THE INFLUENCE OF LOW- DOSE CT ATTENUATION CORRECTION ON ARTEFACTS OF MYOCARDIAL SPECT IMAGES FOR NUCLEAR MEDICINE STUDIES

by

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Thesis submitted in fulfilment of the requirements for the degree

Master of Science: Radiography (Nuclear Medicine Technology)

in the Faculty of Health and Wellness Sciences

at the Cape Peninsula University of Technology

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Bellville

March 2021

DECLARATION

I, Lelanie Lucia Nolan, declare that the contents of this thesis represent my own unaided work, and that the dissertation/thesis has not previously been submitted for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily those of the Cape Peninsula University of Technology**.**

24/03/2021

Signed **Date**

ABSTRACT

Introduction: Myocardial perfusion imaging (MPI) with single photon emission tomography (SPECT) imaging has improved the sensitivity of myocardial scintigraphy in coronary artery disease (CAD), but often at the expense of specificity. Artefacts in SPECT imaging cause poor image quality, which may present as false-positive results that may lead to unnecessary, expensive and invasive procedures. Myocardial perfusion studies performed with Tc-99m sestamibi, consist of stress and rest imaging with patients positioned in a supine or prone position which can be performed on the same day as a one day protocol or on different days as a two day protocol. Breast and diaphragm attenuation may cause anterior and/or inferior soft tissue artefacts during Tc-99m sestamibi imaging and may interfere with the visualisation of the perfusion defects of the myocardium. The application of attenuation correction (AC-A) to the breast tissue and diaphragm of the patient might improve the images and provide a clear view of the myocardium.

Aim: The study aimed at evaluating the efficacy of x-ray- derived attenuation correction in myocardial perfusion scintigraphy. The primary objective of the study was to determine whether hybrid SPECT with computed tomography (CT), will improve the image quality by reducing the soft tissue artefacts with the application of attenuation correction maps in the stress and rest Tc-99m sestamibi myocardial SPECT perfusion studies.

Materials and Methods: A retrospective study was performed on 100 image sets (an image set equals a stress and rest study) of patients with suspected ischaemic heart disease referred to the Nuclear Medicine department between January 2015 and December 2016 for myocardial perfusion scintigraphy. The results of the patients were quantitatively reviewed with a descriptive cross sectional design with a comparison group. The images were given a score of 0-4. A score of 0 implies normal study, 1 equals a defect with no change, 2 equals the defect change <50%, 3 equals the defect change >50% and 4 was given when an artefact was generated by the application of AC on the non- attenuation corrected (NAC) images of the stress and rest studies. An overall score of the results of the improvement (yes) versus no improvement (no) of AC-A to stress and rest studies was also given. The NAC and the attenuation corrected (AC) stress and rest images are the dependent variables of the study. The independent variables which are the relevant factors such as gender, age, weight, height and position of the patients during imaging are also discussed for their influence on the attenuation correction on the stress and rest images. The critical assessment areas were the inferior and anterior wall defects. The image analysis was performed by the two NM physicians, including the co-supervisor of this study. For statistical analysis an inferential multivariate technique, called a Generalized Linear Model, was applied to determined relationships between the dependent and independent variables. Frequency tables for the results are demonstrated in the form of tables and bar charts.

Results: The result of the stress as opposed to rest inferior images (with >50% change of the defect improvement) revealed a score of 46%. The effect of the independent variable on the dependent variable shows with the *p*-value being >0.05, non-significance. The scores showed AC-A improved 49% of the image sets and 51% of the image sets did not improve with the overall outcome. However, this score of 51% with no improvement, excludes 18 images of stress studies and nine images of rest studies which showed improvement (scores 2-3) in the inferior wall of the myocardium.

Discussion: The results demonstrated that with anterior stress and rest SPECT images, the most artefacts were created with AC-A. In the stress studies, the anterior wall showed 45 artefacts and the rest study 55 artefacts. Improvement for the stress inferior images is 61% of which 20 images are less than 50% improvement and 41 images are more than 50% improvement. The stress, as opposed to rest inferior images (with >50% change of the defect) showed an improvement with a score of 46%. AC-A to the stress and rest AC and NAC images scored an improvement of 49% and 51% of no improvement for the overall outcome. In the total amount of stress studies reviewed, it was found that 18 stress studies showed improvement and nine rest studies showed improvement (scores 2-3) in the inferior wall of the myocardium but with no overall improvement. For nine image sets of stress/rest image sets, an improvement was observed in both stress and rest studies in the inferior myocardial walls but AC-A did not improve the results. The relative factors indicate with a *p*-value >0.05, that these factors have no influence on the outcome with the application of AC-A on the images.

Conclusion: There is a significant difference in the AC-A scores of the images in the inferior wall of the myocardium. Therefore, the AC versus NAC with MPI shows a significant influence on the outcome of the study for the inferior wall of the myocardium.

Keywords: myocardial perfusion imaging, Tc-99m MIBI, SPECT/CT, attenuation correction

ACKNOWLEDGEMENTS

The success and outcome of this thesis required a lot of guidance and assistance from many people to whom I am extremely grateful to for the completion of this project.

I wish to thank:

- Ms. Elsie Neo Seane, the supervisor from CPUT, for her endless guidance, encouragement and devotion.
- Mrs. Monique du Toit, co-supervisor from Medical Physics at TBH for her continuous assistance and patience.
- Dr. NA Korowlay as co- supervisor and Dr. M Morkel as co-investigators for their time and enthusiasm to report on the patient data.
- Ms. Carolynn Lackay from CPUT for support and assisting on the Nuclear Medicine issues.
- Medical Physics division, Dr Chis Trauernicht (head of division) and all the medical physics colleagues for their support and willingness to assist when required.
- Tygerberg hospital and Western Cape department of health for the bursary and the chance to expand my knowledge in my work environment.
- Nuclear Medicine division, Prof. A Ellmann and staff for the opportunity to perform my research in the department and especially Dr Janke Kleynhans for her support.
- My immediate colleague, Mr. Tumelo Moalosi for his support and willingness to assist.
- Ms. Corrie Uys, the statistician from CPUT for her assistance in analysing the data.

DEDICATION

Many thanks to the Almighty Lord for giving me the strength and perseverance to complete this thesis and my parents (late William Michael and Wilhelmina Elizabeth Griffiths) for their endless love and sacrifices in giving me the opportunities in life.

I specifically dedicate this thesis to my husband Leroy, children Rudy, Shaun, Lucinda and grandchild Anika for their love and support and being my motivation to complete this journey.

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ABBREVIATIONS AND ACRONYMS

AC:	Attenuation corrected
AC-A:	Application of attenuation correction
ANT:	Anterior
BMI:	Body mass index
CAD:	Coronary artery disease
COR:	Centre of rotation
CS:	Compton scatter
CT:	Computed tomography
CTAC:	Computed tomography attenuation corrected
Cts/s:	Counts per second
ECG:	Electrocardiogram
GSPECT:	Gated single photon emission computed tomography
GLM:	Generalized Linear Model
IAEA:	International Atomic Energy Agency
IHD:	Ischemic heart disease
INF:	Inferior
keV:	Kiloelectron volt
LAD:	Left anterior decending
LCX:	Left circumflex artery
LEHR:	Low energy high resolusion
LV:	Left ventricular
mA:	Milliampere
MBq:	Megabecquerel
MIBI:	Methoxy isobutyl isonitrile
MPI:	Myocardial perfusion imaging
NAC:	Non-attenuation corrected
NEMA:	National Electrical Manufacturers Association
NM:	Nuclear Medicine
OSEM:	Ordered subset expectation maximum
PHA:	Pulse height analyser

PMT:	Photomultiplier tube
QC:	Quality control
QPS:	Quantitative Perfusion Software
RCA:	Right coronary artery
RR:	Resolution recovery
RSS:	Rest summed score
SDS:	Summed difference score
SPECT:	Single photon emission computed tomography
SPSS	Statistical package for social science
SSS:	Summed stress score
Tc-99m:	Technetium-99m
Tl-201	Thallium-201

CHAPTER 1
BACKGROUND AND RATIONALE

1.1 Introduction

Nuclear Medicine (NM) is the administration of radionuclides mainly intravenously or orally into the body but can also be intra-tumoural, subcutaneously or through ventilation for the diagnosis or treatment of diseases. Radionuclides are usually bound to a special compound called a radiopharmaceutical, which concentrates in the organ of interest or part of the body to be examined. The radionuclide decays by emitting gamma rays from the body, and are imaged with a single or dual scintillation detector in a gamma camera. The administered radiopharmaceutical circulates through the body to concentrates in specific areas or organs to provide information about the functions of organs in the body. NM imaging is thus valuable in detecting a range of conditions such as tumours, inflammations, renal function, cerebral blood flow, thyroid function, lung embolism and myocardial perfusion (Cherry *et al*., 2012:1-5). Functional myocardial perfusion is a vital tool for the evaluation and diagnosis of coronary artery disease (CAD), specifically artery stenosis which include ischaemia and infarctions of the myocardium. Myocardial perfusion imaging for CAD can be performed with technetium-99m (Tc-99m) methoxy-isobutyl-isonitrile (MIBI), Tc-99m tetrofosmin or thallium-201 (Tl-201) chloride (Ziessman, 2006:451). When the radionuclide, Tc-99m is bound to six isonitrile (MIBI) ligands it is referred to as Tc-99m sestamibi, which is a cationic complex that accumulates in viable myocardial tissue (Ziessman, 2006:453). After Tc-99m sestamibi is extracted from the coronary circulation, it is bound to intracellular proteins and retained in the cardiac muscle for imaging (Ziessman, 2006:453). Tc-99m sestamibi localises in the liver and maximal accumulation in the gallbladder occurs 60 minutes after intravenous administration, which is then excreted via the hepatobiliary tract into the duodenum (Chamarthy & Travin, 2010, 257).

After intraveneous injection of the radiopharmaceutical, the perfusion as well as the rate of blood flow to the myocardium, can be used as a measure relating the degree of dysfunction to the left ventricle (LV) (Chamarthy & Travin, 2010, 257). The regional myocardial blood flow and myocardial capacity are directly imitated and the uptake in the myocardium is proportional to the pharmaceutical extracted from coronary artery circulation (Chamarthy & Travin, 2010, 257). Therefore, NM imaging provides physiologic information that is different from the anatomic estimation of coronary artery stenosis which is provided by coronary artery angiography. Thus with myocardial perfusion imaging, a decrease in blood flow detected in damaged vessels are due to the narrowing of arteries caused by artery stenosis in the myocardium (Chamarthy & Travin, 2010, 257).

Currently Tc-99m sestamibi is preferred for myocardial perfusion imaging in a routine clinical setting because of the few advantages it has over Tl-201 chloride. The gamma photon of 140 kiloelectron volt (keV) of Tc-99m permits superior image quality than Tl-201, which has a lower photon energy of 81 keV. Tc-99m with its shorter half-life of six hours is beneficial for radiation protection purposes because its fast decay results in less radiation dose and easier decontamination. Tl-201 has more attenuation artefacts on images due to the lower photon instability. Tc-99m sestamibi is much cheaper than Tl-201 and more readily available (Schwaiger, 2020: 110).

During imaging, in cases where perfusion defects (myocardial ischaemia/infarction) exists or are present at the time of imaging, it will reflect as areas of decreased uptake on stress images post-injection of the radiopharmaceutical (Tc-99m sestamibi). When a perfusion defect is present on the stress study, a rest study will be performed. The results of the cardiac stress study are then compared with the rest study. Myocardial ischaemia usually normalises during the resting study, while a persistent defect indicates an infarction (Figure 1.1). Previously various published protocols have used Tc-99m sestamibi in combination with the treadmill or pharmacologic stress to detect ischaemia or infarcts (Chamarthy & Travin, 2010, 257).

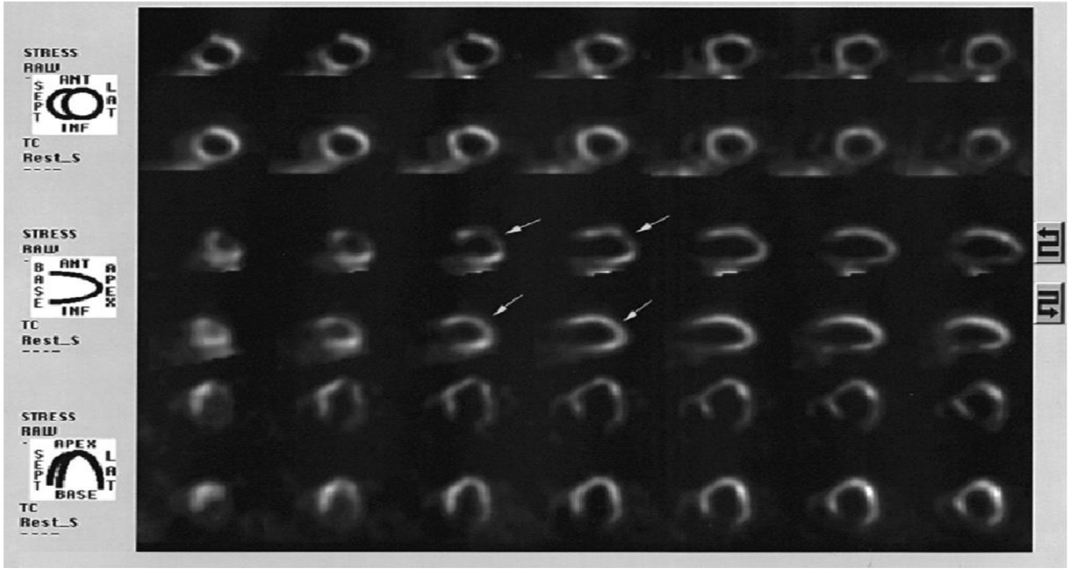

Figure1.1: Combined ischemia and infarction on SPECT images obtained at stress and rest with Tc-99m sestamibi. A large perfusion defect, in the anterior wall on the vertical long axis views (arrows), reveals ischaemia on the rest images and a fixed perfusion defect is present in the inferior wall on the short-axis views (top set of images), which indicates an infarct (Ziessman, 2006:476)

Myocardial perfusion studies consist of a stress and rest study and if performed on the same day, it is a one-day protocol (Figure 1.2). Studies can also be performed on different days which is a two-day protocol (Figure 1.3). The stress study is usually performed first and if the results are normal, there is no need to perform a rest study (International Atomic Energy Agency (IAEA): Nuclear Cardiology, 2016:32-33).

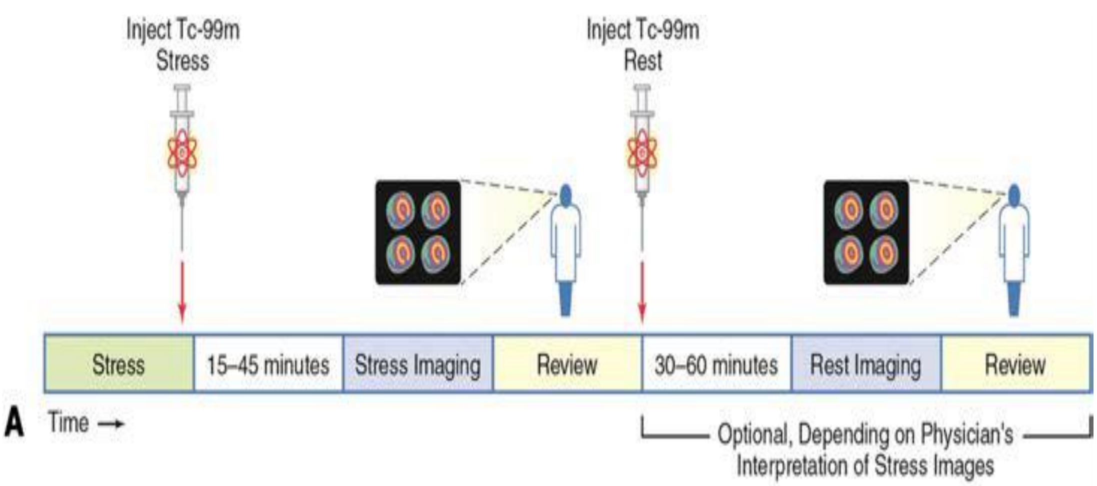

Figure 1.2: Tc-99m sestamibi study performed with one day protocol (IAEA: Nuclear Cardiology, 2016:33)

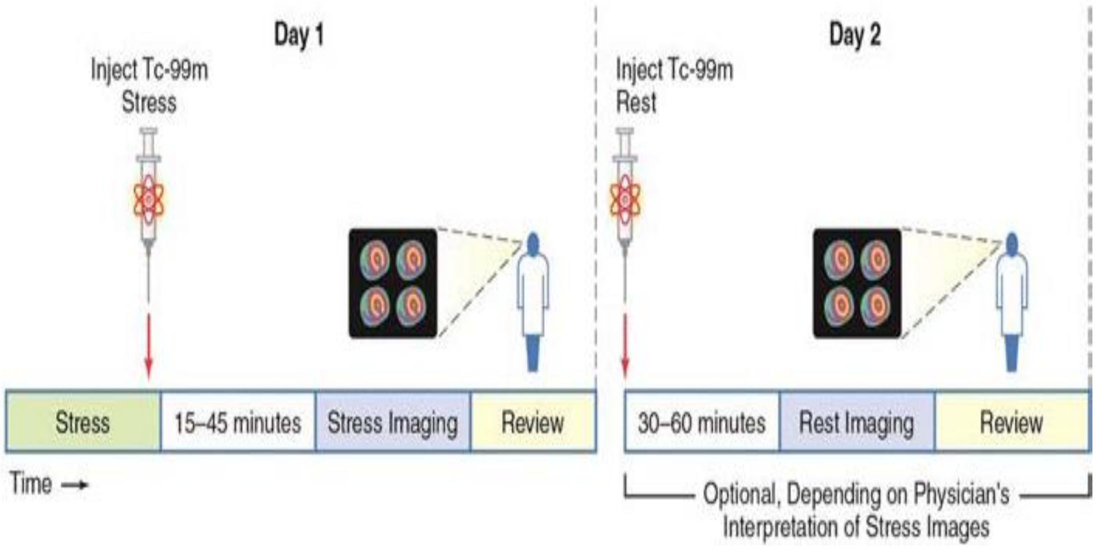

Figure 1.3: Tc-99m sestamibi study performed with two day protocol (IAEA: Nuclear Cardiology, 2016:32)

The stress study is performed by either exercising the patient on the treadmill to reach target heart rate or the patient can be stressed pharmacologically with a dobutamine or dipyridamole intravenous infusion to increase the heart rate. Tc-99m sestamibi is then injected at maximum stress followed by myocardial perfusion imaging on a gamma camera with the electrocardiogram (ECG) integrated. When using a one day protocol, the resting study is usually performed three hours or more after the stress study with a higher dose of the radiopharmaceutical. At the Nuclear Medicine department it is preferred to perform the stress study first and if the outcome is normal, the rest study is not performed as demonstrated in Figure 1.4 (Shackett, 2009:74). For this research study, both protocols either a one or a two day protocol per patient were used.

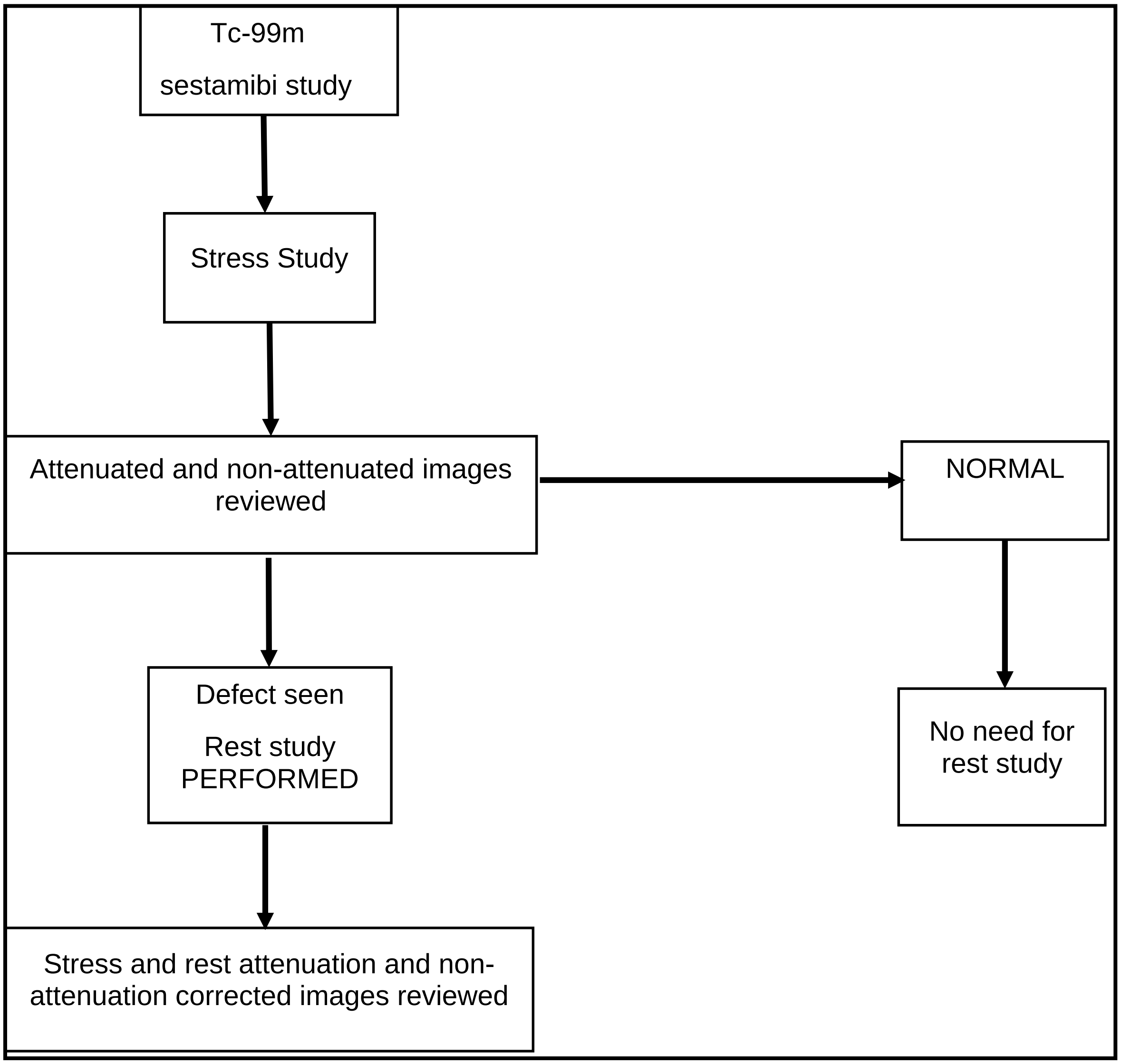

Figure 1.4: Flow diagram of imaging protocol used at the research site

By appropriate adjustment of doses of Tc-99m sestamibi for stress and rest studies, the procedures can be completed on the same day. This allows the total activity for the injection of the entire study to be divided into a third or a quarter for the first study and either two thirds or three quarter for the second study to provide a higher count density when imaged. Retention of activity in the myocardium allows the evaluation to be performed by single photon emission computed tomography (SPECT) techniques (Taylor & Schuster, 2000:3-4).

Gated SPECT (GSPECT) images were performed on a SPECT gamma camera using a dual scintigraphic detector head system with patients connected via leads to an ECG monitor for this research study. ECG gating images should be acquired in a gated mode using a three-lead ECG-trigger to measure the heart rate of the patients for the GSPECT. Eight or 16 frames per cardiac cycles can be used for ECG gating. The 16 frames per cardiac cycle were used for this research study because of improved accuracy to measure the LV ejection fraction, motion and thickening of the myocardial wall or diastolic function (Arumugam *et al*., 2013:820). The GSPECT images are also useful to interpret the findings to differentiate between a reversible defect (ischaemia) or a fixed defect (infarct) (Dvorak *et al*., 2011:2048).

Some gamma cameras have a low-dose computed tomography (CT), for example the gamma cameras used at the research site are equipped with an X-ray tube and X-ray detectors positioned opposite to the tube. The CT images are used for application of attenuation correction (AC-A) during image reconstruction. This option of attenuation correction can assist to improve the images where soft-tissue attenuation can be reduced or eliminated (Ruiz *et al*., 2006:79). A low-dose CT has a function of 2.5 milliamperes (mA) used with the gamma camera in comparison with 50-100 mA used in diagnostic CT and results in a lower radiation dose to the patient (Schillaci, 2005:521). This low-dose CT provides low-resolution images but is useful to adequately locate the anatomical sites of the radiotracer of the SPECT images (Schillaci, 2005:521). Improved image quality is then obtained with low-dose CT based attenuation maps which can eliminate artefacts or false abnormalities and consequently optimise diagnostic evaluation in the myocardium (Dvorak *et al*., 2011:2056). However, AC-A can also introduce artefacts and therefore quality assurance after the reconstruction of images with attenuation correction (AC) is very important. Misregistration of the SPECT and CT images during fusion can also influence the diagnosis. Therefore, to prevent misdiagnosis, the raw images of the SPECT/CT as well the final reconstructed images need to be individually reviewed (Dvorak *et al*., 2011:2057).

MPI can be performed in a supine or a prone position with the arms raised above the patient’s head which allows the gamma camera to rotate easily around the chest and also to avoid attenuation from the patient’s left arm. The SPECT/CT image acquisition takes at least 20 minutes for both stress and rest studies to be completed. The prone position enhances visualisation of the inferior and the septal myocardial walls which is more appropriate to use for men (Iskandrian & Verani, 2003:95; Sayman et al., 2015:268). Women with larger breast will have more attenuation when imaged prone and therefore at research site all the women were scanned in a supine position and men in a prone position. The anterior and lateral myocardial walls are better studied in the supine position (Iskandrian & Verani, 2003:96; Sayman et al., 2015:268).). These soft tissue artefacts (breast and diaphragm attenuation) in the myocardium region can mask perfusion defects that exist and may interfere with visualisation of the myocardial perfusion defects during Tc-99m sestamibi imaging. This may lead to a less accurate diagnosis and in turn result in an incorrect diagnosis that may be the reason for incorrect management of the patients (Iskandrian & Verani, 2003:96; Sayman et al., 2015:268).). Previously when AC-A was not implemented yet, a rest study or repeating of the study was sometimes necessary to clear the origin of these artefacts.

Repeating of studies due to a busy departmental schedule placed a strain on departmental resources and limited time to finish workloads. MPI involves a 15 minute to one hour waiting period after injection for stress and 30 minutes to one hour for rest before imaging; a three hours waiting period between the stress and rest injection and 20 minutes per imaging of a patient. Performing of a rest study with CT further contributes to the patient receiving an additional radiation dose.

It is important for the NM technologist as well as the NM physician involved with the MPI Tc-99m sestamibi to be fully aware of the patients body type and habitus characteristics including the height, weight, gender, chest circumference, breast size and lateral fat on the chest wall of the patient (Crawford & Husain, 2011:48). These factors can influence the counts and attenuation and thus they should to be noted when interpreting the study. Muscle and fat tissue can cause significant attenuation which can influence the myocardium during imaging (Crawford & Husain, 2011:48). When SPECT perfusion myocardial imaging is performed with a 180° orbit, the posterolateral wall of the left ventricle is the most distant from the camera detector. This may result in artifactual abnormalities in the basal half of the posterolateral wall in obese patients (Iskandrian & Verani, 2003:93; Sayman et al., 2015:268).).

The advantages of AC-A has been broadly stipulated in many studies but the question still emerged whether it is essential for myocardial perfusion imaging (Apostolopoulos & Savvopoulos, 2016:89; Denisova & Ansheles, 2018:1-10; Cuocolo, 2011:1887). The reason for this is, although AC-related artefacts can be removed by this technique (AC-A), new false defects may appear and obscure true perfusion abnormalities (Apostolopoulos and Savvopoulos, 2016:82). This may lead to incorrect interpretation of images and affect the patient's results (Apostolopoulos and Savvopoulos, 2016:82). At the research site, a one-day protocol for Tc-99m sestamibi GSPECT stress and rest studies with a CT are already routinely performed with AC-A to images.The current research study was performed to find a decisive answer to uncertainty which still exist whether the routine use of AC-A is necessary on both stress and rest studies and/or adds value to the outcome of patient reports.

1.2 The research problem

SPECT/CT is used for MPI. The CT images are used for application of attenuation correction (AC-A) during image reconstruction. This option of attenuation correction can assist to improve the images where soft-tissue attenuation can be reduced or eliminated (Ruiz *et al*., 2006:79).Breast and diaphragm attenuation may cause anterior and/or inferior artefacts during Tc-99m sestamibi imaging and may interfere with visualisation of the perfusion defects of the myocardium. To minimise these soft-tissue artefacts, low-dose CT attenuation correction is applied to stress studies to improve image quality and eliminate artefacts resulting in optimisation of diagnostic image evaluation of the myocardium (Dvorak *et al*., 2011:2056). AC-A can also introduce artefacts and therefore quality assurance after the reconstruction of images with attenuation correction (AC) is very important. It was suggested that the gated systolic AC images can be used for the interpretation of the apex to mitigate against artefacts created due to AC-A (Apostolopoulos & Savvopoulos, 2016:89-91).

The research site uses preferably one-day MIBI protocol, which has been adjusted for positioning differences, in females a supine position used and in males a prone position is used. AC-A was applied to both stress and rest images where rest studies were indicated. If perfusion defects are not observed on the stress CT attenuated images, the rest study is not performed. This protocol is in line with what has been suggested in the literature (Hesse *et al*., 2005:868). The Tc-99m sestamibi doses are adjusted according to the weight of the patients for both the stress and rest studies. This appropriate adjustment of doses of sestamibi for stress and rest studies permit the procedures to be completed on the same day. Therefore, the total activity for the injection of the entire study is divided into a third or a quarter for the stress study and either two thirds or three quarter for the rest study to provide a higher count density when patients are imaged (Tygerberg Hospital, SOP, 2020).

Although adjustments have been made to improve the image quality in the research site, a question remains whether CT attenuation correction should still be routinely applied to reduce these soft-tissue artefacts. AC-A application in MPI is controversial since it is proposed that false artefacts can be produced in the form of reduction of radioactivity, which can mask real perfusion defects and may lead to uncertainties when interpreting the results (Apostolopoulos & Savvopoulos, 2016:89-91; Denisova & Ansheles, 2018:1-10; Cuocolo, 2011:1887). This study therefore aims to provide more information to solve this controversy.

1.3 Aim of the study

To determine whether the application of attenuation correction maps obtained from low-dose CT will improve image quality or reduce soft tissue artefacts in Tc-99m sestamibi GSPECT myocardial perfusion imaging.

1.4 Objectives of the study

Compare the image quality scores of non-attenuation corrected (NAC) and computed tomography attenuation corrected (CTAC) images when stress was induced physically and pharmacologically to patients. Imaging is performed in the supine and prone positions. Images acquired under physical stress and pharmacological stress were further analysed for the outcome of AC-A of the stress and rest studies in the supine and prone positions.

- Compare the image quality scores of NAC and CTAC images for rest study obtained from patients, imaged in the supine and prone positions

- Determine the influence of the relative factors such as stress, gender, age, weight and height on the CTAC images

1.5 Research Question

Will the use of CTAC maps improve image quality or reduce soft tissue artefacts during the processing of Tc-99m sestamibi GSPECT MPI?

1.6 Significance of the study

The application of CTAC in myocardial perfusion studies can prevent the reporting of false negatives which can occur due to soft tissue artefacts. AC-A to the stress SPECT images can consequently eliminate the need for the rest study or the CT associated with the rest study.The performing of the rest study with an added CT, contributes to an additional radiation dose for the patient. If the findings of this study are statistically significant with improved image quality observed with AC-A, recommendations will be made to include the changes on the routine protocol of SPECT/CT studies at research site regarding patients approved for Tc-99m sestamibi myocardial perfusion studies.

1.7 Presentation of chapters

Chapter 1 presented the the backround to the study as well as the aim, objetctives and rationale for the study. Chapter 2 will outline the literature which discusses the evaluation of CAD using AC-A, the different cardiac stress tests and the patient preparation for MPI. Thereafter the AC-A to SPECT/CT images for breast and diaphragm attenuation. Lastly the quality improvement for MPI and the controversy of the using of AC-A. In Chapter 3 the methods and materials used for this research study will be broadly discussed. The last chapters (3 and 4) presented the results and then the discussion about the results. Chapter 5 provides the conclusion and recommendations for this researh study.

1.8 Conclusion

This chapter presented the the backround to the study as well as the aim, objetctives and rationale for the study. The aim of this study is to determine whether the application of attenuation correction maps obtained from low-dose CT will improve image quality or reduce soft tissue artefacts in Tc-99m sestamibi GSPECT myocardial perfusion imaging. The study will discuss AC-A in MPI and determine whether hybrid SPECT/CT will improve the quality of the images and reduce soft tissue artefacts when attenuation correction maps in stress and rest studies are performed. The next chapter (chapter 2) will aim to provide the reader with the literature background for this study.

CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

The literature review was conducted using Sunsearch associated with Stellenbosch University library system using PubMed and Scopus as search engines. The search included all peer-reviewed articles using the keywords “myocardial perfusion imaging”, “Tc-99m MIBI”, “SPECT/CT” and “attenuation correction”. Nuclear Medicine handbooks were also consulted. Mendeley was used for the referencing. In this chapter, the literature review is provided to inform the reader of all the current AC-A performed on MPI and the different correction factors applied to the image data as the practise is at the moment.This chapter provides the background to the application of attenuatiion correction in MPI studies. The procedures for inducing physical and pharmacological stress, as well as the imaging procedure is discussed.

2.2 Evaluation of coronary artery disease using AC-A for myocardial perfusion imaging

A cardiologist usually refers patients with CAD to the NM department for a Tc-99m sestamibi study. Mainly the study evaluates ischaemia and infarctions caused by coronary artery stenosis (Shackett, 2009:72; Taylor & Schuster, 2000:1).

Stress perfusion scintigraphy (imaging) with SPECT provides valuable information on the degree and severity of CAD for risks assessment, prognosis and better patient management with high accuracy (Ziessman, 2006:458). In the resting state of a patient’s heart, the oxygen demand is low and blood flow adequate, but when the patient exercises the demand increases on the heart with the higher blood flow. Therefore, when patients are resting, most coronary artery stenosis will not be associated with a perfusion abnormality but when exercising, a stenosis in the myocardium causes a reduced blood flow in that region and becomes ischemic (Ziessman, 2006:459). On a scintigraphic image, this ischemic region of the heart will reflect as a photopenic defect, surround by normal blood flow (Ziessman, 2006:459).

NM imaging provides more information regarding physiological activity and processes due to the fact that the biodistribution of a radiopharmaceutical is imaged non-invasively and this is changed by the presence or absence of disease. However, with NM SPECT imaging the visualisation of anatomical landmarks lacks whilst a CT scan provides the anatomical information. The combination of SPECT/CT provide a valuable tool for NM physicians to integrate anatomical and physiological data with the attenuation correction of the registered SPECT and CT datasets. This increases the level of confidence of the NM physicians being able to differentiate between normal and abnormal uptake in the heart (Patton & Turkington, 2008:1).

In a study by Tootell *et al*. (2012: 1122) the clinical evaluation of the possibility for incidental pathology detection with CTAC for MPI was investigated. The CT component of SPECT/CT systems are usually of a low dose radiation, but with advance technology, newer hybrid systems are identically produced as a diagnostic CT scanner (Tootel *et al*., 2012: 1122). The CTAC for MPI is generally of low quality with limited range CT images of the chest. The chest CT includes partly the mediastinum, lung fields and surrounding soft tissues and these images were reported by the NM physicians. The question addressed in their study was whether the low-resolution CTAC images should be interpreted for incidental extra-cardiac disease in these reports. The conclusion was drawn that a multidisciplinary team involving radiology in the final report is necessary (Tootel *et al*., 2012: 1126). At the research site, a radiologist is always available when CT studies are reported or enquiries on these images arise.

According to Genovesi *et al*. (2011), attenuation artefacts can be corrected with GSPECT or CTAC. The CT- based AC-A or GSPECT fast imaging can improve the specificity in the evaluation of CAD in overweight men without affecting the diagnostic sensitivity of the procedure. The fast imaging is when the imaging started within 15 minutes after the stress injection and the second injection is given immediately after completion of the stress study. The conclusion drawn in this study was to use the AC-A on patients with a body mass index (BMI) higher than 27, which was statistically demonstrated in this subgroup of men. A limitation was that the number of overweight women for this study was too small to draw a significant conclusion. For the other patients with a lower BMI, a standard GSPECT study should be significant. This can avoid unnecessary CT scans to reduce the total effective dose to the patients (Genovesi *et al*., 2011:1890). In the current research study, 59% of the population is women and 41% is men with different BMI. The mean BMI for males was 29 kg/m^2 and for women 30 kg/m^2. The BMI was calculated using the weight and height (length) of patients. The equation below was used:

$$BMI = Weight\ (kg)/length\ (m)^2$$

Ou *et al*. (2013), studied 935 patients that had SPECT and CTAC to evaluate the diagnostic value to improve the risk stratification accuracy of MPI. Images with and without AC were rated with a summed stress score (SSS). Results showed AC MPI presented with decreased defects in SSS compared to NAC images. The conclusion was drawn that CTAC may decrease the number of false-positive scan results and can provide valuable information towards patient treatment outcome. The limitation of the study was the absence of an evaluation for the SSS differences on patients with normal perfusion images who did not undertake rest perfusion imaging, to avoid extra radiation exposure (Ou *et al*., 2013:496-499). In the current investigation the patient data on both the stress and the rest studies and AC-A to images were evaluated.

2.3 Cardiac stress tests

Before the patients are imaged they have to be stressed either physically or pharmacologically. Patients are examined in a room that have an availiable treadmill. All the patients for the Tc-99m sestamibi stress studies are connected to a 10-lead ECG monitor via electrodes on the chest for either exercise or pharmacological stress testing. The blood pressure of patients is monitored and recorded in the rest condition before commencing stressing of the heart as well as throughout the procedure in the exercise room (Lomsky *et al*., 2008:169; Shackett, 2009:73). The patient with limited exercise capacity due to medical problems, such as pulmonary disease or lower extremity problems are pharmacologically stressed (Biersack & Freeman, 2007:99). At the research site, physical exercise is the standard method, however pharmacological stress with persantine was performed mostly and to lesser demand dobutamine.

2.3.1 Physical stress test

During physical stress, the an increased heart rate is induced via physical excercise. The patient is positioned on a treadmill with ECG electrodes connected to the monitor for evaluating the heart rate. A NM physician is present while the patient is exercising, to monitor the patient closely for heart rate, blood pressure and ECG changes. The exercise on the treadmill is performed according to the Bruce protocol (Shackett, 2009:73). The Bruce protocol prescribes age and gender corrected values for a normal exercise heart rate between 85 to 100% of 220, minus the age of the patient (Lomsky *et al*., 2008:169). Once the patient reaches maximum or target heart rate according to the Bruce protocol the Tc-99m sestamibi is injected by the NM physician. Exercise will continue after injection for about 1-2 minutes to ensure maximum perfusion of the radiopharmaceutical to the myocardium. The patient will then be handled further as described in section 2.4.

2.3.2 Pharmacologic stress test

Pharmacological stress test is once a pharmaceutical is used to induce an increased heart rate in the patient when physical stress is contraindicated. The three pharmacologic agents used are either dipyridamole (Persantine), dobutamine or adenosine (Biersack & Freeman, 2007:100). The selected agents are administered to the patient via an intravenous infusion connected to a pump with a NM physician always present. Persantine and adenosine are vasodilators, which causes increase blood flow in normal coronary arteries and less in arteries with stenosis (Biersack & Freeman, 2007:99-102). The side effects are chest pain and ECG changes. Persantine side effects (dizziness, vomiting, diarrhea and headaches) can be reversed with an injection of aminophylline (Biersack & Freeman, 2007: 100). If adenosine is used, the infusion can be stopped when side effects occur (chest discomfort, labored breathing, dizziness and tightness in chest). Dobutamine is used as an alternative in patients with contraindications, like asthma or when caffeine was ingested on the day of testing. It does not only increase blood flow but also heart rate and blood pressure, which may cause true ischaemia (myocardial infarction). The common side effects of dobutamine are chest pain and arrhythmias (irregular heart rate) (Biersack & Freeman, 2007:99-102). The Bruce protocol is applied when the target heart rate is reached (Shackett, 2009:73). After the stress test and radiopharmaceutical administration is completed, the patient will be handled as described in section 2.4 before imaging.

2.4 Radiopharmaceutical (Tc-99m sestamibi)

The pharmaceutical MIBI, a manufacturer kit, is radiolabelled with the radionuclide, Tc-99m in a radiopharmacy laboratory under sterile conditions. This radiopharmaceutical (Tc-99m sestamibi) is administered via an intravenous line in accordance to radiation protection practices. The maximum dose is 1600 megabecquerels (MBq) for a one-day stress/rest study (Hesse *et al*., 2005:853; Arumugam *et al*., 2012: 818). As mentioned in chapter 1, the activity is divided into a third or a quarter for the first study and either two thirds or three quarter for the second study to provide a higher count density. For example: the first study's activity can be 400 MBq and 1200 MBq for the second study. This is to ensure that the residual activity of the first study does not influence the MPI quality of the second study (Hesse *et al*., 2005:853; Arumugam *et al*., 2012: 818). For the two-day protocol the injected activity is usually the same amount between 550 to 800 MBq per study but it is not always convenient for the patients to attend two days. The activity for administration is increased on a graded basis according to the weight of the patient as stipulated in Table 3.1 (Hesse *et al*., 2005:853; Arumugam *et al*., 2012: 819).

2.5 Patient preparation

After the stress procedure, the patient has to wait for 15-60 minutes before imaging. This allows hepatobiliary clearance, which can potentially influence the images by increasing the backgroud activity. A longer resting status is required for pharmacological stress because of higher liver uptake relative to exercising the patient (Arumugam *et al*., 2013:819). For quicker clearance from the liver and gallbladder, a fatty meal is offered to the patient before imaging (Arumugam *et al*., 2013:819). At research site, the patient is given chocolate, butter and jam sandwich, and 500 ml of liquids before imaging. A full stomach may also push the intestine away from the inferior myocardium and avoid artefacts on the images (Thientunjakit *etal*., 2017: 268).

2.5.1 Patient positioning

When the waiting period is completed, the patient is ready to be imaged. The protocol of research study required female patients to be imaged in a supine position and the male patients in a prone position. A study by Jeanguillaume *et al*. (1997) assessed the effects of prone and supine positioning to validate the outcome of a change in cardiac axis on the interpretation of Tc-99m sestamibi myocardial SPECT images but without AC-A (Sayman et al., 2015:269). They found the change in the cardiac axis with the different positions can cause a change in the photon attenuation in the heart. Also, the prone position enhances visualisation of the inferior and the septal wall while the anterior and lateral walls are better studied in the supine position (Jeanguillaume *et al*., 1997:1161; Sayman et al., 2015:269). Their images were acquired in both positions to allow the best assessment of the walls (Jeanguillaume *et al*., 1997:1165; Sayman et al., 2015:269). At the current research site, the female study participants were imaged in the supine position and the men in the prone position and AC-A was applied to all the data sets.

2.5.2 Biological factors of patients

The NM technologist as well as the NM physician involved with the study, must be fully aware of the patients' body type and habitus characteristics including the height, weight, gender, chest circumference, breast size and lateral fat on the chest wall of the patient (Crawford & Husain, 2011:48). These factors can influence the count density and attenuation of the nuclear photons and thus they should be noted when interpreting the study. Muscle and fat tissue can cause significant attenuation which influences the myocardium during imaging (Crawford & Husain, 2011:48). The patient data for current research study were categorized for the independent variables to integrate gender, age, weight and height (Addendum A).

Ruiz *et al*. (2007) determined that AC-A to SPECT stress myocardial perfusion studies is time and cost-effective if a rest study is not performed. Their results found that the benefits of AC-A are independent of body mass, clinical history or age. The benefit seemed to be better in men with a greater reduction in false positives after AC-A (Ruiz *et al*., 2007:80). The CTAC is mostly useful in males and obese patients to improve the specificity of MPI in the inferior, inferoseptal and inferolateral wall (Apostolopoulos and Savvopoulos, 2016:91). When SPECT perfusion myocardial imaging is performed with a 180° orbit, the posterolateral wall of the left ventricle is the most distant from the camera detector (Iskandrian & Verani, 2003:93; Sayman et al., 2015:268).). This may also result in artefactual abnormalities in the basal half of the posterolateral wall in obese patients (Iskandrian & Verani, 2003:93). Therefore, the application of AC to images may also be of value to reduce soft tissue artefacts.

2.6 Attenuation correction application to SPECT/CT images

Attenuation occurs when radiation passes through the body and interacts with matter (Hesse *et al*., 2005:880). Different tissue densities have different attenuation coefficients. For gamma-rays of 140 keV, the linear attenuation coefficient is 0.155 cm^{-1} in soft tissue and 0.25 cm^{-1} in bone (Cherry *et al*., 2012:292). One method to compensate for all the attenuation coefficients is to use 2 detectors and to calculate the geometric mean and correcting for the total thickness (D), as seen in figure 2.1 (Cherry *et al*., 2012:292).

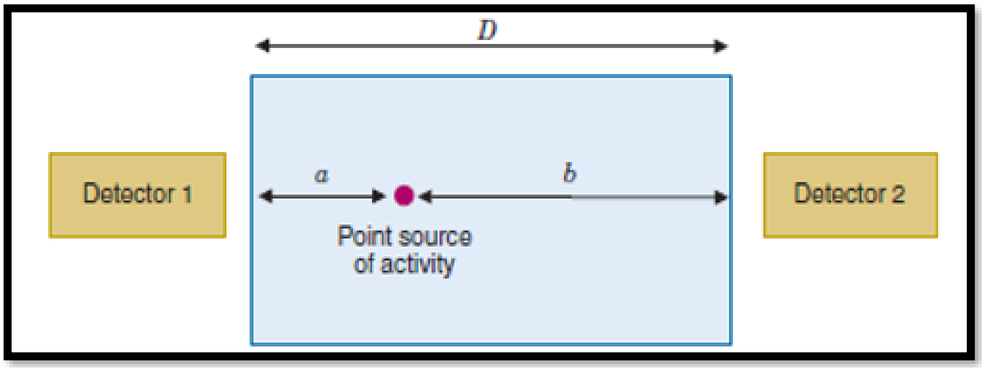

Figure 2.1: Point source of activity within an attenuating medium of thickness D with the attenuation compensates for the geometric or arithmetic mean and a correction for total tissue thickness, (D) (Cherry *et al*., 2012: 292)

According to Hesse *et al*. (2005), the breast and diaphragm cause attenuation of the radiation and can therefore lead to a non-uniform decrease of the activity in the myocardium and may result in artefacts of the images (Hesse *et al*., 2005:880). Artefacts are a major limiting factor for the specificity of SPECT for myocardial perfusion defects. The attenuation characteristics of the tissue imaged and the energy of the radiotracer has an impact on the quality of the final reconstructed images (Dvorak *et al*., 2011:2051). This can be improved by using a reconstruction algorithm that includes a measurement of non-uniform distributions of attenuation coefficients (Tsui *et al*., 1989:497). In older methods, the correction for photon attenuation was assuming that the attenuation coefficient distribution was homogenous, but this was inadequate because the chest cardiac region consists of tissues that have different attenuation coefficients (Tsui *et al*., 1989:497).

A novice way to correct for attenuation is to use of an external transmission radionuclide line source (e.g. gadolinium-153) or a collimated flood source (eg. cobalt-57) with a different emission energy from Tc-99m to allow simultanuous imaging with the two emission energies (Cherry *et al*., 2012:294). According to Ruiz *et al*. (2007), complications with external radioactive sources may occur due to the following:

- truncation of the beam for the fixed linear source,
- the insufficient energy of the sources and also
- the differences between the energy windows of emission and transmission photons.

This may lead to artefacts and misalignment between the emission and transmission data which can also be challenging.

The introduction of SPECT/CT imaging allowed a more accurate method for AC-A (Ruiz *et al*., 2007:78). The gamma camera is combined with a CT (hybrid system). Both data sets, the SPECT images and CT images are acquired in a single imaging session with either one first. The anatomic information delivered by the CT is also helpful with the interpretation of SPECT data (Cherry *et al*., 2012:345). To reduce the number of false positives with myocardial perfusion SPECT the use of AC-A shows improved test specificity (Ruiz *et al*., 2007:78).

SPECT imaging with AC-A represents myocardial perfusion more accurately than NAC images (Fricke *et al*., 2005:741). The AC-A can enhance image quality and improve the sensitivity and specificity of myocardial imaging when processing the data (Dvorak *et al*., 2011:2042). The advantage of AC-A is seen mainly in the inferior wall (Fricke *et al*., 2005:741). Artefacts, which are produced by soft tissue attenuation, can be removed, or reduced on the AC images. Therefore, the need for good quality assurance is essential by reviewing the raw SPECT-CT image data as well as the final reconstructed images during the reporting of images (Dvorak *et al*., 2011:2056-2057).

2.6.1 Attenuation correction application and the need for a rest study

Breast and diaphragm attenuation may cause anterior and/or inferior artefacts during Tc-99m sestamibi imaging and to minimise these soft-tissue artefacts, low-dose CT attenuation correction can be applied to images (Dvorak *et al*., 2011:2042). If perfusion defects are not observed on the stress CT attenuated images, the rest study is not performed. The rest studies are necessary to be performed when a combination of perfusion defects and attenuation defects or true perfusion defects are observed on the stress images (Hesse *et al*., 2005:868).

A retrospective study was done by Ruiz *et al*. (2007) to validate the AC-A techniques with SPECT to post-stress myocardial perfusion studies in patients with ischemic heart disease (IHD). With the AC-A added to the stress study, the authors aimed to reduce the acquisition time and costs in order eliminate the need for a rest study. The results of the MPI AC-A stress studies tests led to excluding 42.9% of patients for a rest study without changing the diagnostic purpose of the study. A conclusion was drawn that the studies could help to eliminate the need for a rest study which prove to be time and cost-effective. These results were more frequently seen in male patients but, it was not dependant on body mass, pre-test probability of ischaemic heart disease (IHD), cardiac risks factors or age. It emphasized the importance for each centre to evaluate its systems because of different AC-A systems, radiotracers, imaging protocols and especially processing protocols (Ruiz *et al*., 2007: 77-87).

Trägårdh *et al*. (2013) evaluated whether the adding of AC images in MPI will reduce the need for a rest study. The gated stress studies and non-gated rest studies were performed in a supine position and with two-day protocols. Rest studies were only scheduled if stress findings were not normal after AC-A was applied to images. The results showed that no rest study required, was substantially higher with NAC and AC than with the NC only on images. In 50% of cases with NAC and NAC+AC of the stress studies no rest study was required but in 31% of the patients the rest studies were required. Trägårdh *et al*. (2013) concluded that 17% of the study population did not require a rest study when AC-A was added to images.

The protocol for the current research study used the patient data of stress and rest image sets with NAC and AC applied to all the studies. The NM physicians evaluated the anterior and inferior walls of the myocardium for both stress and rest, NAC and AC images separately. First the anterior and inferior stress NAC- and then the AC images are reviewed. Then the stress and rest AC images were reviewed and a conclusion of improvement or no improvement was given on whether AC-A changes the outcome of the reports.

2.6.2 Breast attenuation

Breast attenuation artefacts is a regular problem in women who undertake cardiac imaging (Taylor & Schuster, 2000:9). The defects depend on the thickness, density and the position of the breast tissue (Taylor & Schuster, 2000:9). It is preferable to image the women with the bra off during the stress and the rest studies to minimize the thickness of the breast (Iskandrian & Verani, 2003:95; Sayman *et al*., 2015:268).). Breast artefacts commonly appear in the anterior, anterolateral and anteroseptal of the cardiac wall, as shown in Figures 2.2 and 2.3 (Ziessman, 2006:471). However, it is vital for the NM technologists and the interpreting NM physicians to become skilled to distinguish between these attenuation artefacts and minimise the effects where possible (Crawford & Husain, 2011:48).

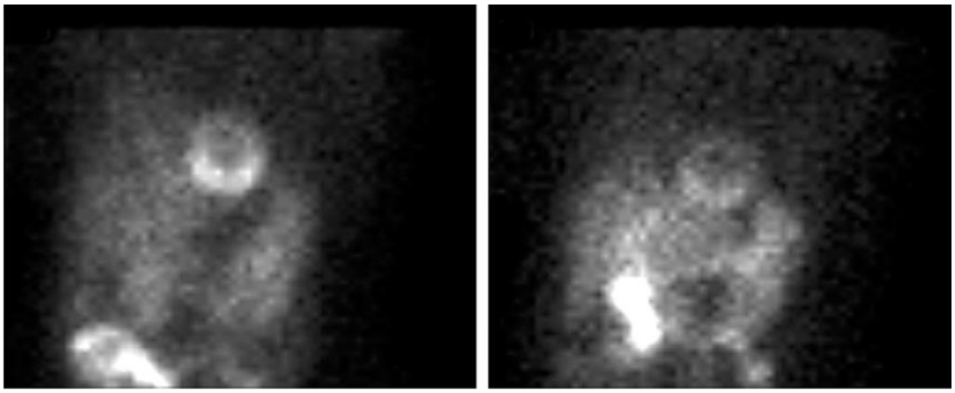

Figure 2.2: Breast attenuation. Single raw data acquisition projection of a cinematic display at stress (left) and rest (right) illustrates the artefact produced by breast attenuation with decreased activity in the upper portion of the heart (Ziessman, 2006:471)

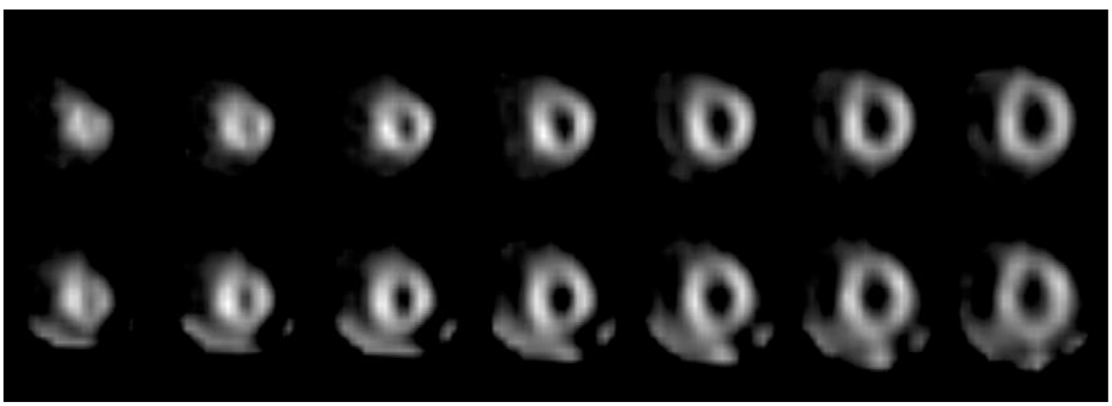

Figure 2.3: Breast attenuation. The SPECT images of the same patient (above) show moderate anterior wall attenuation and are the best demonstrated on this short-axis views (Ziessman, 2006:471)

2.6.3 Diaphragm attenuation

Attenuation of the diaphragm will differ from the stress to the rest study as the diaphragm height changes (Iskandrian & Verani, 2003:93; Sayman *et al*., 2015:268).). Diaphragm attenuation is more commonly seen in male patients, however, muscles in the chest and breast attenuation in males can also be a problem if they are different in tissue mass than the norm (Figure 2.4). In the left hemidiaphragm attenuation normally creates a fixed inferior or inferolateral defect. Imaging in the prone position has been demonstrated to minimise diaphragmatic attenuation artefacts (Iskandrian & Verani, 2003:95; Sayman et al., 2015:268).).

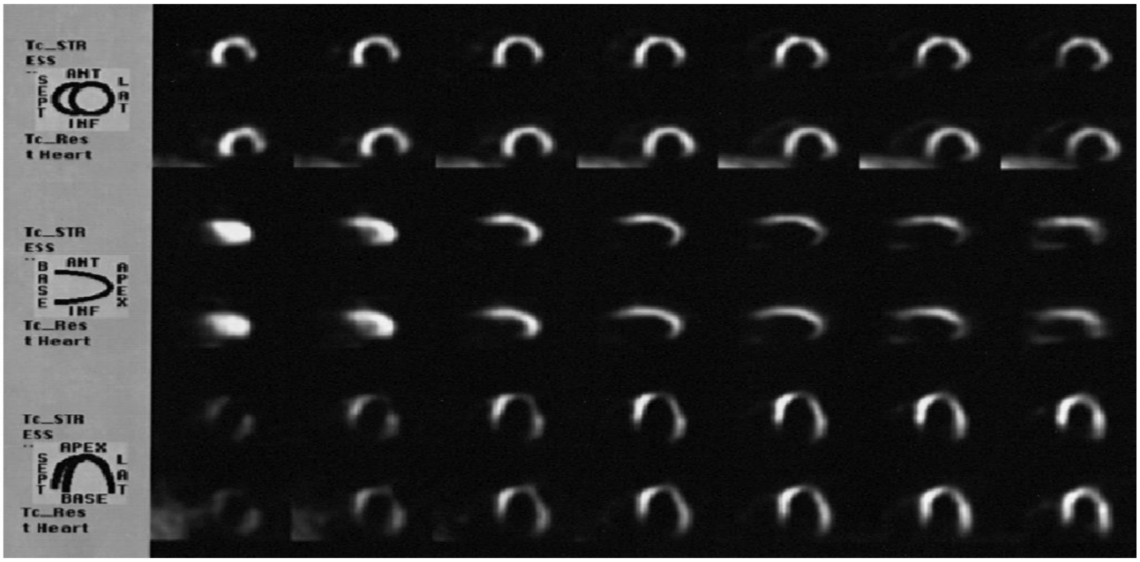

Figure 2.4: Large inferior wall infarction on SPECT images obtained with stress and rest Tc-99m sestamibi study. The large, fixed defect involving the inferior wall of the heart demonstrates the best on the short-axis and vertical long-axis views (Ziessman, 2006:476)

In the prone position, the arms are crossed under the head and therefore shifts the heart upwards and pushes the diaphragm down, which may cause less inferior wall attenuation (Crawford & Husain, 2011:49).

A study on the value of AC-A in myocardial perfusion SPECT/CT on the inferior wall according to BMI was evaluated by Tamam *et al*. (2016). An increased attenuation of the inferior wall was detected in male patients and higher BMI (≥ 30). All patients were imaged in the supine position. The reconstruction with the ordered subset expectation maximum (OSEM) iterative method improved the diagnostic accuracy of the stress only SPECT study significantly in obese patients. The authors found that the method of iterative reconstruction is helpful in differentiating myocardial ischaemia from diaphragm attenuation. Thus, the subsequent rest imaging can be eliminated which reduces radiation dose and unnecessary imaging time. The research site is applying iterative reconstruction with OSEM for Tc-99m sestamibi images which can also be of benefit when interpreting the stress studies (Tamam *et al*., 2016:22).

2.7 Image quality improvements of myocardial images

Quality control reviews all the factors that could influence the image quality and results of the patient's MPI. Quality control ensures that NM equipment is functioning up to standard and the described QC tests is designed to detect issues with equipment before it influences a MPI procedure. The equipment goes through a detailed QC procedure, then the patient's quality of injection is evaluated and finally image quality QC is performed (EANM, 2017:7).

2.7.1 Quality control

Equipment quality control

An important factor to be considered with SPECT/CT imaging, is the QC of the gamma camera and the CT component. The QC tests are necessary to identify artifacts on the SPECT/CT equipment which may interfere with the image quality. The tests should be performed according to the manufacturer recommendations and National Electrical Manufacturers Association (NEMA) standards for QC on SPECT instrumentation (Burell & Macdonald, 2006:200).

The QC tests are: system uniformity, sensitivity and centre of rotation (COR). Extrinsic uniformity is performed to test the response of gamma camera photomultiplier tubes across the entire field of view when exposed to a uniform activity of a Co-57 flood source or Tc-99m point source (Hesse *et al*., 2005:870). According to the NEMA standards, the uniformity for SPECT systems should be equal or less than 5% the reference value. The test for sensitivity of multiple detector cameras is to check the count rate response of the gamma camera. The double head detector systems requires that their sensitivity should not to differ by more than 5%. The test of COR is performed to check the centre of rotation offset, the alignment of Y-axis of the camera and the head tilt in reference of the axis of rotation.The results limit of COR for each detector should not be more than 0.5 pixel per 128x128 matrix size over 360º of camera rotation. Misregistration due to errors in COR will cause a definite artefact such as a distorted anatomical structure or a large area of decreased activity (Hesse *et al*., 2005:871).

Patient quality control

An infiltrated injection may also result in a poor quality study because less of the radiopharmaceutical wil be taken up in the myocardium (Burrell, 2006:195). As part of the protocol used for this research, a static view of the injection site is obtained with every patient. If there is an infiltration of the injection, a calculation is performed of how much is injected. Dependent on the percentage of radioactivity in injection site a protocol is followed: hot compression is placed on the misinjection site, a longer waiting period before scanning is recommended or depending on the type of study a percentage higher than 25% the study will be cancelled (Tygerberg Hospital, Nuclear Medicine departmental protocol, based on international guidelines).

After the stress procedure, the patient has to wait for 30-60 minutes before imaging. This allows hepatobiliary clearance, which can potentially influence the images. A longer resting status is required for pharmacological stress because of higher liver uptake as in the case of physical stress to the patient (Arumugam et al., 2013:819). For quicker clearance from the liver and gallbladder, a fatty meal is offered to the patient before imaging (Arumugam et al., 2013:819). In the research site, the patient is given chocolate, a butter and jam sandwich, and 500 ml of liquids before imaging (Thientunjakit *et al*., 2017: 268). A full stomach may also push the intestine away from the inferior myocardium to avoid artefacts and to improve image quality (Thientunjakit *et al*., 2017: 268).

Image quality control

To ensure that high diagnostic quality in myocardial perfusion studies is reached with imaging, close attention needs to be given to all aspects of the acquisition protocols, processing techniques and image interpretation (Dvorak, 2011:2041). The British Nuclear Cardiac Society published a report in the Nuclear Medicine Communications, setting out different factors affecting the quality of imaging studies (Arumugan et al., 2013:824) in Table 2.1:

Table 2.1 Factors affecting the quality of studies (Arumugan *et al*., 2013:824)

Phase of study	Factors	How does it affect image quality and how is it corrected
Stress	Incorrect agent or protocol	Inadequate stress impacts the sensitivity of this diagnostic technique to access CAD.
	Submaximal stress	
	Medication antagonists if for diagnostic purpose	
Radiopharmaceutical administration	Inadequate activity for patient weight	Issues with radiopharmaceutical delivery degrades the image quality as this influences the counts captured. This decreases diagnostic accuracy and sensitivity of this technique.
	Misadministration e.g., extravascular injection	
Image acquisition	Inadequate camera positioning or orbit selection	Any substandard parameters influence the image quality and indirectly the sensitivity of this technique.
	Inappropriate energy window selection or collimation	
	Patient comfort and motion	
	External attenuating objects	
	Incorrect ECG gating	
Image reconstruction and processing	Inappropriate reconstruction techniques	Inappropriate filtering during tomographic reconstruction degrades the image quality.
	Inaccurate definition of the long axis of LV	
Image display	Inappropriate colour- or grey scale or incorrect widowing	The diagnostic accuracy is influences by inappropriate greyscale.
	Comparison of non-equivalent tomograms	

2.7.2 Compton scatter correction

Compton scatter (CS) happens when the photons emitted from the radionuclide in the patient, interacts with the other atoms in the body, change direction and reduces the initial energy of the photons (Hesse *et al*., 2005:880). They reach the detector and cause a reduction in image quality or contrast which causes artefacts during the reconstruction of images (Hesse *et al*., 2005:880). Hepatic activity in cardiac SPECT MPI studies makes it difficult to interpret the images of the inferior wall of the myocardium due to scattered radiation and creation of artefacts (Ruiz *et al*., 2007:81). In the case of extracardiac hepatic activity it is generally necessary to wait longer before imaging (Ruiz *et al*., 2007:81).

Different ways to compensate for scatter of the emission data are described in the literature. For example, application of an additional energy window to the pulse height spectrum on gamma camera protocol for the scatter component. This will later be subtracted by simply reducing the energy window of the main photo peak to minimize the acquisition of the low energy scattered photons. This method has the advantage of distracting the scatter window but also have the disadvantage, because the use of an additional energy window or reduction of primary energy window increases the noise in the image data and therefore reduce image quality. The method used for this research study was to model the scattered photons based on the emission data to determine an effective attenuation coefficient during the processing of data. The Monte Carlo Scatter correction incorporated into the OSEM iterative reconstruction software was used. This modelling method does not induce noise and is possibly the best option (Cherry *et al*., 2012:296-299). To increase the diagnostic accuracy of image quality with the reconstruction of images, attenuation correction should be incorporated with a scatter correction and not applied alone (Arumugam *et al*., 2013: 820).

2.7.3 Motion correction

The motion of patients during SPECT acquisition is a major problem. The best way to prevent motion artifact can be achieved by convincing the patient not to move during the SPECT acquisition and to make sure the patient is as comfortable as possible (Roach & Parker, 1993). An uncomfortable patient will tend to move. When the patient is in a supine position, the knees are raised with aids such as sponges or a pillow to support the lower back and to keep patient stable (Hesse *et al*., 2005:869). A competent NM technologist is very helpful and by thoroughly explaining the procedure to the patient, helps to reduce excessive movement during the scan (Iskandrian & Verani, 2003:93).

When images show significant patient movement it should be repeated because of the movement of patients, degrade image quality. The raw data can be reviewed by displaying image projections in a cinematic rotating presentation, showed in Figure 2.5 (Ziessman, 2006:467).

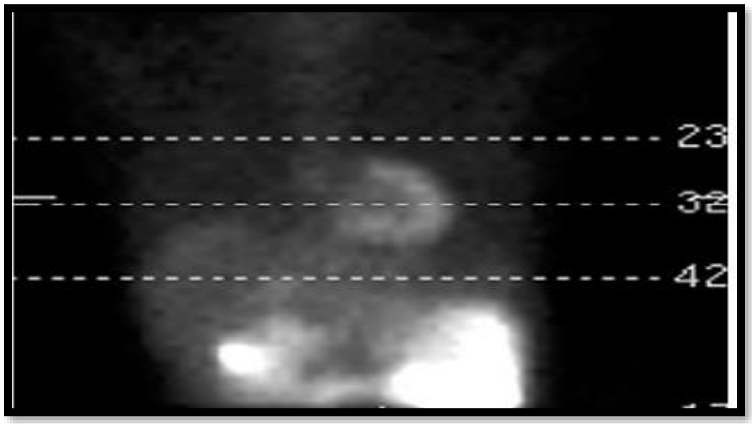

Figure 2.5: Display of image projections (Ziessman, 2006: 467)

Sinograms and linograms display motion and is used to see if there is any movement on images of patients when reporting takes place. With a sinogram which was used for images of research study, each image projection is vertically stacked and compressed. A notable motion will show a break in the sinogram (Figure 2.6) (Ziessman, 2006:467). In some cases, if movement is minimal, motion correction can be applied. Motion correction can only correct movement in the vertical axis but with movement greater than 2-pixel deviation, the study should be reacquired (Ziessman, 2006:467).

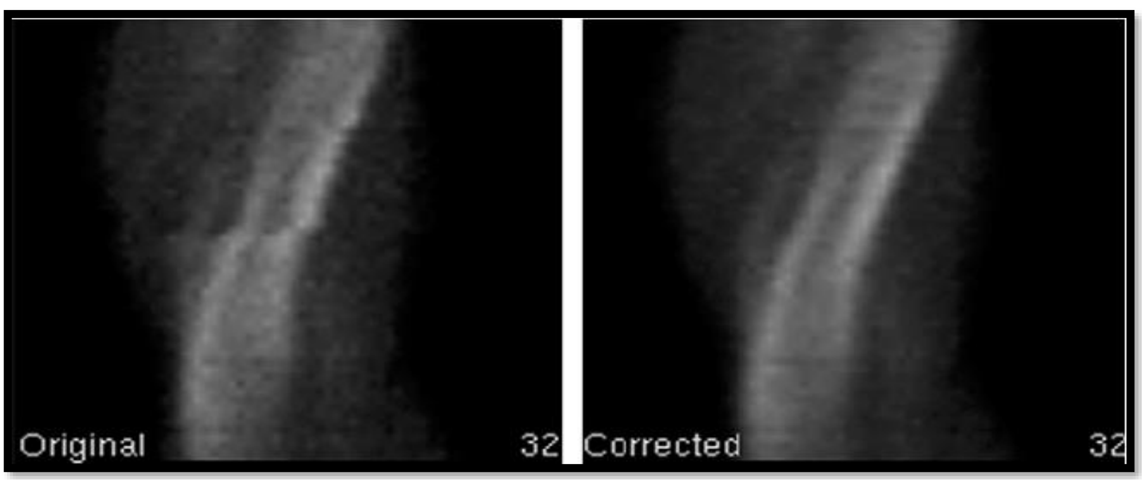

Figure 2.6: Sinogram to detect for motion. Projection images are stacked vertically with a horizontal break in the mid-sinogram (left). The motion-corrected (right) (Ziessman, 2006:467)

The position of the artifact will depend on the direction and time of motion during acquisition and it will be different whether it happened during the middle of acquisition or at the beginning or end (Burerel, 2006:197). After the acquisition is completed and before reconstruction, the acquisition data should be inspected for motion (Burerel, 2006:197). Artefacts in patients with motion defects generally result in false-negative studies for ischaemia which classically present in the anterior and inferior walls (Roach & Parker, 1993:2).

2.8 Controversy about attenuation correction application

Even though the advantages of AC-A in NM has been widely accepted, there is still controversial issues about the application to myocardial perfusion imaging. The CT images function as a transmission map for the images of the SPECT data of the Tc-99m sestamibi study. Artefacts can be produced with the misalignment of emission and transmission image data. These artefacts appear as a reduction of radioactivity with AC-A, which is mostly produced in the apex and is known as false apical defects (Apostolopoulos & Savvopoulos, 2016:89-91; Denisova & Ansheles, 2018:1-10; Cuocolo, 2011:1887). The artefacts can mask real perfusion defects and may lead to uncertainties when interpreting the results. The Tc-99m sestamibi study also needs to determine whether the perfusion defect in the myocardium is reversible or either a result of scatter from extracardiac tracer activity. Therefore it is suggested that both the NAC- and AC images should be reviewed side by side and in consideration of the clinical data of the patient for the final report. It was also suggested that the gated systolic AC images can be used for the interpretation of the apex. The study concluded that CTAC is mostly useful in males and obese patients to improve the specificity of MPI in the inferior, inferoseptal and inferolateral wall. They also suggested that the interpretation of the anterior, anteroseptal, anterolateral walls and the apex should be reviewed in accordance with the reference of the NAC rather than the AC images (Apostolopoulos & Savvopoulos, 2016:89-91; Denisova & Ansheles, 2018:1-10; Cuocolo, 2011:1887).

Although it was mentioned that artefacts can be produced with the misalignment of emission and transmission image data, Plachcinsha *et al*. (2015) investigated the effect of CT misalignment on AC MPI on Tc-99m sestamibi SPECT. The authors found only misalignments exceeding 2-3 pixels have a negative impact on AC images as seen in figure 2.7 below. Therefore, the alignment of SPECT and CT studies should be checked in every patient, even though small misalignments do not effect study interpretation (Plachcinsha *et al*., 2015:80-83).

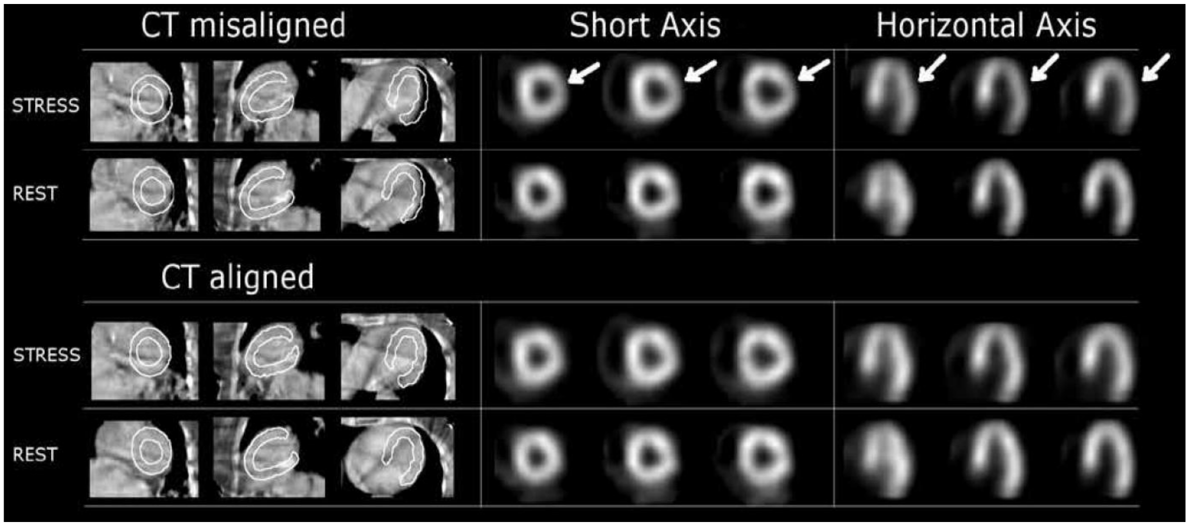

Figure 2.7: Effect of CT misalignment in top images and below realignment on myocardial images (Plachcinsha *et al*., 2015:81)

He *et al*. (2019) investigated the consistency of veterans (experts) in NM to verify incidental findings on AC-A scans of MPI with low-dose CT. Images were separately interpreted by a nuclear cardiologist and a radiologist. Overall the identifying of the incidental findings on the scans by the NM cardiologist and the radiologists were in agreement with observer variability. However, they concluded that it is necessary to standardise the training requirements, and protocols for accurate detection of these findings for the individual divisions (He *et al*., 2019:1691-1692).

2.9 Conclusion

It is clear in the literature that it is necessary to investigate how to improve image quality with AC-A and the possible factors that may contributes to the success of the MPI data. There is much controversy regarding the usefulness of this technique. The literature review discusses the evaluation of CAD using AC-A, the different cardiac stress tests and patient preparation for MPI. Thereafter the AC-A to SPECT/CT images for breast and diaphragm attenuation. Lastly the quality improvement for MPI and the controversy for the using of AC-A worldwide. In the next section, materials and methods for this study will be discussed.

CHAPTER 3
MATERIALS AND METHODS

This chapter aims to provide an in-depth outline regarding the methods followed in the study so that the reader can replicate the study conditions in their own facility. This is also important so that the scientific validity of the study can be evaluated.

3.1 Research methodology

A retrospective study, using a descriptive cross-sectional design with a comparison group was conducted. Retrospective studies are performed after the fact, using information on events that happened in the past. Descriptive cross sectional studies are studies in which the disease or condition and all factors related to them, are measured at a spesific point in time for a population that is defined and described.

Each of the patients' image sets, included in the research study, were subjected to a trial group (AC images) and a control group (NAC images). The NAC and the AC of the stress and rest images are the dependent variables of the study. The relevant patient factors stress, gender, age, weight, and height are the independent variables.

3.1.1 Population

The population was male and female patients over the age of 18 years old residing in the area in the Western Cape that is provided with MPI services by Tygerberg Hospital. The patients chosen for retrospective analysis of MPI was chosen from a patient list provided from the research site used for the patient statistics The population sampling started from the records of January 2015 to December 2016.

3.1.2 Sampling technique and sample size

One hundred patients' image data sets were collected from January 2015 to December 2016. Period starting from January 2015 were chosen because the research site obtained the new software that could allow CTAC on Tc-99m sestamibi studies. The population sample includes 41 males and 59 females.

A systematic sampling technique was used, starting from January 2015, choosing every fifth image set from the patient database (an image set equals a stress and rest study) to ensured an equal chance from all data being selected to be representative of the population. Tygerberg hospital performs around 500 scans per year (1000 over two years) of patients receiving both stress and rest MPI studies. These studies were performed at that stage (January 2015 to December 2016), hence 250 patients (500 scans per two years) received MPI procedures. In systamatic sampling, the patients are selected from a random starting point, but the fixed, periodic interval of sampling is calculated to result in the correct sample size. This method was selected because it is one of the most used methods due to the fact that it is simple and easy to use in a clinical environement (Mostafa & Ahmad, 2018:290). We needed a sample size of 100 patients, therefore we selected every 5th patient. The required sample size of 100 patients of Tc-99m sestamibi studies for myocardial perfusion scintigraphy was chosen from a patient list provided from the research site used for the patient statistics. The statistician approved the sample size of 100 patients to be sufficient to yield statistical significance results for this research study. Systematic unfairness was reduced with this method of sampling thus increasing the validity of the study. This method also meets assumptions of statistical procedures (Grove *et al*., 2013:257), using a statistician to analyse the collected data.

The NAC and AC images for stress and rest images were obtained with the patient in the supine or prone position and a score (0-4) was given to the image data sets by the two NM physicians. A score of 0 implies normal study, 1 means a defect with no change, 2 means the defect change <50%, 3 means the defect change >50% and 4 was given when an artefact was generated by the AC-A on the NAC images of the stress and rest studies. The position of artefacts on the myocardium was also reported by the physicians if it was caused by AC-A and in a separate column, scored yes or no to indicate whether AC-A improved or did not improve the outcome of the results (Addendum B). Incorporated under the data collection method, 20 of the 100 image sets of the research study were separately reported by the two NM physicians. The statistician evaluated the scores of the images with the SPSS using Cohen's Kapp test. This test was used to determine inter-observer variability between the two NM physicians. The conclusion was drawn that no significant observer variability was noticed between the scoring of the two NM physicians. Therefore the remaining 80 image sets were divided between the two physicians.

3.1.3 Inclusion and exclusion criteria

Image data sets were excluded from the population sample if they only underwent a stress study and not the rest study. As per protocol, pregnant patients are not imaged and therefore no pregnant patients form part of the study. Patients that breast feed are also not included since breast feeding patients will have intense breast uptake which can produce uninterpretable images and therefore it is recommended that studies are not performed on breast feeding patients (Arumugam *et al*., 2012: 817).

3.1.4 Ethical considerations

Ethical approval for this research project was granted by the Research Ethics committee of the Faculty of Health and Wellness Sciences in the Cape Peninsula University of Technology (Addendum D), Western Cape Department of Health (Addendum E) and the research site (Addendum F). All patient records were handled confidentially and identifying details such as the name and the hospital number of the patients were masked and not recorded on a image data capture sheet or directly linked to the data set. The image data sets were allocated numbers as identifiers for statistical analysis. The images and all electronic data were stored in a password protected computer on a research folder that were anonymised.

3.1.5 Data preparation

The patient data was divided into two groups: female patients scanned supine and male patients scanned prone according to the protocol of the research site. The prone position enhances visualisation of the inferior and the septal wall of the myocardium since in most cases an elevated diaphragm is observed in male patients. When lying in the prone position the diaphragm automatically move downwards away from the heart (Iskandrian & Verani, 2003:95). Female patients were imaged in a supine position to avoid discomfort concerning pressure on the breasts which may create soft tissue artefacts (Iskandrian & Verani, 2003:95). Patients' weight and height were recorded and used to calculate BMI. The patients were categorised according to different variables including stress, gender, age, weight, height and their position of patient during imaging (Addendum A). This patient-related information was found in the stored records (patient chart, previous reports and request form) at the research site.

3.2 Administered doses of Tc-99m sestamibi

Patients can either undergo the study on a one-day or a two-day protocol as discussed in the introduction. For the two-day protocol, patients received 550 MBq of Tc-99m sestamibi for both the stress and rest studies.The doses, for the one-day protocol for stress/rest Tc-99m sestamibi studies are calculated according to the patient's weight showed as follows (Table 3.1).

Table 3.1: Tc-99m sestamibi doses for a one-day protocol (protocol at research site)

Body mass in kg	**1st dose in MBq**	**2nd dose in MBq**
70 and less	260	740
71-79	330-355	810-870
80-89	380-400	930-990
90-99	430-450	1050-1100
100 and more	480	1150

Technetium-99m with an energy of 140 keV, has a short half-life of 6 hours which is a great benefit in radiation protection perspective. Therefore the radiation absorbed dose to the patient is relatively low, with the colon being the critical target organ. The colon receives about 5.4 cGy/1100 MBq during a Tc-99m sestamibi study (Ziessman *et al*., 2005:543).The tolerance dose for the colon with patients receiving external radiation theraphy for carcinoma of the uterine cervix is between 65 Gy and 70 Gy which shows for Tc-99m sestamibi study that is well below the tolerance level (Teshima *et al*.,1990:2313).

3.3 Imaging equipment and processing

This section describes the imaging equipment and image processing procedures as these components of the procedure has great influence on the outcomes of the study.

3.3.1 Scintillation Detectors

At the research site, the patients were imaged on one of the two-hybrid dual-head gamma cameras (scintillation detectors) combined with a CT component. Studies were performed on either a one-slice CT or a four-slice CT which is mounted on the gamma camera (Figure 3.1). A three-lead ECG monitor was connected to the patients for ECG gating with SPECT imaging.

Figure 3.1: Dual head gamma camera (GE Hawkeye Infinia Gamma Camera)

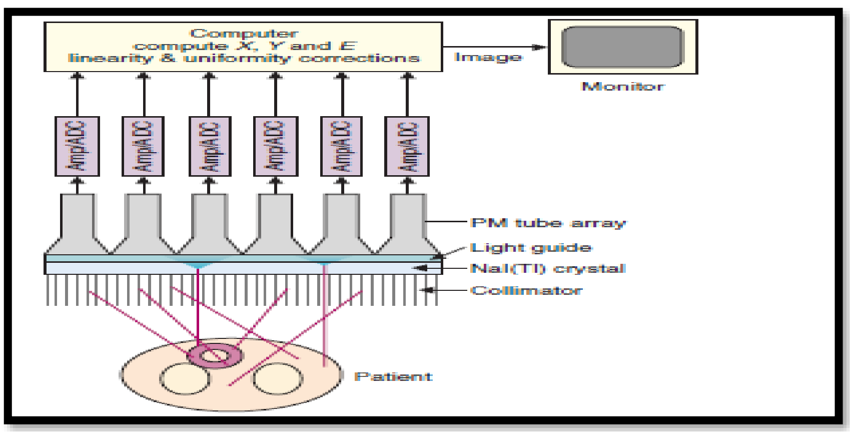

Figure 3.2: Basic principles and components of a modern gamma camera (Cherry *et al*., 2012:196)

Principle of operation for gamma camera

The collimators absorb the scattered gamma rays which are emitted from the patient's body to allow only those gamma rays that are perpendicular to the crystal. The type of detector is a NaI(Tl) scintillation crystal (detector) that transforms gamma rays into light photons.The photomultiplier tube (PMT) is an instrument that converts these light photons into electrical signals. A pulse height analyser (PHA) is used to measure the amplitude of electrical signals from the amplifiers. Finally, the peak height analyser and computer convert these signals into an anatomical image (Cherry *et al*., 2012: 348). See Figure 3.2.

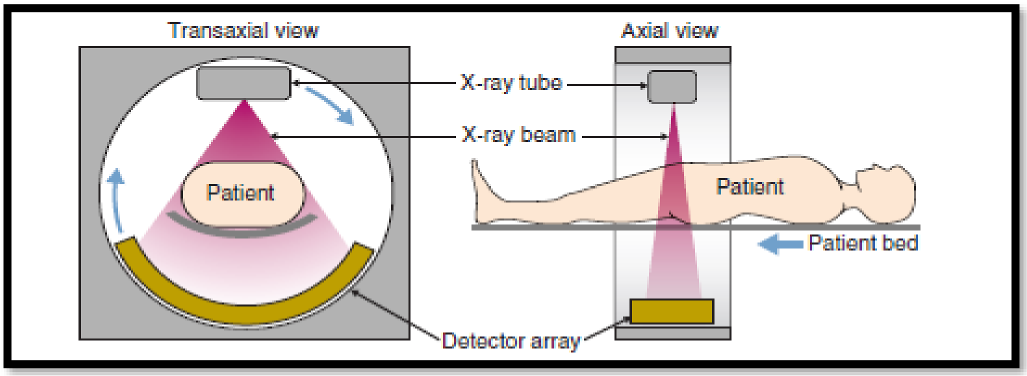

Figure 3.3: Components of the CT scanner (Cherry *et al*., 2012: 348)

The operational principle of CT scanner (figure 3.3) shows the x-ray tube and detector mounted on the gantry of gamma camera rotating in the trans-axial plane. The patient bed moves along the axial direction, resulting in a helical track of the x-ray beam around the patient to acquire multiple image slices rapidly (Cherry *et al*., 2012: 348). The low-dose CT used for research is equipped with X-ray detectors positioned opposite the X-ray tube which is mounted on the gantry of the gamma camera.

3.3.2 Imaging protocol

The data was acquired using the protocol of the research site for stress and rest Tc-99m sestamibi myocardial perfusion imaging. The protocol starts with planar static images taken over the chest area followed by a gated SPECT/CT study. The planar views will indicate the lung- to- heart radiotracer uptake ratio which will show an increase or decrease of the radiotracer uptake in the lungs. This can explain if the patient's symptoms are related to a lung or heart disorder and may affect the medical management of the patient (Wosnitzer, 2012:636).

Planar static images

A good basis for the study is to obtain planar static images, although routinely only SPECT imaging is performed (Henzlova *et al*., 2009: 331). At the research site planar images were obtained with a low energy high-resolution collimator (LEHR), in 256 x 256 matrix size with an acquisition time of 600 000 counts per second (cts/s) over the field of view. A zoom factor of 1.4 and a 20% energy window at 140 keV for Tc-99m was selected. The planar images for all the Tc-99m sestamibi patients at research site are acquired as follows:

i. An anterior planar view of the chest, where the patient is imaged in a supine position with arms along the sides of the patient's body.
ii. A left lateral supine view, the left side of the patient was imaged with the patient lying in a supine position, arms crossed over above the head.
iii. A left lateral side view, the patient was imaged lying on the right side with arms above the head and the detecteor head positioned above the left side.

Gated SPECT/CT

The MPI SPECT/CT data sets were obtained with either one of the two dual-head gamma cameras at the research site. SPECT data were obtained over 180 degrees into and the rotational arc for each gamma camera head was 90 degress with a 3 degree angular step. A 64 $\times$ 64 matrix size was used with an acquisition time of 20 seconds per angular step. A LEHR collimator was used, a frame size of 64 x 64 with a zoom of 1.4 and 20% energy window at 140 keV for Tc-99m was selected. The CT slices were acquired for the region of the heart and not for the whole axial field of view of the gamma camera to reduce the radiation exposure to the patient. A fixed slice thickness of 10 mm, 140 keV voltage and 2.5 milliamperes (mA) current were applied to the low dose CT. ECG gating images for GSPECT study were acquired in a gated mode using a three-lead ECG-trigger to measure the heart rate of the patients with 16 frames per cardiac cycle for the current research study.

3.3.3 Image processing

After imaging, the raw data were electronically transferred to the processing system which is a medical software innovation for NM imaging, operated at the research site. Static views were visually assessed by the NM physician for low count density, interference from the high gut activity and any source of artefacts such as foreign objects in the field of view. The thyroid uptake, breast uptake, pulmonary tumour uptake, or uptake in other thoracic or upper abdominal structures should also be noted (Henzlova *et al*., 2009: 333). The SPECT/CT data was processed by the NM physician with the OSEM reconstruction method, using 15 subsets and 3 iterations with 1.3 cm Gaussian filter. To achieve better image quality on the data, Resolution Recovery software (RR) was used during processing (Arumugam et al. 2013: 820). After the reconstruction of the SPECT images, three sets of slices: short axis, horisontal and vertical long axis were reviewed alongside with Monte-Carlo AC-A of the CT images. The quantitative analysis

(MPI scoring system) is useful to supplement visual interpretation of these slices. The normalised images allowed the comparison to a normal gender-specific database (Holly *et al*., 2010:963). This is a quantitative program, which compares the patient's images with normal databases of males or females (Burrell & MacDonald, 2006:203).

The data was then reported by the NM physician with the multiple slices of stress and rest images AC images with three projections aligned and each set of projections (short axis, horisontal long axis and vertical long axis) displayed directly below each other (Figure 3.4). The NAC stress and rest images can be displayed alongside the AC images for comparison. Polar maps are useful to use in addition with the projected slices but should be presented following viewing conventional display (Dvorak *et al*., 2011:2044-2045).

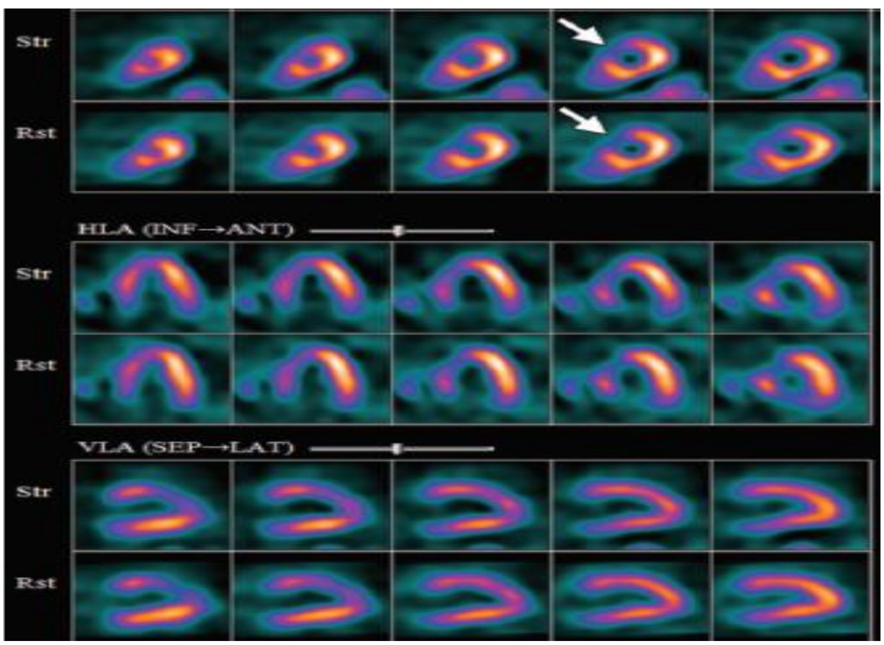

Figure 3.4: Tc-99m sestamibi SPECT/CT images with stress in the upper row on each set of paired images and rest at the bottom row. The short-axis slices are projected in top rows, the horisontal long axis in middle rows and vertical long axis in the bottom rows. A large fixed antero-septal perfusion defect of an infarct is demonstrated with an arrow (Dvorak *et al*., 2011:2052)

All image data sets of patients included in this study were already imaged and stored on the Hermes database. The selected patient studies from January 2015 to December 2016 were anonymised and transferred from the Hermes data base into a research folder which is password protected. The hard copy folders of the patients' results were collected to gain information on the patient-related factors such as stress, gender, weight, height and the position of imaging and whether the patient was physically or pharmacologically stressed.

3.3.4 Reconstruction algorithm

The iterative OSEM algorithm was used for image reconstruction. This is a process applied to obtain an image by using an iterative reconstruction method, which is outlined below as follows.

First, an arbitrary (estimated) image is created. This image is then projected onto the measured image projections. The system compares the arbitrary image to the projected images from where correction factors will be calculated. These factors will either be calculated by using subtracting or dividing methods. The correction factor will be applied to the estimated image. This process will repeat itself until no correction factor is calculated and therefore the estimated projection and measure projection will correspond. The process will end if this is the case and the images will be obtained. (Cherry *et al*., 2012:270). See Figure 3.5 below.

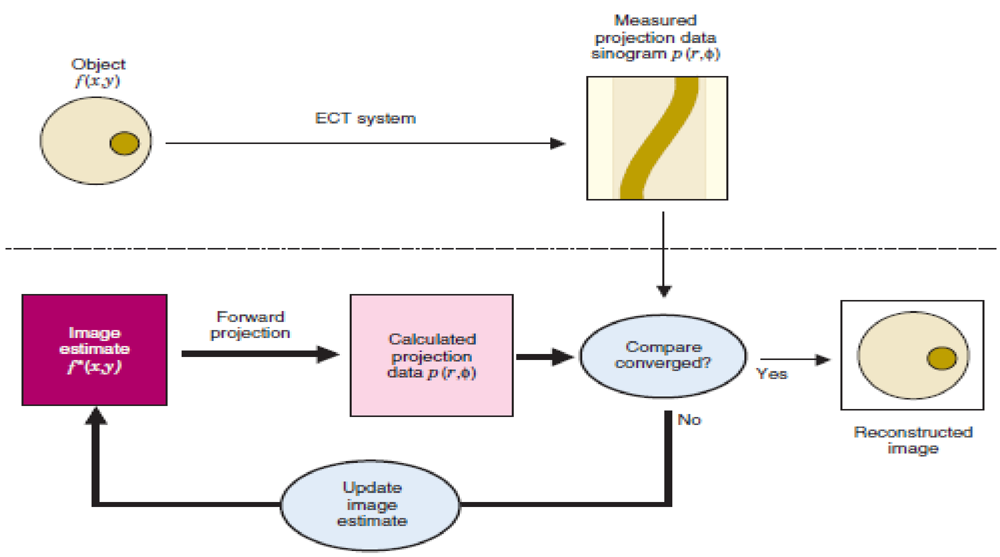

Figure 3.5: Steps to explain iterative construction method (Cherry *et al*., 2012:270)

After the SPECT images were reconstructed, AC-A was integrated. The AC images were produced from the myocardial perfusion datasets that are coregistered with the CT attenuated maps. The specificity of SPECT myocardial imaging can significantly be improved by using attenuation correction methods in conjunction with quantitative analysis during reporting (Dvorak *et al*., 2011:2049). Iterative reconstruction which incorporated attenuation and scatter correction, provides images with increasing diagnostic accuracy if correctly applied (Arumugam *et al*., 2012: 820)

3.4 Reporting of image data

The presence of defects to the images of the myocardium were assessed visually by a NM physician on the stress/rest planar images and quantitatively (by the MPI scoring system indicated in figure 3.6) on the SPECT images during reporting. Images were displayed using a continuous colour scale on all image reproductions for reviewing. The interpretation of the SPECT raw data was visually reviewed for quality control purpose specifically to inspect movement during imaging (Wosnitzer, 2012:636; Dvorak *et al*., 2011:2044).The SPECT images are interpreted according to the American Heart Association which states that the extent and severity of myocardial perfusion defects can be divided in 17 segments on a 0-4 scale. Summed stress score (SSS) is the sum of the scores on the 17 segments of the left ventricular myocardium and so is the summed rest score (RSS). The summed difference score (SDS) is the difference between stress and rest score. Thus the SDS reveals the reversibility (ischaemia) of the LV. A score of 1-3 symbolizes mild ischaemia, 4-7 moderate ischaemia and >7 severe ischaemia (IAEA 2016:50-51).

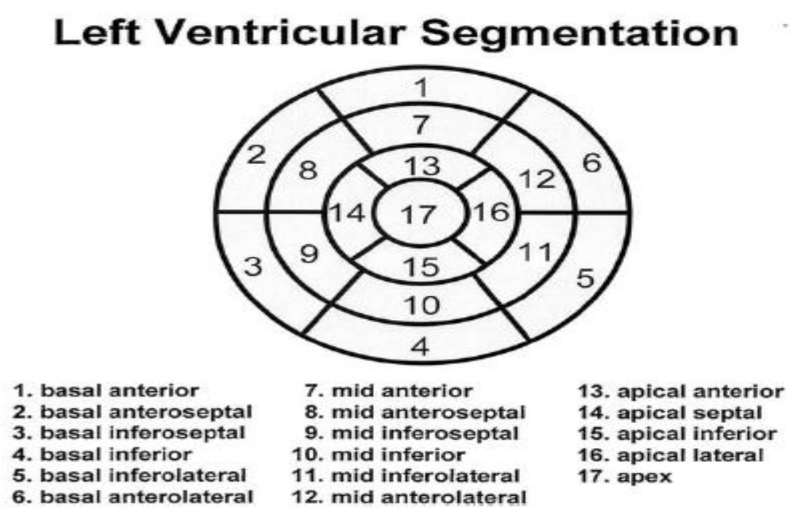

Figure 3.6: The 17 myocardial segments (Hesse *et al*., 2005:885)

The 17 segment model of the LV can also be assigned to the territories of the specific coronary arteries which is the left anterior descending (LAD) artery, right coronary artery (RCA) and the left circumflex artery (LCX) (Hesse *et al*., 2005:885). See Figures 3.6 and 3.7 which is below:

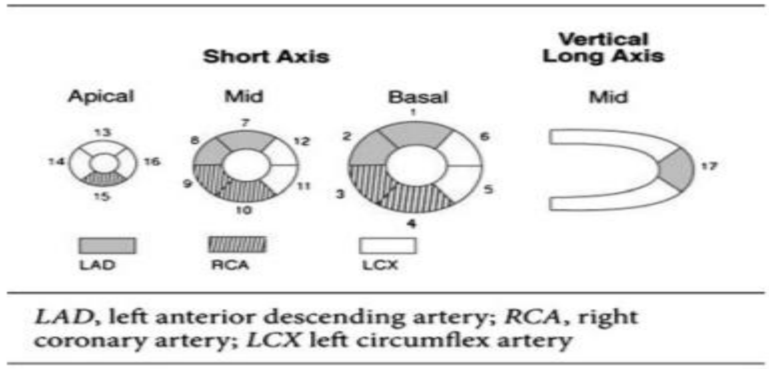

Figure 3.7: SPECT myocardial perfusion imaging: coronary artery territories

(Hesse *et al*., 2005:885)

Polar maps are a display of the evaluation of the presence, extent and location of perfusion abnormalities in the myocardium (Hesse *et al*., 2005:883). It is also called Bull's eye and demonstrates a two-dimensional display of the three-dimensional distribution of the radiotracer activity in the different walls of the LV (IAEA. 2016: 52). See Figure 3.8 below.

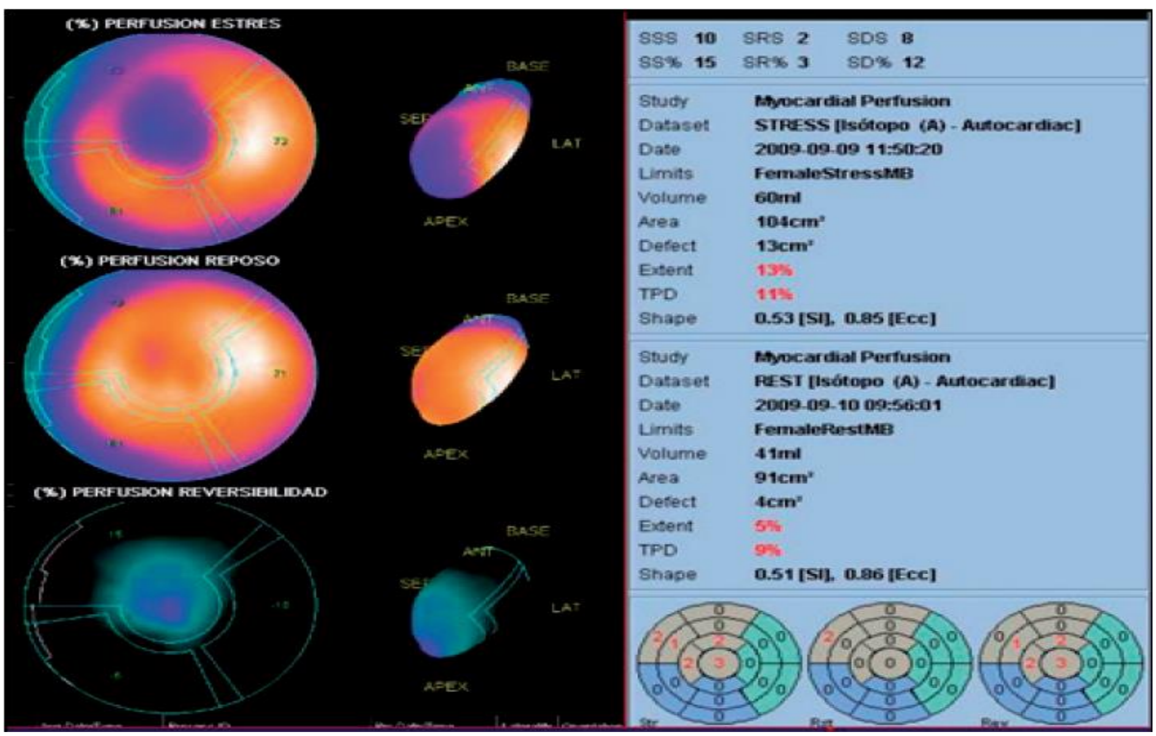

Figure 3.8: Semi-quantitative perfusion analysis with polar plots. The three-dimensional left ventricle displays summed scores with 17-segment model in a patient with anterior and apical ischaemia (IAEA Nuclear Cardiology 2016:74)

A submaximal treadmill protocol with NM stress testing usually produces a negative result for reversible ischaemia (Angelini, 2002:274). When interpreting the GSPECT, it can reveal differentiation between breast or diaphragm attenuation and areas of old myocardial infarction (Biersack & Freeman, 2007:103). The ECG will show normal motion and thickening of the myocardial wall with attenuation, while an infarction absent or moderate motion (Biersack & Freeman, 2007:103). SPECT gating images also improves the diagnostic accuracy of MPI because attenuation artefacts may be wrongly interpreted as infarcts during reporting (Verberne *et al*., 2015:45).

3.5 Clinical interpretation of image sets for research study

The reconstructed SPECT/CT data were quantitatively assessed using a quantitative perfusion software (QPS) program for MPI including the clinical data (Dvorak *et al*., 2011). The accustomed protocol for this research study comprises of four image sets per patient. The four image sets reviewed, were the NAC and AC images of both stress and rest studies respectively. Each patient's image quality on the stress and rest images were assessed for any perfusion defects on the NAC images and then on the AC images by the two NM physicians. The NM physicians evaluated the anterior and inferior walls of the myocardium for both stress and rest studies, NAC and AC images separately. First the anterior and inferior stress NAC- and then the AC stress anterior and inferior images were reviewed and scored. Then the anterior and inferior rest NAC- and AC rest images were reviewed. The scores of current research study for both stress/rest NAC images and AC images were recorded between 0 - 4 accordingly (Addendum B). This scoring was initiated by a study conduted by Ou et al., (2013) to assess the prognostic value of SPECT when using CTAC. The images with and without AC, using the SSS scoring system were classified as normal: SSS = 0 - 3, mildly abnormal: SSS = 4 - 8 and moderately or severely abnormal: SSS > 8. The purpose of their study was to evaluate if there is an improvement of the quality and diagnostic accuracy with the application of CTAC (Ou *et al*., 2013:497).

The flow chart in Figure 3.9 below shows how the clinical interpretation was confirmed. The scores were allocated as follow:

- The four image data sets were reviewed for each patient which included stress NAC and stress AC images and the rest NAC and rest AC images for the anterior and inferior walls of the myocardium. If no perfusion defects (photopenic areas) were seen on anterior and inferior NAC images a score of 0 was given. There was then no need for a rest study or AC to be applied on images. The necessity for the rest studies was due to uncertainty about the observed combination of perfusion defects and attenuation defects or true perfusion defects on stress images.

- If perfusion defects (photopenic areas) were seen on stress NAC then AC images were accessed and if the photopenic areas are confirmed on the AC images the rest study was necessary to be reviewed. When perfusion defects on NAC and AC rest images stay the same as with the stress images, a score of 1 was given.
- If the stress and rest NAC and AC images were reviewed and perfusion defects of the anterior or inferior wall of the myocardium improved less than 50% a score of 2 was given.
- If the stress and rest NAC and AC images were reviewed and perfusion defects of anterior and inferior walls of the myocardium improved more than 50% the score given was 3.
- A score of 4 was given when an artefact was generated by the AC-A to the stress and rest images of the myocardium and the position of the artefacts was indicated.
- In the last column of the scoring sheet, the stress and rest AC images were reviewed and a conclusion of Yes or No was given, where a YES indicated that the application of AC-A changed the outcome of the report; and a NO indicated that the application of AC-A did not change the outcome of the clinical report for the study.

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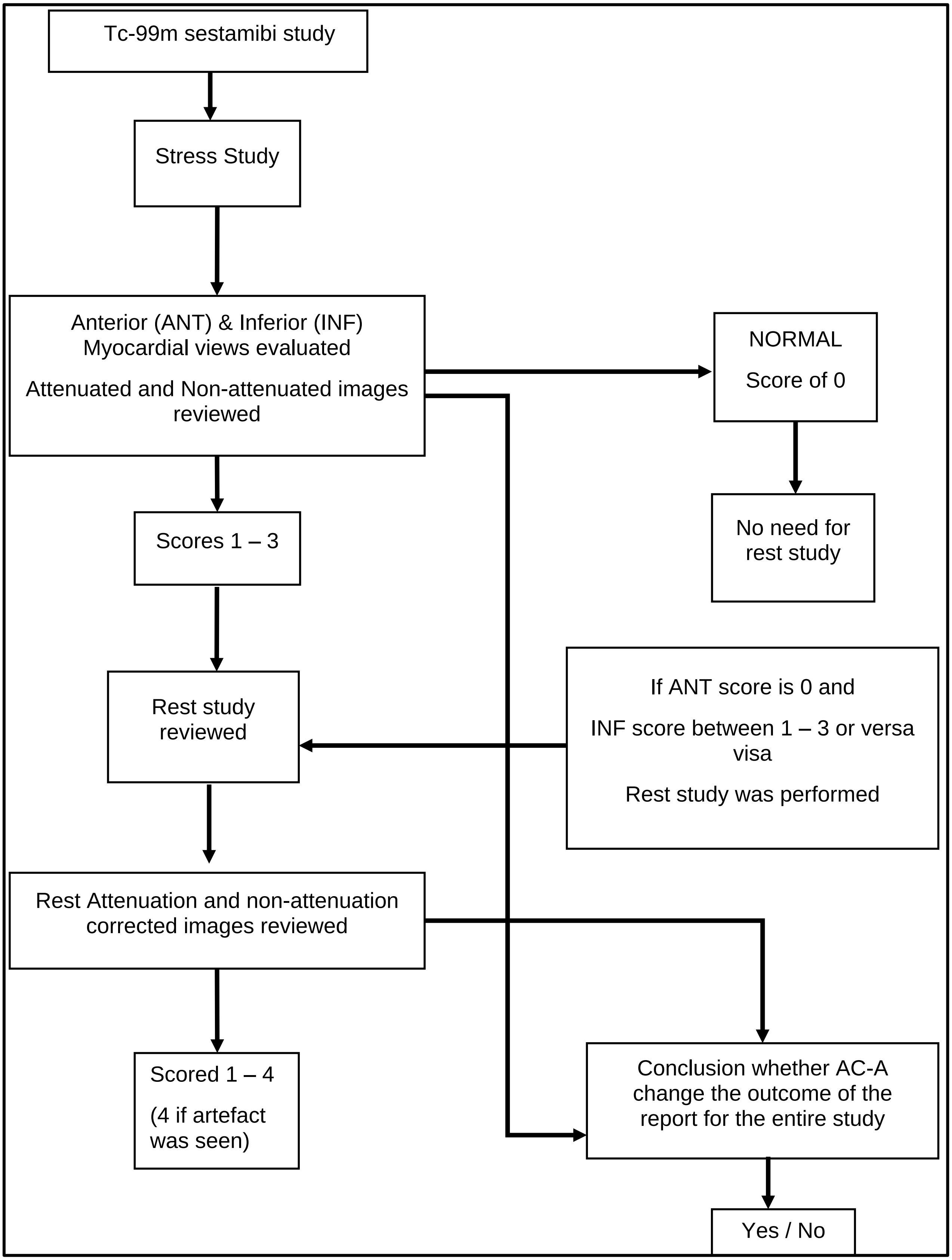

Figure 3.9: Flow diagram of clinical interpretation for research study

3.6 Statistical analysis

The scores of the first 20 image sets were analysed with the statistical package for the social sciences (SPSS) using Cohen's Kapp test. This test was used to determine inter-observer variability between the two NM physicians. The results of the SPSS Kapp test gave an agreement proportion with excluding change agreement of 0.787 and a p-value that is significantly different from 0. Statistically, this points to a substantial agreement between the two physicians. The conclusion was drawn that no significant observer variability was noticed between the scoring of the two NM physicians. In the second phase, the remaining 80 image sets were divided therefore between the two physicians.

An inferential multivariate technique, called a Generalized Linear Model (GLM), was applied by statistician to determine relationships between the categorical variables. The dependent variables (AC images and NAC images) and the independent variables (stress, gender, age, weight are height) were transformed into a dichotomous state (having only two outcomes). The relationships between dependent and multiple independent variables are usually analysed using this linear model, based on several assumptions, of which normality is one (Simonoff, 2003:125-133; Agresti, 2007:66). Since the dependent and independent variables in this study are categorical variables, the assumption of normality cannot happen. Therefore a GLM for non-normal, categorical data was utilised (Simonoff, 2003:125-133; Agresti, 2007:66). This GLM of the family of linear models includes analysis of variance and regression models. The classic linear models assume that all observations are independent of each other and are normally distributed. When working with a categorical dependent variable, the assumption of normality is violated. Theoretically, the GLM consists of three components, a random component, a systematic component and a link function which are outlined as follow:

1) each component of the dependent variable, Y, is independent and normally distributed, having a common variance (random component),
2) the covariates are combined in a linear predictor (systematic component),
3) a link function, which specifies the relationship between the random component and the systematic component (McCullagh & Nelder, 1989:27).

The frequency distribution tables were used to summarise the frequencies or incidences, which is a useful way to organise the data from a list to attain certain outcomes of the samples. Histograms (bar charts) validate the summarised data from frequency tables, for this research.

3.7 Summary

This chapter provided an in depth discussion on the methods followed for this research study. All of these methods where based on standardised methods prescribed by international standards. These methods where performed by experienced and well-trained NM technologists and NM physicians. The next chapter will provide the results that was obtained by following these methods.

CHAPTER 4
RESULTS

In this chapter, the results of AC-A on the stress and rest Tc-99m sestamibi study, imaged in the prone and supine positions are presented. The influence of the related patient factors which includes stress, gender, age, weight and height on these results are also outlined. Excel spreadsheets on the results of the physical and pharmacological stress compared to the supine and prone positions were performed and illustrated by histograms and frequency tables. In this chapter the influence of AC-A on prone and supine stress/rest images will first be analysed, then the analysis of anterior and inferior stress and rest images will be provided. After that a summary of the improvement scores due to AC-A for stress and rest studies will be provided, the influence of AC-A on the one-and two-day protocols and finally the effect of BMI.

4.1 Influence of AC-A on supine and prone stress/rest images

The frequency table (Table 4.1) displays the summary of stress (physical and pharmacological) and rest studies divided into prone and supine positions with the influence of AC-A on each position. The total image sets are divided into improvement (Yes) and no improvement (No) for AC-A. The further analysis of the comparison of the physical and pharmacological stress images is presented in Figures 4.1 and 4.2.

Table 4.1: Physical and pharmacological stress/rest studies divided into prone and supine with the influence of AC-A on each position

	Physical stress/rest prone	Physical Stress/rest supine	Pharmacological Stress/rest prone	Pharmacological Stress/rest supine	Total Image sets
Number image sets	**8**	**8**	**33**	**51**	**100**
Yes (AC-A changed the outcome of the report)	**5**	**5**	**16**	**23**	**49**
No (AC-A did not changed the outcome of the report)	**3**	**3**	**17**	**28**	**51**

A total of 84 patients underwent pharmacologic stress studies (refer to table 4.1) and 16 patients were physically stressed. Out of the 84 patients who had pharmacologic stress, 33 men were performed in a prone position and 51 women in the supine position. The eight men who had physical stress were imaged prone and the eight women in the supine position.

Images acquired under physical stress (Figure 4.1) and pharmacological stress (Figure 4.2) were further analysed for the outcome of AC-A of the stress and rest studies in the supine and prone positions.

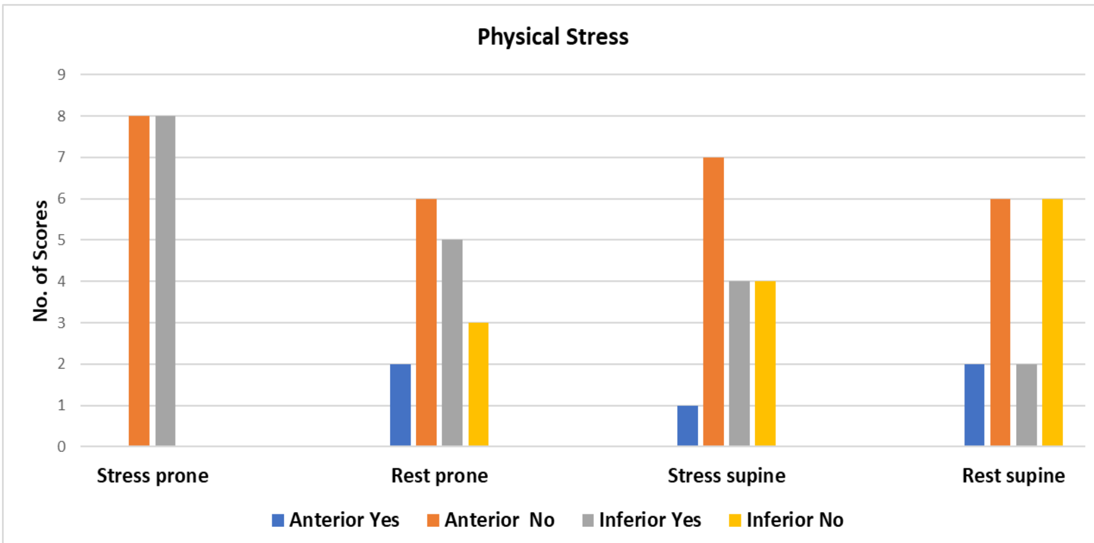

Figure 4.1: Physical stress for prone and supine positions on stress and rest studies for anterior and inferior myocardial walls (Yes=AC-A improved image quality and No= AC-A did not improve image quality for the anterior and inferior walls of myocardium)

Figure 4.1 above represent the histogram for the comparison of the scores of the anterior and inferior walls of the myocardium for stress and rest studies depicting improvement or no improvement for AC-A on the images for the 16 patients who were physically stressed and imaged in the prone or supine positions. The AC-A for the inferior wall myocardium stress images in the prone display improvement in eight patients. There is no improvement for eight patients in the anterior myocardium stress images obtained in the prone position.

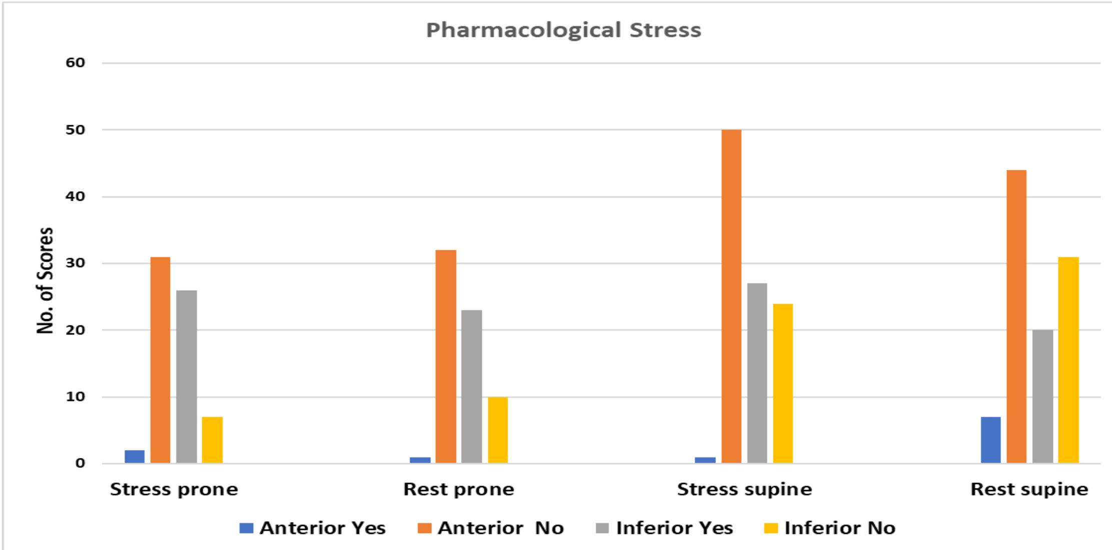

Figure 4.2: Pharmacological stress for prone and supine positions on stress and rest studies for anterior and inferior myocardial walls. (Yes=AC-A improved image quality and No= AC-A did not improve image quality for the anterior and inferior walls of myocardium)

In Figure 4.2 above the histogram presents the comparison of the number of scores for the anterior and inferior walls of the myocardium of the stress and rest studies for 84 patients who were pharmacologically stressed and imaged in the prone or supine positions. The AC-A for this anterior myocardium stress images in the supine position display no improvement in 50 patients. The improvement of AC-A in the inferior myocardium images for pharmacological stress and rest studies in the prone position is in 26 and 23 patients, respectively. The patients imaged in the prone position had no improvement in seven patients for stress studies and 10 patients who underwent rest studies.

4.2 Analysis of anterior and inferior stress and rest images

The four data image sets reviewed by the NM physicians, were the Stress/Rest NAC and AC images as routinely performed for patient reports. Firstly, the anterior and inferior stress NAC- and AC images were reviewed, and scores were given between 0-4 as described in Section 3.6. Then the anterior and inferior rest NAC images and AC images were reviewed in the same manner as the stress images. Lastly the stress and rest AC images were compared to conclude whether AC-A made a difference on the outcome of the report. Figures 4.3 to Figures 4.6 shows the detailed analysis of stress anterior (Figures 4.3), stress inferior (Figures 4.4), rest anterior (Figures 4.5) and rest inferior (Figures 4.6), image sets.

4.2.1 Scores of stress anterior images

Figure 4.3A below displays the stress anterior images with score 0, which indicate a number of perfusion defects observed, 65 image sets were normal and 35 images were not normal, having perfusion defects. Figure 4.3B demonstrates the scores (1-3) which represent the change in the perfusion defects after AC-A, only four of image sets indicated improvement and with 31 image sets, the defects did not change. Figure 4.3C demonstrates 45 artefacts were present with the stress anterior images and in Figure 4.3D the position of these artefacts. The greatest amount of artefacts appeared in the apex of the myocardium with a total of 26 image sets.

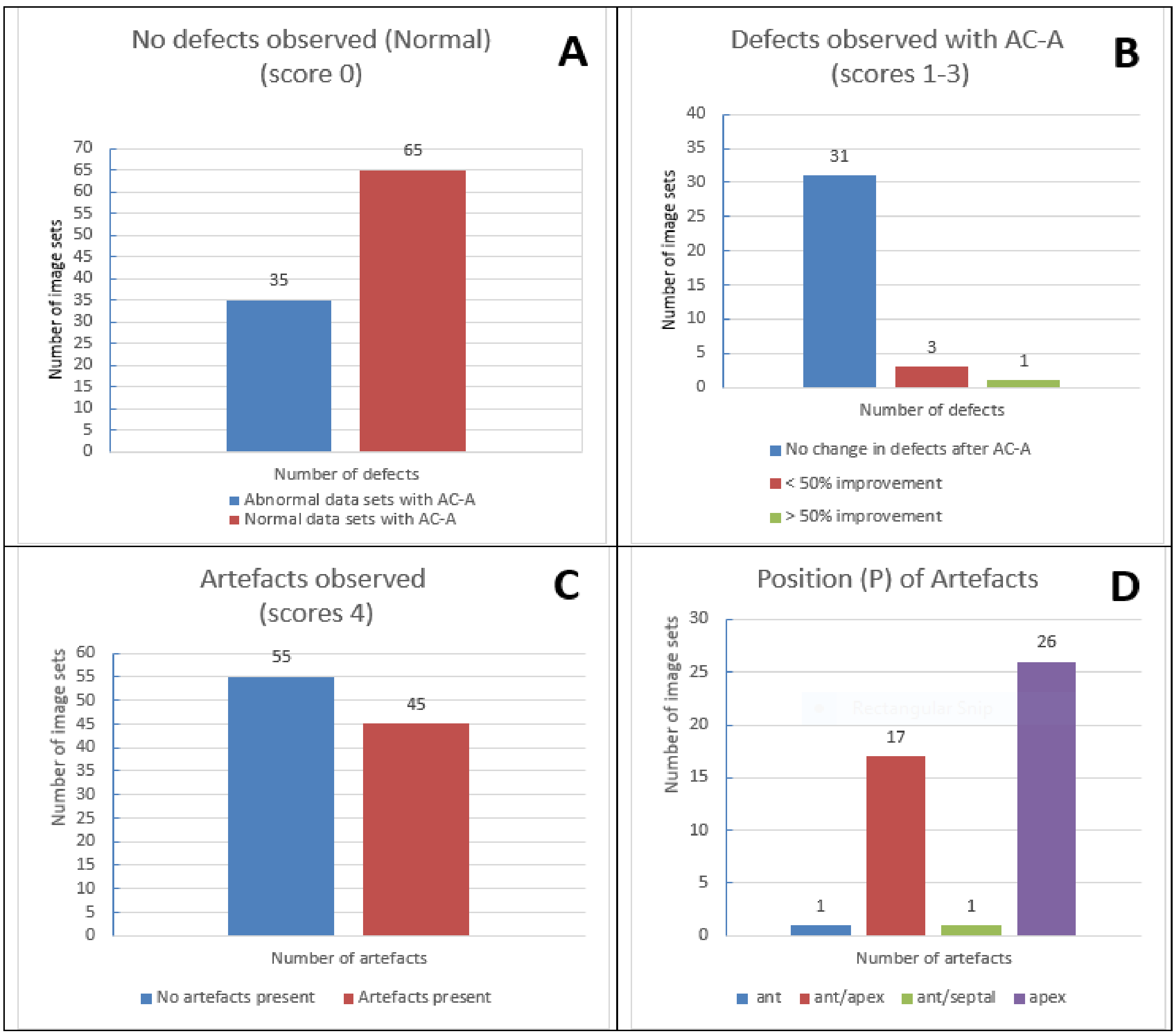

Figure 4.3: Stress Anterior images: No perfusion defects observed (normal) with a score of 0 and the abnormal is the sum of the scores (1-3) of the defects observed with AC-A (A), perfusion defects observed with AC-A (scores 1-3) (B), Artefacts observed (scores 4) (C), Position (P) of Artefacts (D)

4.2.2 Scores of stress inferior images

Figure 4.4A below shows the stress inferior images with score 0, which indicate the number of no defects observed was 24. Figure 4.4B displays the scores (1-3) which indicate the perfusion defects observed after AC-A were 76. The score (>50% in change of defect) is the highest with a score of 41. Figure 4.4C demonstrates only 3 artefacts were present with the stress inferior images and in Figure 4.4D the position of these artefacts is in the inferior position

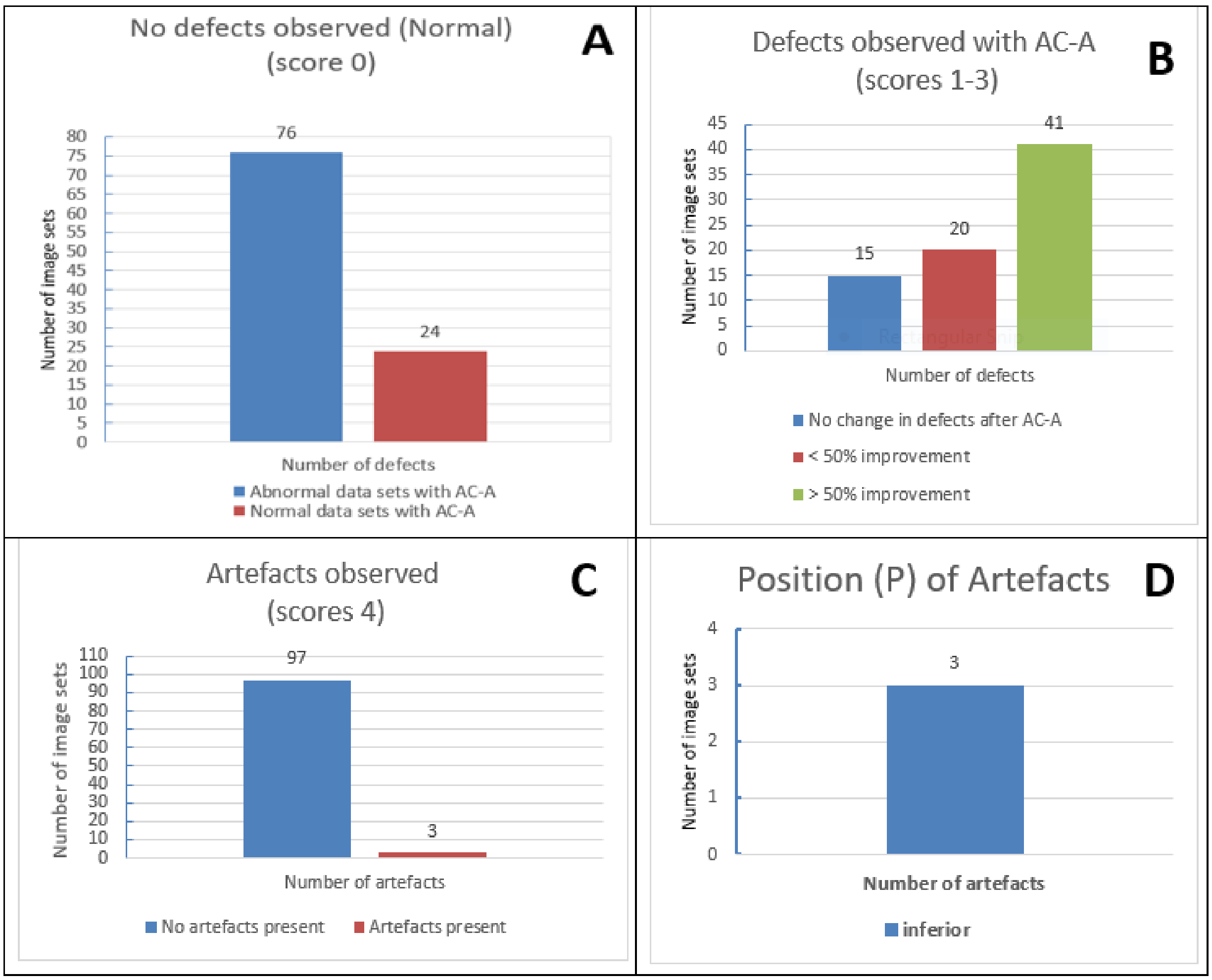

Figure 4.4: Stress Inferior images: No perfusion defects observed (normal) with a score of 0 and the abnormal is sum of the scores (1-3) of the defects observed with AC-A (A) , perfusion defects observed with AC-A (scores 1-3) (B), Artefacts observed (scores 4) (C), Position (P) of Artefacts (D)

4.2.3 Scores of rest anterior images

Figure 4.5A below demonstrates with the rest anterior images and score 0, the number of perfusion defects observed were 33. Figure 4.5B demonstrates the scores (2-3) for the change in the perfusion defects after AC-A, a score of 13 which indicates an improvement was observed in these image sets. Figure 4.5C demonstrates 55 artefacts were present with the rest anterior images and in Figure 4.5D the position of these artefacts. The greatest amount artefacts appeared in the apex of the myocardium with a total of 43.

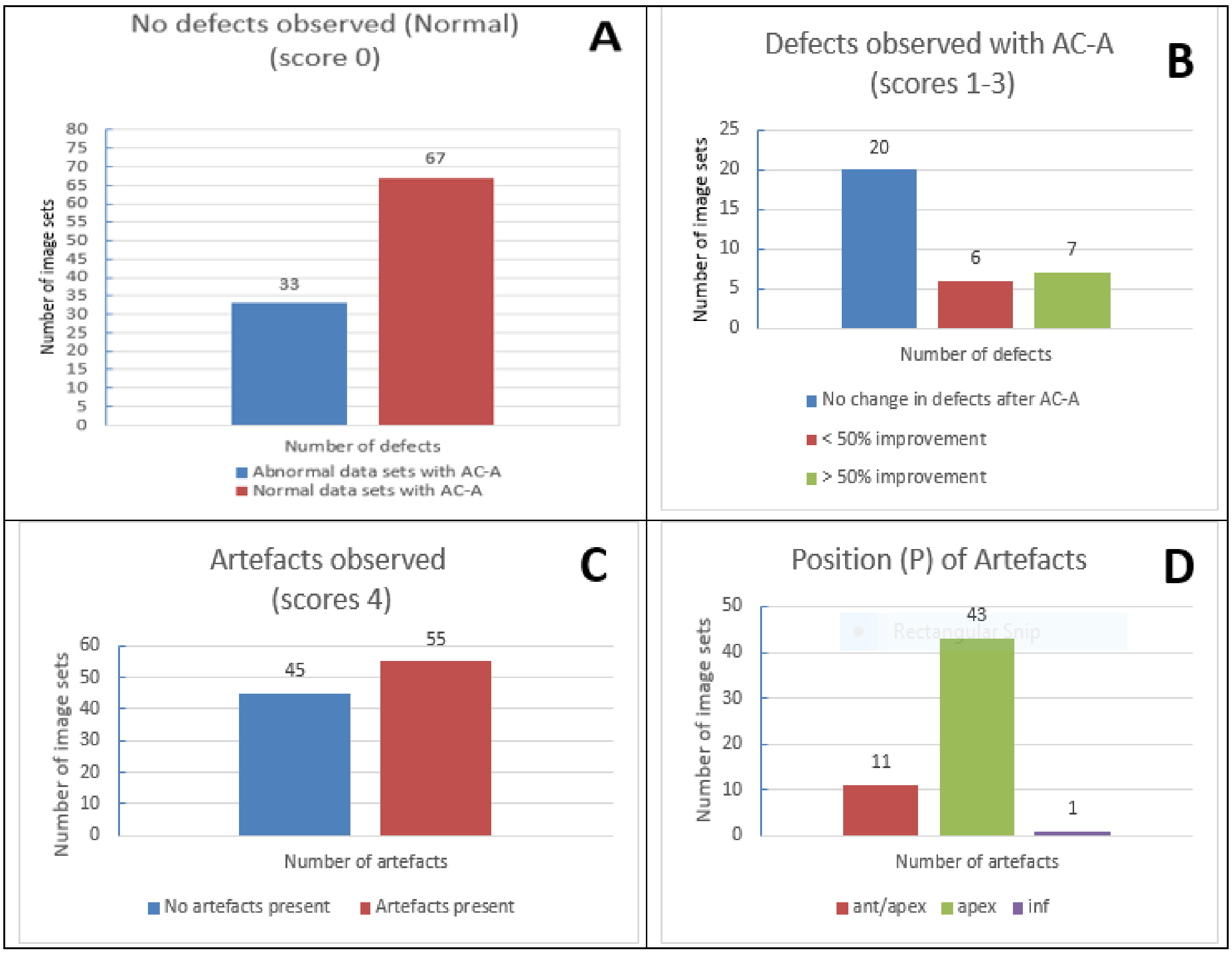

Figure 4.5: Rest Anterior images: No defects observed (normal) with a score of 0 and the abnormal is the sum of the scores (1-3) of the defects observed with AC-A (A), Defects observed with AC-A (scores 1-3) (B), Artefacts observed (scores 4) (C), Position (P) of Artefacts (D)

4.2.4 Scores of rest inferior images

Figure 4.6A below displays 36 image sets for the rest inferior wall were normal with no perfusion defects observed (score 0) and 66 defects were observed (not normal). Figure 4.6B displays the scores (1-3,) which indicate the change of the perfusion defects after AC-A with a score of 34 for > 50% change of perfusion defect. Figure 4.6C shows there is only 4 artefacts present with the stress inferior images and in Figure 4.6D the position of these artefacts are in the inferior wall of the myocardium.

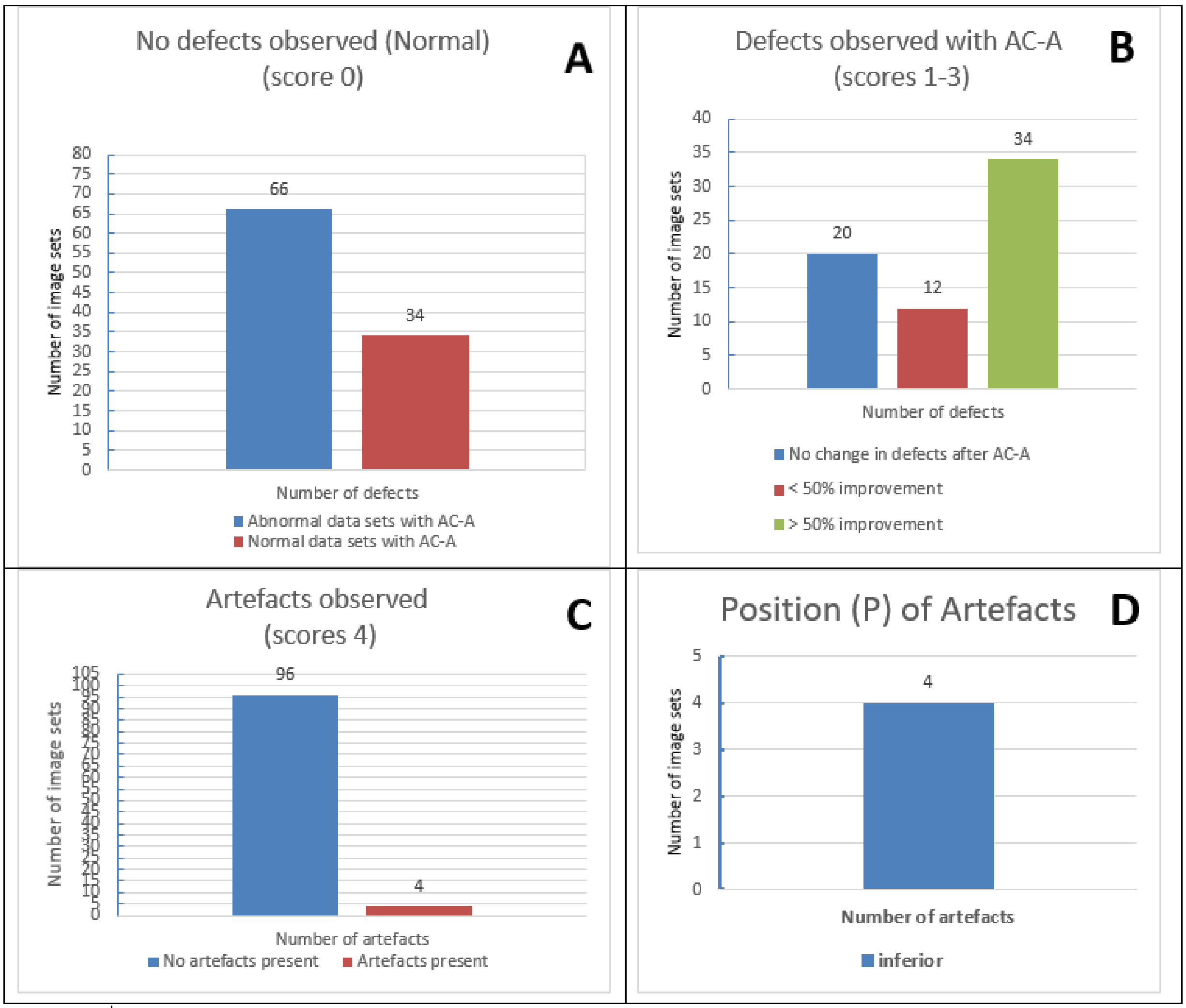

Figure 4.6: Rest Inferior images: No defects observed (normal) with a score of 0 and the abnormal is the sum of the scores (1-3) of the defects observed with AC-A (A), Perfusion defects observed with AC-A (scores 1-3) (B), Artefacts observed (scores 4) (C), Position (P) of Artefacts (D)

4.2.5 Comparison of scores for improvement between stress and rest studies

The bar charts in Figure 4.7 below display a summary of the anterior and inferior myocardial wall scores of stress AC-A images (scores 0-4) alongside the anterior and inferior rest AC-A images (scores 0-4). In Figure 4.7A, the scores (0) for the stress anterior images were 65 and rest anterior images were 67 with no perfusion defects observed. These images also had the most artefacts with stress anterior (45) and rest anterior (55). Stress and rest inferior images scored the highest number for improvement after AC-A, respectively 61:46 (scores 2-3) with a very low number of artefacts (7). The scores of improvement for stress and rest inferior images (defect change >50%) were respectively 41 and 34.

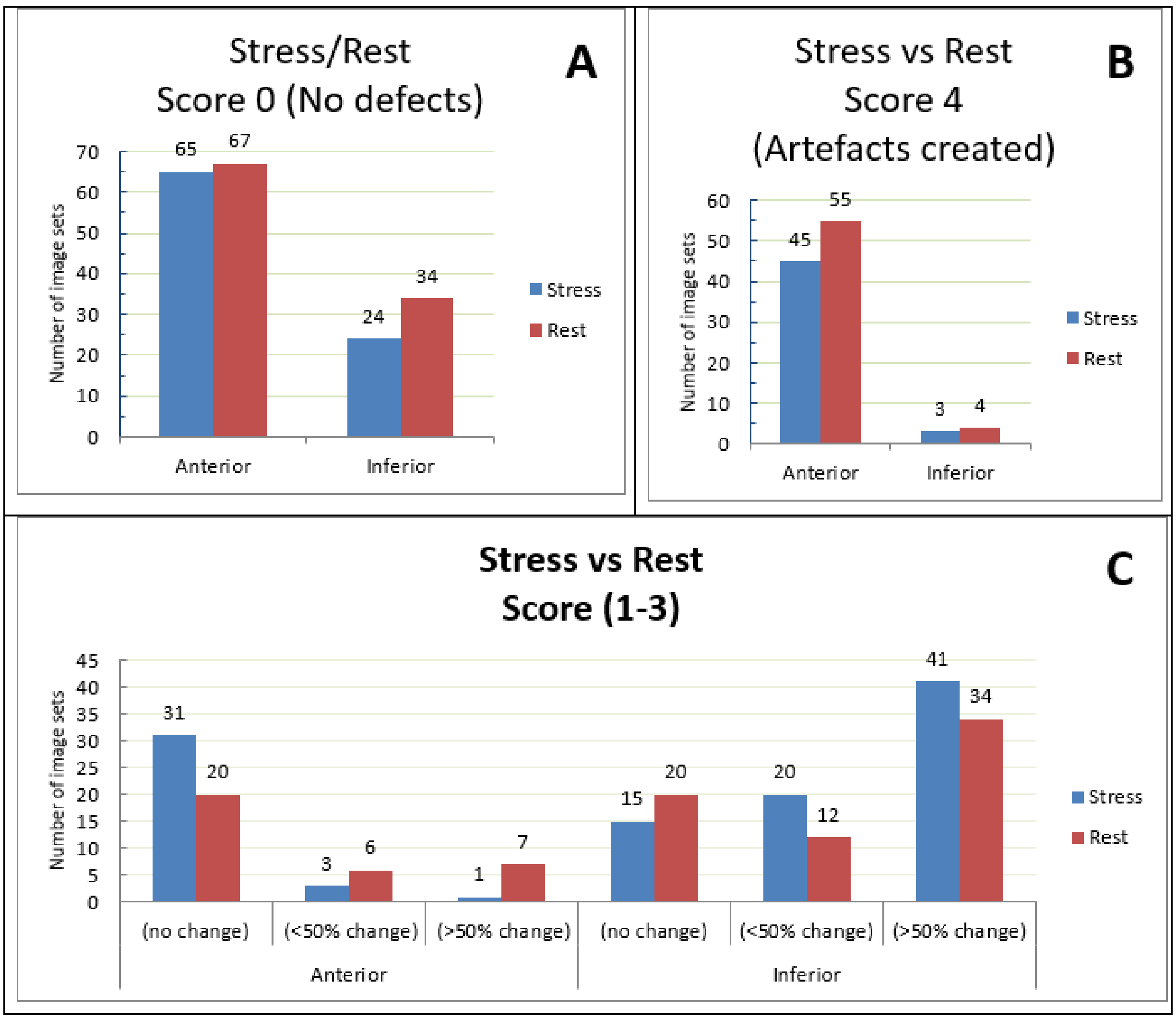

Figure 4.7: Stress/Rest anterior and inferior images: Score 0 (No perfusion defects) (A), Score 4 (Artefacts created) (B), and Scores (1-3) of improvement (C)

4.2.6 Change in perfusion defects from stress to rest images

The bar charts compiled in Figures 4.8A and B below show the percentage change of perfusion defects (0-3) with the AC-A for the anterior and inferior stress images compared to the anterior and inferior rest images (Addendum G and H). The charts in Figure 4.8C and D displays the overall percentage change of the stress anterior and inferior images compared to the rest anterior and inferior images. The overall scores are the total of scores 0-3 from the stress to rest images. The >50% change in the perfusion defects (Figure 4.8B) of the images for stress versus the rest inferior myocardial walls was 46% with the overall percentage change of 41.5% which is the highest value (Figure 4.8D).

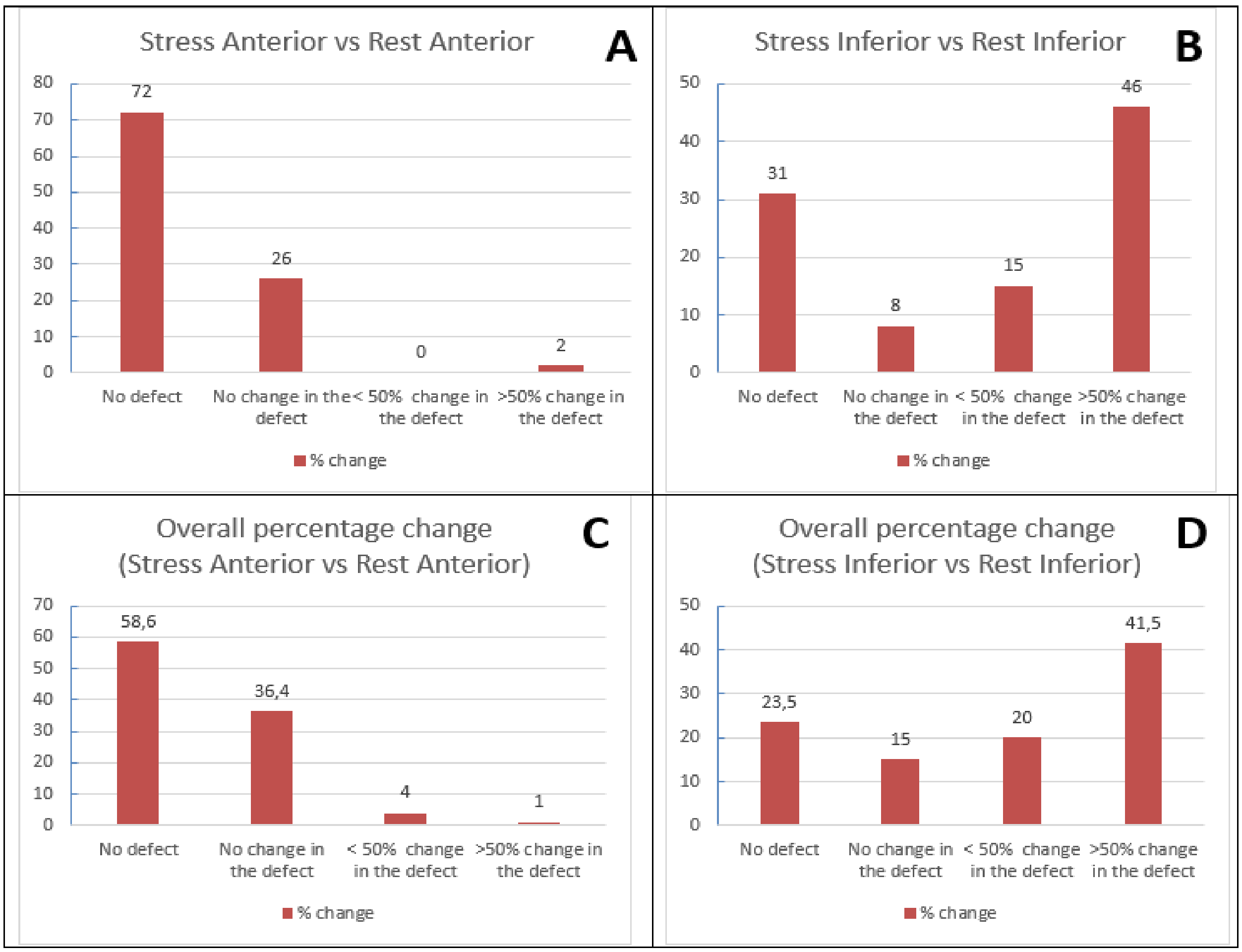

Figure 4.8 Stress Anterior vs Rest Anterior (A), Stress Inferior vs Rest Inferior (B), Overall percentage change (Stress Anterior vs Rest Anterior) (C), Overall percentage change (Stress Inferior vs Rest Inferior) (D). Sheets for statical calculation for Figure 4.8 are available in Addenda G and H

4.2.7 The effect of AC-A on stress and rest studies

The overall results of the improvement versus no improvement of AC-A for stress and rest studies demonstrate a score of 49:51 between the studies respectively (Figure 4.9). This indicates with that AC-A, improvement of the images was 49% and no improvement was 51%. Out of the 41 males, 51.2% improved with AC-A and 48,8% did not improve whereas for the 59 females there was a 47.5% improvement and 52.5% did not improve.

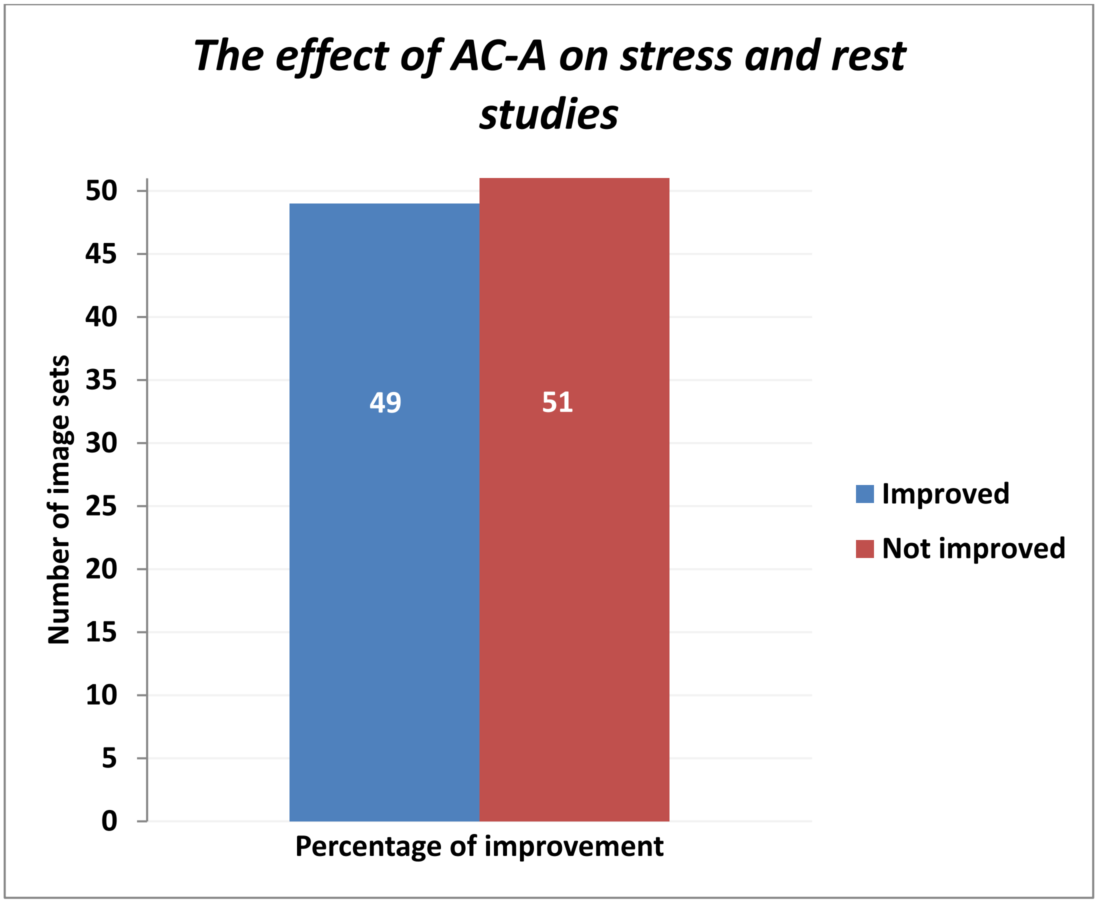

Figure 4.9: The effect of AC-A on the stress and rest studies

4.3 Summary of improvement scores due to AC-A for stress and rest studies

Scores of improvements for anterior and inferior myocardial walls for the stress and rest studies are demonstrated in Tables 4.2 and 4.3. The artefacts created by AC-A and their positions are also indicated.

Table 4.2: Summary of improvement scores for stress studies between NAC (non-attenuation corrected) and AC (attenuation corrected) images

Stress study between non-AC and AC-A							
Anterior (ant) IMPROVEMENT				Inferior (inf) IMPROVEMENT			
Yes	No	Artifact	Artifact position	Yes	No	Artifact	Artifact position
4	96	26	apex	61	39	3	inferior
3-less than 50%	65- normal study	17	ant+apex	20 - less than 50%	24 - normal study		
1 - more than 50%	31-image did not change	2	ant+septal	41 -more than 50%	15- image did not change		
18 image sets improvement inf with AC-A but NO overall improvement for outcome							

In Table 4.2 the stress scores for NAC and AC images, the anterior and inferior myocardial walls are summarised from an excel sheet (addendum C). Improvement for the stress inferior is 61% of which 20 images had a less than 50% improvement and 41 images had a more than 50% improvement. In 18 image data sets improvement was displayed in the inferior wall of myocardium of the stress studies but no improvement on overall outcome was observed.

Table 4.3: Summary of improvement scores for rest studies between NAC (non-attenuation corrected) and AC (attenuation corrected) images

Rest study between non-AC and AC-A							
Anterior (ant) IMPROVEMENT				Inferior (inf) IMPROVEMENT			
Yes	No	Artifact	Artifact position	Yes	No	Artifact	Artifact position
13	87	11	ant+apex	46	54	4	inferior
6 - less than 50%	67- normal study	43	apex	12 -less than 50%	34- normal study		
7 -more than 50%	20 - image did not change	1	inf	34-more than 50%	20-image did not change		
9 image sets improvement inf with AC-A but NO overall improvement for outcome							

In Table 4.3 the rest scores of NAC and AC images for anterior and inferior myocardial walls are summarised from an excel sheet (Addendum C). The improvement for rest inferior images is 46% of which 12 image sets have less than 50% improvement and 34 image sets have more than 50% improvement. The inferior walls of the myocardium for stress and rest studies have the smallest amount (3 and 4 respectively) of artefacts (Tables 4.2 and 4.3). The largest number of artefacts appear in the images of the anterior walls of myocardium but does not interferes with the results because the position is mostly in the apex. The improvement scores for anterior images are only four for stress and 13 for the rest studies. The image data sets which showed improvement, but where the AC-A did not have an influence on the outcome between the stress and rest studies were nine for rest studies and 18 for stress studies. Therefore, for nine image data sets the improvement was in both stress and rest studies, but AC-A was not of significance.

4.4 Analysis of the effect of AC-A on independent variables

Ordinal regression was used to predict the interaction of dependent variables (stress/rest AC-A anterior and inferior images) with one or more independent variables (stress, gender, age, weight and height) as presented in Tables 4.4 and 4.5 below.

Table 4.4: Effects of dependent variables on independent variables of stress anterior and inferior myocardial walls

The effect of AC-A on independent variables

Source	Type III Wald Chi-Square	df	Sig.
Stress	2.583	1	.108
Sex	.552	1	.458
Age	1.690	1	.194
Weight	.629	1	.428
Height	3.684	1	.055

Dependent Variable: Stress Anterior: Change of the defect on scores 1-3
Model: (Threshold), Stress, Sex, Age, Weight, Height

The effect of AC-A on independent variables

Source	Type III Wald Chi-Square	df	Sig.
Stress	.222	1	.637
Sex	1.146	1	.284
Age	.495	1	.482
Weight	.200	1	.655
Height	1.033	1	.309

Dependent Variable: Stress Inferior: Change of the defect on scores 1-3
Model: (Threshold), Stress, Sex, Age, Weight, Height

Table 4.5: Effects of dependent variables on independent variables of rest anterior and inferior myocardial walls

The effect of AC-A on independent variables

Source	Type III Wald Chi-Square	df	Sig.
Stress	.578	1	.447
Sex	1.740	1	.187
Age	.362	1	.547
Weight	1.489	1	.222
Height	3.079	1	.079

Dependent Variable: Rest Anterior: Change in the defect on scores 1-3
Model: (Threshold), Stress, Sex, Age, Weight, Height

The effect of AC-A on independent variables

Source	Type III Wald Chi-Square	df	Sig.
Stress	1.054	1	.304
Sex	3.118	1	.077
Age	.030	1	.862
Weight	.048	1	.827
Height	1.056	1	.304

Dependent Variable: Rest Inferior: Change in the defect on scores1-3
Model: (Threshold), Stress, Sex, Age, Weight, Height

The above tables 4.4 and 4.5 show the effect of AC-A on independent variables: stress, gender, age, weight and height on the dependent variables for the generalized linear model with ordinal regression. The *p*-values for all the variables are >0.05, which indicate that none of the independent variables, have a significant effect on the dependent variables.

4.5 Influence of AC-A on the one-and two-day protocols

MPI studies with AC-A were performed on a one- or two-day protocol. The stress and rest study can be a one day protocol but studies can also be performed on different days with either the stress or rest study on the first day. Normally the stress study is performed first and if findings are normal the rest study was not performed. Due to patient factors eg. if relevant medication which can influence the study is not stopped, the rest study was performed on the day of the appointment and then rebooked for the stress study on another day. The frequency (Table 4.6) below displays the influence of AC-A on these protocols.

Table 4.6: The influence of AC-A on the different day protocols

	One-day protocol	Two-day protocol	Total Image sets
Number image sets	**76**	**24**	**100**
Yes (AC-A improved outcome)	**33**	**12**	**45**
No (AC-A had no influence on outcome)	**43**	**12**	**55**

The 100 data image sets comprised of 76 data image sets for the one-day and 24 image data sets for the two-day protocol. Improvement with AC-A was seen on 45 image sets and on 55 image sets there was no improvement. The two-day protocol showed improvement on 12 image sets and for no improvement on 12 image sets out of the 24 patient studies performed. This is a 50/50 percentage between the improvement and no improvement for AC-A on images for the two-day protocol.

4.6 Body mass index (BMI), gender and age

The BMI of the study population for men (41) and woman (59) for the current research study is presented in Table 4.7 below.

Table 4.7: The BMI of the study population

	Men	Women
Mean BMI	29 kg/m2	30 kg/m2
BMI <30	21 patients	26 patients
BMI >30	18 patients	30 patients

The mean BMI for men is 29 kg/m^2 and women is 30 kg/m^2 for this research study. The number of male patients with a BMI <30 is 21 and BMI >30 is 18 whereas for women patients with a BMI < 30 is 26 and a BMI > 30 is 30. This excluded five patients of whom their height was not presented in the reports. The mean age for men was 62 years and for women was 61 years.

4.7 Summary

In this chapter, the influence of AC-A on prone and supine stress/rest images was analysed, the analysis of anterior and inferior stress and rest images was performed. The improvement scores due to AC-A for stress and rest studies was provided and the influence of AC-A on the one-and two-day protocols as well as the effect of BMI was provided.

CHAPTER 5
DISCUSSION

This research aimed to determine whether SPECT/CT will reduce soft tissue artefacts with the application of attenuation correction maps in Tc-99m sestamibi myocardial SPECT perfusion studies. The AC and NAC images were the dependent variables and the biological and relevant factors such as stress, gender, weight, height and patient position with imaging were the independent variables.

5.1 Influence of AC-A on stress and rest studies

At the research site, it is standard protocol that if the stress study is normal no further imaging is required; but for purposes of the current study, the rest study was performed when the anterior wall was normal but inferior wall was abnormal. The inferior wall had an improvement of less than 50% (score of 2) or improvement more than 50% (scores of 3) on the stress study. The necessity for the rest studies were due to uncertainty about the observed combination of perfusion defects and attenuation defects or true perfusion defects on the stress studies. The patients for current research study had stress and rest studies with AC-A, but the women were positioned supine or and men positioned prone. In 18 image sets of stress studies and nine image sets of rest studies, improvement (scores 2-3) in the inferior wall of the myocardium was observed. In eight image sets, the improvement was observed in both stress and rest studies. In these mentioned image sets for stress and rest studies with AC-A, there were no overall improvement of images on the results. The scores of improvement for the inferior wall of the myocardium of stress AC-A versus rest AC-A were 61% and 46% respectively. On the anterior wall of the myocardium the stress AC-A versus the rest AC-A images the scores of improvement were only 4% and 13% respectively (Table 4.2 and 4.3). AC-A improved the image sets for the current research study in 49% of the study population. The results observed in the current study are therefore in agreement with what was observed by Trägårdh et al. (2013) where the application of AC to images reduced the number of unnecessary rest studies. They found 17% of their study population did not require a rest study and AC-A improved the image quality (Trägårdh *et al*., 2013: 5).

5.2 Effect of AC-A on images acquired in supine and prone positions

The results for current study with males imaged in the prone position and females in the supine position for the stress studies the improvement was 41% and for rest studies the improvement was 34% on the inferior walls of the myocardium. This shows that the inferior walls of the myocardium have the highest score for the more than 50% improvement after AC-A. Therefore, the overall percentage change for the stress versus the rest studies was 41.5% (Figure 4.7 C and 4.8 D in chapter 4). These results agree with the study conducted by Xin *et al*. (2018), where their patients underwent a two-day protocol, imaged in the supine position for stress-rest Tc-99m sestamibi studies. It was found that CTAC was of value for males and overweight patients because of the improved specificity and accuracy which was better for these patients. They concluded when CTAC is used in the clinical application with stress and rest Tc-99m sestamibi myocardial studies, the intergration of NAC and AC image findings should be combined with CAD pre-test probability to improve the diagnostic outcomes. Their results showed improvement of image quality for males positioned in the supine position. This confirms that the patient position did not have an influence on the image quality with AC-A on MPI (Xin *et al*., 2018:48-52).

In this current study, the number of pharmacologically stressed patients that were imaged in the prone position was 33 and 51 in the supine position. The score of improvement for the stress images in the prone position for the inferior myocardium was 26% and for the supine position 27%. Only 16 patients were physically stressed of which eight were in the prone position and eight in the supine position. Out of the 16 patients, images of eight patients showed improvement in the prone position and in the images of eight patients there no improvement in the prone position. The influence of AC-A had an overall score, with the stress and the position of patients, of which 51% did not improve and 49% had improvement (Table 4.1 and Figure 4.9 in chapter). The conclusion can be made that with AC-A for the myocardial studies, there was no significant difference in the results regarding the patient position for supine or prone, therefore all the patients can be performed in the supine position. The results of the current study relate well to the conclusion made by Ou *et al*. (2013) where they imaged all the patients in a supine position and found that CT-AC decrease the number of false positives in their patients' results and improved the image quality.

5.3 The influence of AC-A on the one- and two-day protocols

The British Nuclear Medicine Society (BNMS) revealed in their report that the dose of Tc-99m sestamibi for the two-day protocol is up to 800 MBq on each day which produce a superior image quality (Arumugam *et al*., 2012:17). The preferred protocol for the research site is a one-day protocol. Due to circumstances, it is not always possible for patients to attend for appointments on two separate days. The results for the improvement of AC-A applied to the images for the two-day protocol is 50/50. This indicate that the different days of imaging does not influence the outcome of the results (Table 4.6). According to Fricke et al. (2005), AC-A to the one-day protocol guarantees the perfusion within the myocardium to be more accurate than SPECT alone and therefore also improves image quality (Fricke *et al*., 2005:741).

5.4 Effect of AC-A on BMI of patients

In the current study 18 out of the 41 men had a BMI >30 and 30 out of the 59 women had a BMI >30 (Table 4.7). The analysis of the results of the current study demonstrates no statistical relation between AC-A and the BMI of the patients with the *p*-value of > 0.05 for the influence of the independent variables on the dependent variables (Tables 4.4 and 4.5). These results of the current study agree with what Grüning *et al*. (2006) found in their study. The mean BMI for their study was 29 for males and 30 for females. According to Grüning *et al*. (2006), body mass index and chest circumflex are not useful parameters to predict that patients will benefit from AC-A (Grüning *et al*., 2006:857). Genovesi *et al*. (2011) found in their study that AC-A improved specificity of CAD in overweight men with a BMI >27. Their opinion was that the group of patients with a BMI < 27 could be reported from the GSPECT only without CT and AC-A to images (Genovesi *et al*. 2011:1896).

In a study by Shawgi *et al*. (2012), patients were evaluated for stress and rest SPECT/CT studies with a normal BMI below 25 kg/m^2, with both AC and NAC images. The results visually showed improvement in perfusion images with AC-A, of which 54.4% of the patients with normal BMI had improved images. Of these 84.2% were males and 39.5% females. The changes with the AC images were more common in males than in females as seen in the inferior, inferolateral and anterolateral segments of the myocardium. In females, the apical and anterior segments also improved and the conclusion was that AC-A in patients with a normal BMI could be of great value (Shawgi *et al.,* 2012:217). The results of Ruiz *et al*., (2007) is in agreement with the finding in current research study that the benefits of AC to the images is independent from the body mass index of the patients (Ruiz *et al*., 2007:87).

5.5 Artefacts created by AC-A

In current research study, the position of artefacts is largely in the apex with stress and rest studies (26 and 43 respectively). With the stress anterior images, the artefacts appear also in the anterior walls (Figures 4.3D and 4.5D). The stress and rest inferior images scored 76 and 66 defects (Figures 4.4B and 4.6B) respectively after AC-A, with a very low number of artefacts, only 3 and 4 respectively (Figures 4.4C and 4.6C). According to Denisova and Ansheles (2018), the evaluation of the apex region is helpful to refer to the NAC images and the gated systolic AC images can be useful in the findings of the apical region (Denisova & Ansheles, 2018:11). When using these alternative measurements with reporting, the artefacts should not interfere with the results.

The literature identified that AC-A may improve image quality but artefacts may occur when images are reconstructed. It has been reported that artefacts appear as decrease radioactivity on images and is mostly produced in the apex known as false apical defects (Denisova & Ansheles, 2018:1). These artefacts can mask real defects and may lead to uncertainties when interpreting the results (Denisova & Ansheles, 2018:1). According to Ou *et al*. (2013), studies with CTAC MPI showed a decrease in defect scores in comparison with studies without AC. The images in their study showed new perfusion defects (artefacts) in the apex and anterior walls with CTAC, but an incorrect interpretation of data can be avoided if the interpretation is finalised with the clinical data and ECG of SPECT studies (Ou *et al*., 2013:499). CTAC may decrease the number of false positives but also provide valuable information to guide patient management. The study of Ou *et al*. (2013) observed artefacts created in the apical and anterior walls of the myocardium with CTAC (Ou *et al*., 2013:499). This is in agreement with the results of the current study where the most artefacts of which 45 were in the stress studies and 55 in the rest studies and were created in the apex and anterior walls (Figures 4.3C and 4.5C).

Grüning *et al*. (2006) observed that AC-A was not feasible in a significant proportion of patient images. Both the AC images and the ECG were better evaluated from patient scans with perfusion defects than in normal scans and the diagnostic impact of AC-A on the rest scans were minimal. AC-A can introduce new artefacts mainly in the anterior wall due to over–correction of the images (Grüning *et al*., 2006:857). The normal scans with AC-A had significant lower perfusion in the anterior wall than NAC scans with a significant decrease in the apex (Grüning *et al*., 2006:857). This is also in agreement to what was observed with results of this study in the anterior myocardial walls with stress and rest studies (45 and 55 respectively), delivering the highest number of artefacts with AC-A (Figures 4.3C and 4.5C).

5.6 Interpretation and reporting of images with AC-A

Fricke *et al*. (2004) stated pseudo artefacts can be produced with the misalignment of emission and transmission image data. These artefacts appeared as anterior and apex defects on scans with co-registration of images but after correcting for misalignment of data, it disappeared (Fricke *et al*. 2004:1624). The NAC- and AC images should be reviewed side by side and in consideration of the clinical data of the patient for the final report (Apostolopoulos & Savvopoulos, 2016:91). Denisova and Ansheles (2018:1-11) suggested that the gated systolic AC images can be used for the interpretation of the apex. The results of the current research study demonstrated 45 artefacts with AC-A in anterior wall and apex of myocardium on the stress anterior images. On the contrary, the rest anterior images showed 55 artefacts (Figures 4.3C,D and 4.5C).

According to Fricke *et al*. (2005:736), their results revealed that AC-A causes SPECT images to be more accurate than NAC images and that the benefits can be seen in the inferior wall. In the current research study, the total scores of the improvement in defects observed on the stress inferior wall of the myocardium was 61 (Figure 4.4B) and the rest inferior wall was 46 (Figure 4.6B). These scores show that there is a notable difference in the AC-A score of the images of the inferior wall of the myocardium. Apostolopoulos & Savvopoulos (2016) concluded that interpretation of the anterior, anteroseptal, anterolateral walls and the apex should be reviewed in accordance with the reference to the NAC rather than the AC images alone. (Apostolopoulos & Savvopoulos, 2016:91).

Kuşlu and Öztürk (2017) suggested that prone imaging in addition to supine perfusion SPECT imaging improves the image quality of the inferior wall of the myocardium, especially when reconstructed with an iterative method. This was only of value when CT was not done, and AC-A was not available. If imaging was not performed with the patient in prone position, the ECG-gating was used as a valuable technique for quality control when reporting on the data (Kuşlu & Öztürk, 2017:115). At the current research site, the patients were already imaged in a supine or prone position prior to the AC-A to the protocol. The OSEM iterative reconstruction method was used for reconstruction of images and AC-A for myocardial imaging is performed routinely currently. The patients are usually imaged with ECG-gating and are reported side-by-side with the AC and NAC images, for the final report.

5.7 Conclusion

In conclusion, the results show a 46% improvement with the > 50% change of the defect for the stress as opposed to rest inferior images (Figure 4.8B) with an overall improvement score of 41.5% (Figure 4.8D). The total score of improvement in the defects observed on the stress inferior wall of the myocardium is 61% (Figure 4.4B) and the rest inferior wall 46% (Figure 4.6B) with a very low number of artefacts (Figures 4.4C and 4.6C). These scores show that there is a notable difference in the AC-A score of the images of the inferior wall of the myocardium. The stress and rest anterior images have the most artefacts with the stress anterior delivering 45 artefacts (Figure 4.3C) and the rest studies 58 artefacts (Figure 4.5C). The position of these artefacts is largely in the apex with the stress and rest studies (Figures 4.3D and 4.5D). With the stress study anterior images, the artefacts also appear in the anterior wall of the myocardium (Figure 4.3D). However, the stress and rest inferior images scored the highest number of change in defect after AC-A.

The results also show a *p*-value of >0.05 for the influence of the independent variables on the dependent variables. This indicates that the biological factors and patient position do not have an influence on the outcome of the MPI study (Tables 4.4 and 4.5). The question whether AC-A improves the stress and rest myocardial perfusion imaging, the scores showed a difference between NAC and AC images, with an improvement of 49% and no improvement of 51% for the overall data (Table 4.1 and Figure 4.9). However, this score of 51% with no improvement excludes 18 images of stress studies and nine images of rest studies which showed improvement (scores 2-3) in the inferior wall of the myocardium. In eight image sets, improvement in inferior myocardial walls was observed in both stress and rest studies (Tables 4.2 and 4.3).

CHAPTER SIX
CONCLUSION AND RECOMMENDATIONS

This chapter is a summary of the conclusions that was made during the discussion (chapter 5) based on the procedures that was performed according to the methods section (chapter 3) giving the results in chapter 4.

6.1 Conclusion and recommendations

In view of the findings, the following conclusions can be drawn from this study:

The stress and rest inferior images scored the highest number of improvement (scores 1-3) (Figures 4.4B and 4.6B) after AC-A, with the stress inferior wall a total score of 61% and the rest inferior wall 46%, showing lowest number of artefacts. The results of the stress as opposed to rest inferior images showed (with >50% change of perfusion defect) an improvement with a score of 46% (Figure 4.8B). This score reflects that there is a notable difference in the AC-A scores of the images of the inferior wall of the myocardium. The results also demonstrated that images have the most artefacts with stress and rest anterior studies. The stress anterior walls showed 45 artefacts and the rest study 55 artefacts (Figures 4.3C and 4.5C). The position of these artefacts is largely in the apex with stress and rest studies, but with the stress anterior images the artefacts appear also in the anterior wall (Figures 4.3D and 4.5D). This is an affirmation with the statement by Ou *et al*. (2013) that when the stress study is normal and artefacts could be removed with AC-A, no rest study is needed and this will reduce radiation in a substantial number of patients.

The generalized linear model with ordinal regression demonstrated with the relevant factors that the *p*-values for all the variables are >0.05, and therefore the regression has no influence**.** This indicates that none of the independent variables, such as age, gender, weight, and height have a significant effect on the dependent variables (Tables 4.4 and 4.5). However, these independent variables are important for the patient's studies and final reports. There was no significant difference in the results regarding the patient position for supine or prone with AC-A for the myocardial studies, therefore, all the patients can be performed in the same position. The results for improvement for AC-A applied to the images of the two-day protocol is 50/50. This indicates also that whether a one-day or two-day protocol is used, it does not have an influence on the outcome of the study and validates the protocol used at research site.

The research question whether AC-A improves the images with the stress and rest studies, scores showed a difference where 49% improved and 51% did not improve the overall outcome (Table 4.1 and Figure 4.9). However, this score of 51 with no improvement, excludes 18 images of stress studies and nine images of rest studies which showed improvement (scores 2-3) in the inferior wall of the myocardium. In eight image sets of stress/rest studies, an improvement was observed in both stress and rest studies but AC-A did not improve the overall results (Table 4.2 and 4.3). Nevertheless, the rest study was necessary to be performed due to a combination of perfusion defects and attenuation defects or true perfusion defects observed. The conclusion for AC-A to be beneficial in 49% of stress studies with AC-A, but indecision about perfusion defects on the stress studies may result in a rest study to be performed without a CT, since soft tissue artefacts were already identified on stress study.

The results of the current research study displayed the benefit of AC-A with the highest score of 41.5% (>50% of change of perfusion defect) in this research study for the inferior wall of the myocardium for stress and rest studies although in an additional 18% of stress studies, an improvement in the inferior wall was also identified. There is a significant difference for the AC-A scores of the images in the inferior wall of the myocardium. Therefore, AC versus NAC with MPI shows a significant influence with AC-A on the outcome of the study for the inferior wall of the myocardium.

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ADDENDUM A

MIBI SPECT /CT STUDIES

DATA COLLECTION SHEET

NO	*Stress/ Rest	1 or 2 Day Protocol	Exercise (EX)/Persantin (PERS)	Sex	Age	Weight (kg)	Height (cm)	*Position	Conclusion AC Y	Conclusion AC N
1	S/R	1	PERS	M	70	78.4	1.69	P		X
2	S/R	2	PERS	F	45	154.8	1.695	S		X
3	S/R	1	PERS	F	53	150	1.74	S	X	
4	S/R	2	PERS	F	65	67.8	1.504	S		X
5	S/R	1	EX	M	62	80	1.71	P	X	
6	S/R	1	PERS	F	57	80.5	1.65	S		X
7	S/R	2	PERS	F	70	100.3	1.62	S		X
8	S/R	2	EX	F	47	74.4	1.69	S	X	
9	S/R	1	PERS	F	67	77.3	1.64	S		X
10	S/R	1	PERS	M	55	75.9	1.6	P	X	
11	S/R	2	PERS	F	55	100.1	1.52	S	X	
12	S/R	1	EX	F	60	86.4	1.6	S	X	
13	S/R	1	PERS	M	51	112.2	1.74	P		X
14	S/R	1	PERS	M	69	83	1.68	P		X
15	S/R	1	PERS	M	77	71.4	--------	P		X
16	S/R	1	PERS	M	54	81	1.69	P	X	
17	S/R	1	PERS	F	69	76	1.64	S		X
18	S/R	1	PERS	F	75	89.1	1.65	S		X
19	S/R	1	DOBU	F	61	69.8	1.49	S		X
20	S/R	1	PERS	M	86	62	1.59	P	X	
21	S/R	2	PERS	F	57	85.2	1.49	S		X
22	S/R	1	EX	M	57	95	1.81	P	X	
23	S/R	1	PERS	F	68	68.8	1.61	S		X
24	S/R	1	PERS	F	49	97	1.49	S		X
25	S/R	1	PERS	F	70	109.2	1.53	S		X
26	S/R	1	PERS	M	62	97.2	1.66	P	X	
27	S/R	1	PERS	F	59	87.3	1.69	S	X	
28	S/R	1	EX	M	59	99.6	1.71	P		X
29	S/R	1	PERS	M	64	108	1.71	P	X	
30	S/R	1	PERS	F	70	78.6	1.63	S		X
31	S/R	2	PERS	F	74	71.8	1.55	S		X
32	S/R	2	PERS	F	59	118.4	1.68	S	X	
33	S/R	1	PERS	F	55	95	--------	S	X	
34	S/R	2	PERS	F	61	112	1.63	S	X	
35	S/R	1	PERS	M	84	86.9	--------	P	X	
36	S/R	2	PERS	M	68	82	1.74	p		X
37	S/R	1	PERS	M	53	70.3	1.73	P	X	
38	S/R	1	PERS	M	59	98.6	1.67	P	X	
39	S/R	1	PERS	F	54	60.9	1.54	S		X
40	S/R	1	PERS	F	58	77.7	1.67	S	X	
41	S/R	1	EX	F	64	63.5	1.56	S	X	
42	S/R	1	PERS	M	59	93.6	1.7	P		X
43	S/R	2	PERS	M	68	63.3	1.72	P		X
44	S/R	1	EX	F	73	63	1.71	S		X
45	S/R	1	PERS	F	59	77.5	1.55	S	X	
46	S/R	1	PERS	M	61	80	1.7	P		X
47	S/R	1	PERS	F	64	98	1.55	S	X	
48	S/R	2	PERS	F	61	58	1.52	S		X
49	S/R	1	PERS	M	70	97	1.51	P		X
50	S/R	2	PERS	F	61	58	1.52	S	X	
51	S/R	1	PERS	F	58	84.8	1.65	S		X
52	S/R	1	PERS	F	75	98	169	S	X	
53	S/R	1	EX	F	49	69.7	156.6	S		X
54	S/R	2	PERS	F	61	79	162	S	X	
55	S/R	2	PERS	F	78	75.8	162	S	X	
56	S/R	2	PERS	M	33	78.4	175	P	X	
57	S/R	1	PERS	F	51	144.7	159	S		X
58	S/R	2	PERS	F	69	70.2	153	S	X	
59	S/R	1	DOBU	F	57	124.7	173	S		X
60	S/R	1	PERS	F	52	115.9	156	S		X
61	S/R	1	PERS	M	49	117.5	179	P	X	
62	S/R	1	PERS	F	79	110.9	160.4	S	X	
63	S/R	2	DOBU	M	58	78.1	174	P	X	
64	S/R	2	PERS	F	57	77	154	S	X	
65	S/R	1	EX	M	42	64	170	P		X
66	S/R	1	PERS	F	75	75.6	--------	S	X	
67	S/R	1	PERS	M	70	81.2	171	P		X
68	S/R	1	PERS	M	53	70.7	161	p		X
69	S/R	1	PERS	M	74	73.4	156.6	P	X	
70	S/R	1	EX	M	46	121.5	150.5	P		X
71	S/R	2	PERS	F	84	47	152	S		X
72	S/R	1	PERS	M	65	61	156	P		X
73	S/R	1	EX	F	47	103.4	166	S	X	
74	S/R	1	PERS	M	21	53.6	180	P	X	
75	S/R	1	PERS	M	64	82.5	177	P	X	
76	S/R	1	PERS	M	69	121	172	P		X
77	S/R	1	PERS	F	66	63	170	S	X	
78	S/R	1	PERS	F	77	80	158	S	X	
79	S/R	2	EX	F	65	76.3	162	S		X
80	S/R	1	PERS	F	47	98	155	S	X	
81	S/R	1	EX	F	43	83.7	158	S	X	
82	S/R	1	PERS	F	73	66.5	154	S	X	
83	S/R	2	PERS	M	69	94.3	149.6	P	X	
84	S/R	1	EX	M	69	103.4	168	P	X	
85	S/R	1	EX	M	74	81	175	P	X	
86	S/R	2	PERS	F	68	51.8	156	S		X
87	S/R	1	PERS	F	45	71.3	163	S		X
88	S/R	1	PERS	M	56	56	171	P		X
89	S/R	1	PERS	F	75	57.8	153	S		X
90	S/R	1	PERS	F	61	55.9	161	S		X
91	S/R	1	PERS	F	53	120	149	S	X	
92	S/R	1	PERS	M	63	92	175	P	X	
93	S/R	1	PERS	M	70	93.7	176	P		X
94	S/R	1	PERS	M	69	119	170	P		X
95	S/R	1	PERS	F	49	91	163	S		X
96	S/R	1	PERS	F	47	85.2	168	S		X
97	S/R	2	EX	M	55	93	183	P	X	
98	S/R	1	PERS	F	75	66	162	S	X	
99	S/R	1	PERS	F	43	105	--------	S		X
100	S/R	1	PERS	M	47	86	163	P		X

ADDENDUM B

Scoring sheet of myocardial walls

KEYS	0 = NORMAL	1 = NO CHANGE	2 = <50% CHANGE	3 =>50% CHANGE	4 = ARTIFACT	P = POSTION OF ARTIFACT	Y = IMPROVEMENT with AC-A	N = NO IMPROVEMENT

PT NR	*STRESS*												*REST*												CONCLUSION	
	ANTERIOR						INFERIOR						ANTERIOR						INFERIOR						Y	N
	0	1	2	3	4	P	0	1	2	3	4	P	0	1	2	3	4	P	0	1	2	3	4	P		
1		1					1							1					1							1
2					1	apex			1								1	apex			1					1
3					1	apex				1							1	apex		1					1	
4	1							1									1	apex		1						1
5	1									1			1									1			1	
6					1	apex	1										1	apex	1							1
7	1									1				1				apex		1						1
8	1									1			1					ant/apex	1						1	
9	1				1	apex	1						1				1	apex	1							1
10	1									1			1					apex				1			1	
11	1				1	apex				1			1									1			1	
12	1								1				1				1	apex	1						1	
13		1			1	ant/apex			1					1			1	apex			1					1
14	1				1	apex			1				1				1	apex				1				1
15		1			1	apex		1									1	ant/apex		1						1
16				1						1						1						1			1	
17	1						1						1				1	apex	1							1
18	1						1						1						1							1
19	1				1	apex		1					1				1	apex	1							1
20	1				1	ant/apex			1				1				1	ant/apex			1				1	
21		1						1					1				1	apex	1							1
22		1			1	apex				1						1						1			1	
23	1						1						1						1							1
24	1										1	inferior					1	ant/apex					1	inferior		1
25	1				1	apex		1						1			1	apex		1						1
26	1				1	apex				1			1				1	apex				1			1	
27		1			1	ant/apex		1							1		1	apex				1			1	
28	1								1				1				1	ant/apex		1						1
29	1				1	ant/septal				1			1									1			1	
30		1					1				1	inferior		1						1						1
31		1						1						1						1						1
32	1				1	apex				1							1	x apex		1					1	
33	1				1	apex				1			1				1	apex				1			1	
34		1								1				1								1			1	
35	1									1			1				1	apex				1			1	
36	1				1	apex	1						1				1	apex					1	inferior		1
37			1		1	apex				1				1			1	apex	1						1	
38					1	ant/apex				1			1				1	apex				1			1	
39		1					1							1					1							1
40					1	ant/apex				1			1				1	apex				1			1	
41		1							1				1				1	apex			1				1	
42		1						1					1								1					1
43		1							1					1			1	apex		1						1
44	1				1	apex	1						1				1	inf					1	inferior		1
45	1				1	apex				1			1				1	ant/apex	1						1	
46		1								1				1			1	apex				1				1
47	1									1			1						1						1	
48					1	ant/apex			1								1	apex			1					1
49	1				1	apex	1						1				1	apex	1							1
50					1	ant		1					1								1				1	
51		1								1					1							1				1
52	1									1			1				1	apex	1						1	
53					1	ant/apex					1	inferior	1						1							1
54					1	ant/apex				1			1									1			1	
55	1									1						1						1			1	
56		1								1					1							1			1	
57		1							1				1				1	apex	1							1
58			1				1							1			1	apex	1						1	
59	1				1	apex			1								1	ant/apex	1							1
60		1					1										1	ant/apex	1							1
61	1				1	ant/apex	1										1	apex	1						1	
62		1			1	apex		1								1	1	apex				1			1	
63	1									1				1								1			1	
64	1								1						1						1				1	
65	1				1	ant/apex			1				1						1							1
66	1				1	apex				1			1				1	apex		1					1	
67	1									1			1									1				1
68	1									1			1									1				1
69	1				1	apex			1				1				1	apex			1				1	
70	1				1	ant/apex			1							1	1	ant/apex		1						1
71		1						1					1				1	apex	1							1
72		1						1							1					1						1
73			1				1									1						1			1	
74		1								1			1									1			1	
75		1								1			1									1			1	
76					1	ant/apex			1					1			1	apex		1						1
77		1						1							1							1			1	
78	1									1			1									1			1	
79	1						1									1			1							1
80					1	ant/apex			1								1	apex			1				1	
81	1									1			1				1	apex	1						1	
82	1									1			1				1	apex				1			1	
83	1							1					1									1			1	
84	1				1	apex				1			1				1	apex				1			1	
85	1				1	apex				1			1				1	apex			1				1	
86	1				1	ant/apex			1				1				1	apex			1					1
87		1					1							1					1							1
88		1							1					1						1						1
89	1						1						1				1	apex	1							1
90	1				1	ant/apex			1				1				1	apex					1	inferior		1
91					1	ant/apex				1							1	ant/apex				1			1	
92	1									1							1	apex				1			1	
93		1					1										1	apex	1							1
94		1					1							1					1							1
95	1				1	apex	1										1	ant/apex		1						1
96					1	ant/apex	1										1	ant/apex	1							1
97		1								1				1								1			1	
98		1								1				1								1			1	
99		1					1							1					1							1
100	1				1	apex	1						1				1	apex	1							1

ADDENDUM C

Scoring of stress and rest myocardial walls

Patient	Stress study Between NAC and AC images: Ant Yes	Ant No	Ant Artifact	Ant Artifact position	Inf Yes	Inf No	Inf Artifact	Inf Artifact position	Stress	Rest study Between NAC and AC images: Ant Yes	Ant No	Ant Artifact	Ant Artifact position	Inf Yes	Inf No	Inf Artifact	Inf Artifact position	Rest	Yes/No AC-A improved reporting between Stress and Rest study only for AC-A	Patient
1		1				1					1				0				0	1
2		0	4	apex	2						0	4	apex	2					0	2
3		0	4	apex	3						0	4	apex		1				1	3
4		0				1					0	4	apex		1				0	4
5		0			3						0			3					1	5
6		0	4	apex		0					0	4	apex		0				0	6
7		0			3						1				1				0	7
8		0			3						0				0				1	8
9		0	4	apex		0					0	4			0				0	9
10		0			3						0			3					1	10
11		0			3						0			3					1	11
12		0			2						0	4			0				1	12
13		1	4	apex	2						1	4		2					0	13
14		0	4	apex	2						0			3					0	14
15		1	4	apex		1					1	4	ant+apex		1				0	15
16	3				3					3				3					1	16
17		0				0					0				0				0	17
18		0				0					0				0				0	18
19		0	4	apex		1					0	4	apex		1				0	19
20		0	4	ant +apex	2						0	4	ant+apex	2					1	20
21		1				1					0	4	apex		0				0	21
22		1	4	apex	3					3				3					1	22
23		0				0					0				0				0	23
24		0				0	4	inferior			0	4	ant+apex		0	4	inferior		0	24
25		0	4	apex		1					1	4	apex		1				0	25
26		0	4	apex	3						0	4	apex	3					1	26
27		1	4	apex +ant		1				2	0	4	apex	3					1	27
28		0			3						0	4	ant+apex		1				0	28
29		0	4	ant + septal	3						0				1				1	29
30		1				0					1				1				0	30
31		1				1					1				1				0	31
32		0	4	apex	3						0	4	apex		1				1	32
33		0	4	apex	3						0	4	apex	3					1	33
34		1			3						1			3					1	34
35		0			3						0	4	apex	3					1	35
36		0	4	apex		0					0	4	apex		0	4	inferior		1	36
37	2		4	apex	3						1	4	apex		0				1	37
38		0	4	ant+apex	3						0	4	apex	3					1	38
39		1				0					1				0				0	39
40		0	4	ant+apex	2						0	4	apex	3					1	40
41		1			2						0	4	apex	2					1	41
42		1				1					0			2					0	42
43		1			2						1	4	apex		1				0	43
44		0	4	apex		0					0		inferior		0	4	inferior		0	44
45		0	4	apex	3						0	4	ant+apex		0				1	45
46		1			3						1	4	apex	3					0	46
47		0			3						0				0				1	47
48		0	4	ant+apex	2						0	4	apex	2					0	48
49		0	4	apex		0					0	4	apex		0				0	49
50		0	4	ant		1					0			2					1	50
51		1			3						0				0				0	51
52		0			3						0	4	apex		0				1	52
53		0	4	ant+apex		0	4	inferior			0				0				0	53
54		0	4	ant+apex	3						0			3					1	54
55		0			3					3				3					1	55
56		1			3					2				3					1	56
57		1			2						0	4	apex		0				0	57
58	2					0					1	4	apex		0				1	58
59		0	4		2						0	4	ant+apex		0				0	59
60		1				1				3		4	apex		0				0	60
61		0	4	ant+apex		0					0	4	apex		0				1	61
62		1	4	apex		1				3	0	4	apex	3					1	62
63		0			3						1			3					1	63
64		0			2					2				2					1	64
65		0	4	ant+apex	2						0				0				0	65
66		0	4	apex	3						0	4	apex		1				1	66
67		0			3						0			3					0	67
68		0			3						0			3					0	68
69		0	4	apex	2						0	4	apex	2					1	69
70		0	4	ant+apex	2					3		4	ant+apex		1				0	70
71		1				1					0	4	ant+apex		1				0	71
72		1				1					0	4	apex		0				0	72
73	2					0				3				3					1	73
74		1			3						0			3					1	74
75		1			3						0			3					1	75
76		0	4	ant+apex	2						1	4	apex		1				0	76
77		1			3					2				3					1	77
78		0			3						0			3					1	78
79		0				0				3					0				0	79
80		0	4	ant+apex	2							4	apex	2					1	80
81		0			3						0	4	apex		0				1	81
82		0			3						0	4	apex	3					1	82
83		0				1					0			3					1	83
84		0	4	apex	3						0	4	apex	3					1	84
85		0	4	apex	3						0	4	apex	2					1	85
86		0	4	ant	2						0	4	apex	2					0	86
87		1				0					0	4	apex	2					0	87
88		1			2						1				1				0	88
89		0				0					0	4	apex		0				0	89
90		0	4	ant+apex		2					0	4	apex		0	4	inferior		0	90
91		0	4	ant+apex	3						0	4	ant+apex	3					1	91
92		0			3						0	4	apex	3					1	92
93		1				0					0	4	apex		1				0	93
94		1				0					1				0				0	94
95		0	4	apex		0						4	ant+apex		1				0	95
96		0	4	ant+apex		0					0	4	ant+apex		1				0	96
97		1			3						1			3					1	97
98		1			3						1			3					1	98
99		1				0					1				0				0	99
100		0	4	apex		0					0	4	apex		0				0	100
									19									9	Yes/No	

Stress study between non-AC and AC-A

Anterior (ant) IMPROVEMENT: Yes	No	Artifact	Artifact position	Inferior (inf) IMPROVEMENT: Yes	No	Artifact	Artifact position
4	96	25	apex	60	40	2	inferior
3-less than 50%	65-normal study	15	ant+apex	19 - less than 50%	24 - normal study		
1 - more than 50%	31-image did not change	1	ant=septal	41 -more than 50%	15- image did not change		
	18 image sets improvement inf with AC-A NO				1- less than 50% improvement		

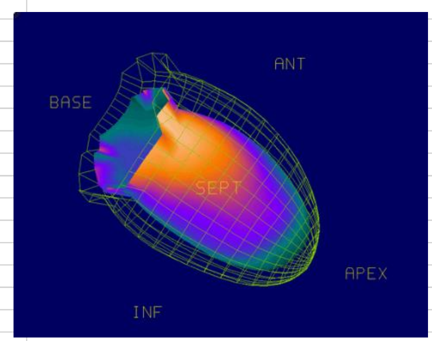
Rest study between non-AC and AC-A

Anterior (ant) IMPROVEMENT: Yes	No	Artifact	Artifact position	Inferior (inf) IMPROVEMENT: Yes	No	Artifact	Artifact position
12	88	11	ant+apex	46	54	4	inferior
4 - less than 50%	68-normal study	43	apex	13 -less than 50%	43-normal study	1	ant+apex
8 -more than 50%	20 - image did not change	1	inf	33-more than 50%	20-image did not change		
	9 image sets improvement inf but with AC-A NO						

0	Normal study. No need to report further
1	Image did not change
2	Less than 50% improvement with AC-A information added
3	More than 50% improvement with AC-A information added
4	Aftifact created on the image, possibly because of the Ac-A

0 and 1 = No
2 and 3 = Yes

NAC	Non- attenuated corrected images
AC	Attenuated corrected
AC-A	Attenuation correction application
ANT	Anterior wall of the myocardium
INFERIOR	Inferior wall of the myocardium
APEX	Lowest area of myocardium
Artifact	Dark area appears due to AC-A on image



Heart muscle(Myocardium) areas

ADDENDUM D

Cape Peninsula
University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

P.O. Box 1906 • Bellville 7535 South Africa
Symphony Road Bellville 7535
Tel: +27 21 959 6917
Email: sethn@cput.ac.za

20 November 2017
REC Approval Reference No:
CPUT/HW-REC 2017/H37

Dear Ms Lelanie Lucia Nolan

Re: APPLICATION TO THE HW-REC FOR ETHICS CLEARANCE

Approval was granted by the Health and Wellness Sciences-REC on 14 September 2017 to Ms Nolan for ethical clearance. This approval is for research activities related to student research in the Department of Medical Imaging and Therapeutic Sciences at this Institution.

TITLE: **The influence of Low-Dosr CT Attenuation Correction applied to Myocardial SPECT imaging on Nuclear Medicine reporting**

Supervisor: Ms E Seane

Comment:

Approval will not extend beyond 21 November 2018. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the HWS-REC in December of that particular year, for the HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Mr. Navindhra Naidoo
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

ADDENDUM E

Western Cape Government
Health

TYGERBERG HOSPITAL
REFERENCE:
Research Projects
ENQUIRIES: **Dr GG Marinus**
TELEPHONE:**021 938 5752**

Ethics Reference: **CPUT/HW-REC 2017/H37**

TITLE: The influence of Low-Dose CT Attenuation ~~Correlation~~ Correction applied to Myocardial SPECT imaging on Nuclear Medicine reporting.

Dear Miss Lelanie Lucia Nolan

PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL.

1. In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital.
2. Researchers, in accessing Provincial health facilities, are expressing consent to provide the Department with an electronic copy of the final feedback within six months of completion of research. This can be submitted to the Provincial Research Co-Ordinator (Health.Research@westerncape.gov.za).

DR GG MARINUS
MANAGER: MEDICAL SERVICES

DR D ERASMUS
CHIEF EXECUTIVE OFFICER
Date: 15 December 2017

Administration Building, Francie van Zilj Avenue, Parow, 7500 Private Bag X3, Tygerberg, 7505
tel: +27 21 938-6267 fax: +27 21 938-4890 www.capegateway.go.v.za

ADDENDUM F

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13 August 2017

To: CPUT MSc Radiography Research Ethics Committee

Dear members of the Research Ethics Committee

RESEARCH PROJECT OF MSc RADIOGRAPHY (NUCLEAR MEDICINE) STUDENT

This is to confirm that the Nuclear Medicine division at Tygerberg Hospital has been informed about a proposed research project by Ms Lelanie Nolan (student number 182009149), which will be performed in the Nuclear Medicine division of Tygerberg Hospital. The title of her project is: *The influence of Low-Dose CT Attenuation Correction applied to Myocardial SPECT Imaging on Nuclear Medicine reporting.*

Please note that the research project must also be approved by Tygerberg Hospital. The student should submit this application before commencing with the research.

Yours sincerely

PROF ANNARE ELLMANN
Head: Nuclear Medicine
Tel: (021) 938-4352
Fax: (021) 938-4694
E-mail: ae1@sun.ac.za

Copy to: Dr N Korowlay, nuclear medicine physician
Mr H Thomas, assistant director Radiography

ADDENDUM G

Stress Anterior: Change in the view of the defect on the NAC image * Rest Anterior: Change in the view of the defect on the NAC image Crosstabulation							
			Rest Anterior: Change in the view of the defect on the NAC image				
			No defect	No change in the view of the defect of the image	Less than 50% improvement of image	More than 50% improvement of image	Total
Stress Anterior: Change in the view of the defect on the NAC image	No defect	Count	38	3	1	3	45
		% Within Stress Anterior: Change in the view of the defect on the NAC image	84.4%	6.7%	2.2%	6.7%	100.0 %
	No change in the view of the defect of the image	Count	7	14	5	2	28
		% Within Stress Anterior: Change in the view of the defect on the NAC image	25.0%	50.0%	17.9%	7.1%	100.0 %
	Less than 50% improvement of image	Count	0	2	0	1	3
		% Within Stress Anterior: Change in the view of the defect on the NAC image	0.0%	66.7%	0.0%	33.3%	100.0 %
	More than 50% improvement of image	Count	0	0	0	1	1
		% Within Stress Anterior: Change in the view of the defect on the NAC image	0.0%	0.0%	0.0%	100.0%	100.0 %
Total		Count	45	19	6	7	77
		% Within Stress Anterior: Change in the view of the defect on the NAC image	58.4%	24.7%	7.8%	9.1%	100.0 %

ADDENDUM H

Stress Inferior: Change in the view of the defect on the NAC image * Rest Inferior: Change in the view of the defect on the NAC image Crosstabulation							
			Rest Inferior: Change in the view of the defect on the NAC image				Total
			No defect	No change in the view of the defect of the image	Less than 50% improvement of image	More than 50% improvement of image	
Stress Inferior: Change in the view of the defect on the NAC image	No defect	Count	19	2	0	1	22
		% Within Stress Inferior: Change in the view of the defect on the NAC image	86.4%	9.1%	0.0%	4.5%	100.0%
	No change in the view of the defect of the image	Count	3	5	2	4	14
		% Within Stress Inferior: Change in the view of the defect on the NAC image	21.4%	35.7%	14.3%	28.6%	100.0%
	Less than 50% improvement of image	Count	4	5	9	1	19
		% Within Stress Inferior: Change in the view of the defect on the NAC image	21.1%	26.3%	47.4%	5.3%	100.0%
	More than 50% improvement of image	Count	6	4	1	28	39
		% Within Stress Inferior: Change in the view of the defect on the NAC image	15.4%	10.3%	2.6%	71.8%	100.0%
Total		Count	32	16	12	34	94
		% Within Stress Inferior: Change in the view of the defect on the NAC image	34.0%	17.0%	12.8%	36.2%	100.0%