

**THE SPECTRUM OF MALE BREAST DISEASE AT CHARLOTTE
MAXEKE JOHANNESBURG ACADEMIC HOSPITAL – A 3 YEAR
RETROSPECTIVE REVIEW**

Dr Darren Rattray

Student Number: 353068



UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

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Master of Medicine in Surgery.

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Declaration

I, Darren Rattray declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Medicine in Surgery at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



(Signature of candidate)

22nd day of June 2020 in Killarney

Abstract

Background: The spectrum of male breast disease (MBD) and their relative proportions is not well documented. This study aims to describe the demographics, clinical, radiological and histopathological characteristics of the spectrum of male breast disease managed at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH).

Methods: This is a retrospective, descriptive study of all male patients diagnosed with MBD at CMJAH between 1 January 2016 and 31 December 2018. Patients' data was extracted from the Breast Imaging Department, CMJAH Breast Clinic and the National Health Laboratory Services patients' records. Data collected included patients' demographics, clinical presentation, radiological findings and histopathological diagnosis, where available. The collected data was captured using REDCap™ and was analysed using Statistica 13 and SAS version 9.2. P value of 0.05 was used for statistical significance.

Results: Of the 269 males imaged, 244 (91%) had a diagnosed breast condition, 90% of which were benign. Gynaecomastia accounted for 85% of all breast disease diagnosed. Patients who presented with benign breast disease were significantly younger than those with malignant breast disease, with a mean age of 45.59 years vs 58.29 years ($p = 0.0007$). 71% of patients had a known HIV status with 39% being HIV positive. There was a significant association between patients with HIV and benign breast disease ($P=0.0129$).

Conclusion:

Gynaecomastia is the most common male breast disease seen at CMJAH. There was a significant association between HIV and benign breast disease. This association should be explored further with respect to the direct effects of the virus and to those of the antiretroviral medication

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1. Introduction

Although most commonly associated with females, breast disease may also manifest in males in a variety of conditions ranging from benign to malignant (1). Despite accounting for a large proportion of outpatient department presentations, due to the relative rarity of male breast disease (MBD), in conjunction with lack of awareness, it often goes under recognized (2). Some of this may have to do with the social stigma MBD carries. Gynaecomastia is the most common benign breast disease in males (2), and due to its association with human immunodeficiency virus (HIV) and anti-retroviral therapy (ART), is of particular interest in the South African context, with an HIV prevalence of 12.9 (9.3-14.3) per 100 000 men between the ages of 15 and 49 (3). In a 9 year retrospective review of HIV positive patients with breast-related pathology, Pantanowitz et al. found that of the HIV positive men with breast-related pathology, 58% had gynaecomastia related to ART of all drug classes (4). A 2016 South African study found that 11% of adverse drug reactions (ADR) reported to the National HIV and Tuberculosis Health Care Worker Hotline between June 2013 and July 2014 were for gynaecomastia (5), while another found gynaecomastia to be the 4th (8.8%) most common ART-associated ADR in South Africa (6). This highlights the significance a diagnosis of HIV has when considering benign diseases of the male breast. In Uganda, a 10 year retrospective review of histopathology reports found gynaecomastia (44%), fibrocystic breast disease (22%) and infiltrating ductal carcinoma (17%) to be the three most common diagnoses among male patients (7). Furthermore, in a Turkish study which looked at all MBD diagnosed by triple assessment, gynaecomastia was the most common diagnosis (87%), followed by primary breast carcinoma (6%) and fat necrosis (2%) (8).

Despite only accounting for less than 1% of all male cancers and less than 1% of all breast cancers (9)(10), male breast cancer (MBC) constitutes the largest proportion of the literature pertaining to MBD. The reported incidence of MBC in sub-Saharan Africa is increasing (7)(9)(11), but as it is so rare the diagnosis may initially not be considered and, for this reason, a thorough understanding of all MBD, benign and malignant, is essential for timely and accurate diagnosis (10). One meta-analysis reviewing data across 27 African countries, revealed that the male-to-female ratio of breast cancer in Africa was 1:24, higher than other parts of the world (9), such as America with an overall male-to-female ratio of 1:152 (12). Of interest, this ratio was even higher in Sub-Saharan Africa than compared to North Africa. This was in keeping with a study by Bunkley et al. (13) that reported a male-to-female breast cancer ratio of 1:14 across 7 sub-Saharan countries, one of which was South Africa, while a

3rd study reported a geographical band in Africa displaying a male:female ratio of 1:17 (16). These researchers also found that the average age at presentation amongst men with breast cancer was 54.6, seven years older than women with breast cancer, versus 67 and 61 for men and women respectively, published in data from the United States (9). A 2017 study by Motloutsi and Lubinga (14) suggested that there may be a genetic explanation for the prevalence of breast cancer in African men. This is supported by the findings of an increased incidence of MBC in sub-Saharan Africa and a 2017 report from the Cancer Association of South Africa, which states that more than 50% of MBC patients were African men (15).

This study aims to describe the spectrum of MBD at Charlotte Maxeke Johannesburg Academic Hospital, South Africa, reviewing the demographics, clinical, radiological and, where available, the histopathological characteristics of MBD at this single institution.

2. Methods

Study Design

This was a retrospective, descriptive study of all male patients who presented at CMJAH with breast disease between 1 January 2016 and 31 December 2018. File numbers of all male patients who underwent breast imaging during the review period were obtained from the CMJAH breast imaging department. Using the patients' file numbers, data relevant to the study was collected from various databases including the CMJAH picture archiving and communication system (PACS), the National Health Laboratory Service (NHLS) database, and patient medical records from the CMJAH Breast Clinic. Data was then entered into a pre-formulated data collection sheet using REDCap™, in a double password protected (computer password and database password) online database. Each patient received a study number, providing the only link to the patient's details. Data collected included patient's age at presentation, self-identified ethnicity, HIV status, presenting complaint, radiological modality, radiological findings as a specific diagnosis and/or BI-RADS grading, and histopathological diagnosis where available. HIV status was established looking at documentation on radiological reports, a search of the NHLS database and/or review of patients' records. Data was then extracted from REDCap™ in the form of an Excel spreadsheet and analysed using Statistica 13 and SAS version 9.2. Descriptive statistics, (frequencies and percentages), were calculated for categorical data, and means and standard deviations were calculated for numerical data. Analytical statistics, the independent t-test and

ANOVA, were used to compare the mean values in two and three groups respectively. Fisher's exact test was used to compare percentages in different groups. The p-value of 0.05 was used for statistical significance. This study was approved by the University of Witwatersrand Human Research Ethics Committee, clearance certificate number M191127.

3. Results

Demographics

During the study period a total of 274 males underwent breast imaging. There were no breast imaging reports available for 5 men, leaving 269 males included in the study. In total, 94% (n=252) of these men were first presentations, while the remaining 6% (n=17) were follow-up patients. Of the men who presented for the first time, the mean age was 46 (SD $\pm$ 17.6) years, the median age - 45 and a range of 13 to 84 years (Figure 1). In terms of ethnicity: 230 (86%) of the men imaged were black, 30 (11%) were white, five (2%) were coloured and four (1%) were Indian. Thirty-nine percent (n=105) were documented to be HIV positive, 32% (n=86) HIV negative, and 29% (n=78) were HIV status unknown (Table 1).

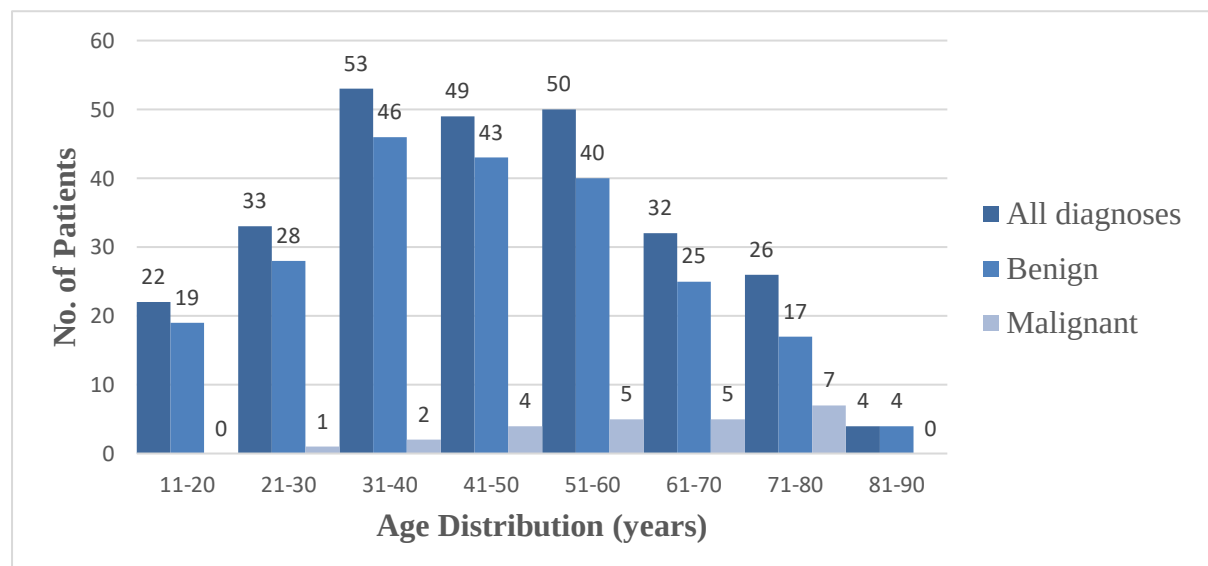


Figure 1. Age distribution of men at presentation for breast imaging

Table 1: Patient characteristics

Total number of patients	269
First presentations	252 (94%)
Follow-ups	17 (6%)
Age at first presentation	46 ± 17.6
<i>Race</i>	
Black	230 (86%)
White	30 (11%)
Coloured	5 (2%)
Indian	4 (1%)
<i>HIV status</i>	
Positive	105 (39%)
Negative	86 (32%)
Unknown	78 (29%)
<i>Presenting complaint</i>	
Enlargement	152 (57%)
Mass	96 (36%)
Mastalgia	30 (11%)
Skin changes	1 (<1%)
Nipple discharge	4 (1%)
Follow-up	17 (6%)
Other	6 (2%)

Breast assessment

The most common presenting complaint was breast enlargement (n=152, 57%), followed by a mass (n=96, 36%) and mastalgia (n=30, 11%). Of the 269 men imaged, 254 (94%) had mammographic imaging as well as ultrasound, while the remaining 15 (6%) only had an ultrasound. Of the breast imaging reports: 75% (n=201) gave both a specific diagnosis and a BI-RADS grading, 19% (n=51) gave only a BI-RADS grading, and 6% (n=17) only a specific diagnosis. 37 males had histologically confirmed breast disease. Invasive carcinoma (n=16) was the most common histopathologically diagnosed MBD, followed by gynaecomastia (n=10). Other notable diseases diagnosed histopathologically included tuberculosis (n=1) and dermatofibrosarcoma protuberans (DFSP) (n=1). Of the 269 men who underwent breast imaging, 244 (91%) had a diagnosed breast condition. 220 (90%) of the

diagnoses were benign, and 24 (10%) were malignant, with or without a concomitant benign diagnosis. Of the patients with malignant disease, seventeen were newly diagnosed, 6 were known with malignant disease, and one was a recurrence. The most common breast disease diagnosed was gynaecomastia, accounting for 85%, while breast cancer accounted for 10% of cases (Figure 2). The most common breast disease diagnosed was gynaecomastia, accounting for 85%, while breast cancer accounted for 10% of cases (Figure 2).

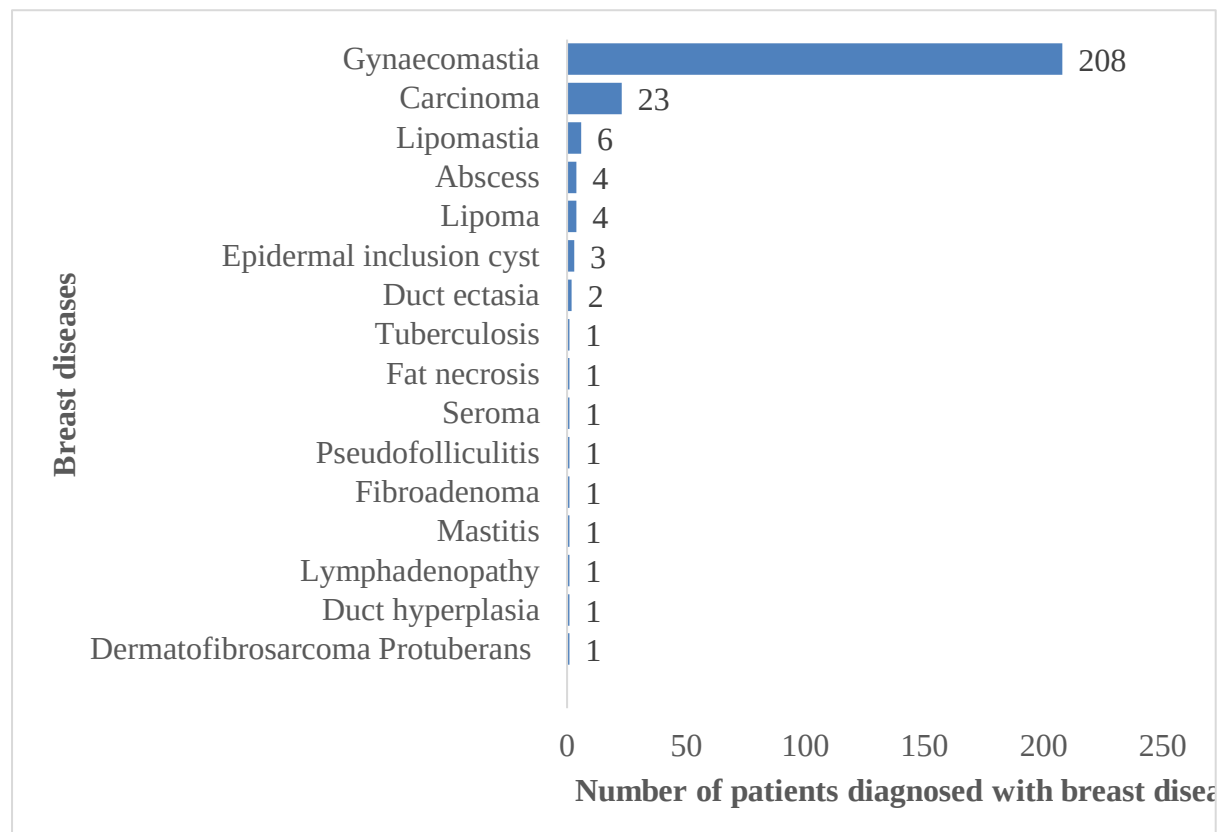


Figure 2: Spectrum of male breast disease identified during the study period

* Although 244 men were diagnosed with breast disease, 15 men had concomitant diagnoses, bringing the total number of diagnosed breast diseases to 259

Associations

Patients' age was significantly associated with benign vs. malignant breast disease, with mean ages of 45.59 years and 58.29 years respectively ($p = 0.0007$). There were no significant associations between ethnicity and benign vs. malignant breast disease ($p = 1.0000$), or disease sub-categories (categorized as gynaecomastia, carcinoma or other) ($p = 0.3985$). The greatest proportion of benign breast disease occurred in patients who were HIV positive, while most of malignant breast disease occurred in patients who were HIV negative

($p=0.0129$). Regarding disease sub-categories, a significantly greater number of patients with gynaecomastia were HIV positive ($p = 0.0111$).

4. Discussion

Spectrum of male breast disease

The main aim of this study was to identify the spectrum of MBD presenting at CMJAH over a 3 year period. There are very few studies which looked specifically at the spectrum of breast disease amongst males, and only one which shared a similar demographic profile to this study. There were only two that could be used to make a comparison.

This study, which included all MBDs diagnosed radiologically and/or histopathologically, identified a total of 269 males, diagnosed with 16 different MBDs over a period of three years. A study from Uganda, which only looked at histopathologically diagnosed MBD, identified a total of 51 males, diagnosed with 8 different MBDs over a period of 10 years. Gynaecomastia was the most common diagnosis, followed by fibrocystic breast disease and infiltrating ductal carcinoma (7). By comparison, the current study identified a total of 37 males with histopathologically confirmed MBD, diagnosed with nine different pathologies, over a period of 3 years: invasive carcinoma was the most common histopathological diagnosis, followed by gynaecomastia. This suggests that CMJAH may diagnose more men with MBD histopathologically, and see a wider variety of pathology than identified in Uganda. The most common diagnoses were proportionately different in each study. While the CMJAH breast imaging department follows a strict protocol regarding which patients warrant biopsies based on their BI-RADS grading, it is not evident if the same protocol was followed in the study done by Ssemmanda et al. This could explain the difference between the most common diagnoses identified by each study. In the Ugandan study it's possible that a greater number of males underwent biopsies for conditions which would be diagnosed radiologically at the CMJAH breast imaging unit.

As in the study by Günhan-Bilgen et al. (8), the current study also found gynaecomastia (87% vs. 85%) and primary breast carcinoma (6% vs. 9%) to be the most commonly diagnosed breast diseases amongst males. Other conditions such as fat necrosis, lipoma, abscess and epidermal inclusion cysts were also found to be present in similar proportions.

Male breast cancer

This study identified 24 males with male breast cancer. Six patients were known with MBC, 17 patients were newly diagnosed with a breast malignancy during the study period, and one was a recurrence. Fifteen were invasive ductal carcinomas, one case of DFSP and in one case no consensus could be made regarding malignant sub-type. The average age at presentation of those newly diagnosed with MBC was 56.8 years. This is in keeping with a 2012 meta-analysis of all MBC in Africa by Ndom et al. who found that the average age at presentation amongst men with breast cancer was 54.6 (9).

Male breast disease and HIV

Gynaecomastia is a well recognized complication of HIV and ART use (4)(5)(6) and, as was suggested in other studies, the current study also identified a significant association between HIV positive males and benign breast disease, specifically gynaecomastia. While Pantanowitz et al. (4) found this association to be due to ART of all drug classes, as this study didn't record ART use or regimen, the same association could not be made. HIV is also associated with infectious breast diseases such as tuberculous mastitis and pyogenic abscess (4). Of the five patients identified with breast abscesses or mastitis in this study, only two (40%) were HIV positive, and another two were HIV status unknown. TB mastitis, once considered a rarity, now accounts for 3-4% of all breast diseases in regions with a high incidence of TB, such as Africa (16). However, TB infection of the male breast is scarcely documented. Interestingly, the only patient documented with tuberculous mastitis in the current series was found to be HIV negative. This suggests that more aggressive screening for HIV should be done in males presenting with infectious breast conditions.

Study limitations

The retrospective nature of this study lends it to some degree of selection bias. As there were no reports available for five of the 274 males who underwent breast imaging during the study period, the missing reports may have resulted in skewing of results. A second limitation of this study was the failure to record clinical examination findings, a major component of the triple breast assessment. Another limitation was the failure to record the details of ART use in the HIV positive patients, something not routinely recorded in patient records. This means that, while there is an association between HIV and gynaecomastia, this study could not

confirm whether the association is due to ART or HIV alone. This could be addressed in a future prospective study. Lastly, as not all patients were biopsied, the radiological diagnosis assigned to patients could not be absolutely confirmed.

5. Conclusion

Gynaecomastia is the most common MBD seen at CMJAH, and in the literature reviewed. There was a significant association between HIV positive status and benign breast disease, an area which deserves to be explored further with regard to the direct (viral) and indirect (treatment) effects of HIV on male breast diseases.

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7. Appendices

A. BI-RADS grading tool

Final Assessment Categories			
Category		Management	Likelihood of cancer
0	Additional imaging needed	Recall for additional imaging	n/a
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably benign	Short interval follow-up, 6 months or continued	>0% but $\leq 2\%$
4	Suspicious	Tissue diagnosis	4a. Low suspicion for malignancy (>2% to $\leq 10\%$) 4b. Moderate suspicion for malignancy (>10% to $\leq 50\%$) 4c. High suspicion for malignancy (>50 to $\leq 95\%$)
5	Highly suggestive of malignancy	Tissue diagnosis	>95%
6	Known biopsy-proven	Surgical excision when clinically appropriate	n/a

(17)

B. Study protocol

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Dr Darren Rattray

Student Number: 353068

Supervisors:

Dr B. Phakathi: MBChB (UKZN); FCS (SA); MMED (UP)

Specialist surgeon – Charlotte Maxeke Johannesburg Academic Hospital

Prof A. Mannell: BSc Med., MBBCh, FRACS, FRCS (London); MS (Univ.Syd)

Associate Professor – Department of Surgery, University of the Witwatersrand, Johannesburg

Department of Surgery

Faculty of Health Sciences

University of the Witwatersrand

2019

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1. Introduction

Although most commonly associated with females, breast disease may also manifest in males in a variety of conditions ranging from benign to malignant (1). Due to the relative rarity of male breast disease (MBD), in conjunction with lack of awareness, it often goes under recognized (2). Despite only accounting for less than 1% of all male cancers and less than 1% of all breast cancers (18)(19), male breast cancer (MBC) constitutes the largest proportion of the literature pertaining to MBD. Almost certainly due to the potentially higher rates of morbidity and mortality related to MBC when compared to other MBDs, this should not undermine the clinical significance and impact of other MBDs. The incidence of MBC in sub-Saharan Africa is increasing (13)(15)(9), but as it is so rare the diagnosis may initially not be considered and, for this reason, a thorough understanding of all MBD, benign and malignant, is essential for timely and accurate diagnosis (10). The objectives of this study therefore, are to describe the demographics and clinical presentation of male patients presenting at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), and to record the radiological and histopathological characteristics of both benign and malignant breast diseases in these patients.

2. Literature Review

Anatomy

Until the age of puberty, breast composition is identical between males and females. Pre-pubertal breast tissue is composed mostly of fat and a few epithelial-lined ducts (11). It occupies the area of the anterior chest wall extending from the 2nd to 6th ribs craniocaudally and sternum to axilla mediolaterally (1). Due to a rise in testosterone levels experienced by

males around the period of puberty, rather than proliferate the ducts atrophy, giving rise to the normal adult male breast, made up mostly of sub-cutaneous fat (2)(10). In comparison, the rise in circulating oestrogen and progesterone experienced by females during puberty results in development of a ductal system, lobules and Cooper's ligaments (1). A good understanding of the differences in the anatomy of male and female breasts is imperative when considering the pathologies most likely to affect each.

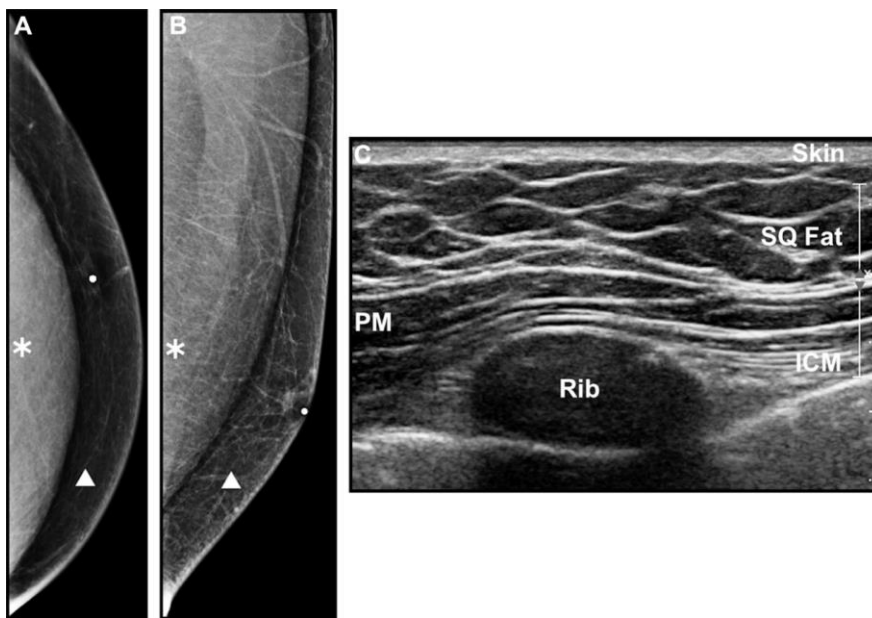


Figure 1 Anatomy of the male breast. Coronal (A) and sagittal (B) mammographic views of normal male breast anatomy. The triangle represents subcutaneous fat, while the star is the pectoralis muscle. Image C is an ultrasound of a normal male breast. SQ = subcutaneous; PM = pectoralis muscle and ICM = intercostal muscle.

(10)

Benign Diseases of the Male Breast

There are numerous benign conditions of the male breast. Some of these conditions affect both men and women, while some affect men exclusively e.g. gynaecomastia. As previously mentioned, most of the literature surrounding MBD is aimed specifically at MBC. The literature does, however, describe some benign male breast conditions which, although relatively rare, are clinically significant and therefore, relevant to this study. Table 1 is a list

of some the most common benign male breast conditions as described in the literature (1)(2)(10)(20)(21)(22)(23)(24)(25)(26).

Breast Malignancies

Epidemiology

MBC is rare. It accounts for less than 1% of all cancers and less than 1% of all breast cancers (18)(19).

As well as being much rarer than female breast cancer, male breast malignancies are also diagnosed much later; on average 5-10 years according to some studies (26)(27)(28)(12). According to the Surveillance, Epidemiology, and End Results database published by Korde, Zujewski and Kamin et al. the median age of diagnosis in

males is 67 years vs. 61 years in females (12). An update on the above database also found that, in a study period between 2005 and 2010, compared to females, MBC patients were older, more likely to be black, married and present with more advanced stage of disease. Men were also more likely to have lymph node (LN) +, estrogen receptor (ER) +, and progesterone receptor (PR) + disease. The above is in keeping

Benign Conditions of the Male Breast

- *Gynaecomastia*
- *Post-traumatic e.g. haematoma or fat necrosis*
- *Haemangioma*
- *Fibro adenoma*
- *Pseudoangiomatous Stromal Hyperplasia (PASH)*
- *Fibrocystic breast disease*
- *Myofibroblastoma*
- *Sclerosing adenosis*
- *Papillary lesions*
- *Granular cell tumour*
- *Epidermal inclusion cysts and sebaceous cysts*
- *Infection e.g. mastitis and abscess*
- *Lipoma and angiolipoma*

Table 1 Common benign male breast diseases as described in the literature.

with a 2018 review published by Fentimen (29) which looked at receptor profile differences between male and female breast cancer patients across 5 different studies (30)(31)(32)(33)(34).

As with benign MBDs, there are numerous malignancies which affect the male breast. Despite the low overall incidence of male breast cancer (18)(19), the different types of malignancies occur in variable proportions, with variable clinical outcomes. By knowing which types of breast cancer are more prevalent in a region, more focused treatment options can be adopted to improve these outcomes. Table 3 is a list of some the most common malignant male breast conditions as described in the literature (1)(2)(18)(22)(35)(36)(37).

Study	Receptor status	Male (%)	Female (%)
Weber-Chappuis	ER+ve	82	75
	PR+ve	77	62
Curigliano	ER+ve	100	64
	PR+ve	96	38
Muir	ER+ve	81	69
	PR+ve	63	56
Shaaban	ER+ve	80	68
	PR+ve	71	72
Shandiz	ER+ve	82	53
	PR+ve	59	50

Table 2 Studies comparing estrogen (ER) and progesterone receptor (PR) status in male breast cancer and female breast cancer.

Male Breast Disease in the African Context

As previously mentioned, on the topic of MBD, most of the available literature is focused specifically on male breast cancer. Furthermore, most of this literature is written in the first world context. This study will be based

Table 3 Types of male breast malignancies as described in the literature.

Types of Male Breast Malignancies
• <i>Ductal carcinoma in situ</i> • <i>Invasive ductal carcinoma</i> • <i>Invasive micropapillary carcinoma</i> • <i>Invasive mucinous carcinoma</i> • <i>Paget's disease</i> • <i>Lymphoma</i> • <i>Metastasis</i> • <i>Leiomyosarcoma</i>

on data collected from a tertiary hospital in Johannesburg, South Africa, but as there is very

Benign breast disease	Females (%)	Males (%)	Total
Fibro adenoma	751 (99.21)	6 (0.79)	757
Fibrocystic breast disease	218 (96.04)	9 (3.96)	227
Sclerosing adenosis	54 (94.74)	3 (5.26)	57
Mastitis	48 (97.96)	1 (2.04)	49
Gynaecomastia	0 (0)	18 (100)	18
Other benign breast disease	161 (98.77)	2 (1.23)	163
Total	1232 (96.93)	39 (3.07)	1271

Table 4 Gender distribution of the most commonly diagnosed benign breast diseases at the Makerere University College of Health Sciences Lab (MakCHS) Histopathology lab for the period 2005-2014.

Cancerous breast disease	Females (%)	Males (%)	Total
Infiltrating ductal carcinoma	319 (97.85)	7 (2.15)	326
Invasive lobular carcinoma	59 (100)	0 (0)	59
Papillary carcinoma	4 (100)	0 (0)	4
Medullary carcinoma	4 (100)	0 (0)	4
Other cancerous breast disease	188 (97.41)	5 (2.59)	193
Total	574 (97.95)	12 (2.05)	586

Table 5 Gender distribution of the most commonly diagnosed cancerous breast diseases at the MakCHS Histopathology Lab for the period 2005-2014.

little literature on MBD published in South Africa, comparisons in our context can best be drawn from the few studies published elsewhere in Africa. The most relevant study in terms of context and aims related to this study, was published by Ssemmanda et al. who looked at all breast disease histologically diagnosed at a tertiary facility in Uganda between 2005 and 2014 (7). Although the study looked at all breast disease for men *and* women, relevant data pertaining specifically to the spectrum of breast disease in males was also obtained. Apart from identifying the spectrum of MBD presenting at a tertiary hospital in Uganda (see table 4 (7)), the

study also found that the male to female breast cancer ratio was 1:48 (see table 5 (7) for the distribution of these cancers by sex) and overall, breast cancers were diagnosed 16 years earlier in women than in men (median age at diagnosis 48 and 64 years respectively) (7).

Another study was published by Ndom et al. (9) who did a meta-analysis of all literature on MBC in Africa, looking specifically at: 1.) the male-to-female ratio of breast cancer in Africa and: 2.) the difference in the age at presentation of men and women with breast cancer in Africa. From this they concluded that the male-to-female ratio of breast cancer in Africa was 1:24, higher than the 1:100 observed in other parts of the world e.g. America, but more interestingly, this ratio was even higher in Sub-Saharan Africa than compared to North Africa. This was in keeping with a study by Bunkley et al. (13) that reported a male to female breast cancer ratio of 1:14 across 7 sub-Saharan countries, one of which was South Africa, while a 3rd study reported a geographical band in Africa displaying a ratio of >6% (1:17) (38). They also found that the average age at presentation amongst men with breast cancer was 54.6, seven years older than women with breast cancer, versus 67 and 61 for men and women respectively, published from data in the United States (9). In their study,

Communicating Male Breast Cancer: Knowledge and Awareness Among South African Youth, Motloutsi and Lubinga (14) suggested that there may be a genetic explanation for the prevalence of breast cancer in African men. This is supported by the findings of an increased incidence of MBC in sub-Saharan Africa and a 2017 report from the Cancer Association of South Africa, which states that more than 50% of MBC patients were African men (15).

Although this study will examine the spectrum of all MBD presenting at a tertiary hospital, including MBC, since the incidence of MBC is increasing in Africa (13)(15)(9), the data collected may be of value for comparison with subsequent studies.

3. Aims and Objectives

Aims

This study aims to identify all males presenting at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) Surgical Breast Unit between January 1st 2016 and December 31st 2018.

Objectives

- 1.) To identify the spectrum of breast diseases amongst males presenting at an urban tertiary level hospital in South Africa.
- 2.) To describe the spectrum of breast disease amongst males presenting at a tertiary level hospital in South Africa in terms of demographics, clinical presentation, radiological and histopathological characteristics.

4. Methods

Study Design

This is a retrospective, descriptive study of all male patients presenting at Charlotte Maxeke Johannesburg Academic Hospital, with radiologically identifiable breast disease, with or without histopathological confirmation, from 1 January 2016 until 31 December 2018.

Inclusion Criteria

All male patients, of any age, with radiologically identifiable breast disease of any aetiology, with or without histopathological confirmation.

Exclusion Criteria

All male patients with or without breast disease, not radiologically confirmed.

Data Collection

Patient file numbers of all males who underwent breast imaging during the review period will be obtained from the CMJAH breast imaging department. The files of all males who underwent breast imaging will be collected, and those with radiologically confirmed breast disease will be included in the study. These file numbers will be cross referenced with the file numbers of all males in the electronic database at the CMJAH Surgical Breast Unit, who attended the unit during the study period. From those included in the study, males who underwent biopsies will be identified, either from their clinical record, or from the biopsy book in the breast imaging department. Using the patient file numbers, biopsy results can be accessed from the National Health Laboratory Service (NHLS) database.

The data will be collected using a pre-formulated data collection sheet and entered into a REDCap™ database (see appendices). All patient information and clinical findings gained as a result of the study will be kept in a double password protected (computer password and database password) online database. Each patient will receive a study number, providing the only link to the patient's details. Only the primary investigator and their supervisors will have access to the password protected database

Data Analysis

Data will be analysed using Statistica software, version 13. Variable patterns such as demographics, clinical presentation and radiological and histopathological diagnoses will be presented in the form of proportions, frequencies and graphs. Pearson chi-squared test will be used to assess associations between demographic, clinical, radiological/histopathological

factors and various male breast conditions, where a p-value of <0.05 will be considered significant.

5. Ethics

This study is currently pending approval by the University of Witwatersrand Human Research Ethics Committee.

6. Funding

This study requires minimal funding, all of which will be covered by the primary investigator.

7. Timeline

Year (2019/20)	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb
Literature review														
Protocol write-up														
Protocol assessment														
Ethics application														
Data collection														
Data analysis														
Thesis write-up														
Submit: marking														

8. Appendices

Data collection sheet

Confidential

The Spectrum of Breast Disease at Charlotte Maxeke Johannesburg Academic Hospital - a 5 Year Retrospective Review
Page 1 of 2

Male breast disease registry

Record ID	
Age at presentation	
Hospital number	
Race	☐ Black ☐ White ☐ Coloured ☐ Indian ☐ Other ☐ Not specified
Specify other race	
HIV Status	☐ Positive ☐ Negative ☐ Unknown
Presenting complaint	☐ Mass ☐ Mastalgia ☐ Skin changes ☐ Nipple discharge ☐ Other
Specify other presenting complaint	
Radiological modality	☐ Ultrasound ☐ Mammography ☐ MRI
Radiological comment	☐ Specific diagnosis ☐ Non-specific diagnosis ☐ BIRADS grading ☐ No comment on diagnosis
Specify specific diagnosis	
Specify non-specific diagnosis	
BIRADS grading	☐ 0 - incomplete ☐ 1 - negative ☐ 2 - benign findings ☐ 3 - probably benign ☐ 4 - suspicious abnormality ☐ 5 - highly suspicious of malignancy ☐ 6 - known biopsy with proven malignancy

Suspicious or indeterminate abnormality

- ☐ 4A - low suspicion of malignancy
- ☐ 4B - moderate suspicion of malignancy
- ☐ 4C - high suspicion of malignancy

Histopathological diagnosis

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C. Ethics Clearance Certificate



R14/49 Dr Darren Rattray

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M191127

NAME: Dr Darren Rattray
(Principal Investigator)
DEPARTMENT: Surgery
Charlotte Maxeke Johannesburg Academic Hospital

PROJECT TITLE: The Spectrum of Male Breast Disease at Charlotte Maxeke Johannesburg Academic Hospital - a 3 Year Restrospective Review

DATE CONSIDERED: 29/11/2019

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr Boitumelo Phakathi and Prof Aylwyn Mannell

APPROVED BY: 
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 29/11/2019

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 Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. 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.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).


Principal Investigator Signature

Date

01/12/2019

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