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Imaging features of male breast cancer in a South African population

Kaloianova, Maria Simeonova

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IMAGING FEATURES OF MALE BREAST CANCER IN A SOUTH AFRICAN POPULATION

Dr Maria Kaloianova

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Diagnostic Radiology

Johannesburg, 2017

Declaration

I, Maria Kaloianova, declare that this research report is my own work. It is being submitted for the degree of MMed (RadD) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

DR MARIA KALOIANOVA

On this 30th day of October 2017.

To my family.

Publications and presentations

This work has never been published.

It has never been presented at a congress.

Abstract

INTRODUCTION: Male breast cancer is a very rare entity, representing less than 1% of all cancers affecting men (1, 2). Only 0.7% of all breast carcinomas are attributed to male breast cancer (3). As a result, there is little published data worldwide and especially from South Africa about the imaging features of breast malignancy in men. This study looked at the mammographic and ultrasound features of male breast cancer in the South African context.

AIM: To describe the imaging features of male breast cancer in a South African population.

METHOD: The histological reports of all patients who met the inclusion criteria were extracted from the National Health Laboratory Services (NHLS) patient records database and printed. The demographic data was used to trace the relevant diagnostic imaging studies that were performed for each patient. Only the mammography and ultrasound reports were reviewed, images were not re-reviewed.

RESULTS: Seventy-six patients between the ages of 31 to 89 with confirmed primary breast malignancy were found in the NHLS database for the predetermined eleven-year period. Only 20 of the 76 had imaging reports available for assessment. Thirty-five percent of malignant lesions demonstrated microcalcifications, while 20% were spiculate, 20% irregular and 25% macrolobulated. On ultrasound, only 35% of lesions were hypoechoic with 20% demonstrating posterior acoustic shadowing.

Invasive ductal carcinoma represented 91% of all primary male malignant breast lesions in our study population, with 8% of lesions attributed to invasive papillary carcinoma and only 1% ductal carcinoma in-situ.

CONCLUSIONS: Male breast cancer in South Africa is similar to male breast cancer elsewhere, not only on imaging but also on histology and immunohistochemistry.

Acknowledgements

I would like to thank the following individuals without whose support, dedication and encouragement this study would never have been possible.

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List of Abbreviations and Terminology

BI-RADS	Breast Imaging Reporting And Data System
DCIS	Ductal Carcinoma In-situ
ER	Oestrogen Receptor
MBC	Male Breast Cancer
MMG	Mammography
MLO	Mediolateral Oblique
NCR	National Cancer Registry
NHLS	National Health Laboratory Service
NS	Not Specified
PR	Progesterone Receptor

1. Introduction

1.1. Background

Male breast cancer (MBC) is a very rare entity, representing less than 1% of all cancers affecting men (1, 2). Only 0.7% of all breast carcinomas are attributed to male breast cancer (3). As a result, there is little published data worldwide and especially from South Africa about the imaging features of breast malignancy in men. This study will look at the mammographic and ultrasound features of male breast cancer in the South African context.

1.2. Anatomy and development of the breast

At birth, the male and female breast is identical, composed predominantly of fibro-adipose stromal tissue and a few primary lactiferous ducts. It is only during puberty and under the influence of oestrogen that the characteristic glandular breast tissue in women develops. The male breast does not develop further and remains primarily unchanged with a lack of significant lobule formation (2). Hence, because of the similarities that male and female breasts share, breast cancer can present in a similar way in both sexes (4). Due to its uncommonness, male breast cancer is far less studied, thus diagnostic and treatment protocols are deduced from those of the extensively studied female breast cancer (4).

1.3. Epidemiology of male breast cancer worldwide

Male breast cancer accounts for less than 1% of all cancers affecting men worldwide, making it an important, but rare disease. Chen describes the incidence of male breast cancer as increasing from 0.86 to 1.08 per 100 000 population over the last 25 years (2). This low incidence implies that since it is so uncommon and there is even less public awareness and education of the disease, no screening guidelines are in place (2, 3, 5, 6).

In Europe, the annual incidence is reported to be 1 in 100 000, making it less prevalent than in developing countries such as Uganda and Zambia, where one study reported the incidence to be 5% and 15% respectively (7). In contrast to the high incidence in Africa, Japan was found to have a prevalence of 1 in 5 000 000 for male breast cancer (7).

There are no absolute risk factors for male breast cancer described thus far, but consistent associations have previously been recognised and published in the literature. Some of these known associations include: family history (especially in a first degree relative), Kleinefelter syndrome, BRCA1 and BRCA2 mutations, ionizing radiation exposure and radiation therapy to the chest, increasing age and conditions resulting in increased oestrogen levels(1, 3, 8, 9). Male breast cancer is often described as having similar characteristics to post-menopausal breast cancer in women (10, 11).

Nahleh et al, in a study in 2007, found significant racial and gender differences in the presentation of breast cancer. In their study population, they found that the male breast cancer patients were more likely to be black. In contrast, the female breast cancer patient was more likely to be white. (12).

1.4. Epidemiology of male breast cancer in the developing world

1.4.1. Africa

A meta-analysis done by Ndom et al found that the female to male ratio of breast cancer in Sub-Saharan Africa and in particular in central and southern African countries was significantly higher (1:0.049) than in their North African counterparts (1:0.027). They also suggested that there is a strong genetic basis of MBC based on observations of males of African origin residing in the United States who displayed a much higher male to female ratio in comparison with the surveyed Caucasian population (13).

The general trend that is observed in African populations with regard to MBC is that it is usually diagnosed late and at a fairly advanced stage (12). A number of reasons contribute to this finding, among which a lack of access to healthcare / resources and poor patient awareness of the disease are just a few (7, 11, 13). These issues are not however limited to just MBC in Africa as similar findings were also demonstrated among the African female population. These are very important factors related to delay in diagnosis and therefore result in an increase in morbidity and mortality (7).

The most common histological type of breast cancer that is observed among African men is infiltrating ductal carcinoma and it is also the predominant type of breast cancer in men worldwide, accounting for more than 90% of all MBC cases (1, 7, 8, 13).

1.4.2. South Africa

There are very few published studies in the literature regarding MBC and its characteristics / features in the South African population. The latest statistics from the National Cancer Registry (NCR) of South Africa published for the year 2012 stated that there were 212 new MBC cases diagnosed in that year, resulting in a 1 in 738 lifetime risk in the South African population (14).

This incidence was higher than the number of diagnosed cases of testis, myeloma and thyroid cancer respectively in South African men of that same year. Of the 212 new MBC cases diagnosed in 2012 in South Africa, 12 were Asian, 103 were African, 28 were coloured and 69 were white (14).

In contrast to the statistical data published by the NCR for the year 2011, there is a clearly observed increase in the total number of newly diagnosed MBC cases from 149 to the 212 reported for 2012 (14, 15). The increase is particularly noted in the black population, previously being 85. The incidence of MBC in the white population was almost doubled from 36 to 69 newly diagnosed cases. The Asian and coloured populations also demonstrated a significant increase from 4 to 12 and 20 to 28 newly diagnosed cases respectively.
In 2011 the lifetime risk was reported to be 1 in 922 (14, 15).

The NCR is the main source for cancer statistics in South Africa and gathers its data only from public and private pathology laboratories across the country. Being a pathology-based registry only, results in under-reporting of many malignancies including that of male breast cancer. Based on the latest NCR data (for the year 2012), MBC in South Africa represents 0.57% of all cancers diagnosed in men. This figure is much higher than the 0.17% reported by Mathew et al and demonstrates an increase from the 0.45% reported by the NCR for the previous year of 2011 (8, 14, 15).

1.5. Imaging of the male breast

Mammography has long been the most reliable method of diagnosing breast cancer in both men and women with a sensitivity of 92% and specificity of 90% respectively (6). Ultrasound is also routinely used as a supplementary investigation to correlate mammography findings and to assist in obtaining image guided tissue biopsy for diagnosis (2, 6, 16).

The most common mammographic feature of MBC is an eccentric, sub-areolar mass (6, 17, 18). These masses are typically solid and often present with spiculated margins (19). Unlike its female equivalent, calcification is not a very common feature of MBC. When present, calcifications tend to be coarse, large and more scattered rather than the microcalcifications that are observed in female breast cancer (2, 17-20).

On ultrasound, most masses are seen as ill-defined, irregular and hypoechoic (2, 17, 20). Cystic lesions in a male breast should always be seen as suspicious because papillary neoplasms commonly present as complex cystic masses (6).

1.6. This project in context: Comparison to literature on the topic

There is extremely little published data on the imaging features of MBC and male breast cancer in general and in the South African context. Recent literature on MBC is summarised in Table 1.1.

Table 1.1. A comparison of recent literature on male breast cancer

Author		Carrasco (2013) (16)	Doyle (2011) (20)	Mathew (2008) (8)	Chen (2006) (2)	Anderson (2005) (5)	Gunhan-Bilgen (2002) (21)	Appelbaum (1999) (1)
No of malignant lesions		6	20	57	14	2984	14	12
Age range (mean)		13 – 83 (48)	64 – 79 (NS)	19 – 80 (62)	(67)	62 – 68 (NS)	53 – 84 (68.7)	NS
Site		NS	Subareolar	Subareolar	Subareolar	NS	Retroareolar	Subareolar
Mammogram	Well-circumscribed	15.7%	15%	15%	NS	NS	23%	50%
	Ill-defined	NS	46%	32%	NS	NS	NS	43%
	Macrolobulated	NS	NS	20%	NS	NS	8%	42%
	Irregular	NS	NS	50%	NS	NS	69%	NS
	Spiculate	NS	39%	33%	NS	NS	NS	NS
	Microcalcifications	NS	15%	29%	NS	NS	7%	25%
Ultrasound	Borders	NS	62% ill-defined 23% well-defined	44% micro-lobulated	NS	NS	NS	NS
	Internal echopattern	NS	93% hypoechoic	76% hypoechoic	hypoechoic	NS	NS	NS
	Posterior echo features	NS	23% post shadowing	NS	14% post shadowing	NS	20% post enhancement	NS
Histology	DCIS	3.8%	NS	11%	NS	NS	35-50%	NS
	Invasive ductal	19.2%	80%	84%	85%	75.6%	85%	75%
	Invasive lobular	NS	5%	3%	NS	NS	NS	NS
	Invasive papillary	NS	5%	7%	NS	23.4%	NS	NS
	Other	NS	10%	NS	NS	NS	14%	NS

NS = Not specified

1.7. Study objectives

The aim of the study was to describe and categorise mammographic and ultrasound features of male breast cancer in our study population.

The study also described the histological and immunohistochemical findings of male breast cancer in our study population.

2. Materials and Methods

This was a retrospective cross-sectional record review of male breast cancer patients in the database of the Division of Anatomical Pathology of the University of Witwatersrand/National Health Laboratory Service (NHLS) over an 11-year period. Ethics clearance was obtained to do the study, certificate number M140852 attached as Appendix A.

2.1. Study population

The study population included all male patients who underwent breast biopsies or surgery and were found in the database of the Division of Anatomical Pathology of the University of Witwatersrand/NHLS.

2.2. Inclusion criteria

All patients with biopsy proven carcinomas were considered for inclusion into the study.

2.3. Exclusion criteria

Patients with incomplete or illegible records were excluded from the study.

2.4. Data collection

The histological reports of all patients that met the inclusion criteria were extracted from the NHLS patient records database and printed. The demographic data was used to trace the relevant diagnostic imaging studies that were performed for each patient. Only the mammography and ultrasound reports were reviewed, images were not reviewed. Data for analysis was collected according to the attached data collection sheet (Appendix B) and captured in an Excel spreadsheet. No personal identifiable information was captured.

2.5. Statistical analysis

The data obtained was analysed using descriptive statistics to determine the frequencies and percentages of pathology as identified on mammogram and ultrasound within the study population. The frequencies and percentages of histological findings were also reported.

3. Results

Within the eleven-year period of 1 January 2004 to 31 December 2014, a total of 76 histologically confirmed male breast cancers were found in the histology database of the University of Witwatersrand/NHLS. Only 20 (26%) of the total 76 were found to have radiological imaging.

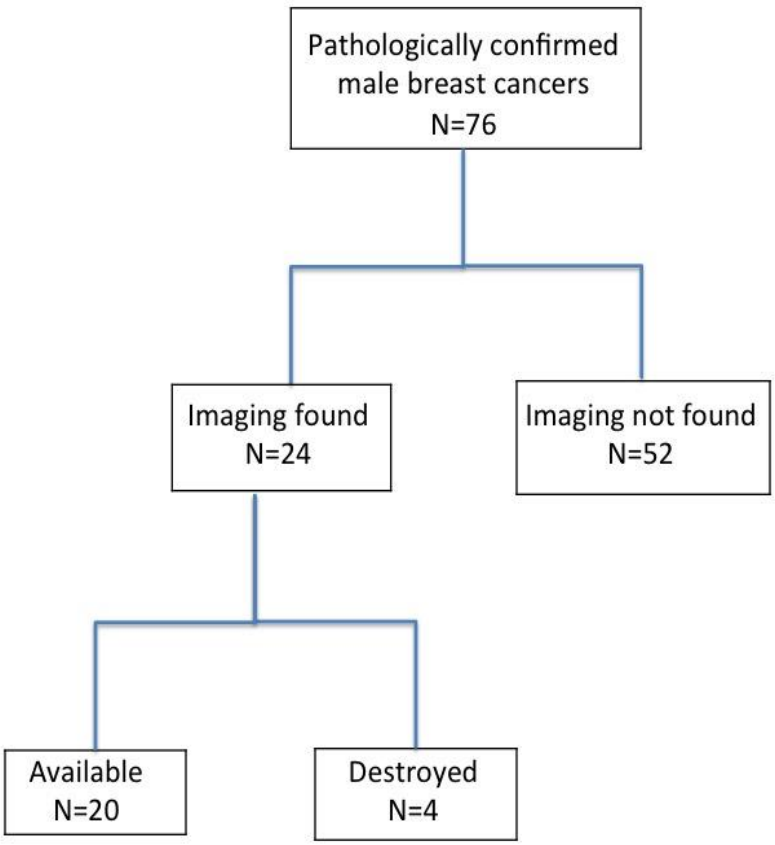


Figure 3.1. Summary of total number of confirmed male breast cancers and available imaging reports

Imaging reports were not available for several reasons

- Imaging was never done - patient had biopsy and / or surgery without any imaging
- Records at some hospitals are destroyed after 5 years, especially if patient demised
- Handwritten reports that were illegible
- Alternative names / misspelling of patient names or surnames

3.1. Demographics

The age range of the sampled population was 31 to 89 years.

The mean age at diagnosis, as well as the median age were both found to be 60 years. The mode was 63 years. Three patients did not have a record of their age.

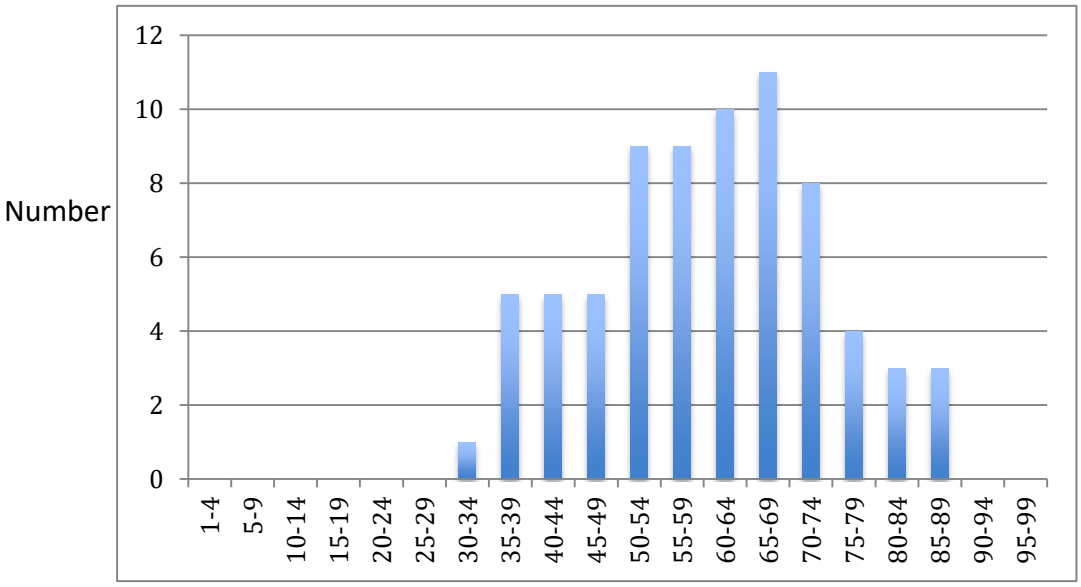


Figure 3.2. Age distribution of male patients with breast cancer

3.2. Mammographic features

The mammographic (MMG) features were recorded on the 20 patients who were found to have imaging reports (Table 3.1).

Table 3.1. Mammographic appearance of malignant lesions and of the contralateral breast

	Mammographic features	Number (%) (N = 20)
Malignancy	Microcalcifications	7 (35%)
	Macrolobulation	5 (25%)
	Irregular	4 (20%)
	Spiculated	4 (20%)
	Well-defined	1 (5%)
Contralateral breast	Gynaecomastia	3 (15%)
	Microcalcifications	1 (5%)
	Normal	12 (60%)
	Unspecified	3 (15%)

NOTE: percentages do not total to 100 because of rounding.

Microcalcifications were demonstrated in 7 patients (35%). A macrolobulated mass lesion was described in 5 cases (25%). Four lesions (20%) were irregular and another 4 (20%) were spiculated. A well-defined lesion was described in only one patient (5%).

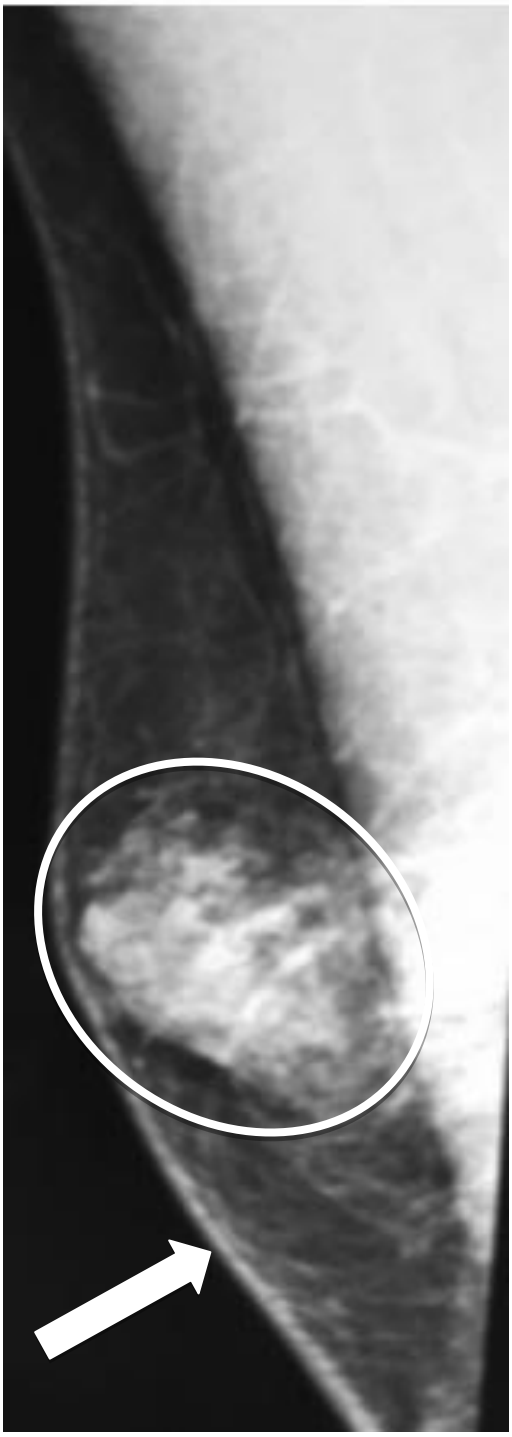
On mammographic review of the contralateral breast (Table 3.1.), three patients (15%) demonstrated gynaecomastia, one (5%) had microcalcifications and 3 (15%) were unspecified. The remaining 12 (60%) demonstrated normal mammographic features with no suspicious characteristics.

Examples of mammographic findings of breast cancer in male patients are shown in Figures 3.3 to 3.6 below.



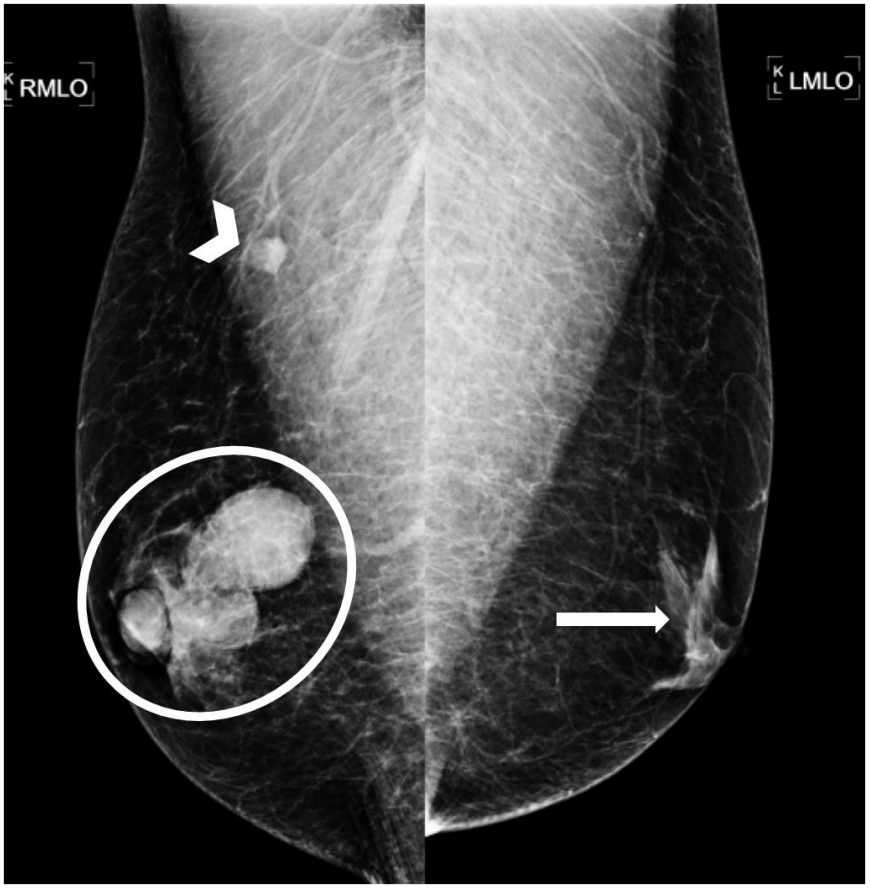
Left mediolateral oblique (MLO) mammogram image of a 45-year-old male patient, showing a retroareolar mass (solid line) with irregular margins and associated microcalcifications (arrow). Additionally, there is overlying skin thickening (arrowhead).

Figure 3.3. Invasive ductal carcinoma with microcalcifications on mammogram in a male patient



Right mediolateral oblique mammogram image of a 59-year-old male patient, showing an irregular retroareolar mass (solid line) with associated skin thickening (arrow). No calcifications were noted in this mass.

Figure 3.4. Invasive ductal carcinoma with no microcalcifications on mammogram in a male patient



Bilateral mediolateral oblique mammographic images of an 82-year-old male patient demonstrating a right retroareolar macrolobulated mass (solid line) with spiculated inferior border and associated nipple retraction. Additionally, there is an involved intramammary lymph node (arrowhead) within the right axillary tail. The contralateral breast demonstrates benign proliferation of retroareolar fibroglandular tissue (arrow) representing gynaecomastia.

Figure 3.5. Invasive papillary carcinoma on mammogram in a male patient with gynaecomastia of the contralateral breast.



Right mediolateral oblique mammographic image of a 79-year-old male patient, demonstrating a retroareolar macrolobulated mass (solid line). There is no involvement of the nipple.

Figure 3.6. Invasive papillary carcinoma on mammogram in a male patient

3.3. Ultrasound features

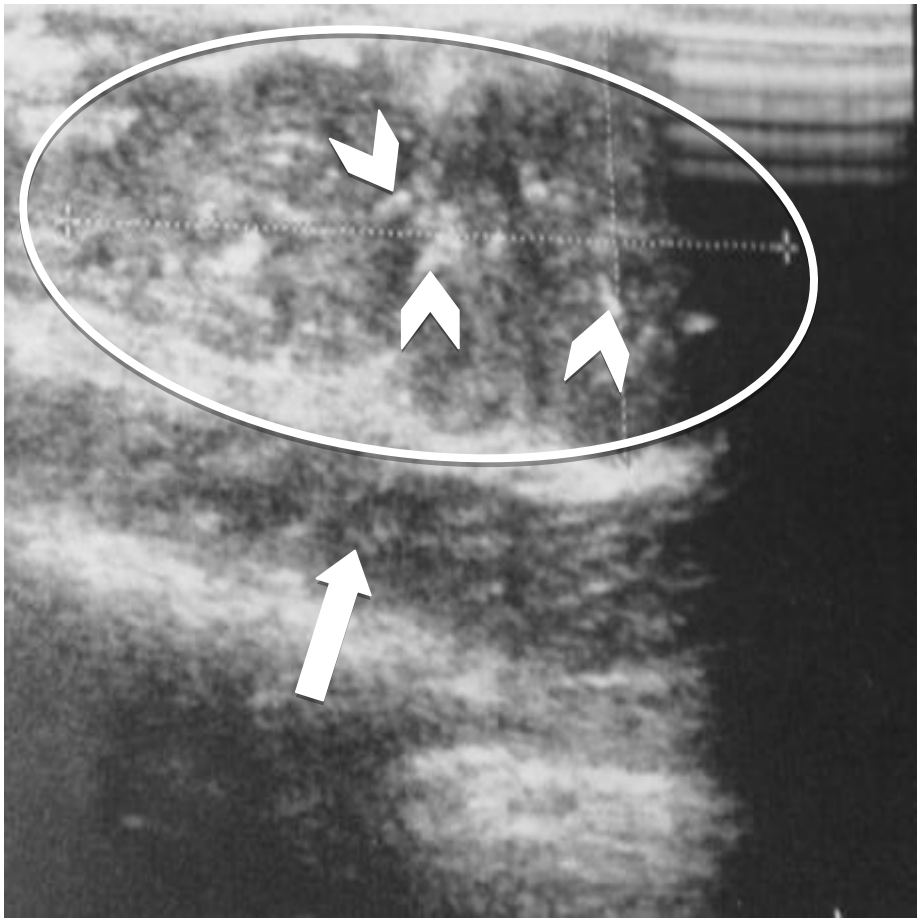
Upon analysis of the 20 available ultrasound reports of histologically confirmed male breast cancers, 5 (25%) were noted to be solid, 3 (15%) were cystic and a further 3 (15%) were mixed solid/cystic.

A hypoechoic internal echopattern was recorded in 7 of the patients (35%) with posterior acoustic shadowing in 4 (20%). Three (15%) of the malignant lesions were found to have irregular borders and only 1 (5%) had spiculated borders on ultrasound (Table 3.2.).

Table 3.2. Ultrasound appearance of malignant lesions

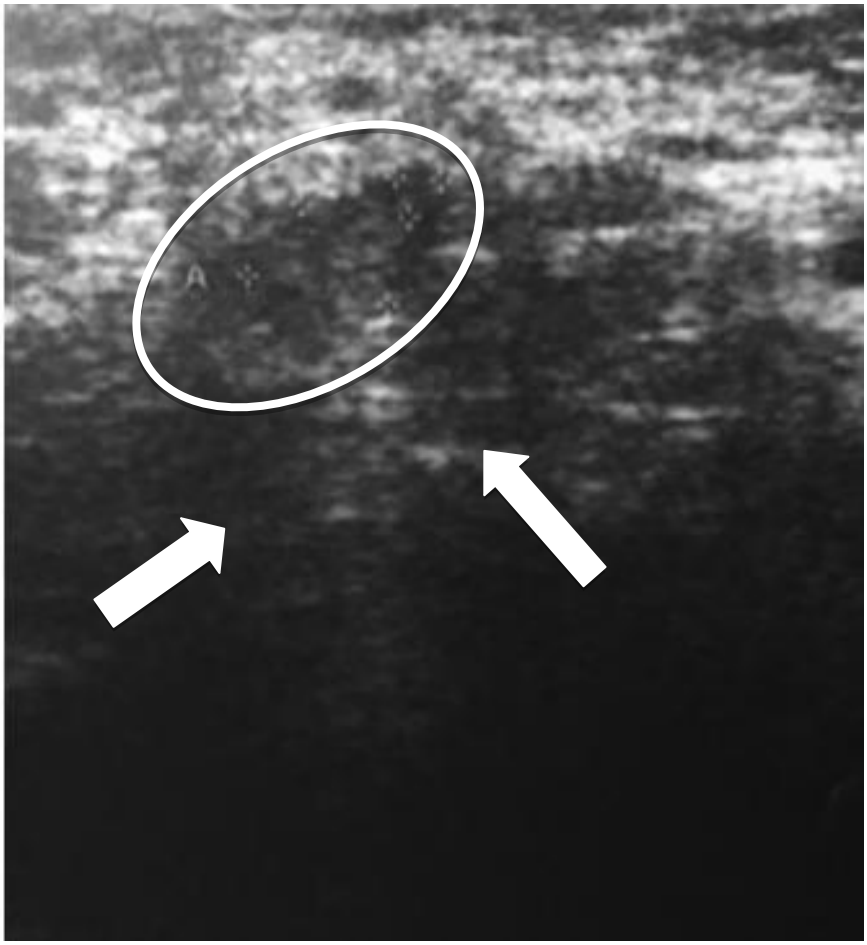
Ultrasound features	Number (%) (N=20)
Solid	5 (25%)
Cystic	3 (15%)
Solid/cystic	3 (15%)
Hypoechoic	7 (35%)
Posterior acoustic shadowing	4 (20%)
Irregular borders	3 (15%)
Spiculated	1 (5%)

NOTE: percentages do not total to 100 because of rounding.



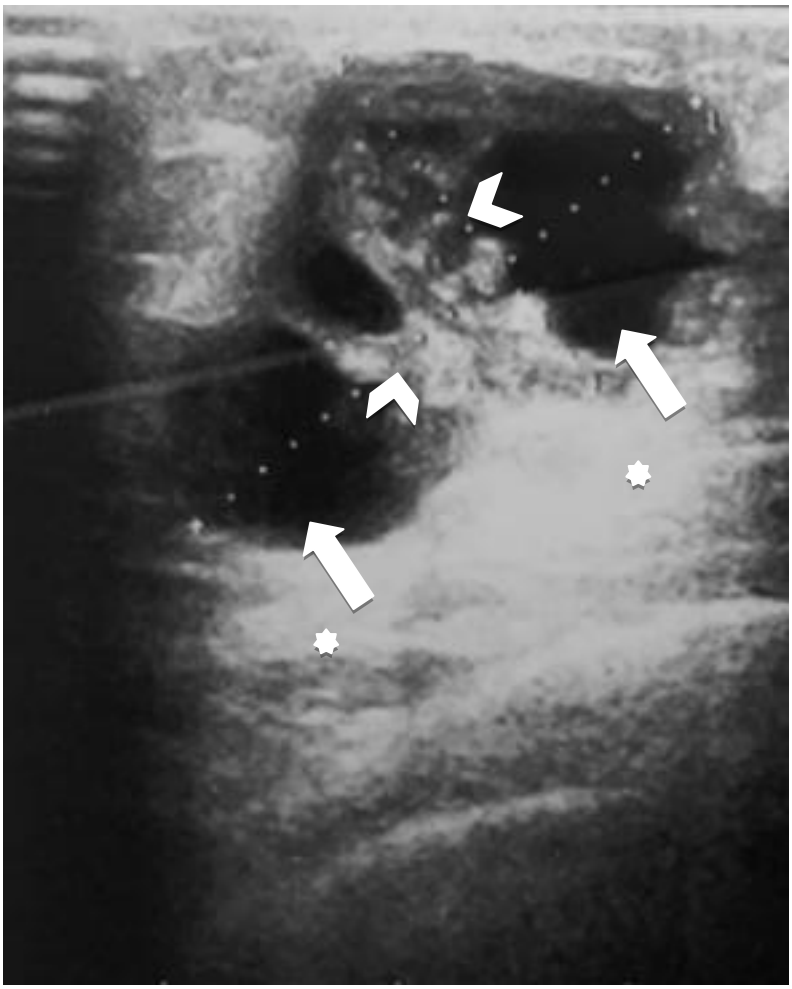
Ultrasound image of the patient seen in Figure 3.3. above with invasive ductal carcinoma, demonstrating a heterogeneous mass with irregular microlobulated margins (solid line) with multiple internal hyperechoic foci (arrowheads) representing microcalcifications. Note that this mass is separable from the underlying pectoralis major muscle (arrow).

Figure 3.7. Invasive ductal carcinoma with microcalcifications on ultrasound in a male patient



Ultrasound image of the patient seen in Figure 3.4. above with invasive ductal carcinoma demonstrating a solid irregular hypoechoic retroareolar mass (solid line) with areas of posterior acoustic shadowing (arrows).

Figure 3.8. Invasive ductal carcinoma on ultrasound in a male patient



Ultrasound image of the patient seen in Figure 3.6. above with invasive papillary carcinoma demonstrating a lobulated mass with anechoic cystic (arrows) and heterogeneous solid (arrowheads) components. There is posterior acoustic enhancement (stars) related to the cystic components.

Figure 3.9. Example of an ultrasound image of male breast cancer – invasive papillary carcinoma

3.4. Histological features

Seventy-six male patients with breast cancer were identified in the NHLS database during the study period. The histological findings were collected on all the patients, whether they had imaging available or not.

Invasive ductal carcinoma was found in 69 patients (91%). Three patients (4%) were noted to have invasive ductal carcinoma with a micropapillary component, and a further 3 (4%) were intraductal papillary carcinomas. Ductal carcinoma in situ was found in only one patient, representing 1% (Table 3.3.).

Table 3.3. Histological features

Histology	**Number (%) (N=76)**
Invasive Ductal Carcinoma	69 (91%)
Invasive Papillary Carcinoma	6 (8%)
Ductal Carcinoma In Situ	1 (1%)
Other	0 (0%)

3.5. Molecular prognostic markers

Oestrogen and progesterone receptor markers were analysed in all but two patients (99%).
Her2NEU analysis was performed in 71 patients (93%).
Ki67 index was performed in only 23 (30%) of the total 76 patients.

3.5.1. Oestrogen receptor status

Sixty-three (83%) patients were found to be Oestrogen receptor (ER) positive and 11 (14%) were ER negative (Table 3.4.). Two patients (3%) had no record of molecular prognostic marker testing and thus ER status was unknown.

Table 3.4. Oestrogen receptor status

Receptor status	Number (%) (N=76)
Positive	63 (83%)
Negative	11 (14%)
Unknown	2 (3%)

3.5.2. Progesterone receptor status

Progesterone receptor (PR) status was tested in all but 2 (3%) patients (Table 3.5.). Fifty-two (68%) of the cancers were found to be receptor positive and 22 (29%) were receptor negative.

Table 3.5. Progesterone receptor status

Receptor status	Number (%) (N=76)
Positive	52 (68%)
Negative	22 (29%)
Unknown	2 (3%)

3.5.3. Her2NEU receptor status

Her2NEU receptor status was tested only on 71 patients (Table 3.6.). A positive receptor status was noted in 16 patients (21%). Of the total 76 patients, 41 (54%) were Her2NEU receptor negative, 14 (18%) were equivocal and 5 (7%) were unknown.

Table 3.6. Her2NEU receptor status

Receptor status	Number (%) (N=76)
Positive	16 (21%)
Negative	41 (54%)
Equivocal	14 (18%)
Unknown	5 (7%)

3.5.4. Ki67 Index

Ki67 index was not consistently tested in all patients. It was performed in only 23 (30%) of the total 76 patients and thus will not be discussed further in this study.

3.5.5. Combined analysis of molecular prognostic markers

A triple negative result (ER, PR and Her2NEU) was noted in only 4 (5%) patients.

3.6. Laterality and site of malignant lesions

Based on histological reports 33 (43%) cancers were left-sided, 36 (47%) right-sided and 7 (9%) were unspecified (Table 3.7.).

Retro-areolar location was noted in 22 patients (29%), followed by lower outer quadrant in 9 (12%), upper outer quadrant in 8 (11%), lower inner quadrant in 5 (7%) and upper inner quadrant in 3 (4%). Quadrant location was unspecified in 29 (38%) patients (Table 3.7.).

Table 3.7. Laterality and site of malignant lesions

		Number (%) (N = 76)
Side	Left	33 (43%)
	Right	36 (47%)
	Unknown	7 (9%)
Location	Retro-areolar	22 (29%)
	Lower outer quadrant	9 (12%)
	Upper outer quadrant	8 (11%)
	Lower Inner quadrant	5 (7%)
	Upper inner quadrant	3 (4%)
	Unspecified	29 (38%)

NOTE: percentages do not total to 100 because of rounding.

4. Discussion

Mammography is the most reliable radiological method of diagnosing breast cancer with a sensitivity and specificity of 92% and 90% respectively (6). The main purpose of this study was to describe the imaging features of breast cancer in male patients in our study population. To our knowledge, this study is the first descriptive study of its kind in South Africa.

There is a paucity of literature on male breast cancer, both internationally and locally. Table 4.1. below compares the mammographic, ultrasound and histological data of our study to six other descriptive studies in the literature. All the studies describing imaging features are rather small, mostly less than 20 patients. The largest study that could be found in the English-speaking literature was done by Mathew et al who reported 57 cases in 2008 (8).

4.1. Results in context

4.1.1. Demographics

Male breast cancer is a very rare entity. According to the NCR between 110 to 145 males have been diagnosed with breast cancer annually in South Africa between the period of 2002 and 2011, with a steep increase of 212 newly diagnosed cases in 2012 (14). This study only identified 76 patients over an 11-year period at the NHLS in Johannesburg.

The age distribution of our study was broad, ranging from 31 to 89 years of age. The mean age at diagnosis was found to be 60 years. This is comparable to the study by Mathew et al who reported a mean age at diagnosis of 62 in their study (8). The studies by Kreiter et al and Otto et al described male breast cancer as having a similar clinical presentation as post-menopausal breast cancer in women (10, 11). This was confirmed by the Anderson study, which found that the incidence of male breast cancer increases with advancing age (5). The demographics in our study reflect a similar pattern.

Table 4.1. Comparison of current study to recent literature on male breast cancer

Author		Kaloianova (2017) Current study	Doyle (2011) (20)	Mathew (2008) (8)	Chen (2006) (2)	Anderson (2005) (5)	Gunhan-Bilgen (2002) (21)	Appelbaum (1999) (1)
No of malignant lesions		76 (20 MMG)	20	57	14	2984	14	12
Age range (mean)		31-89 (60)	64 – 79 (NS)	19 – 80 (62)	(67)	62 – 68 (NS)	53 – 84 (68.7)	NS
Site		Retroareolar	Subareolar	Subareolar	Subareolar	NS	Retroareolar	Subareolar
Mammogram	Well-circumscribed	5%	15%	15%	NS	NS	23%	50%
	Ill-defined	0%	46%	32%	NS	NS	NS	43%
	Macrolobulated	25%	NS	20%	NS	NS	8%	42%
	Irregular	20%	NS	50%	NS	NS	69%	NS
	Spiculate	20%	39%	33%	NS	NS	NS	NS
	Microcalcifications	35%	15%	29%	NS	NS	7%	25%
Ultrasound	Borders	15% irregular 5% spiculated	62% ill-defined 23% well-defined	44% micro-lobulated	NS	NS	NS	NS
	Internal echopattern	35% hypoechoic	93% hypoechoic	76% hypoechoic	hypoechoic	NS	NS	NS
	Posterior echo features	20% post shadowing	23% post shadowing	NS	14% post shadowing	NS	20% post enhancement	NS
Histology	DCIS	1%	NS	11%	NS	NS	35-50%	NS
	Invasive ductal	91%	80%	84%	85%	75.6%	85%	75%
	Invasive lobular	0%	5%	3%	NS	NS	NS	NS
	Invasive papillary	8%	5%	7%	NS	23.4%	NS	NS
	Other	0%	10%	NS	NS	NS	14%	NS

NS = Not specified, MMG = Mammogram

4.1.2. Site and laterality of malignant lesion

Our study found 29% of lesions to be sited in a retroareolar location. In the literature, the terms “retroareolar” and “subareolar” are used interchangeably. All the comparable studies that were found stated either “retroareolar” or “subareolar” as the commonest site for the lesions in their studies. This is in keeping with the fact that the male breast tissue is concentrated in the retroareolar region (4).

There was no statistically significant difference in the laterality of the malignant lesions in our study where 43% were left sided and 47% were right sided. Those with an unknown location accounted for 9% of the total number of lesions.

4.1.3. Mammography findings

Only 20 (26%) of the total 76 patients with histologically confirmed malignancies in our study had breast imaging reports available for analysis. This figure is concordant with only 23% of patients imaged that was reported by Mathew et al (8).
A significant number of our patients had biopsies and / or surgery without any imaging, however there were also cases of lost, destroyed or illegible reports, decreasing the number of imaging reports available for assessment.

The most common finding in our study was that of microcalcifications, found in 35% (7 of 20) of our patients. This was higher that the incidence of microcalcifications described in the international literature. Mathew and Appelbaum reported 29% and 25% respectively (1, 8). Gunhan-Bilgen and Doyle reported even lower incidences of 7% and 15% respectively (20, 21).

Macrolobulation was the second most common finding in our study, with 25% of our patients showing macrolobulation on MMG. This is similar to what Mathew et al have shown, at 20% (8). The frequency of macrolobulation otherwise varies in the literature from 8% (Gunhan-Bilgen et al) to 42% (Appelbaum et al) (1, 21).

4.1.4. Ultrasound features

Ultrasound is commonly used as a supplement to confirm mammographic findings (2, 6, 16). In our centres, it is routinely done for all patients undergoing mammography and it is highly user dependent.

Mathew and Doyle found that more than two thirds of the malignant lesions in their respective studies demonstrated a hypoechoic internal echopattern (8, 20). Internal echopattern was stated in only 35% of patients in our study, and was documented as hypoechoic in all these cases. In the remaining 65% of patients echogenicity of the lesion was not commented upon. In our review, it was noted that 15% of lesions were described as irregular, 5% as spiculated and 20% as demonstrating posterior acoustic shadowing. Review of the ultrasound reports highlighted an inconsistent use of the standardised Breast Imaging Reporting and Data System (BI-RADS) terminology, making it very difficult to extract data that would be comparable with other studies.

4.1.3. Histological features

Invasive ductal carcinoma was by far the most prevalent histological type of breast cancer in our study population, accounting for 91% of all malignant breast lesions. This finding is similar to that noted by Mathew et al and Chen et al, who reported the prevalence of invasive ductal carcinoma to be 84% and 85% in their respective studies (2, 8).

The second most common histological type of breast cancer in this study was invasive papillary carcinoma, which made up 8% of the total. Mathew et al described a comparable finding of 7% in their study population (8). In contrast to the above data, Anderson et al reported a 23.4% prevalence of invasive papillary carcinoma (5).

Ductal carcinoma in-situ (DCIS) was only present in 1% of our study population. Mathew noted an 11% DCIS prevalence (8). There are various factors that could explain this difference. Lack of access to healthcare and delayed presentation due to

poor patient awareness are possible reasons for this apparent discrepancy. (7, 11, 13).

4.1.3. Molecular prognostic markers

Our literature review revealed very few studies that published data relating to molecular prognostic markers in male breast cancer. When reported, only oestrogen and progesterone receptor status were analysed. In our study we considered oestrogen, progesterone and Her2NEU receptor status.

Table 4.2. Comparison of molecular prognostic markers of current study with recent literature

Author		Kaloianova (2017) Current study	Mathew (2008) (8)	Anderson (2005) (5)
Number (%)		N=76 (100%)	N=244 (100%)	N=1855 (100%)
Oestrogen receptor	Positive	63 (83%)	110 (45%)	1097 (59.1%)
	Negative	11 (14%)	11 (5%)	112 (6.0%)
	Unknown	2 (3%)	123 (50%)	646 (34.8%)
Progesterone receptor	Positive	52 (68%)	84 (34%)	936 (50.5%)
	Negative	22 (29%)	26 (11%)	228 (12.3%)
	Unknown	2 (3%)	134 (55%)	691 (37.3%)
Her2NEU receptor	Positive	16 (21%)	NS	NS
	Negative	41 (54%)	NS	NS
	Equivocal	14 (18%)	NS	NS
	Unknown	5 (7%)	NS	NS

NOTE: percentages do not total 100 because of rounding; NS = Not specified

The discordance in data in Table 4.2 above is postulated to be as a result of ethnic genetic differences considering the diverse populations and geographic locations that were surveyed in each study. Further research in this field is needed.

It is extremely important to assess the combined status of the three molecular markers in the context of each tumour. Triple negative breast cancer (ER, PR and Her2NEU negative) in both men and women is known to be particularly resistant to hormonal therapy and other commonly used chemotherapeutic agents (22).
A total of 4 out of 76 patients (5%) in our study were triple negative.

4.2. Current applications

Although primary male breast cancer is rare, it is extremely important to apply the same protocols that are applied in the diagnosis and imaging of female breast cancer. Mammography and ultrasound form the mainstay of this diagnosis. Thus, we recommend performing both mammography and breast ultrasound on all male patients presenting with breast symptoms and supplying the managing clinical team with a standardised report using BI-RADS descriptors.

4.3. Limitations of the current study

A significant limitation of this study is that it is a retrospective review of a single histological laboratory's data set of 76 histologically confirmed MBC, of which only 20 comprehensive imaging reports could be retrieved. An important factor involved in this limitation included poor record-keeping of imaging reports.

Additionally, we found multiple discrepancies and inconsistencies, especially in the ultrasound reports in our centres, which provided only a vague description of lesions. Examples include not providing comments on the internal echo pattern of lesions and simply describing a breast mass as a "space-occupying lesion".

4.4. Future applications

For our study, we compiled a data-collection checklist (Appendix B) that was adapted from common imaging descriptors used in mammography and breast ultrasound in the radiology literature. Based on the widespread use of non-standard descriptors that we found in the imaging reports in our centres, we would strongly like to encourage the use of and adherence to international reporting standards that are outlined in the latest BI-RADS lexicon for the reporting of MMG and ultrasound findings of every patient (male and female) undergoing breast imaging in our centres. Adherence to these guidelines will assist in standardising our imaging reports and greatly facilitate future data collection and analysis. Ultimately this strategy will improve and encourage further research in MBC.

5. Conclusion

We have shown that male breast cancer in South Africa is similar to male breast cancer elsewhere, not only on imaging but also on histology and immunohistochemistry.

Although this is a rare condition, radiologists have an important role to play in communicating findings to clinicians in a concise way in order to facilitate and expedite appropriate treatment.

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Appendix A: Ethics Clearance Certificate

R14/49 Dr Maria Kaloianova

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140852

NAME: (Principal Investigator)	Dr Maria Kaloianova
DEPARTMENT:	Radiology Charlotte Maxeke Johanesburg Academic Hospital Rahima Moosa Mother and Child Hospital Chris Hani Baragwanath Academic Hospital Helen Joseph Hospital and NHLS
PROJECT TITLE:	Imaging Features of Male Breast Cancer in a South African Population
DATE CONSIDERED:	29/08/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Susan Lucas
APPROVED BY:	Professor P Cleaton-Jones, Co-Chairperson, HREC (Medical)
DATE OF APPROVAL:	01/09/2014

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

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature

Date 18/09/2014

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix B: Data collection sheet

Study no		
Age		
Site of lesion		
Mammogram features	Well-defined	
	Ill-defined	
	Irregular	
	Macrolobulated	
	Spiculate	
	Microcalcifications	
	Other breast	
Ultrasound features	Solid	
	Cystic	
	Internal echopattern	
	Posterior echo features	
	Borders	
Histology	DCIS	
	Invasive Ductal Carcinoma	
	Invasive Papillary Carcinoma	
	Invasive Lobular Carcinoma	
	Receptor Status (ER, PR, Her2)	
	Other	

Appendix C: Note on referencing style

Please note that the referencing in this thesis is a modification of the Vancouver Referencing style, done according to the Faculty of Health Sciences Style Guide as set out by the Wits Health Sciences Library.

The information on this WHSL Vancouver Citation Style Guide for Theses, Dissertations and Research Reports is available from http://libguides.wits.ac.za/whsl-vancouver updated on 30 January 2017.