises breast imaging reporting and reduces confusion, 33% agreed that the BI-RADS allows better communication between radiologists and referring physicians, and 40% agreed that the BI-RADS clarifies further management for patients by helping to stratify risk management.

CONCLUSION: The outcome of this study indicated that the use of BI-RADS assessment categories is useful for predicting the likelihood of malignancy when used correctly. The outcome of BI-RADS 4 and BI-RADS 5 had a positive predictive value of 100%, which corresponded well with histology results. The descriptor findings suggested that spiculated mass margins, irregular-shaped masses, hypoechoic echo pattern and posterior shadowing were high predictors of malignancy and warranted a placement in the BI-RADS 5 assessment category.

Keywords: Breast Imaging Reporting and Data System (BI-RADS), BI-RADS lexicon, mammography, breast ultrasound, breast cancer.

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DEDICATION

To my Creator and Sustainer for the knowledge to complete this thesis

I dedicate this thesis to my parents
My mother, Zainonesa Daniels, and late father, Gasant Daniels
&
My husband, Shu-aib Brinkhuis
&
My sisters, Rashieda Daniels and Waseema Craven

Thank you for all the love, encouragement, support and sacrifices that you have made for me.

ABBREVIATIONS AND ACRONYMS

ACR	-	American College of Radiology
ASE	-	Amorphous Selenium
BI-RADS	-	Breast Imaging Reporting and Data System
BRCA	-	Breast Cancer gene
CANSA	-	Cancer Association of South Africa
CC	-	Craniocaudal
DCIS	-	Ductal Carcinoma in Situ
FDA	-	Food and Drug Administration
FNA	-	Fine-Needle Aspiration
HRT	-	Hormone Replacement Therapy
MLO	-	Mediolateral Oblique
MQSA	-	Mammography Quality Standards Act
PACS	-	Picture Archiving and Communication System
PPV	-	Positive Predictive Value

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CHAPTER ONE

AN OVERVIEW OF THE STUDY

1.1 Introduction

Breast cancer is the most common cancer among women in the world; 1.7 million new cases were diagnosed in 2012 (World Health Organisation). In South Africa, according to the National Cancer Registry statistics, breast cancer is the most common cancer in women. The life-time risk of women developing breast cancer in South Africa is 1:45 (South African National Cancer Registry, 2012:5). South Africa has a high mortality rate associated with breast cancer. In 2012 breast cancer was the eighth top cause of death among women in the Western Cape province, with the highest mortality in the West Coast region (Mbombo, 2015).

Breast cancer is an important health problem in South Africa and the number of diagnosed cases and mortality rates have increased over the years (South African National Cancer Registry, 2012:5). Today there are more awareness campaigns, screening programmes and imaging tools available to the public to detect breast cancer in its early stages. Mammography is the 'gold standard' for detecting breast cancer in its early stages. It has been proved that mammography reduces the breast cancer mortality rate (Morrell et al., 2012:29; Puliti et al., 2012:5). The US Mammography Quality Standards Act of 1997 mandated that each mammogram report should include a language of final assessment similar to that in the BI-RADS (Burnside et al., 2009:854-858).

The American College of Radiology (ACR) developed the Breast Imaging Reporting and Data system (BI-RADS). It is an internationally accepted method of assessing and reporting on mammogram and breast ultrasound images. The BI-RADS consists of final assessment categories according to the mammographic and ultrasound findings (Sickles et al., 2013:180). The final assessment categories have been approved by the US Food and Drug Administration (FDA).

The BI-RADS includes various descriptors for mammographic and breast ultrasound images as well as a reporting structure that involves assessment categories. These descriptors are also known as the mammography and ultrasound lexicon. The BI-RADS 4 assessment category is predictive of malignancy (30%), while the BI-RADS 5 assessment category is highly suggestive of malignancy (95%); both BI-RADS 4 and 5 assessment categories recommend biopsy (American College of Radiology, 2013). The BI-RADS recommends a structure for reporting which includes indication of the examination, description of the overall breast composition, clear description of important findings, comparison with previous examinations, and assessment and management (D'Orsi et al., 2013:168).

The BI-RADS is used internationally and many studies have been done. These concluded that the BI-RADS standardises breast imaging reporting and helps to predict the likelihood of malignancy (Liberman et al., 1998:35; Orel et al., 1999:845; Lazarus et al., 2006:385; Burnside et al., 2007:388; Kim et al., 2008:1209). To our knowledge, a few studies on the BI-RADS have been conducted in South Africa. However, there were some limitations in these studies: limited sample size and breast cancer cases that did not include both mammography and ultrasound imaging (Cupido et al., 2013:251-254).

The research site is a well-established radiology department situated in the Western Cape, South Africa, which uses the BI-RADS for mammography and breast ultrasound reporting. This study aimed to obtain data on the imaging screening tool (BI-RADS) for detection of breast cancer as there appeared to be a lack of studies assessing the accuracy of this reporting system.

1.2 Rationale for the research

The purpose of this study was to evaluate the accuracy of the BI-RADS final assessment categories in patients diagnosed with breast cancer using histopathology results as the gold standard as well as to evaluate the accuracy of breast imaging modalities such as mammography and ultrasound.

1.3 Research question

How accurate are the BI-RADS assessment categories when applied in the diagnosis of breast cancer in women?

1.4 Research objectives

1.4.1 Main objective

The main objective was to establish the accuracy of the BI-RADS assessment categories in mammography and breast ultrasound imaging reporting compared with the histopathology results used as the gold standard.

1.4.2 Subsidiary objectives

Subsidiary objectives were:

1. To establish the breast ultrasound findings in the study sample versus the BI-RADS ultrasound lexicon.

2. To establish the mammography findings in the study sample versus the BI-RADS mammography lexicon.

3. To determine whether radiologists' level of experience and training had an influence on the accuracy the BI-RADS lexicon classification.

1.5 Overview of the methodology

Data were obtained from a well-established breast imaging radiology department situated in the northern suburbs of the Cape Metropole, Western Cape, South Africa. A convenient sampling method was employed during this retrospective study.

The mammogram protocol at the research site included right and left craniocaudal and right and left mediolateral oblique views of the breast. A breast ultrasound formed part of the mammogram examination.

The BI-RADS assessment categories of adult women diagnosed with breast cancer between 2013 and 2014 and referred for a mammogram examination and concurrent breast ultrasound, were analysed and compared with the histopathology. A final sample size of 70 met the inclusion criteria.

A data sheet was used to record the raw data. Data retrieved included the following variables: age, clinical history, histopathology results, BI-RADS lexicon mammogram and ultrasound results, radiologists' years of experience and training. The data were analysed using descriptive statistical analysis (numerical discrete measurement for determining the percentage, mean and standard deviation of breast cancer cases and level of radiologist experience and training) and inferential statistics (chi square test; $p<0.05$). The BI-RADS assessment categories were compared with the histopathology results using IBM SPSS cross-tabulation.

Ethics approval was granted by the Faculty of Health and Wellness Sciences Research Ethics Committee of the Cape Peninsula University of Technology. Approval for data collection was granted by the research site.

1.6 Summary and overview of results

The most common malignancy diagnosed was invasive ductal carcinoma with a total of 70% (*n*=54) cases out of 77 cancers detected, followed by ductal carcinoma in situ with 10.4% (*n*=8) and invasive lobular carcinoma with 9.1% (*n*=7). The histology results confirmed breast cancer for all BI-RADS 4 and 5 assessment categories, and confirmed breast cancer in all BI-RADS 3 assessment diagnoses, that is, the probability of malignancy ≥ 2%.

Mammography descriptors: The more common malignancy findings of the 77 breast cancers detected were spiculated mass margin 35.1% (*n*=27) followed by suspicious morphology calcifications 28.6% (*n*=22). Ultrasound descriptors: The more common malignancy findings of the 77 breast cancers detected on ultrasound of the breast were hypoechoic echo pattern

55.8% (*n*=43) followed by posterior shadowing 37.7% (*n*=29). The mammogram was able to detect 93.5% abnormalities, and breast ultrasound 84.4% abnormalities in this study population. Breast ultrasound was used as an adjunct to mammography and hence an overall combined diagnostic rate was 100%.

Fifteen radiologists completed the questionnaire. There was no significant association *(p*=0.152) between radiologists' years of experience and BI-RADS 3, 4 and 5 assessment category reporting. Of the 15 responses, 67% agreed that the BI-RADS standardises breast imaging reporting and reduces confusion, 33% agreed that the BI-RADS allows better communication between radiologists and referring physicians, and 40% agreed that the BI-RADS clarifies further management for patients by helping to stratify risk management. All responses were in agreement that the BI-RADS is excellent and very effective; most importantly, if adhered to, the BI-RADS provides universal language, uniformity and prescriptive care.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

Relevant literature was reviewed in this chapter to evaluate the breast imaging reporting and data system (BI-RADS) used in mammography and breast ultrasound examinations for the detection of breast cancer.

The literature review starts with an overview of the BI-RADS, which includes the lexicon and assessment categories. The following topics have also been included in this literature review: the role of mammography and breast ultrasound in the detection of breast cancer; biopsy techniques; mammography and ultrasound appearance of breast pathology; global breast cancer statistics; and breast cancer risk factors. All literature reviewed is presented as a theoretical framework to enhance the understanding of the accuracy of BI-RADS as a reporting tool and associated findings on breast cancer and the role of breast imaging.

2.2 Breast Imaging Reporting and Data System

The American College of Radiology (ACR) developed the BI-RADS (Breast Imaging Reporting and Data System). It is an internationally accepted method of assessing and reporting mammograms and breast ultrasound images. The ACR aimed to provide a standardised mammographic reporting method to improve communication, reduce confusion regarding mammographic findings, aid research and facilitate outcome monitoring (D'Orsi et al., 2013:27).

The BI-RADS contains important components including: (1) a lexicon of descriptors; (2) a recommended reporting structure, including final assessment categories with accompanying management recommendations; and (3) a framework for data collection and auditing. The BI-RADS includes final assessment categories that reflect the radiologist level of suspicion for malignancy. The first BI-RADS introduced in 1993 included recommendations for mammographic imaging and an overall structure for mammography reports and mammographic density. The ACR developed the first version of the ultrasound BI-RADS lexicon in 2003 in order to standardise breast lesion characterisation with ultrasound as with mammography. The current version of BI-RADS used today is the *BI-RADS Atlas*, 5th edition, which was released by the ACR in 2013; it includes both mammography and ultrasound descriptors (American College of Radiology, 2013).

2.2.1 BI-RADS lexicon

There are various descriptors in the BI-RADS approved by the ACR (2013:29, 34-35) for mammographic findings: breast composition, masses, calcifications, architectural distortion, asymmetries, intra-mammary lymph node, skin lesion, solitary dilated duct, associated features and location of lesion (Table 3.1).

The BI-RADS lexicon serves as an important tool for mammographic reporting; the descriptors for suspicious microcalcifications help predict the risk of malignancy (Burnside et al., 2007:388). The morphology of malignant calcifications includes: fine pleomorphic micro-calcifications and linear branching or segmental distribution, amorphous microcalcifications and coarse heterogeneous calcifications (Burnside et al., 2007:388; Bent et al., 2010:1378; Do Nascimento et al., 2010:94; Badan et al., 2013:210). Architectural distortion and asymmetrical density have been reported as other morphology criteria for malignancy (Wiratkapun et al., 2010: 830).

The breast ultrasound lexicon consists of various descriptors described by the ACR (2013:259): tissue composition, masses, calcifications, associated features and special cases (Table 3.2). The BI-RADS breast ultrasound lexicon shows accuracy in differentiating between benign and malignant lesions (Hong et al., 2005:1260; Heinig et al., 2008:578; Do Nascimento et al., 2010:91; Badan et al., 2013:213); and significant diagnostic reliability especially in dense breast tissue (Abdel-Gawad et al., 2014:1306). Masses in particular can be distinguished by margin, shape, orientation, echo pattern and posterior features on breast ultrasound. The most common descriptors found for malignancy in patients diagnosed with breast cancer were spiculated, microlobulated, indistinct and angular mass margins, irregular shape, non-parallel orientation and posterior shadowing (Hong et al., 2005:1261-1262; Do Nascimento et al., 2010:94; Badan et al., 2013:212; Elverici et al., 2015:192; Trindade-Pacheco et al., 2016:3-4; Yoon et al., 2016:321).

2.2.2 BI-RADS assessment categories

According to the Food and Drug Administration. Department of Health and Human Services (1997:55925), it is mandatory that an assessment category be incorporated in the mammography report. In addition, the assessment categories are to be used by interpreting physicians to evaluate a mammogram ranging from ‘negative’ to ‘highly suggestive of malignancy’ (FDA, 1997:55926). Each mammographic examination requires a single assessment. An overall assessment of the breast is required to be stated at the end of the entire report. In addition, a mammography examination performed concurrently with a breast

ultrasound requires a single final BI-RADS assessment category at the end of the report (FDA, 1997:55926).

The BI-RADS assessment categories range from category 0 to category 6. Category 0 indicates an incomplete exam and additional imaging evaluation such as additional mammographic views, breast ultrasound or prior mammograms for comparison should be considered. The BI-RADS category 1 indicates a negative mammogram in which no benign or malignancy findings have been described in the report; the results indicated a normal mammogram. The BI-RADS category 2 indicates a negative mammogram with at least one benign finding and the likelihood of malignancy is zero (Sickles et al., 2013:180).

The BI-RADS category 3 indicates a probably benign finding in which the finding has a ≤ 2% likelihood of malignancy; however, the characteristics of the finding are essentially 0% likelihood of malignancy (Bent et al., 2010:1382; Badan et al., 2013:209; Sickles et al., 2013:182). The recommendation for category 3 is a six-month follow-up to establish stability of the finding; after surveillance the result will indicate appropriate management. It is recommended that category 3 should be made by physicians only after completion of diagnostic breast imaging examination instead of screening mammography (ACR, 2013: 195). It is essential that lesions are thoroughly evaluated before placing them into the BI-RADS 3 final assessment category (Baum et al., 2011:61; Alimoğlu et al., 2012:10).

Many studies support the BI-RADS category 3 which result in a relatively low malignancy rate ≤ 2% (Orel et al., 1999:845; Kim et al., 2008:1209; Raza et al., 2008:776; Baum et al., 2011:61; Chae et al., 2016:666) with an overall high negative predicative value of 99.2% (Do Nascimento et al., 2010:94; Alimoğlu et al., 2012:3). Not only does BI-RADS category 3 reduce the number of benign biopsies (Chae et al., 2016:666; Lee et al., 2018:1), it is also more cost effective than to do a biopsy (Alimoğlu et al., 2012:3; Giess et al., 2012:1943).

The BI-RADS category 4 is subdivided into 4A, 4B and 4C. Within this assessment category, a wide range of likelihood of malignancy is covered; findings are sufficiently suspicious to justify a recommendation for a biopsy. Category 4A indicates low suspicion for malignancy: the likelihood of malignancy ranges is > 2% to ≤ 10% (ACR, 2013:199; Sickles et al., 2013:180). According to Giess et al. (2012:1943), the incidence of malignancy in category 4A is less than 2%; however, other studies indicated a positive predicative value of malignancy in category 4A of 4.4%, 10% and 6% (Lazarus et al., 2006:385; Burivong & Amornvithayacharn, 2011:728; Yoon et al., 2016:322).

Category 4B indicates moderate suspicion of malignancy; the range of likelihood of malignancy is > 10% to ≤ 50% (Sickles et al., ACR, 2013:180). Studies have indicated the positive predictive value for malignancy in category 4B in the range from 15% to 46.2% (Lazarus et al., 2006:385; Bent et al., 2010:1378; Burivong & Amornvithayacharn, 2011:728; Chaiwerawattana et al., 2012:4063; Trindade-Pacheco et al., 2016:1; Yoon et al., 2016:322). The BI-RADS category 4C indicates findings that have a high suspicion of malignancy; the range of likelihood of malignancy is > 50% to < 95% (ACR, 2013). In addition, studies were concordant, indicating a positive predicative value of 58%, 53%, 75%, 79% and 77.8% (Lazarus et al., 2006:385; Bent et al., 2010:1378; Chaiwerawattana et al., 2012:4063; Trindade-Pacheco et al., 2016:1; Yoon et al., 2016:322).

The subdivision of category 4 has been widely supported by previous studies confirming its accuracy as well as aiding referring physicians in making informed decisions on the management of patients.

The BI-RADS category 5 is highly suggestive of malignancy; the likelihood of malignancy is ≥ 95% and a biopsy is required (ACR, 2013:132). Studies have shown that category 5 indicates 100% accuracy in the diagnosis of malignancy (Bent et al., 2010:1378; Badan et al., 2015:209; Yoon et al., 2016:322). In some studies, the accuracy of malignancy in BI-RADS category 5 has been shown to be not less than 90% (Lazarus et al., 2006:385; Heinig et al., 2008:573; Kim et al., 2008:1209; Raza et al., 2008:773).

BI-RADS category 6 is used for patients with a known biopsy report which confirmed a malignancy. These patients usually return for additional imaging prior to complete excision (ACR, 2013:201; Sickles et al., 2013:183).

2.3 The role of mammography and breast ultrasound for breast cancer detection

The ACR (2013:2) recommends annual mammography screening for asymptomatic women aged 40 years and older who have an average breast cancer risk. Women under the age of 40 years with an increased risk, including genetic mutation and first-degree relative with Breast Cancer Gene (BRCA) mutation, should start annual mammography screening at the age of 30 years. It has also been claimed that there is no age limit at which mammography may not be beneficial (Smith et al., 2003:142; ACR, 2013:2).

Mammography is the ‘gold standard’ for detecting breast cancer in its early stages, with excellent prognosis. Studies have shown that mammography screening programmes reduce the breast cancer mortality rate (Morrell et al., 2012:29; Puliti et al., 2012:5; Weedon-Fekjær et al., 2014:1). Mortality reduction varies from 45% to 51% among women aged 50–69 years

(Puliti et al., 2012:5). However, according to Morrell et al. (2012:29), for biennial participation there has been an 18% reduction in breast cancer mortality, whereas screening participants had a 21% reduction in breast cancer mortality. Weedon-Fekjær et al. (2014:1) published similar results in which mammography reduced breast cancer mortality by about 28%. The breast cancer death rate of participants attending a screening programme was 0.6% compared with 1.2% for non-attenders (Puliti et al., 2012:3).

Mammography has the ability to detect all microcalcifications for early detection of malignancies (Taori et al., 2013:40). Microcalcifications are the most common sign of ductal carcinoma in situ (DCIS), where mammography has detected 85–95% of microcalcifications in patients diagnosed with DCIS (Szynglarewicz et al., 2016:146). Breast ultrasound in the past showed poor detection of microcalcifications compared with mammography. However, advanced technology in ultrasound has vastly improved image quality. The detection of microcalcifications by ultrasound has thus increased over the years from 34% to more than 80%; this detection rate is mostly for malignant calcifications and associated carcinoma (Stöblen et al., 2011:2575; Mansour & Adel, 2012:499). Hashimoto et al. (2015:90-91) published similar results where ultrasound had a diagnostic accuracy of 89.8 % for detecting microcalcifications. The detection was higher in necrotic calcifications than in secretory calcifications.

Dense breasts in young women impact negatively on the accuracy of mammography (Alshayookh et al., 2014:88). Breasts consist of fibroglandular tissue and fat; mammographically fibroglandular tissue appears brighter (Yaffe, 2008:1). The appearance of fibroglandular tissue is referred to as mammographic breast density (Boyd et al. 2011:1). The sensitivity of mammography increases over the age of 60 years and ultrasound is more sensitive than mammography in women younger than 45 years with dense breast tissue (Devolli-Disha et al., 2009:131). Ultrasound of breasts with dense tissue provides good visualisation and detection of malignant and benign lesions and other abnormalities (Taori et al., 2013:40). The major advantage of breast ultrasound is excellent visualisation of dense tissue, especially in young women, pregnant women and women with breast augmentation (Taori et al., 2013:40; Alshayookh et al., 2014:88).

Owing to mammographic breast density's being an independent risk factor, it is important that breast ultrasound is used adjunct to a mammogram for high efficiency (Alshayookh et al., 2014:88). Adding single ultrasound adjunct to mammography will increase the detection rate. However, it will also increase the number of false positives (Berg et al., 2008:2151; Scheel et al., 2015:9-10). According to Nelson et al. (2016:226), the rate of false positives was significantly higher in women with risk factors, including first-degree family history of breast

cancer among women aged 40–69 years. The false positive rate was also higher in women with heterogeneously dense breasts than in women with almost entirely fatty breast tissue (Nelson et al., 2016:229).

A study by Fatima et al. (2011:44) concluded that breast ultrasound should be used as a primary screening tool in younger women and used as an adjunct to mammography in older women to reduce missed breast cancer detection. Based on the sensitivity and detection rates of mammography and breast ultrasound, both these imaging modalities have a combined sensitivity as high as 96–100%, which includes women with dense breast tissue and the detection of benign and malignant masses (Houssami et al., 2003:935; Berg et al., 2008:2151; Taori et al., 2013:40).

2.4 Mammography and ultrasound appearance of breast pathology

Ductal carcinoma in situ (DCIS) is a common pre-malignancy finding of the breast pathology represented in 18.7% (Elverici et al., 2015:190) and 22% (Wiratkapun et al., 2010:834) of breast cancer cases. Microcalcifications are a frequent mammographic sign of DCIS, ranging from 68% to 95% (Evans et al., 1994:1307; Gajdos et al., 2002:246; Szynglarewicz et al., 2016:148). The most common ultrasound appearances of patients diagnosed with DCIS were hypoechoic solid masses with irregular shape, indistinct or angular mass margin and normal acoustic transmission. In some cases, architectural distortion and ductal extension are associated with a solid mass. Microcalcifications can be seen within a mass or within a duct (Chiang et al., 2016:495). However, invasive ductal carcinoma presents with a mammographic appearance of architectural distortion (67%), calcifications (25%) and a mass with calcifications (66%) (Gajdos et al., 2002:249).

Invasive lobular carcinoma of the breast accounts for 5 to 15% of all invasive malignancies (Verkooijen et al., 2003:778; Biglia et al., 2007:550). Mammography findings of ILC showed a mass (46.0%), irregular-shaped mass (88.7%), speculated mass margin (71.0%) and isodense mass density (88.7%). Ultrasound findings showed a mass (96.5%), irregular mass shape (92.7%), speculated mass margin (60.6%), hypoechoic mass echogenicity (91.8%) and posterior shadowing (64.2%) (Menezes et al., 2013:3-4).

Mucinous carcinoma is a rare type of breast cancer. The most common appearance of mucinous carcinoma on mammography includes an oval-shaped mass and circumscribed or microlobulated mass margin (Han et al., 2010:26; Ha et al., 2013:296-297). Ultrasound findings of mucinous carcinoma showed an isoechoic, hypoechoic or heterogeneous mass with oval, round or irregular shape. The mass margin presents as circumscribed, microlobulated and indistinct (Han et al., 2010:26; Ha et al., 2013:296-297). Some masses may even have complex cystic and solid components (Lam et al., 2004:1070-1072; Ha et al., 2013:296-297).

Posterior enhancement and vascularity within or adjacent to the mass are also common features of mucinous carcinoma (Lam et al., 2004:1070-1072; Han et al., 2010: 23-26).
The mammographic appearance of medullary carcinoma includes a non-calcified mass or hypoechoic mass with indistinct and microlobulated margins. The most common shape is a round- or oval-shaped mass with posterior acoustic enhancement (Cho et al., 2002:193; Jeong et al., 2012:W482). Architectural distortion and calcifications are less commonly seen (Matheus et al., 2008:380). Tubular carcinoma is mostly found with screening mammography. Mammography tubular carcinoma often presents as an irregular-shaped mass with speculated margins and a mass with central densities (Leibman et al., 1993:263-265; Shin et al., 2007:103-105). Architectural distortion may also be seen on mammography; calcifications however are less commonly seen (Leibman et al., 1993:263-265; Shin et al., 2007:103-105; Vilaverde et al., 2016:1-2). Studies have indicated the appearance of tubular carcinoma on ultrasound: hypoechoic mass, irregular-shaped mass, indistinct, microlobulated and angular margins, posterior shadowing (Sheppard et al., 2000:253-254; Shin et al., 2007:103-105).

2.5 Biopsy techniques

Various biopsy techniques are used for both mammography and ultrasound imaging. Biopsy methods include fine-needle aspiration (FNA), core biopsy also known as ‘tru-cut’ biopsy, and vacuum-assisted biopsy. Core needle biopsy consists of a firing mechanism in which tissue sample is obtained during single-needle insertion compared with vacuum-assisted biopsy which consists of a vacuum-powered mechanism. Multiple tissue samples are obtained during single-needle insertion (Lui & Lam, 2010:3).

Studies have showed that core needle biopsy is more accurate than fine-needle aspiration for breast lesions (Andreu et al., 1998:1468; Rikabi & Hussain, 2013:125; Dimitrov et al. 2016:126; Shashirekha et al., 2017:497). Core needle biopsy is also easy, less expensive and safe compared with fine-needle aspiration (Pagni et al., 2014:452; Dimitrov et al., 2016:126). The vacuum-assisted biopsy retrieves large amounts of tissue samples and the possibility to remove the entire lesion or groups of calcifications is high. However, this method is more expensive but can reduce expenses related to the need for open surgical biopsy or excision (Lui & Lam, 2010:2-3).

2.6 Global breast cancer statistics

In 2012 there were 14.1 million new cancer cases and 8.2 million cancer deaths worldwide. The second most common cancer was breast cancer, resulting in 1.67 million cases diagnosed among women in 2012 (25% of all cancers); this cancer was rated the fifth cause of death with 522 000 cases (Ferlay et al., 2015:E359-E386). The majority of breast cancer cases and deaths occurred among women in less-developed countries. In more-developed countries,

breast cancer was the second cause of death among women (Ferlay et al., 2015:E359-E386). In South Africa, breast cancer is the most common cancer in women of all races with a lifetime risk of 1 in 26 (Herbst, 2017:2). Men may also develop breast cancer, but it is about 100 times less common than in women. The lifetime risk of men getting breast cancer is about 1 in 6 (Herbst, 2017:2).

The incidence of breast cancer in South Africa increased from 2003 to 2013. In 2003 there were 5602 newly diagnosed breast cancer cases compared with 5923 cases in 2008, 6137 cases in 2010 and 8132 cases in 2013 (South African National Cancer Registry, 2003:2; 2008:2; 2010:2; 2013:1) (Figure 2.1).The majority of breast cancer cases diagnosed from 2008 to 2013 were present in black women and the lifetime risk of breast cancer in black women decreased, resulting in 1:52 in 2008 (South African National Cancer Registry, 2008:6) and 1:45 in 2012 (South African National Cancer Registry, 2012:5), with an increase to 1:51 in 2013 (South African National Cancer Registry, 2013:5).

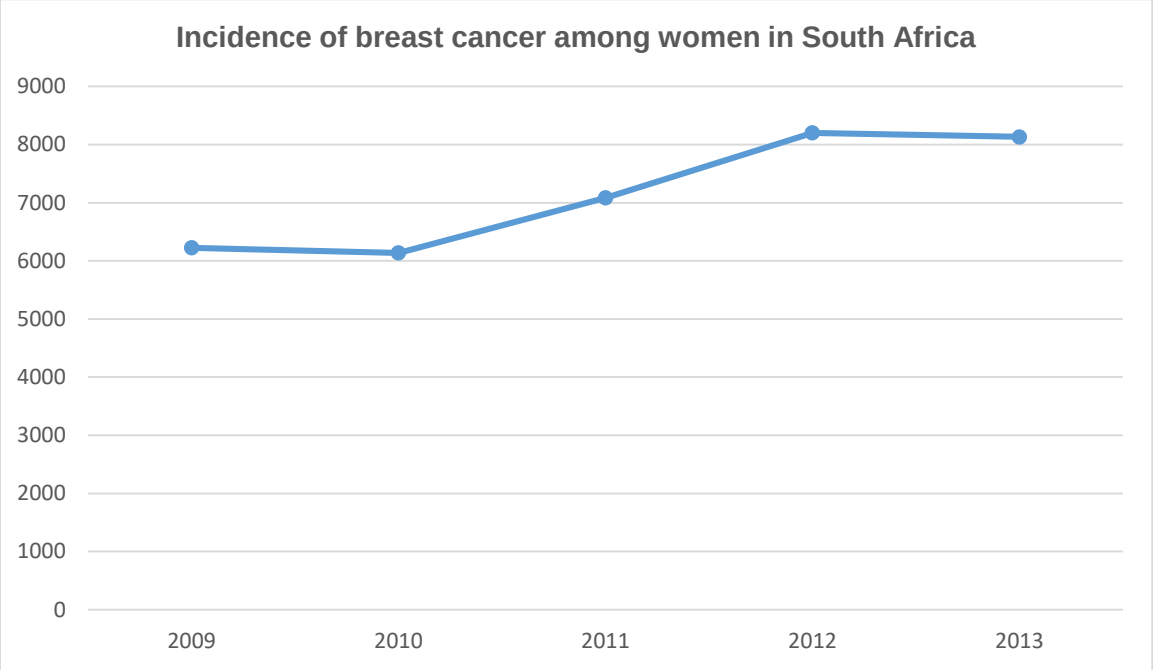

Figure 2.1 Breast cancer statistics in South Africa (2009–2013) (South African National Cancer Registry, 2013)

Among women, there were 6224 breast cancer cases diagnosed in 2009 (South African National Cancer Registry, 2009:2), 6137 cases in 2010 (South African National Cancer Registry, 2010:2), 7085 cases in 2011 (South African National Cancer Registry, 2011:2), 8203 cases in 2012 (South African National Cancer Registry, 2012:1) and 8132 cases in 2013 (South African National Cancer Registry, 2013:1). In 2010 the number of breast cancer cases decreased to 6137 (South African National Cancer Registry, 2010:2) compared with 2009 which had 6224 cases (South African National Cancer Registry, 2009:2). In 2013 the number

decreased to 8132 (South African National Cancer Registry, 2013:1) compared with 2012 which had 8203 cases. The incidence of breast cancer diagnosed in 2012 was the highest, with 8203 cases (South African National Cancer Registry, 2012:1).

According to the American Cancer Society in 2014, it was estimated that about 232 670 new cases of invasive breast cancer would be diagnosed in women in the United States in 2014. It further estimated that 62 570 new cases of carcinoma in situ would be diagnosed and an overall 40 000 women would die from breast cancer in 2014 (American Cancer Society, 2014:9). More than 3000 women die from breast cancer in South Africa annually, of whom 60% are diagnosed with advanced breast cancer (Gonzaga, 2010).

2.7 Breast cancer risk factors

2.7.1 Age

Breast cancer risk increases with age. In South Africa the incidence of breast cancer has increased with age and the majority of diagnosed cases were over 80 years of age in 2012 (South African National Cancer Registry, 2012). In 2013 the age-specific incidence rate per 100 000 for the age group 45–49 years was 125.46, an incidence rate of 151.61 per 100 000 for 75–79 years, and an incidence rate of 235.62 per 100 000 for over 80 years old (South African National Cancer Registry, 2013). Another study concluded that elderly women in the age group of 65–79 years with increased breast density are at greater risk of developing breast cancer (Kerlikowske et al., 2010:3833).

The incidence of women diagnosed with breast cancer at a young age is low, with 12.5% of women diagnosed younger than 35 years of age (Han et al., 2004:1) and 8.8% of women diagnosed younger than 40 years of age (Kheirelseid et al., 2011:1). This incidence of women diagnosed at an early age is more likely to be related to a strong family history of breast cancer and especially women that carry the germline BRCA1 and BRCA2 mutation (Han et al., 2004:1-8). In both studies the histology showed a higher grade and stage of breast cancers (Han et al., 2004:1-3; Kheirelseid et al., 2011:1-3).

There is a worse disease-free survival rate for younger patients diagnosed with breast cancer; the probability of recurrence is greater (Han et al., 2004:1; Kheirelseid et al., 2011:1-3). At five years, the recurrence rate for patients younger than 35 years of age was 30.4%, compared with that of older patients with an 18.7% recurrence rate. At ten years, the recurrence rate for younger patients was 40.1% and for older patients 28.6%. The overall five-year survival rate for patients younger than 35 years of age was 80.0% and 88.5% for older patients (Han et al., 2004:1-3). The study concluded that there is a worse prognosis for overall survival of and recurrence in young breast cancer patients (<35 years old) than for older patients (Han et al., 2004:6).

2.7.2 Breast density

Mammographic breast density is an independent risk factor for breast cancer (Byng et al., 1998:1587-1598; Boyd et al., 2006:2086; Boyd et al., 2007:227; Boyd et al., 2011:1; Schreer, 2009:82-92). There is a link between age and mammographic density: 74% of women with dense breasts were 40–49 years old, 57% women had dense breasts in their 50s, and 36% in their 70s (Checka et al., 2012:W292). There are, however, some postmenopausal women that still have dense breast tissue which reduces the sensitivity of mammography (Checka et al., 2012:W293).

Breast cancer risk increases to 4.6 (95% confidence interval, 1.7–12.6) in premenopausal women with extremely dense breasts and 3.9 (95% confidence interval, 2.6–5.8) in postmenopausal women compared with women of the same age with entirely fatty breasts. Breast cancer was 2.19 times more likely in women with scattered densities, 2.97 times more likely in women with heterogeneously dense breasts and 4.02 times more likely in women with extremely dense breasts (Vacek & Geller, 2004:715-718). Postmenopausal women with extremely dense breasts are at increased risk of breast cancer and should be aware of the added risk of taking hormone therapy, especially a combined hormone therapy of oestrogen and progestin (Kerlikowske et al., 2010:3830-3837).

2.7.3 Hormone Replacement Therapy (HRT)

The use of HRT increases breast cancer risk by 10% for each five years of use with a 36% increased risk after 15 years of HRT use (Ross et al., 2000:330; Beral et al., 2003:419). According to Li et al. (2002), postmenopausal women had a significantly increased risk of breast cancer after long-term use of oestrogen hormone therapy. The risk of breast cancer is much higher when adding progestin to HRT, compared with using oestrogen alone (Ross et al., 2000:330). Women using a combined HRT had a greater risk of invasive ductal and lobular breast carcinoma (Li et al., 2014:481). Canadian women aged 50–69 years had a 9.6% decline in the incidence rate of breast cancer owing to the decreasing use of HRT (De et al., 2010:1489).

2.7.4 Family history

A strong family history remains a risk factor for breast cancer among women. First-degree family history has an estimated risk of 1.8 and second-degree family history has a risk of 1.5 (Nelson et al., 2012:635-648). Women with a BRCA1 mutation have a breast cancer risk of 1.2 for each first-degree family history of breast cancer before the age of 50 years. However, for women with a BRCA2 mutation, the risk of breast cancer increases by 1.7 for each first- degree

family history of breast cancer for women younger than 50 years (Metcalfe et al., 2010:1874). Women with the BRCA mutation have a risk of contralateral breast cancer and risk declines with the age of diagnosis; however, the risk increases with the number of first- degree family members diagnosed with breast cancer (Metcalfe et al., 2011:1384).

2.7.5 Parity status

There was an increased risk of breast cancer among nulliparous women compared with parous women. In addition, women older than 20 years with full-term pregnancy have a higher risk of breast cancer compared with women younger than 20 years with full-term pregnancy (Khalis et al., 2018:4). Another study concluded that the risk of breast cancer in nulliparous women was similar to women in general (Fioretti et al., 1999:1923).

2.8. Summary

Many studies assessing the use of the breast imaging reporting and data system (BI-RADS) have confirmed that when used correctly, the BI-RADS helps predict the risk of breast malignancy. It also serves as a main form of communication with referring physicians and helps patients understand their management options and implications. The most important factors remain early detection, which determines the breast cancer outcome, and mammography and breast ultrasound, which are important imaging tools for early breast cancer detection. The results of this study will add to the body of knowledge on the use of the breast imaging reporting and data system (BI-RADS) to detect breast cancer and the imaging role of mammography and breast ultrasound.

CHAPTER THREE
RESEARCH METHODOLOGY

3.1 Introduction

The aim of this research study was to evaluate the accuracy of the BI-RADS assessment categories in the diagnosis of breast cancer in women, this being the most common cancer among women in South Africa (South African National Cancer Registry, 2012). This study sought to understand how accurate radiologists are when using the BI-RADS lexicon (descriptors) and assessment categories for mammography and breast ultrasound reporting in an urban adult population examined at a private radiology practice in the northern suburbs of the Cape Metropole, Western Cape, South Africa.

This chapter describes the research methodology and research design employed and outlines how the research project was executed.

3.2 Research question

The research question posed for this study was aimed at establishing how accurate the BI RADS assessment categories are when applied in the diagnosis of breast cancer in women.

3.3 Research objectives

3.3.1 Main objective

The main objective was to establish the accuracy of the BI-RADS assessment categories in mammography and ultrasound imaging reporting compared with the histopathology results used as the gold standard.

3.3.2 Subsidiary objectives

Subsidiary objectives are listed below:

1. To establish the accuracy of ultrasound findings versus ultrasound BI-RADS lexicon in the study population.

2. To establish the accuracy of mammography findings versus mammography BI-RADS lexicon in the study population.

3. To determine whether radiologists' level of experience and training had an influence on the accuracy of the BI-RADS assessment category.

3.4 Research design

The study conducted was a retrospective, descriptive quantitative research study aimed at investigating the accuracy of BI-RADS assessment categories as a diagnostic tool used for the diagnosis of breast cancer among female patients. The BI-RADS assessment categories of adult women who had been diagnosed with breast cancer between 2013 and 2014 and referred for a mammogram examination and concurrent breast ultrasound, were analysed and compared with the histopathology results. The data were collected from the mammography report which included the breast ultrasound findings and had a single overall BI-RADS assessment category for both mammography and breast ultrasound findings. The histopathology results for the type of breast cancer were collected from a separate report, all of which were obtained from the patient folders at the study site. In addition, questionnaires were distributed among radiologists at the research site to assess whether their experience and training had an influence on the accuracy of the BI-RADS assessment categories (Appendix A: Participant questionnaire).

3.5 Research site selection

Data were obtained from a well-established breast imaging radiology department situated in the northern suburbs of the Cape Metropole, Western Cape, South Africa. On average about 3400 mammograms are performed per annum, including a breast ultrasound, which is the routine procedure for a mammography examination. The breast facility is operated by qualified and experienced mammographers trained to do mammograms and breast ultrasound examinations.

This centre performs routine mammograms and advanced interventional breast imaging techniques such as breast biopsy techniques, breast hook wire localisations, fine-needle aspiration, as well as breast skin markings under ultrasound and stereotactic guidance. The gold standard biopsy procedures used include ‘tru-cut’ and ‘vacuum’ assisted methods considered to produce excellent breast tissue specimen samples. During the study period, approximately 150–350 interventional procedures were referred to the facility per annum at the time of the study.

All radiologists report on mammograms and breast ultrasound using a single overall BI-RADS lexicon and assessment categories system and descriptive protocol. The BI-RADS system has been used since the establishment of the practice. There are continuous professional development events in the form of seminars, courses and congresses that serve as opportunities for radiologists to undergo training for breast imaging reporting using the BI-RADS lexicon and assessment categories system.

3.6 Research sample selection

3.6.1 Sample size

A convenience sampling method was employed during this study (Welman et al., 2005:69). Data of all patients who had been referred to the radiology practice from 1 January 2013 to 31 December 2014 were retrieved from the Picture Archiving and Communication System (PACS) and biopsy result files. An initial sample of *n*=108 patients was selected. However, a final sample of *n*=70 patients was used as not all the patients from the original sample met the inclusion criteria.

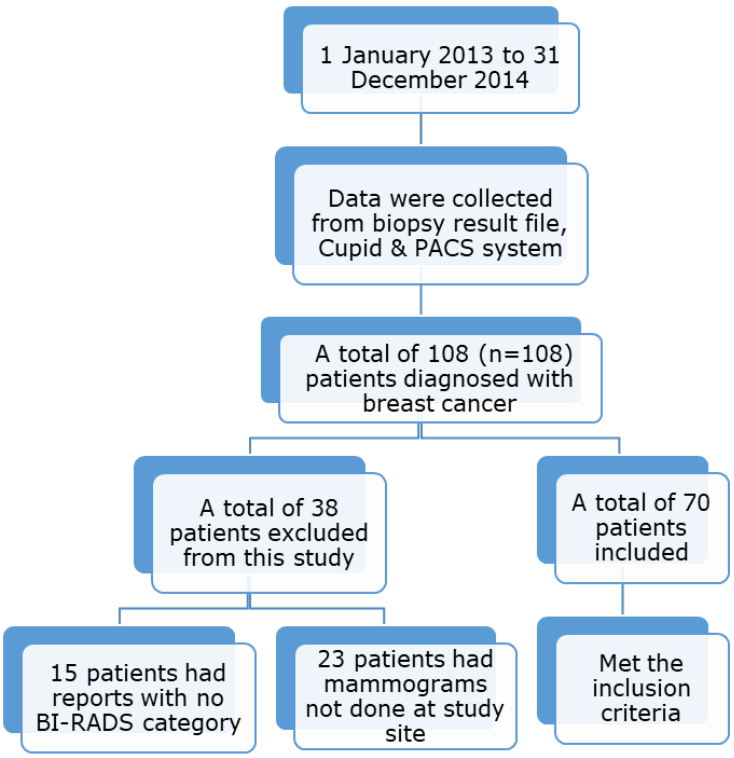

Figure 3.1: The selection of patients for this study

The findings of the results are presented here to give meaning to the main and subsidiary objectives used for this study. The results of demographic data, risk factors of breast cancer and symptoms present at diagnosis have also been included in the data analysis.

3.6.2 Inclusion criteria

The study population included all symptomatic and asymptomatic patients between the ages of 18 and 100 years with confirmed breast cancer referred for a mammogram and breast ultrasound and requiring further evaluation such as breast biopsy and breast localisation during the study period. The inclusion criteria for the study sample were all patients who underwent mammography, ultrasound examination and breast biopsy. Results of vulnerable populations

such as mentally challenged and elderly women were included, as these patients' health and rights were not compromised by the data collection. There was no interaction with patients during the study.

3.6.3 Exclusion criteria

Patients that had been diagnosed with breast cancer before and after the study period (2013 and 2014) were excluded. Data of patients with breast implants, bilateral mastectomy and bilateral reductions for cosmetic reasons with no clinical signs and symptoms were also excluded as this study focused on patients diagnosed with breast cancer.

Male patients as well as patients with no or incomplete BI-RADS assessment category on the mammography report were excluded. Patients who did not undergo all three procedures, namely, a breast ultrasound, mammogram examination at the private radiology practice or without histopathology results were excluded. Patients younger than 18 years of age were also excluded as these participants were not in the specified age group.

3.6.4 Selection of radiologists as participants

Radiologists working at the research site who report on mammograms and breast ultrasound using the BI-RADS were recruited as participants in order to determine whether their level of experience and training had an influence on the accuracy of the BI-RADS assessment categories used in their reports.

There were 33 radiologists employed at the private practice who report on mammograms. All radiologists were requested to complete the questionnaire, distributed via email and as hardcopy. The completed questionnaires were returned via email and/or as hardcopy (Appendix A: Participant questionnaire).

3.6.5 Breast imaging equipment used

3.6.5.1 Breast mammography unit

A digital mammography unit (Siemens Mammomat Inspiration PRIME, Germany) was used for all mammograms and stereotactic biopsy within the study period. An additional tomosynthesis technique was used for patients that needed further evaluation of suspicious areas. Tomosynthesis enables 3D imaging of the breast which allows for better visualisation of breast structures (Phi et al., 2018:1).

3.6.5.2 Breast ultrasound unit

Breast ultrasound formed part of all the mammogram examinations. The Toshiba Xario Prime SSA 660A ultrasound unit was used for all patients within this study period. All patients were scanned with a 7.5 MHz linear transducer probe with a wide field of view.

3.7 Mammogram examination and protocol

The mammogram examination included four images: craniocaudal (CC) of right and left breast and mediolateral oblique (MLO) of right and left breast. Additional mammography views, for example, tomosynthesis and supplementary views, were done for further evaluation of suspicious areas seen on the mammography images (when and if required). The radiologist reviewed the image and results were discussed with the patient; a report was then written with a BI-RADS assessment category and further management suggested. Patients who required further management such as breast biopsy or breast localisation were scheduled for a later date at the same private radiology practice. The images and reports were then stored on the PACS system according to the institutional protocol.

3.7.1 Mammogram protocol

The craniocaudal (CC) view required the patient to stand in front of the mammogram unit with feet facing forward and head turned to the side. The imaging criteria included the entire breast (medial, lateral and subareolar region) with the nipple in profile and 30% of the pectoralis muscle being visualised. By using compression, the breast tissue was evenly distributed to enhance visualisation of any suspicious areas. Patients were provided with a gonadal lead apron for radiation protection. Automatic exposures were used with a tungsten/rhodium filter. Each image was annotated with the correct anatomical marker (Bontrager & Lampignano, 2005:591).

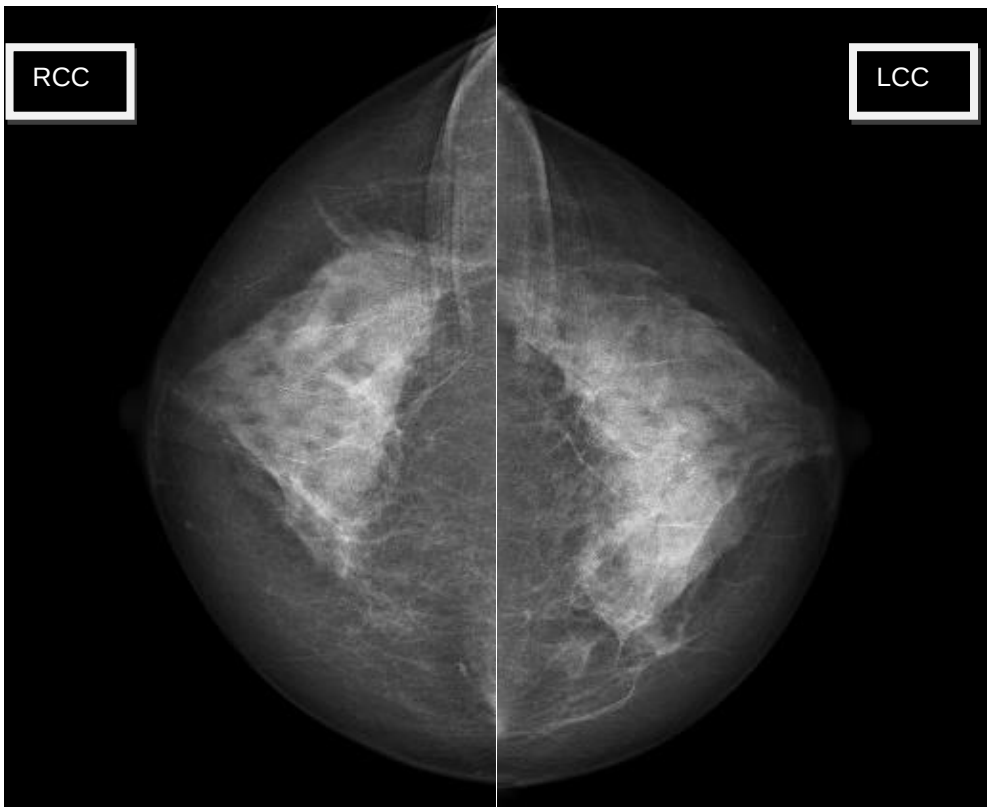

Figure 3.2: Standard right and left craniocaudal (CC) mammography views *(Images courtesy of the radiology practice)*

For the mediolateral oblique (MLO) view, the X-ray tube was turned in a 45° to 50° caudal angle with the patient standing erect facing the unit. The affected arm was raised above the detector of the breast being imaged. The imaging criteria included the entire breast visible from the pectoralis muscle to the level of the nipple. The infra-mammary fold needed to be visible, with the nipple in profile. Patients were further provided with a gonadal lead apron for radiation protection. Automatic exposures were used with a tungsten/rhodium filter. Each image was annotated with the correct anatomical marker. The mammogram examinations were performed by different mammographers at the research site during the study period. All the mammographers are qualified in mammography and the mammographers were trained to use the same technique by following the basic routine mammogram which included right CC, left CC, right MLO, left MLO (Bontrager & Lampignano, 2005: 592).

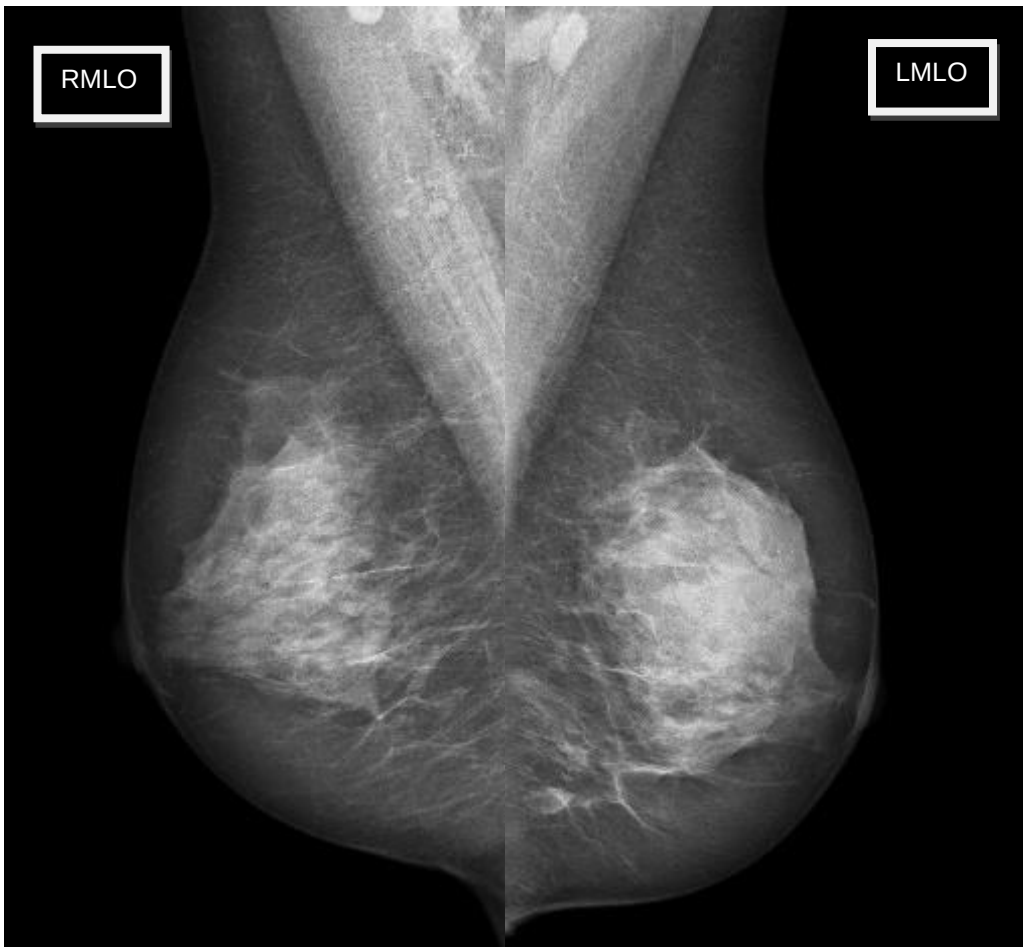

Figure 3.3: Normal standard right and left mediolateral oblique (MLO) mammography views *(Images courtesy of the radiology practice)*

3.7.2 Ultrasound protocol

For the breast ultrasound examination, the patient was supine with the arm raised above the head of the side being scanned. The body is then slightly oblique with the opposite side raised. Various scanning techniques included transverse and longitudinal scanning not parallel to the long axis of the underlying lobar anatomy (Stavros, 2004:46).

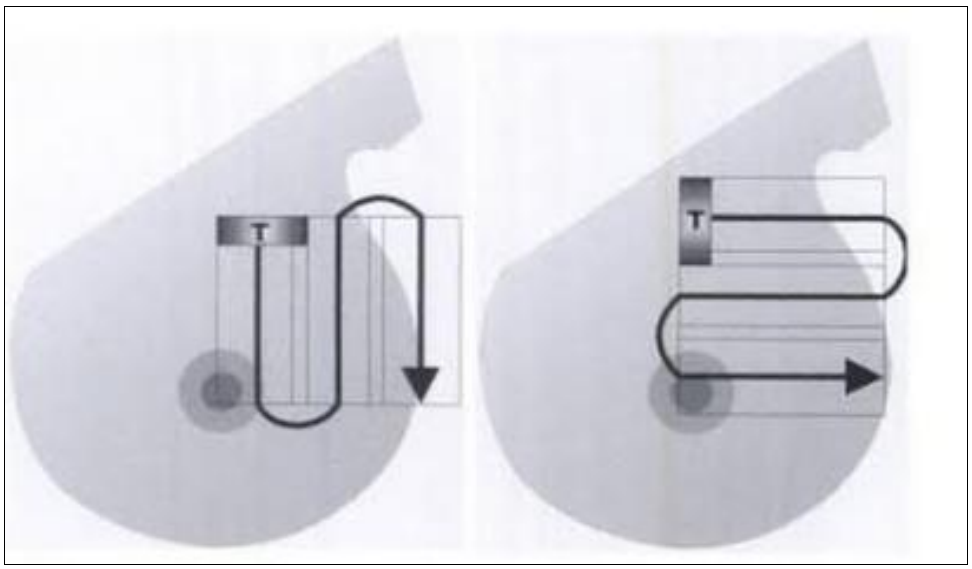

Figure 3.4: Transverse scanning technique (left) and longitudinal scanning technique (right) for breast ultrasound (Stavros, 2004:46)

Another scanning technique used was radial and anti-radial scanning. The breast described and scanned as a clock-face, was scanned starting in the sagittal plane at the 12 o'clock position with the toe of the probe at the nipple and scanning by rotating the probe around the nipple. If pathology was seen in this method, the probe was be rotated 90^0 in the anti-radial plane (Figure 3.4) (Stavros, 2004:47; Ultrasoundpaedia™, 2018).

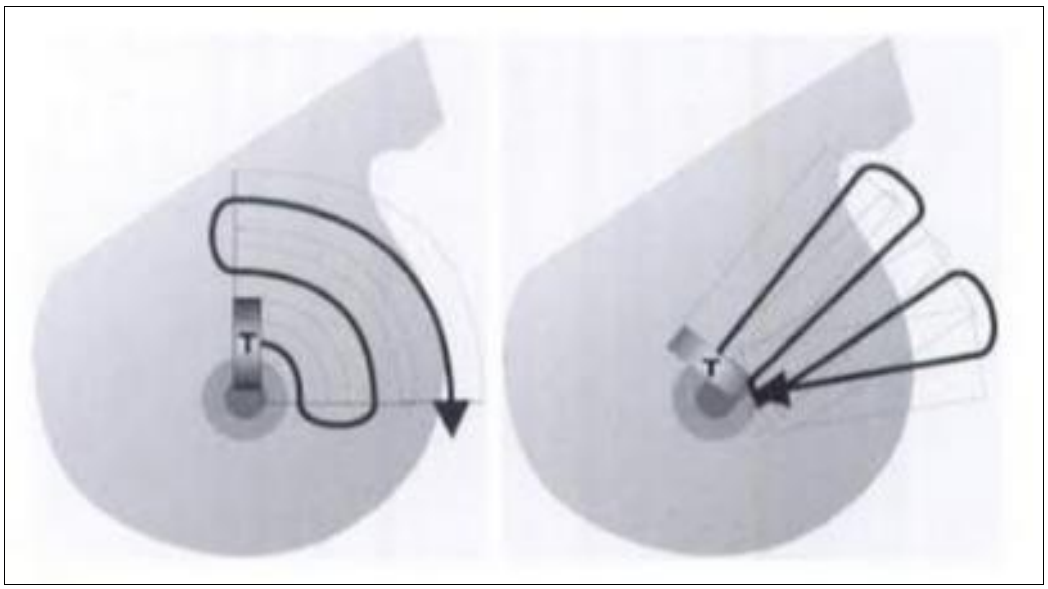

Figure 3.5: Radial scanning technique (left) and anti-radial scanning technique (right) for breast ultrasound (Stavros, 2004: 47)

The scanning method included a basic series of images such as: 12 o' clock, 2 o' clock, 4 o' clock, 6 o' clock, 8 o' clock, 10 o' clock, nipple, axillary tail and axilla (Ultrasoundpaedia™, 2018). Measurements were taken in two planes when pathology was identified and included

the right and left breast with the axillary region and internal mammary nodes. The thickened cortex of the lymph nodes was measured in patients with suspicious masses or areas. Doppler ultrasound was used to determine the presence of vascularity of the area of concern. Ultrasound images and reports were then stored for each patient on the PACS according to institutional protocol. The ultrasound examination was performed by different mammographers and radiologists at the research site during the study period.

3.7.3 BI-RADS mammography and ultrasound lexicon

Based on the evaluation of the mammogram and breast ultrasound images, the BI-RADS lexicon (descriptors) for mammography and breast ultrasound (Appendix D) was used to describe what pathological lesions or areas were seen on these two images (Table 3.1 and Table 3.2).

Table 3.1 : BI-RADS mammography lexicon (ACR 2013; Sickles et al., 2013:34-35)

BI-RADS Descriptives

Breast composition	a. The breasts are almost entirely fatty b. There are scattered areas of fibro-glandular density c. The breasts are heterogeneously dense, which may obscure small masses d. The breasts are extremely dense, which lowers the sensitivity of mammography	
Masses	Shape	Oval
		Round
		Irregular
	Margin	Circumscribed
		Obscured
		Microlobulated
		Indistinct
		Spiculated
	Density	High density
		Equal density
		Low density
		Fat-containing
Calcifications	Typically benign	Skin
		Vascular
		Coarse or 'popcorn like'
		Large rod-like
		Round
		Rim
		Dystrophic
		Milk of calcium
		Suture
	Suspicious morphology	Amorphous
		Coarse heterogeneous
		Fine pleomorphic
		Fine linear or fine-linear branching
	Distribution	Diffuse
		Regional
		Grouped
		Linear
		Segmental
Architectural distortion		
Asymmetries	Asymmetry	
	Global asymmetry	
	Focal asymmetry	
	Developing asymmetry	
Intramammary lymph node		
Skin lesions		
Solitary dilated duct		
Associated features	Skin retraction	
	Nipple retraction	
	Skin thickening	
	Trabecular thickening	
	Axillary adenopathy	
	Architectural distortion	
	Calcifications	
Location of lesion	Laterality	
	Quadrant and clock face	
	Depth	
	Distance from the nipple	

Table 3.2: BI-RADS ultrasound lexicon (ACR, 2013; Mendelson et al., 2013:256)

BI-RADS Descriptives		
Tissue composition	a. Homogeneous background echotexture – fat b. Homogeneous background echotexture – fibroglandular c. Heterogeneous background echotexture	
Masses	Shape	Oval
		Round
		Irregular
	Orientation	Parallel
		Not parallel
	Margin	Circumscribed
		Angular
		Microlobulated
		Indistinct
		Spiculated
	Echo pattern	Anechoic
		Hyperechoic
		Complex cystic and solid
		Hypoechoic
		Isoechoic
		Heterogeneous
	Posterior features	No posterior features
		Enhancement
		Shadowing
		Combined pattern
Calcifications	Calcifications in a mass	
	Calcifications outside a mass	
	Intraductal calcifications	
Associated features	Architectural distortion	
	Duct changes	
	Skin changes	Skin thickening
		Skin retraction
	Oedema	
	Vascularity	Absent
		Internal vascularity
		Vessels in rim
	Elasticity assessment	Soft
		Intermediate
		Hard
Special cases	Simple cyst	
	Clustered microcysts	
	Complicated cyst	
	Mass in or on skin	
	Foreign body including implants	
	Lymph nodes – intramammary	
	Lymph nodes – axillary	
	Vascular abnormalities	AVMs (arteriovenous malformations/pseudoaneurysms
		Mondor disease
	Postsurgical fluid collection	
	Fat necrosis	

3.7.4 BI-RADS final assessment categories

Following the BI-RADS lexicon, a BI-RADS final assessment category was given for further patient management (Table 3.3). Patients diagnosed with BI-RADS 4 and BI-RADS 5 categories required a biopsy as follow-up procedure, and were scheduled for a later date at the same radiology practice.

Table 3.3: BI-RADS final assessment categories (ACR 2013)

Assessments	**Management**	**Likelihood of cancer**
BI-RADS 0: Incomplete – Need additional Imaging evaluation	Recall for additional imaging	N/A
BI-RADS 1: Negative	Routine screening	Essentially 0% likelihood of malignancy
BI-RADS 2: Benign	Routine screening	Essentially 0% likelihood of malignancy
BI-RADS 3: Probably benign	Short-interval follow-up or continued surveillance	>0% but ≤2% likelihood of malignancy
BI-RADS 4: Suspicious 4A – Low suspicion for malignancy 4B – Moderate suspicion for malignancy 4C – High suspicion for malignancy	Tissue diagnosis	>2% but <95% likelihood of malignancy ≥2% ≤10% likelihood of malignancy ≥10% ≤50% likelihood of malignancy ≥50% ≤95% likelihood of malignancy
BI-RADS 5: Highly suggestive of malignancy	Tissue diagnosis	≥95% likelihood of malignancy
BI-RADS 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

3.8 Data collection

The data consisted of the mammography reports, ultrasound reports and histopathology results of the 70 patients diagnosed with breast cancer during the period of data collection. All imaging reports were retrieved from the PACS. Data collected for each patient included age, clinical symptoms, breast cancer risk factors (hormone replacement therapy, family history and

parity status) and previous surgical history (Appendix C). In addition, the level of radiologist training and experience in mammography and ultrasound BI-RADS lexicon descriptors and BI-RADS assessment categories were also recorded (Appendix A: Participant questionnaire).

Each eligible patient was assigned a numerical and chronological participant number starting from 001. Each patient's mammography, ultrasound and histopathology results were transferred to the data-collection sheet corresponding to the participant number for each patient. The patient's participant number was used throughout the data-collection and data-analysis phase. Patient names and hospital identification numbers were not used for data analysis, but only to cross-reference the three different results during the data-collection phase. Thereafter their names were not used any further in order to protect their identities and maintain their privacy and confidentiality.

The mammography and ultrasound findings were recorded in the same detail on the raw data sheet as stated on the initial radiology or histopathology report. The findings on the mammogram and ultrasound images were grouped into codes for the analysis phase. Mammography findings were grouped into the following codes: code 1 – breast mass, code 2 – breast mass with associated features, code 3 − microcalcifications, code 4 – microcalcifications with asymmetry or associated features, code 5 – breast density with a mass or asymmetry or associated features, code 6 – asymmetry, code 7 – asymmetry, with a mass, or associated features. The ultrasound findings were grouped into the following codes: code 1 – breast mass, code 2 – breast mass with posterior features, code 3 – breast mass with associated features, code 4 – calcifications, code 5 – calcifications with associated features, code 6 – special cases (Appendix C: Data-collection sheet).

The data for clinical symptoms, history of surgery, breast cancer risk factors, histology results and radiologist level of training collected for each were given the following codes: Clinical symptoms: code 1 – routine exam, code 2 – routine follow-up, code 3 – palpated nodules or lump, code 4 – tender breast, code 5 – skin or nipple retraction, code 6 – feeling a density or thickening in the breast, code 7 – breast pain, code 8 – itchy nipple, code 9 –enlarged lymph node, code 10 – mass with nipple retraction or skin thickening. History of surgery: code 0 – none, code 1 – right or left benign lumpectomy, code 2 – right or left malignant lumpectomy, code 3 – benign breast biopsies, code 4 – malignant breast biopsies, code 5 – bilateral breast reductions, code 6 – drainage of breast abscess, code 7 – bilateral breast implants, code 8 – breast lift and breast implants, code 9 – mastectomy of one breast and a lumpectomy of the opposite breast (Appendix D: Codes for BI-RADs descriptors for mammography and ultrasound).

Breast cancer risk factors were grouped into the following codes: code 0 – none, code 1 –yes, code 2 – no. Histology results were grouped into the following codes: code 1 – DCIS (grade 1, 2 or 3), code 2 – invasive ductal carcinoma (grade 1, 2 or 3), code 3 – infiltrating ductal carcinoma (grade 1, 2 or 3), code 4 – mucinous carcinoma, code 5 – invasive tubular carcinoma, code 6– invasive lobular carcinoma, code 7 – undetermined lesions. Radiologist level of training was grouped into the following codes: code 0 – none, code 1 – breast imaging congress or conference, code 2 – Tabar or ACR course, code 3 – tomosynthesis workshop (Appendix D: Codes for BI-RAD descriptors for mammography and ultrasound).

The BI-RADS assessment classification, age and number of children for each patient were not grouped into codes as these presented with a number. Opinions and comments of the radiologists with regard to working with the BI-RADS lexicon were also not grouped into codes as the results were individually analysed.

The reporting radiologist was assigned a code ranging from R1, R2, R3, etc., to cross-reference the results for each radiologist to be included in the study. The questionnaires distributed to the participating radiologists were designed to explore training in and experience of working with the BI-RADS as an imaging tool. The questionnaires consisted of open-ended and closed-ended questions and were completed voluntarily by individual radiologists. The results of questionnaires were used anonymously in the data-collection spreadsheet as a code was assigned to each participant; no names were included in the data sheet (Appendix A: Participant questionnaire).

Histology reports of confirmed diagnosis were retrieved from the biopsy results file for the study period. The data retrieved from the electronic biopsy result file at the research site was captured manually by the researcher and a hardcopy was also locked in a filing cabinet.

All data recorded were stored on a password-protected personal computer. All files were also password protected to prevent unauthorised access. Only the researcher and supervisors had access to these files.

3.9 Data analysis

A data-capture sheet was used to record the raw data of the various BI-RADS assessment categories, BI-RADS descriptors for mammography and ultrasound, breast cancer risk factors, histology results, radiologist code that reported on each patient, as well as radiologist level of training and experience.

Descriptive statistical analysis was used as follows: Numerical-discrete measurement was used for determining the percentage, mean and standard deviation of breast cancer cases and level of radiologist experience and training. Inferential statistical analysis (chi-squared test: $p<0.05$) was used to determine significant association between radiologists' experience and BI-RAD reporting.

3.10 Ethical considerations

This study was approved by the Research Ethics Committee of the Faculty of Health and Wellness Sciences at the Cape Peninsula University of Technology in October 2017, Certificate No. CPUT/HW-REC 2017/HI4 (Appendices F–H: CPUT Ethics Certificates). Permission was further granted by the radiology practice of Drs Schnetler, Corbett and Partners for collecting patients' data for this study (Appendix I: Permission to do research study). Permission was granted by the American College of Radiology to use the *BI-RADS Atlas*, 2013 (Appendix J: ACR approval).

No direct human participation was required as this was a retrospective research study analysing data retrieved from databases. There thus was no physical risk of harm to any individual, except breach of patient confidentiality. Since this was a retrospective study, the researcher adhered to the Declaration of Helsinki of the World Medical Association (WMA), thereby protecting the privacy and confidentiality of personal information (World Medical Association Declaration of Helsinki, 2013:2191).

In order to protect the participants' privacy, the data was de-identified. All data recorded were stored on a password-protected personal computer. All files were also password protected to prevent unauthorised access. Only the researcher and supervisors had access to such files.

The data obtained from this research will only be used for the purpose of this research project and related publications; the names of patients and participants will not be revealed either during writing up the results or in publications emanating from this research project. All data will be destroyed after five years.

3.11 Conclusion

This research study aimed to investigate how accurately radiologists were using the BI-RADS assessment categories for diagnosing breast cancer. Questionnaires distributed among the participant radiologists aimed to explore whether personal experience and level of training may have had an influence on the accuracy of applying the BI-RADS assessment categories. This was done to obtain statistical data to inform the accuracy of the BI-RADS assessment

categories applied at this radiology practice and to ascertain whether more training is needed on the use of the BI-RADS in future.

The research design was used to compare the accuracy of the BI-RADS assessment categories used for mammography and ultrasound findings within a defined sample population with the histology results, and to evaluate the BI-RADS descriptors used by a sample of radiologists for mammography and ultrasound findings.

CHAPTER FOUR
RESEARCH RESULTS

4.1 Introduction

The data collected for the study period were guided by the research objectives listed earlier (refer to Chapter 3, Section 3.3). Data collected included the results of the BI-RADS assessment categories and lexicon (descriptors) for mammography and ultrasound findings. These results were compared with the histopathology results for each patient using IBM SPSS software. This allowed the researcher to assess the accuracy of the two diagnostic modalities relative to the histopathology results considered the gold standard. All variables were grouped into codes for descriptive frequency (refer to Chapter 3).

One hundred and eight patients were diagnosed with breast cancer during the study period, 1 January 2013 to 31 December 2014. Of the 108 patients, 38 patients were excluded from this study: 15 patients presented with mammogram reports with no final BI-RADS assessment category and 23 patients had a previous mammogram that was not done at the research site. The final study sample of 70 (*n=70*) met the inclusion criteria for the study (Figure 3.1). All 70 patients were diagnosed with breast cancer within the study period: of the 70 patients, 77 breast cancers were detected.

4.2 Patient age

The mean age of patients diagnosed with breast cancer within this study was 60 (±12.6) years, with their ages ranging from 38 to 84 years.

Table 4.1: Age range of patients in years

	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Patient Age (years)	70	38	84	60.40	12.624
Valid *N*	70				

4.3 Hormone replacement therapy

Table 4.2 overleaf provides an overview of the number of patients receiving hormone replacement therapy (HRT) during the sample period. Among the 70 patients diagnosed with breast cancer, 42.9% (*n*=30) were using HRT and 57.1% (*n*=40) were not. These results indicate that the majority of patients within this sample that were diagnosed with breast cancer, were not using HRT.

Table 4.2: Hormone replacement therapy (HRT)

		Frequency	Percent	Valid Percent	Cumulative Percent
HRT	**Yes**	30	39.5	42.9	42.9
	No	40	52.6	57.1	100.0
	Total	70	92.1	100.0	

4.4 Family history of breast cancer

Table 4.3 below provides an overview of patients diagnosed with breast cancer who had a family history of the disease. In this sample, there were 34.3% (*n*=24) of patients diagnosed with breast cancer that had a family history of breast cancer and 65.7% (*n*=46) of patients without a family history of breast cancer.

Table 4.3: Family history of breast cancer

		Frequency	Percent	Valid Percent (%)	Cumulative Percent
Family history	**Yes**	24	31.6	34.3	34.3
	No	46	60.5	65.7	100.0
	Total	70	92.1	100.0	

4.5 Parity status of patients diagnosed with breast cancer

Table 4.4 overleaf provides an overview of the parity status of patients diagnosed with breast cancer. Of the patients diagnosed with breast cancer, 87.1% (*n*=61) had children. Most of the patients, 41.4% (*n*=29) had two children, followed by 22.9% (*n*=16) with one child, 14.3% (*n*=10) with three children, 5.7% (*n*=4) with four children, 2.9% (*n*=2) with five children, while 12.9% (*n*=9) of patients had zero parity status.

Table 4.4: Parity status of patients diagnosed with breast cancer

		Frequency	Percent	Valid Percent (%)	Cumulative Percent
Parity	**0**	9	11.8	12.9	12.9
	1	16	21.1	22.9	35.7
	2	29	38.2	41.4	77.1
	3	10	13.2	14.3	91.4
	4	4	5.3	5.7	97.1
	5	2	2.6	2.9	100.0
	Total	70	92.1	100.0	

4.6 History of breast surgery

Table 4.5 provides an overview of the history of breast surgery among the patients diagnosed with breast cancer. There were 67.1% (*n*=47) diagnosed with breast cancer that had no previous breast surgery and 33% (*n*=23) who had previous surgery. Of the 33% of patients that had previous surgery, 8.6% (*n*=6) had a lumpectomy which was malignant and one had a total breast mastectomy with a recurrence in the opposite breast. The rest of the patients had benign surgery, there was no malignancy; 10% (*n*=7) patients had a benign lumpectomy; 4.3% (*n*=3) had benign biopsies; 2.9% (*n*=2) had breast abscess drainage; 2.9% (*n*=2) had bilateral reductions; while 2.9% (*n*=2) had bilateral implants with breast lift for cosmetic reasons prior to detecting the breast cancer.

Table 4.5: Breast cancer patients with previous breast surgery

		Frequency	Percent	Valid Percent (%)	Cumulative Percent
History of breast surgery	**None**	47	61.8	67.1	67.1
	Right/left benign lumpectomy	7	9.2	10.0	77.1
	Right/left malignant lumpectomy	6	7.9	8.6	85.7
	Benign biopsies	3	3.9	4.3	90.0
	Bilateral reductions	2	2.6	2.9	92.9
	Drainage of breast abscess	2	2.6	2.9	95.7
	Bilateral implants/breast lift	2	2.6	2.9	98.6
	Mastectomy/ lumpectomy of other breast	1	1.3	1.4	100.0
	Total	70	92.1	100.0	

4.7 Clinical findings

A total of 58.6% (*n*=41) of patients diagnosed with breast cancer experienced no clinical signs or symptoms and presented at the radiology practice for routine screening mammograms. A total of 41.4% (*n*=29) of patients presented with the following signs and symptoms: 22.9% (*n*=16) had palpated a lump, 5.7% (*n*=4) experienced breast pain, 2.9% (*n*=2) had skin and nipple retraction, 1.4% *(n*=1) had skin thickening, 1.4% (*n*=1) had itchy nipple, 1.4% (*n*=1) had enlarged lymph nodes and 5.7% (*n*=4) patients had more than one symptom associated with a mass.

Table 4.6: Clinical findings of breast cancer patients prior to imaging

		Frequency	Percent	Valid Percent (%)	Cumulative Percent
Clinical finding	**Routine follow up/exam**	41	53.9	58.6	58.6
	Palpated nodules/lumps	16	21.1	22.9	81.4
	Tender breast/breast pain	4	5.3	5.7	87.1
	Skin/Nipple retraction	2	2.6	2.9	90.0
	Feeling a density/thickening in left or right breast	1	1.3	1.4	91.4
	Itchy nipple	1	1.3	1.4	92.9
	Enlarged lymph node	1	1.3	1.4	94.3
	Mass with nipple retraction and skin thickening/enlarged lymph node	4	5.3	5.7	100.0
	Total	70	92.1	100.0	

4.8 The accuracy of BI-RADS assessment categories compared with the histopathology results as the gold standard

For this study, the histology results were considered the gold standard and were used to confirm the mammography and ultrasound suspicion of malignancy. Histopathological examination of breast biopsy specimens were performed for all 70 patients diagnosed with breast cancer: a total of 77 cancers were detected which included two patients with bilateral breast cancer and five patients with multifocal breast cancer. The mammogram examination was concurrently done with a breast ultrasound and findings reported in the mammogram report with a single final BI-RADS assessment category. Of the 77 cancers identified, 50 (65%) were classified as BI-RADS 4, 22 (28.5%) as BI-RADS 5, and 5 (6.5%) as BI-RADS 3. BI-

RADS 3 was included in histology findings as five patients had a mammography report with BI-RADS 3 and a biopsy was done instead of a short-term follow-up.

The most common malignancy found in this sample was invasive ductal carcinoma with a total of 70% (*n*=54) cases out of 77 cancers detected, followed by ductal carcinoma in situ with 10.4% (*n*=8) cases and invasive lobular carcinoma with 9.1% (*n*=7) cases. In the BI-RADS 3 assessment category there were five breast cancer cases of which 80% (*n*=4) were invasive ductal carcinoma and 20% (*n*=1) lobular carcinoma.

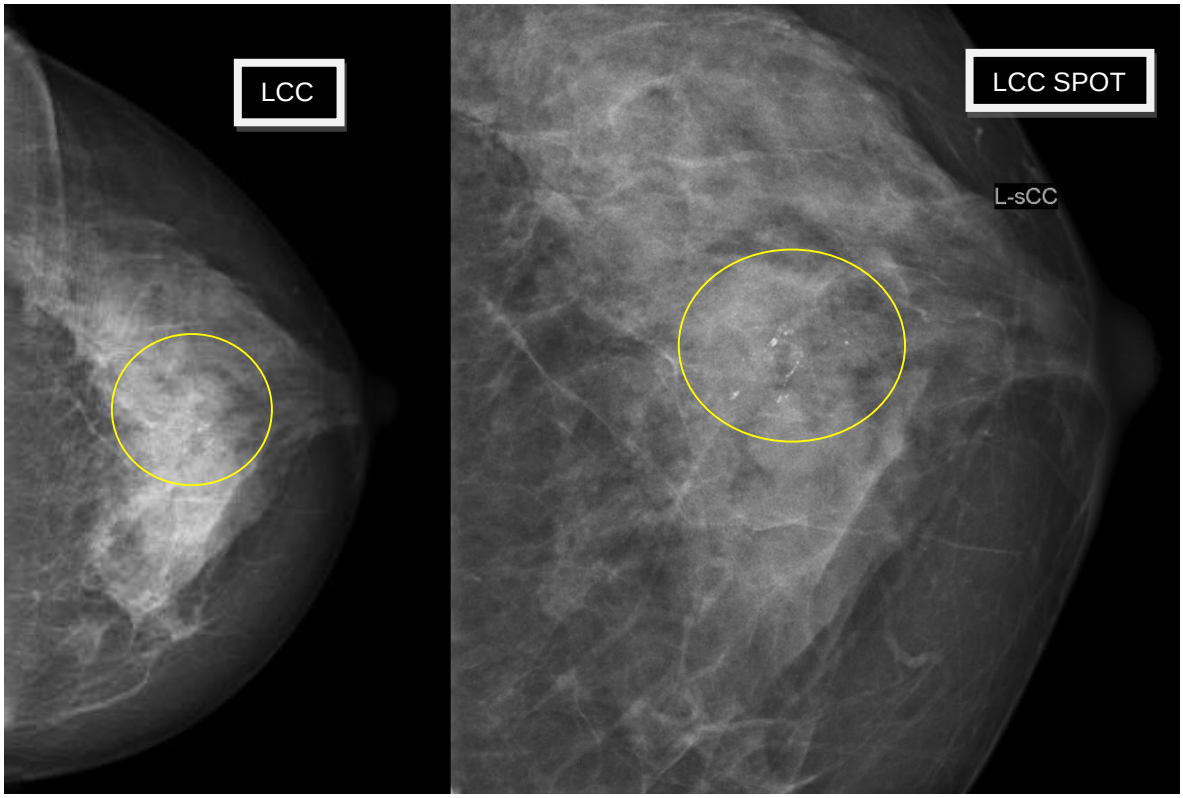

Figure 4.2: The circled area on the left craniocaudal (CC) view (left image) and the spot compression (right image) images demonstrate suspicious calcifications in the left breast. Histopathology confirmed invasive ductal carcinoma grade 2. *(Images courtesy of the radiology practice)*

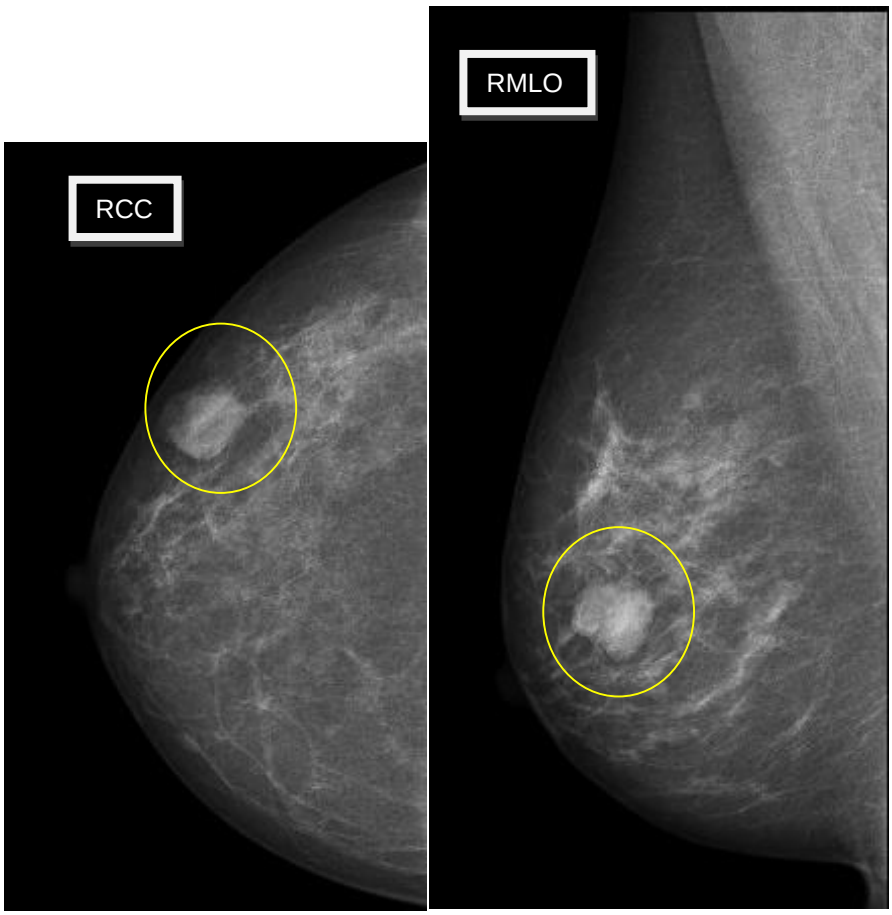

Figure 4.3: The right craniocaudal (CC) (left image) and right mediolateral oblique (MLO) (right image) images demonstrate an irregular, lobulated mass in the right breast. Histopathology confirmed invasive ductal carcinoma grade 3. *(Images courtesy of the radiology practice)*

The accuracy of the BI-RADS assessment categories were assessed with IBM SPSS cross-tabulation. The histology results confirmed breast cancer for the BI-RADS 4 and 5 assessment diagnosis. The histology results confirmed breast cancer in the BI-RADS 3 assessment diagnosis, that is, the probability of malignancy ≥ 2%.

Table 4.7 provides an overview of the BI-RADS assessment category compared with the histopathology results as the gold standard.

Table 4.7: The accuracy of the BI-RADS assessment categories in mammography and breast ultrasound imaging reporting compared to the histopathology results as the gold standard

Histology Results	BI-RADS assessment categories			Total	%
	BI-RADS 3	BI-RADS 4	BI-RADS 5		
DCIS (Ductal carcinoma in situ)	0	6	2	8	10.4%
Invasive ductal carcinoma	4	35	15	54	70%
Mucinous carcinoma	0	4	0	4	5.2%
Invasive tubular carcinoma	0	1	0	1	1.3%
Invasive lobular carcinoma	0	4	3	7	9.1%
Lobular carcinoma	1	0	2	3	4%
Total	5	50	22	77	100%

4.9 BI-RADS mammography descriptors

Seventy patients were diagnosed with breast cancer. There were 110 mammography descriptors described on mammography within the study sample. Of the 70 patients, 44% (*n*=31) had more than one mammography descriptor and 56% (*n*=39) had only one mammography descriptor reported on the mammogram report. According to the ACR (2013), BI-RADS 4 indicates a >2% to <95% likelihood of malignancy and BI-RADS 5 indicates ≥95% likelihood of malignancy. However in this study, five patients had a BI-RADS 3 reported on the mammogram. The BI-RADS 3 category indicates >0 to ≤2% likelihood of malignancy and that a short-term follow-up is recommended (ACR, 2013). The five BI-RADS 3 category patients opted for an immediate biopsy. All five yielded a positive malignancy result. Table 4.8 overleaf provides an overview of the mammography descriptors for this study sample.

Table 4.8: BI-RADS categories 3–5 mammography malignancy descriptors

Mammography descriptors		Number	Percent
Mass shape	**Oval**	1	1.3%
	Irregular	6	7.8%
Mass margin	**Circumscribed**	6	7.8%
	Obscured	1	1.3%
	Microlobulated	7	9.1%
	Indistinct	1	1.3%
	Spiculated	27	35.1%
Density	**High density**	8	10.4%
	Low density	1	1.3%
Calcifications	**Suspicious morphology**	22	28.6%
	Grouped	8	10.4%
Asymmetries	**Focal asymmetry**	5	6.5%
	Global asymmetry	1	1.3%
Associated features	**Nipple retraction**	4	5.2%
	Skin thickening	2	2.6%
	Architectural distortion	7	9.1%
	Axillary adenopathy	3	3.9%
Total		110	100%

On mammography the more common malignancy findings of the 77 breast cancers detected were spiculated mass margin 35.1% (*n*=27), followed by suspicious morphology calcifications 28.6% (*n*=22), grouped calcifications 10.4% (*n*=8), masses with high density 10.4% (*n*=8), microlobulated 9.1% (*n*=7), architectural distortion 9.1% (*n*=7), irregular-shaped mass 7.8% (*n*=6), mass margin and circumscribed mass margins 7.8% (*n*=6), and focal asymmetry 6.5% (*n*=5).

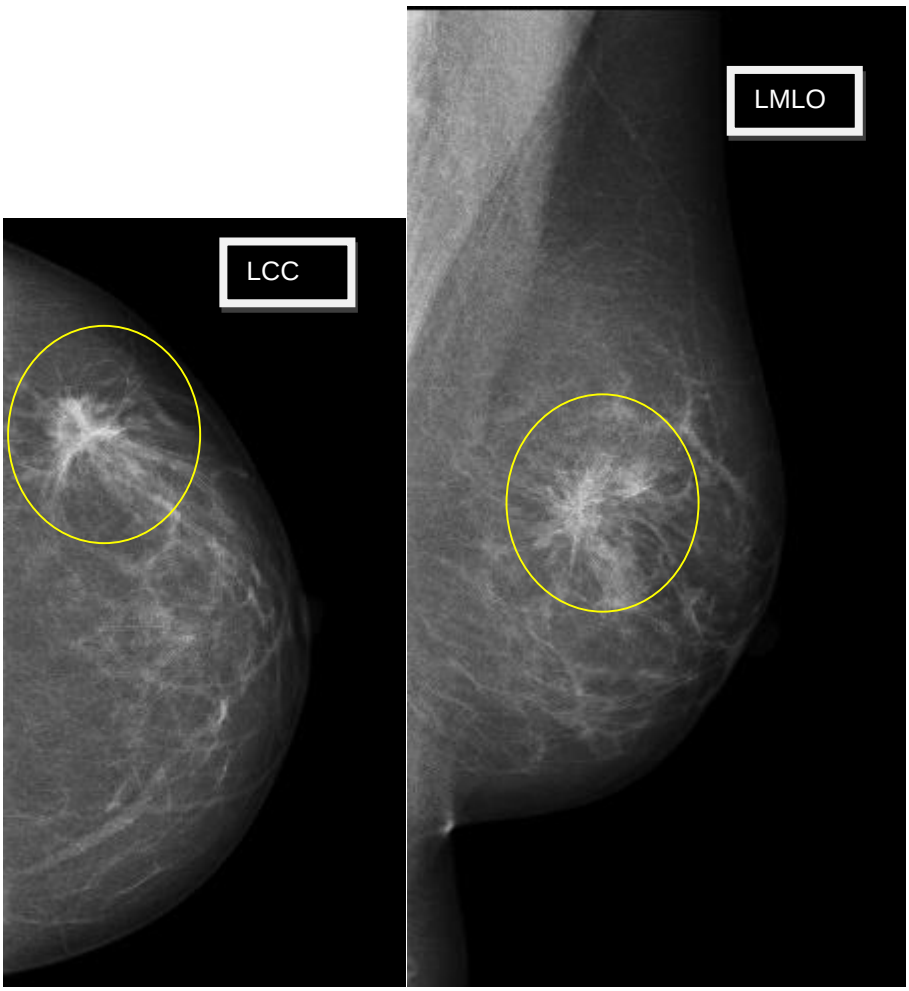

Figure 4.4: The left craniocaudal (CC) (left image) and the left mediolateral oblique (MLO) (right image) images demonstrate a spiculated mass with architectural distortion and isolated microcalcifications. Histopathology confirmed invasive ductal carcinoma grade 3. *(Images courtesy of the radiology practice)*

The following malignancy findings were less common: oval shape mass 1.3% (*n*=1); obscured 1.3% (*n*=1) and indistinct 1.3% (*n*=1) mass margin; low-density masses 1.3% (*n*=1); global asymmetry 1.3% (*n*=1); nipple retraction 5.2% (*n*=4); skin thickening 2.6% (*n*=2); and axillary adenopathy 3.9% (*n*=3).

4.10 BI-RADS ultrasound descriptors

In this study all 70 patients were diagnosed with breast cancer. There were 209 ultrasound descriptors described on breast ultrasound. Of the 70 patients, 73% (*n*=51) had more than one ultrasound descriptor and 27% (*n*=19) had only one ultrasound descriptor reported. Table 4.9 overleaf provides an overview of the ultrasound descriptors found in this study sample.

Table 4.9: BI-RADS 3-5 categories ultrasound malignancy descriptors

Ultrasound Descriptors		Number	Percent
Mass shape	**Irregular**	22	28,6%
Mass margin	**Circumscribed**	3	3,9%
	Indistinct	6	7,8%
	Angular	1	1,3%
	Microlobulated	14	18,2%
	Spiculated	9	11,7%
Echo pattern	**Hyperechoic**	1	1,3%
	Complex cystic and solid	2	2,6%
	Hypoechoic	43	55,8%
	Heterogeneous	1	1,3%
Posterior features	**Posterior enhancement**	2	2,6%
	Posterior shadowing	29	37,7%
Calcifications	**Calcifications in a mass**	3	3,9%
Associated features	**Architectural distortion**	1	1,3%
	Internal vascularity	5	6,5%
Special cases	**Lymph nodes – axillary**	13	16,9%
Total		209	100%

The more common malignancy findings of the 77 breast cancers detected on ultrasound of the breast were hypoechoic echo pattern 55.8% (*n*=43), followed by posterior shadowing 37.7% (*n*=29), irregular-shaped masses 28.6% (*n*=22), microlobulated 18.2% (*n*=14), associated malignant axillary lymph nodes 16.9% (*n*=13), spiculated mass margin 11.7% (*n*=9), indistinct mass margins 7.8% (*n*=6), and internal vascularity 6.5% (*n*=5).

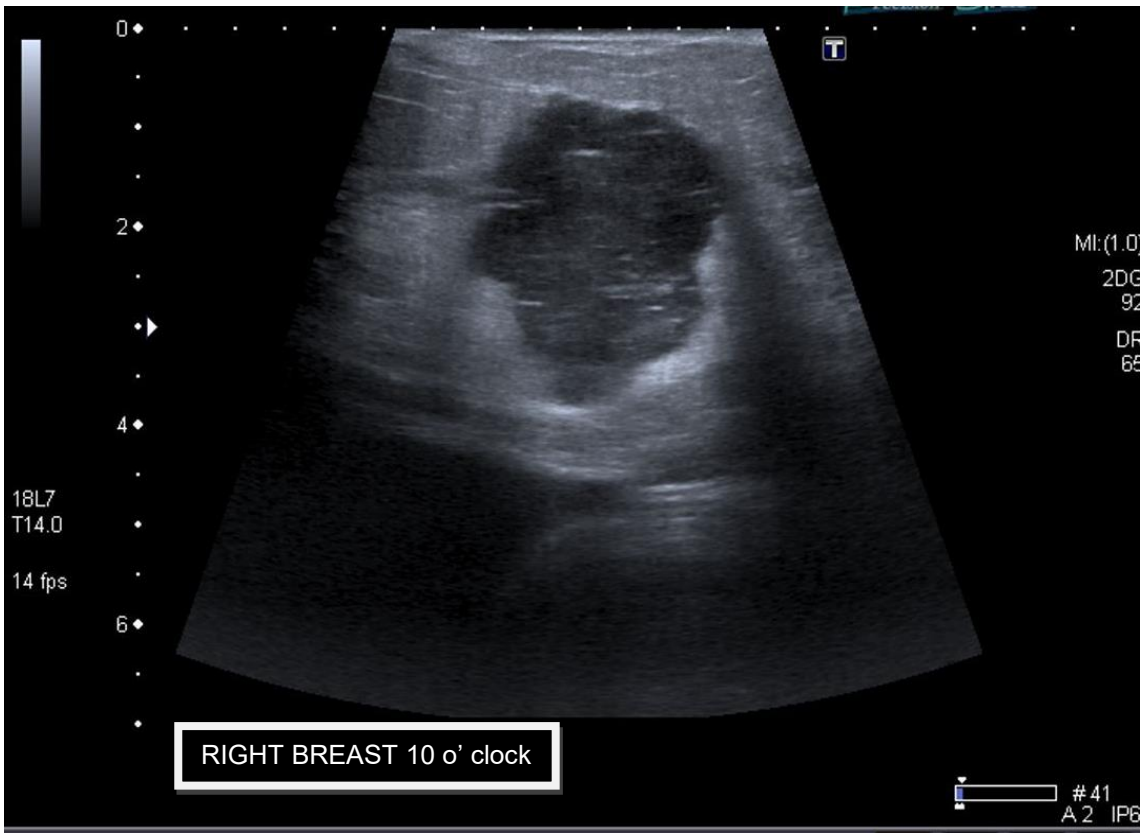

Figure 4.5: Ultrasound of the right breast shows a large lobulated hypoechoic mass at the 10 o'clock radian *(Images courtesy of the radiology practice)*

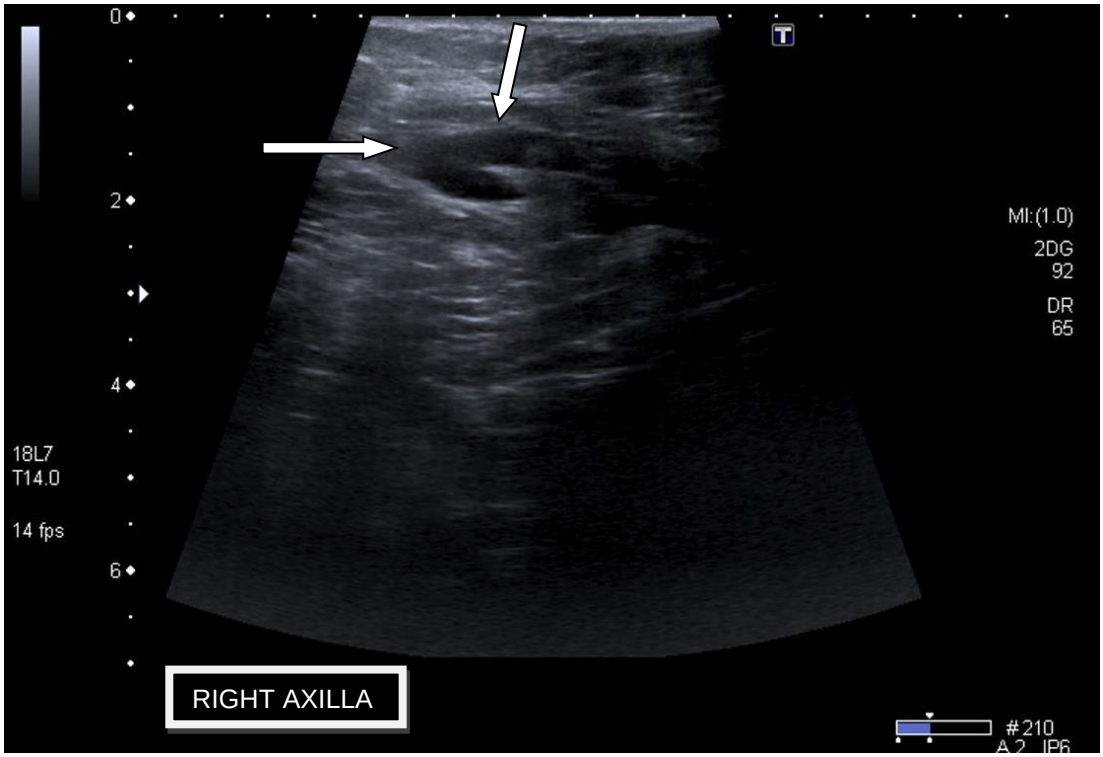

Figure 4.6: Right axillary lymphadenopathy *(Images courtesy of the radiology practice)*

The less common ultrasound findings were circumscribed lesions 3.9% (*n*=3), angular mass margins 1.3% (*n*=1), hyperechoic echo pattern 1.3% (*n*=1), complex cystic and solid echo pattern 2.6% (*n*=2) and heterogeneous echo pattern 1.3% (*n*=1), posterior enhancement 2.6% (*n*=2), calcifications in a mass 3.9% (*n*=3), and architectural distortion 1.3% (*n*=1).

4.11 Diagnostic breast imaging detection

In this study, all the patients diagnosed with breast cancer were detected either by mammography or breast ultrasound, or both.

4.11.1 Mammography detection

The mammograms of all 70 patients were interpreted diagnostically to have an abnormal finding present. The mammograms revealed abnormalities in 93.5% (*n*=72) out of 77 breast cancers diagnosed and no abnormalities in 6.5% (*n*=5) out of 77 breast cancers diagnosed (Figure 4.7).

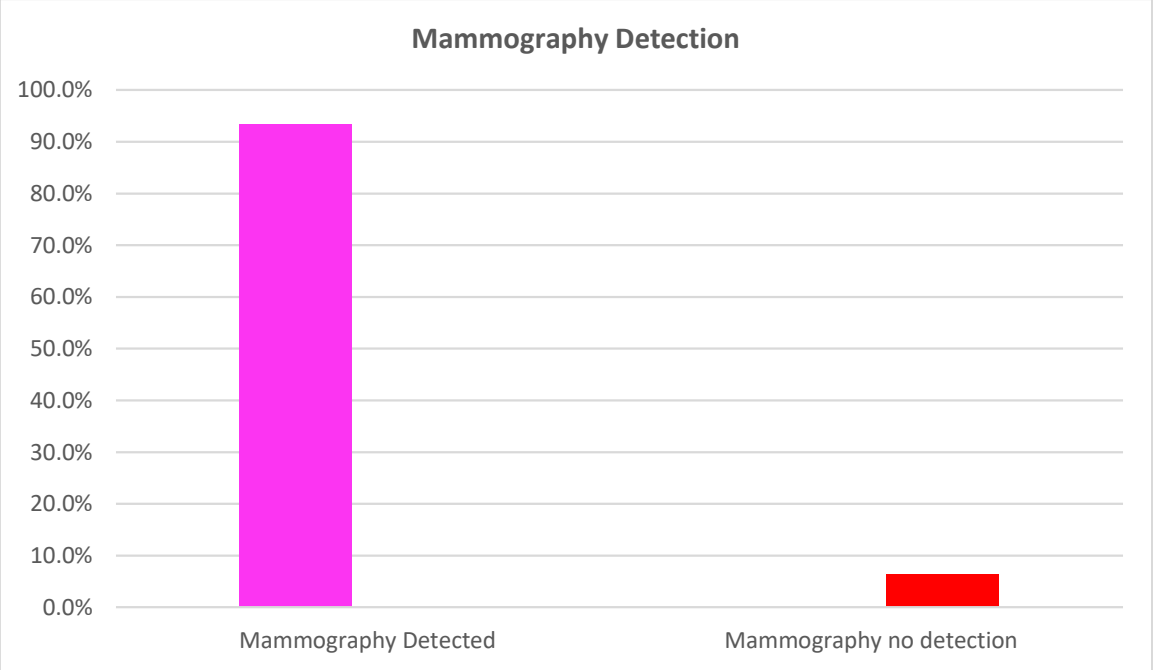

Figure 4.7: Detection of breast cancer using mammography

4.11.2 Pathology diagnosed with ultrasound

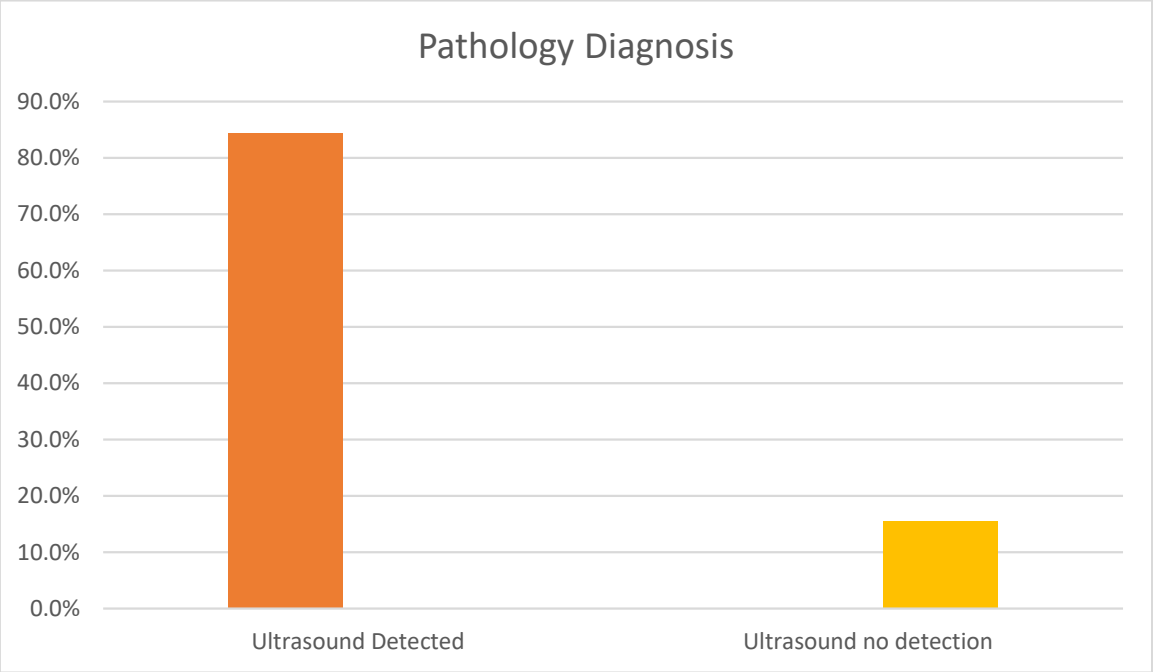

Figure 4.8: Detection of pathology using ultrasound

Breast ultrasound was performed as an adjunct to the mammograms. All 70 patients underwent a breast ultrasound to interpret any abnormal findings. Breast ultrasound revealed abnormalities in 84.4% (*n*=65) out of 77 breast cancers diagnosed and no abnormalities in 15.6% (*n*=12) out of 77 breast cancers diagnosed (Figure 4.8).

4.11.3 Combined mammography and breast ultrasound pathology diagnoses

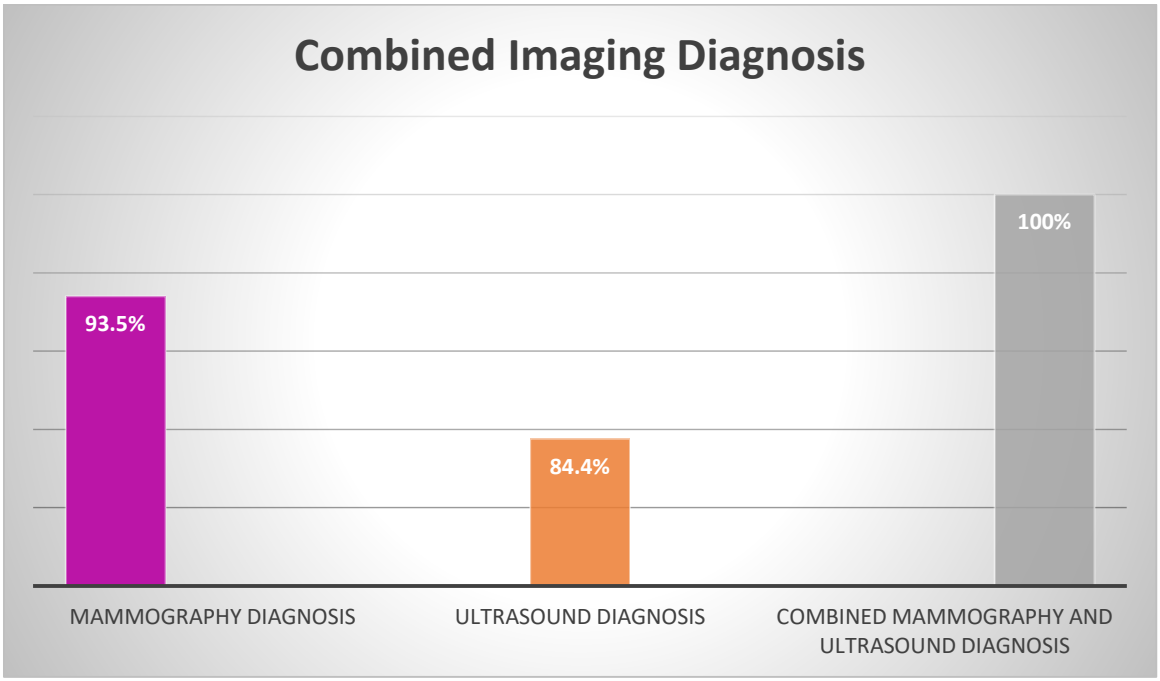

Figure 4.9 Combined mammography and ultrasound diagnoses

Mammography was able to detect 93.5% of abnormalities and breast ultrasound 84.4% of abnormalities within this sample population. Breast ultrasound was used as an adjunct to mammography and had an overall combined diagnostic rate of 100% (Figure 4.9).

4.12 Questionnaire responses

Questionnaires were distributed to all radiologists employed at the private radiology practice who were responsible for mammography and breast ultrasound reporting. The purpose of this questionnaire was to determine whether their level of experience and training had an influence on the accuracy of the BI-RADS assessment categories. The radiologists could complete the questionnaires voluntarily. Twenty-two (22) questionnaires were distributed and fifteen radiologists participated, resulting in a 68% response rate for this study.

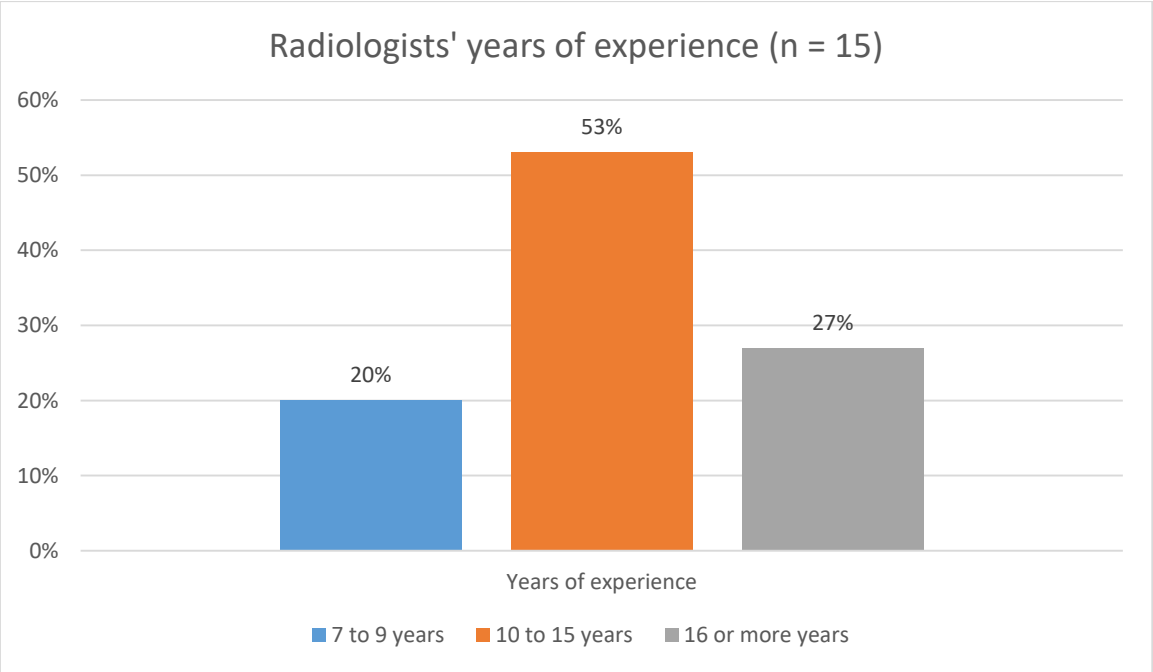

Figure 4.10: Radiologists' years of experience

All radiologists had experience in reporting on mammograms, including breast ultrasound. From the 15 questionnaire responses, three radiologists (20%) had 7–9 years' experience, eight (53%) had 10–15 years' experience and four (27%) had 16 or more years of experience (Figure 4.10). The minimum years of experience were 7 years and the maximum 29 years. The radiologists' mean years of experience in BI-RADS 3, 4 and 5 were 14.60, 11.46 and 13.42 years. All 15 (68%) respondents were very experienced in mammography reporting (Table 4.10).

Table 4.10: Radiologists' mean years of experience in BI-RADS 3, 4 and 5 assessment categories								
BI-RADS	***N***	**Mean**	**Std. Deviation**	**Std. Error**	**95% Confidence Interval for Mean**		**Mini-mum**	**Maxi-mum**
					Lower Bound	Upper Bound		
3	5	14.60	1.517	0.678	12.72	16.48	12	16
4	35	11.46	3.398	0.574	10.29	12.62	8	20
5	12	13.42	6.201	1.790	9.48	17.36	7	29
Total	52	12.21	4.179	0.580	11.05	13.37	7	29

The level of radiologist experience had no influence on the accuracy of the BI-RADS assessment categories as all 70 breast cancer cases were detected accurately when using the BI-RADS assessment categories. Based on the chi-squared test ($p > 0.05$), there was no significance difference (p=0.152) per radiologist average years of experience and BI-RADS 3, 4 and 5 assessment categories (Table 4.11).

Table 4.11: Radiologists' years of experience and BI-RADS 3, 4 and 5 assessment categories					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between groups	65.871	2	32.935	1.957	**0.152**
Within groups	824.802	49	16.833		
Total	890.673	51			

4.13 Radiologist training

With regard to the level of training, the following responses were obtained: Ten radiologists (67%) attended breast congresses/conferences or the Tabar course (formal training), while one (7%) radiologist completed a fellowship in breast imaging. Two (13%) radiologists

attended a BI-RADS course with additional mammography courses and two (13%) radiologists had no additional training on mammography or the BI-RADS (Figure 4.11).

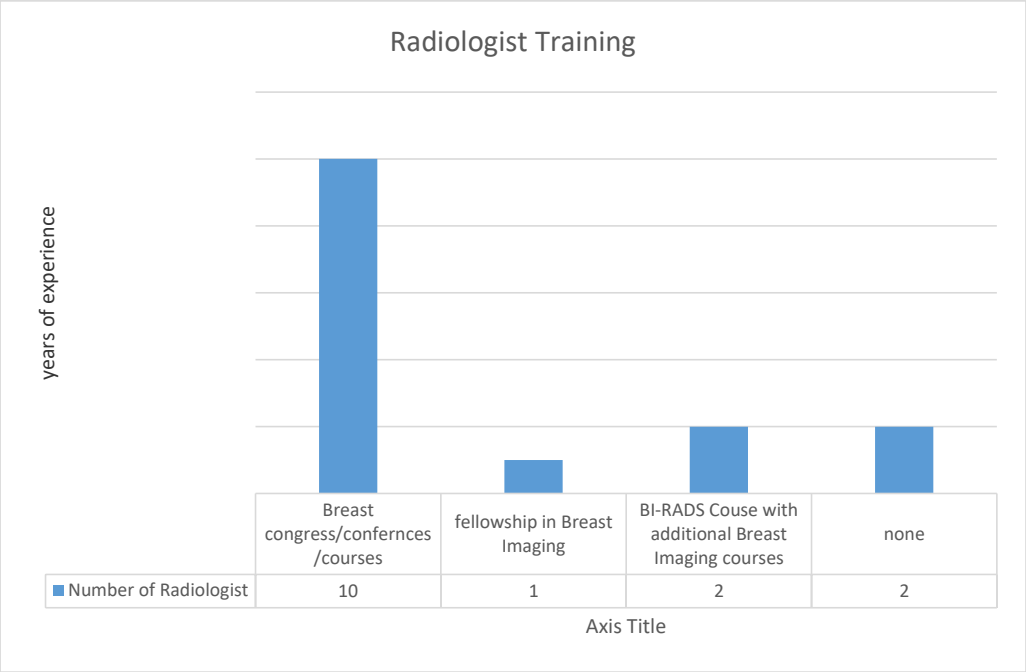

Figure 4.11: Radiologists' additional training in mammography reporting/BI-RADS

4.14 Radiologist opinion of using the BI-RADS descriptors and assessment categories for mammography and breast ultrasound reporting

The open-ended questions in the participants' questionnaire yielded comments from the radiologists. The comments were grouped into the following themes: BI-RADS standardises breast imaging reporting, BI-RADS allows better communication between radiologist and referring physician, and BI-RADS clarifies further management for patients.

Of the 15 responses, 67% agreed that the BI-RADS standardises breast imaging reporting and reduces confusion, 33% agreed that the BI-RADS allows better communication between radiologists and referring physicians, and 40% agreed that the BI-RADS clarifies further management for patients by helping to stratify risk management. All responses were in agreement that the BI-RADS is excellent and very effective; most importantly, if adhered to, the BI-RADS provides universal language, uniformity and prescriptive care (Figure 4.12).

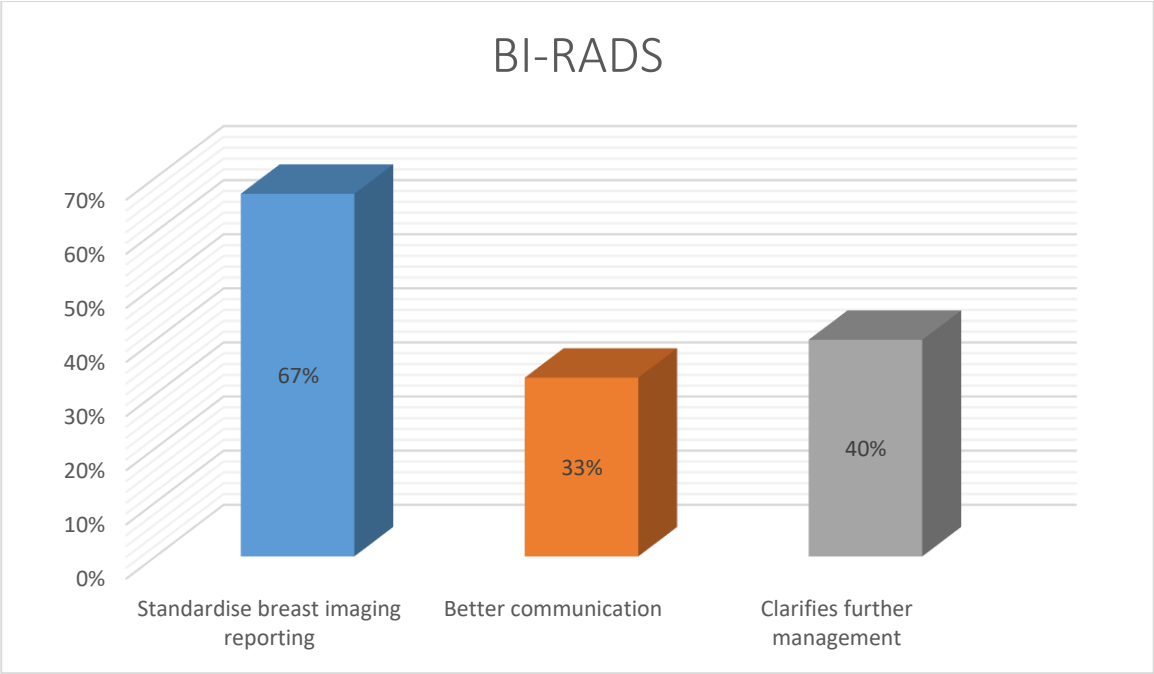

Figure 4.12: Radiologists' comments on using the BI-RADS for mammography and breast ultrasound reporting

4.15 Summary of results

The study population comprised 70 confirmed breast cancer patients with a mean age of 60 (±12.6) years. Thirty patients (42.9%) were on HRT. Twenty patients (34.3%) had a family history of the disease. Forty-one patients (58.6%) experienced no clinical signs or symptoms prior to the mammogram; the remaining 29 patients (41.4%) presented with the following signs and symptoms: 16 (22.9%) had palpated a lump, 4 (5.7%) experienced breast pain, 2 (2.9%) had skin and nipple retraction, 1 (1.4%) had skin thickening, 1 (1.4%) had itchy nipple, 1 (1.4%) had enlarged lymph nodes and 4 (5.7%) patients had more than one symptom associated with a mass. The most common malignancy diagnosed was invasive ductal carcinoma with a total of 70% (*n*=54) cases out of 77 cancers detected, followed by ductal carcinoma in situ with 10.4% (*n*=8) and invasive lobular carcinoma with 9.1% (*n*=7). The histology results confirmed breast cancer for all BI-RADS 4 and 5 assessment diagnoses; and confirmed breast cancer in the BI-RADS 3 assessment diagnoses, that is, the probability of malignancy ≥ 2%.

Mammography descriptors: The more common malignancy findings of the 77 breast cancers detected were spiculated mass margin 35.1% (*n*=27), followed by suspicious morphology calcifications 28.6% (*n*=22), grouped calcifications 10.4% (*n*=8), masses with high density 10.4% (*n*=8), microlobulated 9.1% (*n*=7), architectural distortion 9.1% (*n*=7), irregular-shaped mass 7.8% (*n*=6), mass margin and circumscribed mass margins 7.8% (*n*=6), and focal asymmetry 6.5% (*n*=5).

Ultrasound descriptors: The more common malignancy findings of the 77 breast cancers detected on ultrasound of the breast were hypoechoic echo pattern 55.8% (*n*=43) followed by posterior shadowing 37.7% (*n*=29), irregular-shaped masses 28.6% (*n*=22), microlobulated 18.2% (*n*=14), associated malignant axillary lymph nodes 16.9% (*n*=13), spiculated mass margin 11.7% (*n*=9), indistinct mass margins 7.8% (*n*=6), and internal vascularity 6.5% (*n*=5).

The mammogram was able to detect 93.5% of abnormalities and breast ultrasound 84.4% of abnormalities in this study sample. Breast ultrasound was used as an adjunct to mammography and hence an overall combined diagnostic rate was 100%.

Fifteen radiologists completed the questionnaire. Three radiologists (20%) had 7–9 years' experience, eight (53%) had 10–15 years' experience and four (27%) had 16 or more years of experience. There was no significant difference *(p*=0.152) per radiologists' years of experience and BI-RADS 3, 4 and 5 assessment category reporting. Ten radiologists (67%) attended breast congresses and conferences or the Tabar course (formal training), while one (7%) radiologist completed a fellowship in breast imaging. Two (13%) radiologists attended a BI-RADS course with additional mammography courses and two (13%) radiologists had no additional training on mammography or the BI-RADS. Of the 15 responses, 67% agreed that the BI-RADS standardises breast imaging reporting and reduces confusion, 33% agreed that the BI-RADS allows better communication between radiologists and referring physicians and 40% agreed that the BI-RADS clarifies further management for patients by helping to stratify risk management. All responses were in agreement that the BI-RADS is excellent and very effective; most importantly, if adhered to, the BI-RADS provides universal language, uniformity and prescriptive care.

CHAPTER FIVE
DISCUSSION AND CONCLUSION

5.1 Discussion

The Breast Imaging Reporting and Data System (BI-RADS) is a breast imaging tool used in mammography and breast ultrasound reporting. This study intended to determine the accuracy of the BI-RADS assessment categories compared with histopathology reports, and to establish the accuracy of the BI-RADS lexicon descriptors for mammography and ultrasound in patients diagnosed with breast cancer.

Previously published studies have reported that the positive predictive values (PPVs) for BI-RADS 3, 4 and 5 assessment categories were concordant when compared with histopathology results (Lazarus et al., 2006:385; Bent et al., 2010:1380; Alimoğlu et al., 2012:10; Giess et al., 2012:1945-1946; Badan et al., 2013:211; Chae et al., 2016:671). The current study demonstrated the BI-RADS 4 and 5 assessment categories of the 77 breast cancer cases detected by mammography or breast ultrasound findings corresponded well with histology with a 100% PPV.

Many studies reported a low malignancy rate, ≤ 2%, in the BI-RADS 3 assessment category (Orel et al. 1999:845; Kim et al., 2008:1209; Raza et al., 2008:777; Baum et al., 2011:61; Chae et al., 2016:671). Further literature reported the BI-RADS 4 assessment category to have a malignancy rate between more than 2% to less than 90% (Lazarus et al., 2006:385; Bent et al., 2010:1382; Chaiwerawattana et al., 2012:4063; Yoon et al., 2016:322; Trindade-Pacheco et al., 2016:1) and for the BI-RADS 5 assessment category between 90% to 100% (Heinig et al., 2008:573; Kim et al., 2008:1209; Raza et al., 2008:778; Bent et al., 2010:1382; Badan et al., 2013:211; Yoon et al., 2016:322).

In this study of 77 breast cancer cases, five (6.5%) were classified as BI-RADS 3, 50 (65%) as BI-RADS 4 and 22 (28.5%) as BI-RADS 5. Although a short-term interval follow-up is recommended in the BI-RADS 3 assessment category and not a biopsy (ACR, 2013), a biopsy was performed on all five (6.5%) patients with a BI-RADS 3 assessment category. The main reason for doing a biopsy included patients' anxiety and family history of breast cancer. The histopathology results revealed breast cancer in the 7% of patients with a BI-RADS 3 assessment category. These results were similar to the study of Yoon et al. (2016: 322) in which the BI-RADS category 3 had a malignancy rate of 7.7%. The malignancy rate of the present study is higher than the recommendation for BI-RADS category 3 (ACR, 2013). The reason for the higher malignancy rate may be due to the limited sample size included in this study. Furthermore, out of 77 breast cancer cases, fifty (65%) were classified as BI-RADS 4 assessment category and 22 (28.5%) as BI-RADS 5 assessment category; both categories

had a PPV of 100%. Our results for the BI-RADS 5 assessment category were the same as for previous studies and correlated well with histology (Bent et al., 2010:1382; Badan et al., 2013:211). In addition, the BI-RADS 4 assessment category had a higher malignancy rate of 100% than that of previous studies with a malignancy rate ranging between 2 to ≤ 90 % (Lazarus et al., 2006:385; Bent et al., 2010:1382; Chaiwerawattana et al., 2012:4063; Giess et al., 2012:1948; Trindade-Pacheco et al., 2016:1). The reason for a higher malignancy rate in the BI-RADS 4 may be due to this being a retrospective descriptive quantitative research study consisting only of confirmed breast cancer cases in which no benign cases were included.

All 70 patients in the present study underwent a core needle or vacuum-assisted biopsy under stereotactic or ultrasound guidance. There were two patients with abnormal findings bilaterally and five patients with multiple abnormal findings in one breast. According to the histopathology reports from the 77 breast cancers, the most common malignancy was invasive ductal carcinoma (70%) compared with ductal carcinoma in situ (DCIS) (10.4%) and invasive lobular carcinoma (9.1%). The pathological findings were consistent with previous studies for invasive ductal carcinoma (Wiratkapun et al., 2010:834; Chaiwerawattana et al., 2012:4064; Badan et al., 2013:211; Elverici et al., 2015:191) and DCIS and invasive lobular carcinoma (Chaiwerawattana et al., 2012:4064; Ghate et al., 2012:966; Abdel-Gawad et al., 2014:1305). The less common malignancy findings in the present study were invasive tubular carcinoma (1.3%); the prevalence of tubular carcinoma was similar to a previous study of Elverici et al. (2015:191).

Statistics in South Africa have shown that breast cancer risk increases with age (South African National Cancer Registry, 2013). The mean age range of patients diagnosed with breast cancer in our study was 60 (±12.6) years. Previous studies have reported women with a first- and second-degree family history of breast cancer are at an increased risk for developing breast cancer (Singletary, 2003:479; Nelson et al., 2012:635-648). In our study, there were 34% (*n*=24) of patients diagnosed with breast cancer that had either a first- or second-degree family history of breast cancer, while 65.7% (*n*=46) of patients had no family history of breast cancer. In addition there was no association between parity status and breast cancer risk: 87.1% of patients diagnosed with breast cancer had children and 12.9% had no children. Further research is needed with a larger population size to clarify parity status as a risk factor for breast cancer. The majority of the sample in our study have shown that breast cancer can occur in women without a family history of breast cancer, and therefore it is recommended that all women from the age of 40 years should have a mammogram annually.

The most common signs and symptoms of patients diagnosed with breast cancer in our study was a palpated lump in 16 (22.9%) patients and in 4 (5.7%) patients with more than one symptom associated with a mass. However 41 (58.6%) of patients experienced no clinical signs and symptoms and abnormal findings were detected on mammography or on breast ultrasound. Mammograms revealed abnormalities in 73 (93.5%) out of 77 breast cancers diagnosed and breast ultrasound revealed 64 (84.4%) out of 77 breast cancers diagnosed. Breast ultrasound was used as an adjunct to mammography in our study with a combined diagnostic rate of 100% which was similar to previous studies with a combined sensitivity between 96 to 100% (Houssami et al., 2003:935; Berg et al., 2008:2151; Taori et al., 2013:40).

In this study all 70 patients underwent a mammogram and breast ultrasound. The mammography and breast ultrasound findings were described using the BI-RADS lexicon descriptors. In relation to masses, the most common mammography descriptors for malignancy were spiculated mass margins (35.1%). According to Hong et al. (2005), the prevalence of spiculated mass margins was 97% and indicated a high predictor for malignancy. Another study concluded a high PPV for spiculated mass margins for Observer A was 90% and Observer B was 83.3% (Do Nascimento et al., 2010:94). In the present study, the PPV for spiculated mass margins was lower than in previous studies; studies however were in agreement that spiculated mass margins constitute a high predictor for malignancy. Following spiculated mass margins, another common mammography descriptor for malignancy in the present study was calcifications with suspicious morphology (28.6%). Suspicious morphology includes amorphous, coarse heterogeneous, fine pleomorphic and fine linear or fine-linear branching. Many studies have supported calcifications with suspicious morphology to be a high predictor for malignancy (Burnside et al., 2007:388; Bent et al., 2010:1378; Do Nascimento et al., 2010:94; Badan et al., 2013:213). Micro-calcifications are also frequent mammographic signs of DCIS, ranging from 68%–95% (Evans et al., 1994:1307; Gajdos et al., 2002:246; Szynglarewicz et al., 2016:145). According to Wiratkapun et al. (2010), architectural distortion and asymmetrical density have been reported as further descriptor criteria for malignancy. In the present study, architectural distortion, and focal and global asymmetry were present in 9.1%, 6.5% and 1.3% on mammography.

The most common ultrasound descriptors for malignancy in the present study in relation to masses were irregular-shaped masses (28.6%), microlobulated mass margins (18.2%), spiculated mass margins (11.7%), hypoechoic echo pattern (55.8%) and posterior shadowing (37.7%). Previous studies indicated a high PPV for speculated margins between 80% and 95% (Hong et al., 2005:1262; Raza et al., 2010:1201-1203; Badan et al., 2013:212; Elverici et al., 2015:192) and for microlobulated margins between 33% and 50% (Hong et al., 2005:1262; Heinig et al., 2008:577; Abdullah et al., 2009:669; Elverici et al., 2015:192); however our results

were lower than those of previous studies, with a PPV of 11.7% for speculated margins. Abdullah et al. (2009:669) had similar results with a PPV of 13% for spiculated margins. The lower results in our study may be due to difficulty in radiologists differentiating between spiculated and microlobulated margins as reported in previous studies (Abdullah et al. 2009:669; Elverici et al., 2015:192). Another reason may be due to the small sample size. Hypoechoic echo pattern (55.8%) and posterior shadowing (37.7%) were the highest malignancy descriptors found in our study and these results were similar to those of previous studies (Hong et al., 2005:1262; Abdullah et al., 2009:669; Elverici et al., 2015:192).

In this study the radiologist mean years of experience for the BI-RADS 3, 4 and 5 were 14.60, 11.46 and 13.42 years. All 15 (68%) radiologists were very experienced in mammography reporting. There were no significant differences per radiologist average years of experience and BI-RADS assessment categories with a value of p=0.152. Out of the 15 radiologist responses, 13% had no formal training on the BI-RADS 5th edition; however 7% did a fellowship in breast imaging and 13% attended a BI-RADS course with additional mammography courses. These results indicated that the radiologists predicted malignancy for breast cancer and assigned the correct BI-RADS assessment categories irrespective of the level of training.

Studies concluded that the BI-RADS is useful for differentiating between benign and malignant lesions (Hong et al., 2005:1260; Heinig et al., 2008:578; Do Nascimento et al., 2010:91; Badan et al., 2013:213; Abdel-Gawad et al., 2014:1306). In addition, the BI-RADS standardised breast imaging reporting helps to predict the likelihood of malignancy (Liberman et al., 1998:35; Orel et al.,1999:845; Lazarus et al., 2006:385; Burnside et al., 2007:388; Kim et al., 2008:1209) and is a form of communication between radiologist and referring physicians (Ortiz-Perez et al., 2013:461). There were various responses from radiologists for the use of the BI-RADS in the present study. Among the responses, 67% agreed that the BI-RADS standardises breast imaging reporting and reduces confusion, 33% agreed that the BI-RADS allows for better communication between radiologists and referring physicians, and 40% agreed that the BI-RADS clarifies further management for patients by helping to stratify risk management.

5.2 Limitations and recommendations

This study had several limitations. Firstly, the study population was relatively small and only included one private radiology practice. Thirty-eight patients were excluded from this study owing to no mammogram and no BI-RADS assessment category available at the research site. Secondly, owing to the present study's using only patients confirmed with breast cancer, the BI-RADS descriptors for benign findings or follow-up recommendations were not evaluated. Thirdly, BI-RADS 4 sub-categories (A–C) were not evaluated; instead this study assessed the overall positive predictive value of BI-RADS 4. Additionally in this study, all the radiologists

were experienced in mammography and were familiar with the BI-RADS assessment categories and descriptors.

Further research should be done to include a larger sample size. Although not demonstrated in this study, inconsistent use of the BI-RADS assessment categories and descriptors may vary among radiologists, depending on their experience and training levels, and this provides scope for further investigation.

5.3 Conclusion

Our study results indicated that the BI-RADS assessment categories, 5th edition, are useful for predicting the likelihood of malignancy when used correctly. Additionally the BI-RADS 4 and 5 had a positive predictive value of 100%, which corresponded well with histopathology results. Descriptor findings in this study suggested that spiculated mass margins, irregular- shaped masses, hypoechoic echo pattern and posterior shadowing are high predictors of malignancy and warrant placement in the BI-RADS 5 assessment category. Furthermore, the absence of BI-RADS 4 sub-categorisation had no effect on patient management as the overall BI-RADS 4 assessment category was compatible with histopathology results. Mammography remains the gold standard for detecting breast cancer and when used in conjunction with breast ultrasound, a 100% detection rate is achieved. Our results contributed additional evidence that the BI-RADS 5th edition plays an important role in mammography reporting and provides standardisation among radiologists with good agreement.

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APPENDICES

APPENDIX A: PARTICIPANT QUESTIONNAIRE

8 Bignonia Circle
Belhar
7493
Cape Town
13 August 2015

Dear Dr

Request for participating in research project

I am currently registered for an MSc: Radiography degree at the Cape Peninsula University of Technology.

The title of my study is: BI-RADS final assessment categories breast cancer patients. The aim of my study is to evaluate the accuracy of the BI-RADS lexicon categories in patients diagnosed with breast cancer. The study will compare the accuracy of mammographic, ultrasound and histology reports for patients with confirmed breast cancer. One of the sub-objectives is to ascertain whether there is correlation between the experience and/or level of training of the reporting radiologist and the accuracy of the BI-RADS report.

The study will uphold all ethical requirements and the names of participants or practice will not be revealed during publication of the thesis or the results. Ethics approval for this study has been granted by the Research Ethics Committee of the Faculty of Health and Wellness Sciences at the Cape Peninsula University of Technology.

Should you agree to participate in this study, I should like you to kindly read and answer the following questions. Please sign the attached questionnaire once completed.

I trust that this request will enjoy your favourite consideration.

Yours faithfully
Tasneem Daniels

PARTICIPANT CONSENT FORM

Title of the study

BI-RADS final assessment categories in breast cancer patients

Purpose of the study

To evaluate the accuracy of the BI-RADS lexicon categories for the detection of breast cancer in women.

As participant in this study, I have been informed that:

- My years of experience and/or level of training will be required as part of the data-collection process.
- My name or that of the practice will not be revealed during the publication of the thesis.
- I have been informed that my participation is voluntary and that I can withdraw at any time during the study with no penalties or consequences.
- I have not been coerced to participate in this study whatsoever.

Should you have any further queries, please feel free to contact me or the principal supervisor(s) at the following numbers:

Name: Tasneem Daniels
Contact no: 082 087 1965
Email: tasneemda@gmail.com
Principal supervisor(s)
Name: Ms F. Isaacs:
Contact number: 021 959 6538
Email: isaacsf@cput.ac.za

Please answer the following questions

1. How long have you been reporting on mammogram and breast ultrasound examinations?

   _____
   _____
   _____
   _____
   _____

2. Have you received additional training for mammography reporting?
   Yes ☐ or No ☐
   If yes, please specify

   _____
   _____
   _____
   _____

3. Have you received additional training on the BI-RADS lexicon system or have you attended additional courses?
   Yes ☐ or No ☐
   If yes, please specify

   _____
   _____
   _____
   _____

4. Please give your opinion of the BI-RADS lexicon system for mammography and breast ultrasound reporting?

   _____
   _____
   _____
   _____

Signature of participant:

_____ **Date:** _____

APPENDIX B: PATIENT CONSENT FORM

8 Bignonia Circle
Belhar
7493
Cape Town
October 2018

Dear Ms

Request for consent to use mammogram and breast ultrasound images

I, Tasneem Daniels, am currently registered as a part-time student for a Master of Science degree in Radiography at the Cape Peninsula University of Technology (CPUT). As a course requirement, I am expected to conduct research and publish a thesis. My research study is entitled 'BI-RADS final assessment categories in breast cancer patients'. The aim of my study is to evaluate the accuracy of the BI-RADS lexicon and classification categories in patients diagnosed with breast cancer.

The BI-RADS classification system was established by the American College of Radiology (ACR) and is an international accepted scoring method for assessing findings on a mammogram and breast ultrasound images. Radiologists will describe their findings and indicate a final assessment category. The results standardise mammogram reports and serve as a communication tool between radiologist and referring physicians.

Ethical approval for this study has been granted by the Research Ethics Committee of the Faculty of Health and Wellness Sciences at the Cape Peninsula University of Technology (CPUT). Ethical permission was also granted by Drs Schnetler, Corbett & Partners where the study was conducted.

I hereby request your permission to use your mammogram and breast ultrasound images which demonstrated your pathology prior to diagnosis as part of my research study. The images will be used for display purposes in the thesis, journal publications and conference presentations. All patient information and the name of research site will be kept Unrestricted, so no names or personal identification information will be displayed on any such images. Since all images will be anonymised, no patient identification can be traced to you from any of the images.

Please find attached a consent form that requires your signature if you agree to the above request.

Researcher: Tasneem Daniels
Contact details: 082 087 1965

Consent Form

Consent to use mammogram and breast ultrasound images for research dissertation and publication

- I hereby give consent for mammogram and breast ultrasound images performed at Drs Schnetler, Corbett & Partners to be included in the thesis and journal publication of Ms T. Daniels.

- I understand that all my personal information on images will be anonymised to conceal my identity.

- I understand that the images may be published in a research thesis, journal article or conference presentation. As a result, I understand that the anonymised images will be seen by the general public.

- I have no objection to provide consent and have done so out of free will.

_____ _____

Name of Patient *Signature*

_____

Date

APPENDIX C: DATA-COLLECTION SHEET

PATIENT STUDY NO.	PATIENT DEMOGRAPHICS: AGE	BI-RADS LEXICON: MAMMOGRAPHY RESULTS	BI-RADS LEXICON: ULTRASOUND RESULTS	HISTOPATHOLOGY RESULTS	RADIOLOGIST NUMBER	RADIOLOGISTS: YEARS OF EXPERIENCE & LEVEL OF TRAINING	OTHER COMMENTS
001					e.g R1		
002					e.g R2		
003							
004							
005							
006							
007							
008							
009							
010							

APPENDIX D: CODES OF BI-RADS DESCRIPTORS FOR MAMMOGRAPHY AND ULTRASOUND

Codes	Mammography findings (descriptors)	Codes	Ultrasound findings codes (descriptors)
1	Breast mass (spiculated, circumscribed, indistinct, obscured, microlobulated) (round, oval, irregular) (density-fat, low, equal, high)	**1**	Breast Mass Margin (spiculated, circumscribed,not circumscribed, indistinct, angular, microlobulated) Shape (round, oval, irregular) Echo-pattern (anechoic, hyperechoic, hypoechoic, isoechoic, heterogeneous, complex, cystic/solid)
2	Breast mass with associated features (skin retraction, nipple retraction, skin thickening, trabecular thickening, axillary adenopathy, architectural distortion, calcifications)	**2**	Breast mass with posterior features (no features, enhancement, shadowing, combined pattern)
3	Microcalcifications	**3**	Breast Mass Margin (spiculated, circumscribed, not circumscribed, indistinct, angular, microlobulated) Shape (round, oval, irregular) Echo-pattern (Anechoic, hyperechoic, hypoechoic, isoechoic, heterogeneous, complex, cystic/solid) **with** Associated features (architectural distortion, duct changes, skin thickening, skin retraction, oedema, vascularity - absent, internal, rim & elasticity)
4	Microcalcifications with asymmetry/ associated features (skin retraction, nipple retraction, skin thickening, trabecular thickening, axillary adenopathy, architectural distortion, calcifications)	**4**	Calcifications (inside mass, outside mass or intraductal)
5	Breast density with mass/asymmetry/ associated features (skin retraction, nipple retraction, skin thickening, trabecular thickening, axillary adenopathy, architectural distortion, calcifications)	**5**	Calcifications (inside mass, outside mass or intraductal) **with** Associated features (architectural distortion, duct changes, skin thickening, skin retraction, oedema, vascularity - absent, internal, rim & elasticity)
6	Asymmetry	**6**	Special cases (simple cyst, clustered microcyst, complicated cyst, mass in or on skin, foreign body (including implants), intramammary lymph node, AVM, Mondor ‘s disease, post-surgical fluid collection, fat necrosis)
7	Asymmetry with mass/associated features (skin retraction, nipple retraction, skin thickening, trabecular thickening, axillary adenopathy, architectural distortion, calcifications)		

APPENDIX E: CODES FOR DIFFERENT VARIABLES

Codes	Clinical symptoms	History of surgery	Hormone replacement therapy (HRT)	Family history	Parity status	Histology results	Radiologist level of training
0		None			None		None
1	Routine exam	Right/left benign lumpectomy	Yes	Yes		DCIS grade 1, grade 2 & grade 3	Breast imaging congress/conferences
2	Routine follow up	Right/left malignant lumpectomy	No	No		Invasive ductal carcinoma grade 1, grade 2 & grade 3	Tabar/ACR mammography course
3	Palpated nodules/lumps	Benign biopsies				Infiltrating ductal carcinoma grade 1, grade 2 & grade 3	Tomography workshop
4	Tender breast	Malignant biopsies				Mucinous carcinoma	
5	Skin/Nipple retraction	Bilateral reductions				Invasive tubular carcinoma	
6	Feeling a density/thickening in left or right breast	Drainage of breast abscess				Invasive lobular carcinoma	
7	Breast pain	Bilateral implants					
8	Itchy nipple	Breast lift and breast implants					
9	Enlarged lymph node	Mastectomy one breast with lumpectomy of other breast					
10	Mass with nipple retraction and skin thickening						

APPENDIX F: ETHICS CERTIFICATE

Cape Peninsula
University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

P.O. Box 1906 • Bellville 7535 South Africa
Symphony Road Bellville 7535
Tel: +27 21 959 6917
Email: sethn@cput.ac.za

4 August 2015
REC Approval Reference No:
CPUT/HW-REC 2015/H14

Faculty of Health and Wellness Sciences – Biomedical Sciences Department

Dear Tasneem Daniels

Re: YOUR APPLICATION TO THE HW-REC FOR ETHICS APPROVAL

Approval was granted by the Health and Wellness Sciences-REC to Ms Tasneem Daniels for ethical clearance. This approval is for research activities related to staff research in the Department of Radiography Sciences at this Institution.

TITLE: BI RADS lexicon for the detection of breast cancer

Supervisor: **Ms Ferial Isaacs**

Comment:
Approval will not extend beyond 4 August 2016. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the HWS-REC in December of that particular year, for the HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Mr. Navindhra Naidoo
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

APPENDIX G: ETHICS CERTIFICATE

Cape Peninsula University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

P.O. Box 1906 • Bellville 7535 South Africa
Symphony Road Bellville 7535
Tel: +27 21 959 6917
Email: sethn@cput.ac.za

4 October 2016
REC Approval Reference No:
CPUT/HW-REC 2015/H14(extension)

Faculty of Health and Wellness Sciences – Radiography Sciences

Dear Tasneem Daniels

Re: YOUR APPLICATION TO THE HW-REC FOR ETHICS APPROVAL

Ethics extension approval was granted by the Health and Wellness Sciences-REC to Ms Tasneem Daniels for ethical clearance. This approval is for research activities related to staff research in the Department of Radiography Sciences at this Institution.

TITLE: BI RADS lexicon for the detection of breast cancer

Supervisor: **Ms Ferial Isaacs**

Comment:
Approval will not extend beyond 5 October 2017. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the HWS-REC in December of that particular year, for the HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Mr. Navindhra Naidoo
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

APPENDIX H: ETHICS CERTIFICATE

Cape Peninsula University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

P.O. Box 1906 • Bellville 7535 South Africa
Symphony Road Bellville 7535
Tel: +27 21 959 6917
Email: sethn@cput.ac.za

26 July 2018
REC Approval Reference No:
CPUT/HW-REC 2015/H14(extension)

Faculty of Health and Wellness Sciences – Radiography Sciences

Dear Tasneem Daniels

Re: YOUR APPLICATION TO THE HW-REC FOR ETHICS APPROVAL

Ethics extension approval was granted by the Health and Wellness Sciences-REC to Ms Tasneem Daniels for ethical clearance. This approval is for research activities related to staff research in the Department of Radiography Sciences at this Institution.

TITLE: BI RADS lexicon for the detection of breast cancer

Supervisor: **Ms Ferial Isaacs**

Comment:
Approval will not extend beyond 27 July 2019. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the HWS-REC in December of that particular year, for the HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Dr *Navindhra Naidoo*
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

APPENDIX I: PERMISSION TO DO RESEARCH STUDY

8 Bignonia Circle
Belhar
7493
Cape Town
May 2015

Dear [redacted]

REQUEST FOR PERMISSION TO CONDUCT RESEARCH STUDY

I am currently in my second year of my MTech (master's) degree in Diagnostic Radiography/Mammography at Cape Peninsula University of Technology (CPUT).

I am required to conduct research and write a thesis. My research topic is 'BI-RADS final assessment categories in breast cancer patients'. The aim of my study is to evaluate how accurate the BI- RADS lexicon categories are in patients diagnosed with breast cancer. This will be a quantitative study that will involve using mammographic and histology reports.

The technique used is visual assessment by radiologist and correlation with histology reports. All patient information will remain confidential as a number-coded system will be used and all patient information will be stored in a file locked with a password. I herby request permission to conduct my study at [redacted]

Application for ethics approval for this study has also been submitted to the Research Ethics Committee of the Faculty of Health and Wellness Sciences at the Cape Peninsula University of Technology.

I have also attached a copy of my research proposal for your perusal.

I trust that this request will enjoy your favourite consideration.

Kind regards

Tasneem Daniels

Contact details: (cell) 082 087 1965

Please sign below if permission granted

NAME:....

Signature:..... **Date:.....** 3 June 15

APPENDIX J: AMERICAN COLLEGE OF RADIOLOGY (ACR) APPROVAL

ACR BI-RADS® Atlas — Permission Agreement

Individuals who wish to use the ACR BI-RADS® Atlas for specific, limited purposes should sign and return this form acknowledging that they will comply with the conditions of this permission agreement. If you have any questions about the permission agreement for the ACR BI-RADS® Atlas, please call the American College of Radiology at (800) 227-5463, ext. 4561. Return form to:

American College of Radiology
Department of Quality and Safety
1891 Preston White Drive
Reston, VA 20191
or
Fax to: (703) 648-9467

The American College of Radiology grants permission to the individuals listed below to use this document in the creation of data collection and/or reporting forms and associated software ("related works") as long as:

1) A physician or group of physicians, technologist, breast imaging facility staff, or educational institution uses this document solely for their internal, non-commercial use;
2) any portion of the document so used is reproduced in its entirety without modification;
3) the related works are used solely by the physician(s), technologist, breast imaging facility staff, or educational institution licensed by the College for their internal, non-commercial use, for communications with patients, other physicians and healthcare personnel, for education, or for medical research for the improvement of patient care; and
4) the following statement is included at the content location: ***"Reprinted by permission of the American College of Radiology. All rights reserved. The most current version of the ACR BI-RADS® Atlas can be found at http://www.acr.org/Quality-Safety/Resources/BIRADS."***

The initial term of this Permission Agreement shall commence on the date of execution by the undersigned, and shall extend for one year. This permission agreement shall be automatically renewed thereafter for additional periods of one year unless either party gives at least sixty (60) days, prior written notice to the other of its intention to terminate at the end of the year. Upon termination of this permission agreement by either party, the undersigned must immediately remove BI-RADS® from all future versions of its breast imaging application.

The undersigned acknowledges that s/he has read the above requirements and agrees to abide by them in using this document. Failure to comply with these requirements will result in revocation of the permission agreement.

Tasneem Daniels
Licensee (printed name)

Licensee (signature)

American College of Radiology

25 July 2016
Date