BREAST IMAGING AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL – A CLINICALLY RELEVANT AUDIT

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A Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Master of Medicine in Radiology.

Johannesburg, 2021

Declaration

I, Ilonka Warnich, declare that this research report is my own work. The research report is submitted for the degree of Master of Medicine – Radiology at the University of the Witwatersrand. It is submitted in the format of a publication model with my protocol and an extended literature review and has not been submitted before for any degree or examination at this or any other institution.

DR ILONKA WARNICH

On this 9th day of April 2021.

Student's contribution to article

- Principal investigator.
- Study concept and design.
- Primary compilation of the protocol and extended literature review.
- Collection and analysis of data.
- Construction of the database.
- Primary compilation of the manuscript.
- Submission of the manuscript to the publishing journal.
- Corresponding author in the editing process of the published article.
- Primary author of the published article.

Declaration: Student's contribution to article and agreement of co-authors

I, Ilonka Warnich, student number 1820785, declare that this Dissertation is my own work and that I contributed adequately towards research findings published in the article stated below which is included in my Dissertation.

Signature of Student ..... **Date** 25/11/2020

Name of Primary Supervisor Ilana Viljoen

Signature of Primary Supervisor ..... **Date** 01/12/2020

Agreement by co-authors: By signing this declaration, the co-authors listed below agree to the use of the article by the student as part of her Thesis/Dissertation/Research Report. In cases where the student is not the 1st author of a published article, the primary supervisor must explain (under comments) why the student is entitled to use the paper for his/her degree purposes.

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Dedication

To the women in my family, my mother, Mariëtte, and sister, Janike, for their endless love, inspiration and support.

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Table of Contents

Abbreviations

PDF	Portable Document Format
CHBAH	Chris Hani Baragwanath Academic Hospital
USA	United States of America
ACR	American College of Radiology
BI-RADS	Breast Imaging Reporting and Data System
CAD	Computer-Aided Detection
AI	Artificial Intelligence
FDA	Food and Drug Administration
MQSA	Mammography Quality Standards Act
USPSTF	United States Preventative Services Task Force
NDH	National Department of Health
RSSA	Radiological Society of South Africa
BISSA	Breast Imaging Society of South Africa
PPV	Positive Predictive Value
CDR	Cancer Detection Rate
AIR	Abnormal Interpretation Rate
DCIS	Ductal Carcinoma in Situ
BCSC	Breast Cancer Surveillance Consortium
NMD	National Mammography Database
RSNA	Radiological Society of North America
PACS	Picture Archiving and Communication System
NHLS	National Health Laboratory Service
HIV	Human Immunodeficiency Virus

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Breast imaging at Chris Hani Baragwanath Academic Hospital: A clinically relevant audit

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Background: Breast cancer is a major cause of morbidity and mortality worldwide. From experience, we have found that the disease burden at Chris Hani Baragwanath Academic Hospital (CHBAH) is unique with an advanced stage at presentation.

Objective: To perform a breast-imaging audit at CHBAH, focused on interpretive performance and disease burden.

Method: Demographic and imaging data were retrospectively collected over a 6-month period. Data collected and derived followed the audit definitions and rules described within the American College of Radiology–breast-imaging reporting and data system (ACR–BI-RADS) atlas (5th edn.). A comparison was made to benchmark values published by the Radiological Society of North America (RSNA).

Results: A total of 1549 mammography examinations were analysed. The screening subgroup (n = 808) revealed 11 cancers with a cancer detection rate (CDR) of 13.6 per 1000 studies and a recall rate of 5.94. The diagnostic subgroup (n = 741) revealed 130 cancers with a CDR of 175.4 and an abnormal interpretation rate (AIR) of 39 per 100 studies. Along with the positive predictive values, these performance measures for diagnostic mammography were significantly larger than the RSNA-benchmarks ($p < 0.0001$). In addition, the cancer characteristics showed a greater histological mean tumour length, a lower percentage of minimal cancers (defined as ductal carcinoma *in situ* [DCIS] and invasive cancers ≤ 1 cm) and fewer nodal-negative cancers ($p < 0.0001$), in keeping with a more advanced loco-regional stage at presentation.

Conclusion: The study illustrates the challenges faced by a South African breast-imaging unit confronted with advanced loco-regional disease. The cancer burden is highlighted within a community where there is a lack of national screening mammography. The process of performing a basic, clinically relevant audit is simple and should be a routine practice in breast-imaging units.

Keywords: breast cancer; mammography; BI-RADS; breast-imaging audit; diagnostic mammography.

Introduction

Breast cancer is a major cause of morbidity and mortality worldwide. It is the most common type of female cancer and the leading cause of cancer deaths amongst women.[1]

The need for standardisation in breast imaging has led to the development of the breast-imaging reporting and data system (BI-RADS) by the American College of Radiology (ACR), as summarised in Table 1.[2] Breast-imaging findings are categorised according to the suspicion of malignancy.

Regardless of standardised reporting systems, there still exists an inter-user variation in the interpretive performance of breast imaging and the threshold to obtain tissue diagnosis. Audits have an essential role in monitoring performance within a facility.[3]

The ACR outlines *the basic clinically relevant audit* in the 'follow-up and outcome monitoring' chapter within the ACR–BI-RADS atlas (5th edn.).[4] Annual audits are recommended. The relevance of the audit will be directly proportional to the number of metrics evaluated and should, therefore, be as comprehensive as possible. Separate audits on screening and diagnostic studies are advised, as these show significant statistical differences.[4]

TABLE 1: American College of Radiology breast-imaging reporting and data system final assessment categories.

Category	Management	Probability of cancer
0. Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examination(s)	N/A
1. Negative	Routine screening	Essentially 0%
2. Benign	Routine screening	Essentially 0%
3. Probably benign	Short interval follow-up or continued surveillance mammography	> 0%, but ≤ 2%
4. Suspicious of malignancy	Tissue diagnosis	> 2%, but < 95%
4a. Low suspicion		a. > 2%, but ≤ 10%
4b. Moderate suspicion		b. > 10%, but ≤ 50%
4c. High suspicion		c. > 50%, but < 95%
5. Highly suggestive of malignancy	Tissue diagnosis	≥ 95%
6. Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

Source: Sickles EA, D'Orsi CJ. ACR BI-RADS® Follow-up and outcome monitoring. In: ACR BI-RADS® Atlas, Breast imaging reporting and data system. Reston, VA: American College of Radiology, 2013; p. 21–31.

N/A, not applicable.

TABLE 2: American College of Radiology breast-imaging reporting and data system audit definitions.

Derived data	Definition
True positives (TP)	Positive imaging study with a positive tissue diagnosis of breast cancer.†
False positives (FP)	Positive imaging study with a negative tissue diagnosis for breast cancer.‡
Positive predictive value (PPV)	Reflects true positive cases as a proportion of total positive imaging studies (TP + FP):
1. PPV_1	1. Based on positive screening cases, with any result other than routine follow-up (BI-RADS categories 0, 3, 4 and 5).
2. PPV_2	2. Based on positive examinations with the recommendation for tissue diagnosis (BI-RADS 4 and 5).
3. PPV_3	3. Based on positive examinations where tissue diagnosis was obtained (BI-RADS 4 and 5).
Cancer detection rate (CDR)	Breast cancer-positive cases per 1000 examinations.
Percentage nodal-negative invasive cancers	Reflected as a percentage of total invasive cancer cases.
Percentage 'minimal' cancers	Defined as invasive cancer ≤ 1 cm or ductal carcinoma *in situ* (DCIS). Reflected as a percentage of total cancer cases.
Percentage stage 0 or 1 cancers	Reflected as a percentage of total cancer cases.
Abnormal interpretation rate (AIR)/Recall rate	Positive assessments, leading to additional imaging or biopsy, per 100 examinations:
	1. Diagnostic audit: BI-RADS 3, 4, 5.
	2. Screening audit (recall rate): BI-RADS 0, 3, 4, 5.

Source: Sickles EA, D'Orsi CJ. ACR BI-RADS® Follow-up and outcome monitoring. In: ACR BI-RADS® Atlas, Breast imaging reporting and data system. Reston, VA: American College of Radiology, 2013; p. 21–31.

BI-RADS, breast-imaging reporting and data system.

†, Breast cancer diagnosed within 12 months following the examination; ‡, No breast cancer diagnosed within 12 months following the examination.

Audit guidelines and definitions are provided within the BI-RADS manual (Table 2). Three scenarios for a positive mammogram are described[4]:

- A screening mammogram leading to anything other than routine follow-up (BI-RADS categories 0, 3, 4 and 5).
- A study leading to the recommendation for tissue diagnosis (BI-RADS 4 and 5).
- A study leading to tissue diagnosis being obtained (BI-RADS 4 and 5).

True and false positive, as well as positive predictive values (PPVs) can be derived for each of these scenarios (PPV_1, PPV_2 and PPV_3, respectively). The PPV gives the probability that a positive examination accurately indicates the presence of the disease. Of the subcategories, the PPV_2 is the most useful within an imaging facility. It is a valuable indicator of interpretive performance, as well as the overall biopsy-threshold within the department. The PPV_3 reflects clinical practice, and should equal PPV_2, where biopsies were performed on all cases in which tissue diagnosis was recommended.[5]

Other valuable performance measures include cancer detection rate (CDR) and abnormal interpretation rate (AIR). Abnormal interpretation rate is referred to as recall rate in screening mammography.[4]

In order for sensitivity and specificity to be derived, negative examinations need to be correlated with a population-based tumour registry to verify the true absence or presence of disease (true- or false-negatives).[4] No population-based registry is currently available in South Africa.[6] The data published within the South African national cancer registry lack certain details required for an audit, such as differentiating between screening and diagnostic studies.[7] It is acceptable to exclude false negatives, sensitivity and specificity from audits, where it cannot be reliably derived.[4]

Metrics evaluating tumour characteristics, such as invasive cancer size, lymph node status and cancer stage are encouraged to be included. The percentage of minimal cancers, node-negative cancers and metastatic cancers can then be derived. The ACR–BI-RADS atlas defines minimal cancers as invasive cancers ≤ 10 mm or ductal carcinoma *in situ* (DCIS) of any size.[4] These metrics give an indication of how early disease is detected, which reflects the major goal of screening and early detection programmes within a country.

The ACR–BI-RADS atlas describes the value of comparing a facility's audit results with acceptable performance parameters. One such value set recommended, is the Radiological Society of North America (RSNA) national performance benchmarks for digital mammography.[4] Separate publications for diagnostic and screening studies were released in 2017. The data were collected from the breast cancer surveillance consortium (BCSC) and based on the ACR–BI-RADS 5th edition manual.[3,8]

These benchmarks were not intended for use outside the USA, as they reflect the advanced screening programmes and practices specific to the country.[5] The ACR–BI-RADS manual further describes the limitation of an audit comparison to benchmark data when performed in facilities with relatively small sample sizes, especially a sample obtained from screening-detected cancers. In such cases internal audits or comparison of the facility's trend over time becomes more useful.[4]

Nonetheless, in our opinion, it is of value to analyse deviation from these international benchmarks. Results

need to be interpreted whilst keeping in mind the vast differences in local practices. This is enough motivation for an incentive to obtain a national mammography database and benchmarks, specific to the South African population and resource-limited setting.

The recent addition of tomosynthesis in screening has assisted radiologists in decreasing recall rates,[8] and is routinely used as an adjunct to standard digital mammography in many practices. Similarly, the concurrent use of ultrasound during the initial examination, contributing to a combined assessment with mammography, will greatly influence the performance of a unit.[4] The variable use of these modalities is one of the challenges faced with comparative audits in South Africa, as screening practices are adapted to best suit the population it serves. Immediate reading of screening mammography with the variable addition of ultrasound is a standard practice within many South African breast imaging units. Audit results will differ greatly from facilities where batch reading is performed and patients are subsequently recalled for additional imaging, including tomosynthesis and ultrasound, as commonly done in the USA.[9]

Audit results are also dependent on the screening guidelines within a country. Across the globe there is conflicting data and considerable debate on what these recommendations should entail, particularly in the 40–49 year age group.[10] The ACR recommends women of average risk for the development of breast cancer to commence annual screening mammography from the age of 40.[11] The United States Preventative Services Task Force (USPSTF) advises biennial screening mammography within the age group 50–74, with the recommendation that women aged 40–49 can have optional screening after discussion with their healthcare provider.[12]

The South African National Department of Health (NDH) released the Breast Cancer Prevention and Control Policy in 2017,[6] with the major goal of improving breast cancer awareness, early detection and management within the country. Mammography is recognised as the screening method of choice in developed countries, however, South Africa currently lacks the resources to employ and sustain a national screening programme. It is stated that such a programme should only be introduced if it can be ensured that at least 70% of the target population will benefit from it.[6] A large percentage of women do not have access to screening mammography, especially those within the rural setting. This contributes to a delay in diagnosis and upstaging of disease.[13] The NDH recommends clinical breast examination and breast self-examination for early detection of disease. It is, however, recognised that such methods have not yet been proven as efficient screening tools.[6]

The current recommendations by the relevant imaging societies within South Africa are in favour of regular screening mammography. The Radiological Society of South Africa (RSSA) and Breast Imaging Society of South Africa (BISSA) advise annual screening from the age of 40, which is in accordance with the recommendation from the ACR.[10,11]

Despite there being no national organised screening programme within the USA, there is a high prevalence of opportunistic screening being performed with a reported 65% compliance rate (2015).[5,14] Audit results are expected to differ in countries where a lower frequency of screening is done, particularly when evaluating the size and stage of the screen-detected cancers. Earlier detection of tumours is expected when more screening is performed. In addition, because of the lack of surveillance by an organised screening programme, self-funding and the ever increasing risk of malpractice litigation within the USA, the goal of reducing false positive outcomes is deemed less important. This further limits comparative audits with other countries.[5]

Opportunistic screening mammography is also done within South Africa, however, auditing data are generally not kept or available at most facilities.[10] Therefore, scant research exists on the rate of screening mammography done within the country. The authors suspect the figures to be significantly less than the USA, particularly within the public sector.

There are many countries that do offer national or provincial organised screening programmes, such as Sweden, the Netherlands, Norway, Spain, the United Kingdom, to name a few. Auditing data from these countries are expected to differ. Numerous observational studies from these programmes provide direct proof of the benefit of screening mammography.[10,15]

Chris Hani Baragwanath Academic Hospital (CHBAH) is a major South African tertiary referral institution serving an extensive drainage area.[16] A relatively large proportion of patients receive diagnostic rather than screening mammography, most of which are referred from the CHBAH specialist breast clinic. The exception to this is in the month of October, national breast cancer awareness month,[17] during which screening is promoted.

The relevance of the breast-imaging audit, focused on interpretive performance and disease burden, is to standardise practices, as well as to build a breast-imaging database. The results can be utilised to facilitate quality and skill-improvement methods.

Research methods and design

A retrospective, descriptive study design was used. The objective was to perform a breast-imaging audit at CHBAH, according to the guidelines outlined in the ACR–BI-RADS 5th edition manual.

The study population consisted of patients who received a mammogram between 01 June and 31 November 2018. Cases were excluded where inadequate information was available to classify it as diagnostic or screening. Screening studies

were defined as routine investigations done for asymptomatic patients. Clinical data provided on the radiology report were relied upon to determine these cases. Diagnostic studies included the investigation of breast complaints and the short-term follow-up of previous abnormal assessments. Additional exclusion criteria were BI-RADS six assessments and previous breast augmentation or mastectomy. In patients with a unilateral mastectomy, imaging of the contralateral breast was included.

The standard imaging protocol included digital tomosynthesis mammography (Hologic Selenia Dimensions with AWS 8000, Laurel Bridge Software). Two-dimensional images (craniocaudal and mediolateral-oblique views) were created from breast tomosynthesis using C-view software. The mammography imaging protocol was the same for screening and diagnostic investigations. Breast ultrasound (Aloka – ProSound Alpha 10 system, Version 8 Software) was routinely performed, with the occasional exception of patients presenting with low density breasts (ACR-BI-RADS categories A or B) and unchanged follow-up screening mammography (n = 156). When indicated, tissue diagnosis was obtained within the mammography unit. This included ultrasound-guided fine-needle-aspiration, core needle and stereotactic biopsies.

Data were collected from the hospital picture archiving and communication system (PACS – AGFA IMPAX 6.5.1.501). Consultant-approved mammography reports were used to obtain the clinical demographics, indications and relevant imaging findings (breast composition and ACR–BI-RADS final assessments). In cases where each breast was assigned a separate BI-RADS, the highest category was used.

Histology results were tracked for all positive studies (BI-RADS 4, 5), as well as any other tissue sampling. Results were obtained from the National Health Laboratory Service (NHLS), using the NHLS LABTRAK web-result viewer. Where available, the post-surgical tumour size and nodal involvement were recorded, as stated on the pathology report. These histopathologically proven data were used in the calculation of cancer characteristics. In the presence of multifocal or multicentric disease, the greatest diameter of the largest tumour focus was used as the tumour size.

Data were captured by the primary researcher using Microsoft Excel and the ACR audit definitions and rules were followed (Table 2). It was similar to the methodology used to obtain the RSNA-benchmarks. Derived data were based on mammography examinations with tomosynthesis and additional ultrasound, when performed. Recall rate was defined as any screening investigation with an assessment of BI-RADS 0, 3, 4 or 5. The false-negative values, sensitivity, specificity and presence of metastatic disease were not included in the audit.

Data were analysed using SAS Version 9.2. Descriptive statistics were calculated: numerical data using means with standard-deviations or medians with interquartile ranges (IQRs) and categorical data using frequencies and percentages. The following analytical statistics were used to compare the sample statistics with the published benchmarks: the single proportion binomial test to compare the sample proportion with a proportion in the published benchmarks; the one-sample t-test to compare the sample-mean with a mean in the published benchmarks; the one-sample Wilcoxon-signed-rank test to compare the sample-median with a median in the published benchmarks. The Shapiro–Wilk test was used to investigate if the numerical variables were normally distributed. A significance level of $p < 0.05$ was used.

Ethical consideration

Ethical approval was obtained from the Human Research Ethics Committee, University of the Witwatersrand. Clearance certificate number: M190458.

Results

A total of 1549 mammography examinations were included in the audit, consisting of 808 (52.16%) screening and 741 (47.84%) diagnostic studies. Table 3 shows the demographic and breast-imaging data collected and the cancers detected within the various subgroups. The vast majority (79.66%) of the patients had predominantly fatty or scattered fibroglandular density breast composition (ACR-BI-RADS category A or B). The breast-density distribution showed no significant difference amongst the cancer-positive cases, compared with the non-cancer cases (screening: p = 0.4114, diagnostic: p = 0.0877).

The majority of the final assessments were BI-RADS 1 or 2 (regarded as negative examinations), within both the screening (93.94%) and the diagnostic (58.17%) subgroups.

Abnormal interpretations included BI-RADS categories 3, 4 and 5. The distribution of cancers detected within each of these subcategories is illustrated in Figure 1. The majority of abnormal interpretations and cancers detected were from the diagnostic studies.

Further analysis was done separately for screening and diagnostic studies.

Screening

The patients were all female and 94.18% were over the age of 40 years. The median age screened was 56 (interquartile range [IQR] 48.0–64.0), ranging from 23 to 91 years. A known history of previously treated breast cancer was seen in 34.28% (n = 277). The median age of cancer-positive cases was 55 (IQR 47.0–62.0), with a minimum of 39 and a maximum of 71 years (Table 3).

The majority of patients underwent the standard mammography imaging protocol with digital breast tomosynthesis and additional ultrasound (n = 652, 80.67%).

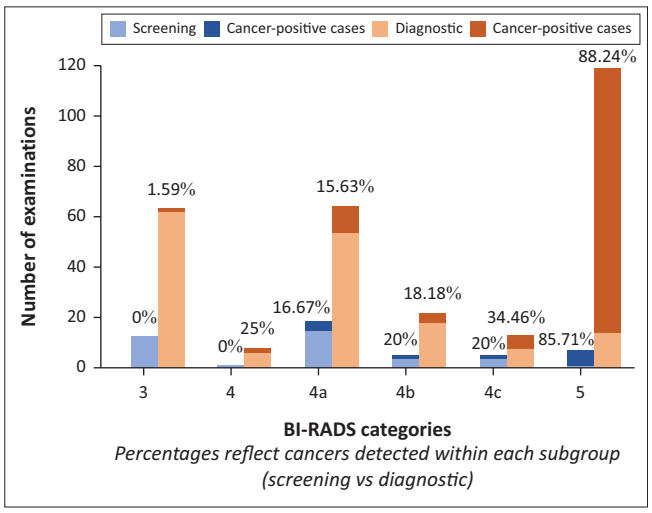
TABLE 3: Audit results for 1549 mammography examinations.

Characteristic	Screening				Diagnostic			
	Total number of examinations	%	Number of cancer-positive cases	%	Total number of examinations	%	Number of cancer-positive cases	%
Age (years)								
< 30	3	0.37	0		16	2.16	5	3.85
30–39	44	5.45	1	9.09	164	22.13	23	17.69
40–49	207	25.62	4	36.36	214	28.88	19	14.62
50–59	247	30.57	2	18.18	160	21.59	37	28.46
60–69	195	24.13	3	27.27	127	17.14	23	17.69
70–79	86	10.64	1	9.09	48	6.8	16	12.31
≥ 80	26	3.22	0	-	12	1.62	7	5.38
Gender								
Female	808	100	11	100	692	93.39	130	100
Male	0	-	0	-	49	6.61	0	-
Personal history of breast cancer								
Yes	277	34.28	6	54.55	24	3.24	4	3.08
No	531	65.72	5	45.45	717	96.76	126	96.92
Breast composition								
Predominantly fatty (A)	318	39.36	2	18.18	216	29.15	34	26.15
Scattered fibroglandular density (B)	373	46.16	6	54.55	325	43.86	62	47.69
Heterogeneously dense (C)	66	8.17	1	9.09	100	13.50	13	10
Extremely dense (D)	6	0.74	0		19	2.56	5	3.85
Not specified (N/S)	45	5.57	2	18.18	81	10.93	16	12.31
BI-RADS classification								
0	0	-	0	-	0	-	0	-
1	295	36.51	N/A	-	123	16.06	N/A	-
2	464	57.43	N/A	-	308	41.57	N/A	-
3	12	1.49	0	-	63	8.50	1	0.77
4 – N/S	1	0.12	0	-	8	1.08	2	1.54
4a	18	2.23	3	27.27	64	8.64	10	7.69
4b	5	0.62	1	9.09	22	2.97	4	3.08
4c	5	0.62	1	9.09	13	1.75	5	3.85
5	7	0.87	6	54.55	119	16.0	105	80.77
Not given	1	0.12	0	-	21	2.83	3	2.31
Total	**808**	**-**	**11**	**-**	**741**	**-**	**130**	**-**

BI-RADS, breast-imaging reporting and data system; N/A, not applicable.

Note: Percentages are based on the total examinations within each column (total values are reported in the last row).

Note: N/A is the number of cancer-positive cases that were not assessed for BI-RADS 1 and 2.



BI-RADS, breast-imaging reporting and data system.

FIGURE 1: Breast-imaging reporting and data system categories and cancers detected for abnormal interpretations in screening and diagnostic mammography.

The remaining studies consisted of mammography with tomosynthesis only (n = 156, 19.31%), and represented patients who came for follow-up screening mammography with low density breast parenchyma (ACR–BI-RADS categories A or B) and unchanged negative assessments (BI-RADS 1 or 2).

Abnormal interpretations (BI-RADS 0, 3, 4 or 5) were reported in 48 of the 808 screening studies, resulting in a recall rate/AIR of 5.94 (Table 4)[8]. These patients were all evaluated using mammography, tomosynthesis and ultrasound and given a final assessment. No patients were categorised as BI-RADS 0. Positive interpretations (BI-RADS 4 or 5) constituted 36 studies. Amongst these, tissue diagnosis was obtained in 32 cases (88.89%). Eleven cancer cases were diagnosed after a positive screening mammogram, with a CDR of 13.6 per 1000 studies. The PPV_1, PPV_2 and PPV_3 were 22.92, 30.56 and 34.38, respectively.

There were nine invasive cancers and two DCIS lesions (Table 5)[8]. The invasive cancer cases with a known pathological tumour size (n = 5) and nodal status (n = 5) demonstrated the following cancer characteristics (Table 5): median tumour length of 20.00 mm (IQR 9.5–26), minimal-

TABLE 4: Derived performance measures for screening mammography (n = 808).

Measure	CHBAH audit value	95% CI	RSNA-benchmark value	95% CI	p
Recall rate (per 100 studies)	5.94	4.51, 7.79	11.6	11.5, 11.6	< 0.0001
Number of abnormal interpretations	48	-	194 668	-	-
Total number of examinations	808	-	1 682 504	-	-
Cancer detection rate (per 1000 studies)	13.6	7.6, 24.2	5.1	-	0.0006
Number of cancers detected	11	-	8529	-	-
Total number of examinations	808	-	1 682 504	-	-
PPV_1	22.92	13.31, 36.54	4.4	4.3, 4.5	< 0.0001
Number of cancers detected	11	-	8529	-	-
BI-RADS 0, 3, 4, 5	48	-	194 668	-	-
PPV_2	30.56	18.01, 46.86	25.6	25.1, 26.1	0.4976
Number of cancers detected	11	-	7376	-	-
BI-RADS 4, 5	36	-	28 785	-	-
PPV_3	34.38	20.41, 51.69	28.6	28.0, 29.3	0.4708
Number of cancers detected	11	-	5945	-	-
BI-RADS 4, 5 with biopsy	32	-	20 763	-	-

Source: Lehman C, Arao R, Sprague B, et al. National performance benchmarks for modern screening digital mammography: Update from the breast cancer surveillance consortium. Radiology. 2017;283(1):49–58. https://doi.org/10.1148/radiol.2016161174

CI, confidence interval; CHBAH, Chris Hani Baragwanath Academic Hospital; RSNA, Radiological Society of North America; PPV, positive predictive value; BI-RADS, breast-imaging reporting and data system.

cancer rate of 42.9% (n = 3) and nodal-negative cancer rate of 60% (n = 3). There were no synchronous bilateral, multicentric or multifocal cancers detected.

The positive cancer cases within the subgroup of women who had a known history of previously treated breast cancer included the following: loco-regional invasive cancer recurrence after previous breast conserving therapy (n = 2; known tumour size 20 mm [n = 1]); invasive cancer involving the contralateral breast (n = 4; known tumour size 12 mm [n = 1]). These patients were all asymptomatic and presented for surveillance screening mammography.

The subgroup of patients with no history of previously treated breast cancer (n = 5) showed the following cancer characteristics: CDR of 9.42 (95% CI [4, 21.8]), invasive cancer median tumour length of 20 mm (n = 3), two DCIS lesions of intermediate- (n = 1; 100 mm) and high-grade (n = 1; unknown size). The age distribution of screen-detected cancers within this subgroup of women were as follows (years): 40–49 (n = 3, 60%), 50–59 (n = 2, 40%), median age of 48 (IQR 45–55.5). These index cancer diagnoses were all screened during the months of October (national breast cancer awareness month) and the beginning of November. Three of these patients represented baseline screening studies, whilst the remaining two patients presented for follow-up screening.

TABLE 5: Derived cancer characteristics for screening mammography (n = 11).

Characteristic	CHBAH audit value	%	RSNA-benchmark value	%	p
Cancer type	-	-	-	-	0.5202
Ductal carcinoma *in situ* (DCIS)†	2	18.2	2644	31.0	-
Low grade	0	-	Unknown	-	-
Intermediate grade	1	-	Unknown	-	-
High grade	1	-	Unknown	-	-
Invasive	9	81.8	5885	69.0	-
Invasive cancer size (mm)‡					0.5782
1–5	0	-	727	12.7	-
6–10	1	20	1461	25.6	-
11–15	1	20	1459	25.5	-
16–20	2	40	840	14.7	-
> 20	1	20	1228	21.5	-
Unknown	4	-	170	-	-
Minimal cancer§	-	-	-	-	0.4658
Yes	3	42.9	4816	57.7	-
No	4	57.1	3527	42.3	-
Unknown	4	-	186	-	-
Axillary lymph node status (invasive cancer)¶	-	-	-	-	0.2745
Positive	2	40.00	1190	20.6	-
Negative	3	60.00	4599	79.4	-
Unknown	4	-	96	-	-
HIV-status	-	-	-	-	-
Positive	2	33.33	Unknown	-	-
Negative	4	66.67	Unknown	-	-
Unknown	5	-	Unknown	-	-
Total number of cancers	**11**	**-**	**8529**	**-**	**-**

Source: Lehman C, Arao R, Sprague B, et al. National performance benchmarks for modern screening digital mammography: Update from the breast cancer surveillance consortium. Radiology. 2017;283(1):49–58. https://doi.org/10.1148/radiol.2016161174

CHBAH, Chris Hani Baragwanath Academic Hospital; RSNA, Radiological Society of North America; HIV, human immunodeficiency virus.

†, DCIS post-surgical tumour size as measured on pathology specimen, where available (n = 1): intermediate-grade 100 mm; high-grade unknown size; ‡, Invasive cancer post-surgical tumour size as measured on pathology specimen, where available (n = 5). Median 20.00 mm (interquartile range 9.5–26), mean 18.2 mm (standard deviation 9.5); benchmark mean 15.9 mm (p = 0.3043); §, Defined as ductal carcinoma *in situ* or invasive cancer ≤ 10 mm; ¶, Refers only to invasive cancers with available nodal pathology results (n = 5).

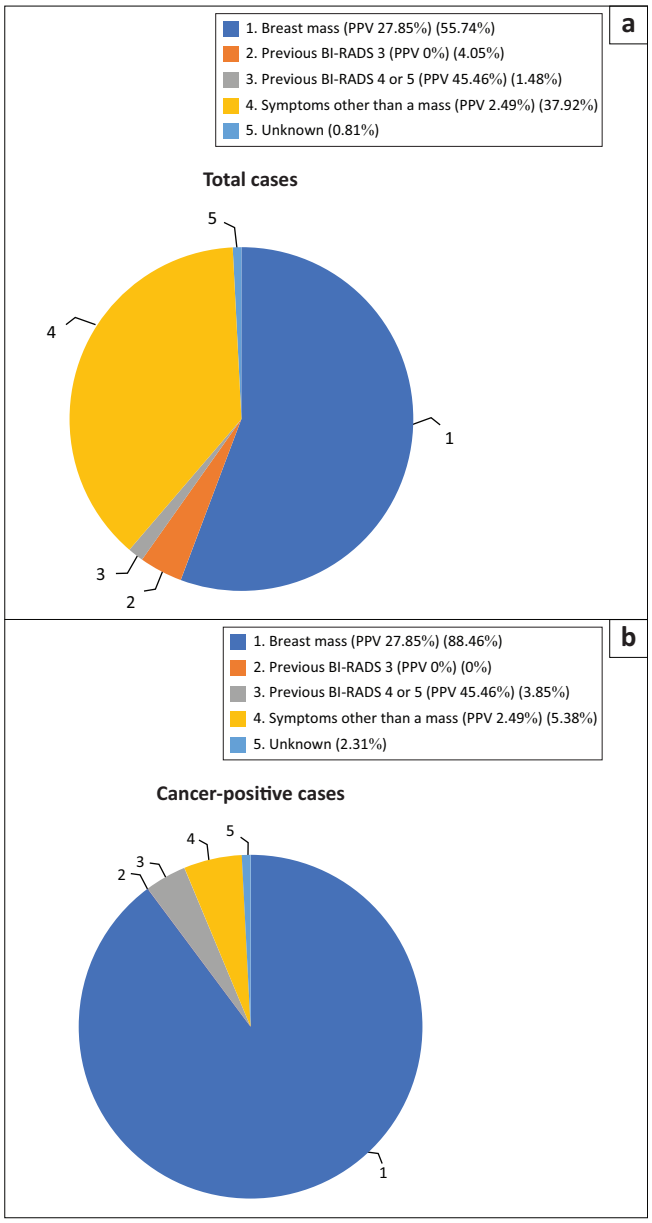
Diagnostic

Similar audit results were derived for the diagnostic subgroup.

The study population consisted of 93.39% (n = 693) female and 6.61% (n = 49) male patients. The median age was 48 (IQR 40.0-60.0), with a range of 19-91 years. A personal history of breast cancer was recorded in 3.24% (n = 24). The median age of cancer-positive cases was 54.5 (IQR 41.0–65.0), with a minimum of 26 and a maximum of 91 years (Table 3).

Amongst the male patients (n = 49), five had abnormal interpretations of their mammograms, consisting of BI-RADS 3 (n = 2), BI-RADS 4c (n = 2) and BI-RADS 5 (n = 1) assessments. Two core biopsies were performed, yielding negative results with no detected breast cancer in males.

The presence of a palpable breast mass constituted 55.74% (n = 413) of the diagnostic indications (Figure 2). Amongst these patients presenting with a mass, 27.85% (n = 115) of the studies resulted in a diagnosis of cancer, contributing



Source: Sprague B, Arao R, Miglioretti D, et al. National performance Benchmarks for modern diagnostic digital mammography: Update from the breast cancer surveillance consortium. Radiology. 2017;283(1):59–69. https://doi.org/10.1148/radiol.2017161519

Note: Data in parentheses are positive predictive values (PPVs).

FIGURE 2: Indications for diagnostic mammography: Total examinations and cancer-positive cases.

88.46% to the cancer cases detected within the diagnostic subgroup.

The remainder of the indications included: mastalgia (n = 176, PPV = 2.27%), nipple discharge (n = 36, PPV = 5.56%), nipple retraction (n = 2, PPV = 0%), skin changes (n = 9, PPV 11.11%), breast abscess (n = 3, PPV = 0%), gynaecomastia (n = 31, PPV = 0%), axillary lymph nodes (n = 4, PPV = 0%), non-specified breast symptoms (n = 17, PPV = 0%), previous BI-RADS 3 (n = 30, PPV = 0%) and previous BI-RADS 4 or 5, where no histology was obtained (n = 11, PPV = 45.46%).

There were 289 (39%) abnormal interpretations (BI-RADS 3, 4 or 5) and 226 (30.50%) positive studies (BI-RADS 4 or 5). In 98.23% (n = 222) of the positive studies, tissue diagnosis was obtained within the unit.

TABLE 6: Derived performance measures for diagnostic mammography (n = 741).

Measure	CHBAH audit value	95% CIs	RSNA-benchmark value	95% CI's	p
Abnormal interpretation rate (per 100 studies)	39	35.55, 42.56	12.6	12.5, 12.7	< 0.0001
Number of abnormal interpretations	289	-	50 659	-	-
Total number of examinations	741	-	401 548	-	-
Cancer detection rate (per 1000 studies)	175.4	149.7, 204.4	34.7	34.1, 35.2	< 0.0001
Number of cancers detected	130	-	13 915	-	-
Total number of examinations	741	-	401 548	-	-
PPV_2	55.75	49.23, 62.08	27.5	27.1, 27.9	< 0.0001
Number of cancers detected	126	-	13 915	-	-
BI-RADS 4, 5	226	-	50 659	-	-
PPV_3	56.76	50.18, 63.32	30.4	29.9, 30.9	< 0.0001
Number of cancers detected	126	-	10 725	-	-
BI-RADS 4, 5 with biopsy	222	-	35 275	-	-

Source: Sprague B, Arao R, Miglioretti D, et al. National performance Benchmarks for modern diagnostic digital mammography: Update from the breast cancer surveillance consortium. Radiology. 2017;283(1):59–69. https://doi.org/10.1148/radiol.2017161519

CHBAH, Chris Hani Baragwanath Academic Hospital; RSNA, Radiological Society of North America; CI, confidence interval; PPV, positive predictive value; BI-RADS, breast-imaging reporting and data system.

The performance measures (Table 6)[3] revealed an AIR of 39, CDR of 175.4 per 1000 studies (n = 130) and a PPV_2 and PPV_3 of 55.75 and 56.76, respectively. These metrics were all significantly higher than the RSNA-benchmark values ($p < 0.0001$).

The vast majority, 96.15% (n = 125), of the cancers detected were invasive and the remaining 3.85% (n = 5) were DCIS (Table 7). One patient with low-grade DCIS presented with a nipple discharge, whilst the remaining intermediate-grade (n = 3) and high-grade (n = 1) DCIS lesions were palpable masses. The median tumour size for DCIS lesions on available pathological specimens was 20 mm (n = 2). Six patients presented with synchronous bilateral breast cancer (4.62%), six with unilateral multicentric cancer (4.62%) and seven with multifocal cancer (5.39%).

Amongst the invasive cancers with a known pathological tumour size (n = 58), 82.76% were greater than 20 mm with a median tumour length of 31 mm (IQR 23.0–45.0). Ten cases (15.87%) were defined as minimal cancers. In approximately half of the cancer-positive cases (50.4%, n = 63) the pathological nodal status was available. Of these, 69.84% (n = 44) were nodal-positive and 30.16% (n = 19) nodal-negative. Figure 3 illustrates the comparison of these tumour characteristics with the RSNA-benchmark values,[3] depicting a larger mean invasive cancer size with a lower percentage of minimal and nodal-negative cancers ($p < 0.0001$).

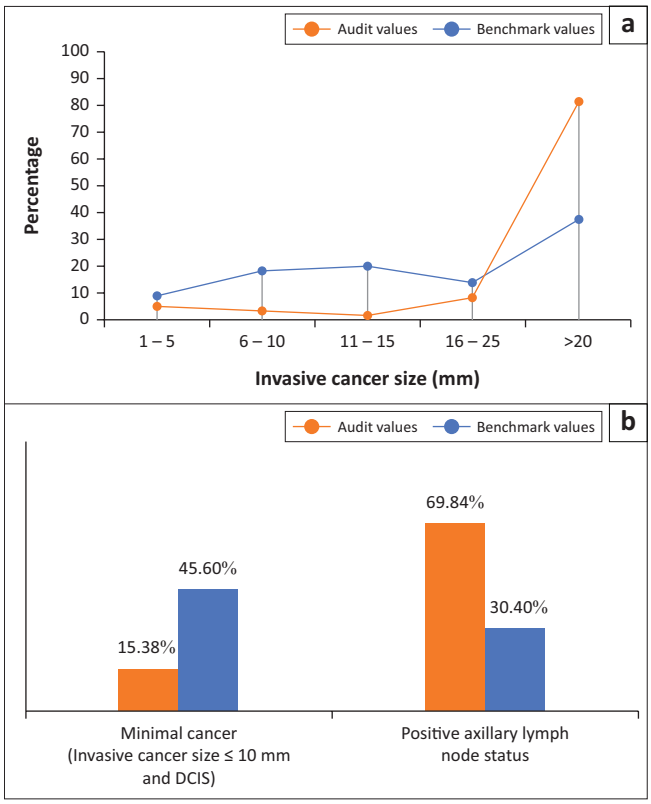
TABLE 7: Derived cancer characteristics for diagnostic mammography (n = 130).

Characteristic	CHBAH audit value	%	RSNA-benchmark value	%	p
Cancer type	-	-	-	-	< 0.0001
Ductal carcinoma *in-situ* (DCIS)†	5	3.85	3329	23.9	-
Low-grade	1	-	Unknown	-	-
Intermediate-grade	3	-	Unknown	-	-
High-grade	1	-	Unknown	-	-
Invasive	125	96.15	10 586	76.1	-
Invasive cancer size (mm)‡	-	-	-	-	< 0.0001
1–5	3	5.17	955	9.5	-
6–10	2	3.45	1858	18.4	-
11–15	1	1.72	2049	20.3	-
16–20	4	6.9	1444	14.3	-
> 20	48	82.76	3767	37.4	-
Unknown	67	-	513	-	-
Minimal cancer§	-	-	-	-	< 0.0001
Yes	10	15.87	6097	45.6	-
No	53	84.13	7260	54.4	-
Unknown	67	-	558	-	-
Axillary lymph node status (invasive cancer)¶	-	-	-	-	< 0.0001
Positive	44	69.84	3083	30.4	-
Negative	19	30.16	7074	69.6	-
Unknown	62	-	429	-	-
HIV-status	-	-	-	-	-
Positive	34	69.91	Unknown	-	-
Negative	79	30.09	Unknown	-	-
Unknown	17	-	Unknown	-	-
Total number of cancers	**130**	**-**	**13 915**	**-**	**-**

Source: Sprague B, Arao R, Miglioretti D, et al. National performance Benchmarks for modern diagnostic digital mammography: Update from the breast cancer surveillance consortium. Radiology. 2017;283(1):59–69. https://doi.org/10.1148/radiol.2017161519

CHBAH, Chris Hani Baragwanath Academic Hospital; RSNA, Radiological Society of North America; HIV, human immunodeficiency virus.

†, DCIS post-surgical tumour size as measured on pathology specimen, where available (n = 2): low-grade unknown size; intermediate-grade 18 mm; high-grade 22 mm; ‡, Invasive cancer post-surgical tumour size as measured on pathology specimen, where available (n = 58): median 31 mm (interquartile range 23–45), mean 36.3 mm (standard deviation 23.9); benchmark mean 21.2 mm (p < 0.0001); §, Defined as ductal carcinoma *in situ* or invasive cancer ≤ 10 mm; ¶, Refers only to invasive cancers with available nodal pathology results (n = 63).



DCIS, ductal carcinoma *in situ*.

FIGURE 3: Comparative illustration of diagnostic audit values and benchmark values for cancer characteristics based on known pathological cancer size and axillary lymph node status.

Discussion

As expected, the data derived from the screening and diagnostic subgroups revealed important differences, illustrating the value of performing separate audits.

Screening

The comparison of the screening audit to RSNA-benchmark values was limited, as expected from the literature review. This was because of the small number of screening-detected cancers limiting the statistical significance of comparing cancer characteristics. Additionally, the differences in screening practices limited the clinical significance of comparing performance measures. The only parameters that showed a statistically significant difference were a lower recall rate/AIR (p < 0.0001), a higher PPV_1 (p < 0.0001) and a higher CDR (p = 0.0006).

The screening audit included patients with a known history of previous breast cancer (n = 277, 34.28%). The ACR audit guidelines advise for these asymptomatic patients to be regarded as screening investigations. Six (54.55%) of the 11 cancers detected were from this high-risk subgroup. In the RSNA screening audit, patients with previous breast cancer constituted only 5.1% of the total patients screened (n = 61 628) and 15% of the cancer cases diagnosed (n = 1022).[6] The majority of patients who received screening mammography at CHBAH had previously presented with a breast complaint, including breast cancer. Therefore, the screening population at CHBAH likely represented a high-risk group for the development of breast cancer, impacting the CDR. The exception to this was the month of October (national breast cancer awareness month), during which screening was promoted. Most of the cancers in the subgroup of women with no history of previous breast cancer were detected during this screening-period, likely representing a more accurate estimate of the CDR in women of average risk within our setting.

The difference in recall rate and PPV_1 can be explained by the difference in screening practices, and is largely influenced by the number of BI-RADS 0 cases. In screening practices where batch reading of mammography is performed, patients are often assessed as BI-RADS 0 and recalled for additional mammography views, tomosynthesis and/or ultrasound. This is standard practice within most facilities in the USA. At CHBAH, immediate reading of screening mammography with tomosynthesis and additional breast ultrasounds are generally performed at the time of first presentation. This is important within a practice serving a large drainage area, where accessibility to breast-imaging units is poor with difficulties in patient recall and follow-up. Consequently,

there were no patients categorised as BI-RADS 0 and the recall rate included final assessments of BI-RADS 3, 4 and 5. This resulted in a significantly lower recall rate and higher PPV_1.

The relative larger size of screen-detected cancers with fewer minimal and nodal-negative invasive cancers, as compared with the RSNA-benchmarks, could be related to the higher frequency of opportunistic screening being performed within the USA. Moreover, the lower PPVs in the RSNA-benchmarks could be attributed to the specific screening environment within the USA (especially regarding self-funding and litigation), where less emphasis is placed on reducing false positive examinations. Despite the comparison of these audit metrics not being statistically significant, the findings are in keeping with what could be expected from the literature review.

The results should, therefore, be interpreted with caution and reflect the differences in screening practices rather than improved performance. This highlights the limitation of comparative audits to international benchmarks. A comparison with follow-up audits in the same unit or units with similar screening practices would be valuable.

The median age of screen-detected cancers was 55 years, which proved to be younger than what was found in the RSNA screening benchmarks. The 40–49 and 50–59 year age groups collectively contributed the majority of cancers detected (36.36% and 18.18%, respectively), compared with the RSNA-benchmarks in which most cancers were detected in women over the age of 60 years (56.3%). In addition, within the subgroup of patients with no personal history of previous breast cancer (n = 5), all screen-detected cancers were in the 40–49 and 50–59 year age groups, (60% and 40%, respectively), with a median age of 48 years. This indicates that screening in our setting should be commenced at the age of 40 and would especially benefit women in their 40s and 50s.

The vast majority of patients, in both the screening and diagnostic audits, had low density breasts (type A or B). This could be related to the demographics of the study population, however, would need further investigation.

Diagnostic

The presence of a palpable breast mass was an important discriminator amongst the reported indications. It was the most common presenting breast complaint and contributed to the majority of cancer cases (88.46%) in the diagnostic subgroup. This was similar to what was reported within the RSNA diagnostic audit. On follow-up audits, the results could be subdivided into 'mass' and 'non-mass' categories, with a different set of performance measures and tumour characteristics for each group.

The performance measures within the diagnostic audit revealed higher CDR and PPVs, as compared with the RSNA-benchmarks. This may be attributed to the fact that patients presented with a significantly larger mean tumour length. The lower percentages of minimal and nodal-negative cancers further reflect an advanced loco-regional stage at presentation.

The reason for the discrepancy between the number of biopsies advised for positive examinations (from which PPV_2 is derived) and the number of biopsies performed (from which PPV_3 is derived) is not clear. Due to the risk of patients defaulting on follow-up, the department strives to perform immediate image-guided biopsies on all positive imaging examinations.

The marked differences in the performance measures, as well as tumour characteristics compared with the RSNA-benchmarks are likely linked to factors contributing to late presentation of disease within our setting. This could include poor breast cancer awareness and accessibility to healthcare facilities, including the lack of a national mammography screening programme. Chris Hani Baragwanath Academic Hospital is a referral centre with a large component of diagnostic studies. There are also multiple delays in the successful diagnosis and referral of these patients by the referring hospitals, mostly because of various human and other resource constraints. Another consideration may be a more aggressive nature of disease in our population. Further investigation in this regard is needed.

The results highlight the need for the promotion of breast cancer awareness and education to all South African women. Furthermore, providing mammography screening facilities in local clinics would increase adherence to recommended screening guidelines and greatly improve early detection and downstaging of cancers.

Study limitations

In addition to the previously mentioned limitations of performing comparative audits using international benchmarks, the following points were noted.

General audit limitations:

- The lack of availability of a national tumour registry precluded the evaluation of metrics, such as false-negative values, sensitivity and specificity.
- The unit does not have a routine patient self-questionnaire. Patient referral forms were relied upon for clinical data acquisition and, where inadequate, the study was omitted. Patient questionnaires within the unit could have facilitated more accurate clinical data collection.

Additional limiting factors on comparison of the audit results with the benchmark values:

- The audit was performed over 6 months from studies done in 2018, whereas the benchmark articles included studies from 2007 to 2013.
- At CHBAH, the BI-RADS assessment is based on digital tomosynthesis mammography with the addition of

ultrasound in most cases. The RSNA-benchmark data is based on digital mammography alone.
- Male patients were included in our diagnostic audit, whereas the RSNA-benchmarks were limited to female patients only. This, however, only constituted a small number of abnormal interpretations (n = 5), with no contribution to the cancers detected.
- Chris Hani Baragwanath Academic Hospital is an academic referral institution, whereas the data collected for the RSNA-benchmarks were largely from non-academic, community-based institutions.

Recommendations for future research

Regular follow-up audits within a facility would be of great value for continuous quality control, especially when a change in practice is implemented. Performance measures could be obtained for each interpreting radiologist. In addition, comparative audits within different South African breast imaging units would provide valuable comparisons of local practices.

We propose a *modified recall rate* to be used in the auditing of screening practices in South Africa. This should be based on the final BI-RADS assessment after further evaluation with digital breast tomosynthesis and ultrasound is complete, as was done in this study. A final BI-RADS assessment leading to anything other than routine follow-up screening mammography (BI-RADS 3, 4 and 5) should be regarded as an abnormal interpretation and used to calculate the *modified recall rate.* This would provide a metric distinct from the internationally accepted *recall rate*, which would be more applicable to many South African screening practices and allow for more relevant comparisons and future research within the country.

The data obtained from these audits could contribute to a breast-imaging database, providing a baseline for the development of benchmarks and recommendations appropriate to the South African setting.

Conclusion

The study highlights the unique challenges faced by a breast-imaging unit within a South African government, tertiary hospital setting. A large proportion of diagnostic mammography is being performed on a population presenting with advanced loco-regional disease, as compared with international, first world benchmarks. It further illustrates the cancer burden within a community where there is a lack of national screening mammography programmes and the additional need for breast cancer awareness.

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Competing interests

The authors have declared that no competing interests exist.

Author's contributions

I.W. was the principal investigator and responsible for the study concept and design, literature review, collection and analysis of data, construction of the database and primary compilation of the manuscript. I.M.V and M.K. were the supervisors and made significant conceptual and editorial contributions to the protocol and final manuscript.

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Data availability statement

Raw data were generated at Chris Hani Baragwanath Academic Hospital. Derived data supporting the findings of this study are available from the corresponding author I.W. on request.

Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors.

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Chapter 2: Protocol with extended literature review

1. Rationale

Breast cancer is a major cause of morbidity and mortality worldwide (1). Breast cancer screening and early detection has been on the forefront of medical innovation with improved breast imaging having a significant impact on the epidemiology of the disease. There is a lack of research in the field of screening mammography within South Africa, with most screening practices not keeping regular audits and statistics (2).

Chris Hani Baragwanath Academic Hospital (CHBAH) is a good representation of a major, South African government hospital with significant financial constraints. The breast cancer disease burden is presumed to be unique with late presentation and advanced disease. This leads the investigator to believe that the breast imaging done at this unit is skewed towards diagnostic investigations as opposed to screening. A clinically relevant audit will be useful to define the disease burden and evaluate operational standards within the breast imaging unit. These can be compared with published benchmarks from developed countries, in an attempt to highlight the impact of the challenges we face in South Africa.

To our knowledge, no such audit has been performed within the CHBAH breast imaging unit. The study will result in a breast-imaging database which can be used for further research in this field. Future follow-up comparative audits can be performed to assess the impact of any new screening or diagnostic implementations or changes. This re-evaluation and outcome monitoring is essential in the quality control of a breast-imaging

unit and the data obtained will be an invaluable addition to cancer research within our country.

2. Introduction

2.1. Epidemiology of breast cancer

2.1.1. International

Breast cancer is the most common type of female cancer worldwide, as well as the leading cause of cancer death amongst women. It accounts for 11,6% of all cancer cases (1). There exists significant global diversity in the epidemiology of the disease, impacted by the degree of economic development as well as social and lifestyle factors. Global statistics are of importance to plan and promote evidence-based cancer control initiatives. For this purpose, adequate national cancer registries are essential, however, the availability of reliable data from most low- and middle- income countries is poor (1).

In the United States of America (USA), cancer surveillance and analysis is made available by the National Cancer Institute. Female breast cancer was estimated as 15,2% of all new cancer cases diagnosed in 2019 with a 5 year survival rate of 89.9% (2009 – 2015) (3).

2.1.2. South Africa

The most recent data published in the 2014 National Cancer Registry (NCR-SA) revealed that the breast is the most common site of cancer affecting South African women of all races. It accounts for 21,78% of all cancers with a lifetime risk of 1 in 27 (4). It should be noted that these statistics are derived from a pathology-based registry which could be an under-reflection of the true cancer incidence. No population-based registry is currently

available in South Africa (5). This fact was further highlighted in a 2016 meta-analysis performed by Jedy-Agba et al. on the stage at diagnosis of breast cancer in sub-Saharan Africa. The paucity of data in this field was reported as an additional issue. The results revealed a major percentage of sub-Saharan African women, including those from South Africa, presenting with late-stage breast cancer. The statistics specific to the black population showed that a larger percentage of women were presenting with late-stage breast cancer in 2010 than what was found within the population of the USA 40 years prior (6).

A more recent study performed in 2019 at a South African government specialist breast-clinic reported that two-thirds of patients were presenting with locally advanced breast cancer. Various population factors contributing to the delay in presentation were described (7). An advanced stage at diagnosis has a poor prognostic implication. The most recently published 5 year survival rate of breast cancer in South Africa is 53.4% (2005 – 2009) (8).

These statistics exemplify the need for additional breast cancer research and disease control within South Africa.

2.2. Advances in breast imaging

Over the past decade there has been a transition from film-screen to digital mammography, which has greatly influenced breast-imaging practices. Because of advances in imaging, more abnormalities, including cancers are diagnosed. Despite this, digital mammography has not shown equally significant improvements in differentiating between benign and malignant disease (9). The result is an increase in false positive (FP)

rates, a decrease in positive predictive values (PPVs) and a subsequent increase in biopsy rates, workload and costs. The recent addition of tomosynthesis in screening has assisted radiologists in decreasing recall rates (10), and is routinely used as an adjunct to standard digital mammography in many practices.

Computer-aided detection (CAD) is another advance in digital mammography, used by readers to improve detection rates. The adjunct of CAD is especially useful in the setting of screening mammography. Ongoing development in artificial intelligence (AI) shows promise to further improve interpretive performance by increasing the specificity of findings. With improved AI algorithms, not only can findings, such as calcifications, be detected by computerised methods, but an improved distinction can be made between benign and suspicious characteristics (11).

Within an era of rapidly changing imaging technology, we believe that regular re-evaluation of a facility's performance becomes essential.

2.3. Reporting of breast imaging - ACR-BIRADS

The American College of Radiology Breast Imaging Reporting and Data System (ACR BI-RADS) is an internationally accepted standardised reporting system on breast imaging findings. The latest ACR BI-RADS Atlas (5th edition) was published in 2013. Using a standardised reporting structure and lexicon of terminology improves performance as well as streamlining "outcome monitoring and quality control". The ACR BI-RADS defines breast composition categories (a-d), with progressively increasing fibroglandular density and subsequently decreasing sensitivity of mammography. The ACR BI-RADS final assessments and management recommendations are categorised in Table 1. The Food

and Drug Administration (FDA) Mammography Quality Standards Act (MQSA) mandates the use of a final assessment in every mammography report. These final assessments do not have to be linked to the management recommendations. However, these categories were designed to be concordant and when used correctly, the BI-RADS assessment categories 1-5 have specific probability ranges for predicting cancer. These predictive values can be evaluated within a specific imaging unit as part of a quality-assurance audit (12).

Table 1: ACR BI-RADS final assessment categories (12).

Category	**Management**	**Probability of cancer**
0 - Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examination(s)	N/A
1 - Negative	Routine screening	Essentially 0%
2 - Benign	Routine screening	Essentially 0%
3 - Probably Benign	Short interval follow-up or continued surveillance mammography	> 0%, but ≤ 2%
4 – Suspicious of malignancy *4a. Low suspicion* *4b. Moderate suspicion* *4c. High suspicion*	Tissue diagnosis	> 2%, but < 95% *4a. > 2%, but ≤10%* *4b. > 10%, but ≤50%* *4c. > 50%, but < 95%*

Category	Management	Probability of cancer
5 - Highly suggestive of malignancy	Tissue diagnosis	≥ 95%
6 - Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

2.4. Screening of breast cancer

A screening study is defined as a routine investigation on an asymptomatic woman. A diagnostic study includes the investigation of a breast complaint and the short-term follow-up of a previous abnormal assessment (9).

The benefits of screening mammography have been recognised for more than 50 years. The main objective is to detect small, clinically occult, node-negative breast cancer resulting in the best possible prognosis (10). However, there has been a recent debate and ongoing research concerning the risk-benefit ratio of screening mammography. The major disadvantage is argued to be overdiagnosis and overmanagement of breast cancer with the psychological, healthcare and financial strain associated with it (7). Additionally, an effective screening programme requires considerable funding. Nevertheless, a meta-analysis of relevant studies, recently published by Lipschitz et al., has shown strong evidence of a significant decrease in the breast cancer mortality rate attributable to screening mammography (7).

2.4.1. International

In most of the world, mammography is the screening method of choice for the detection of early breast cancer. There still, however, exists considerable variation and debate on screening interval guidelines as well as screening practices in the 40 – 50 years age group (7). The American College of Radiology (ACR) recommends women of average risk for the development of breast cancer to commence annual screening mammography from the age of 40 (13). The United States Preventative Services Task Force (USPSTF) advise biennial screening mammography within the age group 50 – 74, with the recommendation that women aged 40 – 49 can have optional screening after discussion with their health care provider (14).

Despite there being no national organised screening programme within the USA, there is a high prevalence of opportunistic screening being performed with a reported 65% compliance rate to recommended guidelines (2015) (15,16). Opportunistic screening refers to unmonitored screening, directed by patient self-request or as advised by a health care professional. Audit results are expected to differ in countries where a lower frequency of screening is done, particularly when evaluating the size and stage of the screen-detected cancers. Earlier detection of tumours is expected when more screening is performed. In addition, due to the lack of surveillance by an organised screening programme, self-funding and the ever-increasing risk of malpractice litigation within the USA, the goal of reducing false positive outcomes is deemed less important. This further limits comparative audits on screening mammography with other countries (16).

There are many countries that do offer national or provincial organised screening programmes, such as Sweden, the Netherlands, Norway, Spain, and the United Kingdom, to name a few. Numerous observational studies from these programmes provide direct proof of the benefit of screening mammography (2,17).

2.4.2. South Africa

The National Department of Health (NDH) released the Breast Cancer Prevention and Control Policy in 2017 (5), with the major goal of improving breast cancer awareness, early detection and management within the country. Promotion of screening and early detection is stated as a key objective. Mammography is recognised as the screening method of choice in developed countries, however, South Africa currently lacks the resources to employ and sustain a national screening program. It is stated that such a program should only be introduced if it can be ensured that at least 70% of the target population will benefit from it (5). A large percentage of women do not have access to screening mammography, especially those within the rural setting (7).

Therefore, currently there is no national mammography screening programme within South Africa. The NDH recommends clinical breast examination and breast self-examination for early detection of disease. It is, however, recognised that such methods have not yet been proven as efficient screening tools (5).

Opportunistic screening mammography is also performed within South Africa, however, auditing data are generally not kept, or available, at most facilities (2). Therefore, scant research exists on the rate of screening mammography done within the country. The

authors suspect the figures to be significantly less than the USA, particularly within the public sector.

The current recommendations by the relevant imaging societies within South Africa are in favour of regular screening mammography. The Radiological Society of South Africa (RSSA) and Breast Imaging Society of South Africa (BISSA) advise annual screening from the age of 40, which is in accordance with the recommendation from the American College of Radiology (2,13).

2.5. Staging of breast cancer

The clinical staging is the first step in the work-up of a patient with newly diagnosed breast cancer. Although referred to as clinical staging, this initial work-up is largely dependent on radiological investigations and image-guided biopsies (18). Important information provided by the radiologist includes the tumour size, number of tumour lesions, local extent of disease, regional nodal status, and distant metastatic disease (19). The result is a clinical tumour-nodal-metastases staging (c-TNM). The importance of the c-TNM is for the planning of primary treatment, which may include neoadjuvant chemotherapy, mastectomy, breast-conserving therapy and sentinel or axillary nodal dissection (18).

The final staging of the patient is based on the histopathology of the surgical specimens, including the primary tumour and resected lymph nodes. Adequate resection margins are necessary for a reliable pathological description of the tumour. This final pathological-TNM (p-TNM) staging, which may differ from the initial c-TNM, will then guide further management of the patient (18).

2.6. The breast imaging audit

2.6.1. Major goals of auditing

Regardless of standardised reporting systems, there still exists an inter-user variation in the interpretive performance of breast imaging and the threshold to obtain tissue diagnosis.

Comparative audits have an essential role in standardising performance within a breast imaging unit, across the country and even across the globe. It provides a quantitative means of quality assurance and subsequent improvement measures. During a breast-imaging audit, certain performance measures derived can be compared to national or international benchmarks and recommendations (9). Additionally, the results can be compared with follow-up audits in the same unit or as a comparison between different units. An internal audit within a unit can also yield comparative results for individual interpreting physicians. The auditing of mammography assessments suspicious for malignancy (BI-RADS 4) and highly suggestive of malignancy (BI-RADS 5) is MQSA mandate within the USA (9).

2.6.2. ACR-BIRADS – the basic clinically relevant audit

Background

The American College of Radiology (ACR) outlines *the basic clinically relevant audit* in the "follow-up and outcome monitoring" chapter within the ACR-BIRADS atlas (5th edition) (20). This audit structure was chosen for this study due to the established audit rules and definitions. Following a widely available, structured audit process allows for accurate comparisons with published benchmarks and recommendations.

Performance measures and tumour metrics

Recommendations for the collection of data and the calculation of derived data are made within the ACR-BIRADS manual, as outlined in Table 2.

Table 2: The basic clinically-relevant audit – derived data to be calculated (20).

Derived data	**Definitions**
True-positives (TP)	Positive imaging study with a positive tissue diagnosis of breast cancer.
False-positives (FP)	Positive imaging study with a negative tissue diagnosis for breast cancer.
Positive predictive value (PPV) *1 – PPV_1* *2 – PPV_2* *3 – PPV_3*	Reflects true positive cases as a proportion of total positives (TP + FP): *1 – Based on positive screening cases, with any result other than routine follow-up (BIRADS categories 0, 3 ,4 and 5).* *2 – Based on positive examinations with the recommendation for tissue diagnosis (BIRADS 4 and 5).* *3 – Based on positive examinations where tissue diagnosis was obtained (BIRADS 4 and 5).*
Cancer detection rate (CDR)	Histology-proven cancer cases per 1000 examinations.
Percentage nodal-negative invasive cancers	Reflected as a percentage of total invasive cancer cases.
Percentage “minimal” cancers	Defined as invasive cancer ≤ 1cm or DCIS.

Derived data	Definitions
	Reflected as a percentage of total cancer cases.
Percentage stage 0 or 1 cancers	Reflected as a percentage of total cancer cases.
Abnormal interpretation rate (AIR) /Recall rate	Positive assessments, leading to additional imaging or biopsy, per 100 examinations: 1. *Diagnostic audit: BI-RADS 3, 4, 5.* 2. *Screening audit (recall rate): BI-RADS 0, 3, 4, 5.*

A positive diagnosis of breast cancer is defined as a histological diagnosis of breast cancer within 12 months following the examination. Similarly, a negative diagnosis is defined as no diagnosis of breast cancer within the 12 months following the examination (9,10).

Three scenarios for a positive mammography examination are described:

1. A screening mammogram leading to anything other than routine follow-up (BI-RADS categories 0, 3, 4 and 5).
2. A study leading to the recommendation for tissue diagnosis (BI-RADS 4 or 5).
3. A study leading to tissue diagnosis being obtained (BI-RADS 4 or 5).

True and false positive as well as positive predictive values (PPVs) can be derived for each of these scenarios (PPV_1, PPV_2 and PPV_3, respectively) (20).

The PPV gives the probability that a positive examination accurately indicates the presence of the disease. Of the subcategories, the PPV_2 is the most useful within an imaging facility. It is a valuable indicator of interpretive performance as well as the overall biopsy threshold within the department. It provides information with regards to cost

containment, while balancing the risk of missing early pathology. The PPV_3 reflects clinical practice, and should equal PPV_2, where biopsies were performed on all cases where tissue diagnosis was recommended (16). PPV_3 is also known as biopsy yield of malignancy or positive biopsy rate (20).

In order for sensitivity and specificity to be derived, negative examinations need to be correlated with a population-based tumour registry to verify the true absence or presence of disease (true- or false-negatives) (20). Even in developed countries, such as the United States of America (USA), the majority of breast-imaging facilities cannot reliably derive these metrics. For this reason, known false negative values are requested by the MQSA, but this metric is not mandatory for the breast imaging audit (20).

No population-based registry is currently available in South Africa (5). The data published within the South African national cancer registry lacks certain details required for an audit, such as differentiating between screening and diagnostic studies (4). It is, therefore, acceptable to exclude false negatives, sensitivity and specificity from audits, where it cannot be reliably derived (20).

Metrics evaluating tumour characteristics, such as invasive cancer size, lymph node status and cancer stage are encouraged to be included in the audit. The percentage minimal cancers (defined as DCIS or invasive cancers $\leq$ 10mm), node-negative cancers and metastatic cancers can then be derived (20). These metrics give an indication of how early disease is detected, which reflects the major goal of screening and early detection programmes within a country.

Further audit rules and recommendations

The American College of Radiology (ACR) recommends audits to be performed at least once a year within breast-imaging facilities. This can consist of either a basic, clinically-relevant audit or a more complete audit, as outlined in the "Follow-up and outcome monitoring" chapter within the ACR-BIRADS atlas (5th edition). The relevance of the audit will be directly proportional to the number of metrics evaluated and should, therefore, be as comprehensive as possible. Separate audits on diagnostic and screening studies are advised, as these show significant statistical differences (20).

2.6.3. Published benchmarks and recommendations

There are currently no published benchmarks or recommendations specific to South African mammography practices. Performance data from imaging facilities is required to analyse national practices and derive such benchmarks. However, currently there is no national mammography database with such data available within South Africa.

Registries such as the Breast Cancer Surveillance Consortium (BCSC) and National Mammography Database (NMD) exist within the USA. These registries greatly facilitating breast cancer research. Breast imaging data, already obtained under MQSA audit regulations, are used to establish national benchmarks and recommendations (21,22). The ACR-BIRADS atlas describes the value of comparing a facility's audit results with acceptable performance parameters.

Three comparator value sets are recommended within the atlas (20):

1. National performance benchmarks based on data from the BCSC.

2. Outcomes reported from the ACR National Mammography Database (NMD).

3. Recommendations made by a panel of breast imaging experts (23).

The benchmark values reflect the performance of breast-imaging practices in the USA, while the recommendations are based on the critical analysis of published literature and personal experience by experts (20).

The Radiological Society of North America (RSNA) national performance benchmarks for digital mammography were published in April 2017, consisting of separate publications and value sets for diagnostic and screening studies. The goal of the publications was to provide relevant benchmarks after the transition from film-screen to digital mammography. The performance measures are summarised in Tables 3 and 4. The data was collected from six BCSC registries and based on the ACR BI-RADS 5th edition manual. Digital mammograms performed between 2007 and 2013 were included. The number of examinations included in the studies were 1 682 504 for screening mammography and 401 548 for diagnostic mammography (9,10).

Table 3: BCSC mammography-screening benchmarks (10)

Performance measure	**Value**
AIR (recall rate) (%)	11.6
CDR (per 1000 examinations)	5.1
False-negative rate (FNR) (per 1000 examinations)	0.8
PPV1, abnormal interpretations (%)	4.4
PPV2, recommendation for biopsy (%)	25.6

PPV3, biopsy performed (%)	28.6
Sensitivity (%)	86.9
Specificity (%)	88.9

Table 4: BCSC mammography-diagnostic benchmarks (9)

Performance measure	**Value**
AIR (%)	12.6
CDR (per 1000 examinations)	34.7
False-negative rate (FNR) (per 1000 examinations)	4.8
PPV2, recommendation for biopsy (%)	27.5
PPV3, biopsy performed (%)	30.4
Sensitivity (%)	87.8
Specificity (%)	90.5

These benchmarks were not intended for use outside the USA, as it reflects the advanced screening practices specific to the country (16).

The ACR-BIRADS manual further describes the limitation of an audit comparison to benchmark data when performed in facilities with relatively small sample sizes, especially the sample obtained from screening-detected cancers. In such cases internal audits or comparison of the facility's trend over time becomes more useful (20).

Nonetheless, in our opinion, deviation from the RSNA benchmarks can be analysed and causative factors hypothesised. Results need to be interpreted whilst keeping in mind the

vast differences in local practices. If the deviation is large, a national incentive to obtain benchmarks specific to our population and resource-limited setting could be motivated for.

2.6.4. Relevance of the breast imaging audit

The relevance of the breast-imaging audit, focused on interpretive performance and disease burden, is to obtain data that will facilitate quality and skill-improvement methods. The aim is to reduce false-positive rates while maintaining high detection rates of invasive, node-negative cancers. In addition, breast cancer awareness and the need for improved screening programmes is promoted.

Relevance to CHBAH

CHBAH is a major South African tertiary referral institution serving an extensive drainage area (24). In our opinion it provides a good representation of the population utilising public healthcare within South Africa. Most patients presenting to CHBAH, including those who receive screening mammography, are referred from other health care facilities. An exception is during the month of October (national breast cancer awareness month) (25) , during which breast imaging in the unit is promoted.

From experience, we have found that the disease burden is unique, with relatively high numbers of diagnostic as opposed to screening investigations and an advanced stage of presentation, contributing to the strain on an already resource-limited setting.

No such study has been performed within the unit and the breast imaging database obtained can be used as a baseline for future comparison within CHBAH as well as other

imaging facilities. A comparison of the performance measures to the published benchmarks from the RSNA will be of value, as the breast imaging practices at CHBAH are also based on the BI-RADS system. A comparison of cancer characteristics to those published by the RSNA (9,10) will add further relevance.

National relevance

The relevance of regular breast-imaging audits within a mammography unit extends to a national level. If such audits were to become regulation, data obtained could be added to a national mammography database. Performance benchmarks and recommendations specific to South Africa could be derived. Additionally, such a database will contribute to further breast cancer research within our country.

3. Aim

To perform a clinically relevant breast-imaging audit, focused on interpretive performance and disease burden, within the CHBAH Breast Imaging Unit.

4. Study objectives

4.1. Primary objective

Perform a breast imaging audit at CHBAH Breast Imaging Unit, according to the guidelines outlined in the ACR BI-RADS 5th edition manual.

4.2. Secondary objectives

- Compare imaging findings (ACR BI-RADS breast composition and final assessments) with histology results.

- Compare data collected and derived with published benchmarks (BCSC Mammography Screening and Diagnostic Benchmarks published by the RSNA) (9,10).

5. Methods

5.1. Research paradigm

This is a retrospective descriptive study.

5.2. Sample

The study population will consist of all patients presenting to CHBAH Radiology Department for breast imaging during the period 1 June to 31 November 2018. According to the Picture Archiving and Communication System (PACS) at CHBAH, approximately 1 500 mammograms were performed during the 6 months and will be considered for the study.

5.2.1. Inclusion criteria

All patients who received a mammogram with or without an additional breast ultrasound.

5.2.2. Exclusion criteria

- No consultant-approved mammography report available.
- Inadequate information available to classify as diagnostic or screening mammography.
- BI-RADS category 6 (known breast cancer). This category does not include patient with treated breast cancer receiving follow-up screening.
- BI-RADS category 0 (incomplete, needing additional imaging), with no follow-up reclassification.

5.3. Materials and methods

The study will evaluate digital mammography and breast ultrasound performed within the CHBAH Mammography Unit. The mammography machine used is a Hologic Selenia Dimensions System. Studies are viewed on mammography-approved monitors. The ultrasound machine used is an Aloka Prosound α 10.

The standard imaging protocol includes tomosynthesis mammography with craniocaudal and mediolateral oblique views. Breast ultrasound is routinely performed, with the general exception of patients presenting with low-density breasts and no change on follow-up screening mammography. However, this varies between radiologists. All studies are reported or reviewed by specialist radiologists, consisting of approximately 10 consultants rotating through the mammography unit. When indicated, tissue diagnosis is obtained within the mammography unit by means of ultrasound-guided or stereotactic core biopsies.

5.4. Data collection

Data will be collected from the hospital PACS at CHBAH. The system in use is the AGFA IMPAX 6.5.1.501. Consultant-approved radiology reports will be used. Histology results will be obtained from the National Health Laboratory Service (NHLS) using the NHLS LABTRAK web results viewer.

Data will be recorded by the researcher, using an Excel spreadsheet.
Separate data sheets will be used for diagnostic and screening studies, as separate audits will be conducted for these two categories.

Data will be collected according to the attached data collection sheets (Appendix A-B). Most of the data will be obtained from the breast-imaging report, which will include the breast composition and ACR-BIRADS final assessment. In cases where each breast was assigned a separate BI-RADS category, the highest category will be used.

In the case of a diagnostic study, subcategories will be recorded as per the indication provided on the breast imaging report. This will include additional imaging or short-interval follow-up imaging of a recent study performed (previous BI-RADS 0 or 3), repeat imaging for a patient lost to follow-up before histology was obtained (previous BI-RADS 4 or 5) or symptomatic evaluation of a breast problem. The presence of a palpable lump will also be recorded. Histology results will be obtained for all positive imaging studies. For positive cancer cases, additional data obtained from the imaging report will include the invasive cancer size in millimetres (c-T). The largest linear dimension of the tumour as measured on mammography and/or breast ultrasound will be recorded. The nodal status as diagnosed on ultrasound within the breast-imaging unit will also be recorded. The post-surgical tumour size and nodal involvement will be recorded as per the pathology report, where available (p-TN).

5.5. Reliability and validity

The study will consist of a large sample size, increasing reliability and validity.
The study relies on radiology reports being available on PACS, which could potentially exclude a significant number of the sample population.

5.6. Bias

- As the audit will be conducted at the breast imaging department of CHBAH, the patient population represents that of a tertiary public hospital and will be unique to this specific unit and patient referral system currently in place.
- Data will be collected from a number of different consultant-approved reports, each with different levels of experience and mammography interpretive skills. Therefore, a study reported by a different set of radiologists may yield slightly different results.

6. Data analysis and statistics

Data captured in Microsoft Excel will then be analysed using SAS Version 9.2. Descriptive statistics will be calculated where numerical data will be analysed using means (M) with standard deviations (SD) or medians (Mdn) with interquartile ranges (IQR). Categorical data will be analysed using frequencies and percentages.

The derived data will be calculated according to the ACR BI-RADS audit definitions and rules. The performance measures will include AIR and recall rates, CDR and PPV. The tumour metrics will include the percentage minimal cancers (DCIS or invasive cancers ≤ 10mm), the median size of invasive cancer (in mm) and the percentage nodal-negative invasive cancers.

The following analytical statistics will be used to compare the sample statistics to the published benchmarks: the single proportion (or one sample) binomial test will be used to compare the sample proportion to a proportion in the published benchmarks; the one

sample t-test will be used to compare the sample mean to a mean in the published benchmarks; and the one sample Wilcoxon signed rank test (which is a non-parametric alternative to one-sample t-test when the data cannot be assumed to be normally distributed) will be used to compare the sample median to a median in the published benchmarks. The Shapiro-Wilk test will be used to investigate if the numerical variables are normally distributed. A significance level (a) of 0.05 will be used.

7. Ethics

Permission from the CHBAH Medical Advisory Committee and Hospital Management has been granted.

The protocol is pending approval by the WITS Human Research Ethics Committee.

7.1. Consent forms

No informed consent will be required as a retrospective study design is used and only patient records will be accessed.

7.2. Data safety

Confidentiality will be ensured by anonymising data on the collecting sheets. Studies will be recorded using study numbers with no patient identification. The data will be kept on the computer of the primary investigator and only the primary investigator and supervisors will have access to the raw data.

8. Timing

Month / Year	Nov 2018	Dec 2018	Jan 2019	Feb 2019	March 2019	April 2019	May 2019	June 2019	July 2019	Aug 2019	Sept 2019
Literature search											
Reading literature											
Summarising literature											
Preparing Protocol											
Protocol Assessment											
Ethics application											
Collecting data											
Data analysis											
Writing up thesis											
Publishing paper											

9. Budget

Travel	R 300
Stationary	R 200
Printing	R 700
Total	R 1 200

The study will be self-funded.

10. Anticipated problems/limitations

- The study will not include patients presenting to CHBAH who undergo non-image guided biopsies outside of the CHBAH breast-imaging unit. The study is limited to the disease burden presenting within the breast-imaging department. This is not expected to be a major limitation, as it is standard practice for patients to be referred for imaging and image-guided biopsy.
- The study will rely on reports being available on PACS. The CHBAH PACS is not consistently working, during which times imaging reports are not saved. Furthermore, the PACS is not linked to the Hospital Information System (HIS), requiring the manual entry of patient details on registration of an imaging examination. This leads to regular errors resulting in untraceable studies and incomplete tracking of patients. This will not pose a major issue to the general audit of the Breast Imaging Unit, as data will be collected using study dates and additional records and statistics of patient details are kept within the unit to assure accuracy. This, however, poses a significant problem when correlating patient details with staging studies to evaluate the percentage metastatic cancers.

The study was, therefore, limited to evaluating locoregional staging as done within the unit. This limitation can be used as motivation for system improvements in order to facilitate future research.

- The false negative rates of breast imaging will not be assessed, due to the lack of cancer ascertainment with a reliable national tumour registry. The sensitivity and specificity, therefore, will be omitted. These metrics, however, are not essential to the basic clinically relevant audit.

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12. Appendices

BI-RADS Final Assessment									Tissue diagnosis	
Not Specified	BR1	BR2	BR3	BR4-NS	BR4a	BR4b	BR4c	BR5	Advised	Biopsy type

Histology Result			Positive Histology			HIV status			Invasive tumour size (mm)			Nodal Status	
Indeterminate	Neg	Pos	Type	Grade	Receptors	Pos	Neg	Unknown	U/S	MMG	Histo	US	Histo

STUDY NUMBER	Demographics		Indication							Composition			
	Age	Gender	Prev. BR0	Prev. BR3	Prev. BR4/5	Lump	Pain	Discharge	Other	a	b	c	d

Turnaround time (days)	
Imaging to histology	Imaging to post-surgical pathology

Appendix A Diagnostic Data Collection Sheet

STUDY NUMBER	Demographics		Composition			
	Age	Gender	A	b	c	d

BI-RADS Final Assessment									Tissue diagnosis	
Not Specified	BR1	BR2	BR3	BR4-NS	BR4a	BR4b	BR4c	BR5	Advised	Biopsy type

Histology Result			Positive Histology			HIV status			Invasive tumour size (mm)			Nodal Status	
Indeterminate	Neg	Pos	Type	Grade	Receptors	Pos	Neg	Unknown	U/S	MMG	Histo	US	Histo

Turnaround time (days)	
Imaging to histology	Imaging to post-surgical pathology

Appendix B Screening Data Collection Sheet

Chapter 3: Appendices

Appendix A: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr I Warnich

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190458

NAME: (Principal Investigator)	Dr I Warnich
DEPARTMENT:	School of Clinical Medicine Department of Radiation Sciences Division of Radiology Medical School University
PROJECT TITLE:	Breast Imaging at Chris Hani Baragwanath Academic Hospital - a clinically relevant audit
DATE CONSIDERED:	2019/04/26
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Drs I Viljoen and M Kuehnast
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/06/24

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 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
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 submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore reports and re-certification will be due early in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

25/06/2019
Date

Appendix B: Turnitin report

1820785:1820785_Warnich_Ilonka.docx

ORIGINALITY REPORT

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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.