AN AUDIT OF PATIENTS PRESENTING WITH CLINICALLY BENIGN BREAST DISEASE TO THE HELEN JOSEPH HOSPITAL BREAST IMAGING UNIT

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Diagnostic Radiology (MC000)

Johannesburg, 2021

Declaration

I, Dr Nicholas Christopher Christofides, declare that this research report is my own work. It is being submitted for the degree of MMed (FC Rad Diag (SA)) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University. It is submitted in publishable format with my protocol an extended literature review.

Dr Nicholas Christopher Christofides
On this 27th day of July 2021

Declaration: Student's contribution to article(s) and agreement of co-author(s)

I, Dr Nicholas Christopher Christofides, 0703131Y / A00025261, declare that this Thesis/Dissertation/Research Report is my own work and that I contributed adequately towards research findings published in the article[s] stated below which are included in my Thesis/Dissertation/Research Report.

Signature of Student ..... Date...20/08/2020.....

Name of Primary Supervisor...Dr Grace Rubin.....

Signature of Primary Supervisor .....Date 28/08/2020

Agreement by co-authors: By signing this declaration, the co-authors listed below agree to the use of the article[s] by the student as part of his/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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Comments by primary supervisor:

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I dedicate this MMed to my family and friends.

Thank you all for the help and support you provided.

Publications and presentations

This work is due to be published in South African Journal or Surgery, volume pending.

AN AUDIT OF PATIENTS PRESENTING WITH CLINICALLY BENIGN BREAST DISEASE TO THE HELEN JOSEPH HOSPITAL BREAST IMAGING UNIT

Abstract

Background: Benign breast pathology is a common presenting complaint and its assessment is important to characterize so as to not miss malignant pathology. At Helen Joseph Hospital (HJH) patients are triaged at the Breast Clinic according to the clinical suspicion of benign versus malignant disease. The patients are assigned a colour label based on their clinical presentation. This triage system affects waiting times between clinical examination and mammography appointments. This study aims to assess the association between clinical examination and the radiological and pathological findings of disorders deemed clinically benign and to ascertain the spectrum of benign breast disorders encountered at HJH.

Method: A retrospective study of imaging results of patients at HJH presenting as clinically benign breast disorders from January – June 2018 was conducted. Assessed BIRADS score was noted and if core biopsies were performed, their results and patient demographics were documented.

Results: Of the 1263 clinically benign patients presenting from January - June 2018 the radiological assessment was: BIRADS 1: 158 (12.5%), BIRADS 2: 685 (54.2%), BIRADS 3: 292 (23.1%), BIRADS 4a: 54 (4.3%), BIRADS 4b: 29 (2.3 %), BIRADS 4c: 21 (1.7%), BIRADS 5: 24 (1.9%). There were 133 biopsies (including 8 BIRADS 3 patients), with 46 (3.6%) confirmed malignancies. The combined specificity of mammography and ultrasound was 65.52 % (54.56% - 75.39%) and combined sensitivity 91.30% (79.21% – 97.58%)

Conclusion: There is a vast spectrum of benign conditions presenting in this population group with only 3.6% confirmed malignancies, confirming an accurate triage system utilised at the breast clinic.

Radiological imaging is highly sensitive but less specific emphasising the triad of clinical, radiological and histological assessment as the gold standard with regard to diagnosis of breast disease.

Keywords: clinically benign breast disease, breast imaging unit, Helen Joseph Hospital

Acknowledgements

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1. Introduction

Benign breast pathology is a common presenting complaint, with benign diseases more common than malignancies in young women(1). In North America, benign breast disorders account for 90% of breast complaints to hospitals. (2) The majority of patients presenting with breast complaints are found to have benign breast disorders, as seen in both developing and developed countries(1, 3). Benign breast disorders have various modes of presentation and comprise multiple entities (4). These disorders require adequate diagnosis and monitoring to identify a mis-assessment of malignant pathology and to review for the small increased risk of breast cancer development associated with some benign pathology(5). Benign breast disease, such as Phyllodes tumour, can carry an increased risk of progression to malignant phyllodes tumours(5).

In order to correctly diagnose these conditions, triple assessment is utilised with the radiological correlation forming an integral part of benign breast disorder diagnosis and monitoring(6). Since breast cancer is the most common cancer in female patients, the diagnosis of a benign breast disorder is a relief to most patients(7, 8). It is therefore important to classify the percentage of patients presenting with these conditions and to ascertain the spectrum of benign disorders seen in our community. Triple (clinical, radiological and pathological) assessment is the gold standard in order to achieve a definitive diagnosis(6).

BIRADS is the radiological classification system used for breast imaging to help standardize breast imaging reporting(9). It is also useful in aiding adequate communication of findings to both radiologists and clinicians alike, as well as providing a method to monitor outcomes of patients(9). The BIRADS classification system and the risk of malignancy is noted in Table 1.

At the Helen Joseph Hospital, patients are triaged at the Breast Clinic according to a clinical suspicion of benign versus malignant breast disease. The patients are assigned a colour label based on their clinical presentation. Patients who present with a clinical suspicion of an abscess, or high suspicion for cancer are triaged as red (deemed high risk clinically and requiring imaging as soon as possible). Those who present with breast pain or breast asymmetry but with no mass, or any non-suspicious mass, milky / infected nipple discharge, or palpable axillary lymph nodes with no definite palpable breast pathology are triaged as

yellow. This triage system affects waiting times between clinical examination and mammography appointments. An assessment was performed of patients triaged as yellow (clinically benign) who received a date for their imaging studies within 6 – 8 weeks of their clinical examination. Thus, the sensitivity of our triage system as well as radiological and histological correlation is vital to patient management.

Table 1.1.: Concordance between BI-RADs assessment categories and management recommendations ACR BI-RADS Atlas 5th Edition(10).

Assessment	Management	Likelihood of Malignancy
BIRADS 0: Incomplete – Needs additional imaging.	Recall Patient	
BIRADS 1: Negative	Routine screening	0%
BIRADS 2: Benign	Routine Screening	0%
BIRADS 3: Probably Benign	Short interval follow up (6 months)	>0% but ≤ 2%
BIRADS 4: 4a: Low suspicion 4b: Moderate suspicion 4c: High suspicion	Biopsy	 >2% but ≤10% >10% but ≤50% >50% but ≤95%
BIRADS 5: Highly suspicious	Biopsy	≥95%
BIRADS 6: Known biopsy proven malignancy	Surgical Management	

This study aims to assess the association between clinical examination and the radiological and pathological findings of disorders deemed clinically benign and to ascertain the spectrum of benign breast disorders encountered at HJH.

2. Methods

This was a retrospective study of mammographic, sonographic and histological (where available) results of all patients group (irrespective of age or gender) presenting to HJH Breast Unit with clinically benign breast disorders from January 2018 to June 2018.
Sample size was calculated based on the population of Johannesburg (as patients can present at any age or gender)
Sample size was calculated with an online calculator using the population of Johannesburg for 2020 (5783000), confidence interval of 5 and confidence level of 99% = sample size of 666.
It was decided to use a six month period, this included 1263 patients.
This included all patients who were classified as benign by the HJH breast unit, based on certain clinical features: breast pain, breast asymmetry, milky or yellow nipple discharge, possibility of palpable lymph nodes with nothing palpable in the breast, palpable mass with no suspicion for cancer. All reports that were illegible or lost were excluded.
The mammogram and ultrasound reports were collected and from them, BIRADS scores, core biopsy reports, and the demographics were collated on a data sheet.
The frequency of all BIRADS classifications found were calculated.
All patients who received a biopsy were documented and the results correlated with their clinical and imaging results.
Histology results were accessed from the NHLS for all patients who underwent a biopsy.
An anonymized database (on Excel) based on demographics, BIRADS score, histology results was collected and documented.

The study is reliable as it is an audit on the department, based on the radiological reports in a unit with a dedicated breast imaging specialist and thus is repeatable.
The study is valid as all lesions classified as BIRADS $\geq$4 receive biopsies (gold standard as per BIRADS) and thus the diagnoses had histological correlation.
Descriptive statics (percentages and frequencies) were calculated for categorical data.
Pearson's Chi Squared test to determine the association between radiological and histological findings was performed.
The sensitivity and specificity were calculated.
Prior to the commencement of this study, ethical clearance was obtained certificate number M191172.

3. Results

There were a total of 1263 patients with a wide variety of ages and 34 male and 1229 female patients.

Table 2.1. Demonstrates the demographics of the patients included within the study.

Table 2.1.: Demographics of study patients and their distribution within BIRADS classification.

Demographics:		**Number of Patients**	**BIRADS 1**	**BIRADS 2**	**BIRADS 3**	**BIRADS 4**	**BIRADS 5**
Age group:	<20	65	15	24	25	1	0
	21 – 30	166	38	56	63	9	0
	31 – 40	176	29	68	54	22	3
	41 – 50	263	28	145	53	31	6
	51 – 60	238	19	152	45	18	4
	61 – 70	243	21	166	35	16	5
	71 – 80	99	7	65	17	6	4
	>80	13	1	9	0	1	2
Gender:	Males	34	1	2	30	0	1
	Females	1229	157	683	262	104	23
Total number of patients involved in the study:		1263	158 (12.6%)	685 (54.2%)	292 (23.1%)	104 (8.2%)	24 (1.9%)

In Figure 1.1. which is shown below, the percentage of patients per age group within each of the BIRADS categories is shown.

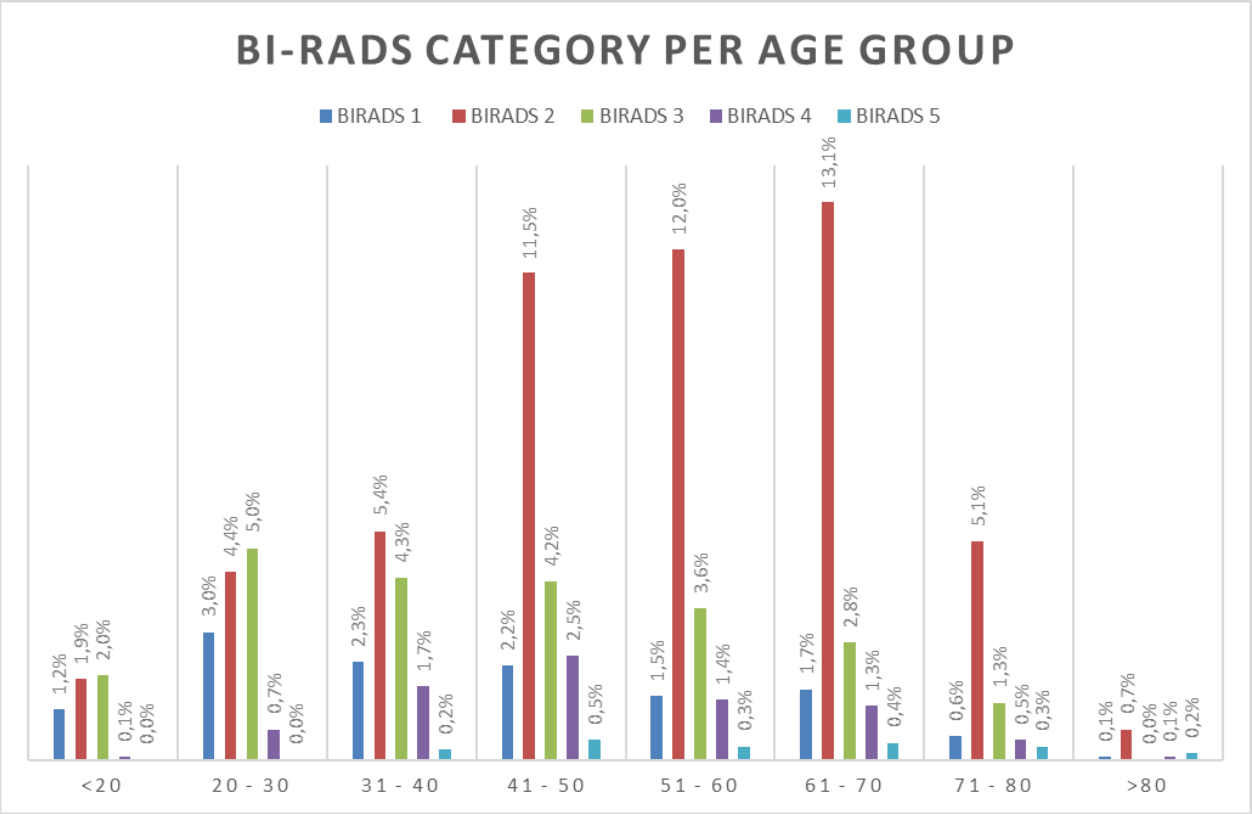

Figure 1.1.: Graph showing the percentage of patients per BIRADS category divided into age groups.

Of the clinically benign patients presenting from January 2018 until June 2018 the spectrum of imaging findings was as follows:
BIRADS 1: 158 (12.5%), BIRADS 2: 685 (54.2%), BIRADS 3: 292 (23.1%), BIRADS 4a: 54 (4.3%), BIRADS 4b: 29 (2.3 %), BIRADS 4c: 21 (1.7%), BIRADS 5: 24 (1.9%)

Table 3.1.: Showing patients that underwent biopsy, their results and BIRADS group as well as the percentage representation in terms of the total number of patients

BIRADS	**Biopsy Result**		**Total**
	Malignant	**Benign**	
3	0	8	8 (0.6%)
4a	4	49	53 (4.20%)
4b	5	24	29 (2.3%)
4c	16	5	21 (1.66%)
5	21	1	22 (1.74%)
Total	46	87	133
Percentage of total patient number	3.6%	6.9%	10.5%

In Table 3.1. above the BIRADS category of every patient that underwent biopsy is recorded and their results are supplied. These results are expressed as a percentage of the total sample number, with only 3.6 % of all patients classified as clinically benign representing malignant disease.

The 8 BIRADS 3 patients who underwent biopsy were to either confirm diagnosis, such as in the case of a giant fibroadenoma or at the request of the patient and all eight were confirmed histologically to be benign.
There were also three patients within the BIRADS 4 and 5 categories who did not undergo biopsy. The reasons were multifocal: patient refusal, patient too unstable or unwell clinically to undergo biopsy or no stock of biopsy needles (these patients were subsequently rebooked).

An assessment of all biopsies was performed, their results and the patients' distribution among the BIRADS categories (Table 3.1.) documented. From these results a Chi Squared Value of 77.307 with a p value of <0.00001 was obtained. This indicates a statistically significant correlation between the radiological findings and the corresponding histological results.

Table 4.1. Biopsy results found within the sample of patients

Types	Number of patients
Biopsy Confirmed Benign Lesions	
Fibroadenoma	24(27.6 %)
Fibrocystic breast disease	21(24.1 %)
Benign breast tissue	20 (23 %)
Fat necrosis	9 (10.3 %)
Epidermal inclusion cyst	2 (2.3 %)
Sclerosing Adenosis	2 (2.3 %)
Benign intraductal papilloma	2 (2.3 %)
Usual ductal hyperplasia	2 (2.3 %)
Periductal inflammation	1 (1.1 %)
Lactational changes	1 (1.1 %)
Mycobacterial infection	1 (1.1 %)
Previous abscess cavity	1 (1.1 %)
Acute mastitis	1 (1.1 %)

Biopsy Confirmed Malignant Lesions	
Invasive carcinoma no specific type	32 (69.6 %)
Ductal Carcinoma In Situ (DCIS)	8 (17.4 %)
Malignant Phyllodes	2 (4.3 %)
Lymphoma	2 (4.3 %)
Mucinous Carcinoma	1 (2.2 %)
Papillary Carcinoma	1 (2.2 %)

Table 4.1 above depicts the spectrum of disease found amongst all the study participants that underwent biopsy. Majority of the patients depicted displayed benign histology in keeping with the clinical findings.

The imaging spectrum of disease within the study population is illustrated in Figure 2.1.

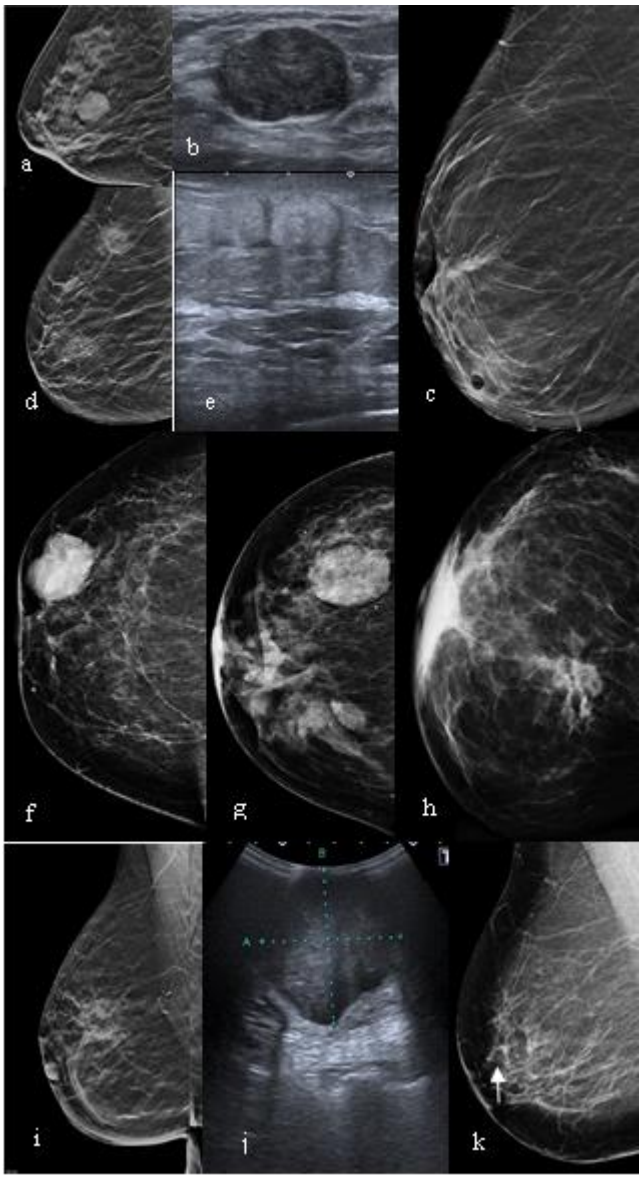

Figure 2.1.: The imaging spectrum of disease seen in this study population. (a) Mammogram (RCC) and (b) ultrasound views of a biopsy confirmed fibroadenoma. (c) Mammogram (RMLO) of a patient with an oil cyst. (d) Mammogram (RMLO) and (e) ultrasound views of fat necrosis post mild trauma to the breast. (f) Mammogram (RCC) of a patient with biopsy confirmed malignant phyllodes. (g) Mammogram (RCC) of a patient with biopsy confirmed mucinous carcinoma of the breast. (h) Mammogram (RCC) of a patient with biopsy confirmed B-cell lymphoma of the breast. (i) Mammogram (RMLO) and (j) ultrasound of a patient with a biopsy confirmed invasive carcinoma. (k) Mammogram (RCC) of a patient with biopsy confirmed DCIS

4. Discussion

Our results demonstrate a wide distribution of ages amongst all the clinically benign patients presenting at an open access breast clinic. The majority of patients were between the ages of 40 and 70, however in more developed countries most patients presenting with benign breast diseases are between the ages of 30 and 50 years(11). This may be related to better access to health care and earlier detection in these more developed countries.

Most of the patients within this clinically benign population fell within the benign or probably benign BIRADS categories with 1135 (89.9%) out of a total 1263 between BIRADS 1, 2 and 3. This is in keeping with the literature as clinical examination alone has a sensitivity of 54% while its specificity is 94% and as such some suspicious lesions may be mis-diagnosed as benign pathology(12).

There were 128 (10.1%) patients within this clinically benign group who were radiologically suspicious (BIRADS 4 – 5). This is higher than expected as per the literature, after a single step triage system (as in our case), 52% of patients with malignancies were given non-urgent dates. Subsequently, after a second stage triage only 4% of patients with malignancies were given non-urgent dates.(13)

A total of 133 biopsies were performed (some performed on BIRADS 3 patients for confirmation of diagnosis or at the patients' request). Three of the radiologically suspicious patients did not undergo biopsy due to refusal, inadequate clinical status or lack of stock of biopsy needles.

Of the 133 patients who underwent biopsies, only 46 were confirmed to have malignancies, representing 3.6% of the total sample (1263) patients. This is comparable with international triage systems as it is expected that 4% patients with breast cancer will be triaged as semi-urgent (or yellow labelled as in our case)(13).

This emphasises that clinical examination is a good screening modality, but cannot be used as a stand alone investigation in our country as well as globally(12).

From Table 4.1 one can see that the majority of malignancies were found to be invasive carcinoma of no specific type (69.6% of all malignancies found) with the next most common malignancy being DCIS (17.4%). This is in keeping with the literature as invasive ductal carcinoma is recognised as the most common subtype of breast cancer(14).

Some other malignant lesions seen were malignant phyllodes, lymphoma and mucinous breast carcinoma, lesions which can mimic benign disease clinically as well as on imaging.

They present as well-defined masses clinically and well circumscribed masses on both mammogram and ultrasound. It is in these cases that histology becomes very important.
With regards to the benign diseases found on biopsy, Table 4.1. shows that the most common findings were fibroadenomas (27.6% of all benign diseases found) which is in keeping with the literature (found in 25% of women)(11) with fibrocystic breast disease (24.1%) and benign breast tissue (23%) being the next most common diagnoses.
From the above results one can conclude that radiological assessment alone has a high sensitivity of 91.30% (79.21 % - 97.58%), however, the specificity in our institution is lower 65.52% (54.56% - 75.39%). According to the literature, however, the sensitivity should be 99% with a specificity of 95.2%(15), thus there is room for improvement, and this further emphasises the need for the gold standard of therapy which is the triple assessment.

This study was limited by the population group sampled, this may not be representative of the full population of our country as it represents only a small subset based on the catchment area of Helen Joseph Hospital.

5. Conclusion

A vast array of BIRADS categories were found within this population clinically assessed as presenting with benign disease with a radiological correlation of the majority (89.9%) being benign. Only 3.6% of the total sample were confirmed radiologically and histologically as malignant disease which is in keeping with international standards.
Radiological imaging alone is highly sensitive but less specific when compared with the histological findings, emphasising that the triad of clinical, radiological and histological assessment is indeed necessary with regards to breast imaging and clinical diagnosis. Of note is the useful application of a triage system at a clinical level to streamline referral for imaging in a resource limited health care setting.

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Appendix 1:

Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr Nicholas Christopher Christofides

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M191172

NAME: (Principal Investigator)	Dr Nicholas Christopher Christofides
DEPARTMENT:	Diagnostic Radiology Helen Joseph Hospital
PROJECT TITLE:	Audit of patients presenting with benign breast disease to the Helen Joseph Hospital Breast Imaging Unit
DATE CONSIDERED:	29/11/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Grace Rubin
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/02/2020

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 03/02/2020

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES