STANDARDIZED UPTAKE VALUE (SUV) AS SEMI-QUANTITATIVE ANALYSIS OF MYOCARDIAL PERFUSION STUDY

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by

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Dissertation submitted in partial fulfillment

of the requirements for the degree

of Bachelor of Health Sciences (Honours) (Medical Radiation)

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CERTIFICATE

This is to certify that the dissertation entitled Standardized Uptake Value (SUV) As Semi-Quantitative Analysis of Myocardial Perfusion Study is the bona fide record of research work done by Ms. Sabturia Kaalam during the period from September 2019 to July 2020 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfillment for the degree of Bachelor Health Science (Honours) (Medical Radiation).

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DECLARATION

I hereby declare that this dissertation is the result of my investigations, except otherwise stated and properly acknowledged. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at Universiti Sains Malaysia or other institutions. I grant Universiti Sains Malaysia the right to use the dissertation for teaching, research, and promotional purpose.

Sabturia Kaalam

Date: 19th August 2020

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LIST OF ABBREVIATIONS AND ACRONYMS

^{18}F-NaF	Fluorine-18 Sodium Fluoride
^{99m}Tc	Technetium-99m
^{99m}Tc-HDP	Tc-99m Hydroxydiphosphonate
CAD	Coronary Artery Disease
CT	Computed Tomography
LAD	Left Anterior Descending artery
LCx	Left Circumflex Coronary artery
MPI	Myocardial Perfusion Imaging
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
ROI	Region of Interest
SPECT	Single Photon Emission Computed Tomography
SUV	Standardized Uptake Value
SSS	Summed Stress Score
SRS	Summed Rest Score
SDS	Summed Difference Score
WHO	World Health Organization

ABSTRAK

Kajian ini bertujuan untuk menyiasat tentang kebolehan pengukuran *SUV* dalam menganalisis keputusan imbasan perfusi miokardium dengan membezakan min *SUV* dan maksimum *SUV*. Menerapkan *SUV* sebagai semi-kuantitatif analisis berkemungkinan untuk memudahkan penganalisisan keputusan imej, yang mana terdapat kebarangkalian tentang ketaktekalan berpunca daripada penilaian visual iaitu pendekatan yang digunakan dalam menganalisis imej *SPECT/CT* pada masa kini. Dalam kajian ini, seramai dua orang pesakit yang diambil secara retrospektif dari Jabatan Pengimejan Perubatan Nuklear Hospital Universiti Sains Malaysia sebagai sampel. Min *SUV*, maksimum *SUV* dan pengambilan penyurih di dalam setiap dinding ventrikel kiri diperoleh menggunakan perisian *GE Myovation Evolution®* dan *GE Q.Matrix*. Setiap Kawasan empat dinding iaitu dinding anterior, lateral, inferior dan septa dilukis secara manual dan bacaan semua *SUV* dan pengambilan penyurih dicatat berdasarkan kawasan yang telah dilukis. Nilai p dengan <0.05 menandakan terdapatnya perbezaan secara statistical. Keputusannya, terdapat tiada perbezaan yang signifikan dijumpai diantara min *SUV* dan maksimum *SUV* dengan pengambilan penyurih di dalam setiap dinding ventrikel kiri dengan nilai-p sebanyak 0.602 ($p>0.05$). Terdapat juga hubungan linear yang kuat diantara kedua-dua min *SUV* dan maksimum *SUV* dengan umur, berat dan tinggi pesakit masing-masing dengan $r=0.873$, $p<0.05$ dan $r=0.768$, $p<0.05$. Secara konklusinya, terdapat peluang yang cerah dalam mengaplikasikan *SUV* sebagai semi-kuantitatif analisis dalam keputusan imbasan perfusi miokardium di masa yang akan datang.

ABSTRACT

This study aimed to investigate the ability of SUV measurement in analyzing the myocardial perfusion finding by comparing the SUV mean and SUV max with the qualitative imaging finding. Applying SUV as semi-quantitative analysis might ease the analyzation process of the image finding due to the probability of inconsistencies finding from the visual evaluation which is the current method used in interpreting the SPECT/CT images. In this study, a sample of two patients from the Nuclear Medicine Imaging Department of Hospital Universiti Sains Malaysia was retrospectively taken. The SUV mean SUV max and uptake of the tracer in each of the left ventricle walls were derived using the GE Myovation Evolution® and GE Q.Metrix software. Every region of the four walls (anterior, lateral, inferior, and septa wall) of the left ventricle were drawn manually and the measurement of the SUVs and uptake was recorded based on the drawn region. A p-value < 0.05 indicates that it is statistically significant. As a result, there were no significant differences between SUV mean and SUV max with the uptake from each of the left ventricle wall with a p-value of 0.602 ($p>0.05$). There was a strong linear relationship found between both SUV mean and SUV max with age, weight, and height of the samples with $r=0.873$, $p<0.05$, and $r=0.768$, $p<0.05$ respectively. In conclusion, there is a bright chance of implementing SUV as a semi-quantitative analysis in myocardial perfusion imaging finding in the future.

CHAPTER 1: INTRODUCTION

1.1 BACKGROUND OF STUDY

Myocardial perfusion imaging (MPI) is one of the techniques used to detect one of the commonest heart diseases which is coronary artery disease. MPI gives images that enable doctors to assess coronary blood flow. Besides, many studies have proven that MPI is the most suitable technique in evaluating the functional hemodynamic aspects of the heart where it can be performed using Single Photon Emission Computed Tomography / Computed Tomography (SPECT/CT) (Spier et al, 2019). SPECT/CT acquires the images from many projections by detecting the gamma rays from decaying radiopharmaceutical such as Technetium-99m, Sestamibi that is being emitted from the patient's body. The distribution of perfusion can be assessed during rest, stress, or both (Strauss et al, 2008). This research project focuses on the assessment of the myocardial perfusion study. MPI assessment can be performed using qualitative and quantitative analysis. The qualitative analysis which is visual evaluation is performed manually by doctors. This is done by evaluating the radiotracer uptake in the myocardial wall of the left ventricle. The presence of radiotracer within a particular region of the left ventricle wall is indicative of normal viable myocardium where else the absence of radiotracer is indicative of otherwise. On the other hand, quantitative analysis is another method of MPI assessment. Conventionally, a 17-segment polar map has been used to describe radiotracer uptake distribution with scores of 1-4 given to each segment. This is a manual visual assessment of radiotracer uptake and is operator dependant. Meanwhile, Standardized Uptake Value (SUV) is one of the quantitative analysis proposed in this study. This study is aimed to assess the feasibility of utilizing SUV in myocardial perfusion study.

1.2 PROBLEM STATEMENT

Currently, visual evaluation is a qualitative analysis used in myocardial perfusion study. In visual evaluation, the inconsistencies in interpreting images might increase due to the absence of fixed values and is operator dependent. Meanwhile, semi-quantitative analysis using SUV is not widely being used as it is only used to assist the visual evaluation method. However, SUV has its benefit compared to qualitative analysis as it enables the quantitative evaluation of the uptake degree in SPECT analysis (Bando et al, 2019). Thus, the problem caused by the uses of visual evaluation analysis can be solved by applying quantitative analysis in myocardial perfusion study. That is why this study is conducted to know whether quantitative SPECT/CT using Standardized Uptake Value (SUV) can be applied in myocardial perfusion study.

1.3 RESEARCH OBJECTIVES

Main Objective

To assess the potential application of SUV SPECT/CT using Tc-99m labeled Sestamibi in myocardial perfusion study.

Specific Objectives

1. To determine the SUV mean and SUV max of the left ventricle wall of the study population.
2. To compare between quantitative SUV mean and SUV max values against qualitative myocardial perfusion imaging finding
3. To correlate between age, weight, and height with SUV mean and SUV max in myocardium perfusion study

1.4 RESEARCH HYPOTHESIS

Alternative Hypothesis

Semi-Quantitative SPECT/CT using Standardized Uptake Value (SUV) is applicable in myocardial perfusion study.

Null Hypothesis

Semi-Quantitative SPECT/CT using Standardized Uptake Value (SUV) is not applicable in myocardial perfusion study.

1.5 JUSTIFICATION OF STUDY

The study of SUV as semi-quantitative analysis in myocardial perfusion can be a tool to make the evaluation of myocardial perfusion images easier and more accurate. Besides, this study is aimed at comparing semi-quantitative analysis such as SUV to the conventional qualitative visual analysis.

CHAPTER 2: LITERATURE REVIEW

2.1 QUALITATIVE ANALYSIS OF MYOCARDIAL PERFUSION STUDY

Interpretation of myocardial perfusion findings is performed based on visual assessment. The evaluation is done by comparing the relative tracer uptake images with a subjective interpretation which includes factors such as pre-test likelihood of disease, image quality, and possible artifacts (Driessen et al, 2018). However, to be an expert in evaluating this MPI finding, a lengthy period of training and experience is needed. Hence, quantitative analysis is needed to assist the medical doctor in image evaluation and interpretation. Driessen et al. (2018), in his study, showed that automated SPECT analysis is as accurate as visual scoring by an expert in the detection of coronary artery disease (CAD).

Research by Bailey et al. (2013), on the potential of quantitative analysis, suggested that SPECT imaging would not reach its full potential if only qualitative analysis is used. In the study, the quantitative SPECT analysis has the potential to match the quantitative Positron Emission Tomography (PET) analysis (Bailey et al, 2013). This proof indicates that quantitative analysis is better than qualitative analyzes in SPECT.

2.2 QUANTITATIVE ANALYSIS OF MYOCARDIAL PERFUSION STUDY

The quantitative analysis of myocardial perfusion study works by comparing data from a patient to normal limits from a pre-defined database. The databases are derived from retrospective studies (Spier et al, 2019). A polar map is a well-known semi-quantitative method to assist visual interpretation by increasing the accuracy and precision in evaluating the images. The distribution of radiotracer throughout the heart is displayed in a two-dimensional polar map. Each data point from the polar map represents a number and color corresponding to the radiotracer uptake (Dvorak et al, 2011).

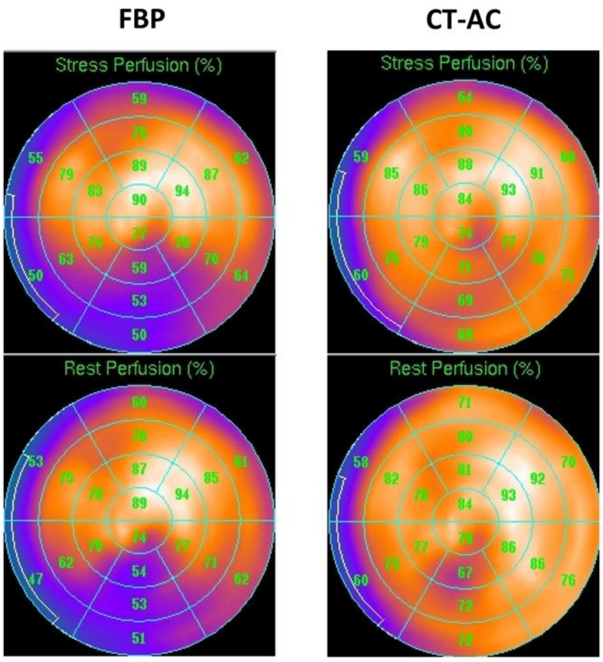

Figure 1 shows the example of a polar map with Filter Back Projection (FBP) and CT Attenuation Correction (CT-AC)

A study from Dvorak et al. (2011) stated that a blackout polar map is mostly being used in interpreting the data. The so-called blackout map displays a black color on an area of the patient’s normalized polar map that has perfusion values exceeding the threshold values. A designated threshold of 2.5 standard deviations below the normal database indicates perfusion defects (Dvorak et al, 2011).

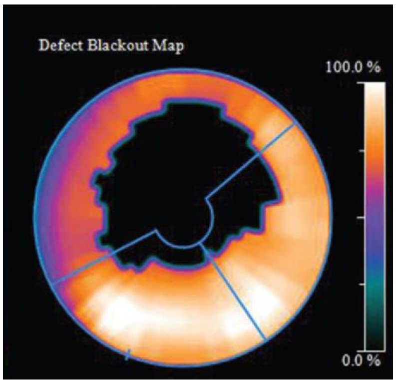

Figure 2 shows the example of defect blackout polar map where the black area indicates perfusion defect below the designated threshold

The semi-quantitative analysis also can be performed by using a 17-segment model where each segment represents a certain score. The scores are then expressed as a summed stress score (SSS), summed rest score (SRS), and summed difference score (SDS) (Burgt, 2019). Through this score, the severity of the abnormality including ischemia and infarction can be determined (Burgt, 2019). A research conducted by Biglands et al. (2018), they reported that quantitative analysis of myocardial perfusion images is highly reliable in terms of diagnosis compared to qualitative image analysis.

2.3 STANDARDIZED UPTAKE VALUE AS A SEMI-QUANTITATIVE ANALYSIS IN SPECT/CT

Generally, SUV acts as a benchmark in determining whether a region is considered as “normal” or “abnormal” levels of uptake. Furthermore, SUV is a common measurement in nuclear medicine, where an SUV of 2.5 or higher is usually considered to be detected as malignant tissue (Caldwell et al, 2008).

SUV as semi-quantitative analysis in SPECT/CT is a common analysis frequently associated with PET but recent advancement in gamma camera technology has applied SUV in SPECT/CT imaging (Toriihara et al, n.d). Many studies have attempted to apply SUV in clinical practice with most of these studies targeted bone SPECT/CT (Toriihara et al, n.d). According to Toriihara et al, SUV has the potentials to improve the accuracy in evaluating numerous studies in nuclear medicine. A study from Arvola et al, comparing SUV of ^{99m}Tc-HDP SPECT/CT and ^{18}F-NaF PET/CT in bone metastases of breast and prostate. Through this study, it is found that all the SUV reading strongly matches between SPECT/CT and PET/CT ($R^2 \geq 0.80$, $p < 0.001$). The correlation of SUV SPECT/CT with PET/CT thus concludes that SUV is an applicable method in clinical quantification of SPECT/CT.

Additionally, research from He et al. (2015) that studied the clinical application of absolute-quantification of SUV SPECT in myocardial perfusion imaging stated that it can evaluate myocardial viability. Moreover, another study on determining the viability of myocardial perfusion quantification by Dhillo (2019) also revealed a similar finding. He stated that the accuracy results from his finding showed a potential for quantification with a low accuracy error (Dhillo, 2019).

CHAPTER 3: RESEARCH METHODOLOGY

3.1 RESEARCH DESIGN

This is a retrospective study analyzing myocardial perfusion study involving two patients who had undergone myocardial perfusion study in the Department of Nuclear Medicine, Radiotherapy & Oncology, Hospital USM from October 2018 to October 2019.

3.2 SCOPE OF STUDY

This study focused on patients referred to the Nuclear Medicine Unit, Hospital USM who had undergone myocardial perfusion study.

3.3 STUDY LOCATION

This study was conducted in the Nuclear Medicine Unit, Department of Nuclear Medicine, Radiotherapy & Oncology, Hospital USM, Kubang Kerian, Kelantan.

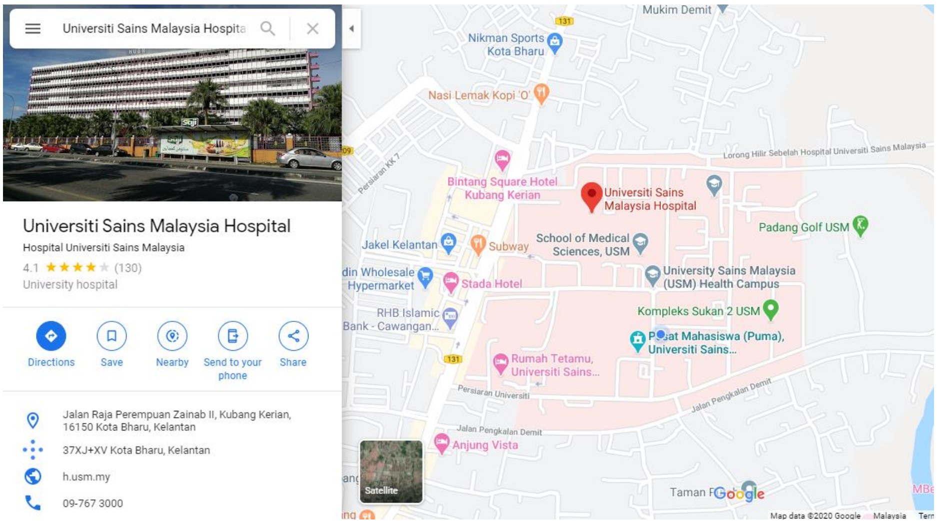

Figure 3 Map of study location

3.4 RECRUITMENT

The sampling method of this study is random sampling where all the patient that undergoes MPI SPECT/CT, we randomly take about n=2 and used their data as this is a retrospective study. A universal sampling method was applied. Data were selected from data of patients who had undergone MPI SPECT/CT from October 2018 to October 2019.

3.5 SELECTION CRITERIA

Inclusion criteria

- A patient that had undergone myocardial perfusion imaging SPECT/CT in the Nuclear Medicine Department in HUSM
- A patient who had undergone two-day stress/rest protocol

Exclusion criteria

- A patient that undergoes other than myocardial perfusion imaging SPECT/CT
- Incomplete Myocardial Perfusion Imaging SPECT/CT such as viability, stress or rest only study
- Pregnancy

3.6 RESEARCH TOOLS

The following tools are used to obtain the necessary data:

1. **GE Myovation Evolution® Software**

GE Myovation Evolution® software was used to derive MPI images to polar maps. This is a semi-quantitative analysis software that analyzed perfusion images during stress and rest studies. CT-attenuation correction method was utilized for better image quality. This software provides the following parameters:

1) Three axial views of the myocardium
    - Short axis
    - Horizontal long axis
    - Vertical long axis

2) Polar maps (Bull's Eye View)

The reconstructed images obtained from this software were processed further using the GE Q.Matrix toolkit whereby SUV values were then derived. SUV values were then compared with the polar map. Theoretically, regions with high uptake of radiotracer will produce high SUV reading and vice versa.

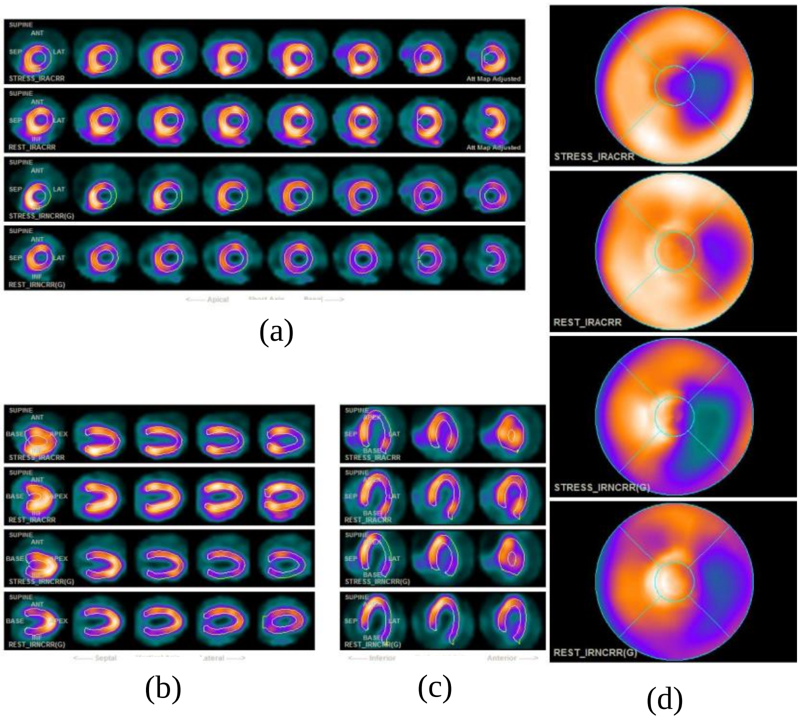

Figure 4(a) Short axis axial view (b) Vertical axis axial view (c) Horizontal axis axial view (d) Polar map of the left ventricle heart wall during stress and rest

2. GE Q.Matrix® Software

This software was used in determining uptake, SUV mean, and SUV max of the four walls of the heart (anterior, lateral, inferior, septa) which is in correlation with the polar map description. This was achieved by manually drawing and outlining regions of interest (ROI) of all 4 walls. This was done by determining the ROI based on the fused CT and SPECT images. Moreover, this software incorporated patient details such as dose of radiotracer inject, weight, and height. SUV values were then derived automatically and SUV values of each of the walls were then recorded. Besides, uptake reading was also obtained which showed the corresponding uptake of each of the drawn heart walls. According to Burgt, (2019) the SUV measurement in g/ml based on bodyweight was derived from PET studies and calculated by the following three equations:

$$SUV = (\text{SPECT image Pixels uptake (Bq/ml)}).\ \text{Bodyweight}/\ (A_{act}\ .1000)$$

$$\text{Bodyweight}_{male} \text{ in kg} = 1.10 \text{ x } W - 120 \text{ x } \left[\frac{W}{H}\right]^2$$

$$\text{Bodyweight}_{female} = 1.07 \text{ x } W - 148 \text{ x } \left[\frac{W}{H}\right]^2$$

Where,

W = Weight in kg

H = Height in cm

A_{act} = The administered activity minus rest-activity corrected for decay

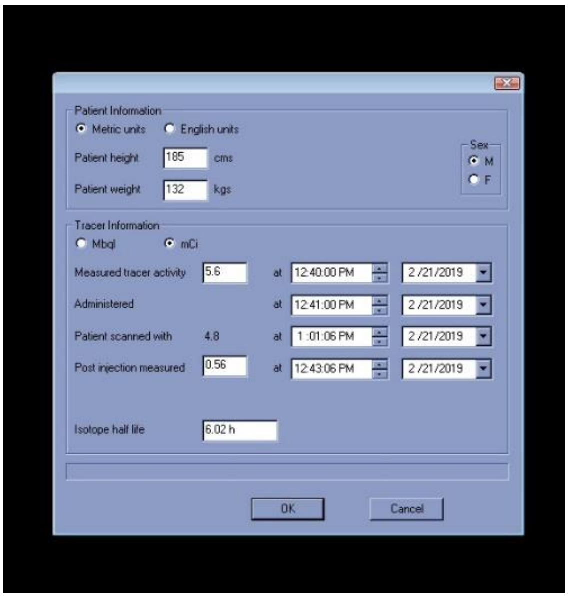

Figure 5 Patient information such as body weight and injection time filled in

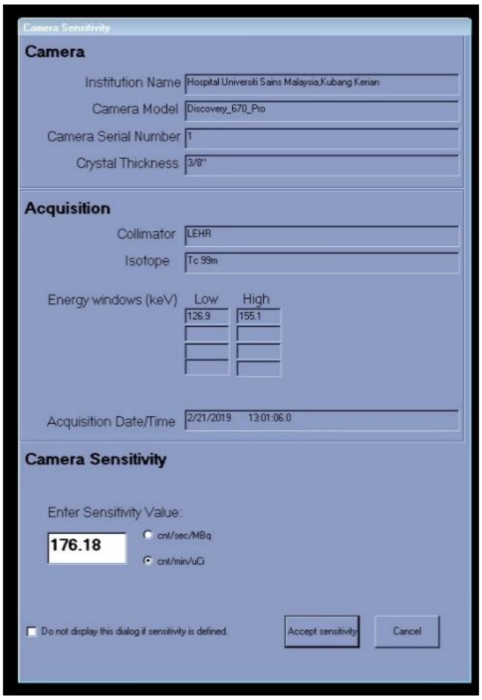

Figure 6 Parameters used in GE Q.Matrix software

Statistical Analysis

Statistical analysis test using SPSS statistic was used to evaluate the normality of the data. Through this test, SUV mean and SUV max was compared with the qualitative image finding of the based on the polar map as well as the 3-axis images. The correlation between age, weight, and height with SUV mean and max also were calculated using statistical analysis. P-value <0.05 indicated significant differences.

3.7 ETHICAL CONSIDERATION

1. Subject vulnerability
   Not applicable.

2. Declaration of the absence of conflict of interest
   I hereby declare that I do not have any personal conflict of interest.

3. Privacy and confidentiality
   All data are anonymous and only research team members can access the data. Data will be presented as grouped data and will not identify the subjects individually.

4. Community sensitivities and benefits
   This study gives the most benefit to medical professionals such as nuclear medicine physicians in accurately interpreting myocardial perfusion study.

5. Honorarium and incentives
   Not applicable.

6. Other ethical review board approval
   Not applicable.

3.8 ETHICAL APPROVAL

This research proposal has been reviewed by the Human Research Ethics Community of USM for ethical consideration and has been approved. This study has been assigned study protocol code **USM/JEPeM/19120864** with ethical clearance validation from 3rd March 2020 until 2nd March 2021. **(Appendix A)**.

CHAPTER 4: RESULTS & DISCUSSION

The primary aim of this project was to find out the possibility of applying SUV as a part of the analysis and interpreting tool in myocardial perfusion imaging. Besides, earlier researchers suggested that SUV was indeed a suitable approach in providing a better way of analysis in SPECT imaging. Among the studies that have shown benefit in utilization of SUV was by Dong et al. (2019) which involved the diagnosis and evaluation of Grave's disease. Thus, the outcome of this project will determine whether SUV can also be applied in myocardial perfusion imaging as suggested by other researchers.

As a result, objective 1 is achieved based on finding in **4.1**. From the polar map, high uptake of tracer for patient 1 visualized at the inferior wall, and the least uptake of tracer was visualized at the lateral wall. Meanwhile, for patient 2 the highest uptake of tracer was visualized at the lateral wall and the lowest uptake visualized at the inferior wall. The insufficiency of the software to provide automatic contouring for the four walls was a challenge in maintaining the same contoured area were shaped to every patient's heart images.

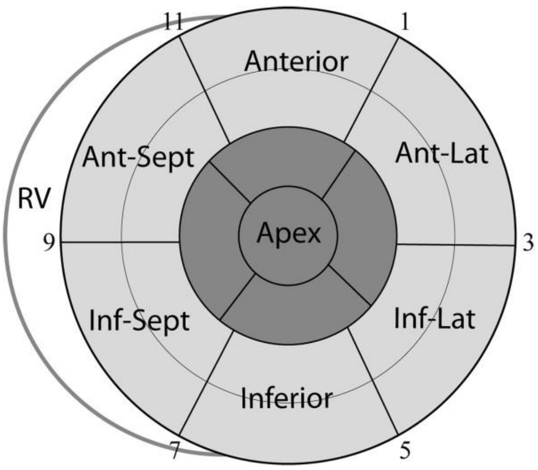

Figure 7 shows the segmentation of the four walls of the left ventricle wall

4.1 VISUAL EVALUATION ANALYSIS IMAGING FINDING

Table 1 shows the patient's result based on qualitative analysis (doctor's report)

Patient	Sex	Finding	Impression
1	Male	Normal	No evidence of myocardial ischemia or infarction
2	Female	Abnormal	Scan evidence of severe stress-induced myocardial ischemia involving mid to distal LAD and LCx territories

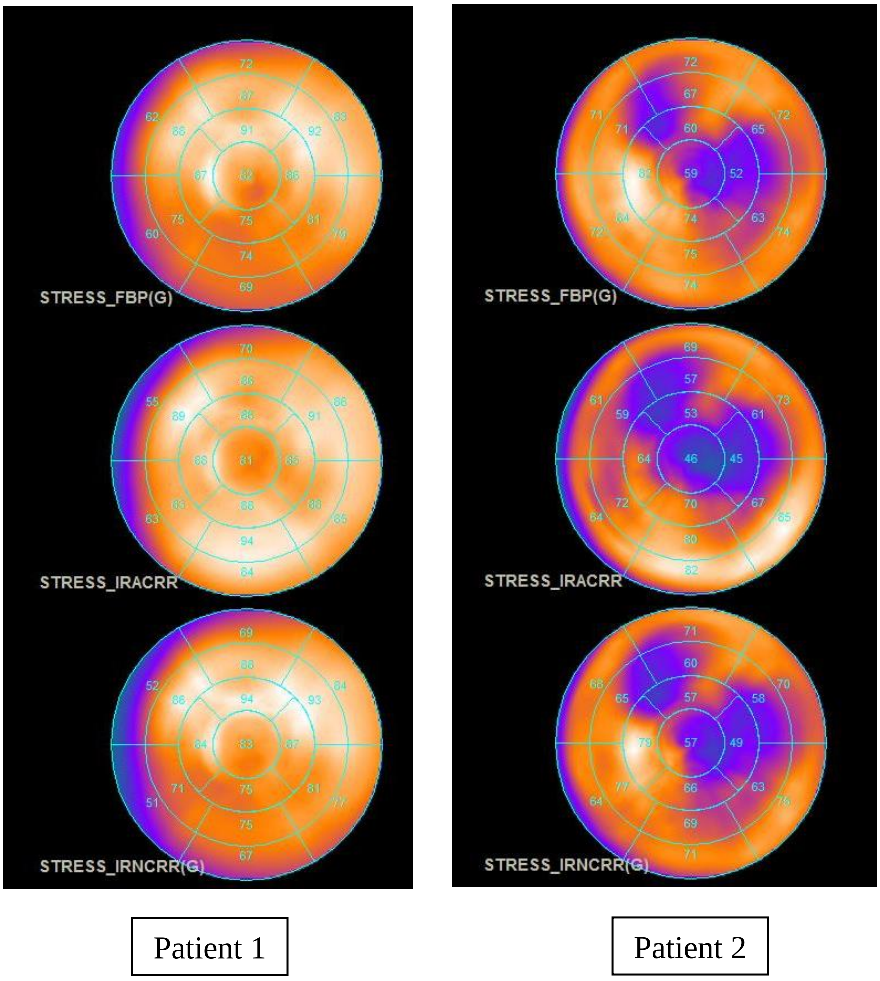

Figure 8 shows Bull's eye image of Patient 1 and Patient 2

Next, objective 2 is achieved in finding **4.2** and **4.3** where the statistical analysis was performed to obtain the p-value for the comparison of SUV mean, SUV max against uptake. A p-value of $p < 0.05$ indicates that there was a significant difference between the two groups. Based on Table 6, there was no significant difference in SUV mean, SUV max and uptake reading ($p > 0.05$) tested using Mann Whitney statistical test. Meaning to say, the outcome of the comparison meets the expectations that were made earlier. Based on patient 1 result in **Table 2**, the lowest reading of SUV mean and SUV max was 4.77 g/ml and 6.87 g/ml which was taken from lateral heart wall measurement. The result from **Table 3** also showed similar findings whereby the lowest mean and maximum uptake were from the lateral heart wall with a reading of 0.04 MBqml and 0.07 MBqml respectively. Additionally, based on patient 2 results in **Table 4** and **Table 5**, the lowest reading of SUV mean, SUV max, mean uptake, and max uptake were from inferior heart wall region with measurement of 3.31 g/ml, 6.47 g/ml, 0.05 MBqml and 0.10 MBqml respectively. The highest uptake of patient 1 and patient 2 heart were both from the inferior and lateral heart wall respectively.

However, the outcome of this project could be deemed inadequate as it only used a small sample size (n=2). As compared to other researches, such as Burgt et al (2019), which studied about 50 patients, where else Vija et al (2019) used about 70 patients. Consequently, large sample size is a factor that contributes to more convincing results. Moreover, due to the lack of automation, the manual drawing of the heart wall was influenced greatly by operator biased and this may also lack standardization between different patients. A patient with a normal heart finding can be easily contoured compared to a patient with an abnormal heart finding. Adequate knowledge of the anatomy of the human heart is a requirement to ensure an accurate result. Above all, the outcome of the comparison between SUV mean, SUV max with uptake still supports the hypothesis made.

4.2 SUV MEAN, SUV MAX, AND UPTAKE FINDING

Patient 1

Gender: Male, Age: 70 years old, Weight: 80 kg, Height: 165cm

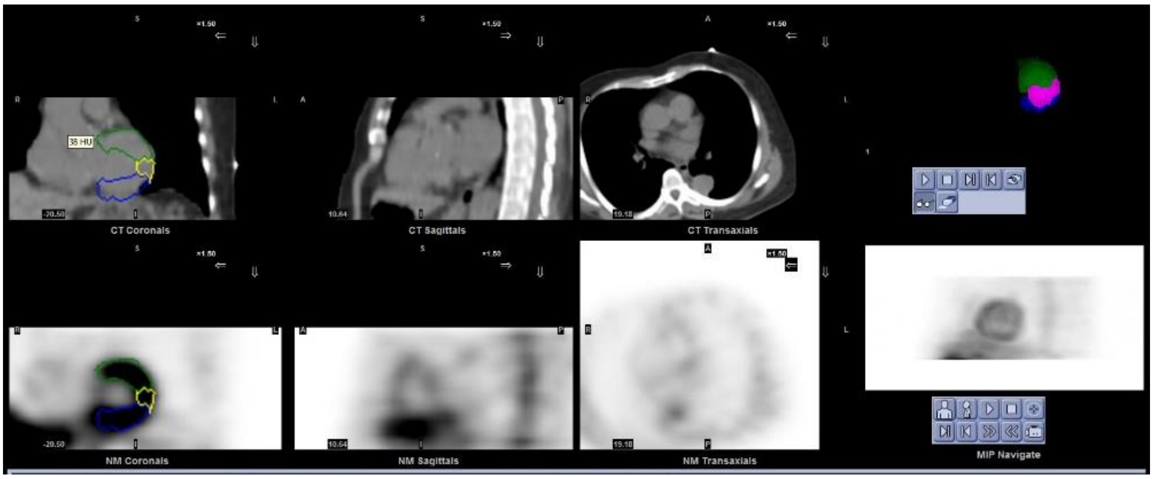

Figure 9 shows the SPECT/CT image of Patient 1

Table 2 Patient 1 SUV reading

Organ	Volume (ml)	Total (g)	Mean (g/ml)	Standard deviation (g/ml)	Maximum (g/ml)	Minimum (g/ml)	Injected dose (%)
Anterior Wall	95.7	596.00	6.22	1.92	10.83	1.73	0.74
Inferior Wall	55.3	407.35	7.36	1.24	10.01	4.65	0.51

Lateral Wall	29.0	138.47	4.77	1.73	8.55	1.87	0.17
Septa Wall	26.6	183.01	6.87	1.43	10.32	2.94	0.23

Table 3 Patient 1 Uptake Reading

Organ	Volume (ml)	Total (MBq)	Mean (MBqml)	Standard deviation (MBqml)	Maximum (MBqml)	Minimum (MBqml)	Injected dose (%)
Anterior Wall	95.7	4.61	0.05	0.01	0.08	0.01	0.74
Inferior Wall	55.3	3.15	0.06	9.6×10^{-3}	0.08	0.04	0.51
Lateral Wall	29.0	1.07	0.04	0.01	0.07	0.01	0.17
Septa Wall	26.6	1.42	0.05	0.01	0.08	0.02	0.23

Patient 2

Gender: Female, Age: 62 years old, Weight: 42 kg, Height: 152 cm

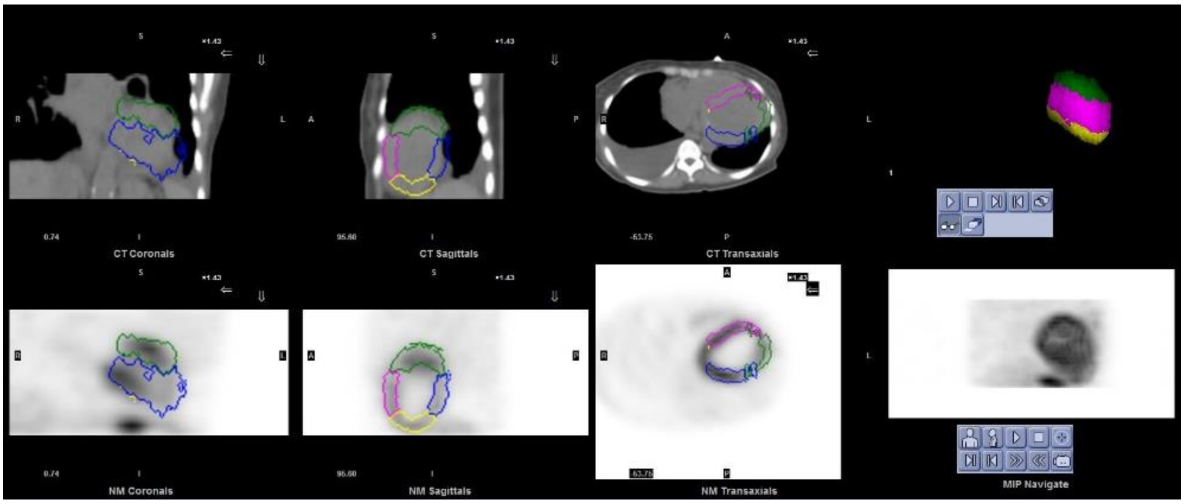

Figure 10 shows the SPECT/CT image of Patient 2

Table 4 Patient 2 SUV

Organ	Volume (ml)	Total (g)	Mean (g/ml)	Standard deviation (g/ml)	Maximum (g/ml)	Minimum (g/ml)	Injected dose (%)
Anterior Wall	106.6	390.96	3.66	1.17	7.12	1.55	0.93
Inferior Wall	58.0	191.97	3.31	1.18	6.57	1.10	0.46
Lateral Wall	65.1	255.35	3.92	1.33	6.84	1.21	0.61
Septa Wall	56.6	206.35	3.64	1.10	6.15	1.38	0.49