DEVELOPMENT AND EVALUATION OF A SOFT-COPY MAMMOGRAPHIC VIEWING PROTOCOL TO IMPROVE RADIOLOGICAL REPORTING

Carin Meyer

Thesis submitted in fulfilment of the requirements for the Ph.D. (Radiographic Sciences) degree in the Faculty of Health Sciences, at the University of the Free State.

Supervisor: **Prof W.I.D. Rae**

Co-Supervisor: **Prof C.P. Herbst**

DECLARATION

I, Carin Meyer, certify that the thesis herby submitted by me for the Ph.D. (Radiographic Sciences) degree at the University of the Free State is my independent effort and had not previously been submitted for a degree at another university/faculty. I furthermore waive copyright of the thesis in favour of the University of the Free Sate.

_____

2 October 2012

DEDICATION

In memory of my father

Adam Johannes Barnard

1934 - 2011

PRESENTATIONS ARISING FROM THIS STUDY

The results of this study were presented as oral and poster presentations at the following forums:

- **48th SAAPMB Congress, UFS, Bloemfontein (24-28 March 2009):**

Optimisation of display of digital images of a mammography QC phantom

- **16th International Society of Radiographers & Radiological Technologists (ISRRT) World Congress, Gold Coast, Australia (9-12 September 2010):**

Assessment of basic soft-copy reporting training on diagnostic accuracy of mammography reporting

Poster: Optimisation of soft-copy display using mammography quality control phantom images

Poster: Image quality assessment of image processing algorithms for clinical soft-copy mammography display

ACKNOWLEDGEMENTS

The mercy of my Heavenly Father, for giving me the strength and perseverance to complete this study.

This study would not have been possible without the assistance of the following persons:

- My study leader, Prof W.I.D. Rae, for his knowledge, assistance, guidance, and encouragement throughout the study;

- Prof C.P. Herbst, my co-leader, for his valuable input and advice;

- Prof G. Joubert; for her valuable input and assistance with the statistical analysis of the data;

- Prof C.S. de Vries and personnel from the Department of Clinical Imaging Sciences for supporting the project;

- Me J. van der Merwe from Philips for the practical training of the viewers on the PACS workstation and for anonymising the patient files

- Prof W.I.D. Rae, Prof. C.P. Herbst and Me A. Sweetlove for participating in the scoring of the phantom images;

- Dr S.F. Otto, for assisting in selecting the clinical images for the study;

- Dr F.A. Gebremariam, Dr M. Naude and Dr J.R. Muller for participating in the reporting of the mammograms;

- Me E.F. Nel, from the mammography unit for obtaining consent from the patients;

- My family and friends for their interest and encouragement. Special thanks to my husband Biebie, without whom I could not have completed this task. Thank you for your love and support throughout the study

TABLE OF CONTENTS

		Page
DECLARATION		ii
DEDICATION		iii
PRESENTATIONS		iv
ACKNOWLEDGEMENTS		v
TABLE OF CONTENTS		vi
LIST OF FIGURES		xvii
LIST OF TABLES		xix
ACRONYMS AND ABBREVIATIONS		xxi
CHAPTER 1	**ORIENTATION TO THE STUDY**	**1**
1.1		I
	INTRODUCTION	1
1.1.1	Incidence of breast malignancies and associated mortality	1
1.1.2	Breast imaging	1
1.1.3	Mammographic features of breast cancer	4
1.1.4	Contrast challenges in mammography	6
1.2	SCREEN-FILM MAMMOGRAPHY	7
1.2.1	Viewing conventional screen-film mammography	8
1.2.2	Limitations and advantages of screen-film mammography	9
1.3	DIGITAL MAMMOGRAPHY	11
1.4	BACKGROUND ON THE SETTING FOR THE STUDY	13

1.4.1 Transition from screen-film mammography to digital mammography at Universitas Academic Hospital 14
1.4.2 Standardising reporting 15
1.5 THE PROBLEM WITH CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY 15
1.6 AIM OF THE STUDY 17
1.7 STRUCTURE OF THE THESIS 17

CHAPTER 2 DIGITAL MAMMOGRAPHY 20

2.1 CONTEXT OF DIGITAL MAMOGRAPHY 20
2.1.1 Image acquisition in DM 21
2.1.1.1 Indirect conversion 21
2.1.1.2 Direct conversion 21
2.1.1.3 Cassette-based CR photostimulable storage phosphor (PSP) imaging plate 22
2.1.2 The digital image 23
2.1.3 Soft-copy display 24
2.1.4 Advantages and limitations of digital mammography 25
2.2 CLINICAL TRIALS FOR COMPARISON OF SCREEN-FILM MAMMOGRAPHY AND DIGITAL MAMMOGRAPHY 27
2.3 DIGITAL IMAGE PROCESSING 30
2.3.1 Image processing algorithms 33
2.3.1.1 Histogram processing 33

2.3.1.1.1 Histogram equalization 33
2.3.1.1.2 Neighbourhood processing 34
2.3.1.1.3 Contrast Limited Adaptive Histogram Equalisation (CLAHE) 34
2.3.1.2 Multi-Scale Image Contrast Amplification (MUSICA) 37
2.4 CLINICAL COMPARISON OF IMAGE PROCESSING ALGORITHMS 39
2.5 CONCLUSION 46

CHAPTER 3 TRAINING REQUIREMENTS FOR RADIOLOGISTS CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY 49

3.1 WHY SHOULD THE RADIOLOGISTS BE TRAINED IN DIGITAL MAMMOGRAPHY? 49
3.2 TRAINING NEEDS FOR RADIOLOGISTS CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY 51
3.2.1 Digital image processing 52
3.2.2 Magnification 53
3.2.3 Manual intensity windowing 54
3.2.4 Invert 55
3.2.5 Summary 55
3.3 CURRENT TRAINING OF RADIOLOGY REGISTRARS AT THE RESEARCH SITE 56

3.4 TRAINING REQUIREMENTS IN THE US vs. THE SA CONTEXT 57

3.5 CONCLUSION 58

CHAPTER 4 IMAGE QUALITY ASSESSMENT OF PROCESSING OPTIONS: PHANTOM BASED METHOD 60

4.1 INTRODUCTION 60

4.2 AIM 61

4.3 METHODS 61

4.3.1 Contrast Detail (CD) Phantom 61

4.3.2 System description and image acquisition 64

4.3.3 Image processing 65

4.3.4 Image evaluation 66

4.3.5 Evaluation of the viewer's observations 67

4.3.6 Image quality quantification 68

4.3.7 Data analysis 68

4.3.8 Statistical analysis 69

4.4 RESULTS 69

4.5 DISCUSSION 77

4.5.1 Unprocessed and Unprocessed Invert 77

4.5.2 MUSICA^2 and MUSICA^2 Invert 77

4.5.3 Invert 78

4.5.4 CLAHE parameter combinations 79

4.5.4.1 Contextual region 79

4.5.4.2 NBins 79
4.5.4.3 Clip limit 80
4.5.4.4 Map level 80
4.5.5 Comparison of mean IQF scores and rank order of processing options 81
4.6 CONCLUSION 83

CHAPTER 5 DEVELOPING THE SOFT-COPY VIEWING PROTOCOL THROUGH PARTICIPATIVE LEARNING 85

5.1 INTRODUCTION 85
5.2 AIM 86
5.3 METHODS 86
5.3.1 Ethics 86
5.3.2 Trainees 86
5.3.3 Training 87
5.3.3.1 Theoretical training 87
5.3.3.2 Hands-on training 88
5.3.3.3 Participative learning 88
5.3.4 Clinical images 89
5.3.5 Processing options 90
5.3.6 Criteria for the clinical evaluation of image quality 93
5.3.7 Rating method 94
5.3.8 Display of the images 95
5.3.9 Instructions to viewers 95

5.3.10	Preliminary familiarisation of viewers with the study	96
5.3.11	Data analysis	96
5.3.12	Feedback to the viewers	96
5.4	RESULTS	97
5.4.1	Image quality evaluation	97
5.4.1.1	Image quality evaluation – Overall anatomical structures (criteria 1-8)	97
5.4.1.2	Image quality evaluation – Individual anatomical structures (criteria 1-8)	99
5.4.1.3	Image quality evaluation – Calcifications (criterion 9) and masses (criterion 10)	101
5.4.1.4	Image quality evaluation – Noise level in the reproduction of the pectoral muscle (criterion 11)	103
5.4.1.5	Image quality evaluation – Is the image quality sufficient for early detection of breast cancer? (Criterion 12)	106
5.5	DISCUSSION	108
5.5.1	Image quality evaluation – Overall anatomical structures (criteria 1-8)	110
5.5.2	Image quality evaluation – Individual anatomical structures (criteria 1-8)	110
5.5.3	Image quality evaluation – Calcifications (criterion 9) and masses (criterion 10)	112
5.5.4	Image quality evaluation – Noise level in the reproduction of the pectoral muscle (criterion 11)	115

5.5.5 Image quality evaluation – Is the image quality sufficient for early detection of breast cancer? (criterion 12) 116
5.5.6 Comparing the results of the phantom study (Chapter 4) with that of the clinical images 117
5.6 CONCLUSION 118

CHAPTER 6 DIAGNOSTIC ACCURACY BEFORE AND AFTER THE DEVELOPMENT OF THE SOFT-COPY VIEWING PROTOCOL 121

6.1 INTRODUCTION 121
6.2 AIM 121
6.3 METHODS 122
6.3.1 Study population 122
6.3.2 Case selection 122
6.3.3 Views included 123
6.3.4 Confirmation of diagnosis 123
6.3.5 Equipment 123
6.3.6 Viewers 124
6.3.7 Viewing of the images 124
6.3.8 Image processing algorithm 124
6.3.9 Reporting 125
6.3.9.1 BI-RADS assessment categories 125
6.3.9.2 Classification of breast parenchyma 126
6.3.9.3 Characterisation of lesions 127

6.3.10	Familiarising the viewers	128
6.3.11	Descriptive data analysis	128
6.3.12	Comparative statistical analysis	130
6.4	RESULTS	131
6.4.1	Histopathology confirmation	131
6.4.2	Viewing sessions	131
6.4.3	Sensitivity	131
6.4.4	Specificity	132
6.4.5	Overall accuracy	133
6.4.6	Positive predictive value (PPV)	134
6.4.7	BI-RADS 3	135
6.4.8	Breast parenchyma	136
6.4.9	Characterisation of lesions	137
6.5	DISCUSSION	139
6.5.1	Sensitivity, specificity, overall accuracy and PPV	139
6.5.2	BI-RADS 3	142
6.5.3	Breast parenchyma classification	145
6.5.4	Characterisation of lesions	147
6.6	CONCLUSION	149

CHAPTER 7 CONCLUSIONS AND RECOMMENDATIONS 151

7.1	CONCLUSIONS	151
7.2	RECOMMENDATIONS	156
7.2.1	Training of radiologists in the new modality	156

7.2.2	Development and refinement of a soft-copy viewing protocol	157
7.2.3	Objectives for the development of a soft-copy viewing protocol	157
7.2.4	Visualisation of masses	157
7.2.5	Visualisation of dense parenchyma in the breast	158
7.2.6	Invert gray scale	158
7.2.7	Clinical images	158
7.2.8	Standardising mammographic reporting	158
7.3	LIMITATIONS OF THE STUDY	159
7.3.1	Small number of viewers	159
7.3.2	Number of cases	159
7.3.3	Type of mammograms	160
7.3.4	Administrative limitations	160
7.3.5	Representivity	160
7.3.6	Software limitations	160
7.3.7	Tabár's classification of breast parenchyma	161
7.3.8	The use of BI-RADS to standardise reporting	161
7.4	FUTURE RESEARCH	161

LIST OF REFERENCES **164**

APPENDICES

Score form CDMAM-phantom	A
Evaluation form CDMAM-phantom	B
University of the Free State: Ethics approval	C
Universitas Hospital: CEO approval	D
Department of Diagnostic Radiology: HOD approval	E
Radiation Control Committee: Approval	F
Information document: English, Afrikaans, Southern Sotho	G
Consent document: English, Afrikaans, Southern Sotho	H
Training programme	I
Evaluation form: Image quality assessment	J
Information document: Image quality assessment	K
Raw data: Image quality assessment	L
p-Values indicating differences in mean IQS (all viewers) per individual anatomical structure (criteria 1 – 8) between the processing options (n=36)	M
A-D: p-Values indicating differences in mean IQS (all viewers) between the individual anatomical structures (criteria 1-8) per processing option (MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert)	N
Mammography reporting: Datasheet	O
Information document: Mammogram reporting	P

Raw data: Initial and Final reporting Q

Simple kappa values for agreement on Tabár's classification of breast parenchyma R

Percentage agreement between viewers on lesion site and calcifications S

Kappa values for agreement between viewers on characterisation of mammogram pattern T

Kappa values for agreement between viewers on lesion extent U

Literature searches with key words that yielded no results V

Recommended soft-copy viewing protocol for mammography W

Implementation of the soft-copy viewing protocol for mammography – Simulation Unit – Faculty of Health Sciences X

SUMMARY

OPSOMMING

LIST OF FIGURES

Figure		Page
Figure 1.1	Characteristic curve of an x-ray film	10
Figure 2.1	Image acquisition with a CR system based on storage-phosphor image plates	23
Figure 2.2	The MUSICA^2 flowchart	39
Figure 4.1	Contrast-Detail phantom ARTINIS CDMAM type 3.4	62
Figure 4.2	A cropped segment of a mammography x-ray image of the ARTINIS CDMAM type 3.4 phantom	63
Figure 4.3	Mean rank score for the different processing options	75
Figure 5.1	A MLO image presented with the different processing options	91
Figure 5.2	A zoomed segment of a limited region of the image in fig 5.1 presented with the four different processing options	92
Figure 5.3	Mean IQS (all viewers) per individual anatomical structure (criteria 1 – 8)	99
Figure 5.4	Mean IQS (all viewers) for calcifications (criterion 9)	102
Figure 5.5	Mean IQS (all viewers) for masses (criterion 10)	102
Figure 5.6(A-D)	Noise level in the reproduction of pectoral muscle for MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert	105
Figure 5.7(A-D)	Sufficiency of image quality for the early detection of breast cancer for MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert	107

Figure 6.1 A MLO view of the breast. In A the image was processed with MUSICA^2, and in B, the image was processed with MUSICA^2 Invert 125

Figure 6.2 Sensitivity before (Initial reporting) and after the viewing protocol (Final reporting) 132

Figure 6.3 Specificity before (Initial reporting) and after the viewing protocol (Final reporting) 133

Figure 6.4 Positive predictive values (PPV) before (Initial reporting) and after the viewing protocol (Final reporting) 135

Figure 6.5 Percentage agreement between viewers on Tabár's classification of breast parenchyma before (Initial reporting) and after the viewing protocol (Final reporting) 137

LIST OF TABLES

Table		Page
Table 4.1	Thickness, diameter and radiation contrast C_r (for standard mammography exposure conditions) of the gold disks within the phantom	64
Table 4.2	Mean IQF (all viewers) for the different processing options	70
Table 4.3	p-Values indicating significance of the paired differences between the different processing options	71
Table 4.4	Mean and total rank scores for the different processing options	74
Table 4.5	Comparison of position based on IQF and mean rank score	76
Table 5.1	Image quality criteria for the MLO projection used for this research study	94
Table 5.2	Mean image quality score (IQS) (all viewers) per image quality criteria (1 – 8 anatomical structures) and anatomical structures overall for the different processing options	97
Table 5.3	p-Values indicating differences in the mean IQS (all viewers) for anatomical structures overall (criteria 1-8) between the processing options	97
Table 5.4	Mean IQS (all viewers) for calcifications (criterion 9) and masses (criterion 10)	101
Table 5.5	p-Values indicating differences in mean IQS (all viewers) for calcifications and masses (criterions 9 and 10) between the processing options	103
Table 5.6	p-Values indicating differences in answers (criterion 11 and criterion 12) (all viewers) between the processing options	104

Table 6.1	American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) classification used in this study	126
Table 6.2	Tabár's classification of breast parenchyma	127
Table 6.3	2 x 2 Contingency table	129
Table 6.4	Overall accuracy before (Initial reporting) and after the viewing protocol (Final reporting)	134
Table 6.5	Cases classified as BI-RADS 3 before (Initial reporting) and after the viewing protocol (Final reporting)	136

ACRONYMS AND ABBREVIATIONS

ACR	American College of Radiology
AHE	Adaptive Histogram Equalisation
AUC	Area Under the Curve
BI-RADS	Breast Imaging Reporting And Data System
CAD	Computer-Aided Detection
CC	Cranio-Caudal
CD	Contrast - Detail
cd/m^2	Candela per square metre
CEO	Chief Executive Officer
CI	Confidence Interval
CME	Continuing Medical Education
CNR	Contrast-to-Noise Ratio
CPD	Continuing Professional Development
CR	Computed Radiography
CsI	Cesium Iodide
DM	Digital Mammography
e.g.	for example
etc.	et cetera
ETOVS	“Etiek Oranje-Vrystaat”
FDA	Food and Drug Administration
FFDM	Full Field Digital Mammography
FN	False Negative
FNA	Fine Needle Aspiration
FoM	Figure of Merit
FOV	Field of View
FP	False Positive
FROC	Free-Response Receiver Operating Characteristic
GE	General Electric
HIW	Histogram-based Intensity Windowing
HPCSA	Health Professions Council of South Africa
IARC	International Agency for Research on Cancer

IBSN	International Breast Cancer Screening Network
IQF	Image Quality Figure
IQS	Image Quality Score
JAFROC	Jack-knife Free-Response Receiver Operating Characteristic
kVp	Peak kilovoltage
lp/mm	line pairs per millimetre
LSR	Lower Spatial Resolution
LUT	Look-up Tables
mAs	milliamps per second
mGy	milligray
MIW	Manual Intensity Windowing
mm	millimetre
MLO	Medio-Lateral Oblique
MMIW	Mixture Model Intensity Windowing
Mo	Molybdenum
Mp	mega pixel
MUSICA	Multi Scale Image Contrast Amplification
MQSA	Mammography Quality Standards Act
MRI	Magnetic Resonance Imaging
n/a	not applicable
NBins	Number of Bins
PACS	Picture Archiving and Communication System
PET	Positron Emission Tomography
PET-CT	Positron Emission Tomography – Computed Tomography
PLAHE	Power Law Adaptive Histogram Equalisation
PMT	Photomultiplier tube
PPV	Positive Predictive Value
PSP	Photostimulable Phosphor
QC	Quality Control
ROC	Receiver Operating Characteristic
RSNA	Radiology Society of North America
SA	South Africa
SD	Standard Deviation
Se	Selenium

SFM	Screen-Film Mammography
TFT	Thin Film Transistor
TN	True Negative
TP	True Positive
UCSF	University of California at San Francisco
µm	micrometre
US	United States
UK	United Kingdom
USA	United States of America
vs.	versus
W	watt
WL	Window Level
WW	Window Width

CHAPTER 1

ORIENTATION TO THE STUDY

1.1 INTRODUCTION

1.1.1 Incidence of breast malignancies and associated mortality

Breast malignancies are globally the most common cancer among women. In both the developed and developing regions in the world, breast cancer is one of the major causes of death among women (GLOBOCAN IARC, 2008) and accounts for almost one in four (23%) cancer cases diagnosed worldwide (Cancer Research UK, 2010). In the female population in South Africa (all ethnic groups), breast cancer is also the most common malignancy (GLOBOCAN IARC, 2008). Survival rates for breast cancer decrease with later stage of the disease at diagnosis (Cancer research UK, 2009). The American College of Radiology (ACR) indicates that the 5-year survival rate for the different stages of breast cancer at diagnosis decreases from 93% for stage 0, to 15% for stage IV (American Cancer Society, 2010). Thus, the probability of successful patient treatment and long term survival of the patient decreases the further the tumour has progressed. For this reason it is of vital importance to breast cancer patients that the malignancy is detected, diagnosed and treated as early as possible.

1.1.2 Breast imaging

Rapid development of technology over the last two decades has changed the practice of breast imaging dramatically compared to what it was in the early days of mammography. Various technologies are now available for acquiring images and

assisting with the detection of breast cancer e.g. screen film mammography (SFM), digital mammography (DM), computer-aided detection (CAD), ultrasound, magnetic resonance imaging (MRI), tomosynthesis, dual energy subtraction contrast-enhanced digital mammography, positron emission tomography (PET), positron emission tomography-computed tomography (PET-CT) and molecular imaging. However, mammography remains the most common imaging examination for the early detection of breast malignancies. Already in 1998, the International Breast Cancer Screening Network (IBSN) collated international data on the results of population-based breast cancer screening programs. They reported at least 22 countries worldwide where some form of mammography screening program has been established (Shapiro *et al*, 1998).

When scrutinising outcomes of mammography breast screening programs around the globe, some have found that annual breast screening programs reduce breast cancer mortality. Shapiro and co-workers studied the effect of screening on breast cancer mortality at the end of a 10 year follow up period. They found the study group's mortality due to breast cancer to be about 30% below that of the control group (1982). A Swedish study by Tabár and co-workers, compared the deaths from breast cancer in the 20 years before the introduction of screening mammography (1958-77) with that of the 20 years thereafter (1978-97). They reported a substantial (44%) reduction in breast cancer mortality in women aged 40-69 years who received screening (2003). Another Swedish study reported between 40% and 45% reduction in breast cancer mortality among screened women (The Swedish Organized Service Screening Evaluation Group, 2006). On the other hand, two Cochrane reviews on screening for breast cancer with mammography, found no reliable evidence that

screening for breast cancer reduces mortality (Olsen & Gøtzsche, 2001) (Gøtzsche & Nielsen, 2009). This significant debate continues today.

What has been demonstrated however is that the important factors in predicting the prognosis for a woman with breast cancer are the size of a breast cancer and how far it has spread at the time of diagnosis. These factors are assessed during mammography and are thus an important contribution made by the procedure.

The principle goal of mammography is to detect breast cancer as early as possible and to differentiate malignant from benign findings. The American College of Radiology (ACR) has categorised these goals as screening mammography and diagnostic mammography. The ACR definitions define the goal of each as follows (ACR, 2008:2):

- Screening mammography

"Screening mammography is a radiological examination performed to detect unsuspected breast cancer in asymptomatic women."

- Diagnostic mammography

"Diagnostic mammography is a radiographic examination performed to evaluate patients who have signs and/or symptoms of breast disease, imaging findings of concern, or prior imaging findings requiring specific follow-up."

The ACR recommends breast screening programs for asymptomatic women 40 years of age or older on an annual basis as they say screening mammography has been found by some to decrease breast cancer mortality (ACR, 2008:2). However, not all are in agreement on the frequency of screening women. A recent report in the U.S. recommends against routine screening in women aged 40 to 49 years and

that the decision to start biennial screening should be based on individual context with regards to benefits and risks. Furthermore biennial instead of annual mammography screening is recommended for women between the ages of 50 to 74 years (U.S. Preventative Services Task Force, 2009). What has been found however, is that the early detection and treatment of breast cancer is essential in order to reduce cancer mortality (Malmgren *et al*, 2012). And as we have mentioned mammography is well established as a good method of doing just that.

1.1.3 Mammographic features of breast cancer

The most common mammographic features of breast cancer are spiculations associated with a mass and / or pleomorphic calcifications. Other mammographic signs of breast cancer are architectural distortion, asymmetric density, a developing density, a round mass, breast oedema, lymphadenopathy, or a single dilated duct (Ikeda, 2011:29). The ACR suggests a standardised method for breast imaging reporting and has therefore developed a breast imaging lexicon to describe lesion features (2003). A concise paraphrased excerpt from the ACR breast imaging lexicon will now be given:

<u>Mass</u>

A mass is defined as “A space occupying lesion seen in two different projections. If a potential mass is seen in only a single projection it should be called a ‘Density’ until its three-dimensionality is confirmed”. A mass with circumscribed (well-defined) margins usually indicates benign disease. On the other hand, a mass with indistinct (ill defined) or spiculated margins suggests infiltration and therefore malignancy.

<u>Architectural distortion</u>

“The normal architecture is distorted with no definite mass visible. This includes spiculations radiating from a point, and focal retraction or distortion of the edge of the parenchyma. Architectural distortion can also be an associated finding.”

Asymmetric density

“This is a density that cannot be accurately described using the other shapes. It is visible as asymmetry of tissue density with similar shape on two views, but completely lacking borders and the conspicuity of a true mass. It could represent an island of normal breast, but its lack of specific benign characteristics may warrant further evaluation.”

Calcifications

Calcifications are deposits of calcium in breast tissue and because they are often very small, they can easily be missed in dense breast tissue. The ACR’s imaging lexicon categorises calcifications as follows:

- Amorphous or Indistinct calcifications

  “These are often round or “flake” shaped calcifications that are sufficiently small or hazy in appearance so that a more specific morphologically classification cannot be determined.”

- Pleomorphic or Heterogeneous calcifications

  “These are usually more conspicuous than the amorphic forms and are neither typically benign nor typically malignant irregular calcifications with varying sizes and shapes that are usually less than 0.5mm in diameter.”

  - Fine, Linear or Fine, Linear, Branching (Casting) calcifications

  “These are thin, irregular calcifications that appear linear, but are discontinuous and under 0.5mm in width. Their appearance suggests filling of

the lumen of a duct involved irregularly by breast cancer." It is also described as having the appearance of little broken needles with pointed ends (Ikeda, 2011:65).

- Benign calcifications

  "Benign calcifications are usually larger than calcifications associated with malignancy. They are usually coarser, often round with smooth margins and are much more easily seen."

From the above it can be seen that some of the features which define breast abnormalities are very subtle, which may render them difficult for the radiologist to detect. Furthermore, the radiologist must be able to adequately characterise the lesion so as to provide, with some degree of confidence, an accurate diagnosis.

1.1.4 Contrast challenges in mammography

Mammography is a technically challenging area of imaging because of the low subject contrast inherent to the breast. In other words, the soft tissue contrast (or lack thereof) poses a problem. Quite often the radiographic density of normal dense breast tissue is nearly the same as the breast cancers embedded therein (Pisano *et al*, 2001). A very small difference exists in the amount of x-ray attenuation that occurs in a tumour and adjacent normal dense breast parenchyma. As a result, the difference in the number of x-rays absorbed in the recording system is also small, complicating the display of subtle differences. Thus although some information may have been recorded on the film, it may not be displayed optimally to the viewer.

A specific and well known problematic area in mammography is the imaging of the thicker and denser breast as it requires a wide image latitude (Ikeda, 2011:1). The lesions in dense breasts are often less conspicuous which renders the

mammographic interpretation in these cases more difficult (Sickles, 1982) (Rosenberg *et al*, 1998). In order to make the subtle signs of breast cancer visible in the final image, excellent soft tissue contrast to allow visualisation of low contrast features (masses and architectural distortion) is crucial. To achieve maximum contrast, conventional mammography is typically performed at between 24 to 32 kVp for molybdenum targets and 26 to 35 kVp for rhodium or tungsten targets (Ikeda, 2011:2). Such a low kVp will deliver a relatively high mean glandular dose [1 – 2 mGy] per image (Feig & Yaffe, 1996). In conclusion it can thus be argued that imaging and display, which allows the perception of low contrast and sometimes subtle lesions, will determine the success of mammography.

1.2 SCREEN-FILM MAMMOGRAPHY

Screen-film mammography was globally accepted as the primary imaging modality for the early detection of breast cancer and is the standard against which newer imaging modalities are compared. Aspects affecting the image quality with SFM have been researched and optimised over many years (Haus,1990). Research was aimed at x-ray tube technology, screen-film combinations, and processing methods. However, the quality and safety of mammography remained a public and professional concern (Bassett, 1996). To address these issues, the Mammography Quality Standards Act (MQSA) of 1992, developed through the Mammography Accreditation Program of the American College of Radiology, set minimum standards for regulating quality in mammography in the USA (FDA, 2001). Despite all the efforts to optimise SFM, a major draw-back remained. Because the subject contrast of breast tissue is poor and normal dense breast tissue often has quite similar radiographic density to breast cancers, they may remain undetected because of a

lack of contrast (Pisano *et al*, 2001). This draw-back is especially problematic with SFM for the estimated 40% of women with dense breasts (Shtern, 1992). Before the advent of DM, the technique of SFM had reached its ceiling in making subtle contrast differences in breast tissue more visible to the observer.

In conventional SFM, as the name implies, an image is produced by making use of a fluorescent screen and photographic film to produce an image. When exposed to x-rays, the fluorescent screen emits visible light. The light pattern is then recorded as an invisible latent image within the film emulsion. The inherent spatial resolution for a "100-speed" mammography screen-film cassette is in the order of 15 to 20 line pairs per millimetre (lp/mm) (Bushberg *et al*, 2012:259). This is commonly achieved by using single-emulsion film against a single intensifying screen. After x-ray exposure, the x-ray film is chemically processed in a film processor with four main stages in the processing cycle namely: development, fixing, washing and drying. The primary purpose of the development stage is to convert the invisible latent image (produced during x-ray exposure) into visible form while the fixing stage "fixes" the image to render it chemically stable so that it is no longer photosensitive as well as to clarify the image and harden the film emulsion. The washing stage follows to remove chemicals from the emulsion which if not removed, will gradually develop a yellow-brown stain during storage. This is done to ensure a reasonable archival life time for the film. The final stage in the processing, namely drying, is to remove all of the surface water and most of that retained in its emulsion to prevent physical damage to the emulsion (Ball & Price, 1995:119).

1.2.1 Viewing conventional screen-film mammography

Unless the conditions under which SFM images are viewed are satisfactory, the effort and skill in producing the images will be wasted, no matter how good the image quality (Bushberg *et al*, 2012:262).

Typically, SFM images are viewed on an illuminator viewing box using several 15W, as 'white' as possible, fluorescent tubes, as well as a high-intensity spotlight (50W tungsten halogen bulb) to view darker (less dense tissue) areas in the image. The minimum luminance on the surface of a mammography viewing box should be at least 3,000cd/m^2. For mammography, adjustable blinds for masking unused areas of the viewing field are used, so preventing contraction of the pupil in presence of a bright light, thus decreasing the eye's sensitivity to dark areas on the mammogram. It is also common for radiologists to use a magnifying glass should it be deemed necessary in evaluating micro-calcifications. It is further important to have the correct balance between viewer light output and ambient light in the viewing room.

1.2.2 Limitations and advantages of screen-film mammography

There are several limitations of SFM despite the degree of excellence that was achieved through research and technical improvement with SFM. A short description of some of the inherent limitations will now follow.

There is a nonlinear relationship between transmitted x-ray intensity and optical density of the displayed film image in SFM which can be seen in Figure 1.1 (Ball & Price, 1995:59). The result thereof is that very little change of optical density on the processed film is seen with changed x-ray intensities in the toe (the region where none of the exposures received by the film is sufficient to produce any photographic effect) and shoulder (the area of maximum density where an increase in exposure

does not significantly increase optical density) of the curve. The gradient or slope of the characteristic curve of the film determines the display contrast in the final film image. It can thus also be said that radiographic film has a low contrast in the exposure range of dense breast tissue (toe area).

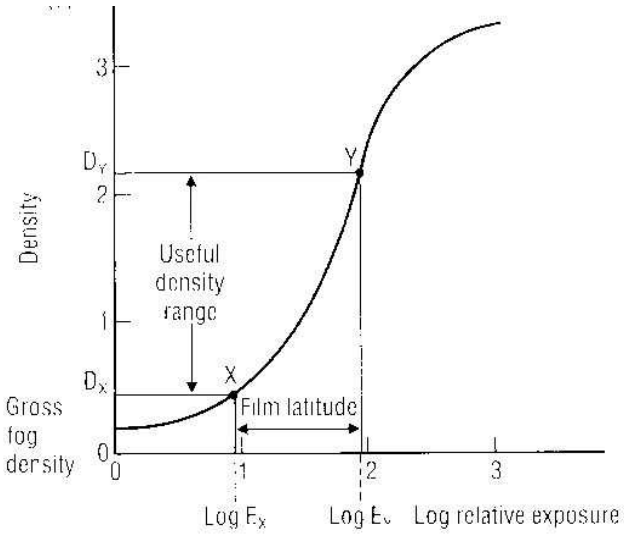


Figure 1.1: Characteristic curve of an x-ray film (Ball & Price, 1995:59)

Screen-film mammography has fixed display characteristics because the image cannot be altered once the film has been processed. All that can be done to improve lesion detection is using a bright light and/or magnifying glass. Should the contrast of the SFM image be regarded as unsatisfactory, the only way to improve the contrast would be to do an additional exposure with the disadvantage that it implies additional radiation to the patient. It is also costly.

Furthermore, the photographic film acts as the medium of image acquisition, storage as well as the display medium in SFM with the disadvantage that these functions cannot be independently optimised.

However, major advantages of SFM compared to DM are its high spatial resolution, familiarity to the radiologist and its relatively inexpensive technology compared to its digital counterpart. It also allows comparison of films imaged over time and in different centres if the standard MQSA is being followed, irrespective of the x-ray unit manufacturer.

1.3 DIGITAL MAMMOGRAPHY

Digital imaging in the medical environment was already introduced in the late 1960s. For mammography however, the mammographic establishment hesitated to accept DM partially because the diagnostic accuracy that had been achieved with SFM had to be matched or improved (Tucker & Ng, 2001:295). Distinct from SFM, the digital acquisition technique allows separation of the detector and display media which allows the possibility to maximise the performance of each independently. In general, digital imaging has two fundamental advantages namely: enhancement of pictorial information for viewing and interpretation by readers; and image data processing for storage, transmission and representation.

Soft-copy viewing of a digital image provides the ability to access and manipulate contrast and brightness in the image using image processing. A much wider dynamic range of up to 4096 gray scale levels is available with digital mammography imaging and the entire range can be utilised to display all areas in the image at visible contrast differences (D'Orsi & Newell, 2007). The small differences in contrast between dense breast tissue and low contrast features such as masses and architectural distortion can thus be made visible to the observer. This increased contrast can enhance cancer detection especially in dense breast parenchyma. In addition, processing options can be applied to the raw data to view all areas in the

image with less user input compared to viewing an unprocessed image. Furthermore, correction for over- an underexposure of the image is much more flexible with DM and can potentially reduce or eliminate the number of re-exposures.

However, a disadvantage of DM is the lower spatial resolution (LSR) compared to standard SFM. Even though the contrast in the image can be manipulated, there was concern that small lesions may not be detected with DM because of the LSR (Pisano, Yaffe & Kuzmiak, 2004:2). Optimal viewing of the digital image is thus important because the LSR can potentially lead to micro calcifications being undetected. All the available information in the image should thus be viewed at a suitable contrast and at full spatial resolution with soft-copy display systems (Pisano, Yaffe & Kuzmiak, 2004:2). To do this, window width and window level adjustments as well as zooming may be necessary to obtain the desired contrast at full spatial resolution. Initially this led to the opinion that soft-copy viewing is not user-friendly enough for routine use in a screening setting with a high work flow (Skaane, Young & Skjennald, 2003). With the introduction of DM, there was also concern that smaller pixel sizes may improve calcification detection even to the extent of causing the identification of artefacts as calcifications and thereby cause more false-positive mammograms (Pisano *et al*, 2001). Because of the different strong points of SFM (increased spatial resolution) and DM (increased contrast resolution), it was uncertain which modality would do better at detecting different types of cancers (Lewin *et al*, 2001). Digital mammography was expected to be superior in detecting densities and masses in dense tissue while SFM was expected to be better in detecting calcifications. However, early evidence was found that despite the lower resolution, DM provides improved detectability of even submillimeter disks of moderate contrast (Nishikawa *et al*, 1987). In another study in the Netherlands, in

which spatial resolution in DM was studied, it was found that a relatively LSR of 0.1mm/pixel does not prohibit high-quality diagnostic performance (Karssemeijer, Frieling & Hendriks, 1993). Evidence was thus found that although DM has a lower spatial resolution compared to SFM, it does not necessarily have a negative impact on diagnostic performance.

It was hypothesized that the ability of digital systems to display subtle differences in the number of photons absorbed in adjacent areas of the breast (improved contrast resolution) might give way to improved lesion detectability, even with reduced spatial resolution. It was presumed that because many cancers are in dense glandular tissue and cannot be detected by SFM, the improved contrast resolution of DM would render it possible to demonstrate some of these cancers. Given the limitations of DM (lower spatial resolution) and SFM (lower contrast resolution), it was expected that each modality would excel at detecting different types of malignant lesion. Because both are important in depicting the features of breast cancer, the trade-off between spatial resolution and contrast resolution characteristics could not be predicted. It was expected that DM would perform better in finding densities and masses in dense fibro-glandular tissue while on the other hand, SFM would perform better in finding calcifications (Lewin *et al*, 2001). Should soft-copy display be used for viewing, a reduced recall rate for DM compared to SFM is a possibility. This is because immediate on-line manipulation of the image is possible for assessing areas of concern that would ordinarily require another patient visit (short-term follow-up) and additional mammographic views. Also, as a result of the lower spatial resolution of DM, fewer benign and malignant findings might be detected. This effect would improve specificity, as most mammographic findings in a screening population are benign (Pisano, Yaffe & Kuzmiak, 2004:29). Because of its

superior contrast properties, it was thus expected that DM would identify at least some cancers in dense lesions.

1.4 BACKGROUND ON THE SETTING FOR THE STUDY

In South Africa (SA), a national breast screening program is not offered. At Universitas Academic Hospital in Bloemfontein, mammography is performed for two different reasons. The one is for "selective" screening purposes in which patients are referred by their physicians for their annual mammogram (selective screening). These mammograms are performed on asymptomatic women to check for breast cancer in the absence of signs or symptoms. The other is for diagnostic purposes on patients referred from the breast-clinic. These mammograms are performed on patients with symptoms of disease such as a lump, or significantly increased risk of the disease such as a strong family history.

In SA all qualified radiologists are allowed to report mammograms and no sub-speciality registration for radiologists (e.g. Mammography) exists with the Health Professions Council of SA (HPCSA, 2001). In the Radiology department at the Universitas Academic Hospital in Bloemfontein, where the study was conducted, mammography reporting is thus part of the job description of all qualified radiologists. A senior specialist is available in a consulting capacity in the department should a junior radiologist or registrar want to seek advice on a mammogram.

1.4.1 Transition from screen-film-mammography to digital mammography at Universitas Academic Hospital

Screen-film-mammography has been performed at Universitas Academic Hospital since 1994. Up until August 2007, when SFM was replaced by an Agfa Computed Radiography (CR) system, all registrars were trained in reporting conventional SFM

on a conventional mammographic light box. In June 2008, a Philips Picture Archiving and Communication System (PACS) was installed and since then, soft-copy mammography viewing and reporting were performed. No standard method of approach was given in the department to radiologists transitioning from SFM to DM and no background training or education was planned for DM.

1.4.2 Standardising reporting

Before the commencement of this study, no standard interpretation form or specific terminology was prescribed for mammography reporting, and no departmental protocol dictated the format of a mammogram report. Radiologists were free to use their own style in reporting. In contrast to this, a standard protocol for reporting and communicating the results to referring physicians is recommended in the literature (ACR, 2003). A need for standardising the report in the department was thus identified before the study and implemented at the time of commencement of the study. The intension of such standardisation would be to standardise the terminology in mammography reporting, the assessment of the findings, and the recommended action to be taken.

1.5 THE PROBLEM WITH CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY

Whenever new digital equipment is installed by a vendor, the vendor would usually informally train the users in the use of their equipment and the users are introduced to the different tools for image viewing available on the workstation. Image processing is usually a matter of using the option and default setting that the vendor offers or recommends. When switching over from SFM to soft-copy viewing it entails much more than merely switching from a viewing box to a computer monitor.

Radiologists also acknowledge that the appearance of the image is different for conventional SFM and soft-copy display. In order to view all parts of the image at full spatial resolution requires an interactive function called: “pan” and “zoom”. Other than with SFM, the radiologists now also need to adjust display parameters for soft-copy viewing in order to display the full range of densities in the breast at optimal contrast – something that they have not been trained to do before. Without knowledge and experience in soft-copy viewing, many of the image processing and display options might not be used optimally by the reporting radiologist and diagnostic accuracy may be sacrificed.

The need for training when moving from film to filmless radiology has been supported by previous studies (Jones, 1999). The ACR states in their practice guideline for image quality in DM, that personnel must have at least 8 hours of training in DM before beginning to use the modality (ACR, 2007) but in SA, no prerequisites are set for radiologists when switching from SFM to DM (HPCSA, 2001).

The Radiology Society of North America (RSNA) also acknowledged the need for training radiologists in soft-copy reading for mammography. At the annual conference of the RSNA in 2005, a self-assessment workshop was conducted for radiologists to gain hands-on experience with the features, functions, and performance of dedicated mammography workstations. It was envisaged as a learning opportunity for radiologists to improve their performance in mammography reading through interactive training sessions using dedicated soft-copy reading workstations. The radiologists also had the opportunity to assess their skills and to discuss false-negative and false-positive results with experts in the field (RSNA, 2005).

Thus, some of the most important challenges in soft-copy viewing are to deal with the limited spatial resolution and the effect of image processing and display options on the overall image quality as well as on breast cancer detection in specific masses and calcifications. The effects of processing and display options have not been fully investigated (ACR, 2007) and very few radiologists are confident when using them. It is therefore reasonable to argue that when changing from conventional SFM to soft-copy viewing, the viewing protocol for the specific clinical setting should be optimised. Furthermore, training in soft-copy viewing (in specific processing and display options) is important as it may affect diagnostic accuracy. The importance of training in soft-copy viewing in mammography is clearly acknowledged in the literature; however, to the best of our knowledge no studies have reported the effect of training for radiologists in soft-copy viewing on diagnostic accuracy. The apparent lack of research on the effect of training of radiologists in soft-copy viewing of a mammogram on diagnostic accuracy was noted and motivated this research study.

1.6 AIM OF THE STUDY

The aim of the study was to improve diagnostic accuracy of soft-copy mammography reading through the development of a viewing protocol. The effect of the mammographic viewing protocol developed through participative learning was evaluated by comparing the diagnostic accuracy before and after the development process.

1.7 STRUCTURE OF THE THESIS

The thesis is divided into seven chapters. An outline of the structure of the study follows.

Chapter 1 outlines the motivation for the study by giving an overview of the problem to be addressed. The differences between SFM and DM are briefly discussed as well as the need for training in using the new modality. In addition the specific aims of this study have been outlined as an intervention to address the problem.

The second chapter is devoted to DM. The aim of a literature review should be to seek to answer the research question by searching for and analysing relevant literature using a systematic approach (Aveyard, 2010:6). A comprehensive and systematic approach will be persued by the researcher to retrieve and review the available literature on the digital technology in mammography, in specific, image processing and interactive soft-copy viewing, to give an overall picture of what is known about the topic. Interpretation of the literature that addressed the topic will be undertaken to draw together all the research and other information on the topic thus giving a clear picture of evidence for the need to answer the research question. The literature on what others have done will be evaluated, organised and synthesised. Sub-areas within the main problem will be identified to peruse in the literature review in order to better understand the main problem and to better answer the research question (Leedy & Ormrod, 2001:82).

In Chapter 3 the training requirements for radiologists changing from SFM to DM are perused. The South African perspective and an international perspective on the issue are given.

The methods and techniques that were applied for the evaluation of the effect of different processing options on image quality of a phantom image in this study are discussed in Chapter 4. The results are presented, discussed and interpreted. A

recommendation is made for processing options to be evaluated on clinical images in Chapter 5.

In Chapter 5 the training of the radiologists is described. Also the development of the soft-copy viewing protocol (through participative learning of the radiologists) is discussed. The methods and techniques applied for the assessment of image processing options on image quality of clinical images are described. The results from the participative training are presented, discussed and interpreted. Based on the results, a recommendation is made for the soft-copy viewing protocol.

The methods and techniques that were applied for evaluation of the effect of the viewing protocol (developed through training) on the diagnostic accuracy of soft-copy viewing are discussed in Chapter 6. The results obtained with the Breast-Imaging-Reporting-Data-System (BI-RADS) of the American College of Radiology (ACR) for both the initial and follow-up surveys are presented and discussed. The possible factors responsible for the differences in results obtained in the initial and follow-up surveys are presented.

The final chapter consists of the conclusions that can be drawn from the study in addition to recommendations for further research in the field of soft-copy viewing for mammography.

The thesis is concluded with a short summary.

CHAPTER 2

DIGITAL MAMMOGRAPHY

2.1 CONTEXT OF DIGITAL MAMMOGRAPHY

At a workshop entitled “Breast Imaging: State-of-the-Art and Technologies of the Future” held by the US National Cancer Institute in 1991, DM was identified as the developing technology with the most potential impact on the management of breast cancer (Shtern, 1992). In the 20 years before DM, significant advances had occurred in SFM, however, inherent limitations to further technical improvements exist (Feig & Yaffe, 1996). Since DM units became commercially available, the technology has been implemented in many clinical settings around the world. Already in May 2010, 65.4% of mammography units in the USA were digital mammography systems (Ikeda, 2011:15).

Two approaches can be employed for the generation of digital mammographic images: secondary digitisation and acquisition of primary digital images. With secondary digitisation, conventional film images are digitised whereby the quality of the images will be limited by the quality of the film (Shtern, 1992). Primary digitisation can be divided into computed radiography (CR) and direct radiography (DR) (Bushberg *et al*, 2012:214). Because of the technical difficulties originally associated with the manufacture of digital detector arrays large enough to image the entire breast, the first DM detectors were able to only image regionally. When technology advanced the first detectors able to image the entire breast were called Full Field Digital Mammography (FFDM) detectors. This term is no longer used as it

is now generally possible to create detectors large enough to cover the entire breast and so the term DM is widely understood to mean imaging of the entire breast using a digital detector.

Direct radiography (DR) systems convert x-rays into electrical charges by means of a direct readout process and can be further divided into direct and indirect conversion groups depending on the type of x-ray conversion used (Körner *et al*, 2007). On the other hand CR systems use a photostimulable phosphor (PSP) detector image plate with a separate image readout process. However, the acquired image is equivalent to that with DR systems, as the detector response is linear in all cases.

2.1.1 Image acquisition in DM

2.1.1.1 Indirect conversion

The detector technology used for the indirect conversion is a thin film transistor (TFT) flat panel array receptor with approximately 100µm sampling pitch. X-rays are absorbed in the caesium iodide (CsI) phosphor and converted into light which is emitted onto a photodiode in each detector element. The photodiode generates a charge and stores the charge on the storage capacitor in that detector element (Bushberg *et al*, 2012:265).

2.1.1.2 Direct conversion

This technology is based on a direct x-ray conversion TFT detector with approximately 70µm sampling pitch. A large voltage is placed across a semiconductor selenium (Se) layer and the charge is directly generated by x-rays within the photoconductor without intermediate signals. As the Se absorbs the incident x-rays, it produces electron-hole pairs. The applied voltage causes the

electrons to travel to the collection electrode where they are captured by the local storage capacitor (Bushberg *et al*, 2012:265).

2.1.1.3 Cassette-based CR photostimulable storage phosphor (PSP) imaging plate

The imaging plates used in CR have a detective layer of PSP crystals, and this functions to replace the conventional films in cassettes. When the PSP imaging plate is exposed to x-rays, x-ray energy is absorbed and temporarily stored by these crystals bringing the electrons to higher energy levels. The exposed imaging plate is subsequently placed in a reader system and scanned by a laser beam with an effective spot size of 50 microns. The stored excited electrons are freed from the traps when they receive energy from the laser beam (Körner *et al*, 2007). When these electrons fall to a lower energy state they emit light – a process called "stimulated luminescence". The light reaches a photomultiplier tube (PMT) which produces an electrical current proportional to the light intensity. The digitised signal from the PMT provides numerical pixel values for the digital image (Bushberg *et al*, 2012:214). With the CR technique, the latent x-ray image is thus obtained in the same manner as in SFM, only the film cassette is replaced by a digital detector. Figure 2.1 illustrates a CR system based on storage-phosphor image plates and shows the two stages of image acquisition namely: the storage of the x-ray energy and the readout process.

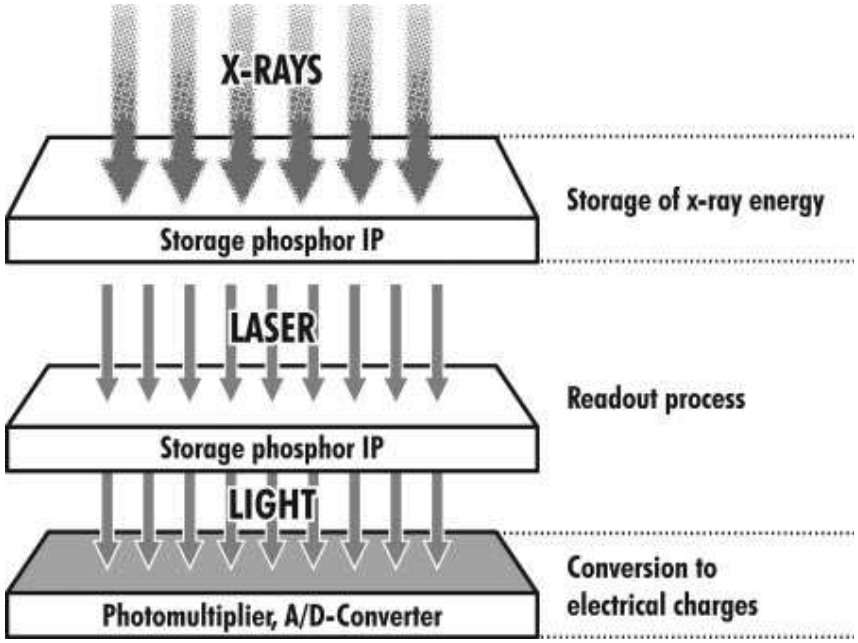


Figure 2.1: Image acquisition with a CR system based on storage-phosphor image plates (Körner *et al*, 2007)

2.1.2 The digital image

A digital image can be described as a two-dimensional grid of square picture elements (pixels) digitally stored in the computer as the image matrix. A pixel is the smallest element of the digital image. The term matrix size refers to the number of pixels in the matrix (Feig & Yaffe, 1996). A larger matrix provides for a less "blocky" or "pixelated" image with a higher resolution (Feig & Yaffe, 1996). The number of pixels in an image defines and limits the maximum spatial resolution. The field of view (FOV) imaged is the area of patient, therefore volume of tissue (in this case of the breast), projected onto the image. The information contained in that volume of tissue is thus summarised by the information stored in the image matrix. This information is then stored in the computer memory and can be displayed with different contrast levels independent of the detector properties (Feig & Yaffe, 1996).

The computers used to process and store images make use of binary numbers, 0 or 1 and because digits in a binary system express multiples of the base 2, each successive digit value increases by a factor of 2, eg, 1, 2, 4, 8, 16 etc (Feig & Yaffe, 1996). In mammography the digital image is represented as a gray scale image on a digital display monitor whereby each pixel is represented as a shade of grey determined by the numerical value of that pixel.

The term bit depth of a digital image is an indication of the number of grey-shades, and thus the number of different intensities of x-rays transmitted through the patient it can depict and is usually expressed as a power of 2 (Feig & Yaffe, 1996). Often groups of 8 bits (known as a byte) are used and because the total value of a binary number equals the sum of values of each bit, a byte thus has a minimum value of 0 and a maximum value of 255. In this range each pixel is thus represented by eight bits, or exactly one byte (Feig & Yaffe, 1996). On the other hand, 2^{10} is referred to as 10 bits of data and can display 1 023 shades of gray and 2^{14} or 14 bits of data, can display 16383 shades of gray (Pisano, Yaffe & Kuzmiak, 2004:9). This thus gives better intensity resolution and thus the ability to distinguish between structures with very little difference in attenuation of the x-ray beam. More shades of grey can thus be displayed if a greater bit depth is used.

2.1.3 Soft-copy display

In DM, the digital data can be displayed in either hard-copy (printed film) or soft-copy (monitor) format (Feig & Yaffe, 1996). One of the main benefits of DM, namely the flexibility of contrast display (independent of the detector properties) according to the preference of the viewer, can only reach its full potential through soft-copy display (Pisano, Yaffe & Kuzmiak, 2004:5). Because the focus in this study is on soft-copy

viewing, only this format of image display will be further discussed. Because the digital display system has a much more limited dynamic range compared to that of digital detectors, interactive image display plays an important role. With soft-copy viewing the viewer can use different contrast levels. This is made possible by adjusting brightness (window-level (WL)) and contrast (window-width (WW)). Look-up tables (LUTs) can be used to display the image independent of the initial x-ray subject contrast values. Differential processing options are also available for e.g. to enhance low contrast structures such as masses and architectural distortion (especially in dense breast tissue), in order to make them more visible to the observer. These processing options will be described in greater detail in section 2.3.1.

2.1.4 Advantages and limitations of digital mammography

With DM many of the limitations of SFM can be effectively overcome. With the digital technique, the three functions of image acquisition and image display are separated and can therefore potentially be optimised independently.

In contrast to the nonlinear response of film, digital detectors have a highly linear response to x-ray input (radiation intensity) which does not significantly change at low or high intensities (Bushberg *et al*, 2012:264) (Pisano, Yaffe & Kuzmiak, 2004:9). Therefore, the dynamic range of digital detectors is much wider than that of conventional film. As a result, they show similar contrast over the entire dynamic range of signals whereas conventional film images suffer contrast loss in underexposed or over-exposed areas of the mammogram. The advantage of the wider dynamic range of digital detectors in clinical practice is that it eliminates the

risk associated with a second exposure to improve image contrast in low and high density areas of the breast (Körner *et al*, 2007).

Because soft-copy viewing of the digital image is possible, it is possible for the viewer to manipulate contrast and brightness in the image according to preference. A much wider dynamic range of up to 4096 gray scale levels is available with digital mammography imaging and the entire range can be utilised to display all areas in the image at visible contrast differences (D'Orsi & Newell, 2007). The small differences in contrast between dense breast tissue and low contrast features such as masses and architectural distortion can thus be made visible to the viewer.

In addition, all digital systems use processing algorithms to perform density equalisation to minimise signal differences caused by the structural anatomy of the breast. Image processing is also used to achieve better visualisation of normal and abnormal tissues.

Furthermore, CAD software can be utilised to analyse data from mammogram images to identify patterns associated with underlying breast cancers (Brancato *et al*, 2008). This technology can thus assist the radiologist in the detection of lesions and thus in interpreting the images.

There are however a few limitations of DM. A major limiting factor is the LSR of DM compared to SFM. Spatial resolution gives an indication of the smallest visible detail in an image and can be quantified in terms of line pairs per unit distance, or dots (pixels) per unit distance (Gonzalez & Woods, 2008:59). The line-pair resolution of screen-film image receptors used for mammography ranges from 15 to 20 lp/mm whereas that of DM systems have spatial resolutions ranging from 5 lp/mm for 100µm pixels, to 10 lp/mm for 50µm pixels (Ikeda, 2011:15). The size of the pixels

(determined by the detector element size) determines the spatial resolution of a digital image. Thus, to equal the resolution of SFM, the digital detector will have to have approximately 32 pixels per mm (30µm pixels). This would result in mammographic images (24 x 30cm) of 120 Mbytes if 2 bytes are stored per pixel. Such small pixels would thus produce storage issues (due to the larger data sets) and it would make the digital technology more expensive (Ikeda, 2011:9). The relatively limited number of pixels commonly used in DM detectors thus limits the spatial resolution of DM. As technology changes this will change, and then the question would arise as to what is required, rather than what can be achieved.

A number of studies compared calcification detection for SFM and DM and found no significant difference (De Maeseneer *et al*, 1992) (Karssemeijer, Frieling & Hendriks, 1993). Cowen and co-workers (1997) found the same minimum detectable size of simulated microcalcifications by the viewers for both SFM and DM (approximately 130µm). A more recent study by Del Turco and co-workers (2007) however found a statistically significant higher detection rate for clustered microcalcifications on DM compared to SFM ($p = 0.007$).

In summary it can thus be said that the lower limiting spatial resolution of digital mammography images compared to conventional film images is compensated for by the increased contrast resolution of digital systems. It allows visibility of the currently understood to be minimum size of significant calcifications even though DM has lower spatial resolution.

2.2 CLINICAL TRIALS FOR COMPARISON OF SCREEN-FILM MAMMOGRAPHY AND DIGITAL MAMMOGRAPHY

Cancer detection with DM was compared to that in SFM in a number of studies. In the USA, the initial studies were initiated by vendors who sought market clearance of their DM systems from the Food and Drug Administration (FDA) (Hendrick *et al*, 2001) (Cole *et al*, 2001). FDA's prerequisites for approval were that, DM should be equivalent to SFM. They defined equivalence as follows: should the SFM be positive, the probability of a positive digital mammogram should be > 0.9. Furthermore, should the SFM be negative, the probability of a negative digital mammogram should be > 0.95. The downfall of the studies was that the presence or absence of malignancy in the patient was based on the SFM interpretations and the DM interpretation had to agree with the former. Histological confirmation of the findings was not obtained. Intra- and inter-reader variability prevented achieving the specified level of agreement for DM with SFM. That level of agreement was not even achievable when SFM was compared to itself. The FDA then revised the requirements of their protocol. Biopsy-proven lesions had to be included in the trials and sensitivity and specificity had to be measured (Pisano, Yaffe & Kuzmiak, 2004:27).

The first completed trial was by Hendrick and co-workers (2000) who compared the GE Senographe 2000D (hardcopy display) with SFM in an enriched diagnostic cohort. FDA approval was granted in January 2000 (Pisano, Yaffe & Kuzmiak, 2004:27) because the results of the study showed no statistically significant difference in diagnostic accuracy between the two modalities. Specificity for DM was higher (55%) compared to that of SFM (53%) while on the other hand the sensitivity for DM was lower (68%) compared to SFM (70%). However it was found with

statistical significance (p = 0.0245) that DM does not have lower sensitivity than SFM. Cole and co-workers (2001) who were responsible for the study that obtained FDA approval for the Fischer SenoScan also reported no statistically significant difference in diagnostic accuracy between SFM and the Fischer SenoScan in a diagnostic mammography population. The average sensitivity for SFM was 74% compared to 66% for DM and the specificity 67% for DM compared to 60% for SFM. A receiver operating characteristic (ROC) analysis was performed which showed a difference of only -0.05 area under the curve (AUC) between SFM and DM (95% confidence interval (CI); -0.101 to 0.002). However, in a later publication on the study by Cole *et al.* (2004), they argued that it is possible that a study with more power might show that SFM is superior to the Fischer SenoScan, because most of the CI is negative in the study.

Since DM was approved by the FDA, many studies have compared the performance of DM and SFM (Lewin *et al*, 2001) (Lewin *et al*, 2002) (Skaane *et al*, 2003) (Yamada *et al*, 2004) (Skaane & Skjennald, 2004) (Pisano *et al*, 2005) (Del Turco *et al*, 2007) (Vigeland *et al*, 2008). Vinnecombe and co-workers (2009) found several differences in study design between the studies which complicate comparisons between the studies. These include: type of population studied - screening population or a diagnostic population, number of subjects included in a study, retrospective or prospective studies, entry bias (should entrance to the diagnostic cohort be predicated only on an abnormal SFM), whether a paired (where the same group of women had a mammogram with both modalities), randomised control, or cohort design was used, multi-centre studies, multi-vendor studies, soft-copy display or hard-copy laser printed films used for reporting for DM, age group of patients included in the study, radiologists used as readers in the studies, double reading

versus single reading of the modalities, method use for arbitration on non-agreement cases, number of radiologists acting as viewers in the study and rating scale for patient outcome - BIRADS or other.

However a meta-analysis of data from eight studies comparing SFM and DM, found a slightly higher detection rate for FFDM, particularly in patients 60 years of age or younger (pooled DM – SFM difference p = 0.1) [95% CI: 0.04, 0.18] (Vinnecombe *et al*, 2009). However, they found no clear differences between the modalities in terms of recall rates or positive predictive values (PPVs).

A more recent UK study compared the performance of DM (hard-copy reading) to SFM in a routine screening population (Vinnecombe *et al*, 2009). The performance of the viewers with the two modalities was compared for a total of 40,198 screening examinations. They found no evidence of any difference in detection rates between the two screening modalities: DM 0.68 [95% CI: 0.47, 0.89] versus SFM 0.72 [95% CI: 0.58, 0.85] respectively (p = 0.74). Their results support those found in the meta-analysis. Also, no significant difference was found in recall rate between the two modalities: DM 3.2% [95% CI: 2.8, 3.6] versus SFM 3.4% [95% CI: 3.1, 3.6] (p = 0.44). The results of this study and that of the meta-analysis support previous findings that suggest that the detection rate of DM is at least as high as that for SFM.

2.3 DIGITAL IMAGE PROCESSING

The goal of image processing is to accentuate certain image features and therefore enhancement techniques are problem orientated (Gonzales & Woods, 2008:25). The inherent information content in the data is however not increased by the enhancement process itself but simply emphasises certain specified image characteristics. However, image processing can be used to correct for differences

as a result of tissue thickness, smooth noise, equalise systematic variations in intensity, and to enhance local contrast and sharpness of small detail such as microcalcifications. Image processing is also beneficial because of its versatility, repeatability and the precision of the preservation of original data (Rao, 2006).

Research in medical image processing has focussed on the development of processing algorithms that can optimise image quality with as little interactive viewing by the viewer as possible (Schaetzing, 2007:31). The unprocessed digital image does not allow easy interpretation by the viewer as such, unless the viewer uses manual intensity windowing (window and level parameters) to adjust and maximise contrast for structure visibility. It has been shown that the success of manual intensity windowing is operator dependant and it can be time consuming. It is possible that an inexperienced viewer can select windows that might obscure lesions that might have been visible with other windows (Pisano *et al*, 2000[b]). The solution to the problem is to make soft-copy viewing more user friendly and less time consuming for the viewer by applying automated image processing algorithms.

Image processing in mammography is used specifically to improve the contrast of lesions so that the viewer can better distinguish them from normal breast tissue (Shtern, 1992). It had been previously reported that at least 10% of palpable breast cancers are not visible with standard SFM (Homer, 1991:4-5). To a certain extent, sensitivity and specificity for a specific reader for mammography will not only be influenced by the interpretation skills of the reader, but also by the visibility of lesions. To be detected on a mammogram, the lesion must be distinguishable from normal breast tissue which can be achieved through image processing. Some authors are of the opinion that the selected image processing for digital images, may meaningfully affect the outcome of clinical trials (Pisano, Yaffe & Kuzmiak,

2004:p29). This is because it is believed that image processing may assist in improving the detection of masses and microcalcifications which in turn may reduce the number of false positives by increasing the visualisation of normal breast tissue.

Image processing algorithms can also optimise contrast and brightness in different regions of the breast in one image. It is possible to visualise the nipple, the skin surface of the breast, and the thoracic wall in one image. This is because image processing algorithms can amplify the fine differences in image contrast between specific structures (Pisano *et al*, 2000[b]).

Image processing has taken major steps toward better visualisation of normal and abnormal tissues, but unfortunately, the optimum processing technique is not yet certain (Nishikawa *et al*, 2009). Some studies even indicated the possibility that different processing algorithms should be used to enhance microcalcifications and masses (Pisano *et al*, 2000[a]) (Zanca *et al*, 2009) (Sivaramakrishna *et al*, 2000). Some argued that with optimisation of image processing, soft-copy viewing could be superior to hard-copy (Nishikawa *et al*, 2009). However, radiologists found it more difficult to compare initial and subsequent mammograms if one was SFM and the other DM in which image processing was applied, because they do not look the same (Hemminger, 2003).

Image processing algorithms are developed by each manufacturer to be used with its acquisition system. Also, independent investigators have developed algorithms for use in DM. Because of competition between vendors it is unfortunately not always possible to obtain details about a specific processing algorithm (Pisano, Yaffe & Kuzmiak, 2004).

Some authors argued that to improve confidence and acceptance of soft-copy reading for inexperienced viewers, specific processing presets should be available on a workstation. In a previous study, processing presets on the workstation were especially preferred by inexperienced radiology residents and referring clinicians (Andriole, Gould & Webb, 1999). The potential advantages of processing presets would include the potential to allow faster reading in soft-copy viewing, improve diagnostic efficacy, standardise display, and facilitate image comparison. However, such pre-sets are not commonly supplied by the vendors.

2.3.1 Image processing algorithms

Apart from manufacturers of digital units that have developed image processing algorithms for use with their own acquisition system, independent investigators have also developed algorithms for use in DM (Pisano *et al*, 2000[a]). This means that not all image enhancement techniques are offered on all digital equipment, and that different manufacturers have different algorithms. The image processing algorithms discussed here will focus on those available for use in the department where the study was conducted.

2.3.1.1 Histogram processing

The histogram represents the relative frequency of occurrence of signal intensities in an image. By using the histogram to manipulate gray levels the display characteristics can be modified. Histogram processing can be done in different ways and will be described briefly.

2.3.1.1.1 Histogram equalisation

With global histogram processing methods the pixels are modified by a transformation function based on the intensity distribution of an entire image (Gonzalez & Woods, 2008:139). With histogram equalisation the image is manipulated to use more of the available gray level range by equalising or flattening its gray-level distribution (Schaetzing, 2007:6). This is done by using a selected subrange of the image intensity values to be displayed with the full available gray level range (Pisano *et al*, 2000[a]). Equalisation thus allows the user to enhance minor intensity variations in an apparently uniform image and thus emphasise low contrast features. However, the global approach is not suitable to enhance details over small areas in an image because the overall enhancement may not have the desired effect on local enhancement (Gonzalez & Woods, 2008:139).

2.3.1.1.2 Neighbourhood processing

This technique is formulated in the context of so-called mask operations. The purpose of a mask operation is to adjust the grey value assigned to a pixel according to a function of both its own pixel intensity and pixel intensities of its neighbours. To achieve local enhancement, a neighbourhood is defined and the centre of the processing region is moved from pixel to pixel. The histogram is then computed from the pixels included in the neighbourhood, and the centre of the neighbourhood region is repeatedly moved to a neighbouring pixel until new values for the entire image have been computed (Gonzalez & Woods, 2008:139). Neighbourhood processing has advantages over computing the histogram of all pixels and various manufacturers have used this basic principle and modified it for their own equipment.

2.3.1.1.3 Contrast Limited Adaptive Histogram Equalisation (CLAHE)

CLAHE is an acronym for Contrast Limited Adaptive Histogram Equalisation and was developed for medical imaging with the aim to enhance low-contrast images (UCSF, 2009). Contrast Limited Adaptive Histogram Equalisation is a specific case of Adaptive Histogram Equalisation (AHE) (Pisano, Yaffe & Kuzmiak, 2004:50). The difference being that with CLAHE the histogram equalisation is performed on a parameterised region-by-region basis to prevent any boundary edges (Mathworks, 2011). CLAHE thus overcame the drawback of the general histogram equalisation method where the computation is performed across the entire image. CLAHE partitions the image into neighbourhoods or contextual regions (called tiles) and calculates a local histogram for each one. Instead of operating on the entire image, each region's contrast is enhanced. Instead of the often narrow range of intensity values of a central pixel and its closest neighbours, the local histogram is equalised to the full range of pixel values available in the newly stored histogram. The full grey spectrum is thus used to display all regions of the image. By applying histogram equalisation to each tile individually, the distribution of grey scale values used is evened out and thus low contrast features of the image are made more visible by using the full gray scale spectrum to display the image. The neighbouring tiles are then combined using bilinear interpolation in order to eliminate artificially induced boundaries (Mathworks, 2011).

With CLAHE a maximum level is set for the contrast that will be displayed in each local histogram (Pisano, Yaffe & Kuzmiak, 2004:50). In order to avoid amplifying the noise which might be present in the image, the contrast (especially in homogeneous areas) can be limited (Mathworks, 2011). These parameter settings (e.g. clip limit

and region size) must be decided on in advance of their application to the images (Pisano, Yaffe & Kuzmiak, 2004:50).

CLAHE is controlled by a number of variable parameters and those parameters available in the department where the research study was conducted will now be described in turn:

Contextual region dimensions ('NumTiles')

The contextual region dimensions specifies the number of rectangular contextual regions (tiles) into which the image is divided. With the CLAHE algorithm, the contrast transform function is calculated for each of these regions individually (Mathworks, 2011). Mathworks describe the value of contextual region as: "A two-element vector of positive integers specifies the number of tiles by row and column, [M N]. Both M and N must be at least 2. The total number of tiles is equal to M*N".

The optimum number of tiles depends on the type of the input image, and is best determined through experimentation. In general, the smaller the block size (larger value for M and N), the tighter the control of the local histogram date, but this leads to local 'noise' (Mathworks, 2011).

Number of bins ('NBins')

'NBins' sets the number of bins for the histogram used in building a contrast enhancing transformation (Mathworks, 2011). Mathworks describe the value of this parameter as: "Positive integer scalar specifying the number of bins for the histogram used in building a contrast enhancing transformation." This parameter thus indicates the number of gray scale levels used to re-bin the histogram data.

Higher values result in greater dynamic range and therefore higher precision of remapping pixel values although at the cost of slower processing.

'ClipLimit'

'ClipLimit' is used to limit contrast enhancement to prevent over-saturation specifically in homogeneous areas of the image. Homogeneous areas are characterised by a high peak in the histogram of the particular image tile due to many pixels falling inside the same gray level range. More contrast can be obtained with higher numbers for 'ClipLimit'. Without the 'ClipLimit', the adaptive histogram equalisation technique could produce results that, in some cases, are worse than the original image. Mathworks (2011) describe the value of 'ClipLimit' as: "Real scalar in the range [0 1] that specifies a contrast enhancement limit" (Mathworks, 2011).

'Map level'

This parameter is an extension of the generic CLAHE algorithm. Selection of '0' for this parameter is the canonical CLAHE algorithm. Selection of '1' or '2' enables the system to generate the required LUT's incurring a much lower computational load with effectively identical results.

2.3.1.2 Multi-Scale Image Contrast Amplification (MUSICA)

MUSICA^2 is the latest processing algorithm trademark of Agfa and is available on the recent Agfa CR systems. The aim of MUSICA^2 is to enhance the visibility of subtle contrast structures that can easily be missed in clinical practice (Pisano, Yaffe & Kuzmiak, 2004:50). The MUSICA^2 processing algorithm focuses on the problem of low contrast enhancement based on multi-resolution representation of the original image. It is a method of generating a contrast enhanced version of a grey value

image by applying contrast amplification to image detail at different scales by a series of gradient functions (US Patent 7155044, 2006). Because structures with high contrast will remain clearly visible even if their contrast is reduced somewhat, MUSICA^2 enhances only subtle contrast at the expense of the high contrast objects.

The contrast equalisation goal with MUSICA^2 is thus to boost subtle contrast relative to their original levels and suppress excessive contrast. MUSICA^2 uses multi-scale to convert the 2-d gray scale input image into a 3-d stack of detail layers. This is called image decomposition using the multi-scale transform whereby the gray scale image is decomposed into frequency sub-bands, or detail layers. Each layer represents local signal differences (local image contrast) in a narrow sub-band of spatial frequencies within the total frequency range (or bandwidth) present in the image. By doing that the various detail layers can be processed individually (e.g. edge enhancement, latitude reduction, noise reduction) in order to precisely control the frequency content of the output image (Schaetzing, 2007:10). In order to do the decomposition, MUSICA^2 uses the so-called Laplacian pyramid. The individually enhanced detail layers are eventually recomposed to form the output image. The concept of MUSICA^2 can be described as follows:

The first step in the processing of the image is analysis of the input image and algorithmic parameters are automatically calculated, without user intervention. The image analysis includes: Histograms, Global noise estimation, Local contrast-to-noise ratio (CNR) estimation, Mask image computation and Global gain calculation. After the image analysis, a number of steps are followed before an enhanced output image is obtained. These steps are: Gain adjustment, Image decomposition, Excess contrast reduction, Subtle contrast enhancement, Edge enhancement, Noise reduction (CNR - based), Image reconstruction and a Gradation processing

(Schaetzing, 2007:8). The different steps in achieving the processed output image with the MUSICA^2 processing algorithm is illustrated in Figure 2.2. The major difference between MUSICA^2 and its predecessor MUSICA, is that MUSICA^2 requires no interaction with the user (e.g. body part images, radiographic projection, patient position and the presence of contrast material). MUSICA^2 also doesn't need collimation or direct x-ray background information (Schaetzing, 2007:5). MUSICA^2 thus depends less on user input which lessens the chance of incorrect information for image processing.

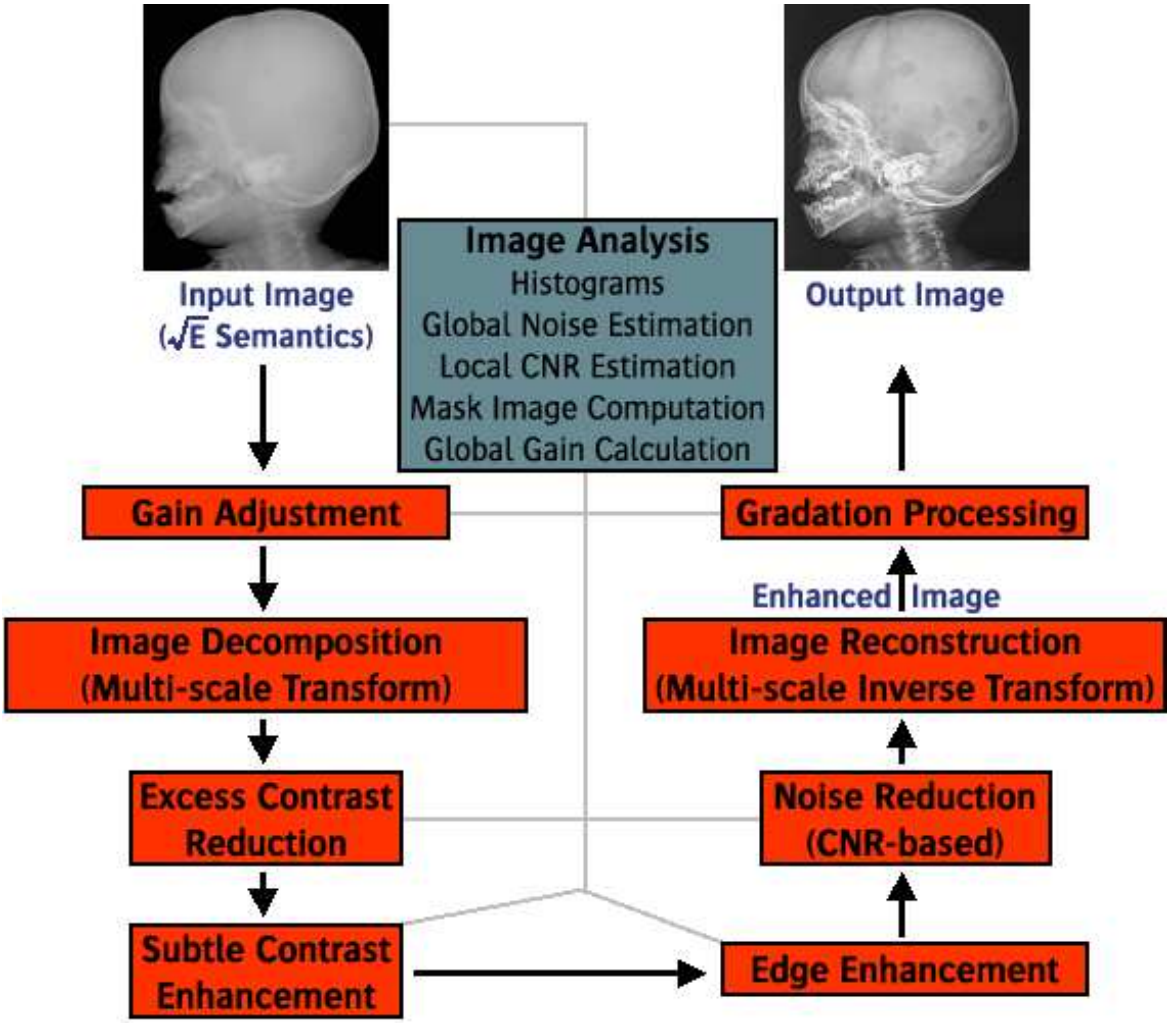


Figure 2.2: The MUSICA^2 flowchart (Schaetzing, 2007:8)

2.4 CLINICAL COMPARISON OF IMAGE PROCESSING ALGORITHMS

A number of studies have been conducted in which the effect of image processing algorithms on interpretation accuracy was investigated. However, differences in study design make it difficult to compare the results of previous studies that investigated the effect of image processing methods on interpretation accuracy (Zanca *et al*, 2009). In many of the studies the images were presented in hard-copy format for evaluation (Cole *et al*, 2003) (Cole *et al*, 2005) (Pisano *et al*, 1997[a]) (Pisano *et al*, 1997[b]) (Pisano *et al*, 1998) (Pisano *et al*, 2000[a]) (Hemminger *et al*, 2001). Very few studies compared the effect of image processing methods on interpretation accuracy with soft-copy display (Sivaramakrishna *et al*, 2000) (Zanca *et al*, 2009) (Kamitani *et al*, 2010). However, although the study by Sivaramakrishna and co-workers (2000) and Kamitani and co-workers (2010) were conducted with soft-copy display, viewers were not allowed to change the monitor settings or use any aids for example the magnifying glass. In some studies (Pisano *et al*, 1997[a]) (Pisano *et al*, 1997[b]) (Pisano *et al*, 1998) (Hemminger *et al*, 2001) student observers were used whereas in other studies radiologists with experience in DM were used. Also, some studies were preference studies (Sivaramakrishna *et al*, 2000) (Pisano *et al*, 2000[a]) whereas others used ROC analyses (Cole *et al*, 2003) (Cole *et al*, 2005) (Kamitani *et al*, 2010) and others used modern ROC/free response receiver operating characteristic (FROC) analyses (Zanca *et al*, 2009). Some studies used self-developed image processing algorithms whereas others used manufacturer recommended algorithms (Zanca *et al*, 2009). The findings of the clinical studies were of some interest even though they varied significantly.

In a study by Cole and co-workers (2003), the effect of three image processing methods on diagnostic accuracy was evaluated in 201 women with dense breasts who underwent diagnostic mammography. Between the image-processing methods [histogram based intensity windowing (HIW), contrast-limited adaptive histogram equalisation (CLAHE), and the preferred algorithm of the manufacturer, they found slight differences with ROC analysis in AUC, sensitivity and specificity, but none were statistically significant (Cole *et al*, 2003). On the other hand, they found that lesion type did influence interpretation accuracy significantly in terms of specificity with the Fischer equipment ($p = 0.0004$) and both AUC and sensitivity with the Lorad unit ($p < 0.0001$). The results thus indicated that diagnostic accuracy depends on lesion type but that it is not influenced by the image processing methods.

Cole and co-workers (2005) investigated the effect of three image-processing algorithms Manufacturer's Default, MultiScale Image Contrast Amplification (MUSICA), and Power Law Adaptive Histogram Equalisation (PLAHE), on interpretation performance of radiologists. They found the AUC for mass cases with the GE system was worse than SFM for all processing options. The AUC for mass cases with the Trex system was better, but only when processed with the manufacturer's default algorithm and sensitivity for mass cases with the GE system was worse than SFM for all digital presentations. On the Fischer system, images processed with Default and PLAHE algorithms, lower specificity was found for cases with calcifications. Lower specificity was also found on the Trex system with MUSICA processed images, for cases with calcifications. Their findings led to the conclusion that different image processing algorithms may be needed for interpretation based on machine and lesion type.

A US study found that the choice of parameters of an algorithm can improve or degrade the detection performance (Hemminger *et al*, 2001). They investigated the effect of HIW and CLAHE on the detection of simulated masses in dense mammograms. They found that HIW processing changed observer detection performance ($p = 0.002$). The best HIW setting performed better than the best fixed-intensity window setting and also better than no processing. However, even with the best CLAHE setting no significant difference was found compared with no processing. It can thus be seen that for the detection of simulated masses, the choice of parameters of an image processing algorithm can improve or degrade viewer performance with some algorithms. The effect was however not tested in a clinical setting.

A study that investigated the effect of CLAHE image processing compared to unprocessed images on the detection of simulated spiculations in dense mammograms, found that the relation of parameters: Contextual region and clip limit, can significantly influence the detection of spiculations (Pisano *et al*, 1998). Improved detection was seen with CLAHE setting: Contextual region 32, clip limit 2 (mean difference in Theta scores: 0.061, $p = 0.0001$). Detection was also improved with CLAHE setting: Contextual region 32, clip limit 4 (mean difference in Theta scores: 0.053, $p = 0.0001$). However, they also found that detection can be adversely affected with CLAHE setting: Contextual region 2, clip level 16 (Pisano *et al*, 1998). Their findings suggest that CLAHE (with specific parameter settings) might be of use to radiologists when subtle spiculations are found to decide if further work-up of the lesion is needed. The effect was not tested in a clinical setting. Furthermore, it was limited to dense breasts and therefore the effect of CLAHE on the appearance of fatty areas of the breast was not taken into account.

The preference of radiologists from among eight different image processing algorithms was studied by Pisano *et al* (2000). The processing algorithms included were: manual intensity windowing (MIW), HIW, mixture model intensity windowing (MMIW), peripheral equalisation, multiscale image contrast amplification (MUSICA), contrast-limited adaptive histogram equalisation, Trex processing, and unsharp masking. Because of the limitations of soft-copy technology at that stage and the preference of radiologists for hard-copy reading, hard-copy display of the digital images was used in the study. All digital images were compared to a corresponding SFM in the same patient. Readers rated the visibility and characterisability of lesions on the different digital images compared to SFM. They found that readers preferred different algorithms depending on the task, lesion type, and machine type for the mass characterisation and calcification characterisation tasks. Readers preferred SFM to all digitally processed images for the screening task. However, images processed with Trex and MUSICA showed no significant difference. In the diagnosis of masses, all printed digitally processed images were preferred to SFM. Digital images processed with unsharp masking were significantly preferred. None of the processed digital images were however preferred to SFM for the diagnosis of calcifications. From the results of this study, it would be fair to argue that soft-copy display would be advantageous because it allows flexibility and easy access to different processing options of the image. The authors suggested that the algorithms to be used for optimal soft-copy display with each mammographic task should be determined by the manufacturers of each DM unit (Pisano *et al*, 2000[a]). However, these are not available on our mammography unit. A disadvantage of studies in which hard-copy display was used is that the benefits of soft-copy display were not taken into account. In clinical practice, soft-copy display allows for user-interface in

terms of window and level adjustment, magnification and panning, as well as image inversion, to name but a few. The flexibility of soft-copy display may impact on the overall performance of radiologists which are not accounted for in studies which used hard-copy display for interpretation by the viewers (Zanca *et al*, 2009).

In another preference study the performance of four image processing algorithms (adaptive unsharp masking, CLAHE, adaptive neighbourhood contrast enhancement, and wavelet-based enhancement) were compared to unprocessed images (Sivaramakrishna *et al*, 2000). Fourty mammogram images with masses and microcalcification of known disorders were displayed in soft-copy format and rated by four radiologists (mammographers) from best to worst on a five-point scale. They found statistically significant differences for all four viewers, among the five images for microcalcifications but not for masses. For microcalcifications, they found the adaptive neighbourhood contrast enhancement algorithm was most preferred in 49% of interpretations ($p \leq 0.011$), the wavelet-based enhancement in 28% ($p \leq 0.030$), and the unprocessed image in 13%. However, for masses the unprocessed image was most preferred in 58% of cases and statistically significant differences were shown. The difference in preference between unenhanced and other processing options were: CLAHE ($p \leq 0.017$), adaptive neighbourhood contrast enhancement ($p \leq 0.017$), and wavelet ($p \leq 0.016$). The results indicate that different image processing algorithms were preferred for different lesions as certain image enhancement can improve the visibility of microcalcifications, but did not improve the visibility of masses. In that study the radiologists preferred algorithms that do not change the appearance of the original image (e.g. adaptive neighbourhood contrast enhancement), while algorithms like CLAHE that changes the appearance of the original image to a larger extend, were least preferred.

Zanca and co-workers (2009) compared the effect of five manufacturer-recommended image processing algorithms for mammography (Agfa MUSICA 1, IMS Raffaello Mammo 1.2, Sectra Mamea AB Sigmoid, Siemens OPVIEW v2 and Siemens OPVIEW v1) on observer detection of simulated microcalcifications. Both jack-knife free-response receiver operating characteristic (JAFROC) and ROC found significant differences for the same six modality pairings, however much lower p-values with JAFROC ($p < 0.0001$) compared to ROC analysis ($p = 0.0305$). The largest JAFROC figure of merit (FoM) difference was found between the newer OPVIEW v2 and the older OPVIEW v1 (JAFORC FoM 0.0548; 95% CI: 0.0311; 0.0785). For OPVIEW v2 the multiscale approach is used for image processing whereas OPVIEW v1 uses conventional image processing algorithms (Zanca *et al*, 2009). The smallest yet significant FoM was found between Agfa MUSICA1 versus Sectra Mamea AB Sigmoid (JAFROC FoM 0.0295; 95% CI: 0.005 82; 0.0532). According to the authors, this was the first study to show significant differences between the performances of manufacturer-developed processing algorithms. This can possibly be attributed to the fact that the JAFROC methodology was used; and this according to them, has higher statistical power than ROC. However, the study did not include masses and other lesions in the breast and the effect of image processing might be different for them.

Goldstraw and co-workers (2009) investigated the effect of Premium View processing software (developed by GE Medical Systems) on patients at a high risk of breast cancer immediately before Premium View was implemented, shortly thereafter, and a few months thereafter. They found a significantly increased indeterminate mammogram rate in the time period immediately after the installation of Premium View from 5.7% to 8.7% ($p = 0.002$). In the follow-up period however,

the indeterminable mammogram rate decreased to 6%, similar to that before Premium View ($p = 0.7$). Also, the stereotactic biopsy rate increased significantly initially from 0.8% to 2.4% ($p = 0.001$) and although decreasing after the delay (1.6%) it remained higher than levels before Premium View ($p = 0.07$). Furthermore, when compared to the original levels, a steady increase in the cancer detection rate (for both microcalcifications and soft-tissue density groups) in the indeterminate mammograms were found both initially (from 3.4% to 4.4%, $p = 0.02$) and after the delay 5% ($p = 0.003$). The results point to possible higher cancer detection rates with the use of Premium View, however at an initial increased recall rate. The authors argued that the interim higher recall rate is due to a technical learning curve which subsided when the operators became familiar with the new technology. Of importance is that as in previous studies, it was shown that image processing and experience with the display modality may affect diagnostic performance.

From what was found in previous studies, it is clear that different image-processing approaches can be of value depending on lesion type (Pisano *et al*, 2000[a]) (Sivaramakrishna *et al*, 2000) (Cole *et al*, 2003) (Cole *et al*, 2005). Evidence was provided that different image processing algorithms may be needed for interpretation based on machine type (Cole *et al*, 2005). Evidence also suggests that different processing algorithms might be of value depending on the mammography task (screening vs diagnostic) (Pisano *et al*, 2000[a]). Evidence was provided that different parameter combinations for image processing algorithms may enhance lesion detection (Hemminger *et al*, 2001) (Pisano *et al*, 1997[a]) (Pisano *et al* 1997[b]) (Pisano *et al*, 1998). Also, evidence was found that even with manufacturer recommended algorithms for mammography, there might be significant differences in observer performance (Zanca *et al*, 2009). Evidence was also found that image processing

may affect diagnostic performance (Goldstraw *et al*, 2009). As the image processing algorithm is commonly determined by the vendor, it can thus be seen that studies to find the best parameter combination for different lesion types and mammography tasks, can improve observer performance in clinical settings. It also becomes apparent that the optimal image processing algorithm for mammography has not been established yet. Interestingly, all the studies mentioned did not include the effect of processing algorithms on the characterisation of lesions.

2.5 CONCLUSION

The mammographic features of breast cancer are subtle and because of the low subject contrast inherent to the breast, mammography is a challenging examination to interpret. Lesions in dense breasts are often less conspicuous, which render the mammographic interpretation of these cases more difficult. A certain degree of distinction was achieved with SFM, especially in terms of its high spatial resolution. However, contrast resolution remained problematic. On the other hand, DM, although offering lower spatial resolution when compared to SFM, compensates by means of increased contrast resolution. Several studies have compared SFM to DM and although the initial studies found no significant difference in cancer detection rates between the two modalities, more recent studies have found DM to be superior to SFM in certain areas. Digital mammography offers many other advantages and since it received FDA approval, it has supplanted SFM in many radiology departments around the globe. In DM, image processing is applied to enhance or accentuate certain image features for a specific application and is therefore problem orientated. However, there is a debate about which processing algorithm is best. No literature was found (see Appendix V) in which the gray scale invert of the digital

image on diagnostic accuracy was documented. Also, no clinical studies were found in which the effect of MUSICA^2 image processing on image quality or diagnostic accuracy was documented. It was noted that although the effect of image processing on lesion detection has been studied, the effect on lesion characterisation was excluded from most studies. Because the choice of processing algorithm usually depends on the vendor, and it was found that full benefit of DM can only be obtained through soft-copy viewing, the viewing protocol for each clinical setting might be unique, depending on the radiologists' preference for different lesion types and mammographic task performed. It is problematic that soft-copy display demands different skills from the radiologist compared to SFM, and radiologists should be trained in the use of the new technology.

In the next chapter the challenges for the radiologist changing to soft-copy viewing will be considered and the training requirements for radiologists changing from SFM to DM will be motivated.

CHAPTER 3

TRAINING REQUIREMENTS FOR RADIOLOGISTS CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY

3.1 WHY SHOULD THE RADIOLOGISTS BE TRAINED IN DIGITAL MAMMOGRAPHY?

Ten years ago it was anticipated that the interpretative performance of radiologists would determine the clinical performance of DM (Lewin *et al*, 2002). Numerous clinical trials have proved that DM is at least as good as SFM for the detection of breast cancer and more recent studies have even found DM to be superior to SFM in certain patient groups (Section 2.2). In some of the studies that compared the diagnostic performance of DM versus SFM, radiologists had very little experience in soft-copy reporting and it was seen as a weakness of the study (Skaane *et al*, 2003). It was argued that the lack of sufficient experience of the viewers in soft-copy viewing might have favoured SFM when compared with DM.

Although the full potential of DM can only be achieved through soft-copy display it is unfamiliar to radiologists qualified during the era of SFM (Obenauer *et al*, 2003). Resistance by users to the use of soft-copy viewing techniques such as magnification, window/level selection and image inversion has been reported when moving from film to filmless radiography (Jones, 1999). The reason being, that because these techniques are not normal routine for radiologists, they can be inefficient and time-consuming. Resistance to soft-copy viewing was predominantly

found for radiologists with many years of experience in SFM which is attributed to bias toward hard-copy interpretation (Kallergi *et al*, 1996). Hard-copy format was particularly preferred by readers with up to 30 years of experience in SFM (Obenauer *et al*, 2003). Personal habits have also been reported to influence the preference of radiologists for hard-copy vs soft-copy reading (Obenauer *et al*, 2003). Lack of suitable soft-copy display systems for mammography was in part responsible for the slow acceptance of digital mammography (Hemminger, 2003). This can be partially responsible for the resistance of viewers to use soft-copy display techniques in early studies with the new technology. Although soft-copy display has improved since the early days of DM, the radiologists still need different skills for soft-copy viewing when changing from SFM to DM.

Although DM uses new technology compared to SFM, the role and responsibility of the radiologist in mammography reporting remain unchanged namely: to detect breast cancer as early as possible, to differentiate malignant from benign findings in order to arrive at the right diagnosis and to facilitate the management of the patient according to the findings (Tabár & Dean, 2001:vii). It would be ideal if the condition is always diagnosed as positive when present and negative when absent.

In the light of their unchanged role, the question could well be asked: Why was it then anticipated that the radiologists' interpretation performance will influence the performance of the new technology? The answer lies in the fact that the characteristics of the mammography image with soft-copy display are completely different in terms of spatial and contrast resolution demands, to that of SFM. Different factors have been argued to have influenced diagnostic accuracy in DM clinical trials. These are image processing algorithms (Cole *et al*, 2005) applied to images and the use of soft-copy display tools for example inability to deal with the

major differences between SFM and DM namely spatial and contrast resolution (Riesmeier *et al*, 2003). In mammography as in many other situations, the presence of a specific object or pathology is not obvious and viewing conditions must be such that the best possible visualisation of any pathology can be achieved by the viewer.

3.2 TRAINING NEEDS FOR RADIOLOGISTS CHANGING FROM SCREEN-FILM MAMMOGRAPHY TO DIGITAL MAMMOGRAPHY

The different technology used in DM compared to SFM leaves the radiologist changing from SFM to DM with a need for knowledge and understanding of the new modality. Some authors argued that the knowledge and understanding required must include: the process of digital image acquisition, advantages and limitations of conventional SFM and DM and the effect of digital image processing on image quality (Pisano *et al*, 2005). Also, previous studies have found experience in soft-copy display to be a need for viewers changing from SFM to DM (Skaane *et al*, 2003) (Jones, 1999). The protocols used for image display are also regarded as crucial to the success of DM with soft-copy viewing (Skaane *et al*, 2003).

In a US study, soft-copy and hard-copy reading for FFDM was compared in 333 cases (Nishikawa *et al*, 2009). They found no statistically significant difference between the two (AUC 0.75 soft-copy vs 0.76 hard-copy, 95% CI, -0.04 to 0.01; $p = 0.36$). However, as the display formats were not optimised, they argued that it is possible that soft-copy reading could be superior to hard-copy reading with proper optimisation.

The only study that was found in which information on the training of viewers for soft-copy reading was provided, was a study by Pisano *et al* (2002). The study

compared the speed and accuracy of soft-copy versus printed film display. Their viewers were radiologists who had no prior experience in interpretation of DM with soft-copy display. Twenty digital mammograms were used to train the viewers in soft-copy viewing before the study. They found no significant difference in the speed of interpretation, sensitivity, specificity or area under the ROC curve between soft-copy versus printed-film display. They argued that soft-copy display is unlikely to significantly influence accuracy or speed. However, they compared digitised SFM with printed digital mammograms. They used manual intensity windowing without other processing for the printed digital mammograms and for the digitised SFM images they used what they referred to as a "standardisation step" to make the appearance of the image on the monitor similar to that of a mammogram on a lightbox. It is not known what the effect on accuracy would be, had the radiologists not been trained in soft-copy viewing. The results shown with this study will possibly not be the same for viewers who are unfamiliar with soft-copy viewing.

The tools for soft-copy viewing of the image on a monitor are more comprehensive than those of SFM and radiologists need knowledge and experience in the use thereof. The tools for soft-copy viewing include the use of image processing, magnification, manual intensity windowing and invert. Discussion of each of these follows:

3.2.1 Digital image processing

Viewers can only take full advantage of digital image processing if they have a reasonable degree of understanding and confidence in its ability (Schaetzing, 2007:24). They need to understand that although the dynamic range of digital detectors is much wider than that of conventional film, the display range is much

more limited and thus some form of image processing is applied (Pisano *et al*, 2005). Subjective experience of radiologists that different image processing algorithms change the apparent image quality of mammograms, has previously been reported (Pisano *et al*, 2000[a]). Radiologists raised concern about the impact that image processing may have on their performance (Zanca *et al*, 2009). Radiologists have even indicated that they find it more difficult to compare initial and subsequent mammograms if one was SFM and the other DM, because they do not look the same (Hemminger, 2003). It has been argued that the success of DM relies heavily on proper image processing. Image processing in DM is important, because it has been found that specific processing is required for different clinical tasks (screening vs. diagnosis) and for the diagnosis of different lesion types (calcifications vs. masses). In addition it has been shown radiologists preference for the type of image processing differed by machine type (Pisano *et al*, 2000[a]). Also, previous investigators found a significant increase in recall rate shortly after the implementation a new image processing algorithm, which reverted to a level similar to that found before implementation after a few months (Goldstraw *et al*, 2009). This perhaps points to the new image processing algorithm leaving the radiologists more uncertain on the mammographic findings so they were assessing the new modality or algorithm by requesting additional diagnostic work-up for confirmation of the diagnosis, compared to before DM.

It would thus be fair to argue that viewers should have knowledge and understanding of the processing options used on their digital units in order to understand why the processed image appears to look different compare to SFM. They should also have knowledge and understanding of the effect of the processing option on image quality and moreover on the effect thereof on the detection of different types of lesions.

3.2.2 Magnification

In a previous study radiologists have reported that they found it less cumbersome to use the magnifying glass in hard-copy display than to use the pan and zoom tools on the soft-copy display (Hemminger, 2003). The zoom function is used to display selected areas of the breast image at full resolution and thus to have a closer view by magnifying or zooming in on the part of interest (Hemminger, 2003). Radiologists should be made aware of the fact that although spatial resolution may be less than one quarter of that of SFM, it is possible to readily visualise the full available spatial resolution through roaming and zooming (or digital magnifying glass) techniques (Pisano *et al*, 2000[a]).

Hundertmark and co-workers (1997) (cited in Pisano, Yaffe and Kuzmiak, 2004:31) found that the diagnostic value of digital mammograms using the direct magnification technique is comparable to standard SFM with regard to the identification of calcifications. Calcifications were seen on both modalities in 86% of cases and additional calcifications were detected on digital (that had not been seen on SFM) in 8% of cases.

The importance of zooming in soft-copy viewing has been shown. Radiologists should not only have knowledge and understanding of the importance thereof, but they should gain experience in the use thereof to be able to confidently apply this tool in clinical soft-copy viewing.

3.2.3 Manual intensity windowing

Conventional manual methods to change image contrast are window width and level adjustments or nonlinear look-up tables. Resistance among viewers for window width and level adjustment when moving from film to filmless radiography has been

reported (Jones, 1999). Pisano and co-workers reported that manual intensity windowing leads to different interpretation by viewers (2000). It is possible that an inexperienced viewer can select windows that might obscure lesions that might be visible with other windows (Pisano *et al*, 2000[b]). Two previous studies have showed significant differences in the detection of simulated calcifications and masses with different window width and window level combinations (Pisano *et al*, 1997[a]), (Pisano *et al*, 1998[b]). The authors argued that pre-set WW/WL settings could address the problem. However, these are not available on our digital mammography unit. The disadvantage of this method to reduce excessive contrast, is that it affects other image contrast as well, making it difficult to standardise image-to-image consistency (Schaetzing, 2007:31). The radiologists thus need knowledge and experience in window width and level adjustment to change the displayed gray scale range of the image according to preference. In other words, they should for example know how to increase contrast in the dense areas of the breast (lower contrast areas) (Pisano *et al*, 2005).

3.2.4 Invert

In a clinical study on soft-copy requirements for DM, radiologists indicated that they regard the ability to invert images in mammography as important (Hemminger, 2003). However, resistance among viewers was reported for image inversion when moving from film to filmless radiography (Jones, 1999). An invert image is obtained by reversing the intensity levels (invert transformation) of an image, producing the equivalent of a photographic negative. This is achieved by linear transformation (Gonzalez & Woods, 2008:108-109). This application is used with the aim to enhance white or near white detail embedded in dark regions and this type of

processing is regarded to be particularly suited to mammography. However, no studies were found that investigated the effect of invert on lesion detection.

3.2.5 Summary

To obtain the full benefit of soft-copy viewing, and to make the task less cumbersome for the viewer, the radiologist needs knowledge and understanding of the tools for soft-copy viewing to ensure that it is performed efficiently and does not take up too much time. The viewer also needs skills to perform soft-copy viewing to ensure reading of the image stays priority and it does not impact negatively on diagnostic accuracy. It is therefore understandable that without additional training in soft-copy viewing, radiologists trained in viewing SFM would be less comfortable with the use of the tools for soft-copy viewing and this might impact negatively on diagnostic accuracy.

3.3 CURRENT TRAINING OF RADIOLOGY REGISTRARS AT THE RESEARCH SITE

The Diagnostic Radiology qualification (M.Med. Rad.D.) offered at the University of the Free State entails a four year curriculum of which Female Imaging is entertained at four academic afternoon sessions. In terms of the theoretical training on Breast Imaging in specific, the topic is covered in two academic afternoon sessions of which one will be a lecture presented by a registrar on mammography. For experiential training all registrars rotate through the mammogram unit at three accredited training sites for an average of 16 weeks during the four year training program. During the rotation, the registrar reports on mammograms at the specific mammography unit and a consultant radiologist is responsible to verify the reports. A practical assessment on mammography is conducted by the consultant radiologist at the end

of a registrar's mammography rotation. This assessment must be passed before the registrar can sit for the final exam in the major subject Diagnostic Radiology (DIR800).

Specific learning objectives for soft-copy mammography viewing and digital image processing are not currently part of the module. Also, the requisites for the mammogram report in the department are not structured. Based on the outcomes of this study, the training of registrars in mammography will be structured to incorporate a teaching file on soft-copy mammography viewing to improve reporting.

3.4 TRAINING REQUIREMENTS IN THE US vs. THE SA CONTEXT

In the US, national quality standards for mammography services are specified by the Mammography Quality Standard Act (MQSA) which was passed in 1992. The mandate includes requirements for equipment and quality assurance as well as requirements for personnel involved in the performance of mammography in the U.S. The MQSA specifies the following requirements in terms of qualifications for interpreting physicians (FDA, 2001):

- Have earned 60 hours of documented mammography continuing medical education (CME) and 8 hours of training in each modality (such as SFM and DM)
- Have read at least 240 examinations in the preceding 6 months under supervision or have read mammograms under the supervision of a fully qualified interpreting physician
- Have read 960 mammograms over a period of 24 months

- Have earned at least 15 Category 1 CME credits in mammography over a 36-month period, with 6 credits in each modality used.
- To perform a new imaging modality e.g. DM, the interpreting physician must have 8 CME credits specific to that modality before starting the modality

In South Africa the Health Professions Council of South Africa (HPCSA) has the responsibility of establishing minimum standards to accredit training programmes and qualifications, and to define the requirements for registration as a specialist and subspecialist (HPCSA, 2001). The HPCSA does not make provision for registration in a sub speciality category (e.g. Mammography) in Diagnostic Radiology.

The Health Profession Act, 1974 (Act No. 56 of 1974) (as amended) endorses Continuing Professional Development (CPD) as the means for maintaining and updating professional competence (HPCSA, 2011). However, no specific requirements exist for radiologists interpreting mammograms.

3.5 CONCLUSION

International acknowledgement of the need for training radiologists in the use of the new modality has been established while on the other hand there is a lack of structure and compulsory guidelines for starting to use the new modality in the South-African context. It was clearly shown that the new modality presents the radiologists with new challenges and many researchers have raised concern that radiologists should be trained in the new modality so as to ensure the same efficacy and quality is achieved in the film-reading process. When buying a new DM unit from a vendor, it is general practice that the product specialist of the vendor will familiarise the radiologist in the use of their equipment.

Thus, although the potential advantages of soft-copy viewing are well documented, it would be fair to argue that the success of this display method will be heavily dependent on the image processing algorithm used and also on the skills of the radiologist to use the tools available for soft-copy viewing. Up until recently, the majority of radiologists in SA have been trained in reading conventional SFM. Digital image processing and soft-copy viewing in mammography have not always been part of the armamentarium of the radiologist. Additional skills must thus be acquired.

In our experience, vendors spend very little time on conceptual and factual training in the new modality, but rather highlight the advantages of their own equipment. Also, although the radiologists are familiarised with the tools available for soft-copy viewing, the skill to address the challenges of LSR compared to SFM, are left to the viewers discretion. Moreover, very little information, on digital image processing is supplied. It is therefore obvious that the information supplied by the vendor's product specialist does not address all the challenges facing the radiologists in terms of soft-copy viewing.

However, in this review of the current international literature, no evidence was found of the effect of training of radiologists in the new modality on diagnostic accuracy achieved with soft-copy viewing. To answer this important question identified from the literature, diagnostic accuracy before and after the development of a viewing protocol through participative learning of a group of radiologists was evaluated (Chapter 6). The development of the viewing protocol through participative learning is discussed in Chapter 5. As sensitivity and specificity in mammography relies heavily on the lesion being detected and correctly classified, the effort in developing the viewing protocol through participative learning will be towards making the fine

anatomy and consequently subtle signs of malignancy, visible to the viewer. It is anticipated that by doing that, the diagnostic accuracy in DM can be improved.

In the next chapter (Chapter 4), a phantom based method was used to assess image quality with different processing options. This was done to narrow down the image processing options to be evaluated on clinical images (Chapter 5).

CHAPTER 4

IMAGE QUALITY ASSESSMENT OF PROCESSING OPTIONS: PHANTOM BASED METHOD

4.1 INTRODUCTION

From the literature review on DM in Chapter 2, it was made clear that image processing is a critical element in the digital radiographic imaging chain. The goal of image processing was described as an attempt to increase the visibility or conspicuity of subtle structures that can easily be overlooked. By doing that, the information in the acquired image can be presented in an optimal way to the observer in an attempt to contribute to better observer performance and indirectly to better patient care. However, image processing was identified as a challenge for the radiologist changing from SFM to DM (Chapter 3), because they really are different.

It was also mentioned in Chapter 2 that on commercially available digital units it is common for the vendor of the DM unit to offer a specific processing algorithm and where applicable, with a default setting. It is therefore reasonable to argue that the reporting outcome might differ from digital unit to digital unit. Where different parameter combinations are available on digital units, a default combination is usually set by the vendor and it is not known if local radiologists might prefer different parameter combinations. Furthermore it is noted in the literature that general consensus on the preferred processing algorithm for breast imaging has not been found. It is argued that these algorithms cannot and should not be evaluated by radiologists in the clinic with real patients (Pisano *et al*, 1997[a]). To find the preferred

processing algorithm will best be achieved with a structured project with dedicated viewers for the purpose.

On the other hand, the value of the radiologist understanding the effect of image processing is acknowledged. However, to conduct clinical trials with all the available processing algorithms and / or combinations of parameters for an algorithm on clinical images and radiologists involved as the readers, will be extremely time consuming and expensive. Moreover, for consistency in quality control procedures, a phantom image will provide more consistency and repeatability for the evaluation of image quality. The European protocol for quality control (QC) of the physical and technical aspects of mammography screening specifies the use of the CDMAM mammography phantom (European Commission, 2006). The phantom allows for fast and simple image quality evaluation and because of the great number of objects it has, evaluation of resolution and contrast properties can be performed with good accuracy. Thus to limit the number of processing options to be evaluated in the clinical situation (Chapter 5), a phantom-based method was pursued in this part of the study.

4.2 AIM

The aim of this part of the study was to assess the effect of the different mammographic processing options (available in the department where the research project was conducted), on the image quality of a phantom image. This was done to identify a smaller set of processing options to be evaluated for image quality assessment on clinical images (Chapter 5).

4.3 METHODS

4.3.1 Contrast Detail (CD) Phantom

A commercially available CD phantom, (CDMAM type 3.4, ARTINIS Medical systems B.V.) was used as the test object to compare the performance of different image processing algorithms. The phantom is 18 x 24cm in area and consists of a 0.5mm thick aluminum base with circular gold disks of variable thickness and diameter arranged in a matrix of 16 rows and 16 columns. The gold disks range in diameter from 0.06 to 2.0mm and in thickness from 0.03 to 2.0µm, resulting in a radiation contrast range of about 0.5 – 30% under standard mammography exposure conditions (ARTINIS, 2007:3). Two disks with the same thickness and diameter are placed in each square – one in the centre and the other placed randomly near one of the corners of the square (Figure 4.1). Within a row the disk-diameter is constant, with an approximately exponential increase in thickness from row to row. The high contrast area of the image is formed where the thickness of the discs is largest. Within a column the disk thickness is constant, with an approximately exponential increase in diameter (Table 4.1).

Figure 4.1: Contrast-Detail phantom ARTINIS CDMAM type 3.4

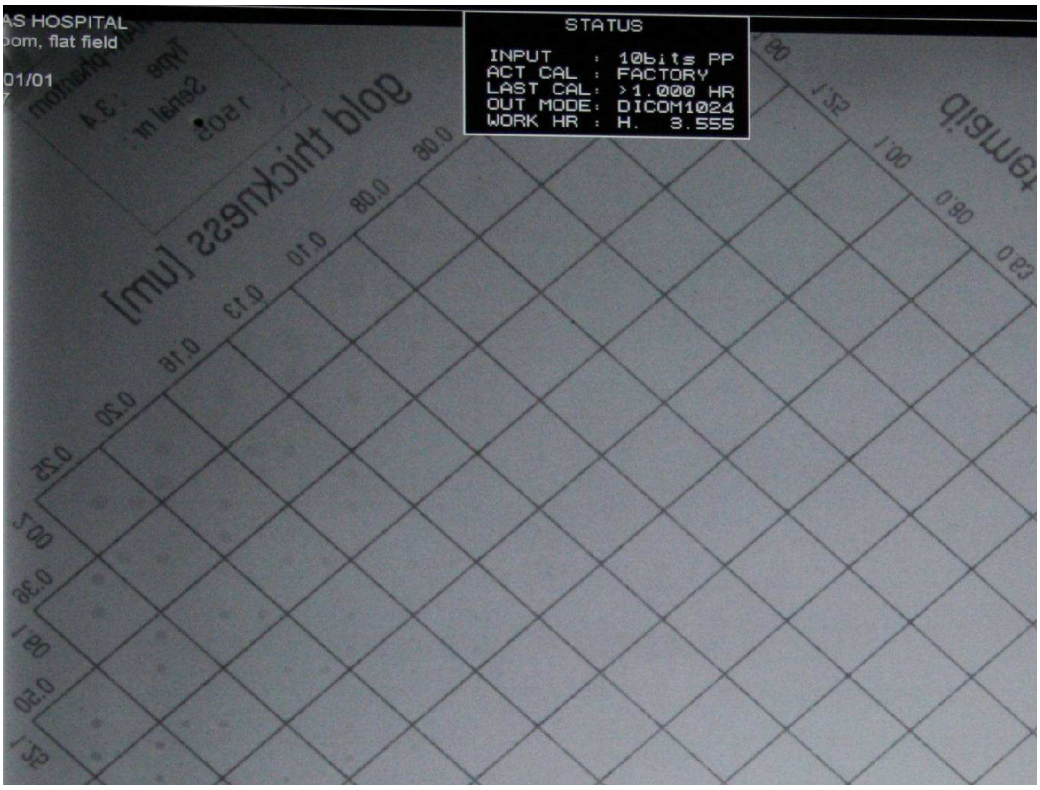


Figure: 4.2 A cropped segment of a mammography x-ray image of the ARTINIS CDMAM type 3.4 phantom

Table 4.1: Thickness, diameter and radiation contrast C_r (for standard mammography exposure conditions) of the gold disks within the phantom (ARTINIS, 2007:7)

Column	Thickness [µm]	Radiation contrast C_r [%]	Row	Diameter [mm]
1	0.03	0.52	1	0.06
2	0.04	0.7	2	0.08
3	0.05	0.87	3	0.1
4	0.06	1.04	4	0.13
5	0.08	1.39	5	0.16
6	0.1	1.73	6	0.2
7	0.13	2.25	7	0.25
8	0.16	2.76	8	0.31
9	0.2	3.44	9	0.4
10	0.25	4.28	10	0.5
11	0.36	6.11	11	0.63
12	0.5	8.38	12	0.8
13	0.71	11.68	13	1
14	1	16.05	14	1.25
15	1.42	22	15	1.6
16	2	29.53	16	2

4.3.2 System description and image acquisition

An x-ray projection image of the phantom was acquired with a GE Senograph DMR Mammographic unit. To obtain the x-ray image of the phantom (Figure 4.2), the directions in the phantom's manual were followed (ARTINIS, 2007:8). The phantom was positioned on the bucky with the smallest disk-diameters at the thorax side. The exposure technique was obtained by using automatic exposure control to limit the mAs with a tube potential set manually to 25kVp. A Mo/Mo target/filter combination, small focal spot and compression plate were used with a mobile grid in place. For

the simulation of an average breast thickness, three Plexiglas plates (each with a thickness of 10mm) were positioned on top of the phantom. The image receptor was a mammography CR plate read by an Agfa CR reader set up for mammo readout.

4.3.3 Image processing

Ten different image processing options selected for evaluation were individually applied to the phantom image. These options were:

- MUSICA^2, trademark of Agfa (generally used in the department for all mammographic image processing)
- MUSICA^2 Invert
- Unprocessed (obtained by changing the device configuration on the Agfa workstation from 'presentation' to 'for processing' before archiving the image to the PACS),
- Unprocessed Invert
- Six different Contrast-Limited-Adaptive-Histogram-Equalisation (CLAHE) parameter combinations, details given below:

On the Philips PACS review station, four different parameters can be manipulated for the CLAHE processing algorithm. The CLAHE parameter combination consisted of the following: Contextual region dimension, Number of bins (NBins), Clip limit, and Map level (see explanation on parameters in Section 4.4.4). For the purpose of this study, the four CLAHE parameters will always be listed in the above mentioned order and the default parameter combination will be indicated in bold, e.g. (**64/256/1.5/1**). For the other parameter combinations included in the study, only the parameter value which is different from the default will be indicated in bold.

For the purpose of this study it was decided to evaluate the default CLAHE parameter combination together with five other parameter combinations. These were derived by changing only one parameter from the default values at a time, and also to change the value of that parameter to the most extreme value compared to that of the default parameter value. The only parameter that was evaluated with two options is the Map Level. Three values are available for this parameter namely "0", "1" and "2". Because the default parameter value is "1", it was decided to include both "0" and "2" for evaluation.

The six CLAHE combinations therefore used in this study were:

- (**64/256/1.5/1**) **default**
- (64/256/**3**/1) higher clip limit
- (**128**/256/1.5/1) larger 'contextual region'
- (64/**384**/1.5/1) larger 'number of 'bins' (NBins)
- (64/256/1.5/**2**) highest map level
- (64/256/1.5/**0**) no map level - canonical CLAHE algorithm

The complete dataset thus included these six processing options plus the MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert.

4.3.4 Image evaluation

Four experienced observers (three medical physicists and a senior lecturer in diagnostic radiography – all with experience in QC), independently evaluated the phantom image processed with the above processing options. The image was archived onto a Philips PACS and reviewed on a workstation with a Matrox MED5Mp-DVI graphic card. The image was displayed on a Fimi (model MML2152)

5Mp high resolution monitor (2048 x 2560 pixels) with a 10 bit gray scale display depth. The viewing conditions were evaluated as part of the departmental QC program and conformed to the acceptance limits.

The “score form CDMAM-phantom” (Appendix A) was used on which a viewer had to indicate the location of the eccentric disks. Previously marked sheets were immediately removed to minimise learning effects. Each viewer evaluated each image three times (total of 30 scores per viewer) in six (6) to nine (9) viewing sessions depending on the time constraints of the individual viewers. The researcher presented each image using one of the ten processing options to the individual observers in a random order. In order to assure objectivity of the viewers, the viewers were blinded to the processing option. The viewers were allowed freedom to adjust window width and window level and magnification, as this type of image enhancement should be performed in mammography soft-copy viewing. No time restriction was placed on the viewing and evaluation of an image.

4.3.5 Evaluation of the viewer’s observations

The indicated positions of the eccentric disks on the score form were compared to the true disk-positions in the phantom using the “evaluation form CDMAM-phantom” (Appendix B). To evaluate the observations, certain rules (correction scheme) were applied taking into account the 4 nearest neighbors of the field under examination (ARTINIS, 2007:9). There are three possibilities for each observation: the eccentric disk was indicated in the true position (T), the eccentric disk was indicated at a false position (F) or the eccentric disk was not indicated at all (N). The two main rules applied in the correction scheme were: A True needed two or more correctly indicated nearest neighbours to remain a True and a False or not indicated disk was

considered as True when it had 3 or 4 correctly indicated nearest neighbours. Exceptions to the two main rules apply only in the corners of the phantom.

4.3.6 Image quality quantification

Image quality is quantified by using the Image Quality Figure (IQF) method which is defined as (ARTINIS, 2007:12)

$$IQF = \sum_{i=1}^{16} Ci \; x \; D_{i,min}$$

where $D_{i,min}$ denotes the smallest diameter in the contrast-column, Ci . Summation over all contrast-columns yields the IQF. A low IQF indicates a high image quality. A completely invisible column will results in a $D_{i,min}$ of 4.00mm and a completely visible column will result in a $D_{i,min}$ of 0.10mm.

4.3.7 Data analysis

Data capturing was done by the researcher onto an Excel spreadsheet. The mean IQF for the different image processing options was calculated for all the viewers combined. Because four viewers scored each processing option three times, the mean IQF score for each processing option represents an averaged value of the assessed image quality for that processing option. A comparison of the IQF for the different processing options was performed. The study was not designed for analysis of the IQF for different viewers. The total ranked order of the processing options (based on the order of the IQF of all viewers) was also calculated. As this was not a preference study (whereby viewers placed the images in a ranked order from best to worst), the processing options were ranked by the researcher in terms

of their IQFs. The processing option with the lowest (best) IQF was ranked one (per individual viewer), whereas the one with the highest (worst) IQF score was ranked ten (per individual viewer). The best total rank score for four viewers could thus be four and the worst score could be forty and the best mean rank score for the four viewers could be one and the worst mean rank score could be ten.

4.3.8 Statistical analysis

The results were summarised using the means, standard deviation (SD) and ranked means of the IQF for all viewers for each processing option. Statistical comparisons between processing options were done using paired t-tests. Differences were considered statistically significant if the p-value was < 0.05.

4.4 RESULTS

The mean IQF for the different processing options are given in Table 4.2.

Table 4.2: Mean IQF (all viewers) for the different processing options

		PROCESSING OPTIONS									
		Unprocessed Invert	**Unprocessed**	**MUSICA² Invert**	**MUSICA²**	**(default) 64/256/1.5/1**	**CLAHE** 64/256/**3**/1	**CLAHE 128**/256/1.5/1	**CLAHE** 64/**384**/1.5/1	**CLAHE** 64/256/1.5/**2**	**CLAHE** 64/256/1.5/**0**
Viewer 1	Batch 1	51.8	64.8	60.7	54.3	66.6	67.3	59.6	65.4	62.9	57.3
	Batch 2	57.5	57.5	59.6	60	59.5	61.9	62.4	62.9	58.7	63
	Batch 3	59.7	51.9	57.8	58.1	58.7	58.2	53.2	53.3	62.5	55.7
Viewer 2	Batch 1	50.2	65.3	51.5	55.6	63.2	65.3	66.2	55.6	63.8	63.7
	Batch 2	45.1	53.9	50.5	48.9	56.1	54.3	52.7	55.3	57.1	58.3
	Batch 3	45.1	57.1	48.2	47.5	57.4	65.3	51.3	52.8	52.5	58.7
Viewer 3	Batch 1	56.7	58.8	51.8	50.2	63.7	57.9	59.9	55.2	58.5	57.9
	Batch 2	53	50.7	58.9	57	54.8	59.1	58.3	58.3	54.1	52.6
	Batch 3	41.9	53.6	53	50.7	55.9	57.1	47.1	47.5	43.1	51.7
Viewer 4	Batch 1	52.2	54.7	53.6	55.1	58	61.2	53	60.3	55.5	65.6
	Batch 2	42.9	53	52.8	56.7	56.6	57.1	55.6	58.1	60.8	62.5
	Batch 3	56.8	55.8	51	59.3	60.3	61.2	56.4	54.3	56.2	60.9
MEAN (All viewers)		**51.1**	**56.4**	**54.1**	**54.5**	**59.2**	**60.5**	**56.3**	**56.6**	**57.1**	**59**
Standard Deviation		**3.9**	**2.3**	**4**	**3.3**	**1.6**	**2**	**1.6**	**3.1**	**3.9**	**3.7**

A low IQF indicates a high image quality

Standard deviation calculated for average IQF scores of the different viewers

From Table 4.2 it can be seen that the mean IQF (all viewers) ranged from 51.1 - 60.5 between the different processing options and the standard deviation (SD) amongst the viewer's mean IQFs, ranged from 1.6 to 4.

The processing option with the best (lowest) mean IQF (all viewers) was Unprocessed Invert (51.1) followed by MUSICA^2 Invert (54.1) and MUSICA^2 (54.5). Unprocessed and CLAHE (**128**/256/1.5/1) (larger contextual region compared to the default), had the next best mean IQFs of 56.4 and 56.3 respectively. The greatest variation in mean IQF between all viewers' mean IQFs was seen with MUSICA^2 Invert (4) but none the less it had the second best (second lowest) average IQF of 54.1. Table 4.3 shows the p-values indicating significance of the paired differences between the different processing options.

Table 4.3: p-Values indicating significance of the paired differences between the different processing options

	Unprocessed Invert	Unprocessed	MUSICA^2 Invert	MUSICA^2	**CLAHE (default) 64/256/1.5/1**	**CLAHE** 64/256/**3**/1	**CLAHE 128**/256/1.5/1	**CLAHE** 64/**384**/1.5/1	**CLAHE** 64/256/1.5/**2**	**CLAHE** 64/256/1.5/**0**
Unprocessed Invert	–	0.0989	**0.0069**	0.0616	**0.0106**	**0.0160**	0.0516	**0.0153**	0.0564	0.0717
Unprocessed		–	0.3787	0.4414	0.0516	**0.0045**	0.8678	0.9305	0.6527	0.2916
MUSICA^2 Invert			–	0.8416	**0.0383**	**0.0487**	0.2773	0.1801	0.2679	0.2208
MUSICA^2				–	**0.0457**	**0.0402**	0.3507	0.0768	0.2270	0.1081
CLAHE (default) 64/256/1.5/1					–	0.1248	**0.0015**	0.0793	0.2300	0.9122
CLAHE 64/256/**3**/1						–	**0.0028**	**0.0456**	0.0536	0.4334
CLAHE 128/256/1.5/1							–	0.8349	0.5946	0.2746
CLAHE 64/**384**/1.5/1								–	0.6292	0.2887
CLAHE 64/256/1.5/**2**									–	0.3548
CLAHE 64/256/1.5/**0**										–

The values in **bold** indicate the rows are significantly better than the columns

The values in ***italic bold*** indicate the rows are significantly worse than the columns

Unprocessed Invert:

It was found that Unprocessed Invert was statistically significantly superior ($p<0.05$) to MUSICA^2 Invert ($p = 0.0069$) and three of the CLAHE parameter combinations namely: default CLAHE (**64/256/1.5/1**) ($p = 0.0106$), CLAHE (64/256/**3**/1) (higher clip limit) ($p = 0.0160$) and CLAHE (64/**384**/1.5/1) (larger NBins) ($p = 0.0153$).

MUSICA^2 Invert:

MUSICA^2 Invert is the processing option with the second best (lowest) IQF (54.1) and was significantly superior to default CLAHE (**64/256/1.5/1**) ($p = 0.0383$) and CLAHE (64/256/**3**/1) (higher clip limit) ($p = 0.0487$) but significantly inferior to only Unprocessed Invert ($p = 0.0069$). No significant difference was seen between MUSICA^2 Invert and MUSICA^2 ($p = 0.8416$).

MUSICA^2:

The image processing option with the third best IQF was MUSICA^2 (54.5). As with MUSICA^2 Invert, a significant superior IQF was seen for MUSICA^2 when compared to that of default CLAHE (**64/256/1.5/1**) ($p = 0.0457$) and CLAHE (64/256/**3**/1) (higher clip limit) ($p = 0.0402$). MUSICA^2 was however close to significantly inferior to Unprocessed Invert ($p = 0.0616$). No significant difference was seen between MUSICA^2 and Unprocessed ($p = 0.4414$) or between MUSICA^2 and MUSICA^2 Invert ($p = 0.8416$).

Unprocessed:

Unprocessed was significantly superior to CLAHE (64/256/**3**/1) (higher clip limit) ($p = 0.0045$) and close to significantly superior to default CLAHE (**64/256/1.5/1**) ($p = 0.0516$). Although CLAHE (**128**/256/1.5/1) (larger contextual region) had a slightly

higher (better) IQF (56.3) compared to Unprocessed (56.4), no significant difference was seen between the two (p = 0.8678).

CLAHE parameter combinations:

Of the six parameter combinations evaluated, CLAHE (**128**/256/1.5/1) (larger contextual region) showed the best (lowest) IQF (56.3) and was significantly superior to default CLAHE (**64/256/1.5/1**) (p = 0.0015) and CLAHE (64/256/**3**/1) (higher clip limit) (p = 0.0028). CLAHE (64/**384**/1.5/1) (larger NBins) showed the second best (lowest) IQF (56.6) of the six CLAHE parameter combinations but was only significantly superior to CLAHE (64/256/**3**/1) (higher clip limit compared to the default) (p = 0.0456). The two processing options with the worst (highest) IQF was CLAHE (64/256/**3**/1) (higher clip limit compared to the default) (60.5) followed by default CLAHE (**64/256/1.5/1**) with an IQF of 59.2. However, no significant difference was seen between the latter two (p = 0.1248). CLAHE (64/256/**3**/1) (higher clip limit) was significantly inferior to CLAHE (**128**/256/1.5/1) (larger contextual region) (p = 0.0028) and CLAHE (64/**384**/1.5/1) (larger NBins). CLAHE (64/256/**3**/1) (higher clip limit) is also the only CLAHE parameter combination which was significantly inferior to all the non-CLAHE processing options. In terms of different map levels, no significant difference was seen between any of the different map levels (p = 0.2300) (p = 0.9122) and (p = 0.3548).

In Table 4.4 the total and mean rank scores for the different processing options can be seen.

Table 4.4: Mean and total rank scores for the different processing options

	Viewer 1	Viewer 2	Viewer 3	Viewer 4	TOTAL RANK SCORE	MEAN RANK SCORE	DIFFERENCE BETWEEN HIGHEST AND LOWEST RANK SCORE
Unprocessed Invert	1	1	1	1	**4**	**1**	**0**
MUSICA^2	2	3	3	5	**13**	**3.25**	**3**
MUSICA^2 Invert	6	2	7	2	**17**	**4.25**	**5**
Unprocessed	3	7	6	3	**19**	**4.75**	**4**
CLAHE 128/256/1.5/1	4	5	8	4	**21**	**5.25**	**4**
CLAHE 64/**384**/1.5/1	7	4	4	7	**22**	**5.5**	**3**
CLAHE 64/256/1.5/**2**	8	6	2	6	**22**	**5.5**	**6**
CLAHE 64/256/1.5/**0**	5	9	5	10	**29**	**7.25**	**5**
CLAHE 64/256/1.5/1 (default)	9	8	10	8	**35**	**8.75**	**2**
CLAHE 64/256/**3**/1	10	10	9	9	**38**	**9.5**	**1**

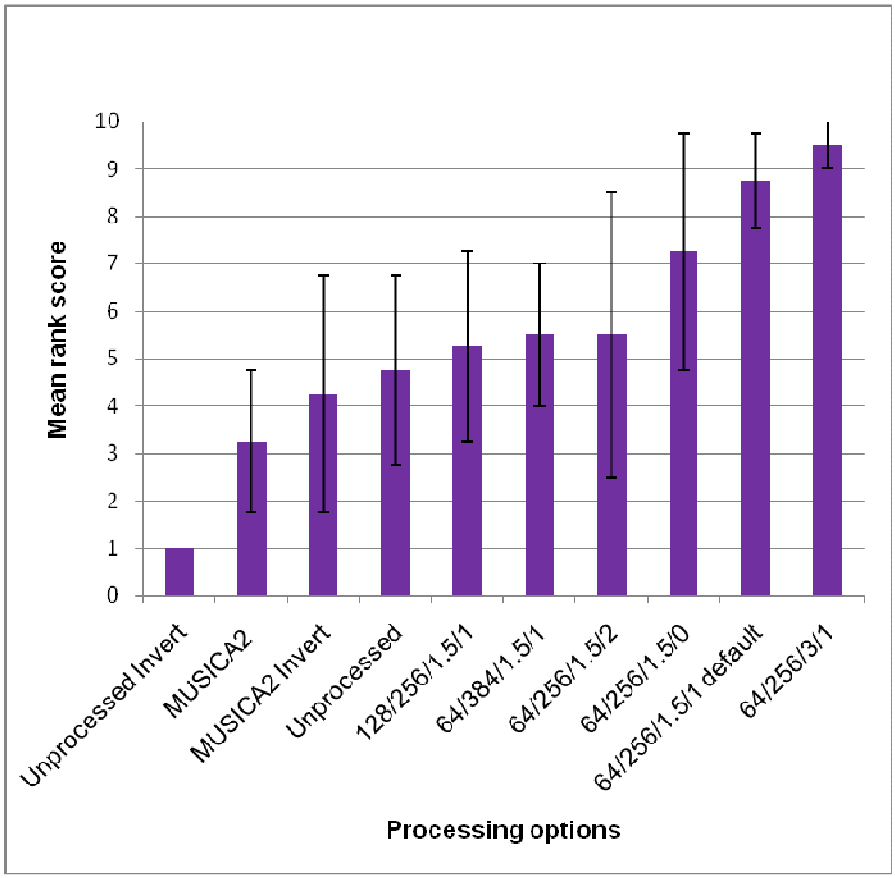


Figure 4.3: Mean rank score for the different processing options

Bars indicate the difference between the highest and lowest rank score between the viewers

From Figure 4.3 it can be seen that Unprocessed Invert showed the best mean rank score (1) (based on lowest (best) IQF score by all viewers. The second best mean rank was seen for MUSICA^2 (3.3), followed by MUSICA^2 Invert (4.3) and Unprocessed (4.8). The processing options with the worst mean rank scores were CLAHE (64/256/**3**/1) (higher clip limit) (9.5) and default CLAHE (**64/256/1.5/1**) (8.8). The largest difference in the next best mean rank score was seen between Unprocessed Invert (1) and MUSICA^2 (3.3).

Table 4.5: Comparison of position based on IQF and mean rank score

Processing option	IQF	Position based on IQF	Position based on mean rank score
Unprocessed Invert	**51.1**	**1**	**1**
MUSICA^2 Invert	**54.1**	**2**	**3**
MUSICA^2	**54.5**	**3**	**2**
CLAHE **(128**/256/1.5/1**)**	**56.3**	**4**	**5**
Unprocessed	**56.4**	**5**	**4**
CLAHE **(**64/**384**/1.5/1**)**	**56.6**	**6**	**6**
CLAHE **(**64/256/1.5/**2)**	**57.1**	**7**	**6**
CLAHE **(**64/256/1.5/**0)**	**59.0**	**8**	**8**
CLAHE default **(64/256/1.5/1)**	**59.2**	**9**	**9**
CLAHE **(**64/256/**3**/1**)**	**60.5**	**10**	**10**

A number of processing options kept their sequence in both IQF and mean rank scores (see Table 4.5). These options are: Unprocessed Invert (position 1), CLAHE (64/256/1.5/**0**) (No map level – canonical CLAHE) (position 6), (**64/256/1.5/1** default) (position 9) and (64/256/**3**/1) (higher clip limit) (position10). The other options only changed by one position. The processing options with which a change in sequence was seen are: MUSICA^2 and MUSICA^2 Invert swapped positions two and three, CLAHE (**128**/256/1.5/1) (larger contextual region) and Unprocessed swapped positions four and five. CLAHE (64/256/1.5/**2**) (higher map level) improved by one position in mean rank score to share the same sixth position as CLAHE (64/**384**/1.5/1) (larger NBins).

4.5 DISCUSSION

4.5.1 Unprocessed and Unprocessed Invert

With the phantom study it was found that Unprocessed Invert showed the best image quality of the CDMAM phantom image with a significantly lower (better) IQF ($p < 0.05$) compared to MUSICA^2 Invert and three of the CLAHE parameter combinations. The European protocol for the quality control of the physical and technical aspects of mammography screening specifies the use of the CDMAM phantom and for current measures of image quality the unprocessed images of the phantom are used (Warren *et al*, 2012). Although no significant difference between Unprocessed Invert and Unprocessed was found in our study, better image quality was found for Unprocessed Invert. Based on the results of our study, we recommend the use of Unprocessed Invert as the processing option to obtain the best image quality of the phantom image.

The characteristics of the Unprocessed image are: wide latitude, digital signals proportional to the detector exposure or the logarithm of exposure and very low contast (Bushberg *et al*, 2012:268). Our results suggest that the signal is well preserved in the Unprocessed Invert image and that the contrast that the viewers were able to obtain with manual window width and window level adjustments was adequate.

4.5.2 MUSICA^2 and MUSICA^2 Invert

The MUSICA^2 processing algorithm was developed for mammography and focuses on the enhancing of low contrast structures at the expense of high contrast structures in the breast which will remain clearly visible even if their contrast is

somewhat reduced (Schaetzing, 2007). In this part of our study MUSICA^2 Invert showed the second best image quality of the phantom image followed by MUSICA^2. As no significant difference was found between Unprocessed and both MUSICA^2 Invert and MUSICA^2 and Unprocessed Invert was found to be significantly superior to MUSICA^2 Invert and close to significantly superior to MUSICA^2, the indications are that the enhancement of lower contrast structures at the expense of high contrast structures does not improve image quality for the phantom image. This could well be explained by the more 'homogeneous' background of the phantom image compared to the background of normal breast structure (Warren *et al*, 2012). When exposed to x-rays, the phantom background will cause less variation in intensities distribution reaching the image receptor. Compared to intensity distribution of a normal breast structure, the intensity distribution is thus smaller and therefore possibly rendering the aim of the processing algorithm less beneficial. The situation might well be different with an image with normal breast structure as background.

4.5.3 Invert

The invert of an image was described as useful in mammography to enhance white or grey detail embedded in dark regions of an image especially in predominantly black areas (Gonzales & Woods, 2008:108-109). The invert can potentially make the visibility of breast tissue more conspicuous to the viewer. With the phantom study it was found that although MUSICA^2 Invert showed a slightly lower (better) IQF compared to MUSICA^2, the difference between the two was not significant ($p = 0.8416$). Also, although Unprocessed Invert showed a better image quality compared to Unprocessed, no significant difference was seen ($p = 0.0989$). Thus although not significant, the indications from the ranking method used were that the invert of the image did provide better image quality. With normal breast structure

background in a mammogram image, different results might be obtained on clinical images.

4.5.4 CLAHE parameter combinations

The CLAHE processing algorithm is influenced by different parameters each contributing to image quality in a different manner (Mathworks, 2011). Of the six CLAHE parameter combinations evaluated in the phantom study, the combination with the larger contextual region CLAHE (**128**/256/1.5/1) showed the best image quality with the phantom image. The fact that the best image quality (lowest IQF score) amongst the six CLAHE parameter combinations evaluated in this study, is not seen for the default CLAHE (**64/128/1.5/1**), pointed to the possibility that the default parameter combination can be improved. The default CLAHE had the second highest (worst) IQF score although the only significant difference between the default CLAHE and the other five CLAHE parameter combinations, was seen with CLAHE (**128**/256/1.5/1) ($p = 0.0015$).

4.5.4.1 Contextual region

The contextual region dimension controls the size of the individual blocks in which the local histograms are computed (Mathworks, 2011). The smaller the block size, the tighter control of the local histogram data, but this also leads to local 'noise' because of poor histogram discrimination. The fact that larger contextual region CLAHE (**128**/256/1.5/1) produced better image quality compared to default CLAHE, might thus have been because less local noise was produced which improved image quality.

4.5.4.2 NBins

The NBins represents the number of gray scale levels used to re-bin the histogram data (Mathworks, 2011). It can thus be expected that the larger number of bins will improve image quality because the higher the number, the higher the precision of remapping pixel values. However in this part of the study, no significant difference was seen for the parameter combination with a larger NBins CLAHE (64/**384**/1.5/1) compared to the default CLAHE ($p = 0.0793$). It can be argued that because of the homogenous background of the phantom, the use of a larger number of bins did not contribute to image quality because the small distribution of intensities in the phantom background was well displayed in the smaller number of bins available in default CLAHE. Different results might however be obtained on clinical images.

4.5.4.3 Clip limit

Clip limit allows a deviation from a flat histogram to be allowed. This is in effect a measure of the maximum slope allowed in the cumulative histogram (Mathworks, 2011). A higher clip limit will thus result in more contrast but will also lead to more perceivable boundaries between the blocks. Although no significant difference between default CLAHE and CLAHE (64/256/**3**/1) (higher clip limit) was found ($p = 0.1248$) in this part of the study, the higher clip limit showed significantly lower image quality compared to CLAHE (**128**/256/1.5/1) (larger contextual region) ($p = 0.0015$) and CLAHE (64/**384**/1.5/1) (larger NBins) ($p = 0.0456$). Our results implied that a higher clip limit (higher contrast) does not contribute to better image quality of the phantom image. The effect on clinical images might well be different.

4.5.4.4 Map level

The study found no significant difference between the CLAHE processing options with different map levels. A map level value of greater than "0" allows iSite to use iSyntax lower resolution data to calculate histograms, which is faster than working from a full resolution image and still very accurate (Mathworks, 2011). The final re-mapping of pixel data still happens on full resolution bitmap. The aim of a map level is to enable the system to generate the required internal look-up tables (LUT's) from lower levels in the wavelet representation and thereby incurring a much lower computational load. It is however expected to give effectively identical results (Mathworks, 2011). The evaluation of the effect of computation load on the time used for image processing was not in the scope of the study.

4.5.5 Comparison of mean IQF scores and rank order of processing options

It can be argued that the mean rank order in which the processing options were placed by the researcher according to the rank scores by the individual viewers, is less precise than the calculated mean IQF for all viewers. It was however used where no significant difference in mean IQF between two next best processing options was found. No significant difference in IQF ($p = 0.8416$) was found between MUSICA^2 and MUSICA^2 Invert, although MUSICA^2 Invert had a slightly lower (better) IQF. In the rank scores however, the two swapped positions (position 2 and position 3) but a larger difference between the highest and lowest rank scores of the individual viewers were seen for MUSICA^2 Invert (five positions difference compared to three positions for that of MUSICA^2).

It was also seen that although CLAHE (**128**/256/1.5/1) (larger contextual region) had a slightly lower (better) IQF compared to Unprocessed, the difference was not

significant (p = 0.0878). In the rank scores, Unprocessed lies one position higher (position 4) compared to that of CLAHE (**128**/256/1.5/1) (larger contextual region) (position 5) and both showed four positions between the highest and lowest rank scores by the individual viewers. In other words, very little difference in apparent image quality between the two were found, however with the rank scores, Unprocessed is favoured compared to CLAHE (**128**/256/1.5/1) (larger contextual region).

No studies were found (see Appendix V) in which the effect of MUSICA^2 on image quality or accuracy was evaluated. Pisano *et al* (1998) investigated the effect of CLAHE parameter combination on the detection of simulated spiculations. They found that the relation of the parameters region size and clip limit can significantly influence the detection of simulated spiculations. Two combinations were found to improve detection namely: region size 32, clip limit 2 (mean difference in Theta scores: 0.061, p = 0.0001), and region size 32, clip limit 4 (mean difference in Theta scores: 0.053, p = 0.0001). On the other hand it was found that the combination of region size 2, clip limit 16 adversely affected detection. This study supports the finding that the parameter combination of region size and clip limit can significantly influence image quality. We found that a higher clip limit (3) alone (CLAHE 64/256/**3**/1 compared to CLAHE **default 64/256/1.5/1**) did not significantly change image quality (p = 0.1248). However a combination with a larger contextual region (128) and lower clip limit (1.5) CLAHE (**128**/256/1.5/1) showed significantly lower image quality compared to a combination with a smaller contextual region (64) and a higher clip limit (3) CLAHE (64/256/**3**/1) (p=0.0015).

Hemminger and co-workers (2001) investigated the effect of CLAHE on the detection of simulated masses and found no combination of CLAHE parameters (contextual

region and clip limit) to improve detection of masses. Our study also found no significantly better image quality for any of the CLAHE parameter combinations compared to Unprocessed.

In a preference study by Sivaramakrishna *et al* (2000) they compared the performance of CLAHE and three other processing options with unprocessed. They reported that unenhanced images were mostly preferred (58%) for masses. Our results found significantly superior image quality with the Unprocessed Invert image. Sivaramakrishna and co-workers also reported that suitable image processing can improve the visibility of microcalcifications. However, they found that processing options that changed image appearance considerably (like CLAHE), are least preferred by radiologists. In our study, the CLAHE parameter combinations with the higher clip limit (64/356/**3**/1) showed significantly lower image quality compared to Unprocessed, Unprocessed Invert, MUSICA^2 and MUSICA^2 Invert.

4.6 CONCLUSION

Different anatomical backgrounds in mammograms are known to influence cancer detection differently. Therefore the image quality findings with the CDMAM phantom are not necessarily an accurate forecaster of image quality in clinical images. A recent UK study investigated the relationship between CDMAM threshold gold thickness (for the 0.1 and 0.25mm disc diameters) and reader performance in the detection of microcalcifications (Warren *et al*, 2012). Although their results have found a lower threshold gold thickness to be a good predictor for the detection of microcalcifications, it is not necessarily related to the ability of the reader to detect masses. The results of the phantom study are thus not conclusive for the complete mammography task and can therefore not replace a clinical study.

A recommendation had to be made on which processing options to be evaluated using clinical images for the training and development of the viewing protocol. Based on providing the best image quality on phantom images, it was decided that Unprocessed Invert, MUSICA^2 Invert, and MUSICA^2 were obvious choices for inclusion. Selecting from CLAHE (**128**/256/1.5/1) (larger contextual region) and Unprocessed, it was decided to include Unprocessed for evaluation on clinical images. This decision was taken upon the assumption that the default CLAHE parameter combination can be improved. Also, because Unprocessed produced very similar image quality to CLAHE (**128**/256/1.5/1), it was decided to rather include Unprocessed for evaluation on clinical images. Furthermore, it seemed to make sense to include two matched processed and invert processed pairs.

In the next chapter the image quality of clinical images will be assessed with the four processing options identified above. The soft-copy viewing protocol will be developed through participative learning of a group of radiologists.

CHAPTER 5

DEVELOPING THE SOFT-COPY VIEWING PROTOCOL THROUGH PARTICIPATIVE LEARNING

5.1 INTRODUCTION

In Chapter 3, the challenges for radiologists changing from SFM to DM were identified from the literature and training needs were identified. In this chapter the training offered to a group of radiologists in order to address the challenges of changing from SFM to DM, will be detailed. Also, the participative learning approach to develop the viewing protocol will be presented. In Chapter 2 evidence was presented that the optimum processing algorithm for DM has not yet been found. The processing options for clinical evaluation through participative learning in this part of the study were the four identified in Chapter 4 (with the aid of the phantom study) namely: Unprocessed Invert, MUSICA^2 Invert, MUSICA^2 and Unprocessed.

It is generally accepted that the early detection and diagnosis of breast cancer is critically dependent on image quality (Ikeda, 2011: 1). The advantages of measuring image quality with a phantom image (Chapter 4) include amongst others: repeatability, accuracy and efficient simple evaluation. Although a CD phantom can be useful in verifying how accurately test objects with various sizes and attenuation characteristics appear in a processed image, the CD phantom results are no substitute for clinical images. They can only point the way as they do not necessarily accurately predict the visibility of anatomical structures and lesions on a mammogram image. The difference between the homogeneous phantom

background and the heterogeneous mammographic background is one of the contributing factors to this effect (Bosmans *et al*, 2006). This emphasises the importance of evaluating image quality on clinical images and is the motivation for the use of clinical images in the development of the viewing protocol in this part of the study.

5.2 AIM

The aim of this part of the study was to develop the viewing protocol through participative learning using the findings of the phantom study.

5.3 METHODS

5.3.1 Ethics

Approval from the Ethics committee of the Faculty of Health Sciences was obtained - ETOVS number 39/08 (see Appendix C). Approval was also obtained from the CEO of the hospital (see Appendix D), the Head of the Department of Radiology (see Appendix E) and the Radiation Control Committee (see Appendix F). An information document regarding the proposed study was available to all patients in one of three languages namely English, Afrikaans and Southern Sotho (see Appendix G). Written consent was obtained from patients willing to participate in the research study by the radiographer performing the mammograms (see Appendix H). Permission was sought from patients to include their mammogram images, relevant information and histo-pathology results in the study. All patient identification was removed from the images and cases were assigned a number for future use.

5.3.2 Trainees

The trainees were the only three qualified radiologists from the department where the study was conducted that had not yet had exposure to digital mammography. None of them were working in the mammography unit on a permanent basis at the time of the study, although reporting the occasional mammogram (when the consultant radiologist responsible for mammography was not present) was part of their job description as consultant radiologists in the department. During their five year training in the specialised field of Diagnostic Radiology, they were exposed to SFM but none of them had previous experience in DM and they had not specifically been trained in this new modality. Their experience as qualified radiologists was one year, two years and five years respectively.

5.3.3 Training

The focus of the training in this study was aimed at providing the radiologists with knowledge and experience to be confident in using soft-copy display tools to improve the visibility of detail and possible lesions in a mammogram. The training of the group of radiologists was structured to include a theoretical and hands-on component, together with a participative learning component to develop the viewing protocol. The program outlining the training can be seen in Appendix I.

5.3.3.1 Theoretical training

A four hour theoretical training course was conducted by a Medical Physicist from the Department of Medical Physics and a Senior Lecturer from the Department of Diagnostic Radiology at the University of the Free State. The content covered the direct radiography and DM sections in Bushberg *et al* (2012:263-270) and the user manuals of the software that had to be demonstrated. The training was aimed at

addressing the needs for radiologists changing from SFM to DM identified in Chapter 3. The training was done with the use of the workstation and thus practically demonstrated. This was done by equipping the radiologist with the factual and conceptual knowledge and understanding of the following:

- The principles of image acquisition in DM
- The advantages and disadvantages of SFM and DM
- The challenges of soft-copy viewing
- The effect of image processing on image quality
- The importance of using tools for soft-copy viewing to achieve the full potential benefit of DM

5.3.3.2 Hands-on training

The Medical Physicist from the Department of Medical Physics and an application specialist for the Philips PACS conducted hands-on training for the viewers at the review station. The radiologists worked at the workstation to equip themselves with the necessary knowledge and skills to confidently use the tools for soft-copy viewing.

5.3.3.3 Participative learning

A participative learning approach was used to develop the viewing protocol. This term was used to describe the active involvement of the viewers in developing the soft-copy viewing protocol. The radiologists had to use the tools for soft-copy viewing to evaluate the image quality of clinical mammography images, processed with different processing options. By doing that they gained experience in the use of the tools for soft-copy viewing as they were exposed to the processed and unprocessed versions of the images. The results of the findings were to serve as the

pool of knowledge for the radiologists on soft-copy viewing in their specific clinical setting. After analysing the results of the participative learning process, the following questions had to be answered in order to establish the viewing protocol:

i) How do the image processing options compare in making anatomical structures visible to the viewer? This would determine the default processing option and whether different processing options should be used in the viewing protocol for viewing all breast anatomy.

ii) Are all anatomical structures equally visualised? This would sensitise the radiologist for possible areas which would need more attention in the viewing protocol.

iii) How do the image processing options compare in making calcifications visible to the viewer? This would determine if specific processing options should be used in the viewing protocol for the viewing of calcifications.

iv) How do the image processing options compare in making masses visible to the viewer? This would determine if specific processing options should be used in the viewing protocol for the viewing of masses.

v) How do the image processing options compare in the visibility of structured noise in a dense area in the breast (pectoral muscle region)? This would determine if a different processing option should be applied whenever excessive noise is apparent in an image.

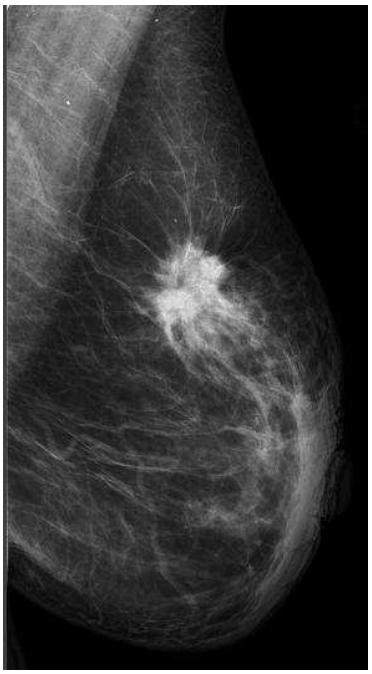
vi) Which processing option(s) is regarded as sufficient for the early detection of breast cancer? This would determine if different processing options should be used in the viewing protocol for a diagnostic mammogram or for “selective screening” performed in the department.

5.3.4 Clinical images

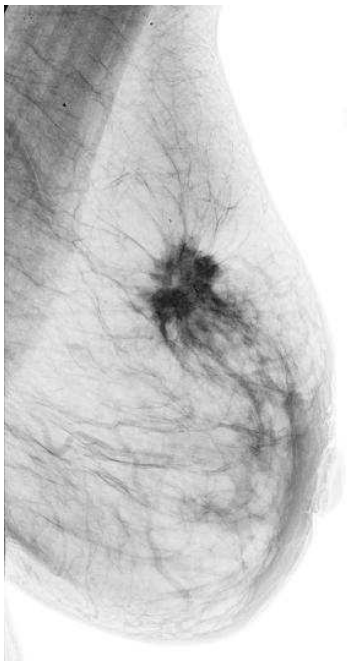
The dataset of clinical images used for the participative learning consisted of 36 medio-lateral oblique view (MLO) images selected retrospectively by the Consultant Radiologist responsible for mammography from routine cases performed in the department during the data selection period (see 6.3.1). Proper positioning of the breast was a prerequisite for inclusion in the dataset. The images were acquired with a GE Sonograph DMR and the image receptor was a mammography CR plate read by an Agfa CR reader set up for mammo readout. The MLO view was selected since it is widely used in single view mammography and it is the view which includes most of the breast tissue (Hemdal *et al*, 2005). The dataset of clinical images included both malignant and benign masses and calcifications. Malignancy was confirmed based on histo-pathology reports whereas normal or benign cases were considered confirmed if both the current and the previous mammogram were reported as benign**.** No clinical information or clinical history was made available to the viewers.

5.3.5 Processing options

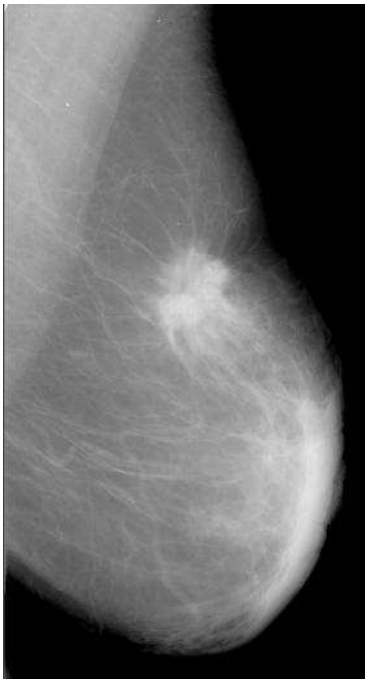
Each of the 36 images was presented with the four processing options: Unprocessed, Unprocessed Invert, MUSICA^2 and MUSICA^2 Invert (as found in Chapter 4 with the phantom study). The full dataset thus consisted of 144 images. Figure 5.1 shows a presentation of a MLO image with the four (4) different processing options and Figure 5.2 shows a zoomed image of a limited region with the four (4) different processing options.



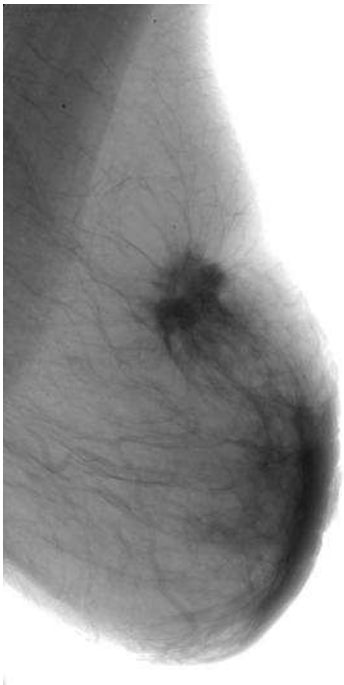
MUSICA^2



MUSICA^2 Invert

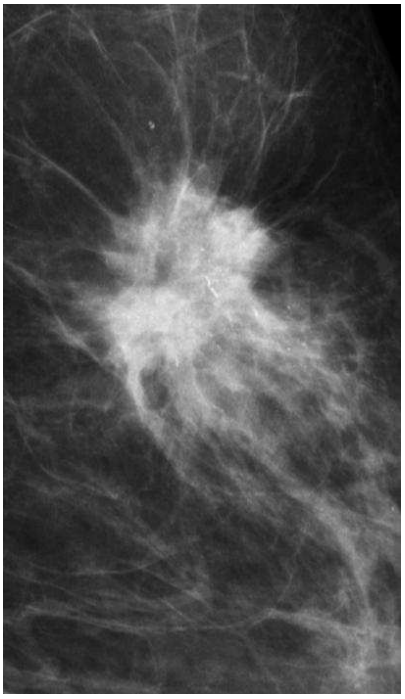


Unprocessed

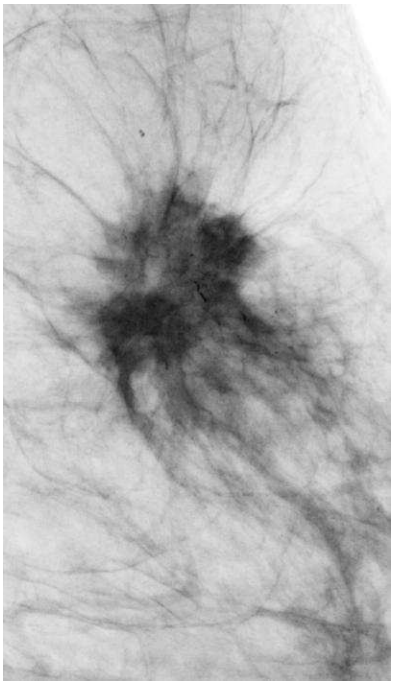


Unprocessed Invert

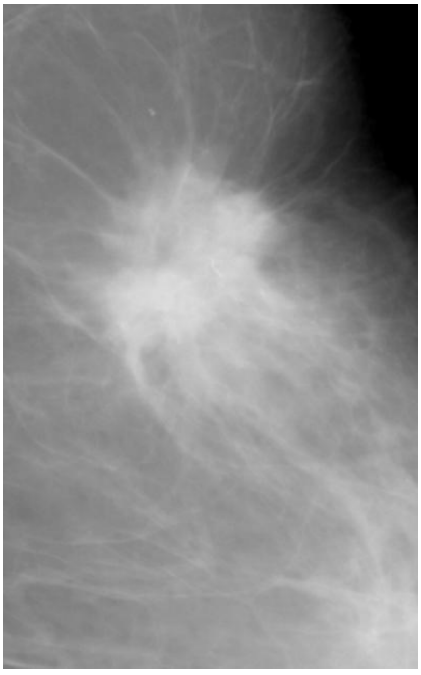
Figure 5.1: A MLO image presented with the different processing options



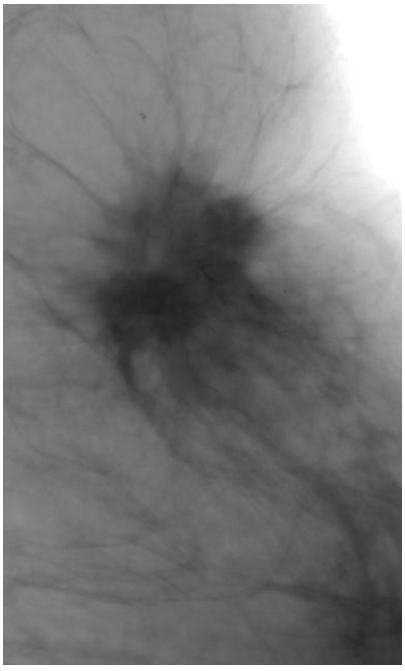
MUSICA^2



MUSICA^2 Invert



Unprocessed



Unprocessed Invert

Figure 5.2: A zoomed segment of a limited region of the image in fig 5.1 presented with the four different processing options

5.3.6 Criteria for the clinical evaluation of image quality

The revised European guidelines for the evaluation of image quality on DM images were used (Hemdal *et al*, 2005). Table 5.1 shows the image quality criteria included which the radiologists had to evaluate on the MLO projection. Criteria 1 – 8 referred to the reproduction of normal anatomical structures (skin outline, skin structure, pectoral muscle margin, vascular structures in dense parenchyma, vascular structures in fat tissue, the combination of all vessels, fibrous strands, and pectoral muscle margin, fibrous strands in fat tissue and glandular tissue). Criterion 9 and criterion 10 on the other hand referred to the evaluation of pathological structures (calcifications and masses). Two criteria were included to evaluate image quality aspects. These were: criterion 11 - Noise level in the reproduction of the pectoral muscle and criterion 12 – Evaluation of the sufficiency of image quality for the early detection of breast cancer.

Table 5.1: Image quality criteria for the MLO projection used for this research study

	IMAGE QUALITY CRITERIA USED IN THIS RESEARCH STUDY
	Reproduction of anatomical structures
1	Reproduction of skin outline
2	Reproduction of skin structure (rosettes from pores) along the pectoral muscle
3	Reproduction of pectoral muscle margin
4	Reproduction of vascular structures seen through most dense parenchyma
5	Reproduction of vascular structures in fat tissue
6	Reproduction of all vessels and fibrous strands and pectoral muscle margin
7	Reproduction of fibrous strands in fat tissue
8	Reproduction of glandular tissue
	Reproduction of calcifications and masses
9	Reproduction of calcifications, when present
10	Reproduction of masses, when present
	Imaging details
11	Noise level in the reproduction of the pectoral muscle
12	Is the image quality sufficient for early detection of breast cancer?

5.3.7 Rating method

A Likert like scale was used to score the image quality criteria for each image. From the recommendations of Hemdal *et al* (2005), the word 'clear' instead of 'visually

sharp' was used in the evaluation of the criteria. For the image quality for criteria 1 – 10, a five-point scale was provided: 1 definitely not clear, 2 almost definitely not clear, 3 probably clear, 4 almost completely clear and 5 completely clear. For criterion 11 (Noise level in the reproduction of the pectoral muscle), a three-point scale was provided: 1 Not seen, 2 Acceptable, 3 Unacceptable. For criterion 12 (Is image quality sufficient for early detection of breast cancer?) viewers were instructed to answer yes / no.

5.3.8 Display of the images

The images were archived onto a Philips PACS and reviewed on a workstation with a Matrox MED5Mp-DVI graphic card. The images were displayed on a Fimi (model MML2152) 5Mp high resolution monitor (2048 x 2560 pixels) with a 10 bit gray scale display depth. The researcher randomly displayed the images to each individual reader and no information on the processing option applied was given to the viewers.

5.3.9 Instructions to viewers

For each of the 144 images the radiologists had to fill in their judgement of the image quality for the set of image quality criteria on an evaluation form (Appendix J). They were instructed to use the zoom and roam function on all images as well as the function of manual intensity windowing. Each viewer received an information document on the image quality criteria (Appendix K). A copy of a MLO image was also supplied on which the anatomical areas were indicated where the different image quality criteria had to be scored (Hemdal *et al*, 2005). For criterion 12, the mammogram in its entirety had to be assessed.

5.3.10 Preliminary familiarisation of viewers with the study

Viewers were individually familiarised with the scoring of the image quality criteria. The preliminary cases consisted of five MLO views, which were not included in the image quality assessment study. The preliminary cases allowed the readers to become familiar with the data collection form and image quality rating scales. Upon completion of the preliminary cases, the viewers began with the actual image quality assessment.

5.3.11 Data analysis

Data capturing was done by the researcher onto an Excel spreadsheet. An image quality score (IQS) was calculated from the sum of the Likert like values for each of the eight criteria (anatomical structures) respectively, averaged over the three viewers. Mean scores (all viewers) for criteria 1-8 (anatomical structures) were also calculated for the different processing options. For criterion 9 (calcifications) and criterion 10 (masses), the image was not included in averaging if any of the three viewers indicated n/a (not applicable) on all four processing options (MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert). The mean scores of the image quality criteria were compared for the different image processing options, as well as for different criteria per processing option using paired samples t-test. Categorical variables (criterion 11 and criterion 12) of the four image processing options were compared using McNemar's test (Fleiss *et. al*., 2003:375). Differences were considered statistically significant if the p-value was < 0.05.

5.3.12 Feedback to the viewers

After analysing the results of the image quality evaluation obtained through participative learning, the researcher presented and thoroughly discussed the

outcomes with the viewers individually. This formed the pool of new knowledge they gained of soft-copy viewing with different processing options used in their clinical setting and which was used to establish the viewing protocol.

5.4 RESULTS

The participative learning was completed in an average of six (6) sessions per viewer in an average of eight hours fifteen minutes per viewer.

5.4.1 Image quality evaluation

The datasheets showing the raw data of all three viewers can be found in Appendix L.

5.4.1.1 Image quality evaluation – Overall anatomical structures (criteria 1-8)

The mean IQS (all viewers) per image quality criteria (1 - 8) and anatomical structures overall for MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert are shown in Table 5.2.

Table 5.2: Mean image quality score (IQS) (all viewers) per image quality criteria (1 – 8 anatomical structures) and anatomical structures overall for the different processing options

The image quality assessment criteria *were: 1 Skin outline, 2 Skin structure, 3 Pectoral muscle, 4 Vascular structures through dense parenchyma, 5 Vascular structures in fat tissue, 6 Vessels, fibrous strands and pectoral muscle, 7 Fibrous strands in fat, 8 Glandular tissue*

	Image quality assessment criteria									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Mean IQS**	**Standard Deviation**
MUSICA^2	4.8	4.1	4.7	2.9	4.8	4.2	4.7	4.7	**4.4**	0.6
MUSICA^2 Invert	4.9	3.9	4.7	2.9	4.7	4.2	4.7	4.7	**4.3**	0.4
Unprocessed	4.7	3.7	4.6	2.6	4.5	4.0	4.6	4.4	**4.1**	1.2
Unprocessed Invert	4.7	3.7	4.6	2.6	4.6	4	4.5	4.5	**4.2**	0.6

The processing options with the highest mean IQS (all viewers) for the anatomical structures were MUSICA^2 (4.4) followed by MUSICA^2 Invert (4.3), Unprocessed Invert (4.2) and Unprocessed (4.1). The standard deviation for mean IQS ranged from 0.4 (MUSICA^2 Invert) to 1.2 (Unprocessed). Although a slightly higher mean IQS for anatomical structures overall was found for MUSICA^2 compared to MUSICA^2 Invert, the invert image showed less variation amongst the viewers; MUSICA^2 Invert (0.4) compared to that of MUSICA^2 (0.6). Also a smaller standard deviation among the viewers was seen for Unprocessed Invert (0.6) compared to that of Unprocessed (1.2). The smallest standard deviation between the viewers was seen for MUSICA^2 Invert (0.4) whereas the largest variation between the viewers was seen for Unprocessed (1.2).

From Table 5.3 it can be seen that for the anatomical structures overall (criteria 1-8), no statistical significant difference was seen between the mean IQS for MUSICA^2 and MUSICA^2 Invert ($p = 0.8396$) or between that of Unprocessed and Unprocessed Invert ($p = 0.6902$). However, MUSICA^2 was significantly superior to Unprocessed ($p < 0.0001$) and Unprocessed Invert ($p < 0.0001$). MUSICA^2 Invert was also significantly superior to Unprocessed ($p < 0.0001$) and Unprocessed Invert ($p = 0.0003$).

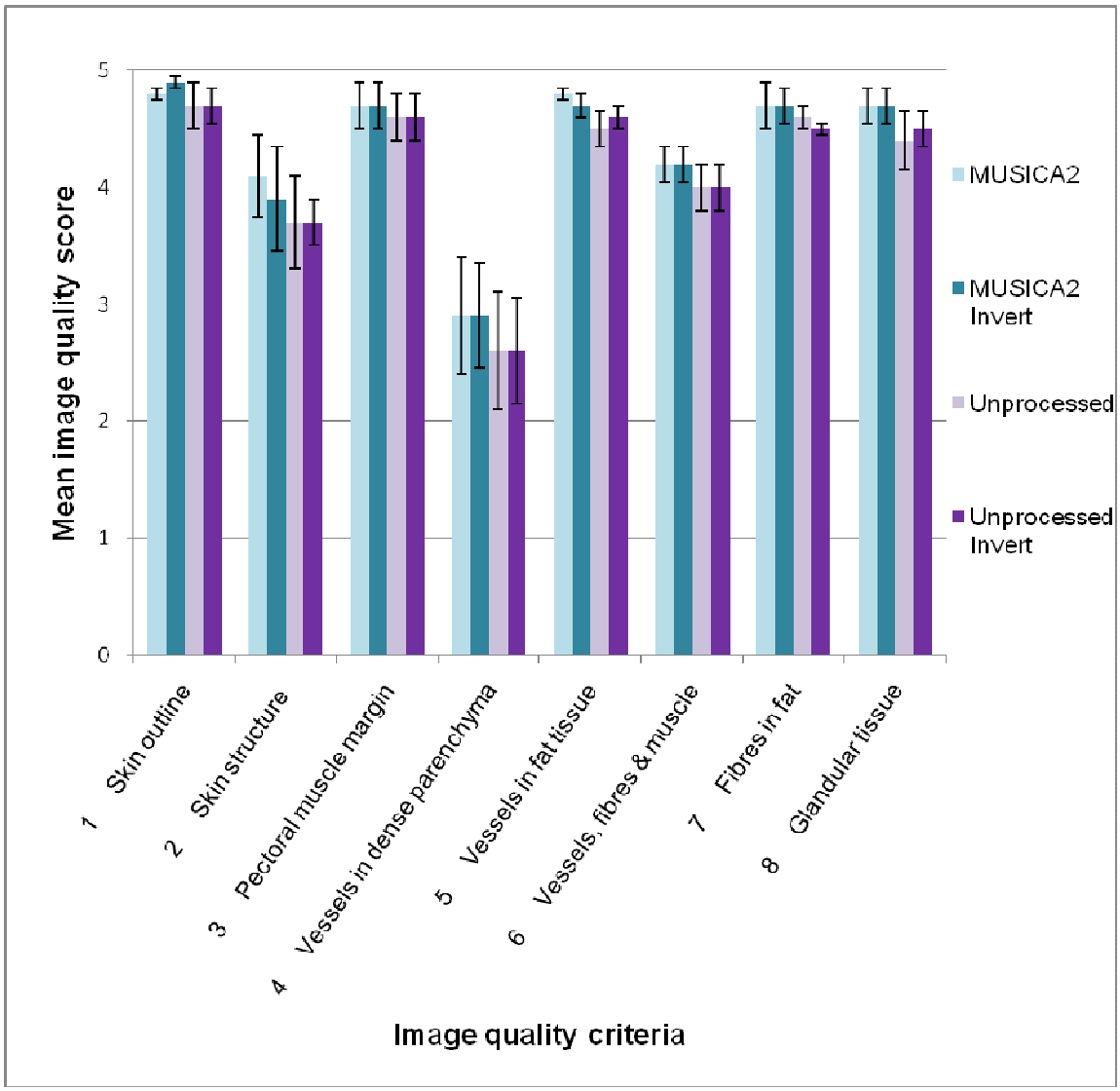
Table 5.3: p-Values indicating differences in the mean IQS (all viewers) for anatomical structures overall (criteria 1-8) between the processing options

	MUSICA^2 Invert	**Unprocessed**	**Unprocessed Invert**
MUSICA^2	0.8396	**<0.0001**	**<0.0001**
MUSICA^2 Invert		**<0.0001**	**0.0003**
Unprocessed			0.6902

(Values in bold indicate significant differences)

5.4.1.2 Image quality evaluation – Individual anatomical structures (criteria 1-8)

Figure 5.3 shows the mean IQS (all viewers) per individual anatomical structure (criteria 1-8). The p-values indicating differences in the mean IQS can be found in Appendix M.



(Bars indicate standard deviation for each processing option)

Figure 5.3: Mean IQS (all viewers) per individual anatomical structure (criteria 1 – 8)

From Appendix M it can be seen that the only single criterion for which a significant difference in mean IQS between MUSICA^2 and MUSICA^2 Invert was seen, was skin outline (criterion 1) where MUSICA^2 Invert was significantly superior ($p = 0.0263$). For pectoral muscle margin (criterion 3) no significant p-values were seen between any of the processing options ($p > 0.05$). Both MUSICA^2 and MUSICA^2 Invert showed significantly superior image quality compared to Unprocessed and Unprocessed Invert for four of the criteria: criterion 4 (Vessels in dense parenchyma) ($p = 0.0042$, $p = 0.0054$, $p = 0.0018$ and $p = 0.0016$ respectively); criterion 5 (Vessels in fat tissue) ($p = 0.0175$, $p = 0.0035$, $p = 0.0405$ and $p = 0.0112$ respectively); criterion 6 (Vessels, fibres and muscle) ($p = 0.0003$, $p = 0.0026$, $p = 0.0003$ and $p = 0.0026$ respectively) and criterion 8 (Glandular tissue) ($p = 0.0005$, 0.0071, $p = 0.0002$ and $p = 0.0195$ respectively). For criterion 7 (Fibres in fat), MUSICA^2 was also significantly superior to Unprocessed Invert ($p = 0.0114$) while MUSICA^2 Invert was significantly superior to both Unprocessed and Unprocessed Invert ($p = 0.0039$ and $p = 0.0086$ respectively). For criterion 2 (skin structure) only MUSICA^2 was significantly superior to Unprocessed ($p = 0.0001$) and Unprocessed Invert ($p = 0.0142$). No significant difference was seen between Unprocessed and Unprocessed Invert.

The p-values indicating differences in IQS between the individual anatomical structures for MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert can be seen in Appendix N. With all four processing options the image quality of vascular structures through dense parenchyma (criterion 4) was significantly inferior to all the other anatomical structures. The image quality of skin structure (criterion 2) was also significantly inferior to all but criterion 4 (vascular structures through dense parenchyma) for MUSICA^2 Invert and Unprocessed. The same was seen for

MUSICA^2 and Unprocessed Invert, except that no significant difference was seen between criterion 2 (skin structure) and criterion 6 (vessels, fibrous strands and pectoral muscle) p-values respectively (p = 0.1927 and p = 0.0531 respectively).

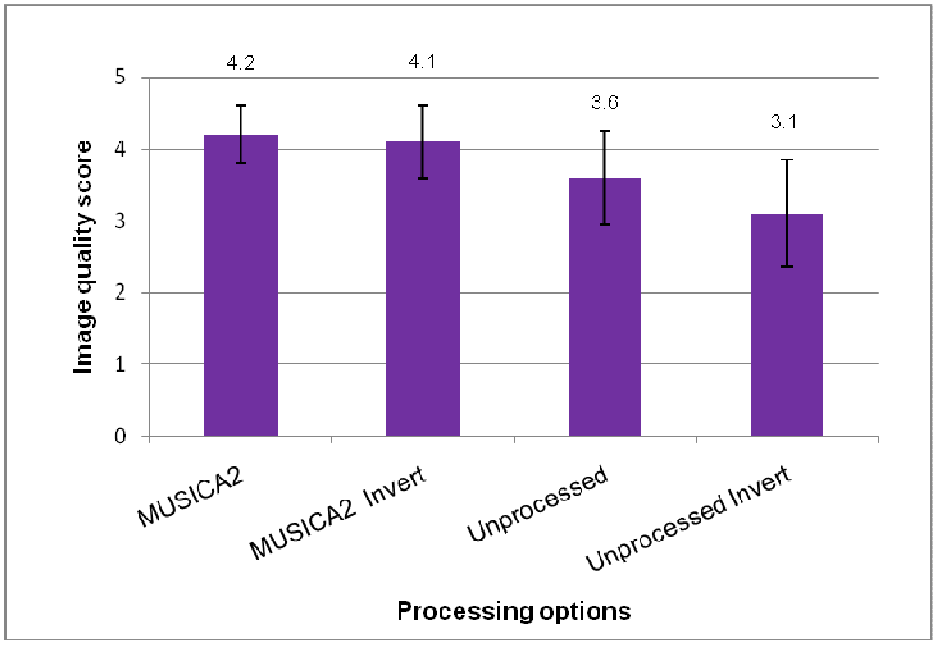
5.4.1.3 Image quality evaluation – Calcifications (criterion 9) and masses (criterion 10)

Table 5.4 shows the mean IQS (all viewers) for calcifications (criterion 9) and masses (criterion 10) for the processing options. Of the 36 images included in the dataset, 30 included calcifications and 20 included masses.

Table 5.4: Mean IQS (all viewers) for calcifications (criterion 9) and masses (criterion 10)

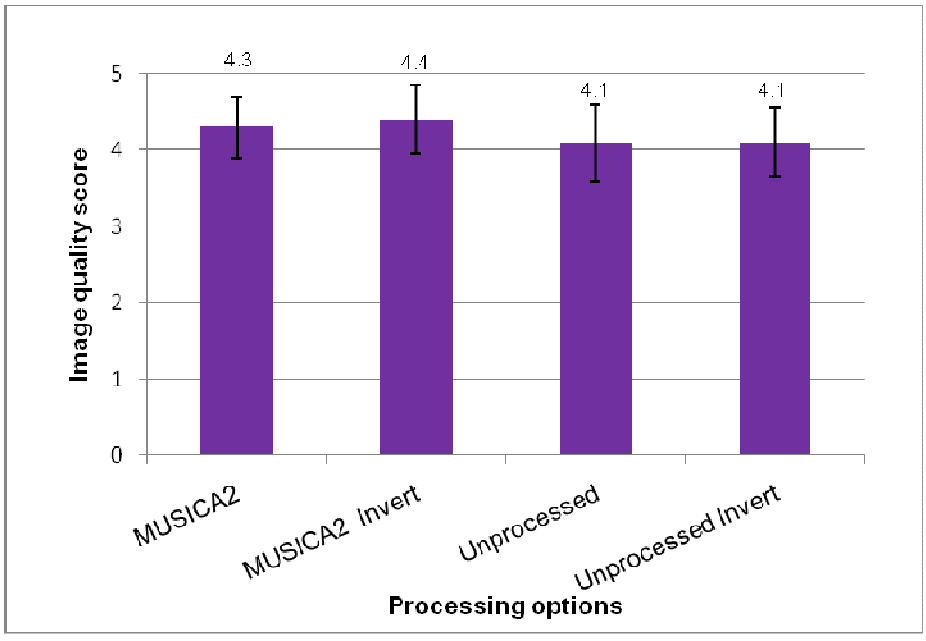
	Calcifications (n = 30)	(IQS) Standard Deviation	Masses (n = 20)	(IQS) Standard Deviation
MUSICA^2	4.2	0.8	4.3	0.8
MUSICA^2 Invert	4.1	1	4.4	0.9
Unprocessed	3.6	1.3	4.1	1
Unprocessed Invert	3.1	1.5	4.1	0.9

Figure 5.4 shows the mean IQS (all viewers) for calcifications (criterion 9) and Figure 5.5 shows that for masses (criterion 10).



(Bars indicate standard deviation for each processing option)

Figure 5.4: Mean IQS (all viewers) for calcifications (criterion 9)



(Bars indicate standard deviation for each processing option)

Figure 5.5: Mean IQS (all viewers) for masses (criterion 10)

From Figure 5.4 it can be seen that for calcifications MUSICA^2 showed statistically significant better image quality compared to both Unprocessed (p = 0.0066) and Unprocessed Invert (p = 0.0001) (see Table 5.5). Unprocessed Invert was significantly inferior to MUSICA^2 (p = 0.0001), MUSICA^2 Invert (p = 0.0003) and Unprocessed (p =0.0169) for calcifications. No significant difference was seen for calcifications between MUSICA^2 and MUSICA^2 Invert. From Figure 5.5 it can be seen that for masses (criterion 10) no significant differences were seen between any of the processing options (see Table 5.5).

Table 5.5: p-Values indicating differences in mean IQS (all viewers) for calcifications and masses (criteria 9 and 10) between the processing options

		Calcifications (criterion 9)	**Masses (criterion 10)**
MUSICA^2	**MUSICA^2 Invert**	0.5335	0.625
	Unprocessed	**0.0066**	0.3321
	Unprocessed Invert	**0.0001**	0.4652
MUSICA^2 Invert	**Unprocessed**	0.0688	0.1062
	Unprocessed Invert	**0.0003**	0.2146
Unprocessed	**Unprocessed Invert**	**0.0169**	0.7414

(Values in bold indicate statistically significant differences)

5.4.1.4 Image quality evaluation – Noise level in the reproduction of the pectoral muscle (criterion 11)

Figure 5.6(A-D) illustrates the noise level in the reproduction of pectoral muscle for the processing options. The only statistically significant difference between the

processing options was seen between MUSICA^2 and Unprocessed Invert (p = 0.0160) (see Table 5.6). With MUSICA^2 the noise level was acceptable to all three viewers in 97.2% (35/36) of cases, compared to 52.8% (19/36) with Unprocessed Invert. However, with Unprocessed Invert, the noise was not even seen by two viewers in 13.9% (5/36) of cases and not seen by one viewer in 30.6% (11/36) of cases.

Table 5.6: p-Values indicating differences in answers (criterion 11 and criterion 12) (all viewers) between the processing options

		Noise level in the reproduction of the pectoral muscle area (criterion 11)	Is the image quality sufficient for the early detection of breast cancer? (criterion 12)
MUSICA^2	**MUSICA^2 Invert**	0.611	0.2009
	Unprocessed	0.1062	**0.0003**
	Unprocessed Invert	**0.016**	**0.0005**
MUSICA^2 Invert	**Unprocessed**	0.2759	0.0699
	Unprocessed Invert	0.0756	**0.0116**
Unprocessed	**Unprocessed Invert**	0.3645	0.0848

The values in bold indicate statistically significant differences

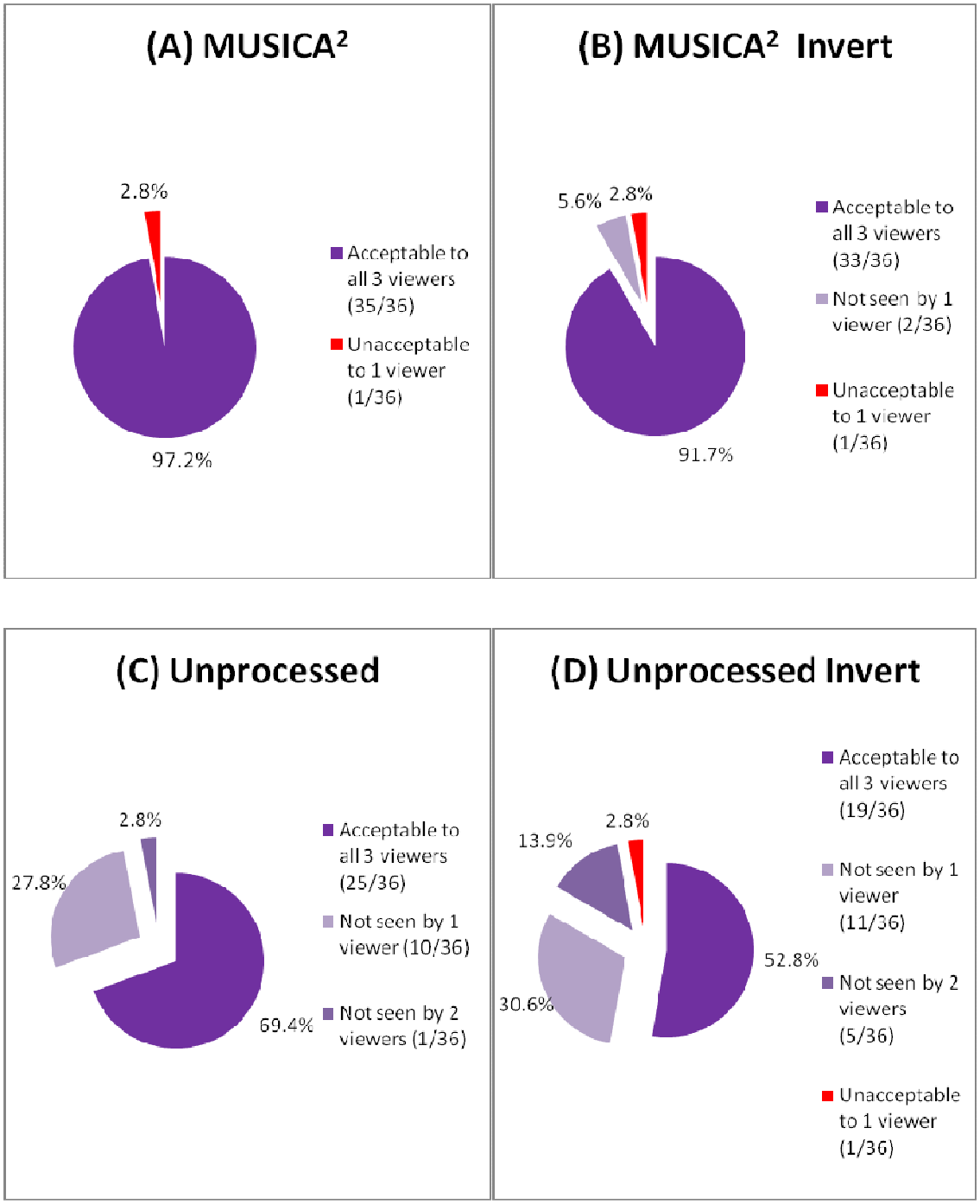


Figure 5.6(A-D): Noise level in the reproduction of pectoral muscle for MUSICA², MUSICA² Invert, Unprocessed and Unprocessed Invert

5.4.1.5 Image quality evaluation – Is the image quality sufficient for early detection of breast cancer? (criterion 12)

The radiologists' opinion on the acceptability of image quality for the early detection of breast cancer for the different processing options is illustrated in Figure 5.7(A-D). The viewers found a significantly larger number of MUSICA^2 images to be suitable for the early detection of breast cancer compared to Unprocessed ($p = 0.0003$) and Unprocessed Invert ($p = 0.0005$). Also significantly more MUSICA^2 Invert images compared to Unprocessed Invert ($p = 0.0116$) and close to significantly more MUSICA^2 Invert images compared to Unprocessed ($p = 0.0699$). No significant difference was found between MUSICA^2 and MUSICA^2 Invert ($p = 0.2009$) or between Unprocessed and Unprocessed Invert ($p = 0.0848$).

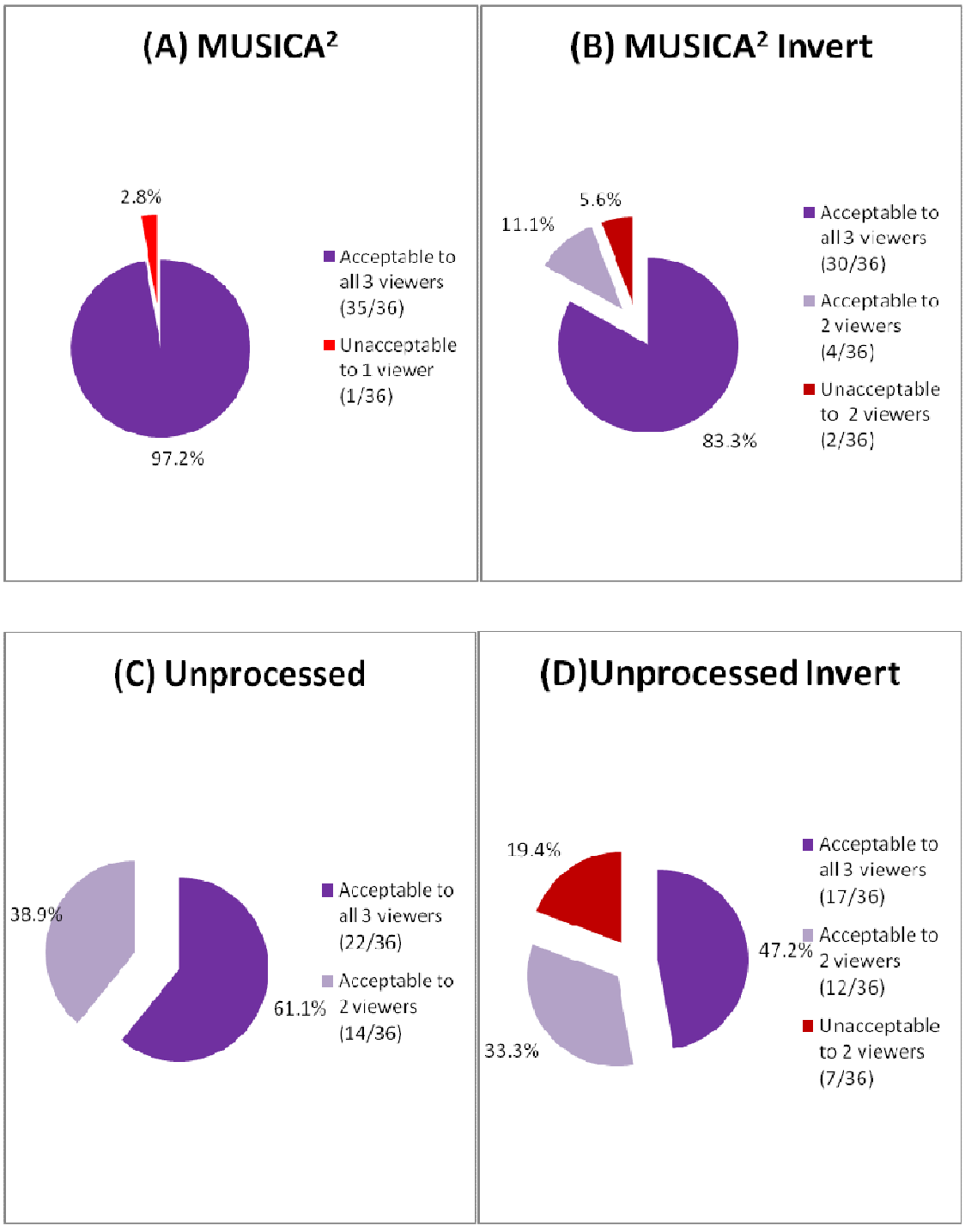


Figure 5.7(A-D): Sufficiency of image quality for the early detection of breast cancer for MUSICA², MUSICA² Invert, Unprocessed and Unprocessed Invert

5.5 DISCUSSION

It is now generally accepted that the full potential of DM can only be achieved through soft-copy reading (Lewin *et al*, 2002) (Kim *et al*, 2006) (Obenauer *et al*, 2002). A previous study has emphasised the importance of appropriate training for radiologists to perform soft-copy reading (Pisano *et al*, 2002). Skaane and co-workers, who performed the Oslo I (2003) and Oslo II (2004) studies, found a higher cancer detection rate for FFDM compared to SFM in the second study. The difference is ascribed to a variety of reasons, one of them being a learning curve effect as they used the same radiologists as readers in both Oslo studies (Skaane, Hofvind & Skjennald, 2007). Before the Oslo I study, the radiologists only had experience in SFM (Skaane *et al*, 2003).

The complexity of soft-copy reading of digital mammograms is widely acknowledged and radiologists have to become familiar with the soft-copy tools (Uematsu, 2009). Furthermore, a much needed knowledge for the radiologists on the image processing algorithm used on a workstation has been expressed (Pisano, 2006). In order for radiologists to accurately evaluate soft-copy images, they should be familiar with the image processing applied (Uematsu, 2009). It was previously reported that viewers are not always provided with sufficient information on the principles of the processing algorithm (Pisano, 2006), and moreover there is still no consensus on the best processing algorithm for DM (Uematsu, 2009). Warren and co-workers (2012) acknowledge that because each manufacturer's system uses a different image processing algorithm, it is important to investigate the effect of each on amongst other things, calcification detection. Moreover in many mammography units across the globe SFM has been replaced with DM and in others the replacement will be

done in due course. The need for radiologists to be trained in the new modality is thus well motivated.

The theoretical training in this study provided the radiologists with knowledge of the new modality and critical awareness of challenges when changing from SFM to DM and the hands-on training enabled the radiologists to learn about the tools for soft-copy viewing and to become familiar with their use. With the participative learning approach to develop the viewing protocol, the radiologists gained experience and confidence in the use of the tools for soft-copy viewing. The results of the participative learning provided them with much needed knowledge and understanding of the processing options in their clinical setting. As they participated in the development of the viewing protocol, they gained first-hand experience of the effect of the processing option on image quality and should therefore be able to confidently apply it in clinical practice.

No previous work was found in which the effect of image processing on the image quality of anatomical structures in the breast was evaluated. Although studies were found in which the effect of processing options on masses and calcifications were investigated, they evaluated the effect of the processing options on viewer performance for the detection of masses and calcifications, not the effect thereof on image quality. However, image quality was demonstrated to be a critical component of early detection of breast cancer (Ikeda, 2011: 1).

The outcomes for the learning objectives defined for the participative learning are as follows:

5.5.1 Image quality evaluation – Overall anatomical structures (criteria 1-8)

The aim of image processing is to improve the display by making it more pleasing to the eye; however it cannot add information to the image (Willison, LaBella & Zuley, 2006). With the unprocessed images, the viewer has to find WW/WL parameters to optimally display the different anatomical structures. The concept of MUSICA^2 on the other hand is to enhance low contrast at the expense of high contrast in order to improve the image quality for the viewer. By reducing the contrast of the structures that use too much of the available dynamic range, the image is manipulated in order to better make use of the available gray level range (Schaetzing, 2007:6-7). In this study both MUSICA^2 and MUSICA^2 Invert showed significantly better image quality for anatomical structures overall (criteria 1-8) compared to Unprocessed and Unprocessed Invert. This can be explained by the better use of the available gray level range for the display of anatomical structures in the breast with the processed images.

5.5.2 Image quality evaluation – Individual anatomical structures (criteria 1-8)

The demand for high contrast in an image to detect subtle lesions in the breast has not changed since the early days of mammography. Compared to conventional SFM, the wide-latitude response of digital detectors makes it possible to capture x-ray information in the over- (near the skin line) and under-penetrated (glandular tissue) regions of the breast. However, the viewer gains more from the improved contrast resolution when image processing enhancement methods are applied (Seibert A, 2006). It would be fair to argue that it is the subtle contrast differences rather than the high contrast differences that are often overlooked in the diagnostic

process in clinical practice (Schaetzing, 2007:p6). In this study both MUSICA^2 and MUSICA^2 Invert demonstrated better image quality for individual anatomical structures (criteria 1-8) compared to Unprocessed and Unprocessed Invert. Of specific importance is the significantly superior image quality for both MUSICA^2 and MUSICA^2 Invert compared to both Unprocessed and Unprocessed Invert in dense (criterion 4 -vessels in dense parenchyma, criterion 8 - glandular tissue) and less dense areas in the breast (criterion 5 - vessels in fat tissue). The gain in image quality is of specific importance in the dense areas of the breast as it has been shown that mammography can potentially be less sensitive when breast tissue is more difficult to penetrate (Saarenmaa *et al*, 2001). Skin structure (criterion 2) was also evaluated in the region of the pectoral muscle area (denser breast area) but only MUSICA^2 was found to be significantly superior to Unprocessed and Unprocessed Invert. Compared to both Unprocessed and Unprocessed Invert; MUSICA^2 Invert showed better image quality (although not significantly). With skin structure, the viewers were instructed to evaluate the rosettes from pores along the pectoralis muscle. Because this is the densest area in the breast, it is also the area where the least dose reaches the image receptor and the area where noise (salt and pepper appearance) could be more readily visible. The latter could degrade the contrast in this area rendering it more difficult to visualise the rosettes from pores. The results of this part of our study leads to the assumption that MUSICA^2 image processing adds to image quality especially in the challenging dense areas of the breast and it can probably be attributed to the better use of the available gray level range to display small intensity differences. In the Unprocessed image, excessive contrast can also be reduced by using WW/WL adjustments, however, the latter will also affect other image contrast and not only the desired contrast adjustment

(Schaetzing, 2007:p16). This explains why the processed image is more beneficial to the viewer because it is less viewer dependant in terms of finding a suitable WW/WL.

With larger structures such as the high contrast pectoral muscle margin, the processed images did not significantly improve visibility perhaps because density differences (contrast) are not as crucial for visualisation of the structure as they are for smaller structures.

In another less dense area in the breast (skin outline - criterion 1) the only significant differences between MUSICA^2 and MUSICA^2 Invert were found; MUSICA^2 Invert being superior to MUSICA^2. MUSICA^2 Invert was also significantly superior to both Unprocessed and Unprocessed Invert. It thus points to the skin outline being better visualised with the invert of the processed image in which the unattenuated background adjacent to the skin outline is displayed in white instead of black and the breast tissue more black instead of more white.

5.5.3 Image quality evaluation – Calcifications (criterion 9) and masses (criterion 10)

Early mammographic signs of breast cancer are often subtle and include masses, calcifications, architectural distortion and bilateral asymmetry (ACR, 2003). Characteristics of calcifications that make them difficult to detect on a mammogram are that they are generally very small in size and therefore often have low contrast compared to the background (especially in dense fibro-glandular tissue). The small size together with a non-homogeneous background can easily lead to misinterpretation as noise (Sampat, Markey & Bovik, 2005:1203).

As mentioned before, no studies were found in which the effects of the different image processing options on the image quality of calcifications were studied. A number of previous authors however reported on the effect of different image processing options on the detection of calcifications and masses.

Calcifications:

Pisano and co-workers (1997[a]) investigated the effect of intensity windowing on the detection of simulated calcifications in dense mammograms. Twenty student observers evaluated the hard-copy images with no windowing applied and nine different window widths and levels applied. They found statistically significant improvement for the detection of calcifications with specific WW/WL settings. These results indicate that manual intensity windowing can have a significant impact on the detection of calcifications and may impact negatively when viewers have to view an unprocessed image. Our results support this. A Japanese study compared the detection of breast cancer by soft-copy reading of DM of a routine image-processing parameter and high-contrast parameters (Kamitani *et al*, 2010). Their study included 154 mammograms obtained with a CR system and five experienced radiologists interpreted the images. In dense breast tissue, they found that high-contrast parameters showed relatively low sensitivity for microcalcifications. Their results indicate that high-contrast parameters do not necessarily improve the detection of a relatively high contrast structure such as calcifications.

Masses:

A very small difference exists in the amount of x-radiation attenuation that occurs in a tumour and adjacent normal dense breast parenchyma. As a result, the difference in the x-rays absorbed in the recording system is also small, complicating the display

of subtle differences. Thus although some information may have been recorded on the film, it may not be displayed optimally to the viewer. Pisano *et al* (1997[b]) studied the effect of intensity windowing on the detection of simulated masses in dense portions of digitised mammograms. Twenty student observers evaluated hard-copy images with no windowing applied and nine different window width and levels applied. They found a statistically significant improvement for the detection of masses with specific window width and window level settings. These results indicate that manual intensity windowing can have a significant impact on the detection of masses and may impact negatively when viewers have to view an Unprocessed image. Hemminger and co-workers (2001) studied the effect of two different image-processing techniques (HIW and CLAHE) on the detection of simulated masses in mammograms. They found that the parameter setting of the algorithms used affected the detection of simulated masses on mammograms with dense backgrounds. No difference in performance was found with the best CLAHE settings compared to no processing. However the best HIW setting performed better than no processing. In our study, we also found no significant difference in image quality between MUSICA[2] and Unprocessed. A Japanese study compared the detection of breast cancer by soft-copy reading of DM of a routine image-processing parameter and high-contrast parameters (Kamitani *et al*, 2010). In contrast to their results in the study where the effect of high-contrast parameters were studied on calcifications (Kamitani *et al*, 2010), they found that high-contrast parameters showed relatively high sensitivity and area under the ROC curves in the detection of masses. Their results indicate that high-contrast parameters can be beneficial for the improvement of the detection of relatively low contrast structures such as masses. As manual windowing is user dependent, the lower mean IQS found for Unprocessed in this

study can be expected as the viewers in this study had little experience in manual windowing for breast images.

In this study, the results strongly indicate that MUSICA^2 provided better image quality compared to Unprocessed and Unprocessed Invert in the demonstration of calcifications and also that MUSICA^2 Invert is significantly superior to Unprocessed Invert for that. However, this study found no significant difference between any of the processing options in the demonstration of masses. These findings suggest that the concept of this processing option was capable of significantly improving the image quality for calcifications (higher contrast structures). However, the enhancement of low contrast structures (masses) was not superior to that which viewers were able to obtain through manual windowing alone. The processed images in which less manual windowing needs to be performed, tend to show better image quality.

5.5.4 Image quality evaluation – Noise level in the reproduction of the pectoral muscle (criterion 11)

Noise can be described as something that interferes with the visibility of useful signal and in the digital image includes quantum noise or mottle as well as electronic noise (present in digital receptors) (Willison, LaBella & Zuley, 2006). A danger of image processing (enhancement) with the aim to enhance low contrast structures is that the noise in the image will also be amplified together with the relevant, subtle contrast. This is because noise is generally also a low-contrast feature (Schaetzing, 2007:12). It would therefore be expected that image noise should be less visible in Unprocessed images compared to processed images. Our results support this by showing significantly less noise was seen by the viewers for Unprocessed. For both these processing options, noise in the image was not acceptable to only one viewer

(1/36), however Unprocessed Invert was significantly superior because noise could not be seen by two viewers in five of the 36 images (5/36), and not seen by one viewer in 11 of the 36 images (11/36). Although a significant difference was not seen between Unprocessed and any of the other processing options, noise was not seen by more viewers with Unprocessed (10/36 by one viewer and 1/36 by two viewers) compared to that of MUSICA^2 (36/36 seen by all viewers) and MUSICA^2 Invert (2/36 not seen by one viewer). Unprocessed Invert was almost significantly superior to MUSICA^2 Invert ($p = 0.0756$). The results thus point to less noise being seen in unprocessed images compared to the processed images, perhaps implicating the possibility that noise becomes more visible to the viewer in the processed image.

5.5.5 Image quality evaluation – Is the image quality sufficient for early detection of breast cancer? (criterion 12)

In a study by Pisano and co-workers (2000) the preferences of radiologists among eight different image processing algorithms for screening and diagnostic imaging task on hard-copy display were determined. The processing options included MUSICA, (the predecessor of MUSICA^2 used in this study). They found that radiologists selected different digital processing algorithms depending on the reading task and for different lesion types. In our results where only MUSICA^2 and Unprocessed were evaluated, the viewers found a significantly larger number of MUSICA^2 images to be suitable for the early detection of breast cancer.

Invert

Our results strongly indicate no significant difference in overall image quality for anatomical structures with the use of the invert for both MUSICA^2 and Unprocessed.

However to demonstrate the skin outline, evidence was found that MUSICA^2 Invert significantly improved image quality compared to MUSICA^2. For the visualisation of calcifications, only Unprocessed Invert significantly improved image quality compared to Unprocessed. We found no significant difference with the use of invert for either MUSICA^2 or Unprocessed in the demonstration of masses or in noise level (in the reproduction of the pectoral muscle area). The invert made no significant difference to the viewers opinion on processing option for the early detection of breast cancer (MUSICA^2 vs MUSICA^2 Invert, and Unprocessed vs Unprocessed Invert).

5.5.6 Comparing the results of the phantom study (Chapter 4) with that of the clinical images

It was interesting to note that the processing option which provided the best image quality with the CD phantom (Chapter 4) was not the same as the processing options which provided the best image quality with the clinical images. The processing option which provided the best image quality (lowest IQF) with the phantom was Unprocessed Invert. With the clinical images, MUSICA^2 and MUSICA^2 Invert showed statistically significantly better image quality compared to that of Unprocessed Invert. This can possibly be because the phantom image consists of a more homogeneous background with regular standard test objects whereas the clinical images are a mix of structures in a heterogeneous background. The enhancement of low contrast structures at the expense of high contrast structures makes sense in a clinical mammography image but not in the type of phantom used in this study. For clinical images however, contrast enhancement of low contrast structures at the expense of high contrast structures renders the available dynamic range for display of more subtle contrast differences better for evaluation of most

anatomical structures and calcifications. The fact that statistically less noise was seen with Unprocessed Invert compared to MUSICA^2 ($p = 0.016$) is perhaps also a good explanation why Unprocessed Invert was found to have superior image quality in the phantom study. Some of the disc diameters in the phantom are very small, and noise can probably influence the visibility of such discs.

5.6 CONCLUSION

The training offered the radiologists factual and conceptual knowledge and insight in the challenges associated with changing from SFM to DM. The participative learning approach to develop the viewing protocol offered them the opportunity to gain experience in soft-copy viewing. They had become accustomed to the process for viewing the image. The recommended processing option for the viewing protocol was made based on the processing option which the radiologists found provided the best image quality. They learned about the processing options and the effect thereof on image quality.

The knowledge gained from the results of the participative learning included the following: Overall, MUSICA^2 and MUSICA^2 Invert showed significantly better image quality compared to Unprocessed and Unprocessed Invert and can be confidently used in clinical practice. Both MUSICA^2 and MUSICA^2 Invert showed significantly better image quality for the visualisation of anatomical structures. Of importance is that both MUSICA^2 and MUSICA^2 Invert also showed significantly better image quality in the denser areas of the breast in which the visualisation of possible pathology is challenging because of low contrast. In addition, both MUSICA^2 and MUSICA^2 Invert can be confidently used for looking at calcifications as it provided significantly superior image quality compared to Unprocessed and Unprocessed

Invert. However, for masses, no significant difference in image quality was seen between the processing options, and it is probably the area in which the processed image contributed the least. Also, although the noise level in Unprocessed Invert was found to be significantly superior to MUSICA^2, the noise level in both MUSICA^2, and MUSICA^2 Invert was found to be acceptable to all three viewers in 97.2% and 91.7% of cases respectively. Also, the viewers found a significantly larger number of MUSICA^2 images to be suitable for the early detection of breast cancer compared to Unprocessed and Unprocessed Invert. The only significant difference between MUSICA^2 and MUSICA^2 Invert was seen with skin outline where MUSICA^2 Invert was found to be superior. Furthermore, a smaller variation between the viewers was observed for MUSICA^2 Invert compared to the other processing options.

On grounds of the knowledge gained from the image quality evaluation study, the following recommendations were made for the soft-copy viewing protocol:

- From the theoretical knowledge gained on the lower spatial resolution for DM compared to SFM, roaming and zooming are essential to view all areas in the breast at full resolution
- Image processing (MUSICA^2 or MUSICA^2 Invert) is recommended for viewing all anatomical structures. The default processing option recommended was MUSICA^2 Invert based on overall image quality performance on anatomical structures in particular skin outline
- Image processing (MUSICA^2 or MUSICA^2 Invert) is recommended for the viewing of calcifications. With MUSICA^2 Invert as the default processing option, it would thus not be necessary to use a different processing option to view calcifications

- Image processing (MUSICA^2 or MUSICA^2 Invert) is recommended for viewing mammograms for the early detection of breast cancer. As for calcifications MUSICA^2 Invert as the default processing option is suitable for the early detection of breast cancer
- Noise level in the densest area of the breast with the processed images (MUSICA^2 or MUSICA^2 Invert) is acceptable. However, the Unprocessed Invert processing option should be applied whenever noise is regarded as a problem
- Special attention should be paid to the dense breast area during viewing as it was identified as the area where even the processed images showed the lowest image quality. Manual intensity windowing should be used to try and improve clear visualization of the area
- As no significant improvement in the image quality of masses was found with the processed images, special attention should be paid in viewing for masses. Manual intensity windowing should be used to try and further improve contrast for the visualization of masses

In the next chapter, the diagnostic accuracy of the radiologists before and after the development of the viewing protocol will be presented.

CHAPTER 6

DIAGNOSTIC ACCURACY BEFORE AND AFTER THE DEVELOPMENT OF THE SOFT-COPY VIEWING PROTOCOL

6.1 INTRODUCTION

It is thus of interest to determine what the effect of the soft-copy viewing protocol (described in Chapter 5) was on the accuracy of radiologists' diagnosis on mammography reporting. To answer the above question, diagnostic accuracy was determined before and after the development of the soft-copy viewing protocol. Diagnostic accuracy in the context of this study relates to the ability of a viewer to discriminate between the target condition (malignant diagnosis on mammogram) and health (normal/benign diagnosis on mammogram). Different measures of diagnostic accuracy can be used to quantify the discriminative ability (Simundic, 2012).

Perfect diagnostic accuracy in this study will imply that the viewer completely discriminated between a mammogram of a patient with breast cancer and a mammogram of a patient without breast cancer. However, in real life the above mentioned scenario is thus far impossible to achieve.

6.2 AIM

The aim of this part of the study was to evaluate the effect of the developed soft-copy viewing protocol on the diagnostic accuracy achieved by the viewers.

6.3 METHODS

6.3.1 Study population

All consecutive consenting patients attending the mammogram unit at Universitas Hospital for a mammogram examination during the study period (June 2008 to May 2009) were considered for the study, and a selection of 120 of these were included.

6.3.2 Case selection

The exclusion criteria for the study were: patients with larger breasts than the field size of the equipment, patients who had a previous mastectomy and patients who had a current normal/benign reported mammogram, but who did not have record of a previous mammogram at least 12 months prior to the current mammogram. Also, all patients with radiology reports of malignancy, for whom histo-pathology reports could not be obtained, were excluded from the study. At the end of the data collection period we had 1263 consented mammograms from which we could obtain histo-pathology confirmation of 60 malignant cases. Because more normal/benign cases were collected during this period compared to malignant cases, a Consultant Radiologist at the mammography unit selected the normal/benign cases to equal the number of malignant cases found. The dataset thus consisted of 120 cases (60 malignant + 60 normal/benign cases).

For the purpose of this study, the data set of images before the development of the viewing protocol will be referred to as “initial data set”, whereas the data set of images after the viewing protocol will be referred to as “final data set”. For the initial data set the first 40 malignant and 40 normal/benign cases were included (total of 80 cases). So as not to use all the same cases for the final data set, only 40 cases in the initial data set were included in the final data set (20 malignant and 20

normal/benign). Forty unseen cases (20 malignant and 20 normal/benign cases) were added to bring the total of the "final data set" also to 80 cases. To avoid image-selection-bias, the cases that were used in both the initial- and final data sets were systematically selected as every second case from the initial dataset.

6.3.3 Views included

A patient case consisted of four standard images namely cranio-caudal (CC) and medio-lateral-oblique (MLO) views of both breasts. If deemed necessary by the reporting radiologist on duty at the time of the examination, spot views that were obtained were also included in the study.

6.3.4 Confirmation of diagnosis

Malignancy was confirmed based on histopathology reports. Current normal/benign cases were considered confirmed if both the current and the previous mammogram were reported as normal/benign.

6.3.5 Equipment

Images were obtained with a GE Senographe DMR mammography unit and an Agfa CR system. The images were archived onto a Philips PACS and reviewed on a workstation with a Matrox MED5Mp-DVI graphic card. The images were displayed on a Fimi (model MML2152) 5Mp high resolution monitor (2048 x 2560 pixels) with a 10 bit gray scale depth. The review station was situated in a dedicated viewing area for mammography with suitable ambient light. Quality control tests on the entire imaging chain, including the viewing equipment and viewing conditions, were performed and approved by the Department of Medical Physics before the commencement of the study.

6.3.6 Viewers

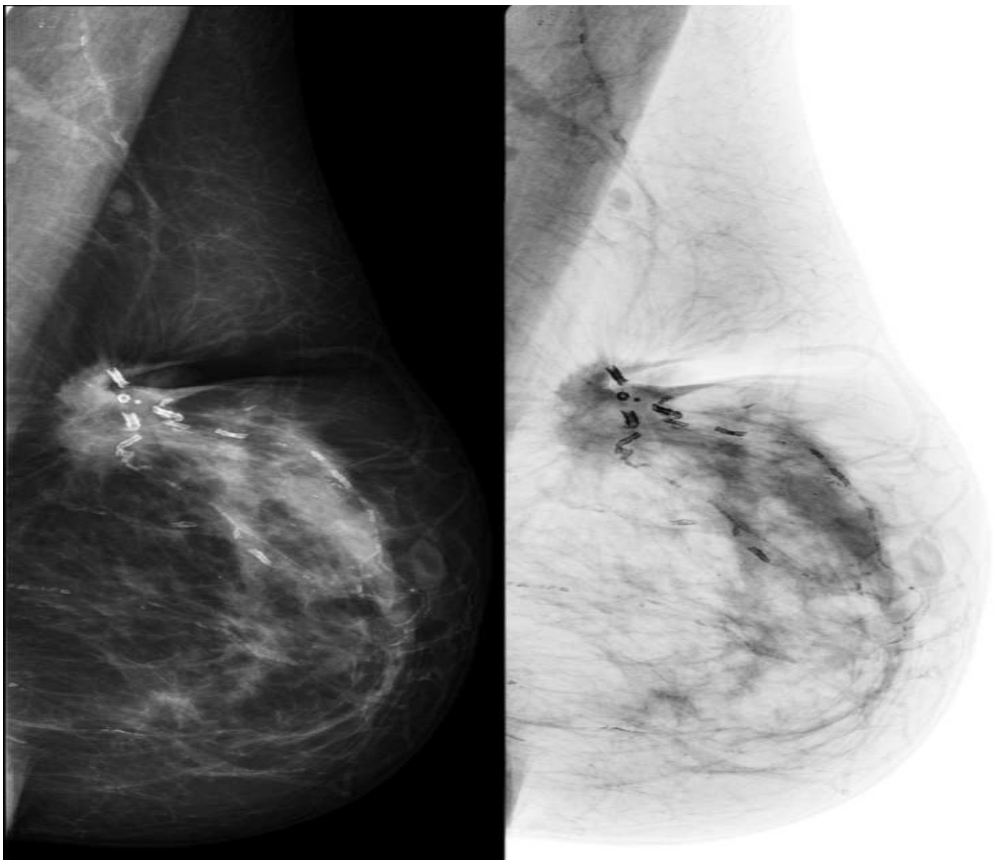
The viewers were the trainees (radiologists) used to develop the soft-copy viewing protocol through participative learning (see 5.3.2).

6.3.7 Viewing of the images

The cases were saved in a personal folder on the PACS workstation, accessible only to the researcher. Malignant and benign cases were randomly displayed by the researcher to each viewer individually. No clinical history or patient information was available to the viewers. For the initial reporting, viewers received no instructions on which display tools to use, but were free to adjust WW/WL and to use roaming and magnification if they so want to. However, for the final reporting, they had to use the guidelines established for the viewing protocol (Chapter 5). No time restriction was placed on the viewing and reporting of images. To avoid recall bias, a minimum 'wash-out' period of three months was allowed between the initial and final reporting.

6.3.8 Image processing algorithm

For the initial reporting, all images were default processed with MUSICA^2 before the soft-copy image was displayed on the computer monitor. For the final reporting the default processing option identified through the development of the viewing protocol (Chapter 5) was MUSICA^2 Invert. In Figure 6.1 an image processed with MUSICA^2 and MUSICA^2 Invert can be seen.



A MUSICA^2 **B MUSICA^2 Invert**

Figure 6.1: A MLO view of the breast. In A the image was processed with MUSICA^2, and in B, the image was processed with MUSICA^2 Invert

6.3.9 Reporting

6.3.9.1 BI-RADS assessment categories

The viewers were instructed to indicate their findings according to the BI-RADS assessment categories on a structured report form (see Appendix O). BI-RADS makes provision for a category 0 where the radiologists can indicate the need for additional imaging which is applicable in screening mammograpy. As the cases in the study were previously worked out, this option was not available to the viewers. BI-RADS 1, 2 and 3 were considered normal/benign and BI-RADS 4 and 5 were

considered malignant. BI-RADS 3 is a category that should be used with caution by radiologists, as it necessitates a short interval follow-up (probably benign finding).

The ACR BI-RADS categories used in the study, together with a description of the finding for each, can be seen in Table 6.1.

Table 6.1: American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) classification used in this study (ACR, 2003)

BI-RADS category	Finding
1	Normal mammogram
2	Benign non cancerous finding
3	Probably benign finding – short interval follow up suggested
4	Suspicious abnormality – biopsy indicated
5	Highly suggestive of malignancy, biopsy and appropriate action needed

For the purpose of this study, the reporting before the development of the viewing protocol is referred to as “initial reporting”, whereas the reporting thereafter is referred to as “final reporting”.

6.3.9.2 Classification of breast parenchyma

The viewers were also instructed to use tick boxes to indicate the breast parenchyma classification as described by Tabàr (Gram, Funkhouser & Tabár, 1997). Table 6.2 shows the breast parenchyma classification by Tabár. Pattern 1

represents the classic appearance of the premenopausal breast. Pattern 2 represents the normal postmenopausal breast with glandular tissue replaced by fatty tissue. Pattern 3 indicates more periductal elastosis. Pattern 4 probably represents proliferation. Pattern 5 represents extensive fibrosis, which may be, but is not necessarily, associated with any malignant or proliferative process.

Table 6.2: Tabár's classification of breast parenchyma

Tabár's classification	Description
1	Mammogram composed of scalloped contours with some lucent areas of fatty replacement, and 1 mm evenly distributed nodular densities
2	Mammogram composed almost entirely of lucent areas of fatty replacement, and 1 mm evenly distributed nodular densities
3	Prominent ducts in the retro-areolar area
4	Extensive nodular and linear densities, with nodular size larger than normal lobules. Prominent ducts in the retro-areolar area
5	Homogeneous, ground glass-like appearance with no perceptible features

6.3.9.3 Characterisation of lesions

The viewers were also instructed to characterise the detected lesions using tick boxes on the supplied report form (see Appendix O). The lesion site had to be indicated using the following tick boxes: 1) Superior-external (lateral), 2) Central-external (lateral), 3) Inferior-external (lateral), 4) Inferior – central, 5) Inferior-internal (medial), 6) Central-internal (medial), 7) Superior-internal (medial), 8) Superior-central, 9) Areolar, 10) Diffuse or 11) Axillary tail and 12) Retro-mammary. For the description of calcifications, the viewers had to tick one of the following descriptors: absent (1), predominatly punctate (2), predominantly pleomorphic/granular (3),

prodominantly linear branching (4) or benign (5). The tick box options to describe opacities included the following: No opacity/asymmetry, Well defined opacity, Poorly defined opacity or Spiculate opacity. To describe the mammogram pattern, the viewers had to tick the following tick boxes where appropriate: Architectural distortion, Asymmetry breast, Asymmetry density, Skin thickening, Skin retraction and Nipple retraction. Lesion extent had to be indicated as either localized, Multifocal or Multicentric. An information document on Tabár's classification of breast parenchyma, BI-RADS assessment categories and the ACR's Breast Imaging Lexicon was given to each radiologist to serve as a reference in case it was needed (see Appendix P).

6.3.10 Familiarising the viewers

Before the start of this part of the study, the report form was explained to the viewers and each viewer received an information document which explained the BI-RADS categories, details about the report form (see Appendix P). Before the start of the first viewing session for each individual viewer, the viewer was instructed to report on five mammogram studies (not included in the study) using the report form in order to familiarise themselves with the procedure to be followed during the study.

6.3.11 Descriptive data analysis

Data capturing was done by the researcher onto an Excel spreadsheet. Sensitivity, specificity, overall accuracy, PPV and the percentage of BI-RADS 3 cases (undesirable category for probably benign lesions as it necessitates a short interval follow-up) were calculated per viewer. Table 6.3 was used to calculate sensitivity, specificity, overall accuracy and PPV.

Table 6.3: 2 x 2 Contingency table

	Reference standard	
Test results	**Subjects with the disease**	**Subjects without the disease**
Positive	True positive (TP)	False positive (FP)
Negative	False negative (FN)	True negative (TN)

Sensitivity in this study defines the proportion of true malignant findings on mammograms in the total group of mammograms with a confirmed diagnosis of malignancy.

$$Sensitivity = \frac{TP}{TP + FN}$$

Specificity on the other hand defines the proportion of true normal/benign findings on mammograms in the total group of mammograms with a confirmed normal/benign diagnosis.

$$Specificity = \frac{TN}{TN + FP}$$

The overall accuracy in this study defines the proportion of correct findings on mammograms in relation to all the mammograms included.

$$Overall\ Accuracy = \frac{TP + TN}{TP + FN + FP + TN}$$

The positive predictive value (PPV) in this study defines the probability of breast cancer among the mammograms with a positive test result.

$$Positive\ predictive\ value = \frac{TP}{TP + FP}$$

6.3.12 Comparative statistical analysis

Sensitivity, specificity, overall accuracy, PPV and percentage BI-RADS 3 were compared between initial and final reporting using chi-squared or Fisher's exact tests. In the initial reporting, specificity for one viewer was calculated for 39 cases as that viewer used BI-RADS category 0 (which was not allowed for this study) to indicate the management of one truly benign case. The agreement between the viewers on Tabár's classification of breast parenchyma, as well as agreement on lesion characterisation was calculated using kappa with a 95% CI. Cut-off points for kappa values proposed by Landis and Koch as reported by Fleiss *et. al*. (2003: 604) was used: < 0.4 (weak to moderate agreement), 0.4 – 0.75 (fair to good agreement) and > 0. 75 (strong agreement). For lesion site and calcifications the percentage agreement between pairs of viewers were calculated. The same statistical analysis was conducted for the initial reporting and the final reporting.

6.4 RESULTS

The datasheets showing the raw data of all three viewers can be found in Appendix Q.

6.4.1 Histopathology confirmation

Histopathology revealed the malignant lesions included examples of ductal carcinoma Gr II (24), ductal carcinoma Gr III (14), ductal carcinoma in-situ (DCIS) (4), ductal carcinoma Gr I (3), lobular carcinoma (3), angiosarcoma (1), medullary carcinoma (1), and Pagets infiltrating carcinoma (1). Nine (9) cases were considered malignant based on Fine-Needle-Aspiration (FNA) only as they were lost to follow-up.

6.4.2 Viewing sessions

Initial reporting (80 cases) was completed in an average of seven (7) individual sessions per reader in an average of seven (7) hours and 20 minutes per viewer. On completion of the initial reporting by all three viewers, the development of the viewing protocol through participative learning commenced (Chapter 5). Final reporting (80 cases) were completed in an average of five (5) individual sessions per reader in an average of five hours 16 minutes per viewer.

6.4.3 Sensitivity

The sensitivity for the different viewers before and after the development of the viewing protocol can be seen in Figure 6.2. For viewer A, sensitivity stayed unchanged after the viewing protocol on 95% ($p = 1.000$). For both viewer B and viewer C on the other hand, a non significant increase in sensitivity was noted after

the viewing protocol from 90% to 95% (p = 0.6752) and from 90% to 97.5% (p = 0.3589) respectively.

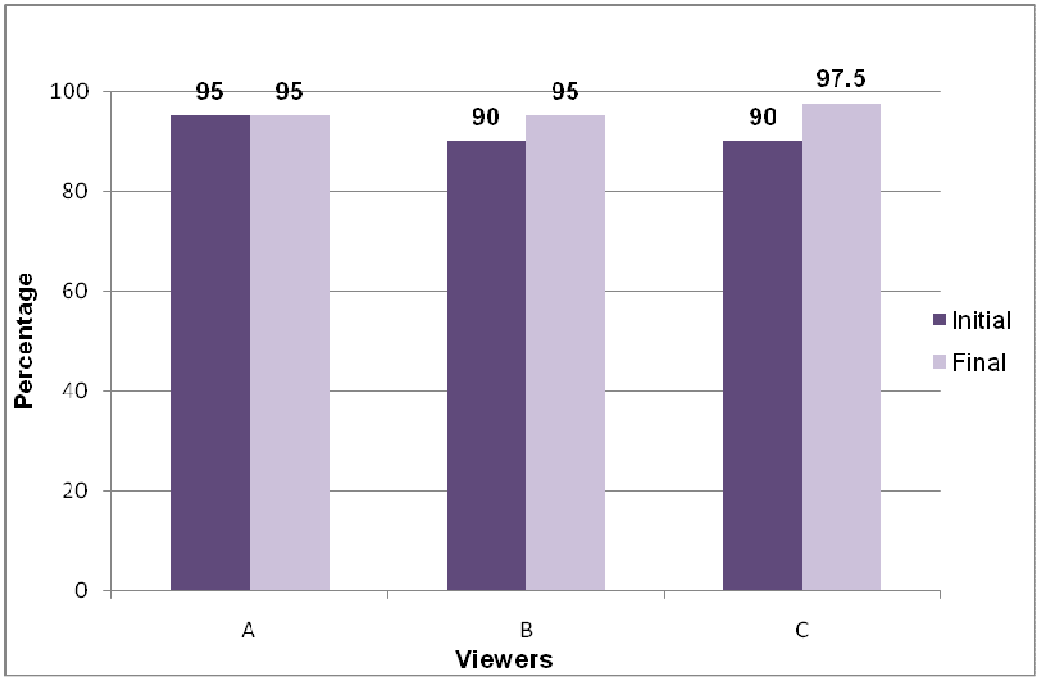


Figure 6.2: Sensitivity before (Initial reporting) and after the viewing protocol (Final reporting)

6.4.4 Specificity

From Figure 6.3 it can be seen a non significant increase in specificity was noted for two of the viewers (viewer A and viewer B) after the viewing protocol from 61.5% to 72.5% (p = 0.2999) and 70% to 85% (p = 0.1082) respectively. However, for one of the viewers (viewer C), specificity stayed unchanged after the viewing protocol (82.5%) (p = 1.000).

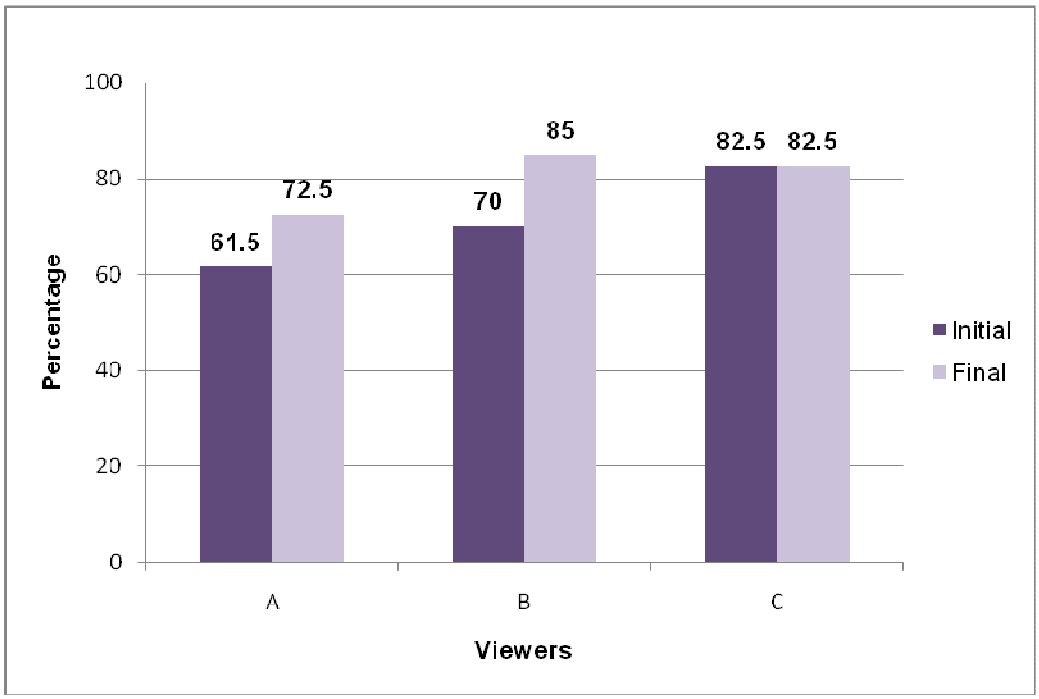


Figure 6.3: Specificity before (Initial reporting) and after the viewing protocol (Final reporting)

6.4.5 Overall accuracy

The overall accuracy in the initial and final reporting is presented in Table 6.4. Although an increase in overall diagnostic accuracy for all three viewers was found after the development of viewing protocol, it was not significant ($p = 0.3959$, $p = 0.0765$ and $p = 0.4635$).

Table 6.4: Overall accuracy before (Initial reporting) and after the viewing protocol (Final reporting)

	Initial			Final		
Viewer	**Sensitivity**	**Specificity**	**Overall accuracy %**	**Sensitivity**	**Specificity**	**Overall accuracy %**
A	38/40	24/39	78.5 (62/79)	38/40	29/40	83.8 (67/80)
B	36/40	28/40	80 (64/80)	38/40	34/40	90 (72/80)
C	36/40	33/40	86.3 (69/80)	39/40	33/40	90 (72/80)

6.4.6 Positive predictive value (PPV)

Figure 6.4 shows the PPV for the viewers before and after the viewing protocol. It can be seen that PPV increased for all three viewers after the viewing protocol, from 71.7% to 77.6% ($p = 0.6198$), 75% to 86.4% ($p = 0.1699$), and 83.7% to 84.8% ($p = 0.8907$) respectively which was not significant.

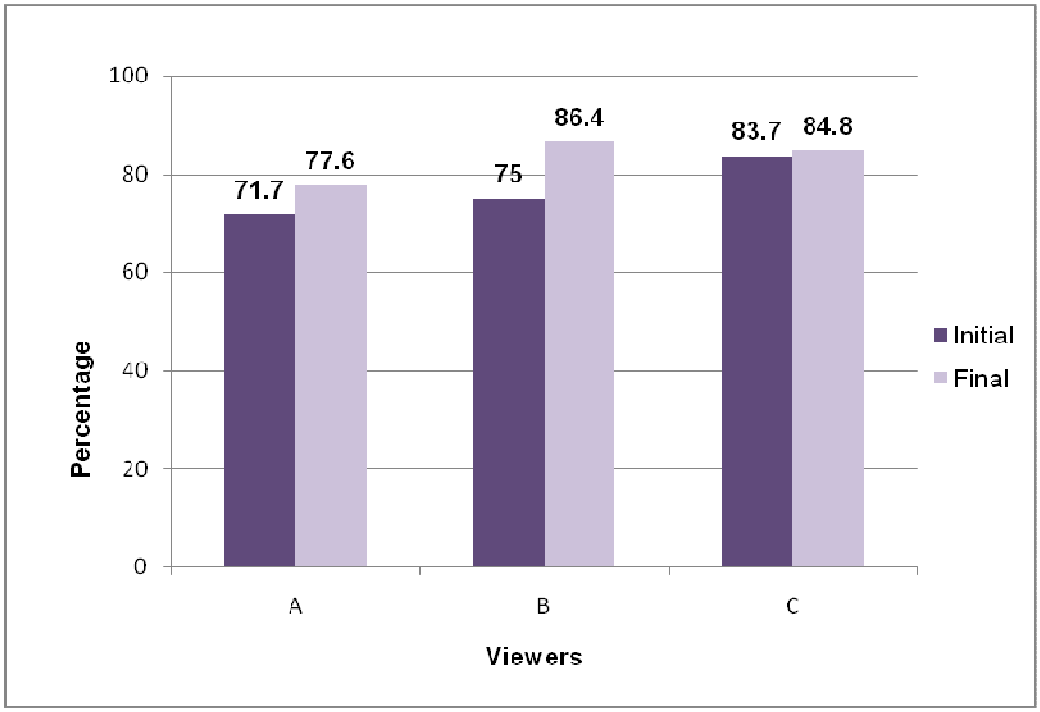


Figure 6.4: Positive predictive values (PPV) before (Initial reporting) and after the viewing protocol (Final reporting)

6.4.7 BI-RADS 3

The cases reported as BI-RADS 3 before and after the viewing protocol are presented in Table 6.5. When comparing all cases in BI-RADS 3 before and after the viewing protocol, it was found that both viewer A and viewer C showed a slight decrease in the percentage cases classified as BI-RADS 3: from 15% (12/80) to 12.5% (10/80) ($p = 0.6461$) and from 28.8% (23/80) to 22.5% (18/80) ($p = 0.2810$) respectively. However for viewer B a slight increase was seen from 30% (24/80) to 32.5% (26/80) ($p = 0.7330$). The percentage of BI-RADS 3 cases that had proven malignancy increased slightly for viewer A from 8.3% to 10%. However, for both viewers B and C a decrease was found from 16.7% to 7.7% ($p = 0.4092$) and from 17.4% to 5.6% ($p = 0.3629$) respectively.

Table 6.5: Cases classified as BI-RADS 3 before (Initial reporting) and after the viewing protocol (Final reporting)

Viewers	A		B		C	
	Initial	**Final**	**Initial**	**Final**	**Initial**	**Final**
Percentage of all cases (n = 80)	15% (12)	12.5% (10)	30% (24)	32.5% (26)	28.8% (23)	22.5% (18)
Percentage of true malignant cases (n=40)	2.5% (1)	2.5% (1)	10% (4)	5% (2)	10% (4)	2.5% (1)
Percentage of true benign cases (n=40)	27.5% (11)	22.5% (9)	50% (20)	60% (24)	47.5% (19)	42.5% (17)
Percentage of BI-RADS category 3 cases that had proven malignancy	8.3%	10%	16.7%	7.7%	17.4%	5.6%

6.4.8 Breast parenchyma

The percentage agreement between the viewers on Tabár's classification of breast parenchyma is shown in Figure 6.5. The highest percentage agreement for a viewer pair in the initial reporting was 61.3%, compared to 66.3% in the final reporting. It can be seen that after the viewing protocol the percentage agreement between all three viewers on breast parenchyma classification, increased from 31.3% to 43.8% ($p = 0.1025$). The calculated simple kappa values for the agreement on Tabár's classification of breast parenchyma between the viewers before and after the viewing protocol can be seen in Appendix R. It can be seen that weak to moderate agreement (kappa < 0.4) was found for two of the three viewer pairs in both the initial and final reporting, and fair to good agreement for one viewer pair in each (kappa 0.4 – 0.75). Strong agreement (kappa > 0.75) was not found for any viewer pair either before or after the viewing protocol.

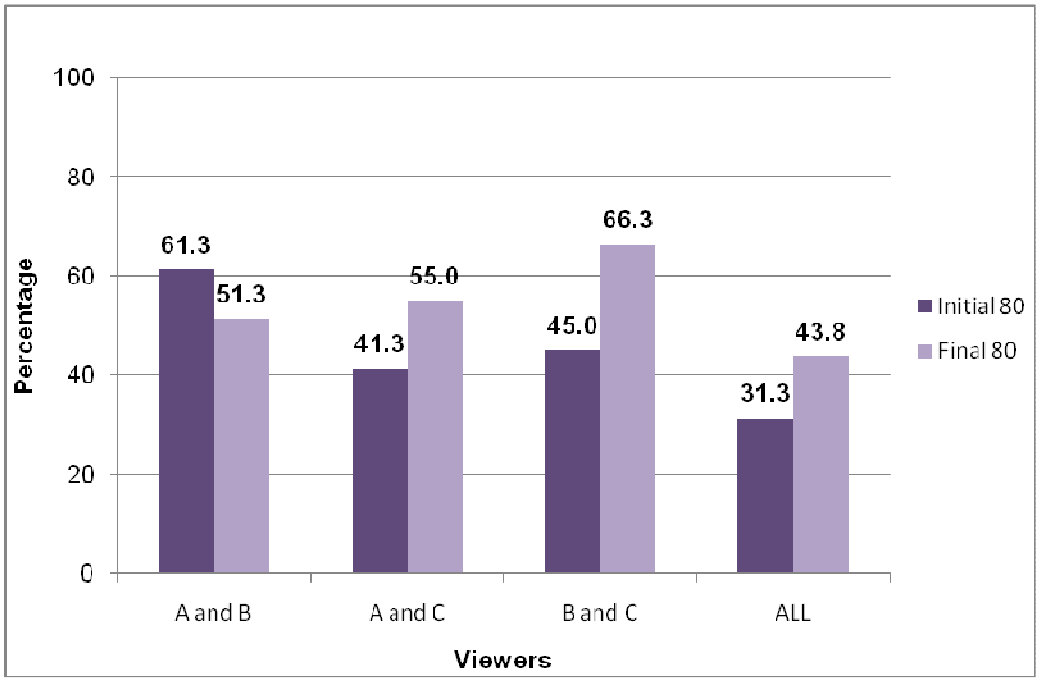


Figure 6.5: Percentage agreement between viewers on Tabár's classification of breast parenchyma before (Initial reporting) and after the viewing protocol (Final reporting)

6.4.9 Characterisation of lesions

Lesion site

The percentage agreement between the viewers on lesion site can be seen in Appendix S. The lowest percentage agreement between any viewer pair in the initial reporting was 46.3% compared to 56.3% in the final reporting. The highest percentage agreement between any viewer pair in the initial reporting was less than 64% and in the final reporting less than 73%. An increase in both the lowest percentage agreement and highest percentage agreement was thus found in the final reporting compared to the intial reporting.

Calcifications

The percentage agreement between the viewers on the description of calcifications can be seen in Appendix S. The highest percentage agreement between any viewer pair in the initial reporting was less than 63% and in the final reporting less than 58%. The percentage agreement between most viewer pairs in both the initial and final reporting was less than 50%.

Mammogram pattern

The kappa values indicating agreement between the viewers for the descriptors used to characterise the mamogram pattern can be seen in Appendix T. Because the viewers did not indicate the lesions as being in the same site, the mammographic pattern descriptor for the lesion as either a well defined opacity, poorly defined opacity or spiculate opacity could not be further analysed and is therefor not incuded in Appendix T.

The total number of viewer pair agreements calculated for the seven (7) mammogram pattern descriptors was 42 for the intial and final reporting respectively. In the initial reporting weak to moderate agreement (kappa < 0.4) was found for 17 pairs compared to 12 pairs in the final reporting. Fair to good agreement (kappa 0.4 – 0.75) was found for 22 pairs in the initial reporting compared to 20 pairs in the final reporting. Strong agreement (kappa > 0.75) was found for three (3) pairs in the intial reporting compared to 10 pairs in the final reporting. The improvement in agreement was found in particular for the descriptors pertaining to skin thickening, skin retraction, and nipple retraction In the initial reporting strong agreement was found for three (3) viewer pairs for these descriptors, compared to nine (9) viewer pairs in the final reporting.

Lesion extent

The agreement between the viewers on lesion extent can be seen in Appendix U. It can be seen that lesion extent was not indicated in the largest percentage of cases in both initial and final reporting. This could be because 50% of the cases (n=40) were benign/normal. Fair to good agreement (kappa 0.4 – 0.75) was found between most viewer pairs in both initial and final reporting. Strong agreement (kappa > 0.75) was not found between any viewer pair in either the initial or final reporting.

6.5 DISCUSSION

The two basic steps for radiologists in interpreting mammograms are perception and analysis (Tabár & Dean, 2001:vii). The aim with the development of the viewing protocol in this study was to improve the perceptibility of anatomical structures and subsequently the subtle signs of breast malignancies to improve radiological reporting. The training of the radiologists in the new modality with the emphasis on digital image processing and soft-copy viewing also contributed towards improving perceptibility of information in the digital image.

6.5.1 Sensitivity, specificity, overall accuracy and PPV

Several studies have been performed to establish performance benchmarks for diagnostic mammography (Sickles *et al*, 2005). Dee and Sickles (2001) performed a medical audit of diagnostic mammography examinations and compared that with screening outcomes that were obtained concurrently. They found substantially different results for diagnostic mammography examinations compared with those of screening examinations. The US National Cancer Institute reported sensitivity and specificity for 4,032,556 screening mammography examinations from 1996 to 2005 to be 78.7% and 89.5% respectively (BCSC, 2007). They also reported sensitivity

and specificity benchmarks based on 401,572 diagnostic mammography examinations from 2002 to 2006 (BCSC, 2010). Sensitivity and specificity for all diagnostic examinations were found to be 84.1% and 92.0% respectively. Higher sensitivity and specificity were thus found for diagnostic examinations compared to screening examinations.

Bearing in mind the difficulty of comparing our results with that of benchmarks, the sensitivity of all three viewers in this study (both initial and final reporting) was found to be higher than the reported benchmark of 84.1% for diagnostic mammography (BCSC, 2010) - viewer A: both initial and final 95%, viewer B: initial 90%, final 95%, and viewer C: initial 90%, final 97% respectively. The specificity of all three viewers was however found to be lower than the reported benchmark value of 92.0% for diagnostic mammograms (BCSC, 2010) - viewer A: initial 61.5 and final 72.5%, viewer B: initial 70%, final 85% respectively; and viewer C: both initial and final 82.5%).

Several factors have been found to influence radiologists' performance in mammography (Barlow *et al*, 2002). They found among others that previous mammography decreased sensitivity but increased specificity. In our study where radiologists did not have access to previous mammograms, it could well have contributed to our higher sensitivity and lower specificity. Barlow and co-workers (2002) also found that self-reported breast lump increased sensitivity but decreased specificity. In our setting where predominantly diagnostic mammograms are performed this could well have contributed to our higher sensitivity and lower specificity. Sickles and co-workers (2005) found a higher cancer diagnosis rate at diagnostic mammography, and the cancers identified at diagnostic mammography were found to be larger, with more frequently positive node involvement and more

advanced stage tumours compared to those detected at screening. The reason for these phenomena has been attributed by some as due to the fact that visible symptoms or clinical findings in diagnostic mammography may point toward a more advanced tumor that is easier to locate and identify (Barlow *et al*, 2002). An audit of diagnostic mammography examinations by Dee and Sickles (2001), also found several differences between patients for screening and patients for diagnostic mammography. These included different patient demographics, higher number of positive biopsies, higher cancer detection rates; and larger, more advanced-stage cancers for diagnostic mammograms. Again in this study, the more advanced stage breast malignancy found in diagnostic mammography could have contributed to our high sensitivity especially if taken into account that a national based screening mammography program is not available in South Africa.

It is thus clear that diagnostic accuracy in screening mammography studies cannot be compared to that in diagnostic mammography studies. The mammogram examinations performed at our mammography unit are predominantly diagnostic although 'selective' screening is also performed (see section 1.4). Furthermore, our dataset consisted of only 80 cases of which 50% had proven malignancy. Thus although comparison with benchmarks for diagnostic mammography will be more appropriate, accurate comparison is not possible because of the differences in study design. Apart from different study populations, the viewers in our study did not have access to any clinical history on the cases and they did not have access to previous mammograms.

As mentioned before, the focus of this part of the study was to find out if the development of the viewing protocol had an effect on the performance of the

viewers. It was not to compare sensitivity and specificity values found in this study with benchmarks in the literature.

The challenge for radiologists reporting on mammograms is to balance the need for high sensitivity for abnormalities with the need to limit the number of false-positives (call-backs for additional work-up and/or biopsy) (Jamal *et al*, 2006). In our study although the highest sensitivity was found for viewer A before the viewing protocol, that viewer also showed the lowest specificity and the lowest PPV. Although it was found that the viewing protocol made no difference for this viewer on sensitivity, specificity on the other hand increased by 11% and PPV by 5.9%. For viewer B the viewing protocol improved the relationship between sensitivity and specificity (before the viewing protocol 90% and 70% respectively and after the viewing protocol 95% and 85% respectively). Viewer B also showed the best improvement in PPV (an increase of 11.4%). Before the viewing protocol, the best relationship between sensitivity and specificity was found for viewer C (90% and 82.5% respectively). After the viewing protocol a higher sensitivity was found for viewer C while specificity stayed unchanged on 82.5%. Thus, an increase in overall diagnostic accuracy was found for all three viewers after the viewing protocol although it was not significant ($p = 0.3959$, $p = 0.0765$ and $p = 0.4635$). The high sensitivity of the viewers in initial reporting, together with a limited number of cases in the dataset, might be the reason why a significant increase in diagnostic accuracy was not found.

6.5.2 BI-RADS 3

BI-RADS 3 is an intermediate category which implies a short-term (six (6) months) follow up mammogram is to be done (ACR, 2003). Opposite to BI-RADS 4 and 5 that lead to biopsies and thereby “true answers”, BI-RADS 3 allows a period of indecision. In the ideal world, the assessment of mammograms should be such that

no cases are classified as BI-RADS 3. However, in the real world BI-RADS 3 is a recognized method to reduce the number of tissue confirmation procedures in patients with a low probability of malignancy (Varas *et al*, 2002). Although contributing to cost reduction, high emphasis is placed by some on unnecessary patient anxiety during the six-month follow-up period. A finding placed in this category should have a high probability of being benign and should thus have a very low PPV (PPV < 2%) (ACR, 2003). Some suggest that BI-RADS 3 should not exceed 7% of all mammograms (ECR, 2011). An Uruguayan study suggests a benchmark of less than 5% incidence of BI-RADS 3 (Varas *et al*, 2002). They suggest that a higher incidence of this category in a facility might indicate a too large percentage of benign lesions being included in BI-RADS 3. On the other hand, they support the benchmark of the ACR and suggest a less than 2% incidence of false-negative results in BI-RADS 3. If the percentage cases with malignancy found in BI-RADS 3 were found to be higher, it indicates a too large percentage of probably malignant lesions being included in this category. There is a debate on the latter two percentages, and no established guidelines for BI-RADS 3 exist.

In our study a much higher percentage of cases were classified in BI-RADS 3 in both the initial and final reporting by all three viewers. This can perhaps be attributed to inexperience of the viewers (general radiologists see section 5.3.2) in this study compared to expert mammographers who are often used in studies to establish benchmarks. Furthermore, our viewers did not have the opportunity to review the patient's clinical history or previous mammogram(s) to assist them in their BI-RADS assessment. Moreover, our dataset of cases was selected to include 50% malignant and 50% benign cases. All of the above could well have led to more uncertainty

among our viewers which caused them to use BI-RADS 3 more often and to have the opportunity to re-assess their findings with short term follow-up.

However as mentioned before, the main aim of our study was to evaluate the effect of the viewing protocol on the diagnostic accuracy of the viewers. This study found a slight decrease in the percentage of cases in BI-RADS 3 for two of the viewers after the development of the viewing protocol. However, a slight increase was found for viewer B (from 30% to 32.5%). Previous work assessing the effect of Premium View post-processing software on DM reporting showed interim results with a higher recall rate which was ascribed to a technical learning curve (Goldstraw *et al*, 2009). They thus ascribed the higher interim recall rate to more uncertainty among the viewers with the appearance of the image with the new processing software. In this study, BI-RADS 0 (recall) which is used in screening mammography (for additional imaging), was not an option. In this study if viewers felt uncertain about their finding, they would use BI-RADS 3 (probably benign finding with a recommendation for short interval follow up). After the training offered to the viewers in this study, together with the development of the viewing protocol through participative learning, one would presume that the viewers should have been more confident with the processed image. Our study found a small decrease in BI-RADS 3 for the majority of viewers after the development of the viewing protocol. It thus appears that the viewing protocol could well have improved the majority of viewers' confidence not to use short term follow-up in so many cases.

In our study the percentage true malignant cases found in BI-RADS 3 was much higher than the benchmark suggested by some of <2%. This indicates a too large percentage of probably malignant lesions were placed in this probably benign category. Because of the small number of malignant cases (40) in both initial and

final reporting, even one case in this category delivered a percentage value above the benchmark of <2%. However, after the development of the viewing protocol, the number of malignant cases found in BI-RADS 3 decreased by more than 50% for viewer B and by more than 67% for viewer C. It thus appears the viewing protocol probably improved the perceptibility of the subtle signs of breast cancer for the majority of viewers.

6.5.3 Breast parenchyma classification

Previous studies have found proof that increased breast density significantly reduces the sensitivity of mammography (Carney *et al*, 2003) (Kerlikowske *et al*, 1996). Furthermore, there is substantial evidence that shows that mammographic densities are an indicator of increased risk of breast cancer (Harvey & Bovbjerg, 2004) (Oza & Boyd, 1993). The ACR recommends in BI-RADS that a description of breast density should be included in every mammography report to inform the referring clinician about how the mammographic density of the patient may affect the sensitivity of the examination (ACR, 2003). However there is no standard method of quantifying breast density and the debate on a reproducible method to classify breast density is ongoing. Breast density classification on mammograms can be grouped into two broad categories: subjective classification (by radiologists) and objective classification (computerised assessment) (Jamal *et al*, 2007). Different subjective classifications have been reported e.g.: Wolfe's classification (Wolfe, 1976), Tabár's classification (Gram, Funkhouser & Tabár, 1997) and the BI-RADS density classification (ACR, 2003). According to Sickles (2007) breast density as an indicator of future cancer risk has largely replaced the Wolfe mammographic parenchyma pattern classification. In our study, the radiologists were instructed to use Tabár's classification of breast parenchyma pattern as they were using this

classification in SFM before the study and it was presumed that they were more familiar with it.

A number of studies on variability in interobserver and intraobserver agreement for the various breast density assessment methods have been reported. Berg and co-workers (2000) reported on interobserver agreement of five (5) experienced mammographers who assessed among other things breast density on 103 screening mammograms using BI-RADS (the mammographers were not specifically trained in BI-RADS). They found an overall interobserver kappa value of 0.43 which indicates moderate agreement. In another study Ciatto *et al* (2005) reported on interobserver agreement of 12 dedicated breast radiologists who assessed 100 mammograms according to BI-RADS breast density classification. They also found the average interobserver agreement to be moderate (kappa 0.54, range 0.02-0.77). Our study also found weak to moderate agreement between the majority of viewer pairs in both the initial (highest agreement 61.3%) and final reporting (highest agreement 66.3%) for breast parenchyma classification. On the other hand a study by Ooms *et al* (2007), in which four experienced breast radiologists assessed 57 mammograms for breast density, they found a weighted overall kappa of 0.77 (95% CI: 0.69-0.85) which indicates substantial overall interobserver agreement. The difference in their study is that the radiologists received instructions regarding the use of BI-RADS. In our study, because the radiologists used Tabár's classification of breast parenchyma on SFM before, it was assumed that they were familiar with it and they only received a copy of the parenchyma breast pattern with their information document pertaining to the study (Appendix P). It is possible that the inconsistency among the viewers is probably due to the viewer's incorrect perception of the classification criteria rather than the classification system per se. However, as this study found the dense

parenchyma in the breast to be the anatomical area with the lowest image quality (section 5.3.1.2), it is possible that the BI-RADS density assessment might be more suitable for the processed digital image than Tabár's classification of breast parenchyma. However, the measure of breast density is still qualitative and is observer-dependent because it involves the judgement of the radiologist. A recent study by Lobbes *et al* (2012) compared breast density assessment by an experienced and inexperienced reader in 200 mammograms. The images were scored according to BI-RADS classification and density assessment using dedicated software. They found that in 42% of cases the experienced and inexperienced reader disagreed on the BI-RADS density category and thus only moderate agreement (kappa 0.52) was found. With the semi-automated analysis, they found excellent intra-class correlation coefficient of 0.91 [95% confidence interval; 0.88-0.93] for both left-sided and right-sided breast densities alike. Comparison between the semi-automated analysis and the BI-RADS classification assigned showed that the correct BI-RADS classification was assigned in 58.5% of cases by the experienced reader. On the other hand, the inexperienced viewer was found to assign the correct BI-RADS classification in only 42.0% of cases. Their study demonstrated that the objective assessment of breast density could be used to improve agreement between viewers on breast density classification. To improve agreement on density assessment between viewers, the development of an objective (computer-based) assessment of breast density should probably be investigated.

However, what our study did find using the subjective Tabár's breast parenchyma assessment method, was that the viewing protocol improved agreement between viewers on parenchyma classification although not significantly. This could probably

be ascribed to the radiologists' improved experience in viewing the digitally processed image which probably allowed them to better have viewed the dense parenchyma in the breast.

6.5.4 Characterisation of lesions

To improve the intrinsic variability in mammographic interpretation the ACR introduced BI-RADS in 1993. It is also the reason why it has become compulsory with the MQSA that all mammograms in the US be reported using BI-RADS assessment categories. The aim was to standardise the interpretation of mammograms and to improve communication between clinicians and radiologists. This was also the motivation for establishing the BI-RADS lexicon to describe the features of mammographic lesions. To standardise the reporting in our own setting (see section 1.4), BI-RADS assessment together with the BI-RADS lexicon were introduced for the assessment of mammograms with the start of this study.

The aim of our study was not to compare our results with the results of others, but rather to determine the effect of our viewing protocol on viewer agreement. Our study found improved agreement among the viewers on the characterization of lesions after the development of the viewing protocol. The improvement in agreement was predominantly found for the descriptors pertaining to the skin and also the nipple. In the development of the viewing protocol (Chapter 5), MUSICA^2 Invert was found to provide significantly better image quality for the evaluation of skin outline and this was why it was recommended as the default processing option for the viewing protocol. This is probably the reason for the improved interobserver agreement found in this study for the descriptors pertaining to the skin and nipple with the recommended viewing protocol.

The radiologists in this study did not have training in the use of BI-RADS per se. Previous authors, who investigated predictors of interobserver agreement in mammography using BI-RADS, suggested that training in the use of BI-RADS and focusing on mass description may increase agreement in mammography interpretation (Antonio & Crespi, 2010). This is supported by another US study in which 23 experienced breast imagers reviewed mammograms before and after a day's lectures on BI-RADS (Berg *et al*, 2002). Improved agreement was found among others for mass margins and/or asymmetries (kappa 0.36 improved to kappa 0.41 after training) and also for the description of calcification morphology (kappa 0.36 improved to kappa 0.44 after training). Training the radiologists in our setting on the use of BI-RADS could probably improve agreement between them on the characterization of lesions.

6.6 CONCLUSION

The theoretical training offered to the radiologists was aimed at improving the radiologists' factual and conceptual knowledge of the new modality with special emphasis on how to address the challenges which radiologists face when switching from SFM to DM soft-copy viewing.

The development of the viewing protocol was aimed at improving image quality in soft-copy viewing and thereby subsequently the perceptibility of the subtle signs of breast cancer to improve diagnostic accuracy in mammography reporting. The radiologists also gained experience in soft-copy viewing through the participative learning method in developing the viewing protocol.

Our study found that although not significantly, the viewing protocol did improve radiological reporting in terms of the sensitivity and specificity for the majority of

viewers. Also, although not significantly, the overall accuracy and PPV increased for all the viewers. The high percentage BI-RADS 3 cases found in this study could probably be attributed to the fact that our radiologists were not experienced mammographers. In addition they did not have access to previous mammograms or the clinical history of the cases to assist them in interpreting their findings. However, although not significantly, the development of the viewing protocol did contribute to the majority of radiologists' confidence to categorize their findings as either benign or malignant without the need for short term follow-up.

What this study also found is that although there was an improvement between all the viewers on Tabár's classification of breast parenchyma after the viewing protocol, the agreement was still weak to moderate for the majority of viewer pairs. The qualitative method of using the radiologists' judgement on Tabár's classification of breast parenchyma is perhaps not ideal for the digitally processed image.

Furthermore, the study found variability among viewers in the use of the BI-RADS descriptors to communicate their findings. The recommended viewing protocol with MUSICA^2 Invert did contribute to improved agreement among the viewers on the descriptors pertaining to skin thickening, skin retraction, and nipple retraction. In order to achieve the goal of BI-RADS, namely to standardise the interpretation of mammograms to improve communication between clinicians and radiologists, the radiologists should clearly be specifically trained in the use thereof.

CHAPTER 7

CONCLUSIONS AND RECOMMENDATIONS

7.1 CONCLUSIONS

Since the aim of mammography is to detect breast carcinoma in its earliest possible stages, great emphasis should be placed on the perceptibility of the subtle signs of breast malignancies in the development of a soft-copy viewing protocol for mammography. The first step for the radiologists is to detect the abnormality on the mammogram, and only thereafter can the radiologist analyse the mammogram to arrive at the correct diagnosis. Good image quality is thus of the utmost importance in mammography and the development of a soft-copy viewing protocol should address the need for the clear visualization of anatomical structures in the breast and subsequently the subtle signs of breast carcinoma.

When switching from SFM to DM the radiologist needs additional knowledge on and understanding of the new modality (Chapter 2). They should be aware of the differences between SFM and DM and they should know how to address the challenges for the radiologists when switching from SFM to DM. As they need different skills to perform soft-copy viewing and reporting, they need knowledge of and experience in using the tools for soft-copy viewing. Of great importance is that they should have a reasonable knowledge of the effect of digital image processing on image quality. The theoretical training offered to the radiologists in this study (Chapter 5) equipped them with the necessary knowledge and understanding of among others the principles of DM and the advantages and disadvantages of the

new technology. They also learned about the principles of good soft-copy viewing and the effect of image processing on the appearance of the image.

The development of the viewing protocol in this study (Chapter 5) was aimed at improving the clear visualization of breast anatomy and thereby subsequently the perceptibility of the subtle signs of beast carcinoma. Based on our findings, recommendations were made for the processing option which provided the best image quality for anatomical structures overall, individual anatomical structures, masses and calcifications. Also, the processing option with the least visible noise was identified so as to assist radiologists whenever visible noise poses to be a problem. The processing option which the viewers regarded as suitable for the early detection of breast cancer was also identified. The processed image (MUSICA^2) was found to provide significantly better overall image quality compared to the unprocessed image. From the results of this study, it is understandable why the vendor (Agfa) has superseded its MUSICA software with MUSICA^2. This study (Chapter 5) is a confirmation of the superiority of the new software.

However, the clear visualization of masses was found to be an area in which the processed images did not significantly improve image quality. Recommendations were made that the viewer should pay special attention in viewing to attempt to make subtle contrast differences more visible by applying manual intensity windowing (WW/WL) especially in the dense breast parenchyma.

The only significant difference in image quality between MUSICA^2 and MUSICA^2 Invert was found for skin outline. MUSICA^2 Invert was found to improve the visualization of the skin and nipple area significantly and should be used in clinical practice for that. The MUSICA^2 Invert image was thus recommended as the default

processing option for our setting. With the characterisation of lesions, the agreement between the viewers showed good improvement in the evaluation of skin thickening, skin retraction and nipple retraction with MUSICA^2 Invert (Chapter 6).

The image processing algorithm on a digital unit is vendor dependant, and there is no standard processing option. Processing algorithms will therefore differ between mammography units and radiologists should have knowledge and experience of the effect of the processing option on the appearance of the image. They should know if different processing options should be used in their unit for different tasks (screening mammography versus diagnostic mammography) and/or for different lesion types (calcifications and masses). They should thus invest time to learn about their processing options.

Also, with the MUSICA^2 processing algorithm, the viewer cannot vary any processing parameter. However, with some other processing options for e.g. CLAHE a number of parameters can be varied. In such cases, knowledge of the effect of each parameter on image quality is essential for the radiologists viewing and reporting on the images. The participative learning approach used in this study, enabled the radiologists to obtain the necessary knowledge of the effect of the different parameter combinations on image quality.

Furthermore, should the vendor of a DM unit upgrade the image processing software, the participative learning method used in this study can also be used to learn about the effect thereof on image quality.

The phantom-based assessment of image quality (Chapter 2) and the assessment on clinical images (Chapter 5) did not find the same processing options to provide superior image quality. The phantom based study found little difference between the

Unprocessed images and the MUSICA^2 processed images. Only Unprocessed Invert was found to be significantly superior to MUSICA^2 Invert. However, although not significantly, Unprocessed Invert was found to provide better image quality compared to Unprocessed and MUSICA^2. In the clinical study on the other hand, the processed images (MUSICA^2 and MUSICA^2 Invert) were found to provide significantly better image quality compared to the Unprocessed images for the anatomical structures overall, for most of the individual anatomical structures, and for calcifications. This difference in the results with the phantom based study and the clinical images indicates that the phantom based study can be a useful tool, but cannot supplant the clinical study.

The small change in diagnostic accuracy after the viewing protocol (Chapter 6) can possibly be ascribed to the fact that a relatively high sensitivity was found among the radiologists before training. The relatively large number of cases with malignancy could have contributed to the high sensitivity because 'diagnostic mammography' may be considered as "easier" to report. Even before the development of the viewing protocol through participative learning, the radiologists fared well in identifying lesions that indicated malignancy.

The small difference in the processing algorithm proposed for the viewing protocol (Chapter 5) also limited the chance to show a significant improvement in diagnostic accuracy (Chapter 6). MUSICA^2 and MUSICA^2 Invert were not found to be significantly different. It was only for skin outline that MUSICA^2 Invert was found to be significantly superior. Should a more profound difference in image quality be found, it may well have a greater impact on diagnostic accuracy.

Although the viewing protocol was aimed at improving the first step in mammography reporting, namely to perceive subtle signs of breast carcinoma, the second step, namely analyzing the imaging findings to arrive at the correct diagnosis, was not in the scope of this study. The variability in interobserver agreement on lesion characterization found in both the initial and final reporting in this study (Chapter 6), points towards a need for training the radiologists to analyse their findings using the BI-RADS descriptors. Radiologists need to communicate their findings to the referring physician, patient and surgeon and in this area a lot of disagreement was found among the viewers irrespective of the viewing protocol. The use of terminology to communicate the findings should also be consistent otherwise the reporting becomes inconsistent. The study found evidence for a need to train radiologists in using standardised terminology for the characterisation of lesions. However, this study laid a good foundation for further improvement in radiology reporting by ensuring that the best image quality is available for viewing.

What we have showed is that the viewing protocol did improve agreement between the radiologists (Chapter 6) in areas where the proposed default processing option (MUSICA^2 Invert) were found to provide significantly superior image quality. This is attributed to the better visualization of the skin outline achieved with MUSICA^2 Invert as the default processing option for the recommended viewing protocol.

The participative learning approach in developing the viewing protocol (Chapter 5) could be of value to any radiologists changing from SFM to DM. It can improve their confidence in soft-copy viewing and can provide them with first-hand experience of the effect of image processing options in their clinical setting on image quality. Should even small changes be made in image processing, this participative learning

approach can be of great value to the viewers to familiarise them with the effect thereof on image quality.

After the training and the participative learning (Chapter 5), the radiologists had first-hand experience of the influence of image processing on the appearance of the mammogram image and one would assume that they were more confident in interpreting the digitally processed image. The proposed viewing protocol could be used confidently by the radiologists because they have found it to provide them with the best image quality to assess mammograms to perceive the subtle signs of breast malignancies. Also, they now had the necessary knowledge of digital mammography, experience in soft-copy viewing and a better understanding of the effect of image processing on image quality. They can now confidently perform soft-copy mammography viewing for reporting.

The outcomes of this study will be used in the future training of radiologists. Based on the findings of this study, a teaching file on the mammography module was created for the M.Med. (Rad.D.) qualification at the University of the Free State (see Appendix X). This teaching file is in the process of being implemented at the Simulation-unit (which is currently under construction) in the Faculty of Health Sciences at the University of the Free State. The teaching file includes theoretical training as conducted during the research, as well as 80 mammography cases (used in the current study) for viewing with the proposed viewing protocol. The viewers (registrars) will do structured reporting as proposed in this study with the aid of BI-RADS descriptors. The outcomes are based on the findings in this study namely a good understanding of digital imaging principles and soft-copy viewing principles, the use of the proposed viewing protocol, and standardising reporting according to BI-RADS. On completion of the teaching file, the registrars will be assessed on 40

mammography cases (used in the current study) to determine the registrar's sensitivity, specificity and the use of BI-RADS category 3 and thus their performance post-training. The theoretical training and the teaching file will also be evaluated from the registrars' point of view.

7.2 RECOMMENDATIONS

7.2.1 Training of radiologists in the new modality

The training of radiologists in the new modality when switching from SFM to DM is regarded as essential. Radiologists should be aware of the challenges of soft-copy viewing and how to address these in order to achieve the full potential of soft-copy viewing. Radiologists cannot confidently interpret digitally processed images unless they have reasonable knowledge and experience of the effect of the processing option on the appearance of the image. The participative learning approach used in this study is recommended for developing a soft-copy viewing protocol for radiologists changing from SFM to DM. This approach can provide them with first-hand experience in soft-copy viewing and the effect of the image processing options in their clinical setting on image quality.

7.2.2 Development and refinement of a soft-copy viewing protocol

The development and refinement of a soft-copy viewing protocol for each clinical setting will be relevant as long as vendors use different processing algorithms. The radiologist must be able to perceive the subtle signs of breast cancer in order to analyse them for diagnosis. A high standard of image quality in mammography is essential for optimal perception by the viewer and each mammography unit should develop or refine their own soft-copy viewing protocol to ensure the best image quality is obtained. The participative learning approach is also recommended to

refine a viewing protocol in any mammography unit should even small changes in image processing options or software be implemented. The advantage thereof is that it provides the opportunity for all radiologists to learn about the effect of the change on image quality so that they can confidently apply it in clinical practice.

7.2.3 Objectives for the development of a soft-copy viewing protocol

We regard the objectives (questions) set for the development of our viewing protocol to be relevant for the development of a soft-copy viewing protocol for any mammography unit. It will enable the radiologists to find the best processing option(s) in their clinical setting for different types of lesions (calcifications and masses) and also for different mammography tasks (screening versus diagnostic).

7.2.4 Visualisation of masses

Because this study found the processed images (MUSICA^2 and MUSICA^2 Invert) not to be significantly superior to the unprocessed images for the visualisation of masses, radiologist should pay special attention to viewing for masses. Manual WW/WL adjustments should be used to try and improve the visual contrast to perceive the low subject contrast of masses.

7.2.5 Visualisation of dense parenchyma in the breast

Also, although the processed images (MUSICA^2 and MUSICA^2 Invert) are significantly superior to the unprocessed images for the clear visualisation of vessels through dense parenchyma, it remains an area which has significantly less image quality compared to the other anatomical areas. As for viewing masses, radiologists should exercise special precaution and use manual WW/WL adjustments to try and improve visual contrast to perceive detail through the dense parenchyma.

7.2.6 Invert gray scale

The Invert of MUSICA^2 is recommended specific for the viewing of the skin and nipple area as it has been found to provide significantly better image quality in those areas. For image quality control tests with the CDMAM type 3.4 phantom, the processing option Unprocessed Invert should be used as it was found to provide best image quality.

7.2.7 Clinical images

Clinical images should be used for developing a soft-copy viewing protocol for a mammography unit as this study found that a phantom-based study (like the one used in this study), cannot supplant image quality evaluation on clinical images.

7.2.8 Standardising mammographic reporting

Standardising mammographic reporting is important to improve communication between clinicians and radiologists. Training in the use of BI-RADS is regarded as important to improve agreement between viewers on the descriptors for lesion characterisation. It should not be assumed that because standardized descriptors are used, all radiologists will interpret them in the same way.

7.3 LIMITATIONS OF THE STUDY

7.3.1 Small number of viewers

The power of the study is somewhat limited by the small number of radiologists (viewers) included in the study. The setting where the study was conducted only had eight consultant radiologists at the time of which two were doing a fellowship in interventional radiology and were therefore not available for the study. The time the viewers had to spend participating in the research adds up to an average of just less

than 25 hours per viewer (initial reporting 7 hours 20 minutes, training 4 hours, developing the viewing protocol 8 hours 15 minutes and final reporting 5 hours 16 min) which is a considerable time for a radiologist. Time constraints on the part of the radiologists limited the number of radiologists that could participate in the study and we could also only include those who had not been exposed to DM before. Only readers with no previous experience in digital mammography were included in the study. This was specifically to address the aim of our study in evaluating the effect of developing the soft-copy viewing protocol for radiologists changing from SFM to DM.

7.3.2 Number of cases

The significance of this study is somewhat hampered by the small sample size (120 patient cases). Equal numbers of malignant and benign / normal cases were needed so that random guesses would not skew the results. Because we wanted to include true malignant cases, only patients for whom histopathology confirmation of all noted lesions/masses could be obtained were included. The 60 confirmed malignant cases together with the 60 benign/normal cases formed a balanced set of test images that allowed adequate testing of the proposed viewing protocol.

7.3.3 Type of mammograms

Our setting does not offer a mammography screening programme. Because diagnostic mammograms are predominantly performed in our setting, it could have hampered the improvement in accuracy that could be obtained. A different finding could be a possibility for a screening population in which earlier signs of breast malignancies can be expected compared to diagnostic mammography.

7.3.4 Administrative limitations

These include poor record keeping and exclusion of patients due to limited follow-up. Although more radiology reports were found in which malignancy was suspected, we were unable to obtain histopathology confirmation because the patients were apparently followed-up at other hospitals or no record could be found.

7.3.5 Representivity

The population only includes patients from one tertiary hospital and one group of patients. Also only one digital unit and the processing options on that unit were included in the study.

7.3.6 Software limitations

The fact that the default processing option (MUSICA^2) on our digital unit (before the development of the viewing protocol) provided good image quality compared to the proposed processing option for the viewing protocol (MUSICA^2 Invert), left little room to show an improvement in diagnostic accuracy after the development of the protocol. However, it is anticipated that, should a processing option be identified which provided much better image quality, a larger improvement in diagnostic accuracy is possible. Also, different results would be possible in a screening population in which the perception of earlier signs of breast malignancy could be expected compared to those in a diagnostic population.

7.3.7 Tabár's classification of breast parenchyma

The study showed that Tabár's classification of breast parenchyma is an area of disagreement among radiologists. The subjective classification described by Tabár was not found to be a reproducible method to classify breast parenchyma on the

digital image in our study. An alternative classification based on DM characteristics would be more useful.

7.3.8 The use of BI-RADS to standardise reporting

It was envisaged that the local reporting radiologists could standardise mammography reporting by using BI-RADS developed by the ACR, together with the BI-RADS lexicon descriptors for mammographic findings. The results of this study showed that radiologists can interpret the descriptors differently.

7.4 FUTURE RESEARCH

This study brought to the fore some areas in this field of research that will require further attention in future:

- How do we identify masses

- How do we better image dense areas so as to more accurately identify masses and other signs of breast malignancy

- How do we reproducibly classify breast density

- How do we consistently and standardly describe and classify our findings in mammography

- Evaluation of the protocol in everyday practice

- Proof that the protocol improves radiological reporting

Digital mammography soft-copy viewing protocols that are developed based on the principles of this study can make a meaningful contribution in the transition to digital mammography. It will enable radiologists to confidently use their recommended viewing protocol in clinical practice. And so although we have laid a good foundation for the transition to digital mammography, there are still significant questions to be answered…

LIST OF REFERENCES

American Cancer Society, 2010. *Survival rates for breast cancer.* [Online] Available: www.cancer.org/Cancer/BreastCancer/OverviewGuide/breast-cancer-overview-survival-rates [Accessed 25 April 2012]

American College of Radiology, 2003. *BI-RADS: mammography*, 4th ed. In: Breast imaging reporting and data system: BI-RADS atlas, Reston, VA: American College of Radiology.

American College of Radiology, 2007. *ACR-AAPM-SIIM practice guideline for determinants of image quality in digital mammography. (Res.35)*. [Online] Available: http://www.google.co.za/#hl=en&output=search&sclient=psy-ab&q=American+College+of+Radiology.+++2007.++ACR-AAPM-SIIM+practice+guideline+for+determinants+of+image+quality+in+digital+mammography.++(Res.35).+&oq=American+College+of+Radiology.+++2007.++ACR-AAPM-SIIM+practice+guideline+for+determinants+of+image+quality+in+digital+mammography.++(Res.35).+&gs_l=hp.12...22235.22235.0.25188.1.1.0.0.0.0.0.0..0.0...0.1...1c.dCvYvV58kvk&pbx=1&bav=on.2,or.r_gc.r_pw.r_qf.&fp=2a7aa3db6754adfb&biw=1024&bih=549 [Accessed 15 November 2010]

American College of Radiology, 2008. *ACR practice guideline for the performance of screening and diagnostic mammography (Res. 24)*. [Online] Available: http://www.acr.org/~/media/3484CA30845348359BAD4684779D492D.pdf [Accessed 8 September 2010]

American College of Radiology, 2012. *ACR statement on reporting breast density in mammography reports and patient summaries*. [Online] Available http://www.acr.org/About-Us/Media-Center/Position-Statements/Position-Statements-Folder/Statement-on-Reporting-Breast-Density-in-Mammography-Reports-and-Patient-Summaries [Accessed 25 April 2012]

Andriole, K.P., Gould, R.G., Webb, W.R., 1999. Finding Specific Display Presets for Computed Radiography Soft-copy Reading. *Journal of Digital Imaging*;12(2), Supplement 1:3-5.

Antonio, A.L.M. & Crespi, C.M., 2010. Predictors of Interobserver Agreement in Breast Imaging using the Breast Imaging Reporting and Data System. *Breast Cancer Res Treat*;120:539-46.

ARTINIS Manual Contrast-Detail phantom CDMAM type 3.4, 2007.

Aveyard, H., 2010. *Literature review in health and social care: A practical guide*. 2nd ed. Open University Press: Glasgow.

Ball, J. & Price, T., 1995. *Chesneys' radiographic imaging*. 6th ed. Oxford: Blackwell Science.

Barlow, W.E., Lehman, C.D., Zheng, Y., Ballard-Barbash, R., Yankaskas, B.C., Cutter, G.R., Carney, P.A., Geller, B.M., Rosenberg, R., Kerlikowske, K., Weaver, D.L., Taplin, S.H., 2002. Performance of Diagnostic Mammography for Women with Signs or Symptoms of Breast Cancer. *Journal of the National Cancer Institute*;94(15):1151-59.

Bassett, L.W., 1996. The Regulation of Mammography. *Seminars in Ultrasound, CT, and MRI*;17(5):415-23.

BCSC, 2007. *Sensitivity and specificity for 4,032,556 screening mammography examinations from 1996 – 2005*. [Online] Available: http://www.breastscreening.cancer.gov/data/benchmarks/screening/tableSensSpec.html [Accessed 27 January 2012]

BCSC, 2010. *Sensitivity and specificity by indication of examination for 401,572 diagnostic mammography examinations from 2002 – 2006 --- based on BCSC data as of 2009*. [Online] Available: http://breastscreening.cancer.gov/data/benchmarks/diagnostic/2009/tableSensSpec.html [Accessed 27 January 2012]

Berg, W.A., Campassi, C., Langenberg, P., Sexton, M.J., 2000. Breast Imaging Reporting and Data System: Inter- and Intraobserver Variability in Feature Analysis and Final Assessment. *AJR*;174:1769-77.

Berg, W.A., D'Orsi, C.J., Jackson, V.P., Bassett, L.W., Beam, C.A., Lewis, R.S., Crewson, P.E., 2002. Does Training in Breast Imaging Reporting and Data System (BI-RADS) Improve Biopsy Recommendations or Feature Analysis Agreement with Experienced Breast Imagers at Mammography. *Radiology*;224:871-80.

Bosmans, H., Carton, A.K., Rogge, F., Zanca, F., Jacobs, J., Van Ongeval, C., Nijs, K., Van Steen, A., Marchal, G., 2006. Image Quality Measurements and Metrics in Full Field Digital Mammography: An Overview. *Radiation Protection Dosimetry*;117(1-3):120-30.

Brancato, B., Houssami, N., Francesca, D., Bianchi, S., Risso, G., Catarzi, S., Taschini, R., Rosselli Del Turco, M., Ciatto, S., 2008. Does Computer-aided Detection (CAD) Contribute to the Performance of Digital Mammography in a Self-referred Population? *Breast Cancer Res Treat*;111(2):373-76.

Bushberg, J.T., Seibert, J.A., Leidholdt, E.M. (Jr.), Boone, J.M., 2012. *The essential physics of medical imaging*. 3rd ed. Philadelphia: Wolters Kluwer / Lippincott Williams & Wilkins.

Cancer Research UK, 2009. *Breast cancer: survival statistics.* [Online] Available: http://info.cancerresearchuk.org/cancerstats/types/breast/survival/breast-cancer-survival-statistics [Accessed 27 Sept 2010]

Cancer Research UK, 2010. *Cancer cases and deaths across the world and in the UK.* [Online] Available: http://info.cancerresearchuk.org/cancerstats/reports/ [Accessed 27 October 2010]

Carney, P.A., Migliorettie, D.L., Yankaskas, B.C., Kerlikowske, K., Rosenberg, R., Rutter, C.M., Geller, B.M., Abraham, L.A., Taplin, S.H., Dignan, M., Cutter, G., Ballard-Barbash, R., 2003. Individual and Combined Effects of Age, Breast Density, and Hormone Replacement Therapy Use on the Accuracy of Screening Mammography. *Ann Intern Med;*138:168-75.

Ciatto, S., Houssami, N., Apruzzese, A., Bassetti, E., Brancato, B., Carozzi, F., Catarzi, S., Lamberini, M.P., Marcelli, G., Pellizzoni, R., Pesce, B., Risso, G., Russo, F., Scorsolini, A., 2005. Categorizing Breast Density: Intra- and Interobserver Reproducibility of BI-RADS Density Categories. *Breast*;14(4):269-75.

Cole, E.B., Hill, C., Pisano, E.D., Hanna, L.G., Braeuning, M.P., Kuzmiak, C.M., Rice, L.Z. *et al*., 2001. Multi-center Clinical Assessment of the Fischer SenoScan Digital Mammography System. *Radiology*;(supplement) 221:285.

Cole, E., Pisano, E.D., Brown, M., Kuzmiak, C., Braeuning, P., Kim, H.H., Jong, R., Walsh, R., 2004. Diagnostic Accuracy of Fischer SenoScan Digital Mammography versus Screen-film Mammography in a Diagnostic Mammography Population. *Acad Radiology*;11:879-86.

Cole, E.B., Pisano, E.D., Kistner, E.O., Muller, K.E., Brown, M.E., Feig, S.A., Jong, R.A., Maidment, A.D.A., Staiger, M.J., Kuzmiak, C.M., Freimanis, R.I., Lesko, N., Rosen, E.L., Walsh, R., Williford, M., Braeuning, M.P., 2003. Diagnostic Accuracy of Digital Mammography in Patients with Dense Breast who underwent Problem-solving Mammography: Effects of Image Processing and Lesion Type. *Radiology*;226:153-60.

Cole, E.B., Pisano. E.D., Zeng, D., Muller, K., Aylward, S.R., Park, S., Kuzmiak, C., Koomen, M., Pavic, D., Walsh, R., Baker, J., Gimenez, E.I., Freimanis, R., 2005. The Effects of Gray Scale Image Processing on Digital Mammography Interpretation Performance. *Acad Radiol*;12:585-95.

Cowen, A.R., Launders, J.H., Jadav, M., Brettle, D.S., 1997. Visibility of Microcalcifications in Computed and Screen-film Mammography. *Phys Med Biol*;42:1533-48.

Dähnert, W., 2002. *Radiology review manual*. 5th ed: Baltimore:Lippencott, Williams & Wilkins.

D'Orsi, C.J. & Newell, M.S., 2007. Digital Mammography: Clinical Implementation and Clinical Trials. *Seminars in Roentgenology*;42(4):236-42.

De Maeseneer, M., Beeckman, P., Osteaux, M., Mattheus, R., Hoste, M., Bastaerts, Y., Jong, B., 1992. Detecting Clustered Microcalcifications in the Female Breast: Secondary Digitized Images versus Mammograms. *J Belge Radio*;75(3):173-78.

Dee, K.E. & Sickles, E.A., 2001. Medical Audit of Diagnostic Mammography Examinations – Comparison with Screening Outcomes obtained Concurrently. *AJR*;176(3):729-33.

Del Turco, M.R., Mantellini, P., Ciatto, S., Bonardi, R., Martinelli, F., Lazzari, B., Houssami, N., 2007. Full-field Digital versus Screen-film Mammography: Comparative Accuracy in Concurrent Screening Cohorts. *AJR*;189:860-66.

ECR, 2011. *BI-RADS 3 arouses controversy, poses management challenges*. [Online] Available: www.auntminnieeurope.com/redirect/redirect.asp?ItemID=604819 [Accessed 27 January 2012]

European Commission, 2006. *European Guidelines for quality assurance in breast cancer screening and diagnosis. The European protocol for the quality control of the physical and technical aspects of mammography screening, Part B: Digital mammography*,. 4th ed. Luxembourg: European Commission.

Feig, S.A. & Yaffe, M.J, 1996. Current status of digital mammography. *Seminars in Ultrasound, CT and MRI*;17(5):424-43.

Fleiss, J.L., Levin, B., Paik, M.C., 2003. *Statistical methods for rates and proportions*. 3rd ed. New Jersey: Wiley-Interscience.

Food and Drug Administration, 2001. *The Mammography Quality Standards Act Final Regulations: Preparing for MQSA Inspections; Final Guidance for Industry and FDA.* [Online] Available: http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm094441.pdf [Accessed 26 October 2011]

Food and Drug Administration (2010*). The Mammography Quality Standards" Final Rule*. [Online]. Available: http://www.fda.gov/CDRH/MAMMOGRAPHY/mqsa-act.html [Accessed 30 September 2010]

GLOBOCAN (IARC), 2008. *Cancer fact sheet: Breast cancer incidence and mortality worldwide in 2008 - Summary*. [Online] Available: http://globocan.iarc.fr/factsheets/cancers/breast.asp [Accessed 25 October 2010]

GLOBOCAN (IARC), 2008. *South African Republic: most frequent cancers: women.* [Online] Available: http://globocan.iarc.fr/factsheets/populations/factsheet.asp?uno=710 [Accessed 27 September 2010]

Goldstraw, E.J., Castellano, I., Ashley, S., Allen, S., 2009. The Effect of Premium View Post-processing Software on Digital Mammographic Reporting. *The British Journal of Radiology*;000:1-7.

Gonzalez, R.C., & Woods, R.E., 2008. *Digital image processing*. 3rd ed. New Jersey: Pearson Education International.

Gøtzsche, P.C. & Nielsen, M., 2009. *Screening for breast cancer with mammography (Review) - The Cochrane Collaboration*. [Online] Available: http://www.cochrane.dk/research/Screening%20for%20breast%20cancer,%20CD001877.pdf [Accessed 20 April 2012]

Gram, I.T., Funkhouser, E., Tabár, L., 1997. The Tabár Classification of Mammographic Parenchymal Pattern. *European Journal of Radiology*;24:131-36.

Harvey, J.A. & Bovbjerg, V.E., 2004. Quantitative Assessment of Mammographic Breast Density: Relationship with Breast Cancer Risk. *Radiology*;230:29-41.

Haus, A.G., 1990. Technologic Improvements in Screen-film Mammography. *Radiology*;74:628-37.

Hemdal, B., Andersson, I., Grahn, A., Håkansson, M., Ruschin, M., Thilander-Klang, A., Båth, M., Börjesson, S., Medin, J., Tingberg, A., Månsson, L.G., Mattsson, S., 2005. Can the Average Glandular Dose in Routine Digital Mammography Screening be Reduced? A Pilot Study using Revised Image Quality Criteria. *Radiation Protection Dosimetry;*114(1-3):383-8.

Hemminger, B.M., 2003. Soft Copy Display Requirements for Digital Mammography. *Journal of Digital Imaging*;16(3):292-305.

Hemminger, B.M., Zong, S., Muller, K.E., Coffey, C.S., DeLuca, M.C., Johnston, R.E, Pisano, E.D., 2001. Improving the Detection of Simulated Masses in Mammograms through Two different Image-processing Techniques. *Academic Radiology*;8:845-55.

Hendrick, R.E., Lewin, J.M., D'Orsi, C.J., Kopans, D.M., Conant, E., Cutter, G.R., Sitzler. A., 2001. Non-inferiority Study of FFDM in an Enriched Diagnostic Cohort: Comparison with Screen-film Mammography in 625 Women. In: Yaffe, M.J., ed. IWDM 2000: *5th International workshop on digital mammography*. Madison, WI: Medical Physics Publishing 2001:475-81.

Homer, M.J., 1991. *Mammographic interpretation: a practical approach*. New York:McGraw-Hill.

HPCSA, 2001. *Regulations relating to the specialities and subspecialities in medicine and dentistry, No. R. 590.* [Online] Available: http://www.hpcsa.co.za/downloads/medical_dental/regulations/r590_of_29_june_2001.pdf [Accessed 31 January 2011]

HPCSA, 2011. Continuing Professional Development: CPD Overview. Available: http://www.hpcsa.co.za/cpd_overview.php [Accessed 31 January 2011]

Hundertmark, C., Breiter, N., Hermann, K.P. *et al*, 1997. Digitale VergröBerungsmammographic in Speicherfolientechnik. Erste klinische Ergebnisse. *Radiologe*;37(8):597-603. In: Pisano, E.D., Yaffe, M.J. & Kuzmiak, C.M., 2004. *Digital Mammography*. Philadelphia: Lippincott Williams & Wilkins.

Ikeda, D.M., 2011. *Breast Imaging: the requisites*. 2nd ed. Missouri: Elsevier Mosby.

Jamal, N., Ng, K.H., Looi, L.M., McLean, D., Zulfiqar, A., Tan, S.P., Liew, W.F., Shantini, A., Ranganathan, S., 2006. Quantitative Assessment of Breast Density from Digitized Mammograms into Tabár's Patterns. *Phys Med Biol*;51(22):5843-57.

Jamal, N., Ng, K.-H., Ranganathan, S., Tan, L.K., 2007. Comparison of Computerised Assessment of Breast Density with Subjective BI-RADS Classification

and Tabár's Pattern from Two-view CR Mammography. *IFMBE Proceedings*;14(3):1405-1408.

Jones, W.G., 1999. Crossing the Digital Divide – Moving from Film to Filmless Radiology. *Journal of Digital Imaging*;12(2), Suppl. 1:47-49.

Kallergi, M., Clarke, L.P., Qian, W., Gavrielides, M., Venugopal, P., Berman, C.G., Holman-Ferris, S.D., Miller, M.S., Clark, R.A., 1996. Interpretation of Calcifications in screen/film, Digitized, and Wavelet-enhanced Monitor-displayedMmammograms: A Receiver Operating Characteristic Study. *Acad Radiol*;3:285-93.

Kamitani, T., Yabuuchi, H., Soeda, H., Matsuo, Y., Okafuji, T., Sakai, S., Setoguchi, T., Hatakenake, M., Ishii, N., Honda, H., 2010. Detection of Breast Cancer by Soft-copy Reading of Digital Mammograms: Comparison between a Routine Image-processing Parameter and High-contrast Parameters. *Acta Radiologica*;1:15-20.

Karssemeijer, N., Frieling, J.T., Hendriks, J.H., 1993. Spatial Resolution in Digital Mammography. *Invest Radiol*;28(5):413-19.

Kerlikowske K, Grady, D., Barclay, J., Sickels E.A., Ernster, V., 1996. Effect of Age, Breast Density, and Family History on the Sensitivity of First Screening Mammography. *JAMA*;276:33-8.

Kim, H.H., Pisano, E.D., Cole, E.B., Jiroutek, M.R., Muller, K.E., Zheng, Y., Kuzmiak, C.M., Koomen, M.A., 2006. Comparison of Calcification Specificity in Digital Mammography using Soft-copy versus Screen-film Mammography. *AJR*;187:47-50.

Körner, M., Weber, C.H., Wirth, S., Pfeifer, K.J., Reiser, M.F., Treitl, M., 2007. Advances in Digital Radiography: Physical Principles and System Overview. *Radiographics*;27(3):675-86.

Leedy, P.D. & Ormrod, J.E., 2001. *Practical research: Planning and design*. 7th ed. Prentice Hall Inc: New Jersey.

Lewin, J.M., Hendrick, R.E., D'Orsi, C.J., Isaacs, P.K., Moss, L.J., Karellas, A., Sisney, G.A., Kuni, C.C., Cutter, G.R., 2001. Comparison of Full-field Digital

Mammography with Screen-film Mammography for Cancer Detection: Results of 4,945 Paired Examinations. *Radiology*;218:873-80.

Lewin, J.M., D'Orsi, C.J., Hendrick, R.E., Moss, L.J., Isaacs, P.K., Karellas, A., Cutter, G.R., 2002. Clinical Comparison of Full-field Digital Mammography and Screen-film Mammography for Detection of Breast Cancer. *AJR*;179:671-77.

Lobbes, M.B.I., Cleutjens, J.P.M., Passos, V.L., Frotscher, C., Lahaye, M.J., Keymeulen, K.B.M.I., Beets-Tan R.G., Wildberger, J., Boetes, C., 2012. Density is in the Eye of the Beholder: Visual versus Semi-automated assessment of breast density on standard mammograms. *Insights Imaging*;3:91-9.

Malmgren, J.A., Parikh, J., Atwood, M.K., Kaplan, H.G., 2012. Impact of Mammography Detection on the Course of Breast Cancer in Women Aged 40 – 49 years. *Radiology*;262(3):797-806.

Mathworks (2011). Image processing toolbox support- Contrast-limited adaptive histogram equalization (CLAHE) [Online] Available: http://www.mathworks.com/help/toolbox/images/ref/adapthisteq.html [Accessed 17 June 2011]

Nishikawa, R.M., Mawdsley, G.E., Fenster, A., Yaffe, M.J., 1987. Scanned-projection Digital Mammography. *Med Phys*;14(5):717-27.

Nishikawa, R.M., Acharyya, S., Gatsonis ,C., Pisano, E.D., Cole, E.B., Marques, H.S., D'Orsi, C.J., Farria, D.M., Kanal, K.M., Mahoney, M.C., Rebner, M., Staiger, M.J. for the Digital Mammography Image Screening Trial investigator group, 2009. Comparison of Soft-copy and Hard-copy Reading for Full-field Digital Mammography. *Radiology*;251(1):41-9.

Obenauer, S., Luftner-Nagel, S., von Heyden, D., Munzel, U., Baum, F., Grabbe,E., 2002. Screen Film vs Full-field Digital Mammography: Image Quality, Detetectability and Characterization of Lesions. *Eur Radiol*;12(7):1697-702.

Obenauer, S., Hermann, K.P., Marten, K., Luftner-Nagel, S., von Heyden, D., Skaane, P., Grabbe, E., 2003. Soft Copy versus Hard Copy Reading in Digital Mammography. *Journal of Digital Imaging*;16(4):341-44.

Olsen, O. & Gøtzsche, P.C., 2001. Cochrane Review on Screening for Breast Cancer with Mammography. *The Lancet*;358:1340-42.

Ooms, E.A., Zonderland, H.M., Eijkemans, M.J., Kriege, M., Mahdavian Delavary, B., Burger, C.W., 2007. Mammography: Interobserver Variability in Breast Density Assessment. *Breast*;16(6):568-76.

Oza, A.M. & Boyd, N.F., 1993. Mammographic Parenchymal Patterns: A Marker of Breast Cancer Risk. *Epidemiol Rev*;15:196-208.

Pisano, E.D., Chandramouli, J., Hemminger, B.M., DeLuca, M., Glueck, D., Johnston, R.E., Muller, K., Braeuning, M.P., Pizer, S., 1997[a]. Does Intensity Windowing Improve the Detection of Simulated Calcifications in Dense Mammograms? *Journal of Digital Imaging*;10(2):79-84.

Pisano, E.D., Chandramouli, J., Hemminger, B.M., Glueck, D., Johnston, R.E., Muller, K., Braeuning, M.P., Puff, D., Garrett, W., Pizer, S., 1997[b]. The Effect of Intensity Windowing on the Detection of Simulated Masses Embedded in Dense Portions of Digitized Mammograms in a Laboratory Setting. *Journal of Digital Imaging*;10(4):174-82.

Pisano, E.D., Zong, S., Hemminger, B.M., DeLuca, M., Johnston, E., Muller, K., Braeuning, M.P., Pizer, S.M., 1998. Contrast Limited Adaptive Histogram Equalization Image Processing to Improve the Detection of Simulated Spiculations in Dense Mammograms. *Journal of Digital Imaging*;11(4):193-200.

Pisano, E.D., Cole, E.B., Major, S., Zong, S., Hemminger, B.M., Muller, K.E., Johnston, R.E., Walsh, R., Conant, E., Fajardo, L.L., Feig, S.A., Nishikawa, R.M., Yaffe, M.B., Williams, M.B., Aylward, S.R., for the International digital mammography development group, 2000[a]. Radiologists' Preference for Digital Mammographic Display. *Radiology*;216(3):820-30.

Pisano, E.D., Cole, E.B., Hemminger, B.M., Yaffe, M.J., Qylward, S.R., Maidment, A.D.A., Johnston, R.E., Williams, M.B., Niklason, L.T., Conant, E.F., Fajardo, L.L., Kopans, D.B., Brown, M.E., Pizer, S.M., 2000[b]. Image Processing Algorithms for Digital Mammography: A Pictorial Essay. *RadioGraphics*;20:479-91.

Pisano, E.D., Kuzmiak, C., Koomen, M., Cance, W., 2001. What Every Surgical Oncologist should know about Digital Mammography. *Semin Surg Oncol*;20:181-86.

Pisano, E.D., Cole, E.B., Kistner, E.O., Muller, K.E., Hemminger, B.M., Brown, M.L., Johnston, R.E., Kuzmiak, C.M., Braeuning, M.P., Freimanis, R.I., Scott Soo, M., Baker, J.A., Walsh, R., 2002. Interpretation of Digital Mammograms: Comparison of Speed and Accuracy of Soft-copy versus Printed-film Display. *Radiology*;223:483-88.

Pisano, E.D., Yaffe, M.J. & Kuzmiak, C.M., 2004. *Digital Mammography*. Philadelphia: Lippincott Williams & Wilkins.

Pisano, E.D., Gatsonis, C., Hendrick, E., Yaffe, M., Baum, J.K., Acharyya, S., Conant, E.F., Fajardo, L.L., Bassett, L., D'Orsi, C., Jong, R., Rebner, M., 2005. Diagnostic Performance of Digital versus Film Mammography for Breast Cancer Screening – The Results of the American College of Radiology Imaging Network (ACRIN) Digital Mammographic Imaging Screening Trial (DMIST). *N Engl J Med*;353(17):1773-83.

Pisano, E.D., 2006. Digital Mammography: What Next? *Radiology*;3:583-85.

Rao, K.M.M., 2006. *Overview of image processing. National Remote Sensing Agency (NRSA)* [Online] Available: http://www.drkmm.com/resources/INTRODUCTION_TO_IMAGE_PROCESSING_29aug06.pdf [Accessed 15 November 2010]

Riesmeier, J., Eichelberg, M., Hellemann, H.P., Kieschke, J., Wilkens, T., 2004. Experiences with a Workstation Prototype for Softcopy Reading within the Bavarian Mammography Recertification Program: Workstations and Education. *Acad Radiol;*11(4):407-18.

Rosenberg, R.D., Hunt, W.C., Williamson, M.R., Gilliland, F.D., Wiest, P.W., Kelsey, C.A., Key, C.R., Linver, M.N., 1998. Effects of Age, Breast Density, Ethnicity, and Estrogen Replacement Therapy on Screening Mammographic Sensitivity and Cancer Stage at Diagnosis: Review of 183,134 Screening Mammograms in Albuquerque, New Mexico. *Radiology*;209:511-18.

RSNA, 2005. *Digital Mammography*. [Online] Available: http://rsna2005.rsna.org/rsna2005/V2005/conference/event_display.cfm?em_id=4421378 [Accessed 9 March 2011]

Saarenmaa, I., Salminen, T., Geiger, U., Heikkinen, P., Hyvärinen, S., Isola, J., Kataja, V., Kokko ML, Kokko, M.L., Kokko, R., Kumpulainen, E., Kärkkäinen, A., Pakkanen, J., Peltonen, P., Piironen, A., Salo, A., Talviala, M.L., Hakama, M., 2001. The Effect of Age and Density of the Breast on the Sensitivity of Breast Cancer Diagnosis by Mammography and Ultrasonography. *Breast Cancer Research and Treatment*;67:117-23.

Sampat, M.P., Markey, M.K. & Bovik, A.C., 2005. Computer-Aided Detection and Diagnosis in Mammography. In: Bovik, A.C. (ed), 2005. *Handbook of Image and Video Processing*. Amsterdam: Elsevier Academic Press.

Schaetzing, R., 2007. *Agfa's MUSICA$^{2\ TM}$ White Paper: Taking image processing to the next level*. [Online]. Available: http://www.google.co.za/#hl=en&source=hp&q=Agfa%27s+MUSICA2+Taking+image+processing+to+the+next+level%2C+Schaetzing&btnG=Google+Search&oq=Agfa%27s+MUSICA2+Taking+image+processing+to+the+next+level%2C+Schaetzing&aq=f&aqi=&aql=&gs_sm=s&gs_upl=4078l30250l0l32734l68l68l0l57l0l1l765l3671l3-3.4.0.1l8l0&fp=fde8dfd2ad8f06ff&biw=1024&bih=549. [Accessed 28 April 2010]

Seibert, J.A., 2006. Experience with a Computed Radiography Mammography System and Comparison with other Systems. *Applied Radiology*;45(9)supplement:10-16.

Shapiro, S., Venet, W., Strax, P., Venet, L., Roeser, R., 1982. Ten- to Fourteen-year Effect of Screening on Breast Cancer Mortality. *J Natl Cancer Inst*;69(2):349-55.

Shapiro, S., Coleman, E.A., Broeders, M., Codd, M., de Koning, H., Fracheboud, J., Moss, S., Paci, E., Stachenko, S., Ballard-Barbash, R., 1998. Breast Cancer Screening Programmes in 22 Countries: Current Policies, Administration and Guidelines. International Breast Cancer Screening Network (IBSN) and the European Network of Pilot Projects for Breast Cancer Screening.for the International

Breast Cancer Screening Network (IBSN) and the European Network of Pilot Projects for Breast Cancer Screening. *Int J Epidemiol;*27(5):735-42.

Shtern, F., 1992. Digital Mammography and Related Technologies: A Perspective from the National Cancer Institute. *Radiology*;183:629-30.

Sickles, E.A., Migliorettie, D.L., Ballard-Barbash, R., Geller, B.M., Leung, J.W.T., Rosenberg, R.D., Smith-Bindman, R., Yankaskas, B.C., 2005. Performance Benchmarks for Diagnostic Mammography. *Radiology*;235:775-90.

Sickles, E.A., 2007. Wolfe Mammographic Parenchymal Patterns and Breast Cancer Risk. *AJR*;188:301-3.

Simundic, A.M., 2012. *Measures of diagnostic accuracy: basic definitions* [Online] Available: www.ifcc.org/.../**measures-of-diagnostic-accuracy**-basic-definitions/ [Accessed 25 January 2012]

Sivaramakrishna, R., Obuchowski, N.A., Chilcote, W.A., Cardenosa, G., Powell, K.A., 2000. Comparing the Performance of Mammographic Enhancement Algorithms: A Preference Study. *AJR*;175:45-51.

Skaane, P., Young, K., Skjennald, A., 2003. Population-based Mammography Screening: Comparison of Screen-film and Full-field Digital Mammography with Soft-copy Reading – Oslo I study. *Radiology*;229:877-84.

Skaane, P. & Skjennald, A., 2004. Screen-film Mammography versus Full-field Digital Mammography with Soft-copy Reading: Randomized Trial in a Population-based Screening Program – The Oslo II study. *Radiology*;232 (1):197–204.

Skaane, P., Hofvind, S., Skjennald, A., 2007. Randomized Trial of Screen-film versus Full-field Digital Mammography with Softcopy Reading in Population-based Screening Program: Follow-up and Final Results of Oslo II Study. *Radiology*;244(3):708-17.

Tabár, L. & Dean, P.B., 2001. *Teaching atlas of mammography*. 3rd revised ed. Stuttgart:Thieme.

Tabár, L., Yen, M.F., Vitak, B., Chen, H.H.T., Smith, R.A., Duffy, S.W., 2003. Mammography Service Screening and Mortality in Breast Cancer Patients: 20-year Follow-up Before and After Introduction of Screening. *Lancet*;361:1405-10.

The Swedish Organized Service Screening Evaluation Group, 2006. Reduction in Breast Cancer Mortality from Organized Service Screening withMmammography: 1. Further Confirmation with Extended Data. *Cancer Epidemiol Biomarkers & Prevention*;15(1):45-51.

Tucker, A.K. & Ng, Y.Y., 2001. *Textbook of mammography*. 2nd ed. Edinburgh: Churchill Livingstone: Edinburgh.

U.S. Preventive Services Task Force, 2009. Screening for Breast Cancer: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*;151(10):716-726.

UCSF, 2009. *Contrast-Limited Adaptive Histogram Equalization (CLAHE). Tutorial on EPID-Chapter 2- Image Processing – Lesson 7 - Contrast-limited Adaptive Histogram Equalization (CLAHE)*. [Online] Available: http://radonc.ucsf.edu/research_group/jpouliot/tutorial/HU/Lesson7.htm [Accessed 17 June 2009]

Uematsu, T., 2009. Detection of Masses and Calcifications by Soft-copy Reading: Comparison of Two Postprosessing Algorithms for Full-field Digital Mammography. *Jpn J Radiol*;27:168-75.

US Patent 7155044 – Multiscale gradation processing method. [Online] Available: http://www.patentstorm.us/patents/7155044/claims.html [Accessed 2 March 2010]

Varas, X., Leborgne, J.H., Leborgne, F., Mezzera, J., Jaumandreu, S., Leborgne, F, 2002. Revisiting the Mammographic Follow-up Category 3 Lesions. *AJR*;179:691-95.

Vigeland, E., Klaasen, H., Klingen T.A., Hofvind, S., Skaane, P., 2008. Full-field Digital Mammography Compared to Screen Film Mammography in the Prevalent Round of a Population-based Screening Programme: The Vestfold County Study. *Eur Radiol*;18:183-91.

Vinnicombe, S., Pinto Pereira, S.M., McCormack,V.A., Shiel, S., Perry, N., Dos Santos Silva, I.M., 2009. Full-field Digital versus Screen-film Mammography: Comparison within the UK Breast Screening Program and Systematic Review of Published Data. *Radiology*;251(2):347-58.

Warren, L.M., Mackenzie, A., Cooke, J., Given-Wilson, R.M., Wallis, M.G., Chakraborty, D.P., Dance, D.R., Bosmans, H., Young, K.C., 2012. Effect of Image Quality on Calcification Detection in Digital Mammography. *Med Phys*;39(6):3202-13.

Willison, K., LaBella, J., Zuley, M.L., 2006. Introduction to Digital Mammography: The Technologist' Perspective. *Applied Radiology*;35(9) supplement:3-9.

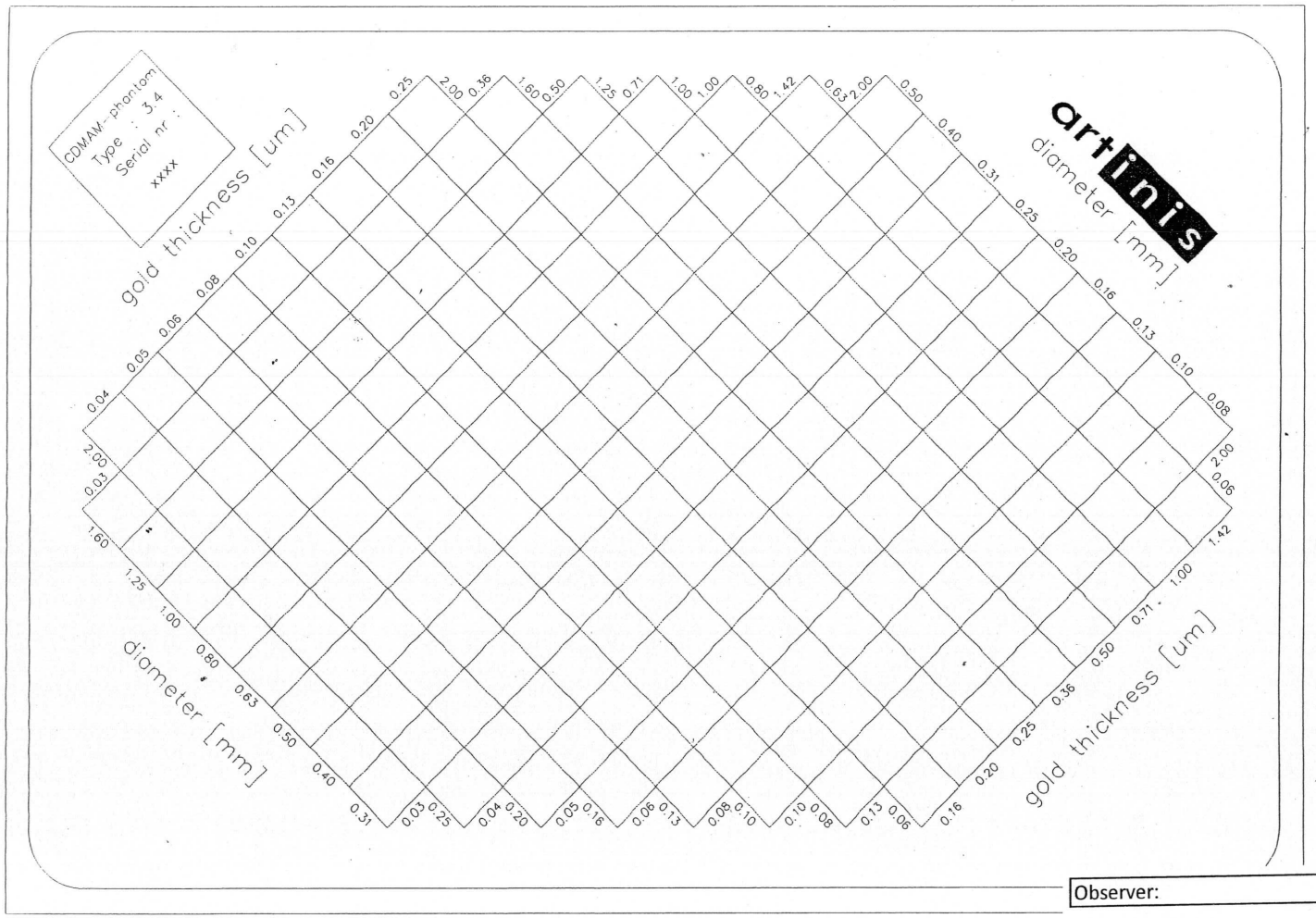
Wolfe, J.N., 1976. Breast Patterns as an Index of Risk for Developing Breast Cancer. *AJR*;126:1130- 9.

Yamada, T., Saito, M., Ishibashi, T., Tsuboi, M., Matsuhashi, T., Sato, A., Saito, H., Takahashi, S., Onuki, K., Ouchi, N., 2004. Comparison of Screen-film and Full-field Digital Mammography in Japanese Population-based Screening. *Radiation Medicine*;22(6):408-12.

Zanca, F., Jacobs, J., Van Ongeval, C., Claus, F., Celis, V., Geniets, C., Provost, V., Pauwels, H., Marchal, G., Bosmans, H., 2009. Evaluation of Clinical Image Processing Algorithms used in Digital Mammography. *Med Phys*;36(3):765-75.

APPENDIX A

Score form CDMAM-phantom



APPENDIX A

Observer:

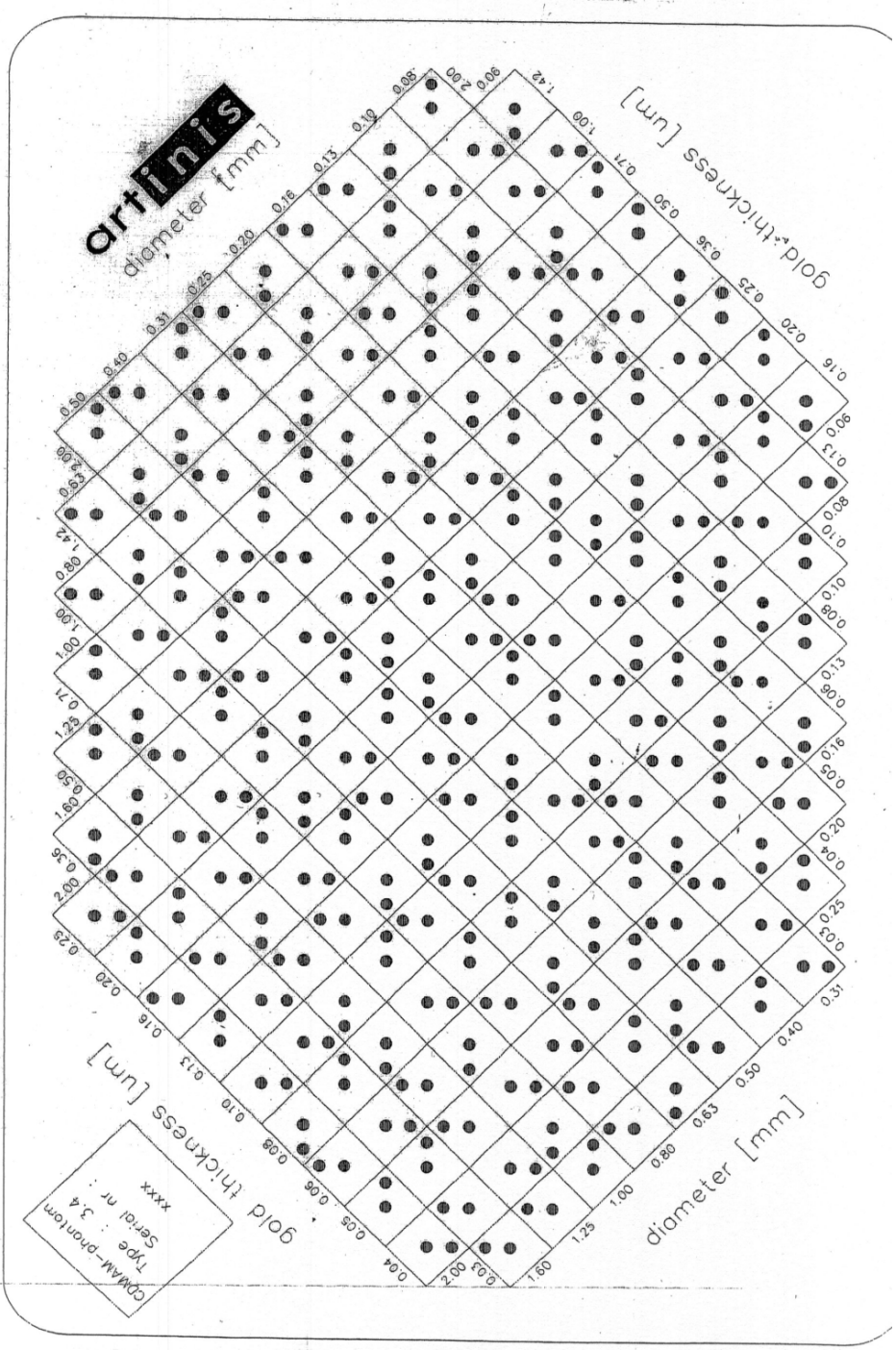
Date:

Manipulation:

Score form CDMAM-phantom, type 3.4

APPENDIX B

Evaluation form CDMAM-phantom


artinis
diameter [mm]
gold thickness [um]
0.04 0.05 0.06 0.08 0.10 0.13 0.16 0.20 0.25 0.31 0.40 0.50 0.63 0.80 1.00 1.25 1.60 2.00
0.23 0.20 0.16 0.13 0.10 0.08 0.06 0.05 0.04 0.03 0.03 0.03 0.03 0.04 0.05 0.06 0.08 0.10 0.13 0.16 0.20 0.25 0.31
0.36 0.50 0.71 1.00 1.42 2.00 2.83
0.50 0.63 0.80 1.00 1.25 1.60 2.00
0.71 0.80 1.00 1.25 1.60 2.00 2.83
1.00 1.25 1.60 2.00 2.83
1.42 1.60 2.00 2.83
2.00 2.83
2.83
gold thickness [um]
diameter [mm]
CUMM-phantom
Type : 3.4
Serial nr :
xxxx

APPENDIX C

University of the Free State: Ethics approval

APPENDIX C

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Direkteur: Fakulteitsadministrasie / Director: Faculty Administration
Fakulteit Gesondheidswetenskappe / Faculty of Health Sciences

Research Division
Internal Post Box G40
☎(051) 4052812
Fax nr (051) 4444359

E-mail address: gndkhs.md@mail.uovs.ac.za

Ms H Strauss

2008-03-14

MS C MEYER
DEPT OF DIAGNOSTIC RADIOLOGY
FACULTY OF HEALTH SCIENCES
UFS

Dear Ms Meyer

ETOVS NR 39/08
MS C MEYER **DEPT OF DIAGNOSTIC RADIOLOGY**
PROJECT TITLE: DEVELOPMENT AND EVALUATION OF A SOFT COPY MAMMOGRAPHIC VIEWING PROTOCOL TO IMPROVE RADIOLOGICAL REPORTING.

- You are hereby informed that The Ethics Committee approved the above-mentioned at the meeting on 11 March 2008 on condition that the Information Leaflet and Informed Consent are available in the language the trial person prefers.
- Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.
- Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
- The Committee must be informed of any serious adverse event and/or termination of the study.
- A progress report should be submitted within one year of approval of long term studies and a final report at completion of both short term and long term studies.
- Kindly refer to the ETOVS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

for PROF BB HOEK
CHAIR: ETHICS COMMITTEE

ETHICS COMMITTEE

OF THE FACULTY OF HEALTH SCIENCES

ATTENDANCE LIST OF THE MEETING HELD ON 11 MARCH 2008

FACULTY MEMBERS (CLINICAL)

Prof BB Hoek	Chairperson M.B. Ch.B. (Pret) M.Med. (Paed.)(UOFS), D.G.G. (UOFS) Department: Paediatrics and Child Health	Present
Prof R Barry	Vice-chair M.B. Ch.B. (Stell.), M.Med. (Surgery)(UOFS) Department: Surgery	Present
Prof L Goedhals	M.B. Ch.B. (U.C.T.) M.Med (Rad.T.) UOFS Department: Oncotherapy	Present
Prof PH Wessels	MB. Ch.B; M.Med.(O. et G.) (UFS), L.K.O.G. (SA); MD (UOFS) Department: Obstetrics and Gynaecology	Absent
Dr WJ Steinberg	MBBch (Wits) DPH; DTM & H (Wits) M.Fam.Med (UOFS) Dip. Obst (SA) Dept of Family Medicine	Present
Prof JH van Zyl	M.B. Ch.B (Pret) Dip. Av Med. M.Med (Internal Medicine) Add. Qualification: Gastro-enterology Dept of Internal Medicine	Present
Prof WH Kruger	M.B. Ch.B (UOFS) M.Med. (Community Health) (UOFS), MBA (PU for CHE) Dept of Community Health	Present
Ms M Nel	B.A. (Urbanology) B.A. Hons. (Statistics) M.Med (Biostatistics) (UOFS) IRENSA Diploma in International Research Ethics 2006 Dept of Biostatistics	Present

SCHOOL OF NURSING REPRESENTATIVE		
Prof Y Botma (lady)	B. Soc.Sc (Nursing) Honn, M. Soc.Sc., Ph.D. (UFS) IRENSA Diploma in International Research Ethics 2005 School of Nursing	Absent
Dr DE Botha (lady)	M. Soc.Sc (Nursing) (UOFS) Ph.D (Nursing) (UOFS) School of Nursing	Absent
REPRESENTATIVE OF SCHOOL OF ALLIED HEALTH PROFESSIONS		
Dr S van Vuuren (lady)	B. Occupational Therapy (Stell.), M. Occupational Therapy (UFS), Ph.D Health Professions Education (UFS) Head: School of Allied Health Professions	Present
Ms SM van Heerden (lady)	M. Occupational Therapy (UOFS) Dept of Occupational Therapy	Absent
REPRESENTATIVE OF THE CENTRAL UNIVERSITY OF TECHNOLOGY, FREE STATE		
Prof L de Jager	Director: School of Health Technology Faculty of Health and Environmental Sciences Central University of Technology, Free State Bloemfontein	Absent
RELIGIOUS/LAY MEMBER		
Rev MJ Kofa (Coloured)	MA Practical Theology (UOFS) Department: Biblical Studies	Present
Ms KM Jingosi (Lady)	Social Auxiliary Work (SA Council for Social Service Professions) Child and Family Welfare Society	Present
LEGAL MEMBER		
Prof H Oosthuizen	B.Iur., LL.B., LL.D. (UOFS) Department: Criminal Law	Present
Adv R-M Jansen (secundus) (lady)	B.Soc.Sc. (Nursing) Honn. B.Iur., LL.B., LL.M. (UOFS) Department: Private Law	Absent

11/03/08

EX OFFICIO MEMBERS *(not entitled to vote)*

Dr S Kabane	M.B. Ch.B. (Medunsa) Chief Executive Officer Universitas Hospital Bloemfontein	Absent
Dr NRJ van Zyl	M.Med. (UOFS) Business MBL (UNISA) Clinical Head: Universitas Hospital Bloemfontein	Absent
Ms MA Mabandla	Representative Universitas Hospital Bloemfontein	Absent
Mr ST Mohapi	Senior Executive Officer Free State Psychiatric Complex Bloemfontein	Absent
Dr BM Masitha	M.B.Ch.B. B.Sc Hons Health Sciences IFE - Nigeria B.Sc NBLS – ROMA H.O.C.S. – Chief Medical officer Free State Psychiatric Complex Bloemfontein	Absent
Mr MP Tsibolane	Chief Executive Officer Pelonomi Hospital Bloemfontein	Absent
Ms AS Sesing	M.Soc.Sc. (Nursing) (UFS) Chief Executive Officer National District Hospital Bloemfontein	Absent

Før .....
PROF BB HOEK
CHAIR: ETHICS COMMITTEE

APPENDIX D

Universitas Hospital: CEO approval

APPENDIX D

FREE STATE PROVINCE

Ref. no.: 13/2

22 February 2008

Me C Meyer
Department Diagnostic Radiology
Universitas Academic Hospital

Dear Me Meyer

RESEARCH PROJECTS: DEVELOPMENT AND EVALUATION OF A SOFT COPY MAMMOGRAPHIC VIEWING PROTOCOL TO IMPROVE RADIOLOGICAL REPORTING.

Herewith permission for the mentioned project to be done at Universitas Academic Hospital on condition that approval is obtained from the Ethics Committee.

The Chief Executive officer must be notified if the findings of the project will be published.

Yours sincerely

DR NIC R J VAN ZYL
HEAD: CLINICALSERVICES
UNIVERSITAS ACADEMIC HOSPITAL

DR NRJ VAN ZYL
2008 -03- 22
HEAD: CLINICAL SERVICES
UNIVERSITAS ACADEMIC HOSPITAL

HEAD: CLINICAL SERVICES: **DR N R J VAN ZYL**, UNIVERSITAS TERTIARY HOSPITAL ● Private Bag X20660, Bloemfontein,9300 ● Tel. no.: 051-4052866 ● Fax: 051-4440792 ● Room 1129, First Floor, Universitas Tertiary Hospital ● E-mail: vanzylnr@fshealth.gov.za

APPENDIX E

Department of Diagnostic Radiology: HOD approval

APPENDIX E

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Departement Diagnostiese Radiologie / Department of Diagnostic Radiology
Skool vir Geneeskunde / School of Medicine
Fakulteit Gesondheidswetenskappe / Faculty of Health Sciences

22 February 2008

TO WHOM IT MAY CONCERN

RE: RESEARCH PROJECT - ME CARIN MEYER
TITLE: " DEVELOPMENT AND EVALUATION OF A SOFT COPY MAMMOGRAPHIC VIEWING PROTOCOL TO IMPROVE RADIOLOGICAL REPORTING"

I hereby grant permission that Me C Meyer may conduct the above mentioned study in the Department of Diagnostic Radiology at Universitas Hospital. Permission is also granted for the use of patient's mammographic images for the purpose of the project during the period of March 2008 – March 2009.

Yours sincerely

PROF CS DE VRIES
HEAD OF DEPARTMENT DIAGNOSTIC RADIOLOGY

339 (G61), Bloemfontein 9300, ☎ (051) 405 3471, (051) 444 3248, gndrmsd.md@mail.uovs.ac.za
Republiek van Suid-Afrika, Republic of South Africa

APPENDIX F

Radiation Control Committee: Approval

APPENDIX F

APPROVAL FOR USE OF IONISING RADIATION

RADIATION CONTROL COMMITTEE

UNIVERSITAS/PELONOMI HOSPITALS

Project title: **Development and evaluation of a soft copy mammographic viewing protocol to improve radiological reporting**

Principle Investigator: **Me C Meyer**

Department: **Diagnostic Radiology**

Laboratories: **Diagnostic Radiology**

Number of Patients: **90**

Radionuclide: **N/A**

Activity MBq (mCi)	Dose per subject (mSv)	Annual limit Radiation worker	Annual limit Public
		20 mSv	1 mSv

Patients undergoing routine mammographic examinations will be used. No additional radiation will be given to either patients or staff. The project is intended to develop and evaluate of a soft copy mammographic viewing protocol to improve radiological reporting

Conditions: Project approved on condition that no additional radiation will be given to patients or staff. Any deviation from these conditions will require a new application.

.....
CHAIRPERSON
Radiation Control Committee

26/2/08
.....
DATE

.....
SECRETARY
Radiation Control Committee

26/2/08
.....
DATE

APPENDIX G

Information document: English, Afrikaans, Southern Sotho

APPENDIX G

INFORMATION DOCUMENT

Study title: Development and Evaluation of a Soft Copy Mammographic Viewing Protocol to Improve Radiological Reporting

Ethics Approval Number: ETOVS

Greetings! Would you be willing to help me in my research?

I, Carin Meyer am doing research on soft copy viewing and reporting of mammographic images. Research is simply the process of finding the answer to a question. In this study I want to learn how to optimally manipulate post-processing parameters to help me to implement a protocol for optimal viewing of soft copy mammographic images in an attempt to improve radiological reporting. To do this I need to use the breast images of many patients, and I need information about any disease that may be affecting those patients' breasts.

Invitation to participate: I request your permission to use the x-ray images of your breasts (mammograms) in this study and I also need permission to obtain information from your files about any diseases influencing your breasts.

What is involved in the study: The study is being done at Universitas Hospital. I intend using all mammograms from all the patients who are referred to Universitas Hospital for mammography and who are willing to grant us permission. I plan to implement a protocol for optimal viewing and reporting of soft copy mammographic images. As a participant, you should be totally unaware that the study is taking place, as there will be no change in your treatment or management whatsoever. All x-ray images of your breasts will simply be used to develop the program for the duration of the study, which is scheduled to end in February 2010. I will need to obtain information from your files or reports about what diseases, if any, are affecting your breasts. Other personal information should not be required or obtained for the study. You will be given all necessary information about the study while you are involved in the project and after the results are available.

No risks are associated with involvement in the study, as there will be no change in your management or treatment in any way whatsoever. No adverse effects are foreseen.
No benefits are expected for those participating in the study, as the computer-aided diagnosis program will only be used after the study has been completed and we are certain that it works properly.
Participation is voluntary, and refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled; you may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.
No reimbursements will be made, as this study involves no additional costs to you or the hospital.

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law. Organisations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Ethics Committee for Medical Research and the Medicines Control Council where appropriate. Publication of results is anticipated and this would mean that it would be known that patients having mammography at Universitas Hospital are involved in this study, but no individual identification should occur.

To contact researchers – for further information or reporting of study-related information, contact:
Me Carin Meyer, Ground flour Universitas Hospital, Room G86, Department of Diagnostic Radiology, Faculty of Health Sciences, University of the Free State, Bloemfontein, 9301, Tel: 051 405 3471 or 051 405 3468, E-mail: gndrcm.md@ufs.ac.za

To contact the Research Ethics Committee Secretariat and Chair – for reporting of complaints or problems contact: Ms Henriette Strauss, Research Division (Ethics Committee), Block D, Dean's Division, Room D115, Faculty of Health Sciences, P O Box 339 (Internal Post Box G40), University of the Free State, Bloemfontein, 9300 Tel: 051 4052812, Fax: 051 4444359, E-mail: gndkhs.md@ufs.ac.za

INLIGTINGSDOKUMENT

Titel van studie: Ontwikkeling en Evaluering van 'Mammografiese Besigtigings Protokol vir Rekenaarwerkstasies om Radiologiese Rapportering te Verbeter

Etiekkomitee-goedkeuringsnommer: ETOVS

Goeie dag! Sal u dalk bereid wees om ons met hierdie navorsingstudie te help?
Ek Carin Meyer is tans met navorsing besig oor besigtiging en rapportering van mammografie beelde op rekenaarwerkstasies. Navorsing is slegs die proses om antwoorde op vrae te verkry. In hierdie studie wil ek graag uitvind hoe om die post-prosesserings parameters optimaal te manipuleer om my te help om 'n protokol vir optimale besigting van mammografiese beelde op rekenaarwerkstasies te implementeer, in 'n poging om diagnostiese akkuraatheid te verbeter. Om dit te kan doen benodig ek die x-straalbeelde van 'n aantal pasiënte se borste en die inligting rakende enige siekte wat die betrokke pasiënte se borste mag affekteer.

Uitnodiging om deel te neem: Hiermee vra ek u toestemming om die x-straalbeelde van u borste tydens hierdie studie te gebruik en ek benodig ook u toestemming om inligting rakende enige siektes wat u borste kan beïnvloed, uit u pasiëntelêer te trek.

Wat die studie behels: Die studie word slegs by Universitas Hospitaal gedoen. Ek beplan om die mammografieë van al die pasiënte wat na Universitas Hospitaal verwys word vir 'n mammogram te gebruik, mits ons u toestemming het. Ek beplan om 'n protokol vir optimale besigtiging en rapportering van mammografie beelde op rekenaar werkstasies te implementeer. As deelnemer sal u totaal onbewus wees van die studie. Daar sal hoegenaamd geen verandering in u hantering of bestuur wees nie. Alle x-straalbeelde van u borste sal slegs gebruik word om die program te ontwikkel vir die duur van die navorsingstudie, wat geskeduleer is om teen Februarie 2010 afgehandel te wees. Ek sal alle inligting of verslae van u pasiëntelêer rakende enige siektes wat u borste affekteer, indien enige, benodig. Geen ander persoonlike inligting sal vir hierdie studie benodig of ingewin word nie. Die nodige inligting rakende die studie sal aan u voorsien word tydens u deelname aan die projek, asook wanneer die resultate beskikbaar word.

Geen risiko word met u deelname aan hierdie studie geassosieer nie, aangesien dit geen verandering in u hantering of bestuur sal veroorsaak nie. Geen ongunstige effekte word verwag nie.
Geen voordele word in die vooruitsig gestel vir diegene wat aan hierdie studie deelneem nie, aangesien **die** slegs gebruik sal word wanneer die studie gefinaliseer is en ons oortuig is dat dit behoorlik werk.
Deelname is vrywillig, en indien u sou versuim in u deelname, sal u nie gepenaliseer word of enige voordele verloor waarop u andersins geregtig is nie. U mag u op enige stadium van deelname onttrek sonder penalisering of verlies aan voordele waarop u andersins geregtig is.
Geen vergoeding sal aangebied word nie, aangesien hierdie studie geen addisionele kostes vir u of die Hospitaal inhou nie.

Vertroulikheid: Pogings sal aangewend word om persoonlike inligting vertroulik te hou. Absolute vertroulikheid kan egter nie gewaarborg word nie. Persoonlike inligting mag bekend gemaak word indien dit deur wetgewing vereis word. Organisasies wat u navorsingsrekords mag ondersoek en/of kopieer vir gehalteversekering en data–analise, sluit groepe in soos die Etiekk omitee vir Mediese Navorsing en die Medisynebeheerraad waar gepas. Publikasie van resultate is 'n moontlikheid en dit beteken dat dit bekend sal wees dat pasiënte wat mammografieë by Universitas Hospitaal ondergaan het, by hierdie studie betrokke was. Geen individuele identifikasie behoort egter plaas te vind nie.

Kontakbesonderhede van navorser: Vir enige verdere inligting, kontak asb. Carin Meyer, Departement Diagnostiese Radiologie, Grondvloer Universitas Hospitaal, kamer G61, UV, Bloemfontein, 9301 Tel.: 051 405 3471 of 051 405 3468, E-pos: gndrcm.md@ufs.ac.za

Kontakbesonderhede van die sekretaresse en voorsitter van die Navorsingsetiekkomitee – vir enige rapportering van klagtes of probleme. Mev. Henriëtte Strauss, Navorsingsafdeling (Etiekkomitee), Blok D, Dekaanskantoor, kamer D115, Fakulteit Gesondheidswetenskappe, Posbus 339 (Interne Bus G40), UV, Bloemfontein, 9300 Tel.: 051 4052812, Faks.: 051 4444359, E-pos: gndkhs.md@ufs.ac.za

TOKOMANE YA THLAHISOLESEDING

Lebitso la Diphuputso: Ho Thehwa le ho Kenngwa Tshebetsong ha Tekolo ya Matswele ya Seipone ka Thuso ya Khomphuta (Mammography Computer Aided Diagnosis Development and Implementation).
Nomoro ya Tumello ya tsa Tshebetso: ETOVS

Dumela! na o ka rata ho re thusa ka dipatlisiso tsa rona?

Nna, **Carin Meyer**,ke etsa dipatlisisong tse bitswang: Ho Thehwa le ho Hlahlojwa ha Prothokole ya Tekolo ya Matswele ya Seipone ho Ntlafatsa Ditlaleho tsa Radioloji (**Development and Evaluation of a Soft Copy Mammographic Viewing Protocol to Improve Radiological Reporting**).Ho etsa dipatlisiso ke mokgwa wa ho fumana karabo ya potso. Dipatlisisong tsena, ke batla ho ithuta ho sebedisa dipharamitara tsa kamora tshebetso ka katleho e phethahetseng ho nthusa ho kenya tshebetsong prothokole ya tjhebo ya dikhopi tsa ditshwantsho tse bobebe tsa matswele ka sepheo sa ho ntlafatsa tlaleho ya radioloji. Ho etsa sena re hloka ditshwantsho tsa seipone tsa matswele tsa bakudi ba bangata le ho fumana tlhahisoleseding ka mahloko a tshwereng matswele a bona.

Memo ya ho nka karolo: Re kopa hore o re dumelle ho sebedisa ditshwantsho tsa X-ray tsa matswele a hao tsa diphuputsong tsena mme hape re tla hloka tumello ya hao ho fumana dinthla tse mabapi le mahloko a tshwereng matswele a hao ho tswa faeleng ya hao.

Dipatlisiso tsee di tla o hloka eng: Dipatlisiso tsena di etswa sepetleleng sa Universitas feela. Re ikemiseditse ho sebedisa diipone tsa matswele kaofela tsa bakudi ba romellwang Sepetleleng sa Universitas, mme e le tsa bakudi ba ikemiseditseng ho re fa tumello ya ho etsa jwalo. Re rerile ho rala prokreme ya tlhahlobo la khomphuta.. Wena jwalo ka monkakarolo, ha o na ho tseba ho hang hore dipatlisiso tsa mofuta ona di a etsahala ka ha ho ke ke ha eba le diphetoho tsa mofuta ofe kapa ofe kalafong le tlhokomelong ya hao jwalo ka mokudi. Ditshwantsho tsa x-ray tsa matswele a hao di tla sebediswa ho hlabolla prokreme ya khomphuta nakong yohle eo dipatlisiso tsena di tla beng di etsahala ka yona. Dipatlisiso tsena di lebeletswe ho fela ka kgwedi ya Hlakola selemong sa 2010. Re tla hloka dinthla kaofela, ho tswa faeleng ya hao, ka mahloko a tshwereng matswele a hao, haeba a le teng. Ha hona dintlha ka wena tse tla sebediswa dipatlisisong tsena. O tla fuwa tlhahisoleseding ka kgatelopele ya projeke ena, o be o fumane le diphetho tsa yona hang ha di fumaneha.

Ha ho Menyetla ya Kotsi e teng ka ho nka karolo dipatlisisong tsena, ka ha ho se diphetoho tse tlang ho etsahala tlhokomelong le kalafong ya hao jwalo ka mokudi.
Ha ho Melemo e lebeletsweng bakeng sa bakudi ba nkang karolo dipatlisisong tsena, hobane prokreme ena e tla sebediswa ha dipatlisiso tsena di se di phethetswe, mme re na le bonnete ba hore e sebetsa hantle.
O nka karolo ka ho ithaopa, mme ha o sa ikutlwe ho nka karolo dipatlisisong tsena, ha o na ho lahlehelwa ke melemo ya letho eo o nang le yona.
Ha ho tjhelete eo o tla e buseletswa , kaha diphuputso tsena ha di na ho baka ditjeho tsa letho ho wena kapa sepetlele.

Sephiri: Boikgathatso bo tla etswa ho boloka tlhahisoleseding ya hao sephiring. O ke ke wa fuwa tiisetso ya sephiri se feletseng kahohlehohle. Tlhahisoleseding e mabapi le wena e ka hlahiswa haeba molao o hloka jwalo. Mekgatlo e ka hlahlobang le/kapa ya kopitsa direkoto tsa hao tsa diphuputsong bakeng sa netefatso ya boleng le tlekodiso ya data e kenyeletsa dihlopha tse jwalo ka Ethics Committee for Medical Research le Medicines Control Council moo ho lokelang. Phatlalatso ya sephetho e lebeletswe hore e ka etsahala mme sena se tla bolela hore ho tla tsebahala hore bakudi ba nkilweng seipone sa matswele Universitas Hospital ba kenetse diphuputso tsena, empa ha ho tsebahatso ya batho ka bonngwe e tla etsahala.

Ho ikopanya le ba etsang dipatlisiso – bakeng sa tlhahisoleseding le dintlha tse feletseng ka dipatlisiso tsena, o ka b uisana le:
Mof Carin Meyer, Ground floor, Universitas Hospital, Room G86, Department of Diagnostic Radiology, Faculty of Health Sciences, University of Free State, Bloemfontein, 9301, Founu: **051 405 3471**, kapa **051 405 3468,**

Imeile: raewid.MD@ufs.ac.za

Ho ikopanya le ba Bongodi le Modulasetulo ba Komiti ya Dipatlisiso tse Molaong – ho tlaleha ditletlebo le mathata, ikopanye le: Me. Henrietta Strauss, Research Division (Ethics Committee), block D, dean's Division, Room D115, Faculty of Health Science, P O Box 339 (Internal Post Box G40), University of Free State, Bloemfontein, 9300, Founu: 051 405 2812, Fekse: 051 444 4359
Imeile: gndkhs.md@mail.uovs.ac.za

APPENDIX H

Consent document: English, Afrikaans, Southern Sotho

APPENDIX H

CONSENT TO PARTICIPATE IN RESEARCH

Name: _____

Reference Number: _____

You have been asked to participate in a research study entitled "Development and Evaluation of a Soft Copy Mammographic Viewing Protocol to Improve Radiological Reporting". Ethics Approval Number: ETOVS. 39 |08

You have been informed about the study by ....

You may contact Ms Carin Meyer at the Department of Diagnostic Radiology, Faculty of Health Sciences, University of the Free State, Bloemfontein (Tel: 051 405 3471) at any time if you have questions about the research or if you are concerned about the research.

You may contact the Secretariat of the Ethics Committee of the Faculty of Health Sciences, UFS at telephone number (051) 405 2812 if you have any questions about your rights as a research subject.

Your participation in this research is voluntary, and you will not be penalised or lose benefits if you do not wish to participate in the study or decide to stop participating in the study.

If your mammograms are not suitable for inclusion in the study for any reason, then your participation in the study will end and no further use will be made of your information for the study.

There will be no additional costs to you or to the hospital if you participate in the study, and you will receive no remuneration for participation in the study.

If you agree to participate in the study, you will be given a signed copy of this document together with the participant information sheet, which is a written summary of the research study.

The research study, including the above information, has been verbally described to me. I understand what my involvement in the study means and I voluntarily agree to participate.

_____ _____
Signature of Participant Date

_____ _____
Signature of Witness Date
(Where applicable)

_____ _____
Signature of Translator Date
(Where applicable)

«Merge Record #»

TOESTEMMING VIR DEELNAME AAN NAVORSING

Naam: _____

Verwysingsnommer: _____

U is gevra om aan 'n navorsingstudie getiteld "Ontwikkeling en evaluering van 'n mammografiese besigtigingsprotokol vir rekenaarswerkstasies om radiologiese verslagdoening te verbeter" deel te neem. Etiekkomitee-goedkeuringsnommer: ETOVS 39/08

U is van die studie in kennis gestel deur .....

U kan me. Carin Meyer by die Departement Diagnostiese Radiologie, Fakulteit Gesondheids-wetenskappe, UV, Bloemfontein (tel.: 051 405 3471) enige tyd kontak indien u navrae aangaande hierdie studie het.

U kan die sekretaresse van die Etiekkomitee, Fakulteit Gesondheidswetenskappe, Universiteit van die Vrystaat, Bloemfontein, kontak indien u enige navrae het oor u regte as navorsingsubjek (tel.: 051 405 2812).

U betrokkenheid by hierdie navorsing is vrywillig en u sal nie gepenaliseer word of enige voordele verloor indien u nie deel van die studie wil vorm en/of u deelname aan die studie staak nie.

Indien u mammogramme om een of ander rede nie geskik is om by hierdie studie ingesluit te word nie, sal u deelname aan die studie beëindig word en u inligting sal nie verder gebruik word nie.

Daar sal geen addisionele kostes vir u of die Hospitaal wees indien u sou deelneem aan die studie nie, en u sal ook geen vergoeding ontvang vir deelname aan die studie nie.

Indien u instem om deel te wees van die studie, sal u 'n getekende afskrif van hierdie dokument ontvang asook die Deelnemerinligtingsdokument, wat 'n opsomming van hierdie navorsingstudie is.

Die navorsingstudie, sowel as bogenoemde inligting is mondelings aan my verduidelik. Ek verstaan wat my betrokkenheid by die studie behels en stem vrywillig in om deel te neem.

_____ _____

Handtekening van deelnemer Datum

_____ _____

Handtekening van getuie Datum
(waar van toepassing)

_____ _____

Handtekening van vertaler Datum
(waar van toepassing)

<< Rekord # >>

KAMOHELO YA HO NKA KAROLO DIPATLISISONG

Lebitso: _____

Nomoro ya Referense: _____

O kopilwe ho nka karolo dipatlisisong tse bitswang: Ho Thehwa le ho Hlahlojwa ha Prothokole ya Tekolo ya Matswele ya Seipone ho Ntlafatsa Ditlaleho tsa Radioloji (**Development and Evaluation of a Soft Copy Mammographic Viewing Protocol to Improve Radiological Reporting**). Nomoro ya Phano ya Tumello ya Tshebetso e Molaong: ETOVS 39/08

O hlaloseditswe ka dipatlisiso tsena ke .....

O ka ikopanya le Mof Carin Meyer wa **Department of Diagnostic Radiology, Faculty of Health Sciences,**, University of Free State, Bloemfontein (Founu: **051 405 3471**) nako efe kapa efe ha o na le dipotso mabapi le dipatlisiso.

O ka ikopanya le mongodi wa komiti ya dipatlisiso tse melaong ya Faculty of Health Sciences, UFS nomorong ena ya mohala (051) 405 2812 ha o na le dipotso mabapi le ditokelo tsa hao jwalo ka monkakarolo dipatlisisong.

Ho nka karolo ha hao dipatlisisong tsena, ke ka ho ithaopa, mme o keke wa sehollwa kapa wa lahlehelwa ke letho haeba o sa batle ho nka karolo kapa o se o sa ikutlwe ho tswela pele.

Haeba diipone tsa matswele a hao di sa loka hore di ka sebetsa dipatlisisong tsena, ka lebaka lefe kapa lefe, ho nka karolo ha hao ho tla kgaotswa mme tlhahisoleseding e mabapi le wena e faeleng ya hao ha e na ho sebediswa kamora moo.

Ha ho tjhelete eo o tla e lefiswa ka ho ithaopela ho nka karolo dipatlisisong tsena, le wena ha ho tjhelete eo o tla e fumana bakeng sa ho nka karolo.

Ha o dumela ho nka karolo, o tla fuwa setlankana se saennweng mmoho le tokomane e nang le dintlha ka bokgutshwane mabapi le dipatlisiso tse o nkang karolo ho tsona.

---------o0O0o---------

Dintlha ka dipatlisiso le tlhahisoleseding e boletsweng mona ke e hlaloseditswe ka molomo. Ke utlwisisa se bolelwang ke ho nka karolo ha ka dipatlisisong tsena, hape ke ithaopa ho nka karolo.

_____	_____
Monkakarolo	Letsatsi
_____	_____
Paki (Ha e hlokeha)	Letsatsi
_____	_____
Toloko	Letsatsi

TRANSMAXIMUS

Suzette Botha
B.Soc.Sc.(MW), B.Ed.(Psig.), H.O.D. en Magistergraad in Vertaling

Nanette Lötter
B.A., H.E.D. and Master's Degree in Translation

AAN WIE DIT MAG AANGAAN

Hiermee word verklaar dat Suzette Botha (Geakkrediteerde Vertaler: Suid-Afrikaanse Vertalersinstituut, APVert en APRed, nr. 1000775), en Nanette Lötter (Geakkrediteerde Vertaler: Suid-Afrikaanse Vertalersinstituut, APTrans en APEd, nr. 1001099) onderskeidelik die taalversorging van die volgende twee dokumente behartig het:

"Ontwikkeling en evaluering van mammografiese besigtigingsprotokol vir rekenaarwerkstasies om radiologiese verslagdoening te verbeter (Etiekkomitee-goedkeuringsnommer ETOVS 39/08)"; en

"Development and Evaluation of a Soft Copy Mammographic Viewing Protocol to Improve Radiological Reporting (Ethics Approval Number ETOVS 39/08)".

Die uwe

Suzette Botha en Nanette Lötter
3 Maart 2008

(2008/03/12) Carin Meyer - FAX-12387007.tif

Att: Ms Carin Meyer
Fax: 0866329343

This is to confirm that I, Thabiso Ntsielo, translated the medical document numbered ETOVS 39/08 into Sesotho.

I am a SATI accredited translator in the Sesotho/English languages.

Membership No.: 1001161

Signed: 3/7/2008

APPENDIX I

Training programme

TRAINING PROGRAMME

UNDERSTANDING DIGITAL IMAGE AND PROCESSING

Date: 5 November 2009

Time: 13.00 – 17:00

Venue: Mammography Unit – Universitas Hospital

Presenters: Dr W.I.D. Rae (Medical Physicist)

Me C. Meyer (Senior lecturer: Department Diagnostic Radiology)

Me J. vd Merwe (Application Specialist – Philips PACS)

13:30 Welcoming and aim of training - **Me C. Meyer**

13:40 Digital Imaging - **Dr W.I.D. Rae**

Acquisition of the digital image

Advantages and disadvantages of SFM and DM

- Spatial resolution
- Contrast resolution

Challenges of soft-copy viewing

Digital image processing

- General concepts of Histogram equalisation
- CLAHE
- MUSICA^2

Display for feature selection

- Magnification, MIW, Invert, LUT, Greyscales
- Edge enhancement / Median filter / Edge detection

Display tools demonstration

- Histogram information, WW/WL manipulation, Magnification / roaming / magnifying glass, Flip, Rotate etc
- Signal measurement: ROI, freehand ROI
- Image measurement: Rulers / Angles
- Annotation overlay

15:00 Tea

15:15 Image quality assessment of the digital image - Me C. Meyer

- Results of our phantom study
- Participative learning method of image quality assessment for the study

15:45 Radiologists hands-on at workstation - Me J. vd Merwe

Hanging protocol

Manual Intensity Windowing

Zooming, roaming, magnifying glass

Viewing the histogram

Display: Invert, LUT, Flip, rotate

Signal measurement: ROI, point

Image measurement: Rulers, Angles

Annotation overlay

16:45 Summary and acknowledgements – Me. C. Meyer

APPENDIK I

APPENDIX J

Evaluation form: Image quality assessment

IMAGE QUALITY ASSESSMENT - SOFT-COPY MAMMOGRAPHY MLO VIEW

DATE:
CASE #:
RADIOLOGIST:
MANIPULATION:

1	Definitely not clear
2	Almost definitely not clear
3	Probably clear
4	Almost completely clear
5	Completely clear

	1	2	3	4	5	
1. Reproduction of skin outline						
2. Reproduction of skin structure (rosettes from pores) along the pectoralis muscle						
3. Reproduction of pectoral muscle margin						
4. Reproduction of vascular structures seen through most dense parenchyma						
5. Reproduction of vascular structures in fat tissue						
6. Reproduction of all vessels and fibrous strands and pectoralis muscle margin (absence of movement)						
7. Reproduction of fibrous strands in fat tissue						
8. Reproduction of glandular tissue						
9. Reproduction of calcifications, when present						N/A
10. Reproduction of masses, when present						N/A

1	Not seen
2	Acceptable
3	Unacceptable

	1	2	3
11. Noise level in the reproduction of the pectoral muscle			

	Yes	No
12. Is image quality sufficient for early detection of breast cancer?		

Comments:

_____

_____

_____

APPENDIX K

Information document: Image quality assessment

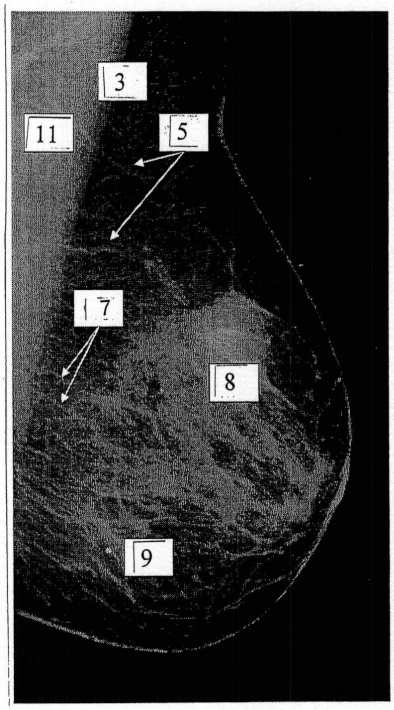
Information Document
Image Quality Assessment

Development and Evaluation of a Soft-Copy Mammographic Viewing Protocol to Improve Radiological Reporting

Carin Meyer

European guidelines on image quality criteria

This image gives an indication of where the image quality criteria could be assessed in a mammogram (Hemdal, B. *et al.* Can the average glandular dose in routine digital mammography screening be reduced? Radiat. Prot. Dosim. 114(1-3),385-390 (2005).



3. Reproduction of pectoral muscle margin
5. Reproduction of vascular structures in fat tissue
7. Reproduction of fibrous strands in fat tissue
8. Reproduction of glandular tissue
9. Reproduction of calcifications (when present)
11. Noise level in the reproduction of the pectoral muscle

Noise

Every source of image noise contributes to image degradation to some extent.

Major sources of random noise in a digital image are electronic noise from the digital chain and quantum noise from statistical fluctuations in x-ray photon density. A well-designed digital system should not further degrade the image by addition of more noise. There is nothing inherent in digital radiography that necessarily leads to a noisier image.

Quantum mottle, caused by the statistical fluctuations in the number of photons that exit the patient, is ultimately a limiting factor for all x-ray imaging. Increasing exposure reduces quantum mottle and smaller detail becomes more visible as dose is increased, but at the cost of a higher dose to the patient. Increasing the dose M times reduces quantum mottle by $\sqrt{M}$ times. In Mammography (as in all other X-ray examinations), limiting the dose (ALARA principle) is of the essence.

Higher subject contrast lessens the importance of noise, but in Mammography the subject contrast is extremely low, and noise might well play an important role in image quality assessment.

Quantum mottle is much less significant for detecting large structures than for detecting small ones because the larger structures have both higher inherent subject contrast and cover larger areas. In Mammography, micro-calcifications might be some of the structures that need to reproduced, and thus quantum mottle will once more play an important role in image quality assessment.

Practical hint: The visual prominence of noise increases as the display window is narrowed.

What does quantum noise look like in an image?
A grainy (salt and pepper) appearance.

Where will you most probably see quantum noise in an image?

- The area in the image that represents the densest anatomical area (on a MLO Mammogram the pectoral muscle area),
- where the highest attenuation of the X-ray beam took place,
- and thus where the least number of X-ray photons reached the image receptor.

APPENDIX L

Raw data: Image quality assessment

APPENDIX L

IMAGE QUALITY ASSESSMENT - DATASHEET

Algorithm

1 MUSICA^2

2 MUSICA^2 invert

3 Raw

4 Raw invert

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
1	**A**	1	5	2	5	1	5	4	4	5	**31**	5	N/A	2	Y
1	A	2	5	1	5	1	5	4	5	5	**31**	N/A	5	2	Y
1	A	3	5	1	5	1	5	5	5	5	**32**	5	N/A	2	N
1	A	4	5	1	5	3	5	3	4	5	**31**	5	N/A	1	N
1	**B**	1	5	4	5	2	5	4	5	4	**34**	4	N/A	2	Y
1	B	2	5	5	5	2	5	5	5	4	**36**	5	4	2	Y
1	B	3	5	5	5	1	4	4	4	4	**32**	4	N/A	2	Y
1	B	4	4	1	4	2	4	3	3	3	**24**	4	N/A	1	N
1	**C**	1	5	4	3	3	5	3	5	4	**32**	5	N/A	2	Y
1	C	2	5	3	3	3	4	3	5	4	**30**	4	N/A	2	Y
1	C	3	5	3	4	3	4	3	5	4	**31**	5	N/A	2	Y
1	C	4	5	3	4	2	3	3	4	3	**27**	4	N/A	2	Y
2	**A**	1	5	4	5	1	5	4	4	5	**33**	N/A	N/A	2	Y
2	A	2	5	1	5	1	4	4	5	5	**30**	N/A	N/A	1	N
2	A	3	5	4	5	2	2	3	5	5	**31**	N/A	N/A	2	N
2	A	4	5	5	5	2	2	4	5	5	**33**	N/A	N/A	2	Y
2	**B**	1	5	5	5	2	5	4	5	4	**35**	4	N/A	2	Y
2	B	2	5	2	4	1	4	3	4	3	**26**	4	N/A	2	N
2	B	3	5	4	5	1	3	4	4	3	**29**	5	N/A	2	Y
2	B	4	5	4	4	1	4	4	4	4	**30**	4	N/A	2	Y
2	**C**	1	5	5	4	3	4	3	5	5	**34**	4	N/A	2	Y
2	C	2	4	4	5	3	4	4	5	4	**33**	N/A	4	2	Y
2	C	3	4	4	5	3	4	3	5	4	**32**	3	N/A	2	Y
2	C	4	5	4	5	4	4	4	5	4	**35**	N/A	N/A	1	Y
3	**A**	1	5	5	5	1	5	5	5	5	**36**	N/A	5	2	Y
3	A	2	5	4	5	1	5	5	5	5	**35**	5	N/A	2	N
3	A	3	5	5	5	1	5	5	5	5	**36**	5	N/A	2	Y
3	A	4	5	5	5	3	5	5	5	5	**38**	N/A	N/A	2	N
3	**B**	1	5	5	5	1	5	5	5	4	**35**	4	N/A	2	Y
3	B	2	5	5	4	1	4	4	5	3	**31**	5	N/A	2	Y
3	B	3	5	5	5	1	5	4	5	3	**33**	4	N/A	2	Y
3	B	4	5	5	5	1	5	5	5	4	**35**	5	N/A	2	Y
3	**C**	1	5	5	4	3	5	4	5	5	**36**	4	N/A	2	Y
3	C	2	5	5	5	2	4	4	7	8	**40**	4	N/A	2	Y
3	C	3	5	5	5	4	5	4	5	5	**38**	4	N/A	2	Y
3	C	4	3	5	5	4	5	4	5	5	**36**	4	2	2	N

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
4	**A**	1	4	1	5	3	5	5	3	5	**31**	N/A	5	2	Y
4	A	2	5	2	5	3	5	4	4	5	**33**	N/A	5	2	Y
4	A	3	5	1	5	1	4	4	4	5	**29**	N/A	5	1	N
4	A	4	5	2	5	1	4	3	3	5	**28**	N/A	5	2	N
4	**B**	1	4	1	4	1	4	4	5	3	**26**	1	3	2	Y
4	B	2	5	5	5	2	5	5	5	5	**37**	4	5	2	Y
4	B	3	5	4	5	1	4	4	5	4	**32**	N/A	4	2	Y
4	B	4	5	4	5	1	4	4	4	4	**31**	4	4	2	Y
4	**C**	1	4	2	4	3	4	3	4	4	**28**	3	5	2	Y
4	C	2	5	3	3	4	5	3	5	4	**32**	4	5	1	Y
4	C	3	4	3	3	3	4	3	4	4	**28**	3	N/A	2	Y
4	C	4	4	3	3	3	4	3	4	4	**28**	4	5	2	Y
5	**A**	1	5	3	5	3	5	4	3	5	**33**	5	N/A	2	Y
5	A	2	5	2	5	3	5	3	4	5	**32**	N/A	N/A	2	Y
5	A	3	5	1	5	3	5	3	4	5	**31**	N/A	N/A	2	N
5	A	4	5	4	5	1	5	3	3	5	**31**	N/A	N/A	2	N
5	**B**	1	5	5	5	2	5	5	5	5	**37**	4	N/A	2	Y
5	B	2	5	5	5	2	5	5	5	5	**37**	3	N/A	2	Y
5	B	3	3	3	4	4	1	4	4	3	**26**	N/A	N/A	2	Y
5	B	4	5	4	5	1	5	4	5	5	**34**	N/A	N/A	2	Y
5	**C**	1	5	4	4	3	4	3	5	5	**33**	4	N/A	2	Y
5	C	2	5	4	4	3	5	3	5	4	**33**	5	4	2	Y
5	C	3	4	2	5	2	3	3	3	4	**26**	4	**N/A**	1	Y
5	C	4	5	3	5	3	4	3	4	4	**31**	2	3	3	Y
6	**A**	1	5	2	5	3	5	4	5	5	**34**	4	N/A	2	Y
6	A	2	5	2	5	3	5	4	4	5	**33**	N/A	N/A	2	Y
6	A	3	5	3	5	4	5	5	5	5	**37**	N/A	N/A	2	N
6	A	4	5	3	5	1	5	4	5	5	**33**	N/A	N/A	1	N
6	**B**	1	5	5	5	1	5	4	5	5	**35**	4	N/A	2	Y
6	B	2	5	5	5	2	5	5	5	5	**37**	3	N/A	2	Y
6	B	3	5	5	5	2	5	4	5	4	**35**	N/A	N/A	2	Y
6	B	4	4	4	4	1	4	4	5	4	**30**	N/A	N/A	2	Y
6	**C**	1	5	4	4	4	5	4	5	5	**36**	4	N/A	2	Y
6	C	2	5	5	4	4	5	4	5	5	**37**	4	4	2	Y
6	C	3	5	4	4	4	5	4	5	5	**36**	4	N/A	2	Y
6	C	4	4	3	4	3	4	4	4	4	**30**	**N/A**	N/A	1	Y
7	**A**	1	4	5	5	4	5	4	4	5	**36**	N/A	5	2	Y
7	A	2	4	5	5	3	5	4	4	5	**35**	N/A	5	2	Y
7	A	3	5	5	5	1	5	4	5	5	**35**	N/A	5	2	N
7	A	4	5	5	5	4	5	4	5	5	**38**	N/A	5	2	Y
7	**B**	1	4	5	5	1	5	4	5	5	**34**	3	4	2	Y
7	B	2	5	5	5	2	5	5	5	5	**37**	4	5	3	Y
7	B	3	2	4	4	1	4	3	4	3	**25**	4	4	2	Y
7	B	4	3	5	4	1	3	3	4	4	**27**	4	4	2	Y
7	**C**	1	3	5	5	4	5	4	5	5	**36**	4	5	2	Y
7	C	2	3	5	3	4	5	3	5	5	**33**	4	5	2	Y
7	C	3	4	2	3	3	4	4	4	3	**27**	4	N/A	2	Y
7	C	4	3	4	4	4	5	4	5	4	**33**	4	5	1	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
8	**A**	1	4	4	5	2	5	4	4	5	**33**	5	5	2	Y
8	A	2	5	2	5	1	5	4	4	5	**31**	5	N/A	2	Y
8	A	3	5	3	5	2	5	5	5	5	**35**	5	5	2	Y
8	A	4	5	4	5	2	5	4	4	3	**32**	5	5	2	Y
8	**B**	1	4	5	5	2	5	4	5	5	**35**	4	4	2	Y
8	B	2	4	5	4	2	5	4	4	3	**31**	5	4	2	Y
8	B	3	4	5	5	2	4	4	4	4	**32**	4	4	2	Y
8	B	4	5	5	5	3	5	5	5	5	**38**	4	5	2	Y
8	**C**	1	5	4	4	4	5	4	5	4	**35**	5	5	2	Y
8	C	2	5	4	4	4	5	4	4	4	**34**	N/A	4	2	Y
8	C	3	5	4	3	4	5	4	4	4	**33**	5	5	1	Y
8	C	4	4	4	4	4	5	4	4	5	**34**	5	4	1	Y
9	**A**	1	5	2	5	2	5	5	5	5	**34**	5	5	2	Y
9	A	2	5	2	5	2	5	5	5	5	**34**	5	5	2	Y
9	A	3	5	1	5	2	5	5	5	5	**33**	5	5	2	Y
9	A	4	5	3	5	1	5	5	5	5	**34**	N/A	5	2	N
9	**B**	1	4	4	4	1	5	4	4	3	**29**	4	4	2	Y
9	B	2	5	5	5	3	5	5	5	5	**38**	5	5	2	Y
9	B	3	5	4	5	1	4	4	4	4	**31**	4	4	2	Y
9	B	4	5	4	5	2	5	5	5	5	**36**	4	4	2	Y
9	**C**	1	4	4	5	3	4	4	4	4	**32**	N/A	N/A	2	Y
9	C	2	5	3	3	4	5	3	5	5	**33**	5	5	2	Y
9	C	3	5	4	3	3	4	3	5	4	**31**	5	5	2	Y
9	C	4	5	3	4	3	4	3	5	4	**31**	4	5	2	N
10	**A**	1	5	3	5	4	5	4	4	5	**35**	N/A	N/A	2	Y
10	A	2	5	1	5	4	5	4	4	5	**33**	N/A	N/A	2	Y
10	A	3	5	1	5	1	5	3	3	4	**27**	N/A	N/A	2	N
10	A	4	5	5	5	1	5	4	5	3	**33**	N/A	N/A	1	Y
10	**B**	1	5	5	5	3	5	5	5	5	**38**	4	N/A	2	Y
10	B	2	5	5	5	2	5	5	5	5	**37**	4	N/A	2	Y
10	B	3	3	4	4	4	4	4	4	4	**31**	N/A	N/A	2	Y
10	B	4	5	5	4	3	5	5	5	5	**37**	3	N/A	2	Y
10	**C**	1	5	4	4	5	5	5	5	5	**38**	4	N/A	2	Y
10	C	2	5	5	5	5	5	5	5	5	**40**	4	N/A	2	Y
10	C	3	5	3	5	4	5	4	5	5	**36**	3	**N/A**	1	Y
10	C	4	4	4	5	5	5	5	5	5	**38**	4	N/A	2	Y
11	**A**	1	5	4	5	3	5	5	5	5	**37**	5	N/A	2	Y
11	A	2	5	5	5	4	5	5	5	5	**39**	N/A	5	2	Y
11	A	3	5	4	5	2	5	4	4	5	**34**	N/A	5	2	Y
11	A	4	5	3	5	1	5	5	4	5	**33**	N/A	5	2	N
11	**B**	1	5	5	5	3	5	5	5	5	**38**	4	4	2	Y
11	B	2	5	5	5	3	5	5	5	5	**38**	5	5	2	Y
11	B	3	4	5	5	4	1	4	5	5	**33**	4	5	2	Y
11	B	4	4	3	4	2	4	4	5	4	**30**	3	4	2	Y
11	**C**	1	5	5	5	4	5	5	5	5	**39**	5	5	2	Y
11	C	2	5	5	5	5	5	5	5	5	**40**	4	5	2	Y
11	C	3	4	4	5	4	5	4	5	5	**36**	4	5	2	Y
11	C	4	4	3	5	4	5	4	5	4	**34**	3	5	2	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
12	**A**	1	5	4	5	2	4	3	2	5	**30**	5	N/A	2	Y
12	A	2	5	2	5	1	5	4	2	5	**29**	N/A	5	2	N
12	A	3	5	3	5	1	5	4	2	5	**30**	5	N/A	2	N
12	A	4	5	1	5	1	5	4	4	5	**30**	N/A	N/A	2	Y
12	**B**	1	5	4	4	1	3	4	4	4	**29**	3	N/A	2	Y
12	B	2	5	5	2	1	3	3	4	4	**27**	4	N/A	2	Y
12	B	3	3	3	4	1	3	3	3	3	**23**	3	N/A	2	Y
12	B	4	4	4	5	1	4	4	4	4	**30**	3	N/A	2	Y
12	**C**	1	5	4	4	3	4	3	5	4	**32**	5	3	2	N
12	C	2	5	5	4	3	4	3	4	4	**32**	4	N/A	2	Y
12	C	3	4	4	4	2	4	3	4	4	**29**	4	N/A	2	Y
12	C	4	3	3	4	3	4	3	4	4	**28**	4	N/A	2	N
13	**A**	1	5	5	5	4	5	5	5	5	**39**	5	5	2	Y
13	A	2	5	4	5	5	5	5	5	5	**39**	5	5	2	Y
13	A	3	5	4	5	4	5	4	4	5	**36**	5	5	2	Y
13	A	4	5	5	5	4	5	4	5	4	**37**	5	5	1	Y
13	**B**	1	4	4	4	3	4	4	5	4	**32**	4	3	2	Y
13	B	2	5	5	5	3	5	5	5	5	**38**	4	4	2	Y
13	B	3	5	5	5	3	5	5	5	5	**38**	4	4	2	Y
13	B	4	5	4	5	3	5	5	5	5	**37**	4	5	2	Y
13	**C**	1	4	5	5	5	5	5	5	4	**38**	5	5	2	Y
13	C	2	5	5	4	5	5	4	5	5	**38**	5	5	2	Y
13	C	3	4	5	5	4	5	4	5	5	**37**	4	5	2	Y
13	C	4	5	4	4	4	5	4	5	5	**36**	4	5	1	Y
14	**A**	1	5	5	5	5	5	5	5	5	**40**	5	N/A	2	Y
14	A	2	4	5	5	5	5	4	5	5	**38**	5	N/A	2	Y
14	A	3	5	5	5	5	5	5	5	4	**39**	5	N/A	2	N
14	A	4	5	5	5	5	5	5	5	5	**40**	5	N/A	2	Y
14	**B**	1	4	5	5	3	5	5	5	5	**37**	5	N/A	2	Y
14	B	2	5	5	5	3	5	5	5	5	**38**	5	N/A	2	Y
14	B	3	3	4	4	4	4	4	4	4	**31**	4	N/A	2	Y
14	B	4	4	4	5	3	4	4	4	5	**33**	4	N/A	2	Y
14	**C**	1	5	5	5	5	5	5	5	5	**40**	5	N/A	2	Y
14	C	2	5	4	5	5	5	5	5	5	**39**	5	N/A	2	Y
14	C	3	5	4	4	5	5	4	5	4	**36**	5	N/A	1	Y
14	C	4	5	4	4	5	5	4	5	5	**37**	4	N/A	2	Y
15	**A**	1	5	1	5	3	5	5	5	5	**34**	5	N/A	2	Y
15	A	2	5	4	5	3	5	5	5	5	**37**	5	N/A	2	Y
15	A	3	5	4	5	2	5	5	5	5	**36**	5	N/A	2	y
15	A	4	5	1	5	1	5	5	5	5	**32**	5	N/A	2	Y
15	**B**	1	5	5	5	2	5	4	5	4	**35**	4	N/A	2	Y
15	B	2	5	5	5	2	5	5	5	4	**36**	5	N/A	2	Y
15	B	3	5	5	5	1	5	4	5	4	**34**	5	N/A	2	Y
15	B	4	4	4	5	1	4	4	4	3	**29**	4	N/A	2	Y
15	**C**	1	5	4	4	3	5	4	5	5	**35**	5	N/A	2	Y
15	C	2	5	3	4	3	5	3	5	5	**33**	5	N/A	2	Y
15	C	3	5	4	5	4	5	4	5	5	**37**	5	N/A	1	Y
15	C	4	5	4	4	4	5	4	5	5	**36**	5	N/A	2	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
16	**A**	1	5	5	5	3	5	5	5	5	**38**	4	N/A	2	Y
16	A	2	5	3	5	4	5	5	5	5	**37**	N/A	N/A	2	Y
16	A	3	5	4	5	1	5	5	5	5	**35**	N/A	N/A	2	Y
16	A	4	5	5	5	4	5	4	4	5	**37**	N/A	N/A	2	Y
16	**B**	1	5	5	4	1	5	5	5	5	**35**	N/A	N/A	2	Y
16	B	2	4	4	4	1	4	4	4	3	**28**	N/A	N/A	2	Y
16	B	3	3	4	4	1	4	4	5	4	**29**	N/A	N/A	2	Y
16	B	4	5	5	4	2	5	4	5	5	**35**	N/A	N/A	2	Y
16	**C**	1	5	5	4	4	5	4	5	5	**37**	3	5	3	Y
16	C	2	5	4	5	4	5	5	5	4	**37**	1	N/A	2	Y
16	C	3	5	5	5	4	5	4	5	5	**38**	N/A	N/A	1	Y
16	C	4	5	5	4	4	5	4	5	5	**37**	N/A	N/A	2	Y
17	**A**	1	5	5	5	3	5	4	4	4	**35**	5	N/A	2	Y
17	A	2	5	3	5	4	5	5	5	5	**37**	5	N/A	2	Y
17	A	3	5	4	5	2	5	4	4	2	**31**	4	5	2	Y
17	A	4	5	5	5	2	5	4	3	4	**33**	5	N/A	2	Y
17	**B**	1	5	5	5	2	5	5	5	5	**37**	4	4	2	Y
17	B	2	5	4	4	1	4	4	4	4	**30**	5	3	2	Y
17	B	3	5	5	5	2	5	5	5	5	**37**	4	N/A	2	Y
17	B	4	5	4	5	3	5	5	4	5	**36**	5	N/A	2	Y
17	**C**	1	5	5	5	4	5	4	5	5	**38**	4	4	2	Y
17	C	2	5	4	5	4	5	4	5	4	**36**	4	4	2	Y
17	C	3	5	4	4	4	5	4	5	5	**36**	5	N/A	2	Y
17	C	4	5	4	5	4	5	4	5	5	**37**	4	4	2	Y
18	**A**	1	4	4	5	5	5	4	4	5	**36**	5	5	2	Y
18	A	2	4	2	5	4	5	4	4	5	**33**	N/A	5	2	Y
18	A	3	5	1	5	1	5	5	5	5	**32**	5	N/A	1	N
18	A	4	5	2	5	1	4	4	4	5	**30**	N/A	5	1	Y
18	**B**	1	3	4	5	1	5	4	5	4	**31**	4	5	2	Y
18	B	2	5	5	5	2	4	4	4	4	**33**	4	5	2	Y
18	B	3	3	4	4	2	4	3	4	3	**27**	4	3	1	Y
18	B	4	4	4	4	1	4	4	4	4	**29**	3	3	2	Y
18	**C**	1	3	3	2	3	4	3	5	4	**27**	4	5	2	Y
18	C	2	3	3	3	4	4	4	5	4	**30**	4	N/A	2	Y
18	C	3	4	3	3	3	4	3	4	3	**27**	3	4	2	Y
18	C	4	3	3	3	4	5	3	5	5	**31**	4	5	2	Y
19	**A**	1	5	2	5	1	1	4	4	5	**27**	N/A	5	2	Y
19	A	2	5	2	5	2	5	4	4	5	**32**	N/A	5	2	Y
19	A	3	5	1	5	1	5	5	5	5	**32**	N/A	5	2	Y
19	**A**	4	5	1	5	2	5	4	4	5	**31**	N/A	5	2	N
19	**B**	1	5	5	5	1	4	4	4	4	**32**	4	5	2	Y
19	B	2	5	4	5	1	4	4	4	4	**31**	4	4	2	Y
19	B	3	4	3	5	1	4	3	3	3	**26**	4	4	2	Y
19	B	4	4	4	5	1	3	4	4	4	**29**	5	4	1	Y
19	**C**	1	5	4	4	3	5	3	4	4	**32**	4	N/A	2	Y
19	C	2	5	2	2	3	4	3	5	5	**29**	4	5	2	Y
19	C	3	5	3	3	4	5	3	5	5	**33**	N/A	5	2	Y
19	C	4	4	2	4	3	4	3	4	3	**27**	3	N/A	1	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
20	**A**	1	5	1	5	4	5	5	4	5	**34**	5	5	2	Y
20	A	2	5	1	4	4	5	4	4	5	**32**	5	5	2	Y
20	A	3	5	1	4	2	5	4	4	4	**29**	4	4	2	Y
20	A	4	5	2	3	3	5	5	5	5	**33**	5	5	2	N
20	**B**	1	5	3	4	2	5	4	5	5	**33**	4	5	2	Y
20	B	2	5	4	5	3	5	4	4	5	**35**	4	4	2	Y
20	B	3	4	3	5	1	5	3	4	4	**29**	4	4	2	Y
20	B	4	4	3	3	2	5	4	4	4	**29**	4	3	1	Y
20	**C**	1	5	3	1	4	5	2	5	4	**29**	5	5	2	Y
20	C	2	5	3	2	3	4	3	4	4	**28**	4	5	2	Y
20	C	3	5	3	3	3	5	3	5	4	**31**	5	5	2	Y
20	C	4	4	2	1	4	5	2	5	4	**27**	4	N/A	1	N
21	**A**	1	5	4	5	3	5	4	4	5	**35**	5	5	2	Y
21	A	2	5	3	5	3	5	4	4	5	**34**	5	5	2	Y
21	A	3	5	3	5	1	5	4	4	5	**32**	N/A	N/A	2	Y
21	A	4	5	5	5	4	5	4	4	5	**37**	5	5	2	Y
21	**B**	1	4	5	4	2	5	4	5	4	**33**	4	4	2	Y
21	B	2	5	4	5	3	5	5	5	5	**37**	5	4	2	Y
21	B	3	5	5	5	1	5	5	5	5	**36**	5	4	2	Y
21	B	4	5	5	5	1	5	5	5	5	**36**	5	3	2	Y
21	**C**	1	5	4	5	3	4	5	5	4	**35**	5	5	2	Y
21	C	2	4	4	4	4	5	4	5	5	**35**	5	5	2	Y
21	C	3	5	4	3	4	4	3	5	5	**33**	5	5	2	Y
21	C	4	4	4	4	3	4	3	4	4	**30**	5	5	1	Y
22	**A**	1	5	4	5	2	5	4	4	5	**34**	N/A	5	2	Y
22	A	2	5	4	5	1	4	4	5	5	**33**	5	5	2	Y
22	A	3	5	4	5	1	5	5	5	5	**35**	N/A	5	2	Y
22	A	4	5	3	5	1	5	5	5	5	**34**	N/A	5	2	N
22	**B**	1	5	5	5	1	4	4	4	5	**33**	3	3	2	Y
22	B	2	5	5	5	1	4	5	5	5	**35**	4	4	2	Y
22	B	3	4	5	5	1	5	4	5	4	**33**	4	4	2	Y
22	B	4	5	4	5	4	4	4	4	4	**34**	4	3	2	Y
22	**C**	1	4	5	4	4	5	4	5	5	**36**	4	5	2	Y
22	C	2	4	4	4	3	4	4	5	5	**33**	4	5	2	Y
22	C	3	5	4	3	3	4	3	5	4	**31**	4	5	2	Y
22	C	4	5	4	4	3	4	3	4	4	**31**	3	4	1	N
23	**A**	1	4	1	5	2	5	3	3	5	**28**	N/A	5	2	Y
23	A	2	5	3	5	3	5	4	4	5	**34**	4	N/A	2	Y
23	A	3	5	3	5	1	5	4	4	5	**32**	N/A	5	2	Y
23	A	4	5	4	5	1	4	3	3	5	**30**	N/A	5	2	N
23	**B**	1	4	4	4	4	4	4	5	4	**33**	3	4	2	Y
23	B	2	5	5	4	2	4	4	5	5	**34**	4	4	2	Y
23	B	3	4	5	3	1	3	3	4	3	**26**	N/A	3	2	Y
23	B	4	5	3	3	2	4	3	4	4	**28**	N/A	3	2	Y
23	**C**	1	4	3	4	3	4	3	5	4	**30**	4	4	2	Y
23	C	2	4	4	4	4	4	4	5	5	**34**	4	5	2	Y
23	C	3	4	4	3	3	4	3	4	4	**29**	4	4	1	Y
23	C	4	5	3	3	3	4	3	4	5	**30**	3	5	2	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
24	**A**	1	5	5	5	5	5	5	5	5	**40**	5	N/A	2	Y
24	A	2	5	5	5	4	5	5	5	5	**39**	N/A	5	2	Y
24	A	3	5	5	5	2	5	5	5	5	**37**	5	N/A	2	Y
24	A	4	5	4	5	2	5	5	5	5	**36**	5	N/A	2	N
24	**B**	1	5	5	5	2	4	4	4	4	**33**	4	N/A	2	Y
24	B	2	5	5	5	3	5	5	5	5	**38**	5	N/A	2	Y
24	B	3	5	5	5	1	5	3	5	4	**33**	5	N/A	2	Y
24	B	4	5	4	5	2	4	4	4	4	**32**	4	N/A	2	Y
24	**C**	1	4	5	4	4	5	4	5	5	**36**	5	N/A	2	Y
24	C	2	4	4	4	4	5	4	5	5	**35**	5	N/A	2	Y
24	C	3	5	5	4	4	5	4	5	5	**37**	5	N/A	2	Y
24	C	4	5	4	5	3	4	3	5	4	**33**	4	N/A	1	Y
25	**A**	1	5	4	5	2	5	5	5	5	**36**	5	N/A	2	Y
25	A	2	5	4	5	2	5	5	5	5	**36**	5	N/A	2	Y
25	A	3	5	4	5	3	5	5	5	5	**37**	5	N/A	2	Y
25	A	4	5	4	5	4	5	5	5	5	**38**	5	N/A	2	Y
25	**B**	1	5	5	5	3	5	5	5	5	**38**	4	4	2	Y
25	B	2	5	4	5	2	4	4	5	4	**33**	5	N/A	2	Y
25	B	3	5	5	4	3	5	5	5	5	**37**	4	N/A	2	Y
25	B	4	5	5	5	3	5	5	5	5	**38**	4	N/A	2	Y
25	**C**	1	5	5	5	4	5	4	5	5	**38**	5	N/A	2	Y
25	C	2	5	5	5	4	5	4	5	4	**37**	4	N/A	2	Y
25	C	3	5	4	5	5	5	5	5	5	**39**	5	N/A	2	Y
25	C	4	5	4	5	4	5	4	5	5	**37**	4	N/A	2	Y
26	**A**	1	5	1	5	1	5	5	5	5	**32**	5	N/A	2	Y
26	A	2	5	2	5	2	5	5	5	5	**34**	N/A	N/A	2	Y
26	A	3	5	1	5	2	5	5	5	5	**33**	N/A	N/A	2	Y
26	A	4	5	1	5	2	5	5	5	5	**33**	N/A	N/A	2	Y
26	**B**	1	5	5	5	3	5	5	5	5	**38**	4	N/A	2	Y
26	B	2	5	4	5	2	5	4	5	4	**34**	3	N/A	2	Y
26	B	3	5	4	4	2	5	4	5	4	**33**	3	N/A	2	Y
26	B	4	5	5	5	2	5	4	5	4	**35**	N/A	N/A	2	Y
26	**C**	1	5	4	5	5	5	5	5	5	**39**	4	N/A	2	Y
26	C	2	5	4	5	4	5	4	5	5	**37**	4	N/A	2	Y
26	C	3	5	4	4	4	5	4	5	5	**36**	4	N/A	2	Y
26	C	4	4	3	4	3	5	3	5	5	**32**	4	N/A	2	Y
27	**A**	1	5	5	5	2	5	4	3	5	**34**	N/A	N/A	2	Y
27	A	2	5	5	5	1	2	4	4	5	**31**	5	N/A	2	N
27	A	3	5	4	5	2	4	5	5	5	**35**	N/A	N/A	2	N
27	A	4	5	4	5	1	4	3	4	5	**31**	N/A	N/A	2	N
27	**B**	1	5	5	5	1	5	4	5	4	**34**	3	N/A	2	Y
27	B	2	5	5	5	1	4	4	5	4	**33**	4	N/A	2	Y
27	B	3	5	5	5	1	4	4	5	3	**32**	N/A	N/A	2	Y
27	B	4	5	5	5	1	4	4	4	3	**31**	4	N/A	2	Y
27	**C**	1	5	5	4	4	5	4	4	5	**36**	4	N/A	2	Y
27	C	2	5	5	5	5	5	5	5	5	**40**	4	N/A	2	Y
27	C	3	5	5	5	4	4	4	4	4	**35**	4	N/A	2	Y
27	C	4	5	4	4	3	4	3	4	5	**32**	4	N/A	2	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
28	**A**	1	5	5	5	5	5	5	4	5	**39**	5	N/A	2	Y
28	A	2	5	5	5	4	5	4	4	5	**37**	5	N/A	2	Y
28	A	3	5	5	5	5	5	5	5	5	**40**	N/A	N/A	2	Y
28	A	4	5	5	5	5	5	5	5	5	**40**	5	N/A	2	Y
28	**B**	1	5	5	5	2	5	4	5	4	**35**	4	N/A	2	Y
28	B	2	5	5	5	2	5	4	5	4	**35**	5	N/A	2	Y
28	B	3	4	5	4	2	5	4	4	4	**32**	5	N/A	2	Y
28	B	4	5	5	5	3	5	4	5	5	**37**	5	N/A	2	Y
28	**C**	1	5	5	5	5	5	5	5	5	**40**	5	5	2	Y
28	C	2	5	5	5	4	5	4	5	4	**37**	4	3	2	N
28	C	3	5	5	4	5	5	4	5	4	**37**	5	4	2	Y
28	C	4	5	5	4	5	5	5	5	5	**39**	4	4	2	Y
29	**A**	1	5	1	5	1	5	5	4	5	**31**	5	5	2	Y
29	A	2	5	2	5	1	5	4	4	5	**31**	5	5	2	Y
29	A	3	5	1	5	3	5	4	4	5	**32**	5	5	2	N
29	A	4	5	3	5	1	5	4	4	5	**32**	5	5	2	Y
29	**B**	1	5	5	5	1	5	4	5	4	**34**	5	5	2	Y
29	B	2	5	5	5	2	5	5	5	4	**36**	5	5	2	Y
29	B	3	5	4	5	1	4	4	4	3	**30**	4	4	2	Y
29	B	4	5	4	5	5	5	5	5	5	**39**	5	4	2	Y
29	**C**	1	5	4	4	4	5	4	5	5	**36**	5	5	2	Y
29	C	2	5	4	4	5	5	4	5	4	**36**	5	5	2	Y
29	C	3	4	4	5	4	5	4	5	4	**35**	5	5	2	Y
29	C	4	5	4	4	2	4	3	4	4	**30**	4	5	2	N
30	**A**	1	5	3	5	5	5	5	5	5	**38**	5	5	2	Y
30	A	2	5	5	5	4	5	5	4	5	**38**	5	5	2	Y
30	A	3	5	3	5	4	5	5	5	5	**37**	N/A	5	2	Y
30	A	4	5	3	5	4	5	5	5	5	**37**	N/A	5	2	N
30	**B**	1	5	5	5	3	5	5	5	5	**38**	4	5	2	Y
30	B	2	5	5	5	3	5	5	5	5	**38**	3	5	2	Y
30	B	3	5	5	5	3	5	4	5	5	**37**	4	5	2	Y
30	B	4	5	5	5	2	5	4	5	4	**35**	4	5	2	Y
30	**C**	1	5	5	5	5	5	5	5	5	**40**	4	5	2	Y
30	C	2	5	4	5	5	5	5	5	5	**39**	5	5	2	Y
30	C	3	5	4	5	4	5	4	5	5	**37**	4	4	2	Y
30	C	4	5	4	5	4	5	4	5	4	**36**	N/A	4	2	Y
31	**A**	1	5	4	5	4	5	5	4	4	**36**	3	5	2	Y
31	A	2	5	3	5	5	5	3	4	5	**35**	5	5	2	Y
31	A	3	5	4	5	4	5	3	4	5	**35**	N/A	5	2	Y
31	A	4	5	4	5	4	5	5	5	5	**38**	N/A	5	2	N
31	**B**	1	5	5	4	3	5	5	5	5	**37**	4	5	2	Y
31	B	2	5	5	5	3	5	5	5	5	**38**	5	5	2	Y
31	B	3	4	4	5	3	5	5	4	5	**35**	3	5	2	Y
31	B	4	4	5	5	2	4	4	5	5	**34**	4	4	2	Y
31	**C**	1	5	4	5	5	5	5	5	5	**39**	5	5	2	Y
31	C	2	5	4	5	4	5	4	5	5	**37**	4	5	2	Y
31	C	3	5	4	5	4	5	4	5	5	**37**	3	5	1	y
31	C	4	4	4	5	4	5	4	5	4	**35**	3	5	2	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
32	**A**	1	5	2	5	1	4	3	4	5	**29**	5	N/A	2	Y
32	A	2	5	1	5	2	5	4	4	5	**31**	5	N/A	2	N
32	A	3	5	1	5	1	4	3	4	5	**28**	N/A	N/A	2	N
32	A	4	5	3	5	1	5	4	4	5	**32**	N/A	N/A	2	N
32	**B**	1	5	5	5	1	4	4	5	4	**33**	4	N/A	2	Y
32	B	2	5	4	5	1	5	4	5	4	**33**	5	N/A	2	Y
32	B	3	4	3	4	3	3	2	3	3	**25**	3	3	2	Y
32	B	4	5	4	5	1	3	3	4	3	**28**	3	N/A	2	Y
32	**C**	1	5	4	4	4	5	4	5	5	**36**	4	N/A	2	Y
32	C	2	5	4	4	3	4	3	4	5	**32**	5	N/A	2	N
32	C	3	5	4	4	3	4	3	4	4	**31**	4	N/A	2	Y
32	C	4	4	3	4	2	4	2	4	4	**27**	4	N/A	2	N
33	**A**	1	5	1	5	4	5	4	4	5	**33**	5	5	2	Y
33	A	2	5	3	5	5	5	5	5	5	**38**	5	5	2	Y
33	A	3	5	2	5	4	5	5	5	5	**36**	5	5	2	Y
33	A	4	5	4	5	3	5	5	5	5	**37**	5	5	2	Y
33	**B**	1	5	5	4	2	5	4	5	4	**34**	5	5	2	Y
33	B	2	5	5	5	3	5	4	5	4	**36**	5	5	2	Y
33	B	3	4	5	4	3	5	4	4	4	**33**	4	4	2	Y
33	B	4	5	5	5	1	5	5	4	4	**34**	4	4	2	Y
33	**C**	1	5	4	5	5	5	5	5	5	**39**	5	4	2	Y
33	C	2	5	4	5	5	5	5	5	5	**39**	5	4	2	Y
33	C	3	5	4	5	4	5	4	5	5	**37**	5	5	2	Y
33	C	4	5	4	5	4	5	4	5	5	**37**	5	5	1	Y
34	**A**	1	5	2	5	4	5	4	3	5	**33**	5	5	2	Y
34	A	2	5	3	5	4	5	4	4	5	**35**	5	5	2	Y
34	A	3	5	4	5	2	5	5	5	5	**36**	5	5	2	Y
34	A	4	5	1	5	2	5	4	4	5	**31**	N/A	5	2	N
34	**B**	1	5	5	5	3	5	4	5	4	**36**	5	5	2	Y
34	B	2	5	5	5	2	5	5	5	5	**37**	4	4	2	Y
34	B	3	5	5	5	2	5	4	4	4	**34**	4	4	2	Y
34	B	4	5	4	5	1	4	4	4	4	**31**	4	4	2	Y
34	**C**	1	5	3	4	3	5	3	4	4	**31**	5	5	2	Y
34	C	2	5	4	4	4	5	4	5	4	**35**	5	5	2	Y
34	C	3	4	4	4	3	5	3	4	5	**32**	5	5	2	Y
34	C	4	4	3	4	4	4	3	4	4	**30**	5	5	2	N
35	**A**	1	5	4	5	4	5	5	5	5	**38**	5	5	2	Y
35	A	2	5	4	5	3	5	4	5	5	**36**	5	5	2	Y
35	A	3	5	4	5	3	5	5	5	4	**36**	5	5	2	N
35	A	4	5	5	5	1	5	4	4	5	**34**	5	5	2	Y
35	**B**	1	5	5	5	2	5	5	5	5	**37**	4	5	2	Y
35	B	2	5	5	5	3	5	5	5	4	**37**	4	5	2	Y
35	B	3	4	5	5	1	5	4	5	4	**33**	4	5	2	Y
35	B	4	4	5	5	2	5	5	5	5	**36**	5	4	2	Y
35	**C**	1	5	5	5	4	5	4	5	5	**38**	4	5	2	Y
35	C	2	5	4	4	4	5	4	5	5	**36**	5	5	2	Y
35	C	3	4	5	5	4	5	4	5	4	**36**	5	5	1	Y
35	C	4	4	4	4	4	5	4	5	4	**34**	4	N/A	1	Y

			IMAGE QUALITY ASSESSMENT												
Image #	**Radiologist**	**Algorithm**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**T**	**9**	**10**	**11**	**12**
36	**A**	1	5	4	5	1	5	5	5	5	**35**	5	5	2	Y
36	A	2	5	3	5	2	5	4	4	5	**33**	N/A	5	2	Y
36	A	3	5	2	5	1	5	5	5	5	**33**	4	N/A	2	Y
36	A	4	5	4	5	1	5	5	5	5	**35**	N/A	5	2	Y
36	**B**	1	5	4	4	1	4	4	5	4	**31**	3	4	2	Y
36	B	2	5	5	5	1	4	4	5	4	**33**	4	4	2	Y
36	B	3	5	4	5	1	4	3	4	3	**29**	3	3	2	Y
36	B	4	5	3	5	1	4	4	4	4	**30**	N/A	4	2	Y
36	**C**	1	4	5	5	3	5	3	5	5	**35**	4	N/A	2	Y
36	C	2	5	5	5	4	5	4	5	4	**37**	4	4	2	Y
36	C	3	5	4	5	4	5	4	5	4	**36**	5	5	2	Y
36	C	4	5	4	4	3	4	3	5	4	**32**	4	3	1	Y

APPENDIX M

p-Values indicating differences in mean IQS (all viewers) per individual anatomical structure (criteria 1 – 8) between the processing options (n=36)

APPENDIX M

p-Values indicating differences in mean IQS (all viewers) per individual anatomical structure (criteria 1 – 8) between the processing options (n = 36)

		1 Skin outline	2 Skin structure	3 Pectoral muscle margin	4 Vessels in dense parenchyma	5 Vessels in fat tissue	6 Vessels, fibres and muscle	7 Fibres in fat	8 Glandular tissue
MUSICA^2	MUSICA^2 Invert	**0.0263**	0.3060	0.6891	0.2825	0.5933	0.8721	0.3033	0.9002
	Unprocessed	0.1293	**0.0159**	0.3139	**0.0042**	**0.0175**	**0.0003**	0.1017	**0.0005**
	Unprocessed Invert	0.3530	**0.0142**	0.1978	**0.0054**	**0.0035**	**0.0026**	**0.0114**	**0.0071**
MUSICA^2 Invert	Unprocessed	**0.0001**	0.0974	0.4188	**0.0018**	**0.0405**	**0.0003**	**0.0039**	**0.0002**
	Unprocessed Invert	**0.0032**	0.2212	0.4828	**0.0061**	**0.0112**	**0.0026**	**0.0086**	**0.0195**
Unprocessed	Unprocessed Invert	0.5347	0.9444	1.0000	0.9356	0.8035	0.8864	0.5363	0.1044

Values in bold indicate statistically significant differences (p <0.05))

APPENDIX N

A-D: p-Values indicating differences in mean IQS (all viewers) between the individual anatomical structures (criteria 1-8) per processing option (MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert)

APPENDIX N

A-D: p-Values indicating differences in mean IQS (all viewers) between the individual anatomical structures (criteria 1-8) for MUSICA^2, MUSICA^2 Invert, Unprocessed and Unprocessed Invert

A - MUSICA^2

	Skin structure	Pectoral muscle	Vascular structures through dense parenchyma	Vascular structures in fat	Vessels, fibrous strands, pectoral muscle	Fibrous strands in fat	Glandular tissue
Skin outline	**<0.0001**	0.172	<0.0001	0.8346	**<0.0001**	0.1764	0.1931
Skin structure		**<0.0001**	**<0.0001**	**<0.0001**	0.1927	**0.0001**	**<0.0001**
Pectoral muscle			**<0.0001**	0.0897	**<0.0001**	0.893	0.744
Vascular structures through dense parenchyma				**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Vascular structures in fat					**<0.0001**	**0.0141**	0.0631
Vessels, fibrous strands, pectoral muscle						**<0.0001**	**<0.0001**
Fibrous strands in fat							0.5971

Values in bold indicate statistically significant differences (p < 0.05)

B - MUSICA² Invert

	Skin structure	Pectoral muscle	Vascular structures through dense parenchyma	Vascular structures in fat	Vessels, fibrous strands, pectoral muscle	Fibrous strands in fat	Glandular tissue
Skin outline	**<0.0001**	**0.0008**	**<0.0001**	0.0749	**<0.0001**	**0.0293**	**0.0083**
Skin structure		**<0.0001**	**<0.0001**	**<0.0001**	**0.0051**	**<0.0001**	**<0.0001**
Pectoral muscle			**<0.0001**	0.1356	**<0.0001**	0.1862	0.5427
Vascular structures through dense parenchyma				**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Vascular structures in fat					**<0.0001**	0.6392	0.3928
Vessels, fibrous strands, pectoral muscle						**<0.0001**	**<0.0001**
Fibrous strands in fat							0.6679

Values in bold indicate statistically significant differences (p < 0.05)

C - Unprocessed

	Skin structure	Pectoral muscle	Vascular structures through dense parenchyma	Vascular structures in fat	Vessels, fibrous strands, pectoral muscle	Fibrous strands in fat	Glandular tissue
Skin outline	**<0.0001**	0.334	**<0.0001**	0.2491	**<0.0001**	0.0898	**<0.0001**
Skin structure		**<0.0001**	**<0.0001**	**<0.0001**	**0.0443**	**<0.0001**	**<0.0001**
Pectoral muscle			**<0.0001**	0.727	**<0.0001**	0.5488	**0.0032**
Vascular structures through dense parenchyma				**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Vascular structures in fat					**<0.0001**	0.9123	**0.046**
Vessels, fibrous strands, pectoral muscle						**<0.0001**	**<0.0001**
Fibrous strands in fat							**0.026**

Values in bold indicate statistically significant differences (p < 0.05)

D - Unprocessed Invert

	Skin structure	Pectoral muscle	Vascular structures through dense parenchyma	Vascular structures in fat	Vessels, fibrous strands, pectoral muscle	Fibrous strands in fat	Glandular tissue
Skin outline	**<0.0001**	0.238	**<0.0001**	0.186	**<0.0001**	**0.0425**	**0.0063**
Skin structure		**<0.0001**	**<0.0001**	**<0.0001**	0.0531	**<0.0001**	**<0.0001**
Pectoral muscle			**<0.0001**	0.8557	**<0.0001**	0.3475	0.2983
Vascular structures through dense parenchyma				**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
Vascular structures in fat					**<0.0001**	0.2637	0.2219
Vessels, fibrous strands, pectoral muscle						**<0.0001**	**<0.0001**
Fibrous strands in fat							1

Values in bold indicate statistically significant differences (p < 0.05)

APPENDIX O

Mammography reporting: Datasheet

BI-RADS DATASHEET

Case #	
Initial / Final	
Radiologist #	
Date	

Please indicate the Tabar classification of the breast parenchyma on the image by marking the relevant number with an X

1	2	3	4	5

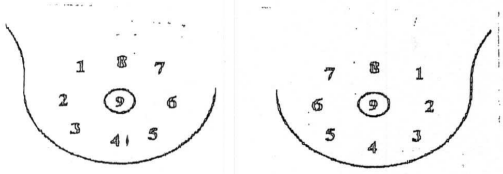
Selected Window Width/Level

ww/l		

Please complete the BI-RADS assessment categories for the case by marking the relevant number with an X

1	Negative
2	Benign Finding
3	Probably Benign Finding - Short interval follow-up suggested
4	Suspicious Abnormality - Biopsy should be considered
5	Highly suggestive of Malignancy - Appropriate action should be taken

Please indicate with an X where applicable and write down the ww/l where applicable.



R	LESION SITE	L
	1. Superior-external (lateral)	
	2. Central-external (lateral)	
	3. Inferior-external (lateral)	
	4. Inferior-central	
	5. Inferior-internal (medial)	
	6. Central-internal (medial)	
	7. Superior-internal (medial)	
	8. Superior-central	
	9. Areolar	
	10. Diffuse	
	11. Axillary tail	
	12. Retro-mammary	

R	MAMMOGRAM PATTERN	L
ww/l		ww/l
	No opacity or asymmetry	
	Well defined opacity	
	Poorly defined opacity	
	Spiculate opacity	
ww/l		ww/l
	Architectural distortion	
	Asymmetry breasts	
	Asymmetry density	
	Skin thickening	
	Skin retraction	
	Nipple retraction	
ww/l		ww/l
	Other (specify):	

R	CALCIFICATIONS	L
ww/l		ww/l
	Absent	
	Predom. amorphous,indistinct	
	Predom. pleomorphic/granular	
	Predom. linear branching	
	Benign	

R	DISEASE EXTENT	L
	Localized	
	Multifocal (more foci in the same quadrant)	
	Multicentric (syncr. lesions in different quadrants)	

* Parenchymal Breast Pattern classification - Laszlo Tabar

* BI-BIRADS assessment categories - American College of Radiology

Comment:

Diagnosis:

For researcher use only

Confirmed diagnosis:

APPENDIX P

Information document: Mammogram reporting

Information Document
Mammography Reporting

Development and Evaluation of a Soft-Copy Mammographic Viewing Protocol to Improve Radiological Reporting

Carin Meyer

American College of Radiology – Breast Imaging Reporting and Data System (BIRADS), 2003

ASSESSMENT CATEGORIES

Close window

• Category 0 / Need Additional Imaging Evaluation	Finding for which additional imaging evaluation is needed. This is almost always used in a screening situation and should rarely be used after a full imaging work up. A recommendation for additional imaging evaluation includes the use of spot compression, magnification, special mammographic views, ultrasound, etc. Whenever possible, the present mammogram should be compared to previous studies. The radiologist should use judgment in how vigorously to pursue previous studies.
• Category 1 / Negative	There is nothing to comment on. The breasts are symmetrical and no masses, architectural disturbances or suspicious calcifications are present
• Category 2 / Benign Finding	This is also a negative mammogram, but the interpreter may wish to describe a finding. Involuting, calcified fibroadenomas, multiple secretory calcifications, fat containing lesions such as oil cysts, lipomas, galactoceles, and mixed density hamartomas all have characteristic appearances, and may be labeled with confidence. The interpreter might wish to describe intramammary lymph nodes, implants, etc. while still concluding that there is no mammographic evidence of malignancy.
• Category 3 / Probably Benign Finding - Short Interval Follow-Up Suggested	A finding placed in this category should have a very high probability of being benign. It is not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability. Data are becoming available that shed light on the efficacy of short interval follow-up. At the present time, most approaches are intuitive. These will likely undergo future modification as more data accrue as to the validity of an approach, the interval required, and the type of findings that should be followed.
• Category 4 / Suspicious	These are lesions that do not have the characteristic morphologies of breast cancer but have a definite

Abnormality - Biopsy Should Be Considered	probability of being malignant. The radiologist has sufficient concern to urge a biopsy. If possible, the relevant probabilities should be cited so that the patient and her physician can make the decision on the ultimate course of action.
• Category 5 / Highly Suggestive of Malignancy - Appropriate Action Should Be Taken	These lesions have a high probability of being cancer

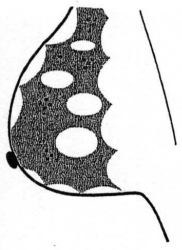
( )

( )

Dähnert, W., 2002: 545. Radiology review manual. 5th ed: Lippencott, Williams & Wilkins.

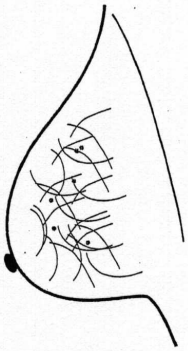
Parenchymal Breast Pattern (Laszlo Tabar)

Pattern I
Concave contour from Cooper's ligaments evenly scattered 1-2 mm nodular densities
Named QDY = quasi dysplasia (for Wolfe classification)
(= normal terminal ductal lobular units)
oval-shaped / circular lucent areas (= fatty replacement)



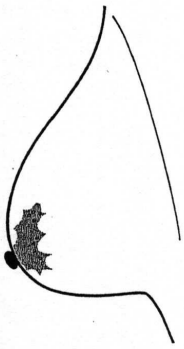
Pattern I

Pattern II
Total fatty replacement
NO nodular densities
Similar to N1 (Wolfe)



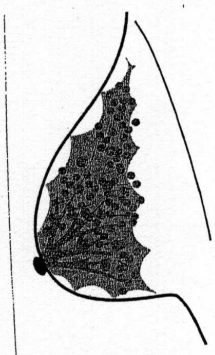
Pattern II

Pattern III
Normal parenchyma occupying <25% of breast volume in retroareolar location
Similar to P1 (Wolfe)



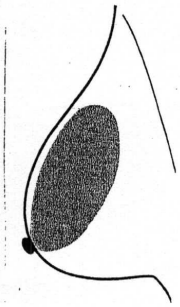
Pattern III

Pattern IV
Adenosis pattern
Cause: hypertrophy + hyperplasia of acini within lobules
Histo: Small ovoid proliferating cells with rare mitoses scattered 3-7 mm nodular densities (= enlarged terminal ductal lobular ~~lobular~~ units) = adenosis
Tick linear densities (= periductal elastic tissue proliferation with fibrosis) = fibroadenosis
No change with increasing age (genetically determined)
Similar to P2 (Wolfe)



Pattern IV

Pattern V
Uniformly dense parenchyma with smooth contour (=extensive fibrosis)
Similar to DY (Wolfe)



BI-RADS BREAST IMAGING LEXICON

Close window

MASS

A "Mass" is a space occupying lesion seen in two different projections. If a potential mass is seen in only a single projection it should be called a "Density" until its three-dimensionality is confirmed.

- **Circumscribed (well-defined or sharply-defined) margins**: The margins are sharply demarcated with an abrupt transition between the lesion and the surrounding tissue. Without additional modifiers there is nothing to suggest infiltration.
- **Indistinct (ill defined) margins**: The poor definition of the margins raises concern that there may be infiltration by the lesion and this is not likely due to superimposed normal breast tissue.
- **Spiculated Margins**: The lesion is characterized by lines radiating from the margins of a mass.

ARCHITECTURAL DISTORTION

- The normal architecture is distorted with no definite mass visible. This includes spiculations radiating from a point, and focal retraction or distortion of the edge of the parenchyma. Architectural distortion can also be an associated finding.

ASYMMETRIC DENSITY

- This is a density that cannot be accurately described using the other shapes. It is visible as asymmetry of tissue density with similar shape on two views, but completely lacking borders and the conspicuity of a true mass. It could represent an island of normal breast, but its lack of specific benign characteristics may warrant further evaluation. Additional imaging may reveal a true mass or significant architectural distortion.

CALCIFICATION

- **Amorphous or Indistinct Calcifications:** These are often round or "flake" shaped calcifications that are sufficiently small or hazy in appearance that a more specific morphologic classification cannot be determined.
- **Pleomorphic or Heterogeneous Calcifications:** These are usually more conspicuous than the amorphic forms and are neither typically benign nor typically malignant irregular calcifications with varying sizes and shapes that are usually less than 0.5 mm in diameter.
- **Fine, Linear or Fine, Linear, Branching (Casting) Calcifications:** These are thin, irregular calcifications that appear linear, but are discontinuous and under 0.5 mm in width. Their appearance suggests filling of the lumen of a duct involved irregularly by breast cancer.
- **a. Benign Calcifications:** Benign calcifications are usually larger than calcifications associated with malignancy. They are usually coarser, often round with smooth margins and are much more easily seen.

APPENDIX Q

Raw data: Initial and Final reporting

Initial Reporting: Pages 1 – 22

Final Reporting: Pages 23 – 40

INITIAL MAMMOGRAM EVALUATION - MUSICA

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
1	1.1.13	A	4	5	Tru-cut biopsy - Infiltrating duct	4 , 5	1 , 2		2	5			x	
		B	1	5	Ca gr II		7		3	1				x
		C	2	5			1 , 10 , 9		3	5			x x	
2	2.1.22	A	4	2	Benign -Follow-up	1 , 2, 3		6	1	1	x			
		B	1	3				2	2	2	x			
		C	4	4			8 , 12	8	5	5				
3	3.1.4	A	2	5	Lumpectomy - Infiltrating duct	4 , 5	6		2					x
		B	2	5	Ca gr II		2		3	1				x
		C	4	5			6		2	5				x
4	4.2.15	A	2	2	Benign -Follow-up	1 , 2, 3		8	5					
		B	2	3				8	5	1	x			
		C	2	3				8	5	5				
5	7.2.13	A	5	2	Benign -Follow-up	1 , 2, 3			5	5				
		B	4	3					5	5	x			
		C	1	2					5	5	x			
6	8.2.10	A	2	5	Biopsy - Infiltrating duct ca Gr II	4 , 5		8 , 9		2				
		B	1	5				8	1	3	x			
		C	2	5				8 , 9	5	3				
7	21.2.4	A	1	5	Benign	1 , 2, 3	6		5					x
		B	1	4	Biopsy - intraduct papilloma				5	5	x			
		C	1	4			4		5	5				x
8	131.13.1	A	3	5	Needle biopsy - Infiltrating duct	4 , 5		5		3,5				
		B	5	5	Ca gr II with mucinous Ca			3	3,5	3,5	x			
		C	3	5	component			5 , 9	5	3				

APPENDIX Q

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
9	9.2.9	A	2	3	Benign - Follow-up	1 , 2, 3	1		1					
		B	2	2			12		5	5		x		
		C	2	4			1	9	5	5			x	
10	12.2.1	A	3	0	Benign - Follow-up	1 , 2, 3	8							
		B	4	2			12		1	1		x		
		C	4	3			2 , 11		5	5		x	x	
11	135.13.13	A	1	5	FNA - malig cells present	4 , 5		8		3				
		B	1	5	consistent with duct ca with		6	8 , 7 , 7	3 , 5	3 , 5		x		
		C	4	4	mucinous component			8 , 1	5	3 , 3			x	
12	170.13.1	A	1	5	Mastectomy - Extensive DCIS	4 , 5	7		5				x	
		B	1	4			7 , 7 , 7		5	1				
		C	4	4			8	1 , 12	5	1			x	
13	15.2.1	A	4	4	Benign - Follow-up	1 , 2, 3			5	3				
		B	5	3					5	5	x			
		C	4	3					x	x	x			
14	138.13.13	A	3	5	Mastectomy - Extensive High gr	4 , 5		1	5	5				
		B	3	4	DCIS				5	5				
		C	3	3				2	1	5				
15	133.13.13	A	1	5	Needle biopsy -Infiltrating duct	4 , 5		7						
		B	1	5	Ca gr II		11 , 11	2	5	1		x x		
		C	1	5				7	1	1				
16	145.13.5	A	2	5	Mass resection - Adenocarcinoma	4 , 5	8 , 12		5	5				
		B	2	5	highly suggestive of infiltrating		2		5	5			x	
		C	2	4	duct Ca gr III		12		1	1			x	

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
17	134.13.13	A	2	5	Biopsy - Medullary Ca	4 , 5		2 , 6	5	3 , 5				
		B	1	5			7 , 9	5 , 3 , 3	5	2 , 5		x		
		C	4	4			1	1 , 6,12, 5	1	2				
18	13.2.4	A	1	3	Benign - Follow-up	1 , 2, 3			5					
		B	4	3					5	5	x			
		C	4	2					5	5	x			
19	144.13.10	A	3	5	Tru-cut biopsy - Infiltrating duct	4 , 5	11						x	
		B	1	5	Ca gr II		7		5	5				x
		C	1	5			11		5	1				x
20	18.2.10	A	4	4	Benign - Follow-up	1 , 2, 3	1						x	
		B	4	3					1	5	x			
		C	5	2					1	5	x			
21	136.13.13	A	2	5	Mastectomy - Infiltrating duct Ca	4 , 5		1 , 5		3		x	x	
		B	2	5	gr III + lymphovascular invasion			7 , 4	1	2 , 5				x x
		C	2	5			9	1 , 9	1	3			x	
22	153.13.4	A	1	5	Biopsy - Infiltrating duct Ca gr III	4 , 5		9		1				
		B	2	5			2	9	1	1				
		C	4	5			12	9	1	1			x	
23	10.2.3	A	5	3 , 4	Benign - Follow-up	1 , 2, 3	1 , 2	6	1	1				
		B	5	3 , 4			9	9	5	5			x	
		C	5	2			9	12 , 9	5	5		x		
24	250.20.10	A	2	5	Benign - Biopsy - granulomar infection	1 , 2, 3	5		1			x		
		B	2	4	No mass found - chronic absess		3		5	1			X	
		C	2	4			5		1	1		x		

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
25	152.13.14	A	4	5	Biopsy - Infiltrating duct Ca gr II	4 , 5	8		3				x	
		B	3	5			9		3	1			x	
		C	4	4			10		3	5			x	
26	160.13.11	A	4	3	Biopsy - Infiltrating duct Ca gr II	4 , 5								
		B	1	3					1	1	x			
		C	1	3				1	1	1				
27	23.2.13	A	1	5	Mastectomy - Infiltrating duct Ca gr	4 , 5		5		3				
		B	1	4	III / Background of high grade DCIS				1	3	x			
		C	3	4				5 , 9		3				
28	41.4.1	A	1	1 , 2	Benign - Follow-up	1 , 2, 3								
		B	1	3					1	1	x			
		C	4	2					1	1	x			
29	26.3.11	A	3	5	Mastectomy - Infiltrating duct Ca gr	4 , 5		5		1				
		B	3	4	II. Mucious component present			3	5	2 , 5	x			
		C	1	4				5	5	5				
30	42.5.8	A	1	5	Benign - Follow-up	1 , 2, 3	3		1				x	
		B	1	4			4		5	5		x		
		C	4	3			9			5		x		
31	29.3.1	A	3	4	Excision biopsy - Infiltrating duct Ca	4 , 5		1	5	5				
		B	1	3	Gr I / Low grade DCIS			7	5	3 , 5	x			
		C	4	4				1 , 1	5	3 , 5				
32	27.3.1	A	2	4	Excision biopsy - Infiltrating duct Ca	4 , 5	1		3					
		B	2	4	gr II with areas of DCIS		7		3 , 5	5				x
		C	2	4			1		2					x

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
33	30.3.9	A	1	2	Benign - Follow-up	1 , 2, 3								
		B	1	3			7		5	5		x		
		C	4	2					5	5	x			
34	31.4.1	A	3	2	Benign - Follow-up	1 , 2, 3			5	5				
		B	1	3			7	7	5	5		x		
		C	4	3			10	10	5	5		x		
35	34.4.1	A	2	2	Benign - Follow-up	1 , 2, 3			5	5				
		B	1	2			11	11	5	5		x		
		C	1	2					5	5		x		
36	25.3.12	A	4	5	Biopsy - Moderately differentiated	4 , 5		4						
		B	4	5	duct Ca gr II			4	1	1	x			
		C	4	4				4	1	1				
37	32.4.1	A	1	3 , 4	Benign - Follow-up	1 , 2, 3			5	5				
		B	1	3					5	5	x			
		C	4	3					5	5				
38	33.4.13	A	1	2	Benign - Follow-up	1 , 2, 3			5					
		B	1	2					5	5	x			
		C	4	3				1	2	2				
39	46.5.14	A	2	5	Mastectomy - Invasive lobular Ca,	4 , 5		1	5	3 , 5				
		B	2	5	classic subtype			7	5	5	x			
		C	2	4				1	5	5				
40	48.5.14	A	3	3	Benign - Follow-up	1 , 2, 3		1	5	5		x		
		B	1	3					5	5	x			
		C	1	3				9	5	5				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
41	50.6.8	A	1	1	Benign - Follow-up	1 , 2, 3								
		B	1	2					1	1	x			
		C	1	1					1	1				
42	53.6.14	A	3	5	Mastectomy - Infiltrating duct Ca gr	4 , 5		1	5	3				
		B	3	5	II			6	5	3	x			
		C	4	5				2	5	3				
43	60.7.1	A	2	2	Benign - Follow-up	1 , 2, 3								
		B	2	1							x			
		C	2	1					5	1	x			
44	61.8.1	A	2	3,4	Benign - Follow-up	1 , 2, 3		2						
		B	2	4				6	5	5	x			
		C	2	0 , 3				2	5	5				
45	65.8.1	A	5	5	Trucut biopsy - Infiltrating Lobular Ca	4 , 5	8	1	3 , 5	3 , 5				x
		B	4	5				7	3 , 5	3 , 5				
		C	5	4			8	1 , 10	3 , 5	5			x	
46	66.8.13	A	2	5	Mastectomy - Infiltrating duct Ca gr	4 , 5		9 , 1	5	5				
		B	2	5	II			4	5	2 , 5	x			
		C	2	5				9 , 1	1	1				
47	69.10.1	A	1	5	Mastectomy - Infiltrating duct Ca gr	4 , 5	1					x		
		B	2	4	III		7		2	1		x		
		C	2	4			1		2				x	
48	73.10.1	A	1	3	Benign - Follow-up	1 , 2, 3	8			5				
		B	3	2					5	5	x			
		C	4	3				12	5	2				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
49	74.10.19	A	3	2 , 3	Benign - Follow-up	1 , 2, 3		1				x		
		B	1	2					5	5	x			
		C	4	2						5				
50	75.11.13	A	2	3 , 4	Benign - Excision biopsy no features of	1 , 2, 3		1		2				
		B	1	4	malignancy. Traumatic fat necrosis		5	7	5	3	x			
		C	4	4	and dystrophic calcifications			1 , 2		3 , 2				
51	76.11.13	A	1	1	FNA - Malignant cells compatible	4 , 5								
		B	1	3	with ductal carcinoma				1	3 , 5	x			
		C	4	3	Recurrent Ca					3	x			
52	77.11.16	A	1	4	Excision biopsy - Infiltrating duct Ca gr	4 , 5	1 , 10					x		
		B	4	3	III with areas of high grade DCIS				5	1				
		C	5	3			8	8	5	5			x	
53	78.11.1	A	3	3	Benign - Follow-up	1 , 2, 3		1	5	5				
		B	3	3				7 , 7	5	5	x			
		C	4	3			9	1	5				x	
54	79.11.1	A	2	5	Biopsy - Infiltrating duct Ca gr III	4 , 5		2		3				
		B	2	4				6	3	2				
		C	4	5			8 , 5, 12		3	3			x x	
55	81.11.13	A	2	5	FNA - Mucinous Ca/ ductal Ca cannot	4 , 5	5		5	5		x		
		B	2	4	be excluded		3		5	5			x	
		C	2	4	Pt transferred - No file		6		5	5			x	
56	86.11.13	A	2	5	Mastectomy - Infiltrating duct Ca gr II	4 , 5		1						
		B	1	5	and extensive DCIS			6	1	5	x			
		C	1	4				2	5	2				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
57	88.11.13	A	1	5	Mastectomy - Infiltrating duct Ca gr III	4 , 5	1		3				x	
		B	1	5	Extensive lymphovascular invasion		7		3 , 5	5				x
		C	4	5			1 , 9		3	5			x	x
58	89.12.26	A	2	3	Benign - Follow-up	1 , 2, 3		8		5				
		B	2	3					5	5	x			
		C	2	3			2	8	5	5		x		
59	90.12.10	A	3	5	Mastectomy - Infiltrating duct Ca gr II	4 , 5	5		5	5		x		
		B	2	4			3		5	5			x	
		C	4	4			5		2 , 4	2 , 5			x	
60	91.12.8	A	1	4	Benign - Follow -up	1 , 2, 3		1		5				
		B	1	3					5	5	x			
		C	3	2					5	5	x			
61	93.12.5	A	2	5	Biopsy - DCIS	4 , 5		6		3				
		B	2	5			7	2	5	3 , 5		x		
		C	2	5			1	6	5	3		x		
62	94.12.13	A	2	5	FNA - Malignant cells compatable with	4 , 5		1		5				
		B	1	5	duct Ca		7	7	1	2 , 5	x			
		C	1	5	Pt refused surgery - grading unknown		1	1	1	3		x		
63	96.12.8	A	1	5	Benign - Follow-up	1 , 2, 3			3	3				
		B	4	4					3 , 5	3 , 5				
		C	4	3			10		2	2				
64	98.12.18	A	2	5	Biopsy - Infiltrating duct Ca gr III	4 , 5		8		2 , 5				
		B	2	5			7	8	5	2 , 5	x			
		C	2	5				8	5	3	x			

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
65	99.13.3	A	2	3	Benign - Follow-up	1 , 2, 3	2		5				x	
		B	2	3			6		5	5				
		C	2	3			2 , 9	2	5	5			x x	
66	100.13.16	A	4	5	Mastectomy - Infiltrating duct Ca gr II	4 , 5		11		5				
		B	2	5	Lymphovascular infiltration, infiltration			11	5	5				
		C	4	5	into adjacent skeletal muscle			10 , 11	5	5				
67	101.13.12	A	2	3	Benign - FNA periductal mastitis	1 , 2, 3			5	5				
		B	2	4					5	5	x			
		C	4	3			9	10	5	5			x	
68	104.13.12	A	1	5	Benign - Excision Biopsy Fibroadenoma	1 , 2, 3	5	11				x		
		B	1	4			3		5	5		x		
		C	4	3			5		5	5		x		
69	105.13.1	A	1	1	Benign - Follow-up	1 , 2, 3								
		B	1	3					1	5				
		C	4	2					5	5	x			
70	107.13.10	A	2	5	Biopsy - Infiltrating duct Ca gr II	4 , 5		9 , 11		3				
		B	2	5				9	5	3 , 5				
		C	2	5				9	5	4				
71	110.13.20	A	1	5	Benign - Lymph node BX - Caseous	1 , 2, 3		10						
		B	1	4	TB lymphadenitis				1	1	x			
		C	1	4				10	1	2				
72	111.13.13	A	2	5	Histology - Angiosarcoma	4 , 5	5		5	5		x		
		B	2	4			3		5	5		x		
		C	4	4			5		5	5			x	

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
73	113.13.23	A	1	4	Benign - Follow-up	1 , 2, 3	1	1				x		
		B	1	4			7	7	5	5			x	
		C	5	3			1 , 2, 10	1 , 10	1	2		x	x	
74	118.13.4	A	1	3	Benign - Follow-up	1 , 2, 3		8						
		B	4	3					5	5				
		C	4	2					5	1				
75	119.13.13	A	3	5	Benign - TB breast	1 , 2, 3	10							
		B	3	4					5	5				
		C	1	4			10		5	5				
76	121.13.1	A	2	5	FNA - Malignant cells compatable with	4 , 5		8 , 8 , 1 , 9	5	3 , 5				
		B	2	5	duct Ca			9	5	2 , 3 , 5	x			
		C	2	5	Pt refused surgery - grading unknown			8 , 2 , 9	5	3				
77	122.13.3	A	4	5	FNA - Malignant cells compatable with	4 , 5		8						
		B	4	5	duct Ca			9		2				x
		C	4	5	Pt refused surgery - grading unknown		10	1	1	2				
78	126.13.11	A	2	2	Benign - Biopsy Intraduct Papilloma	1 , 2, 3			5	5				
		B	3	3	No signs of malignancy			7	5	5	x			
		C	4	3				9	5	5				
79	128.13.8	A	5	2	Benign - Follow-up	1 , 2, 3			5	5				
		B	4	3					5	5	x			
		C	5	3					2 , 5	2 , 5	x			
80	130.13.1	A	2	3	Benign - Follow-up	1 , 2, 3	1					x		
		B	2	3			8		5	5		x		
		C	4	3										

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	**Lesion extent** R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
1	1.1.13	A	x	x	x	x	x												x					
		B	x			x	x	x	x												x			
		C	x	x	x	x	x			x														
2	2.1.22	A								x												x		
		B									x				x							x		
		C									x								x			x		
3	3.1.4	A	x																x					
		B	x						x											x				
		C	x																x					
4	4.2.15	A								x										x				
		B								x														
		C								x													x	
5	7.2.13	A								x					x									
		B							x						x									
		C							x															
6	8.2.10	A											x	x		x		x					x	
		B										x	x	x		x	x	x						x
		C										x x	x	x		x	x	x					x	
7	21.2.4	A																	x					
		B							x										x					
		C																	x					

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	**Lesion extent**								
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
8	131.13.1	A											x	x		x						x		
		B										x	x	x		x	x	x				x		
		C									x	x	x	x		x	x	x				x		
9	9.2.9	A																	x					
		B																	x					
		C									x		x	x				x				x		
10	12.2.1	A		x	x									x	x		x	x						
		B											x	x		x		?	x					
		C											x	x		x		x	x					
11	135.13.13	A									x											x		
		B								x x	x				x							x		
		C									x			x	x							x		
12	170.13.1	A																		x				
		B			x					x x x												x		
		C		x	x					x														
13	15.2.1	A																						
		B							x															
		C							x															
14	138.13.13	A									x												x	
		B			x																			
		C									x			x	x							x		

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L		
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric				
15	133.13.13	A										x	x										x					
		B										x	x					x										
		C										x	x					x				x						
16	145.13.5	A																	x									
		B		x															x									
		C	x	x					x										x									
17	134.13.13	A																										x
		B									x x			x														x
		C									x x		x	x														x
18	13.2.4	A														x												
		B							x																			
		C							x																			
19	144.13.10	A	x																x									
		B	x	x															x									
		C	x	x		x	x												x									
20	18.2.10	A																	x									
		B							x																			
		C							x																			
21	136.13.13	A			x								x		x								x					
		B	x			x																						x
		C									x x		x	x		x	x		x									x

Lesion extent

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	**Lesion extent**						
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	R Locallized	R Multifocal	R Multicentric	L Locallized	L Multifocal	L Multicentric
22	153.13.4	A									x		x				x	x				x		
		B			x						x		x	x		x	x	x					x	
		C									x		x	x	x	x	x	x						
23	10.2.3	A																			x	x		
		B									x								x			x		
		C								x														
24	250.20.10	A																	x					
		B	x			x			x										X					
		C																	x					
25	152.13.14	A	x			x	x	x											x					
		B	x	x		x	x	x	x											x				
		C	x	x	x	x	x	x													x			
26	160.13.11	A										x			x									
		B													x									
		C									x			x								x		
27	23.2.13	A									x													
		B		x	x																			
		C									x		x	x									x	
28	41.4.1	A																						
		B							x															
		C							x															

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
																			Lesion extent					
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
29	26.3.11	A								x												x		
		B								x												x		
		C								x			x									x		
30	42.5.8	A																	x					
		B							x															
		C																	x					
31	29.3.1	A																				x		
		B													x							x		
		C										x	x										x	
32	27.3.1	A																	x					
		B							x										x					
		C																	x					
33	30.3.9	A													x									
		B							x										x					
		C							x															
34	31.4.1	A																						
		B								x														
		C		x	x					x				x	x						x			
35	34.4.1	A																						
		B								x										x			x	
		C								x														

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L	**Lesion extent**
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric	
36	25.3.12	A																				x			
		B								x			x	x			x					x			
		C									x		x	x	x							x			
37	32.4.1	A													x										
		B													x										
		C												x	x										
38	33.4.13	A																							
		B													x										
		C									x				x							x			
39	46.5.14	A										x	x									x			
		B										x	x			x							x		
		C										x	x	x		x									
40	48.5.14	A																				x			
		B							x																
		C									x				x							x			
41	50.6.8	A																							
		B							x																
		C																							
42	53.6.14	A										x	x									x			
		B										x	x									x			
		C										x	x	x	x		x					x			

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L		
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric			
43	60.7.1	A																									
		B							x																		
		C							x																		
44	61.8.1	A								x												x					
		B								x												x					
		C								x												x					
45	65.8.1	A	x	x								x	x	x		x	x		x			x					
		B			x							x	x	x		x	x					x					
		C	x								x	x				x	x										x
46	66.8.13	A								x	x					x	x	x									x
		B										x	x	x		x	x	x					x				
		C									x	x	x	x		x	x	x									x
47	69.10.1	A			x	x		x																			
		B				x			x										x								
		C	x			x													x								
48	73.10.1	A													x				x								
		B							x																		
		C									x											x					
49	74.10.19	A																				x					
		B							x																		
		C																									

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L	**Lesion extent**
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric	
50	75.11.13	A									x															
		B								x					x										x	
		C									x		x		x										x	
51	76.11.13	A																								
		B				x			x							x										
		C				x			x							x										
52	77.11.16	A			x														x							
		B			x				x																	
		C									x															
53	78.11.1	A						x										x			x					
		B								x x																
		C								x									x			x				
54	79.11.1	A								x			x									x				
		B			x						x		x								x	x				
		C	x							x			x								x	x				
55	81.11.13	A																	x							
		B	x	x															x							
		C	x		x	x													x							
56	86.11.13	A										x	x									x				
		B										x	x	x								x				
		C										x	x	x								x				

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
57	88.11.13	A	x			x													x					
		B	x	x		x	x	x												x				
		C	x	x		x		x												x				
58	89.12.26	A								x												x		
		B													x									
		C									x													
59	90.12.10	A				x																		
		B							x										x					
		C	x		x	x													x					
60	91.12.8	A									x				x							x		
		B							x															
		C							x															
61	93.12.5	A									x							x				x		
		B									x		x				x					x		
		C										x	x				x	x	x			x		
62	94.12.13	A										x	x									x		
		B										x	x			x	x					x		
		C										x	x			x	x					x		
63	96.12.8	A																						
		B			x										x						x			x
		C																						

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
																				Lesion extent					
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
64	98.12.18	A										x	x				x					x		
		B										x	x	x		x	x	x				x		
		C										x	x	x		x	x	x				x		
65	99.13.3	A																	x					
		B			x				x										x					
		C			x					x									x					
66	100.13.16	A									x	x			x	x						x		
		B										x	x	x		x	x					x		
		C										x	x	x		x	x							x
67	101.13.12	A													x									
		B													x									
		C		x	x									x	x				x				x	
68	104.13.12	A								x									x			x		
		B																	x					
		C																	x					
69	105.13.1	A																						
		B			x				x															
		C							x															
70	107.13.10	A										x				x	x	x						x
		B										x	x	x		x	x	x						x
		C										x	x	x	x	x	x	x					x	

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L		Lesion extent						
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
71	110.13.20	A									x					x		x						
		B												x	x	x								
		C											x	x		x	x							
72	111.13.13	A																	x					
		B	x						x										x					
		C		x	x														x					
73	113.13.23	A								x										x			x	
		B									x										x		x	
		C			x					x	x				x						x		x	
74	118.13.4	A									x											x		
		B																						
		C		x										x										
75	119.13.13	A		x	x	x		x																
		B		x	x	x			x															
		C																			x			
76	121.13.1	A								x	x													x
		B									x		x	x										x
		C				x				x	x x					x								x
77	122.13.3	A										x				x	x	x				x		
		B	x	x		x	x	x														x		
		C				x						x	x	x	x	x	x	x			x			x

			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
78	126.13.11	A						x										x						
		B								x														
		C								x												x		
79	128.13.8	A		x																				
		B							x															
		C							x															
80	130.13.1	A																						
		B																	x					
		C				x									x									

FINAL MAMMOGRAM EVALUATION - MUSICA INVERT

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
1	**1.1.13**	A	2	5	**Tru-cut biopsy - Infiltrating duct**	**4 , 5**	1		3 , 5					x
		B	1	5	**Ca gr II**		1		3 , 5	5				x
		C	4	5			1 , 11		3	5			x	x
2	**250.20.10**	A	2	4	Benign - Biopsy granulomar infection	1 , 2 , 3	5		5			x		
		B	2	4	No mass found - chronic absess		5		5	1			x	
		C	2	4			6		5	5		x		
3	**2.1.22**	A	2	2	Benign - follow-up	1 , 2 , 3			5					
		B	1	3					5	5				
		C	1	3				9	5	5				
4	268.22.3	A	4	5	**Excision biopsy - duct Ca gr 1**	**4 , 5**	8							
		B	1	5			8		2	5				x
		C	4	5			8		3					x
5	249.20.10	A	3	2	Benign - Follow-up	1 , 2 , 3	3		5	5		x		
		B	3	2			2		5	5		x		
		C	3	2			9		5	5		x		
6	**7.2.13**	A	1	2	Benign - Follow-up	1 , 2 , 3			5	5				
		B	1	3					5	5	x			
		C	1	2					5	5	x			
7	246.20.2	A	4	5	Benign - Follow-up	1 , 2 , 3		1	5	5		x		
		B	4	4			8	1	5	5			x	
		C	4	3			2	1	2	2			x	
8	**8.2.10**	A	2	5	**Biopsy - Infiltrating duct Ca Gr II**	**4 , 5**		9 , 7						
		B	2	5				9	1	3	x			
		C	2	5				9 , 9	5	3				
9	262.20.2	A	2	5	**Mastectomy - Infiltrating duct Ca gr II**	**4 , 5**		1		3				
		B	3	5				2	5	3 , 5				
		C	2	5				1, 1	2	3 , 4				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
10	**10.2.3**	A	1	3	Benign - Follow-up	1 , 2 , 3	1 , 1	8	1	1		x x		
		B	5	3			8	9	5	5		x		
		C	4	3			9 , 9	9	2 , 5	2 , 5			x	
11	236.19.3	A	1	2	Benign - Follow-up	1 , 2 , 3			5					
		B	3	3					5		x			
		C	1	3				4	5	5	x			
12	**13.2.4**	A	1	4	Benign - Follow-up	1 , 2 , 3			5	5				
		B	4	3					5	5	x			
		C	4	2					5	5	x			
13	**25.3.12**	A	4	5	**Biopsy - Moderately differentiated**	**4 , 5**		4						
		B	4	4	**duct Ca gr II**			4	5	5				
		C	4	4				4		2			x	
14	233.19.13	A	1	1	Benign - Follow-up	1 , 2 , 3								
		B	1	3					5	1				
		C	4	4				1	5	2				
15	**21.2.4**	A	3	2	Benign - Intraduct papilloma	1 , 2 , 3			5	5				
		B	3	3					5	5			x	
		C	1	4			9		5	5			x	
16	259.20.13	A	2	5	**Incision biopsy - Infiltrating duct Ca**	**4 , 5**		11		5				
		B	2	5	**gr III**			1 , 10	5	3	x			
		C	2	5				1 , 11		2				
17	**27.3.1**	A	2	2	**Excision biopsy - Infiltrating duct Ca**	**4 , 5**			5	5				
		B	2	5	**gr II with area of DCIS**		9		3, 5	5				x
		C	2	4			1		3	5				x
18	230.19.2	A	4	3	Benign - Follow-up	1 , 2 , 3		1	5	5				
		B	4	4					5	5				
		C	4	4					3	3				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
19	**31.4.1**	A	1	2	Benign - Follow-up	1 , 2 , 3								
		B	1	3			1	1	5	5		x		
		C	1	3					2	2	x			
20	258.20.11	A	4	5	**Biopsy - Infiltrating duct carcinoma**	**4 , 5**		2		3				
		B	4	5	**(grading mastectomy after 15/10/08)**			2	5	3	x			
		C	4	5	**Pt transferred - no file**			2 , 11	5	3				
21	**46.5.14**	A	2	5	**Mastectomy - Invasive lobular Ca,**	**4 , 5**		1	5	5				
		B	2	5	**classic subtype**			1	5	5	x			
		C	2	5				2	4	3 , 4				
22	244.20.13	A	3	5	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**		9						
		B	3	5				4	5		x			
		C	1	5				9	5	5				
23	229.19.16	A	3	4	Benign - Follow-up marker no clear	1 , 2 , 3		1	5	5				
		B	1	3	lesion				1	1	x			
		C	1	2					5	5	x			
24	**65.8.1**	A	4	5	**Trucut biopsy - Infiltrating lobular Ca**	**4 , 5**	8	1	3	3				
		B	4	5			8	1	3 , 5	3 , 5				x
		C	4	5			9	1	3	3			x	
25	**33.4.13**	A	4	1	Benign - Follow-up	1 , 2 , 3								
		B	1	3				5	1		x			
		C	1	3				1	5	5				
26	227.19.5	A	2	5	**Tru-cut biopsy - Invasive Ca? Lobular Ca**	**4 , 5**		1						
		B	2	5	**(did not qualify for surgery)**			2	5	2 , 5				
		C	2	5				1 , 1	5	3			x	x
27	228.19.3	A	1	2	Benign - Follow-up	1 , 2 , 3								
		B	2	2					5	5	x			
		C	2	2					5	5				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
28	**41.4.1**	A	1	1	Benign - Follow-up	1 , 2 , 3								
		B	1	3					1	1	x			
		C	1	2					5	5	x			
29	**69.10.1**	A	2	5	**Mastectomy - Infiltrating duct Ca gr III**	**4 , 5**	1					x		
		B	2	5			1		2	1		x		
		C	1	5			1 , 1		5	1		x		
30	221.19.11	A	1	2	Benign - Follow-up	1 , 2 , 3								
		B	2	2					5	1	x			
		C	2	2					5	5	x			
31	**48.5.14**	A	1	4	Benign - Follow-up	1 , 2 , 3		8	5	3 , 5				
		B	1	2					5	5	x			
		C	1	2					5	5	x			
32	225.19.1	A	2	5	**Mastectomy - Infiltrating duct Ca gr**	**4 , 5**		1		2				
		B	2	5	**II**			2	5	2	x			
		C	2	5				1	5	2				
33	215.19.19	A	1	1	Benign - Follow-up	1 , 2 , 3								
		B	1	2					5		x			
		C	1	2					5	2	x			
34	**77.11.16**	A	1	4	**Excision biopsy - Infiltrating duct Ca**	**4 , 5**	8					x		
		B	5	3	**gr III with areas of high grade DCIS**				5		x			
		C	5	4			9		2				x	
35	224.19.13	A	3	4	**Biopsy - Pagets Infiltrating duct CA with**	**4 , 5**	1,1,1,8,8	1				x x x x x		
		B	1	4	**extreme high grade DCIS (not**		9		3	1				
		C	1	4	**possible to grade**		1,9,11	1	3	2		x		

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
36	**81.11.13**	A	2	4	**FNA - Mucinous Ca/ ductal Ca cannot**	**4 , 5**	7		5	5			x	
		B	2	4	**be excluded**		6		5	5		x		
		C	2	4	**Pt transferred - no file**		5		5	5			x	
37	60.7.1	A	2	1	Benign - Follow-up	1 , 2 , 3								
		B	2	2					5	5	x			
		C	2	1					5	5	x			
38	212.19.5	A	1	2	Benign - Follow-up	1 , 2 , 3			5	5				
		B	4	3				8	5	5	x			
		C	1	3				1	5	5				
39	223.19.3	A	4	5	**Biopsy - Ca (final classification on**	**4 , 5**		1						
		B	4	4	**excision after 26/2/09)**			1			x			
		C	4	4			1 , 9	1	5	5			x	
40	**88.11.13**	A	1	5	**Mastectomy - Infiltrating duct Ca gr**	**4 , 5**	1		3					x
		B	1	5	**III. Extensive lymphovascular invasion**		1		3 , 5	5				x
		C	1	5			1	1	3	5				x
41	222.19.20	A	3	5	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**		1		3				
		B	3	5				1	5	3 , 5	x			
		C	3	5				1, 10	5	3	x			
42	**73.10.1**	A	1	3	Benign - Follow-up	1 , 2 , 3	9	5	5			x		
		B	2	3					5	5	x			
		C	2	2					5	5	x			
43	**93.12.5**	A	2	5	**Biopsy - DCIS**	**4 , 5**		5		3				
		B	2	5			2	6	5	3 , 5		x		
		C	2	5			1	6	5	3		x		
44	220.19.4	A	1	4	**Lumpectomy - Infiltrating duct Ca gr**	**4 , 5**	5		5	5		x		
		B	2	4	**III**		5		5	5			x	
		C	2	4			5		2	5			x	

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
45	211.19.3	A	1	2	Benign - Follow-up	1 , 2 , 3			5	5				
		B	2	2					5	5	x			
		C	2	2					5	5	x			
46	**75.11.13**	A	1	4	Benign - Excision biopsy no features	1 , 2 , 3		1		3				
		B	2	4	of malignancy. Traumatic fat necrosis			1		3				
		C	2	4	and dystrophic calcifications			1	1	3				
47	209.19.6	A	3	5	Benign - Follow-up	1 , 2 , 3								x
		B	4	5			6		2 , 5				x	
		C	1	4			6		2	5				x
48	**98.12.18**	A	1	5	**Infiltrating duct Ca gr III**	**4 , 5**		8		2				
		B	2	5				8		2 , 5	x			
		C	4	5				8	5	3				
49	217.19.19	A	3	5	**Tru-cut biopsy - Infiltrating duct Ca gr**	**4 , 5**	5						x	
		B	2	4	**III**		5		2	1			x	
		C	1	4			6		5	5				
50	**107.13.10**	A	2	5	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**		9	5	5				
		B	2	5				9	5	3 , 5	x			
		C	2	5				9, 11	5	3	x			
51	**89.12.26**	A	1	3	Benign - Follow-up	1 , 2 , 3	2	8	5	5				
		B	2	3				8	5	5	x			
		C	2	3			9	8	5	5		x		
52	214.19.13	A	3	5	**Mastectomy - Infiltrating duct Ca gr I**	**4 , 5**		1	5	5				
		B	4	5				1	5	5	x			
		C	1	5				1	5	3				
53	195.16.1	A	1	3	Benign - Follow-up	1 , 2 , 3		4						
		B	2	2					5		x			
		C	4	2					5	5	x			

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
54	**96.12.8**	A	1	3	Benign - Follow-up	1 , 2 , 3	5		5	5			x	
		B	5	3					5	5	x			
		C	**5**	**3**					5	5	x			
55	192.16.1	A	1	3	Benign - Follow-up	1 , 2 , 3	2	1				x		
		B	1	3					5					
		C	1	3			1		5	5			x	
56	**101.13.12**	A	1	4	Benign - FNA periductal mastitis	1 , 2 , 3		1	5	5				
		B	3	3				2	5	5	x			
		C	2	3			9		5	5			x	
57	**121.13.1**	A	2	5	**FNA - Malignant cells compatable with**	**4 , 5**		8 , 8	5	3 , 5				
		B	2	5	**duct Ca**			8	5	3 , 5	x			
		C	2	5	**Pt refused surgery - grading unknown**		1	9 , 1	3		x			
58	213.19.13	A	1	5	**Biopsy - Infiltrating duct Ca at least**	**4 , 5**	8		3					x
		B	2	5	**gr II**		6	3 , 5	5					x
		C		5			9 , 10		3	2			x	
59	180.14.14	A	1	2	Benign - breast aspirate no malignant	1 , 2 , 3								
		B	4	3	cells were identified				5	1				
		C	4	2			1		5	5			x	
60	**131.13.1**	A	3	5	**Needle biopsy - Infiltrating duct Ca**	**4 , 5**		5	5	5				
		B	3	5	**gr II with mucinous Ca component**			5	5	3 , 5	x			
		C	1	5				6		3				
61	193.16.20	A	3	5	**Mastectomy - Infiltrating duct Ca (too**	**4 , 5**	9							x
		B	2	5	**autolytic to grade). High grade DCIS**		9		5	5				x
		C	2	5	**present**		9		3	5				x
62	**134.13.13**	A	3	5	**Biopsy - Medullary Ca**	**4 , 5**		1 , 4, 5	5	3 , 5		x x x		
		B	2	4				1 , 5, 7	5	2 , 5	x			
		C	1	4			1 , 2, 9	1 , 6	5	3		x		

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
63	105.13.1	A	1	3	Benign - Follow-up	1 , 2 , 3	8						x	
		B	4	3			5		5	1				
		C	1	3			9		5	5			x	
64	190.16.12	A	2	5	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**	9					x		
		B	2	4			9		2	1		x	x	
		C	2	5			9		2	5		x		
65	**136.13.13**	A	2	5	**Mastectomy - Infiltrating duct Ca gr III**	**4 , 5**		1		2				
		B	2	5	**Lymphovascular invasion**		9	1, 4		2				
		C	2	5			9	1 , 9	5	3			x	
66	185.14.1	A	2	5	**FNA - Ductal Ca**	**4 , 5**		1 , 8				x	x	
		B	2	4				8 , 8	1	5	x			
		C	2	4	**Pt transferred - no file**			1 , 9		2				
67	**144.13.10**	A	3	5	**Tru-cut biopsy - Infiltrating duct Ca**	**4 , 5**	11							x
		B	3	5	**gr II**		1		1	1				x
		C	1	5			1		1	5				
68	179.14.12	A	1	5	Benign - Follow-up	1 , 2 , 3	1 , 4		5	5				x
		B	2	3			4		5	5				
		C	1	3				1	5	5				
69	**113.13.23**	A	4	4	Benign - Follow-up	1 , 2 , 3	4	1 ,1, 1				x x		
		B	2	3			3	1 , 1, 1, 1	1	5		x x		
		C	4	3			1 , 2	1 , 1 , 1	5	5		x		
70	178.14.8	A	1	3	Benign - Follow-up	1 , 2 , 3	1						x	
		B	3	3			1		5					
		C	1	3			1 , 9		5	5			x	
71	**119.13.13**	A	1	5	Benign - TB breast	1 , 2 , 3								
		B	2	4	**Biopsy - Caseating tuberculous**			9	5	5	x			
		C	3	5	**lymphadenitis**		10		5	5				

							R	L	R	L	R	R	R	R
Patient number	Patient code	Reader	Tabar	BI-RADS	TRUTH	BI-RADS TRUTH	Lesion site	Lesion site	Calcifications	Calcifications	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity
72	182.14.14	A	1	5	**Tru-cut biospy - Infiltrating duct Ca gr**	**4 , 5**	1		2					x
		B	3	5	**III**		1		2 , 5	5				x
		C	1	5			8 , 10	9	3	5				x
73	169.13.10	A	1	2	Benign - Follow-up	1 , 2 , 3		1 , 5, 5	5	5				
		B	4	3			10	10	5	5		x		
		C	4	3					5	5				
74	**128.13.8**	A	1	2	Benign - Follow-up	1 , 2 , 3			5	5				
		B	5	3					5	5	x			
		C	4	3					5	5	x			
75	143.13.16	A	3	2	Benign - Follow-up	1 , 2 , 3								
		B	2	2					5	1				
		C	1	2					5	5	x			
76	139.13.13	A	2	1	Benign - Follow-up	1 , 2 , 3								
		B	2	2					5	1	x			
		C	2	2					5	5	x			
77	**152.13.14**	A	3	5	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**	8		3					x
		B	3	5			8		3					x
		C	3	5			8		3	5				x
78	177.14.14	A	1	5	**Confirmed Infiltrating duct Ca g II**	**4 , 5**		8		3				
		B	1	5				8		3				
		C	1	5				8 , 10		3				
79	**160.13.11**	A	1	3	**Biopsy - Infiltrating duct Ca gr II**	**4 , 5**								
		B	1	3					1	1	x			
		C	1	3				1	5	5				
80	171.13.4	A	2	5	**Mastectomy - Infiltrating ductal Ca gr**	**4 , 5**	1 , 4		5	5			x x	
		B	2	5	**III**		1 , 5		5	5		x		x
		C	2	5			1 , 9		5	5		x		x

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
1	**1.1.13**	A	x	x			x												x					
		B	x	x		x	x		x											x				
		C	x	x		x	x		x										x					
2	**250.20.10**	A				x													x					
		B				x			x										x					
		C							x										x					
3	**2.1.22**	A													x									
		B													x							x		
		C			x						x				x							x		
4	268.22.3	A																						
		B	x																x					
		C	x																x					
5	249.20.10	A																	x					
		B							x															
		C							x										x					
6	**7.2.13**	A																						
		B							x															
		C							x															
7	246.20.2	A																				x		
		B									x		x						x			x		
		C				x				x						x			x			x		
8	**8.2.10**	A										x , x	x , x			x	x	x					x	
		B										x	x	x		x	x	x						x
		C										x	x	x	x	x	x	x						x
9	262.20.2	A										x	x			x	x					x		
		B										x	x	x		x	x	x					x	
		C									x	x	x		x	x							x	

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
10	**10.2.3**	A								x										x				
		B								x									x			x		
		C																						
11	236.19.3	A																						
		B													x							x		
		C									x													
12	**13.2.4**	A																				x		
		B							x															
		C							x															
13	**25.3.12**	A								x							x					x		
		B								x												x		
		C	x																			x		
14	233.19.13	A																						
		B							x															
		C									x		xx	x	x							x		
15	**21.2.4**	A																						
		B																		x				
		C																	x					
16	259.20.13	A									x		x							x				
		B									x		x	x		x							x	
		C									x		x	x	x	x							x	
17	**27.3.1**	A																						
		B							x										x					
		C																	x					
18	230.19.2	A								x												x		
		B			x										x						x		x	
		C																			x			x

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
19	**31.4.1**	A																						
		B								x										x			x	
		C		x					x					x										
20	258.20.11	A								x												x		
		B									x												x	
		C									x		x		x									x
21	**46.5.14**	A										x	x									x		
		B										x	x				x						x	
		C										x	x	x		x	x						x	
22	244.20.13	A										x	x	x			x	x				x		
		B										x	x	x			x	x				x		
		C										x	x	x	x	x	x	x				x		
23	229.19.16	A										x										x		
		B							x															
		C							x															
24	**65.8.1**	A																	x			x		
		B	x									x	x			x	x		x			x		
		C	x									x	x	x		x	x				x			x
25	**33.4.13**	A																						
		B			x																			
		C									x													
26	227.19.5	A										x										x		
		B											x									x		
		C	x																				x	
27	228.19.3	A																						
		B							x															
		C											x											

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
28	**41.4.1**	A																						
		B							x															
		C							x															
29	**69.10.1**	A																	x					
		B				x		x	x										x					
		C	x	x	x	x													x					
30	221.19.11	A																						
		B							x															
		C							x															
31	**48.5.14**	A										x										x		
		B							x															
		C							x															
32	225.19.1	A										x	x	x		x	x	x				x		
		B										x	x	x		x	x	x				x		
		C										x	x	x	x	x	x	x				x		
33	215.19.19	A																						
		B							x															
		C							x															
34	**77.11.16**	A																	x					
		B							x															
		C																	x					
35	224.19.13	A								x														
		B			x																			
		C								x												x	x	
36	**81.11.13**	A																						
		B							x										x					
		C	x			x													x					

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
37	60.7.1	A																						
		B							x															
		C							x															
38	212.19.5	A													x									
		B													x									
		C									x											x		
39	223.19.3	A									x												x	
		B									x												x	
		C									x		x	x					x				x	
40	**88.11.13**	A	x	x		x		x											x					
		B	x	x		x	x	x	x											x				
		C	x	x	x	x	x	x			x								x			x		
41	222.19.20	A								x				x		x						x		
		B										x	x	x		x								
		C										x	x	x	x	x	x							x
42	**73.10.1**	A																						
		B							x															
		C							x															
43	**93.12.5**	A										x	x	x				x				x		
		B										x	x	x				x				x		
		C										x	x					x	x			x		
44	220.19.4	A																	x					
		B							x										x					
		C	x																x					
45	211.19.3	A																						
		B							x															
		C							x															

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
46	**75.11.13**	A									x				x							x		
		B								x													x	
		C									x												x	
47	209.19.6	A																	x					
		B	x	x		x	x	x	x											x				
		C	x	x	x	x	x	x											x					
48	**98.12.18**	A										x	x	x		x	x					x		
		B										x	x	x		x	x	x				x		
		C										x	x	x		x	x	x				x		
49	217.19.19	A	x				x												x					
		B							x										x					
		C									x		x						x					
50	**107.13.10**	A										x	x	x		x	x	x				x		
		B										x	x	x		x	x	x						x
		C										x	x	x	x	x	x	x						x
51	**89.12.26**	A									x											x		
		B													x							x		
		C									x													
52	214.19.13	A										x	x	x		x	x	x				x		
		B										x	x	x		x	x	x				x		
		C										x	x	x	x	x	x					x		
53	195.16.1	A								x												x		
		B							x															
		C							x															
54	**96.12.8**	A																	x					
		B							x															
		C							x															

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
55	192.16.1	A								x									x			x		
		B							x															
		C																						
56	**101.13.12**	A									x				x									
		B													x							x		
		C																	x					
57	**121.13.1**	A								x	x			x									x	
		B								x	x			x				x					x	
		C								x	x		x	x	x				x					x
58	213.19.13	A				x													x					
		B	x			x		x	x															
		C	x	x	x	x															x			
59	180.14.14	A																						
		B							x															
		C																	x					
60	**131.13.1**	A										x										x		
		B										x	x			x	x	x						
		C										x	x	x	x	x	x	x				x		
61	193.16.20	A	x	x		x	x	x											x					
		B	x	x		x	x	x	x										x					
		C	x	x	x	x	x	x											x					
62	**134.13.13**	A																			x			
		B								x x	x												x	
		C								x x				x	x						x			x
63	105.13.1	A																	x					
		B			x				x										x					
		C							x										x					

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
64	190.16.12	A			x	x													x					
		B		x		x			x											x				
		C	x	x		x													x					
65	**136.13.13**	A										x	x	x		x	x		x					
		B			x							x	x	x	x	x	x							x
		C									x	x	x	x	x		x		x					x
66	185.14.1	A	x	x			x																x	
		B								x x				x									x	
		C								x x			x										x	
67	**144.13.10**	A	x	x		x	x												x					
		B	x	x		x	x		x										x					
		C										x	x	x	x	x	x					x		
68	179.14.12	A	x	x		x	x	x												x				
		B			x				x															
		C									x											x		
69	**113.13.23**	A								x x										x			x	
		B								x x									x					
		C								x x											x		x	
70	178.14.8	A																	x					
		B			x				x															
		C																	x					
71	**119.13.13**	A																						
		B	x	x		x				x									x					
		C	x	x	x	x															x			
72	182.14.14	A	x		x	x													x					
		B	x			x			x										x					
		C	x	x	x	x					x								x					

																				Lesion extent					
			R	R	R	R	R	R	L	L	L	L	L	L	L	L	L	L	L	R	R	R	L	L	L
Patient number	Patient code	Reader	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	No opacity/asymmetry	Well defined opacity	Poorly defined opacity	Spiculate opacity	Architectural distortion	Asymmetry breasts	Asymmetry density	Skin thickening	Skin retraction	Nipple retraction	Locallized	Multifocal	Multicentric	Locallized	Multifocal	Multicentric
73	169.13.10	A																							x
		B								x												x			x
		C																							
74	**128.13.8**	A																							
		B							x																
		C									x														
75	143.13.16	A																							
		B																							
		C							x																
76	139.13.13	A																							
		B							x																
		C							x																
77	**152.13.14**	A				x	x	x											x						
		B	x	x		x	x	x	x										x						
		C	x	x	x	x	x	x											x						
78	177.14.14	A									x		x	x								x			
		B										x	x									x			
		C									x		x	x	x								x		
79	**160.13.11**	A									x											x			
		B							x																
		C									x											x			
80	171.13.4	A	x	x			x	x											x						
		B	x	x		x	x	x	x													x			
		C	x	x	x	x	x	x														x			

APPENDIX R

Simple kappa values for agreement on Tabár's classification of breast parenchyma

APPENDIX R

Calculated simple Kappa values for the agreement on Tabar's classification of breast parenchyma between the three viewer pairs (n=80) before (Initial reporting) and after the viewing protocol (Final reporting)

Viewers	Initial	95% CI	Final	95% CI
A and B	*0.46*	0.33 ; 0.60	0.34	0.21 ; 0.48
A and C	0.26	0.14 ; 0.38	0.36	0.22 ;0.51
B and C	0.3	0.18 ; 0.42	*0.54*	*0.41 ; 0.67*

Kappa values:

<0.4: – weak to moderate agreement,

0.4 – 0.75: – fair to good agreement,

>0.75: – strong agreement

APPENDIX S

Percentage agreement between viewers on lesion site and calcifications

APPENDIX S

Percentage agreement between viewers on lesion site and calcifications

		INITIAL (n = 80)		FINAL (n = 80)	
	Viewer	**n**	**Percentage**	**n**	**Percentage**
Lesion site					
Left	A and B	42	52.5	51	63.8
	A and C	46	57.5	45	56.3
	B and C	37	46.3	48	60
Right	A and B	42	52.5	58	72.5
	A and C	51	63.8	46	57.5
	B and C	37	46.3	49	61.3
Calcifications					
Left	A and B	25	31.3	38	47.5
	A and C	23	28.8	26	32.5
	B and C	41	51.3	34	42.5
Right	A and B	31	38.8	35	43.8
	A and C	29	36.3	31	38.8
	B and C	50	62.5	46	57.5

APPENDIX T

Kappa values for agreement between viewers on characterisation of mammogram pattern

APPENDIX T

Agreement amongst viewers on mammogram pattern (Initial reporting and Final reporting)

	INITIAL (n = 80)					FINAL (n = 80)				
MAMMOGRAM PATTERN	**Viewer**	**Frequency used (%)**	**Viewer pairs**	**Kappa**	**95% CI**	**Viewer**	**Frequency used (%)**	**Viewer pairs**	**Kappa**	**95% CI**
No opacity/asymmetry (Right)	A	1.3	A and B	0.03	-0.02 ; 0.08	A	0.0	A and B	<0.01	-0.02 ; 0.02
	B	48.8	A and C	-0.02	-0.07 ; 0.02	B	47.5	A and C	<0.01	-0.04 ; 0.05
	C	15.0	B and C	0.21	0.05 ; 0.37	C	25.0	B and C	*0.44*	0.26 ; 0.61
No opacity/asymmetry (Left)	A	0.0	A and B	<0.01	-0.03 ; 0.03	A	0.0	A and B	0	-0.02 ; 0.02
	B	35.0	A and C	0.01	-0.07 ; 0.10	B	50.0	A and C	0.01	-0.05 ; 0.06
	C	15.0	B and C	*0.43*	0.23 ; 0.63	C	23.8	B and C	0.38	0.20 ; 0.55
Architectural distortion (Right)	A	7.5	A and B	*0.59*	0.29 ; 0.88	A	11.3	A and B	*0.51*	0.23 ; 0.79
	B	12.5	A and C	*0.67*	0.41 ; 0.94	B	15.0	A and C	0.28	0.02 ; 0.53
	C	13.8	B and C	*0.51*	0.23 ; 0.79	C	21.3	B and C	*0.71*	0.51 ; 0.91
Architectural distortion (Left)	A	15.0	A and B	*0.67*	0.47 ; 0.88	A	15.0	A and B	**0.79**	0.62 ; 0.96
	B	22.5	A and C	*0.49*	0.29 ; 0.70	B	21.3	A and C	*0.61*	0.41 ; 0.81
	C	31.3	B and C	*0.65*	0.47 ; 0.84	C	28.8	B and C	*0.67*	0.48 ; 0.86
Asymmetry breast (Right)	A	6.3	A and B	0.08	-0.20 ; 0.36	A	8.8	A and B	*0.58*	0.28 ; 0.88
	B	10.0	A and C	0.05	-0.19 ; 0.30	B	11.3	A and C	0.35	0.05 ; 0.65
	C	12.5	B and C	0.38	0.07 ; 0.68	C	15.0	B and C	*0.73*	0.50 ; 0.95
Asymmetry breast (Left)	A	5.0	A and B	*0.40*	0.12 ; 0.68	A	12.5	A and B	*0.75*	0.54 ; 0.96
	B	17.5	A and C	0.13	-0.04 ; 0.30	B	16.3	A and C	*0.55*	0.32 ; 0.77
	C	31.3	B and C	*0.50*	0.30 ; 0.71	C	23.8	B and C	*0.54*	0.31 ; 0.76
Asymmetry density (Right)	A	7.5	A and B	0.15	-0.13 ; 0.43	A	2.5	A and B	-0.04	-0.09 ; 0.00
	B	13.8	A and C	0.03	-0.20 ; 0.27	B	8.8	A and C	0.13	-0.14 ; 0.40
	C	12.5	B and C	0.07	-0.18 ; 0.32	C	12.5	B and C	-0.11	-0.17 ; -0.06
Asymmetry density (Left)	A	12.5	A and B	0.26	-0.02 ; 0.55	A	5.0	A and B	*0.51*	0.15 ; 0.88
	B	15.0	A and C	0.01	-0.21 ; 0.23	B	8.8	A and C	0.02	-0.16 ; 0.19
	C	18.8	B and C	0.24	-0.02 ; 0.51	C	21.3	B and C	0.05	-0.16 ; 0.26

Kappa values: < 0.4 (Weak to moderate agreement), values indicated in *italic : 0.4 - 0.75 (Fair to good agreement)* values indicated in bold : **> 0.75 (Strong agreement)**

	INITIAL (n = 80)					FINAL (n = 80)				
MAMMOGRAM PATTERN	**Viewer**	**Frequency used (%)**	**Viewer pairs**	**Kappa**	**95% CI**	**Viewer**	**Frequency used (%)**	**Viewer pairs**	**Kappa**	**95% CI**
Skin thickening (Right)	A	7.5	A and B	*0.63*	0.34 ; 0.93	A	11.3	A and B	*0.69*	0.45 ; 0.92
	B	11.3	A and C	*0.54*	0.25 ; 0.84	B	16.3	A and C	*0.48*	0.20 ; 0.75
	C	13.8	B and C	*0.54*	0.26 ; 0.82	C	16.3	B and C	**0.82**	0.64 ; 0.99
Skin thickening (Left)	A	11.3	A and B	*0.58*	0.32 ; 0.84	A	10.0	A and B	**0.82**	0.63 ; 1.00
	B	16.3	A and C	*0.58*	0.34 ; 0.82	B	13.8	A and C	*0.58*	0.33 ; 0.84
	C	20.0.8	B and C	**0.87**	0.74 ; 1.00	C	17.5	B and C	**0.76**	0.57 ; 0.96
Skin retraction (Right)	A	2.5	A and B	*0.66*	0.21 ; 1.00	A	10.0	A and B	*0.63*	0.34 ; 0.93
	B	5.0	A and C	**0.79**	0.40 ; 1.00	B	8.8	A and C	*0.53*	0.20 ; 0.86
	C	3.8	B and C	*0.55*	0.10 ; 1.00	C	7.5	B and C	**0.92**	0.75 ; 1.00
Skin retraction (Left)	A	8.8	A and B	*0.50*	0.21 ; 0.80	A	11.3	A and B	**0.77**	0.56 ; 0.99
	B	13.8	A and C	*0.51*	0.25 ; 0.78	B	13.8	A and C	*0.62*	0.36 ; 0.87
	C	17.5	B and C	**0.76**	0.57 ; 0.96	C	15.0	B and C	**0.85**	0.68 ; 1.00
Nipple retraction (Right)	A	6.3	A and B	0.18	-0.20 ; 0.55	A	6.3	A and B	*0.64*	0.32 ; 0.97
	B	5.0	A and C	0.26	-0.18 ; 0.70	B	8.8	A and C	**0.79**	0.50 ; 1.00
	C	2.5	B and C	*0.66*	0.21 ; 1.00	C	6.3	B and C	***0.82***	0.58 ; 1.00
Nipple retraction (Left)	A	12.5	A and B	*0.41*	0.10 ; 0.72	A	7.5	A and B	*0.72*	0.47 ; 0.98
	B	8.8	A and C	*0.62*	0.36 ; 0.88	B	12.5	A and C	*0.75*	0.48 ; 1.00
	C	13.8	B and C	*0.75*	0.52 ; 0.98	C	8.8	B and C	**0.80**	0.59 ; 1.00

Kappa values: < 0.4 (Weak to moderate agreement), values indicated in italic *: 0.4 - 0.75 (Fair to good agreement)* values indicated in bold : **> 0.75 (Strong agreement)**

APPENDIX U

Kappa values for agreement between viewers on lesion extent

APPENDIX U

Agreement amongst viewers on the descriptors for lesion extent (Initial reporting and Final reporting)

		INITIAL (n= 80)							FINAL (n = 80)							
		Frequency used (%)							Frequency used (%)							
DESCRIPTOR	Viewer	Not indicated	Localised	Multifocal	Multicentric	Viewer pair	Kappa	95 % CI	Viewer	Not indicated	Localised	Multifocal	Multicentric	Viewer pair	Kappa	95 % CI
Lesion extent (left breast)	A	57.5	31.3	6.3	5	A & B	*0.62*	0.48 ; 0.77	A	61.3	31.3	6.3	1.3	A & B	*0.45*	0.29 ; 0.62
	B	62.5	22.5	6.3	8.8	A & C	*0.45*	0.29 ; 0.61	B	62.5	18.8	13.8	5	A & C	0.38	0.22 ; 0.52
	C	55	26.3	8.8	10	B & C	*0.46*	0.31 ; 0.62	C	57.5	20	11.3	11.3	B & C	*0.51*	0.35 ; 0.66
Lesion extent (right breast)	A	70	23.8	3.8	2.5	A & B	*0.4*	0.23 ; 0.57	A	66.3	27.5	5	1.3	A & B	0.34	0.17 ; 0.51
	B	70	20	5	5	A & C	0.36	0.18 ; 0.54	B	67.5	21.3	7.5	3.8	A & C	*0.45*	0.28 ; 0.61
	C	67.5	23.8	1.3	7.5	B & C	*0.53*	0.35 ; 0.71	C	57.5	32.5	0	10	B & C	*0.44*	0.28 ; 0.59

Kappa values:

< 0.4 (Weak to moderate agreement),

values indicated in *italic: 0.4 – 0.75 (Fair to good agreement)*,

values indicated in **bold: > 0.75 (Strong agreement)**

APPENDIX V

Literature searches with key words that yielded no results

+You Search Images Maps Play News Gmail Drive Calendar Translate More

digital image, grayscale invert, diagnostic accuracy, clinical studies

Sign in

Web Images Maps More Search tools

About 1,010,000 results (0.27 seconds)

Scholarly articles for **digital image, grayscale invert, diagnostic accuracy, clinical studies**
Clinical evaluation of JPEG2000 compression for ... - Sung - Cited by 36
Digital radiography of the chest: promises and ... - Goodman - Cited by 57
Unsupervised border detection in dermoscopy **images** - Emre Celebi - Cited by 63

Gray-Scale Reversal for the Detection of Pulmonary Nodules on a ...
www.ajronline.org/doi/full/10.2214/AJR.11.6625
by DW De Boo - 2011 - Cited by 1 - Related articles
We therefore decided to reevaluate with modern **digital image** and monitor equipment whether ... and represent the standard processing used in routine **clinical studies**. ... the original **gray-scale** values (bones white) to their **inverted** counterparts. ..... Digital chest radiography: effect on **diagnostic accuracy** of hard copy, ...

[PDF] Evaluating quality of compressed medical **images** - Information ...
code.ucsd.edu/cosman/web-05.pdf
File Format: PDF/Adobe Acrobat - Quick View
by RA OLSHEN - 1994 - Cited by 244 - Related articles
developed methods for determining **diagnostic accuracy** of lossy ... for any **digital image** processing that produces images different from the ... P. C. Cosman and R. M. **Gray** are with the Information Systems ... images measured by **clinical** simulation and statistical ... and recall **studies** because the overwhelming quantity of ...

ScienceDirect.com - **Clinical Imaging** - **Gray-scale** inversion ...
www.sciencedirect.com/science/article/pii/S0899707112000150
The purpose of this **study** was to investigate **gray-scale** inversion in nodule detection ... during three reading sessions: traditional presentation, **inverted gray-scale**, and a ... Sensitivity and specificity were used to assess **accuracy** based on presence or ... Pulmonary nodule;; Chest radiograph;; Lung cancer;; **Digital imaging** ...

[PDF] **Gray Scale** Inversion in **Digital Image** for Measurement of ... - S...
www.scielo.br/pdf/bdj/v23n6/v23n06a13.pdf
File Format: PDF/Adobe Acrobat - Quick View
by ML OLIVEIRA - 2012 - Related articles
All **images** were treated with Positive, a **digital** tool that **inverts** the **grayscale** value. ... files, since it did not improve the **accuracy** of measurements. ... of **diagnostic** tools, comparative studies are critical to .... Additionally, as in a **clinical trial**, the ...

Journal of Applied Oral Science - Comparison between **inverted** and ...
www.scielo.br/scielo.php?pid=S1678-77572007000600007...sci...
by G Scaf - 2007 - Cited by 12 - Related articles
The advances in **digital imaging** technology in dentistry have provided an ... The purpose of this **study** was to compare **inverted** and unprocessed ... Digitization was performed at 600 dpi and in **gray scale**. ... **diagnostic accuracy** between these images regarding periodontal bone loss .... New **clinical** methods of diagnosis.

F-speed film and **digital images** for detection of osseous defects in ...
dmfr.birjournals.org/content/36/8/500.full.pdf
by T Jorgenson - 2007 - Cited by 8 - Related articles
73190, USA; 4General **Clinical Research** Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA. Objectives: The aim of the present study was to compare the **diagnostic accuracy** of F-speed .... 1024 £ 768 lines and a **greyscale** range of 0–225. Optimal .... However, **inverted digital images** ...

The **Digital Imaging** Workstation
www.ncbi.nlm.nih.gov › ... › J Digit Imaging › v.16(1): Mar 2003
by RL Arenson - 2003 - Cited by 156 - Related articles
The effects on **diagnostic accuracy** of using **digital** workstations rather than film for these ... resolution will vary substantially based on the modality and **clinical** question. ... Summary of **Studies** on Pixel Size Requirements for Chest **Imaging** .... To avoid digitization noise they recommend **digital gray**-level spacing no wider ...

[PDF] Breast Cytology **Diagnosis** Via **Digital Image** Analysis 1 ... - Cite...
citeseerx.ist.psu.edu/viewdoc/download?doi...1... - United States
File Format: PDF/Adobe Acrobat - Quick View
by WH Wolberg - Cited by 67 - Related articles
Clinical Sciences Center, 600 Highland Avenue, Madison, WI 53792. ... 5Mr. Street is a Ph.D. student and **Research** Assistant in Computer Sciences. ... the cytological **diagnosis** of breast cancer with the **accuracy** of **digital image** .... This term allows the snake to take on a reasonable shape even in regions where **gray** ...

[PDF] Cone-Beam CT **Diagnostic** Applications: Caries, Periodontal Bo...
www.aae.org/...**Research**/.../Cone- ...
File Format: PDF/Adobe Acrobat - Quick View
by DA Tyndall - Cited by 89 - Related articles
Digital imaging has been an advancement, yet the imaging geometry has not changed .... tem had a lower **diagnostic accuracy** for caries detection than the intraoral or LCBCT .... In a **clinical study** conducted by Simon and coworkers [52], CBCT was found to be ... granulomas from cysts) using **grayscale** values in the lesions.

[PS] Breast Cytology **Diagnosis** Via **Digital Image** Analysis - p.cs.wisc...
ftp://ftp.cs.wisc.edu/math-prog/tech-reports/olm098.ps
File Format: Adobe PostScript - View as HTML
by WH Wolberg - Cited by 67 - Related articles
Clinical Sciences Center, 600 Highland Avenue, Madison, WI 53792. ... 5 Mr. Street is a Ph.D. student and **Research** Assistant in Computer Sciences. ... the cytological **diagnosis** of breast cancer with the **accuracy** of **digital image** .... This term allows the snake to take on a reasonable shape even in regions where **gray** ...

+You Search Images Maps Play News Gmail Drive Calendar Translate More

MUSICA2 image processing, digital mammography, diagnostic accuracy mam

Sign in

Web Images Maps More Search tools

About 3,380 results (0.35 seconds)

Effect of **image quality** on calcification detection in **digital ...**
pdfserv.aip.org/MPHYA6/vol_39/iss_6/3202_1.pdf
May 17, 2012 – qualities were processed with Agfa (**Musica-2**) **image processing** only. ... Key words: **digital mammography**, dose, **image processing**, observer performance, calcification ... cal **trials** have provided insight on the **clinical** performance of ... overall **diagnostic accuracy** for screen-film and digital to be similar, but ...

Effect of **image quality** on calcification detection in ... - Medical Physics
online.medphys.org › RADIATION IMAGING PHYSICS
Images of the CDMAM **mammographic** test phantom were acquired using ... These **images** were modified to the additional **image** qualities used in the observer **study**. ... in detection between the two **image processing** algorithms used ($p > 0.05$). ... 2Jarvis Breast Screening and **Diagnostic** Centre, Guildford GU1 1LJ, United ...

[PDF] Agfa's **MUSICA2** TM Taking **Image Processing** to ... - Agfa Heal...
www.agfahealthcare.com/global/en/he/library/libraryopen?ID...
File Format: PDF/Adobe Acrobat - Quick View
The displayed **image quality** in a **digital** projection radiography system depends ... imperfect input for human interpretation.3 Clearly, if the relevant **clinical** ... tutorial on the Role of **Image Processing** on the **Musica2** CD) can usually resolve any .... on **diagnostic accuracy**. ..... method for **mammographic** contrast enhancement.

[PDF] There 12 - Agfa HealthCare
www.agfahealthcare.com/he/global/.../THERE_12_tcm541-95647.pd...
File Format: PDF/Adobe Acrobat - Quick View
Educational initiatives strengthen **mammography** ... **Quality** of **image processing** software key in ... strives to provide as **accurate** information as possible, but shall not be responsible for any ... activities, or can enhance **clinical** care ... Integrating **digital** radiology and pathology ..... **diagnostic** imaging **studies**, the region is ...

[PDF] DX-D 100 Datasheet (US) - Agfa HealthCare
www.agfahealthcare.com/global/en/he/library/libraryopen?ID...
File Format: PDF/Adobe Acrobat - Quick View
range of general radiography X-ray **studies**, even for the least mobile ... efficiency . What's more, the higher **image quality** also means potential ... facilitates **diagnostic** confidence. The DX-D ... control. • **MUSICA2 processing** for superior contrast detail and ... NX adds the exposure parameters used to the **digital image** file, and ...

AGFA.com - Agfa HealthCare at RSNA 2010
www.agfahealthcare.com › ... › News and Events › News from Agfa
Oct 14, 2010 – Imaging excellence, **clinical** confidence - Agfa HealthCare is ... by **MUSICA2**, Agfa HealthCare's gold standard **image processing** ... will provide the potential to yield **diagnostic quality images** at lower dose. ... Agfa HealthCare's DX-M is a **digital** radiography solution able to handle CR **mammography**, as well ...

Results for similar searches

CR 30-Xm - AGFA HealthCare
www.agfahealthcare.com › ... › Products › Computed Radiography (CR)
Mar 1, 2013 – Complete solution' for **digital mammography** and all general radiography applications; No compromises in **image quality**; Fits in small spaces and is suited ... that wants a single, digital solution for carrying out the maximum number of types of **studies**. .... Advanced **Image Processing** Technology. **MUSICA 2** ...

More results for **musica2 image processing digital mammography diagnostic** ~~accuracy~~ **mammography clinical study image quality**

Digital Mammography (Medical Radiology / **Diagnostic** Imaging ...
www.amazon.com › ... › Cancer › Breast Cancer
Digital Mammography (Medical Radiology / **Diagnostic** Imaging) [Ulrich Bick, Felix ... At the end of the free **trial**, your membership will automatically upgrade to a full year ... of **digital mammography**, including detector technology, **image processing**, ... acceptance, and **quality** assurance of **digital mammography** between the ...

More results for **musica2 image processing digital mammography diagnostic ~~accuracy~~ mammography clinical study image quality**

Agfa HealthCare's CR **digital Mammography** Solution with FDA ...
www.ehealthserver.com/.../1019-agfa-healthcares-cr-**digital-mammo**...
Jan 23, 2012 – Home, Industry, **Research** & Development, Conferences & Events, Downloads ... Excellent **image quality** and enhanced detail ... The DX-M comes with Agfa HealthCare's **MUSICA2** advanced **image processing** software for ... capturing, managing and processing **diagnostic** images and **clinical**/administrative ...

More results for **musica2 image processing digital mammography diagnostic ~~accuracy~~ mammography clinical study image quality**

APPENDIX W

Recommended soft-copy viewing protocol for mammography

APPENDIX W

SOFT-COPY VIEWING PROTOCOL FOR MAMMOGRAPHY

1 Pre-requisites for soft-copy mammography reporting: Training of viewers to have a good understanding of digital imaging principles and soft-copy viewing principles

2 Apply zooming or image magnification on all images to ensure the entire breast is viewed at full resolution

3 Use MUSICA^2 Invert as the default processing option for viewing all anatomical structures in the breast

4 Pay special attention to viewing the dense parenchyma in the breast. Use window-width and window-level adjustments to improve the contrast to better visualise the dense parenchyma

5 Use MUSICA^2 Invert (default processing option) for viewing of calcifications

6 Pay special attention to viewing for masses. Use window-width and window-level adjustments to improve the contrast to better visualise masses

7 Use MUSICA^2 Invert for both the screening and diagnostic mammographic tasks

8 Use the Unprocessed image whenever noise in the dense areas of the breast poses a problem

9 Use a structured report form

10 Use BI-RADS to standardise reporting

11 Use BI-RADS lexicon to communicate findings

APPENDIX X

Implementation of the soft-copy viewing protocol for mammography

APPENDIX X

IMPLEMENTATION OF THE SOFT-COPY VIEWING PROTOCOL FOR MAMMOGRAPHY
SIMULATION UNIT – FACULTY OF HEALTH SCIENCES (UFS)

Delegates: All registrars in the Department Clinical Imaging Sciences
Date: Friday – date to be decided
Time: Departmental Academic Afternoon
Venue: Theoretical training - Lecture room (Department Clinical Imaging Sciences)
Teaching file and assessment (Simulation Unit - on appointment)

1 **THEORETICAL TRAINING PROGRAM**

- **Prof WID Rae**
  Understanding the digital image and image processing

- **C Meyer**
  The effect of image processing on image quality (in specific MUSICA^2)

- **Dr SF Otto**
  Reporting of the Mammogram
  - Structured report form
  - Tabar's classification of breast parenchyma
  - BI-RADS lexicon
  - BI-RADS assessment categories

- Assessment of theoretical training by registrars

2 **TEACHING FILE (SIMULATION UNIT – On appointment)**
- Registrar reports on 80 Mammograms
- Use structured report form
- Aid: Drop boxes with explanation of Tabar's classification of breast parenchyma, the ACR lexicon and ACR assessment categories
- Assessment of the teaching file by registrars
- Assessment of the registrar's sensitivity / specificity / BI-RADS category 3
- Feedback to the registrar

3 **ASSESSMENT (SIMULATION UNIT – On appointment)**
- Registrar reports for assessment when ready – The simulation unit will allocate a date and time
- Registrar reports on 40 Mammograms
- Use structured report form
- No drop boxes as in teaching file
- Evaluation of the registrar's sensitivity / specificity / BI-RADS category 3
- Feedback to the registrar

SUMMARY

INTRODUCTION

Switching from screen-film mammography to digital mammography entails a lot more for the reporting radiologists, than switching from a light box to a computer monitor. Soft-copy viewing of the digitally processed image demands different skills and thus knowledge from the radiologist. The image processing option on digital mammography units is vendor dependant and the optimal processing options have not yet been established.

The main aim of this study was to develop and evaluate a soft-copy viewing protocol for mammography through participative learning to improve radiological reporting.

METHODS

A phantom-based method was used to identify a smaller set of processing options to be evaluated for image quality assessment on clinical images. Three (3) radiologists were trained in the new modality with specific emphasis on how to address the challenges of soft-copy viewing. The viewing protocol was developed through participative learning. The radiologists scored the image quality on thirty six (36) medio-lateral oblique images processed with four (4) different image processing options (MUSICA^2, MUSICA^2 Invert, Unprocessed, and Unprocessed Invert). An image quality score was calculated to find the best processing option for the anatomical structures overall, anatomical structures individually, masses, calcifications, noise, and the early detection of breast cancer. A viewing protocol was recommended based on the findings. The effect of the viewing protocol was assessed by comparing diagnostic accuracy of the radiologists before and after the viewing protocol. They reported on eighty (80) mammograms using the breast imaging and reporting data system (BI-RADS) of the American College of Radiology. Sensitivity,

specificity, positive predictive value (PPV) and BI-RADS category 3 were calculated and compared.

RESULTS

The phantom-based method found Unprocessed Invert, MUSICA^2, MUSICA^2 Invert, and Unprocessed to provide the best image quality. These processing options were therefore identified for image quality assessment on clinical images. For the anatomical structures overall, MUSICA^2 provided significantly superior image quality compared to Unprocessed ($p<0.0001$) and Unprocessed Invert ($p<0.0001$). MUSICA^2 Invert also provided significantly superior image quality compared to Unprocessed ($p<0.0001$) and Unprocessed Invert ($p=0.0003$) for that. The only significant difference between MUSICA^2 and MUSICA^2 Invert was found for skin outline for which MUSICA^2 Invert showed superiority ($p=0.0563$). The image quality of vessels in dense parenchyma was found be significantly inferior to that of all other anatomical structures with all processing options, even with the processed images ($p<0.0001$). For calcifications MUSICA^2 provided significantly superior image quality compared to Unprocessed and its Invert ($p=0.0066$ and $p=0.0001$ respectively). However, no significant difference was found between any of the processing options for masses ($p>0.05$). Noise was significantly less visible for Unprocessed compared to MUSICA^2 ($p = 0.016$) although it was still acceptable to all three radiologists in 97.2% of cases with MUSICA^2. For the early detection of breast cancer, MUSICA^2 was found to be significantly superior to Unprocessed ($p=0.0003$) and Unprocessed Invert ($p=0.0005$). The recommended default processing option for the viewing protocol was MUSICA^2 Invert. After the development of the viewing protocol, sensitivity increased for two of the radiologists [from 90% to 95% ($p=0.6752$)], and from 90% to 97.5% ($p =0.3589$) respectively]; specificity increased for two of the radiologists [from 61.5% to 72.5% ($p=0.2999$), and from 70% to 85% ($p=0.1082$) respectively]; PPV increased for all three radiologists [from 71.7% to 77.6% ($p=0.6198$), from 75% to 86.4% ($p=0.1699$), and from 83.7% to 84.8% ($p=0.8907$) respectively]. The percentage BI-RADS

category 3 cases decreased for two of the radiologists [from 15% to 12.5% (p=0.6461) and from 28.8% to 22.5% (p=0.2810) respectively].

CONCLUSIONS

Although not significant, the study found improvement in diagnostic accuracy after the development of the viewing protocol. Training of radiologists in the new modality and knowledge of the effect of image processing on image quality is regarded as important. The development of the viewing protocol through participative learning of the radiologist provided evidence to the radiologists that they could confidently use the proposed viewing protocol in clinical practice.

KEYWORDS

Digital mammography, soft-copy display, viewing protocol, digital mammography training, image quality assessment, digital image processing, MUSICA^2, unprocessed image, BI-RADS, diagnostic accuracy

OPSOMMING

INLEIDING

Vir die rapporterende radioloog behels die oorskakeling vanaf skerm-film mammografie na digital mammografie baie meer as slegs die oorskaling vanaf ‘n ligboks na ‘n rekenaarskerm. Sagte-kopie besigtiging van die digital geprosesseerde beeld vereis ander vaardighede en dus kennis van die radioloog. Die beeldprosesserings-opsie op ‘n digitale mammogafie eenheid hang af van die vervaardiger daarvan en die optimal prosesserings-opsies is nog nie vasgestel nie.

Die hoof doel van die studie was om ’n sagte-kopie besigtigingsprotokol vir mammografie te ontwikkel en te evaluaeer deur middel van deelnemende leer om sodoende radiologiese rapportering te verbeter.

METODES

‘n Fantoom-gebaseerde metode is gebruik om ‘n kleiner aantal prosesseringsopsies te identifiseer vir die assessering van beeldkwaliteit op kliniese beelde. Drie (3) radioloë is opgelei in die nuwe modaliteit met spesifieke klem op hoe om die uitdagings van sagte-kopie besigtiging die hoof te bied. Die besigtigingsprotokol was ontwikkel deur middel van deelnemende leer. Die radioloë het die beeldkwaliteit bepunt op ses-en-dertig (36) medio-lateraal skuins beelde wat met vier (4) verskillende beeldprosesseringsopsies (geïdentifiseer met die fantoom-gebaseerde metode) geprosesseer is. ‘n Beeldkwaliteitspunt is bereken om die prosesseringsopsie te vind vir die anatomiese strukture in geheel, anatomiese strukture individueel, massas, kalsifikasies, steuring en die die vroeë opsporing van kanker. ‘n Besigtigingsprotokol is op grond van die bevindinge aanbeveel. Die effek van die besigtigingsprotokol is geëvalueer deur die diagnostiese akkuraatheid van die radioloë voor en

na die besigtigingsprotokol te vergelyk. Die radioloë het op tagtig (80) mammogramme gerapporteer deur gebruik te maak van die 'breast imaging en reporting data system' (BI-RADS) van die Amerikaanse Kollege vir Radiologie. Sensitiwiteit, spesifisiteit, positiewe voorspelbaarheidswaarde (PPV) en BI-RADS kategorie 3 was bereken en vergelyk.

RESULTATE

Die fantoom-gebaseerde metode het bevind dat Ongeprosesseerd Invers, MUSICA^2, MUSICA^2 Invers en Ongeprosesseerd die beste beeldkwaliteit verskaf het. Hierdie prosesseringsopsies is dus geïdentifiseer vir gebruik om beeldkwaliteit op kliniese beelde te evalueer. Vir die anatomiese strukture in geheel, het MUSICA^2 betekenisvol beter beeldkwaliteit gelewer in vergeyking met Ongeprosesseerd ($p<0.0001$) en Ongeprosesseerd Invers ($p<0.0001$). MUSICA^2 Invers het ook betekenisvol beter beeldkwaliteit daarvoor gelewer in vergelyking met Ongeproseesserd ($p<0.0001$) en Ongeprosesseerd Invers ($p=0.0003$). Die enigste betekenisvolle verskil tussen MUSICA^2 en MUSICA^2 Invers was gevind vir die buitelyn van die vel waarvoor MUSICA^2 Invers superior was ($p=0.0563$). Die beeldkwaliteit van vate in digte parenchiem was betekenisvol laer as al die van ander anatomiese strukture, selfs met die geprosesseerde beelde ($p<0.0001$). MUSICA^2 het betekenisvol beter beeldkwaliteit gelewer vir kalsifikasies in vergelyking met Ongeprosesseerd en sy Invers ($p=0.0066$ en $p=0.0001$ onderskeidellik). Vir massas aan die anderkant is geen betekenisvolle verskil tussen enige van die prosesserings-opsies gevind nie ($p>0.05$). Steuring was betekenisvol minder sigbaar vir Ongeprossesseerd in vergelyking met MUSICA^2 hoewel dit steeds aanvaarbaar was vir al drie radioloë in 97.2% van gevalle met MUSICA^2. Vir die vroeë opsporing van borskanker was MUSICA^2 betekenisvol meer aangedui as Ongeprosesseerd ($p=0.0003$) en Ongeprosesseerd Invers ($p=0.0005$). Die aanbevole "default" prosesserings-opsie vir die besigtigingsprotokol was MUSICA^2 Invers. Na die ontwikkeling van die besigtigingsprotokol het sensitiwiteit vir twee van die radioloë verhoog

[van 90% tot 95% (p=0.6752) en van 90% tot 97.5% (p=0.35890] onderskeidellik; spesifisiteit het verhoog vir twee8van die radioloë [van 61.5% tot 72.5% (p=0.2999) en van 70% tot 85% (p=0.1082) onderskeidellik]; PPV het toegeneem vir al drie radioloë [van 71.7% tot 77.6% 9p=0.6198), van 75% tot 86.4% (p=0.1699) en van 83.7% tot 84.8% (p=0.8907) onderskeidellik]. Die persentasie BI-RADS kategorie 3 gevalle het afgeneem vir twee van die radioloë [van 15% tot 12.5% (p=0.6461) en van 28.8% tot 22.5% (p=0.2810) onderskeidellik].

GEVOLGTREKKINGS

Alhoewel nie betekenisvol nie, het die studie ‘n verbetering in diagnostiese akkuraatheid van die radioloë gevind na die ontwikkeling van die besigtingingsprotokol. Opleiding van radioloë in die nuwe modaliteit en kennis van die effek van beeldprosessering op beeldkwaliteit word beskou as belangrik. Die ontwikkeling van die besigtigingsprotokol deur middel van deelnemende leer van die radioloog het aan die radioloë bewyse verskaf dat hulle die voorgestelde besigtigingsprotokol met vertroue in kliniese praktyk kan gebruik.