UNIVERSITI PUTRA MALAYSIA

QUANTIFICATION OF STANDARDISED UPTAKE VALUE FOR ^{18}F-FDG POSITRON EMISSION TOMOGRAPHY IN MALAYSIA

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QUANTIFICATION OF STANDARDISED UPTAKE VALUE FOR ^{18}F-FDG POSITRON EMISSION TOMOGRAPHY IN MALAYSIA

By

MUHAMMAD HAFIZ BIN HANAFI

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November 2017

Chair : Assoc. Prof. Fathinul Fikri Ahmad Saad, PhD
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The role of Positron Emission Tomography/Computed Tomography (PET/CT) modalities is becoming more important concomitantly with the increase of oncology cases in Malaysia. Thus, it is the perfect time to perform a study to standardise the PET/CT image quality in Malaysia. This study aimed to compare the quantification of image quality of PET/CT with a standardised uptake value (SUV) parameter. In general, this study was carried out with the purpose of identifying the standardisation of quantification of standardised uptake value, $SUV_{controlled}$ for ^{18}F-FDG PET between two independent PET modalities at two different institutions.

The analysis was done on the $SUV_{controlled}$ of technical techniques (PET phantom) as a control standard for the validation of the PET-CT images of selected subjects with Fasting Blood Glucose index as the adjusted index to synchronise the two independent data sets. It was found that the $SUV_{controlled}$ was a potential conversion marker to validate the in vivo standardisation techniques for the two independent PET/CT modality systems based on the reference standard of the matched FBS and the in vitro ^{18}F-FDG phantom. This study confirmed that the two independent PET modalities at paired-centre could potentially be standardised on the independent image quality based on the SUV_{max} quantification as the two independent measured were insignificantly different.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk Ijazah Master Sains

PENGKUANTITIAN NILAI PENGAMBILAN TERPIAWAI UNTUK TOMOGRAFI PANCARAN POSITRON ^{18}F-FDG DI MALAYSIA

Oleh

MUHAMMAD HAFIZ BIN HANAFI

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Pengerusi : Prof. Madya Fathinul Fikri Ahmad Saad, PhD
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Peranan modaliti Tomografi Pancaran Positron/Tomografi Berkomputer (PET/CT) adalah semakin penting seiring dengan peningkatan kes-kes onkologi di Malaysia. Rentetan itu, kajian ini menyasarkan untuk membandingkan pengkuantitian kualiti imej berdasarkan parameter nilai pengambilan terpiawai (SUV) Secara amnya, kajian ini bertujuan untuk mengenalpasti pemiawaian pengkuantitian nilai pengambilan terpiawai (SUV) ^{18}F-FDG di antara dua modaliti PET yang tidak bersandaran di dua institusi berbeza.

Analisis dijalankan terhadap $SUV_{controlled}$ teknik teknikal (fantom PET) sebagai piawaian kawalan bagi tujuan pengesahan imej PET/CT bagi subjek terpilih dengan indeks FBS sebagai indeks penyelarasan untuk menyelaraskan dua data tidak bersandaran. Kami mendapati bahawa $SUV_{controlled}$ in vitro berpotensi sebagai penanda pertukaran untuk pengesahan pemiawaian teknik in vivo bagi dua modaliti PET/CT yang tidak bersandaran berdasarkan pemiawaian rujukan bagi FBG yang sepadan dan fantom in vitro ^{18}F-FDG. Kajian ini mengesahkan bahawa dua modaliti PET yang tidak bersandaran di pusat-berpasangan adalah perbezaan tidak ketara pengkuantitian terpiawai setelah kolerasi SUV_{max} antara pusat-pusat dilakukan.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

^{18}F-FDG	2-deoxy-2-[18F]-fluoro-D-glucose
ACR	The American College of Radiology
Bq	The becquerel is the SI derived unit of radioactivity
C-11	Carbon-11 (C-11) radiotracers
Ci	The curie (symbol Ci) is a non-SI unit of radioactivity
EANM	European Association of Nuclear Medicine
EARL	European Association of Nuclear Medicine (EANM) Research Ltd
F-18	Fluorine-18
FBS	Fasting blood sugar
Ge-68	Germanium-68
IAEA	International Atomic Energy Agency
keV	Kiloelectron-volt
kg	Kilogram/s
kVp	Peak kilovoltage
mAs	milliampere-seconds
mL	millilitre
mm	millimetre
MOE	Ministry of Education
MOH	Ministry of Health
N-13	Nitrogen-13
O-15	Oxygen-15
PET	Positron Emission Tomography
PET/CT	Positron Emission Tomography/Computed Tomography

QAP	Quality Assurance Programme
QC	Quality Control
ROI	Region-of-interest
SUV	standardised uptake value
VOI	Volume-of-interest

CHAPTER 1

INTRODUCTION

1.1 Background

The function of Positron Emission Tomography/Computed Tomography (PET/CT) modalities has increasingly becoming more important, concomitantly with the increase of cancer cases in Malaysia. As stated by the National Cancer Council Malaysia (2014), cases of cancer continue to increase; however, studies regarding the standardisation of PET modalities in Malaysia based on comparable quantification of SUVs remain unknown.

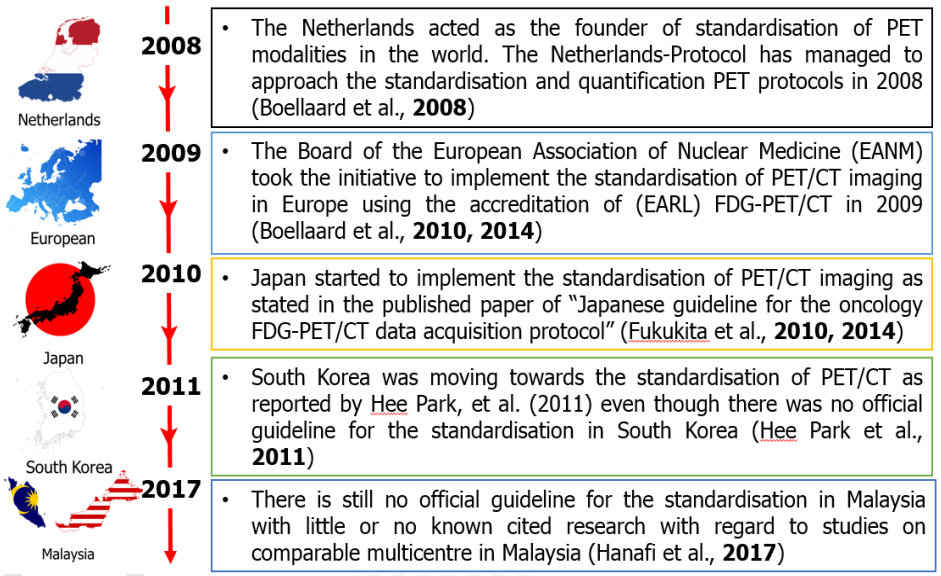

Figure 1: The chronology the standardisation of PET in world healthcare since 2008.

As illustrated in Figure 1, the Netherlands has started the standardisation of PET quantification protocols on all PET/CT modalities in the country since 2008. The standardisation of the quantification protocols is known as the Netherlands-Protocol (Boellaard, et al., 2008). Since the Netherlands is a member of the Board of the European Association of Nuclear Medicine (EANM), EANM suggested that the country standardised PET/CT imaging in the Europe using (EARL) FDG-PET/CT accreditation programme in 2009 (Boellaard, et al., 2010,

2014). EARL stands for the European Association of Nuclear Medicine Research Ltd (European Association of Nuclear Medicine Research Ltd, 2017).

In addition, developed Asian countries such as Japan has also started to standardise PET/CT imaging as stated in the published paper of *Japanese guideline for the oncology FDG-PET/CT data acquisition protocol* (Fukukita, et al., 2010; 2014). Although certain parts of the European and Asian countries have become more advanced when it comes to the standardisation and harmonisation of PET/CT SUV_{max} (quantification) since the last decade, it is never too late for Malaysia to start the standardisation of PET modalities in the country based on a comparable-multicentre study.

1.2 Problem Statement and Justification

The Ministry of Health, Malaysia (MOH) is serious in improving the quality of nuclear services in Malaysia. It has implemented a Quality Assurance Programme (QAP) for both the government and private nuclear medicine centres since 2013. Various requirements for quality control (QC) have been performed according to the medical terms stated under the Atomic Energy Licensing Act 1984 (The Commissioner of Law Revision Malaysia, 2006, 2010). The implementation of QC is compulsory as stated in the technical quality control Protocol Handbook of Positron Emission Tomography/ Computed Tomography (PET/CT) Systems by MOH (Medical Radiation Surveillance Division, 2015). The performance of PET/CT systems assures that the PET/CT modality is qualified to interpret the PET/CT image quality of maximum standardised uptake value (SUV_{max}) in each stand-alone PET/CT at each centre (Medical Radiation Surveillance Division, 2015).

However, the implementation of the QAP programme as approached by MOH is only applicable for a stand-alone PET modality at a nuclear medicine institution. Thus, the programme has limited access for a standardisation of comparable quantification (image quality of maximum standardised uptake value, SUV_{max}) of PET modalities in Malaysia. Consequently, the variations of quantification of PET modalities in Malaysia remain unknown. The impact is that it limits the PET study to only one particular centre that has validated a baseline image to ensure the measured parameter i.e. the SUV_{max} is reproducible and construed to the current status of a disease.

This study sought to ascertain the potential of validating two independent in vivo ^{18}F-FDG PET/CT modalities based on the variation of SUV_{max} as a potential conversion marker. This is with regard the derived transferable calibration constant of phantom (in vitro ^{18}F–FDG uptake) to verify whether the SUV_{max} quantification between PET modalities are comparable.

1.3 Limitations of the Study

Many PET modalities have been installed in Malaysia since 2006 by various parties such as the Ministry of Health Malaysia (MOH), Ministry of Education (MOE) as well as the private sector. Thus, this study aimed to have the participation of more than two nuclear imaging institutions in the Klang Valley which were equipped with a PET/CT modality and referred patients undergoing the PET/CT examination.

The institutions selected for the study were the Centre for Diagnostic Nuclear Imaging (PPDN) UPM, Beacon International Specialist Centre (BISC) and Prince Court Medical Centre (PCMC) since these institutions are equipped with PET/CT modalities. However, as Beacon International Specialist Centre was reluctant to participate in the research due to internal reasons (the official letter from the management of BISC is attached in the Index Section), only two nuclear imaging institutions were involved in the study.

1.4 Research Questions

The research questions have been divided into two parts. The first part is the technical phantom technique questions, and the second part is the clinical assessment questions.

The first part of the research questions are as follows:

i. What is the quantitative measurement value of $SUV_{controlled}$ for standard activation of PET phantom for the two independent PET modalities?
ii. What is the significant difference of the variation of $SUV_{controlled}$ PET phantom for the two independent PET modalities?
iii. From the above questions, is there a possibility to derive the transferable calibration constant (k) using $SUV_{controlled}$ of PET phantom?

The second part of the research questions are as follows:

i. What is the quantitative measurement value of SUV_{max} of PET images?
ii. What is the post-variation of SUV_{max} using the transferable calibration constant (k)?
iii. What is the correlation of post-variation SUV_{max} with the variation of SUV_{max} of the patients?

1.5 Objectives of the Study

1.5.1 General Objective

The overall aim of this study was to identify the standardisation of quantification of SUV_{max} for ^{18}F-FDG PET between two independent PET modalities at two different institutions by analysing the $SUV_{controlled}$ of technical techniques (PET phantom) and clinical assessment of SUV_{max} (PET images of patients). It is hoped that the research findings gained from the pilot study can be a source of reference towards the standardisation and harmonisation of ^{18}F-FDG PET modalities in oncology imaging in Malaysia.

1.5.2 Specific Objectives

a) To identify the quantitative measurement value of $SUV_{controlled}$ of activation standard PET phantom for two independent PET modalities.
b) To derive the transferable calibration constant (k) using the $SUV_{controlled}$ of PET phantom.
c) To analyse the post-variation of SUV_{max} using a transferable calibration constant (k).
d) To analyse the correlation of post-variation SUV_{max} with the variation of SUV_{max} of the patients.

1.6 Organisation of the Thesis

This thesis is divided into six chapters organised as follows: Chapter 1 provides an introduction to the study by providing the background, problem statement, justification, limitation, research questions and objectives of the pilot study; Chapter 2 presents the literature review on the fundamental operation of PET modality, PET imaging, image quality, quantification and comparable-multicentre study as well as highlights the current and previous studies that have been carried out by other researchers with regard to the factors that affect SUV_{max} measurement; Chapter 3 describes the research methodology applied in the study and provides a brief description on how the research methodology was developed, the materials, the comparison of the paired-centre study regarding the two independent PET modalities and also explains the statistical methods used in analysing the results of the study; Chapter 4 and Chapter 5 discuss the results and assessment outcomes of the findings; and Chapter 6 explains the conclusion, limitation and provides recommendations for future studies.

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