QUANTITATIVE AND QUALITATIVE STUDIES OF EXTRINSIC AND INTRINSIC UNIFORMITY ON GAMMA CAMERA DETECTORS USING CO-57 FLOOD SOURCE & Tc-99m POINT SOURCE: EXPERIMENTAL AND CLINICAL STUDIES

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by

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LIST OF ABBREVIATIONS

CFOV	Central Field of View
Co-57	Cobalt-57
FFOV	Full field of View
FOV	Field of View
HUSM	Hospital Universiti Sains Malaysia
LEHR	Low Energy High Resolution
NaI(TI)	Thallium Doped Sodium Iodide
NEMA	National Electrical Manufacturers Association
PACS	Picture Archiving and Communication System
PHA	Pulse Height Analyzer
PMT	Photomultiplier Tube
ROI	Region of Interest
SCD	Source-to-Collimator Distance
SDD	Source-to-Detector Distance
SNR	Signal-to-Noise Ratio
SPECT	Single-Photon Emission Computed Tomography
Tc-99m	Technetium-99m
UFOV	Useful Field of View

LIST OF SYMBOLS

λ	Decay constant
t	Elapsed time
A_0	Initial activity
A_t	Activity at time t
$T_{1/2}$	Half-life of radionuclide

LIST OF APPENDICES

KAJIAN KUANTITATIF DAN KUALITATIF UJIAN KESERAGAMAN EKSTRINSIK DAN INTRINSIK KAMERA GAMA MENGGUNAKAN SUMBER CO-57 & SUMBER TITIK Tc-99m: KAJIAN EKSPERIMEN DAN KLINICAL

ABSTRAK

Pengenalan: Ujian kawalan kualiti, seperti ujian keseragaman, memastikan operasi optimal kamera gamma dengan menilai respons pengesan terhadap fluks foton yang seragam di seluruh medan pandangan (FOV). Ujian keseragaman harian termasuk jenis ekstrinsik dan intrinsik. **Kaedah:** Sumber *Cobalt-57* digunakan untuk ujian ekstrinsik, dan sumber titik *Technetium-99m* untuk ujian intrinsik. Kiraan latar belakang diukur tanpa sumber. Untuk ujian ekstrinsik, pengambilan data untuk kedua-dua detektor dilakukan menggunakan matriks 256 x 256 dengan jumlah kiraan 5 juta pada jarak sumber 5 cm, 10 cm, dan 15 cm dari pengkolimat. Parameter yang sama digunakan untuk ujian intrinsik pada jarak sumber 2FOV, 3FOV, dan 4FOV dari pengesan. Analisis data menggunakan *Xeleris Workstation* melibatkan penciptaan *region of interest (ROI)* dalam FOV penuh (FFOV), berguna (UFOV), dan Tengah (CFOV) untuk mengukur kiraan purata dan mengira nisbah isyarat kepada hinggar (SNR) dan kontras. Ujian Kruskal-Wallis H menilai hubungan antara SNR, kontras dan jarak yang berbeza. Penilaian kualitatif gambar ekstrinsik yang diperoleh pada 10 cm dan gambar intrinsik yang diperoleh pada 4FOV dilakukan oleh seorang pemerhati pakar dan tiga pemerhati rakan. Lima gambar klinikal disemak untuk artifak. **Keputusan:** Untuk ujian ekstrinsik, SNR dan kontras berkurangan sedikit dalam kedua-dua UFOV (SNR: 124.603 to 124.263; kontras: 151.282 to 150.869) dan CFOV (SNR: 124.401 to 123.611; kontras: 151.036 to 150.077) Pengesan 1 apabila jarak sumber dari pengkolimat meningkat. Untuk ujian intrinsik, SNR dan kontras dalam semua FOV adalah yang terendah pada 2FOV. Untuk kedua-dua ujian, analisis kuantitatif menunjukkan bahawa tiada perbezaan yang signifikan secara statistik dalam SNR dan kontras pada jarak yang berbeza dalam setiap FOV ($p > 0.05$) untuk kedua-dua detektor. Secara kualitatif, ketidakseragaman diperiksa dalam gambar ekstrinsik pada 10 cm (min skor visual= 2.75), menunjukkan corak tiub foto pengganda (PMT), manakala tiada ketidakseragaman kelihatan dalam gambar intrinsik pada 4FOV (min skor visual= 1). Gambar klinikal menunjukkan artifak disebabkan oleh faktor berkaitan pesakit tetapi tiada artifak berkaitan foto pengganda. **Kesimpulan:** Tiada hubungan yang signifikan antara keseragaman ekstrinsik dan intrinsik pengesan kamera gamma dan jarak yang berbeza ($p > 0.05$). Artifak PMT yang diperhatikan dalam ujian ekstrinsik tidak dilihat dalam gambar klinikal, mencadangkan ia mungkin berpunca dari tenaga rendah *Co-57*, bendasing *Co-57*, penembusan septa pengkolimat, atau penyerakan foton dan bukannya kerosakan kamera gamma.

QUANTITATIVE AND QUALITATIVE STUDY OF EXTRINSIC AND INTRINSIC UNIFORMITY TESTING ON GAMMA CAMERA DETECTORS USING CO-57 FLOOD SOURCE & Tc-99m POINT SOURCE: EXPERIMENTAL AND CLINICAL STUDIES

ABSTRACT

Background: Quality control tests, such as uniformity tests, ensure optimal operation of gamma cameras by evaluating the detectors' response to a spatially uniform photons flux across the field of view (FOV). Daily uniformity tests include extrinsic and intrinsic types. **Methods:** A Cobalt-57 flood source was used for the extrinsic test, and a Technetium-99m point source (0.8 mCi) for the intrinsic test. Background counts were measured without the source. For extrinsic test, data acquisition for both detectors was done using a 256 x 256 matrix with 5 million total counts at source-to-collimator distances of 5 cm, 10 cm, and 15 cm for the extrinsic test, and at source-to-detector distances of 2FOV, 3FOV, and 4FOV for the intrinsic test. Data analysis using Xeleris Workstation involved creating regions of interest within full, useful, and central FOV to measure mean counts and calculate signal-to-noise (SNR) and contrast. The Kruskal-Wallis H test assessed associations between SNR, contrast and varying distances. Qualitative assessments were made by one expert observer and three peer observers acquired for extrinsic images at 10 cm and intrinsic images acquired at 4FOV. Five clinical bone images were reviewed for artifacts. **Result:** For the extrinsic test, SNR and contrast slightly decreased in both the UFOV (SNR: 124.603 to 124.263; contrast: 151.282 to 150.869) and CFOV (SNR: 124.401 to 123.611; contrast: 151.036 to 150.077) of Detector 1 with increased source-to-collimator distances. For the intrinsic test, SNR and contrast in all FOVs were the lowest at 2FOV. For both tests, quantitative analysis showed no statistically significant differences in SNR and contrast at varying distances within each FOV ($p > 0.05$) for both detectors. Qualitatively, nonuniformity was inspected in the extrinsic images at 10 cm (mean visual score= 2.75), showing photomultiplier tubes (PMTs) pattern, whereas no nonuniformities were visible in intrinsic images at 4FOV (mean visual score= 1). Clinical images revealed artifacts due to patient-related factors but no gamma camera-related artifacts. **Conclusion:** There was no significant association between the extrinsic and intrinsic uniformity of gamma camera detectors and different distance ($p > 0.05$). PMTs artifacts observed in the extrinsic test were not seen in clinical images, suggesting they might result from low energy of Co-57, impurities, collimator septa penetration, or photon scattering rather than gamma camera malfunctions.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

A single-photon emission computed tomography (SPECT) system consists of gamma (scintillation) cameras that are able to rotate the entire detector head around the patient. The acquisition of planar views showing the distribution of in vivo radioactivity from various angles is made possible by this rotational movement. These data can then be employed to generate the necessary projections for image reconstruction through computed tomography (IAEA, 2020; Sayed, 2021). Basic components of a gamma camera consists of detector (NaI(TI)) crystal, photomultiplier tubes (PMTs), collimator, pulse height analyzers (PHAs), position logic circuitry, computer, and display monitor.

Quality control (QC) is crucial in recognizing variations in a gamma camera's functionality and ensure optimum operation of the gamma camera (IAEA, n.d.; Islam et al., 2022; O'connor, 1999; Pandey et al., 2017). There are various quality control tests of gamma camera such as spatial resolution test, spatial linearity test, uniformity test and count rate performance test. This research will focus on the extrinsic and intrinsic uniformity test. The purpose of the uniformity test is to evaluate how well the detector responds to a spatially uniform incident photons flux across the field of view (FOV) (Ziada et al., 2010).

According to Bolstad et al. (2011) and Tuncman et al. (2019), an intrinsic uniformity test is performed without a collimator, by using a Tc-99m point source. Conversely, an extrinsic uniformity test, conducted with a collimator, reveals system non-uniformity and evaluates collimator integrity. There are two sources applicable for extrinsic uniformity test, which are the Cobalt-57 (Co-57) planar sheet source and the Technitium-99m (Tc-99m) water-filled sheet source. Bolstad et al. (2011) and Tuncman et al. (2019) also recommend using a Co-57 planar sheet source as it exhibits less than 1 % of nonuniformity. This source is considered to be more dependable and practical when compared to the water-filled sheet sources. Tc-99m water-filled sheet source may contain air bubbles, exhibit incomplete mixing, and are prone to bulging, leading to non-uniformities (Ziessman et al., 2013). Consequently, it is advised against using Tc-99m water-filled sheet sources for extrinsic uniformity assessment.

Typically, uniformity assessment involves visual inspection and computation of uniformity indices such as the integral and differential uniformity of the useful field of view (UFOV) and central field of view (CFOV) (Pandey et al., 2017). As outlined by the National Electrical Manufacturers Association (NEMA) (2018) NU 1 standard, the UFOV represents the portion of the detector designated for imaging gamma rays and x-rays. Conversely, the CFOV denotes the imaging area on the detector obtained by scaling all linear dimensions of the UFOV by 75%. Notably, the UFOV comprises the central 95 % of the full field of view (FFOV), excluding 5% of edge pixels (Murray et al., 2014). According to NEMA NU 1 (2018), the differential uniformity measures the count density change per specified unit distance when the incident gamma ray on the detector forms a homogeneous flux across the field of view, while the integral uniformity measures the maximum differences in count density across the entire field of view.

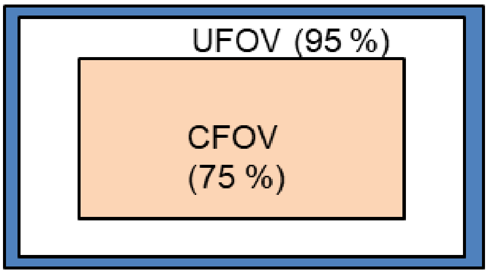

Figure 1.1: Illustration of the Useful Field of View (UFOV) and Central Field of View (CFOV) on the Detector.

Non-uniformity refers to variations in detector response across different areas of the scintillator crystal (Daniel, 1991). Non-uniformity might be caused by poor performance or malfunction of PMTs. This will result in artifacts like edge packing or ring artifact (Nautiyal et al., 2019; A. T. Oktaviana et al., 2022; Pandey, Karunanithi, et al., 2015). Other causes such as defective collimator or reflection of photons by the detector crystals' sidewalls will also result in edge packing (Després et al., 2006). As a result, artifacts will affect the image quality and might lead to diagnostic misinterpretation (Daniel, 1991; Nautiyal et al., 2019).

1.2 Problem Statement

Uniformity images are taken and examined every day to make sure that there are not any significant changes to the detector uniformity. For example, such changes may be caused by a malfunctioning photomultiplier tube. However, visual inspection of uniformity is subjective, and pixel value-based method frequently fall short in detecting finer structures that could be clearly visible and clinically unacceptable (Lofton, 2010; Nelson and Samei, 2020; Pandey et al., 2017), therefore, minor changes in crystal or PMT malfunctioning that could cause artefacts are typically disregarded due to lenient pixel value-based acceptable limit. Moreover, the GE Xeleris Flood Uniformity Protocol does not address uniformity for the FFOV; it only offers uniformity measurements for the UFOV and CFOV (Nelson et al., 2014a; Pandey et al., 2017). This may result in difficulties detecting non-uniformity at the edges that lead to edge packing artifacts. This poses a challenge when imaging targets located at the edge of the detector field of view. Furthermore, many studies only emphasized the relationship between intrinsic integral and differential uniformity within UFOV and CFOV and the source-to-detector distances, excluding the FFOV (Abdullah et al., 2013; Osman and Zobly, 2010; Saad, 2013; Sarah et al., 2015). Therefore, the first problem statement highlights the limitations of existing approaches to uniformity assessment. To address this, this research aims to quantify uniformity within FFOV, UFOV, and CFOV using signal-to-noise ratio (SNR), and contrast, and investigate their relationship with different distances, complemented by visual inspection for a comprehensive evaluation of the image.

Many studies verify the second problem statement, which emphasize the impact of source-to-camera distance on intrinsic uniformity (Abdullah et al., 2013; Elkamhawy et al., 2000; Sarah et al., 2015). However, there is lack of exploration in the literature currently available on how source-to-collimator distance affects extrinsic uniformity. Hence, by investigating the relationship between extrinsic uniformity and source-to-collimator distance, this study aims to bridge this gap.

1.3 Objectives

1.3.1 General Objective

To investigate the relationship between the extrinsic/intrinsic uniformity of gamma camera detectors and different source-to-collimator distances/source-to-detector distances.

1.3.2 Specific Objectives

1. To calculate the extrinsic/intrinsic uniformity of full field of view (FFOV), useful field of view (UFOV), and central field of view (CFOV) at different source-to-collimator distances/source-to-detector distances.
2. To analyse the gamma camera detector performance according to the presence of artifacts, signal-to-noise ratio (SNR) and contrast.
3. To interpret any detected artifacts on selected clinical bone images.

1.4 Hypotheses

1.4.1 Null Hypothesis

There is no significant association between the extrinsic/intrinsic uniformity of gamma camera detectors and different source-to-collimator distances/source-to-detector distances.

1.4.2 Alternative Hypothesis

There is significant association between the extrinsic/intrinsic uniformity of gamma camera detectors and different source-to-collimator distances/source-to-detector distances.

1.5 Research Questions

1. What is the relationship between the extrinsic/intrinsic uniformity of gamma camera detectors and different source-to-collimator distances/source-to-detector distances?

2. What is the extrinsic/intrinsic uniformity within FFOV, UFOV, and CFOV in terms of signal-to-noise ratio (SNR) and contrast at different source-to-collimator/camera distances?

3. How does the performance of gamma camera detectors vary in the presence of artifacts, SNR and contrast?

4. What types of artifacts are detected in the selected clinical bone images?

1.6 Significance of Study

Artifacts in nuclear medicine imaging are not only cause visual mistakes, but they also have can affect the precision of diagnosis and treatment planning. According to Dittrich & Chowdhury (2024), these artifacts often lead to misinterpretation of anatomical structures as diseased. Such misrepresentations potentially leading to incorrect clinical decisions.

One of the primary causes of artifacts is the non-uniformity of detector response, as highlighted by Marin et al. (2020). These non-uniformities, which can result from issues such as photomultiplier tubes (PMTs) malfunction, cracked sodium iodide crystals, or damaged collimators (Dittrich and Chowdhury, 2024; Nautiyal et al., 2019). Besides, Nautiyal et al. (2019) also reported that artifacts can be generated spontaneously during image acquisition, which appear randomly. These artifacts reduce the image quality, make the image interpretation more difficult, and may result in false-positive imaging results (Nautiyal et al., 2019; Sarah et al., 2015).

Moreover, making an accurate imaging result is restricted by the artifacts such as edge packing or ring artifacts, which have been linked to the poor PMTs performance, PMTs malfunction or defective collimators (Nautiyal et al., 2019; A. T. Oktaviana et al., 2022; Pandey, Karunanithi, et al., 2015; Ziessman et al., 2013), especially when the target is located at the edges of the detector field of view. These artifacts impair both the accuracy of imaging results and the precise localization of abnormalities.

Considering these challenges, the present study aims to provide insight into the status of gamma camera detectors and clinically used collimators through the uniformity tests. The potential detection of edge-packing artifacts or ring artifacts during the tests act as signs of potential PMTs malfunction or poor functioning. In addition, this study aims to address the limitations of traditional pixel value-based method by evaluating nonuniformities using alternative methods, with focus on signal-to-noise ratio (SNR) and contrast. These alternative approaches might improve the accuracy of nuclear medicine imaging by improving the precision of artifact detection image interpretation.

In summary, this study aims to make meaningful contributions to clinical practice by overcoming the problems of artifacts in nuclear medicine imaging, which will enhance diagnostic accuracy and patient care outcomes.

1.7 Operational Definition

Table 1.1: Operational Definitions of Variables

Variables	Operational Definition
Artifacts	Visualized non-uniform region observed in the images that can affect the image quality.
Contrast	The difference in count density between the image regions.
Signal-to-noise ratio (SNR)	The ratio of the difference between the mean count in the region of interest (ROI) and the mean count in background to the standard deviation of the background count.
Source-to-Camera Distance	The physical separation between the collimator and the radiopharmaceuticals (Tc-99m point source) during uniformity testing, measured in centimeter (cm).
Source-to-Collimator Distance	The physical separation between the collimator and the radiopharmaceuticals (Co-57) during uniformity testing, measured in centimeter (cm).

CHAPTER 2

LITERATURE REVIEW

2.1 Daily Uniformity Test

2.1.1 Intrinsic Uniformity Test

Before the acquisition of patient images, an intrinsic uniformity test is required to identify any changes in gamma camera performance that could potentially impact the interpretation of clinical studies (Ejeh and Adedapo, 2012). This test assesses the gamma camera's spatially correlated sensitivity without involving a collimator (DiFilippo et al., 2006). For this test, a Technetium-99m (Tc-99m) point source is used (Bolstad et al., 2011; Tuncman et al., 2019). This test does not account for the potential of collimator to generate nonuniformities in the images (Bailey et al., 2014; Bolstad et al., 2011).

2.1.2 Extrinsic Uniformity Test

Extrinsic uniformity test is to assess the gamma camera's spatially correlated sensitivity with a collimator installed (DiFilippo et al., 2006). The extrinsic uniformity test and intrinsic uniformity test should be compared in order to differentiate between nonuniformities related to the collimator and those related to the gamma camera detectors (DiFilippo et al., 2006). A Tc-99m water-filled sheet source and a Cobalt-57 (Co-57) planar sheet sources are the two types of radionuclides that can be used for extrinsic uniformity test (Nichols and Tosh, 2019; Pandey et al., 2015). It is more practical and convenient to use the Co-57 sheet source. This is because using the Tc-99m water-filled sources has a potential to result in air bubbles, insufficient mixing, and bulging, which cause nonuniformities (Ziessman et al., 2013).

2.2 Impacts of Image Nonuniformities

Quality control of gamma camera detectors should be performed regularly to detect any technical malfunctions. If these problems are ignored, it will lead to undetected technical issues that cause artifacts in the clinical image (Grootjans, 2017). One of the quality control tests of gamma camera is the daily uniformity test. Uniformity of gamma camera is defined as the ability to produce a uniform image in response to a uniform source of γ-radiation. The purpose of daily uniformity test is to detect nonuniformities that could affect image acquisitions (Murray et al., 2014). Abnormalities in the images can be caused by nonuniformities as small as 1 % (Bolstad et al., 2011). Nonuniformities can be caused by many factors. For instance, the study conducted by Pandey et al. (2015) showed that instability or poor performance of the photomultiplier tubes (PMTs) will produce fluctuations in the PMTs response across the field of view (FOV), resulting in nonuniformities. Moreover, Hasan et al. (2017) also reported that the image uniformity can be influenced by the stability of the PMTs.

2.2.1 Edge Artifacts, Ring Artifacts and Photomultiplier Artifacts

Non-uniformity will result in artifacts. As evidence, according to the study carried out by Nautiyal et al. (2019), they emphasized that malfunctioning of PMTs can lead to edge packing artifacts, characterized by bright rings at the edges of the image. Besides, the appearance of edge packing artifacts can also be due to the multi-reflected photons approaching the detector crystal’s edge (Castro, 2017; Cherry et al., 2012; Ricci et al., 2019). Other than that, ring artifacts are produced primarily by the gamma camera detectors due to the degraded or poor functioning of photomultiplier tubes (PMTs) (Bashir et al., 2017; Oktaviana et al., 2024; Oktaviana et al., 2022). Oktaviana et al. (2024) also reported that ring artifacts can arise from the uncorrected collimator.

Besides that, several authors have noted a common problem with Co-57 sheet sources used in extrinsic uniformity test, which is the presence of impurities from other isotopes of cobalt, namely Co-56 and Co-57 (Busemann Sokole et al., 1996; DiFilippo, 2014; DiFilippo et al., 2006; Zimmermann, 2018). These authors reported that the high-energy photons released by the Co-56 and Co-58 can lead to nonuniformities in photomultiplier tubes (PMTs) pattern, a phenomenon known as PMT artifacts. This is because, in contrast to the 122-keV gamma rays from Co-57, the high-energy photons from Co-56 and Co-58 more readily pass through the collimator and interact more deeply in the detector crystal, resulting in PMT artifacts (DiFilippo et al., 2006). Moreover, Co-57 decays with 692-keV gamma rays at 0.16 % in addition to 122 keV (85.5 %) and 136 keV (11 %) gamma rays. As a result, there are constantly high-energy gamma rays with 692 keV (Busemann Sokole et al., 1996; DiFilippo, 2014), could be a cause in the PMT artifacts.

2.2.2 Clinical Image Misinterpretation

As reported by Qutbi and Ahmadi (2022), artifacts have the potential to affect the visual interpretation and quantitative analysis of clinical images. For example, there is a possibility that nuclear cardiology and non-cardiac nuclear medicine studies will be misinterpreted due to difficulties in identifying the ring artifacts (Mezzenga et al., 2022). In addition, edge packing artifacts may resemble pathological lesions on whole-body bone scans (Nautiyal et al., 2019). These will result in false-positive or false-negative diagnostic results (Elkamhawy et al., 2000). Moreover, according to Hossain et al. (2022), artifacts might easily be confused for lesions, which could cause the study to be misinterpreted.

2.3 Physical Factors Influence Uniformity

2.3.1 Source-to-Collimator Distances and Source-to-Detector Distances

Source-to-collimator and source-to-camera distances are one of the factors affecting the uniformity of gamma camera. As proof, Sayed (2021) reported that a patient's size may affect the distance of collimator from them, potentially influencing the quality of the image. The study's result showed that a greater patient-to-collimator distance has negative image impacts, such as hot, cold, and ring artifacts. Besides, an increased phantom-to-collimator distance reduces overall contrast and SNR.

In contrast, by increasing the source-to-detector distance, it is possible to improve the gamma camera detectors' uniformity (Abdullah et al., 2013; Sarah et al., 2015). Their studies also indicated that a source-to-detector distance of 3 meters achieved the best intrinsic uniformity. Moreover, in the study by Saad (2013), various distances from the detector, specifically, 20, 40, 60, 80, 100, 120, 140, 160, 180, 200, and 220 cm, were included as locations for placing a point source. His findings indicated that both integral and differential uniformity demonstrated improvement as the distance between the source and the detector increased, with 200 cm being the distance that achieved the best uniformity. Furthermore, the study carried out by Osman and Zobly (2010) involved altering source-to-detector distances within the range of 85 cm to 120 cm to evaluate its impacts on intrinsic uniformity. Their findings also indicated that uniformity improved as the source-to-detector distance increased, with both differential and integral uniformity showing the best results at a distance of 100 cm, particularly between 95 cm and 105 cm. Other than that, based on the findings from Hasan et al. (2017) and Hossain et al. (2022), it can be concluded that maintaining a distance of at least four times the field of view (4FOV) diameter between the point source and the detector is deemed sufficient.

2.3.2 Collimator

As it relates to clinically utilised collimators, extrinsic uniformity test should be checked on routinely to enable evaluation of the collimator's integrity (Bolstad et al., 2011; DiFilippo et al., 2006; Tuncman et al., 2019). Image nonuniformities may result from collimator defects (Saad Mohamed, 2018). For example, if the collimator is collided with an external object, it may become faulty and show variations in local sensitivity of the collimator. This could result in uniform-related artifacts (DiFilippo et al., 2006). In addition, if the septa of the collimator is deformed, it may also result in variations in local sensitivity (Bolstad et al., 2011). Furthermore, Bolstad et al. (2011) reported that it is also possible for nonuniformities to occur within the collimator during the fabrication process. Efficiency is the term used to describe these nonuniformities, which represent the regional differences in rates of photon passing through the collimator. Such differences are due to inconsistent mechanical parts produced throughout the fabrication process, including the variations in septal thickness and any deformation that occurs during fabrication.

In addition, once photons exit the patient, they can be classified into three different image components based on their interactions with the collimator: a geometric component (passing through the collimator holes), a penetration component (passing through the collimator septa without being attenuated), and a scatter component (photons scattered within the septa at least once) (Sadremomtaz and Telikani, 2016). There is certain probability that photons that are not parallel to the collimator holes will reach and interact with the detector crystal due to the incomplete attenuation by the collimator (Polo, 2014). Therefore, septa penetration and scatter make the functioning of the collimator more difficult, which could lower the quantitative precision and overall image quality (NEMA 2018; Sadremomtaz and Telikani, 2016).

2.3.3 Field of View

The gamma camera detectors comprise three specific areas, which are full field of view (FFOV), useful field of view (UFOV), and central field of view (CFOV), as shown in Figure 1.1. FFOV refers to the field of view that includes the detector's whole surface ("QC of Planar Imaging," 2023). According to the National Electrical Manufacturers Association (NEMA) (2018) NU 1 standard, the UFOV refers to the part of the detector used for imaging. On the other hand, the CFOV refers to the imaging region on the detector that results from scaling all linear dimensions of the UFOV by 75%. Crucially, the central 95 % of the FFOV is included in the UFOV (Murray et al., 2014).

The relationship between integral or differential uniformity values and the field of view can be summarized as follows: FFOV $\geqslant$ UFOV $\geqslant$ CFOV ("QC of Planar Imaging," 2023). The uniformity within FFOV is typically poorer than UFOV and CFOV. This is primarily because there is greater light collection efficiency for events near the edge as opposed to the central regions of the detector crystal (Cherry et al., 2012). Such discrepancy is due to the internal reflections of photons within the crystal's edge (Castro, 2017; Cherry et al., 2012; Ricci et al., 2019). Consequently, the FFOV is more likely to experience edge packing artifacts, which might cause count fluctuations at the FFOV's extreme edges and falsely raise the integral or differential value ("QC of Planar Imaging," 2023). In contrast, the performance within the CFOV is generally superior due to fewer edge effects.

2.4 Methods of Uniformity Evaluation

Nelson et al. (2014) and Pandey et al. (201) reported that the accessibility of the GE Xeleris Flood Uniformity Protocol (GE Healthcare) for uniformity analysis. This protocol is a commercially available program designed to calculate the estimated integral uniformity from the nuclear medicine images in both useful field of view (UFOV) and central field of view (CFOV). However, this pixel value-based programs might not be able to detect finer structures or patterns, which could lead to incorrectly pass an image with visually obvious non-uniformities (Nelson et al., 2014; Nelson and Samei, 202(. Lofton (2010) also reported that at present, routine quality control (QC) is typically overseen through a pass or fail approach, relying on visual inspection to detect evident artifacts.

Therefore, alternative evaluation methods were developed to solve the drawbacks of current methods in assessing uniformity, such as by calculating signal-to-noise ratio (SNR) and contrast. Firstly, SNR measures the level of the signal in the presence of noise. Both Abdullah et al. (2013) and Cherry et al. (2012) explain the meaning of image noise and emphasized that image noise can generally be divided into random noise and structural noise. According to the authors, structural noise is related to non-random fluctuations in count rates that disrupt the structure of the object of interest. Abdulla and Clarke also noted that structural noise can arise from the distribution of radionuclides and artifacts of the imaging system, citing nonuniformities in gamma camera images as an example. This relates to the focus of my research on gamma cameras nonuniformities. When the SNR is high, it suggests that the signal is meaningful rather than random fluctuations. As a result, better image quality is indicated by a high SNR, whereas worse quality is indicated by a low SNR (Shirazu et al., 2017).

They also explain the meaning of image contrast. Abdulla and Clarke (2020) defined contrast as the difference in appearance between a lesion and adjacent normal tissue. Similarly, Cherry et al. (2012) defined contrast as variations in intensity in different areas of the image that represent varying radioactivity uptake levels by the patient.

For example, according to the study conducted by Sayed (2021), a R.A. Carlson SPECT phantom with hot and cold region inserts was used for data acquisition. Then, using ImageJ software, a region of interest (ROI) was drawn on the reconstructed image. This approach was to analyze the non-uniformity of the image by calculating standard deviation, SNR and contrast. In his study, the SNR and contrast were computed by using the formula as follows:

$$C_{cold\ region}=\frac{D_{cold\ region}-D_{background}}{D_{background}} \quad ...(1)$$

$$C_{hot\ region}=\frac{D_{hot\ region}-D_{background}}{D_{hot\ region}+D_{background}} \quad ...(2)$$

$$SNR=\frac{C}{\sqrt{D_{background}}} \quad ...(3)$$

where,

$D_{hot/cold\ region}$ = Mean counts in hot or cold regions

$D_{background}$ = Mean counts in background

Besides that, Baldelli et al. (2020) also suggested a uniformity evaluation method by creating an ROI on the image and calculating its SNR and pixel value (PV). In his study, the ratio of the mean pixel value (MPV) to the standard deviation (SD) is used to compute the signal-to-noise ratio. Furthermore, the study carried out by Noori-Asl (2020) highlighted that the effects of various factors on the SPECT images quality can be assessed using three mathematical criteria, which are relative noise of the background (RNB), SNR, and image contrast. The SNR and contrast were computed by using formula as follows:

$$SNR=\frac{Mean\ Counts\ in\ Background\ ROI\text{-}Mean\ Counts\ in\ ROIs}{Standard\ Deviation\ in\ Background\ ROI}\ x\ 100\% \qquad ...(4)$$

$$Contrast=\frac{Mean\ Counts\ in\ Background\ ROI\text{-}Mean\ Counts\ in\ ROIs}{Mean\ Counts\ in\ Background\ ROI}\ x\ 100\% \qquad ...(5)$$

There are also standard formulas that can be used to calculate the SNR and contrast, which are stated as follows (Abdulla and Clarke, 2020; Bushberg, 2012; Cherry et al., 2012):

$$SNR=\frac{Mean\ Counts\ in\ ROIs\text{-}Mean\ Counts\ in\ Background}{Standard\ Deviation\ in\ Background} \qquad ...(6)$$

$$Contrast=\frac{Mean\ Counts\ in\ ROIs\text{-}Mean\ Counts\ in\ Background}{Mean\ Counts\ in\ Background} \qquad ...(7)$$

2.5 Overall of the Previous Studies: Daily Uniformity Test and Its Impact

In nuclear medicine, gamma cameras are essential as they provide insights into the physiological and pathological processes within the human body. Therefore, to ensure an optimum performance of the gamma cameras, a daily uniformity test is crucial. The uniformity test ensures that the gamma cameras respond well to a spatially uniform incident photons flux across the field of view and produce high quality images. The uniformity test can be classified as intrinsic or extrinsic. Intrinsic uniformity test is conducted without a collimator by using a Tc-99m point source, while extrinsic uniformity test is conducted without a collimator by using Co-57 sheet source. Nonuniformities can result in a variety of artefacts, including ring, edge, and photomultiplier (PMT) artefacts, which lower image quality and impair the diagnostic accuracy of the images. These artifacts often caused by from PMTs malfunctions, fluctuations in PMT response, or collimator defects. Besides that, physical factors such as source-to-collimator and source-to-camera distances, field of views, collimator defects, septa penetration, photon scattering have a significant impact on uniformity. To evaluate uniformity, several methods are used, including pixel value-based programs and visual inspection. However, these methods could miss subtle patterns in the images, thereby alternative approaches have been developed to evaluate the uniformity such as ROI analysis and SNR and contrast calculations. Table 2.1 provides a summary of all these important findings from the previous studies.

Table 2.1: Summary of Key Findings and Methods in the Literature Review

Criterion	Key Findings	Authors
Daily Uniformity Test	- Extrinsic uniformity test assesses the gamma camera's spatially correlated sensitivity with a collimator installed,	DiFilippo et al. (2006), Bolstad et al. (2011), Pandey et al. (2015), Nichols and

		while intrinsic uniformity test assesses the gamma camera's spatially correlated sensitivity without a collimator. - The source used in extrinsic uniformity test is Co-57, while the source used in intrinsic uniformity is Tc-99m.	Tosh (2019), Tuncman et al. (2019)
Impacts of Image Nonuniformities	Edge Artifacts, Ring Artifacts and Photomultiplier Artifacts	- Artifacts in nuclear medicine images result from non-uniformity caused by technical malfunctions in gamma camera detectors. - Fluctuations in PMT response across the FOV induce non-uniformity and lead to artifacts. - Malfunctions in PMTs can cause edge packing and ring artifacts, affecting image quality and clinical interpretation. - Ring artifacts can be caused by defective collimator. - Presence of impurities in Co-57 sheet source result in PMT artifact.	Pandey et al. (2015), Hasan et al. (2017) Busemann Sokole et al. (1996), DiFilippo et al. (2006), DiFilippo (2014), Bashir et al. (2017), Zimmermann (2018), Nautiyal et al. (2019), Oktaviana et al. (2022)
	Clinical Misinterpretation	- The potential of artifacts to resemble lesions, which can result in the misinterpretation of the clinical images.	Elkamhawy et al. (2000), Castro (2017), Grootjans (2017), Ricci et al. (2019), Mezzenga et al. (2022) Qutbi & Ahmadi (2022)
Physical Factors Influence Uniformity	Source-to-Collimator and Source-to-Camera Distances	- Greater patient-to-collimator distance may lead to hot, cold, and ring artifacts,	(Abdullah et al., 2013; Hasan et al., 2017; Hossain

		reducing contrast and SNR. - Greater source-to-camera distance increases gamma camera detector uniformity.	et al., 2022; Osman and Zobly, 2010; Saad, 2013; Sarah et al., 2015)
	Collimator	- Nonuniformities can arise from collimator defects and deformation of the septa. - Septa penetration and scatter affect collimator performance, reducing image quality	DiFilippo et al. (2006), Bolstad et al. (2011), Sadremomtaz and Telikani (2016), NEMA (2018), Polo (2014), Saad Mohamed (2018)
	Field of View	- Uniformity in FFOV is poorer than UFOV and CFOV due to internal photon reflections at crystal's edge that result in greater light collection efficiency near the edge.	Cherry et al. (2012), Castro (2017), Ricci et al. (2019), "QC of Planar Imaging" (2023)
Methods of Uniformity Evaluation		- Current methods for uniformity evaluation rely on pixel value-based programs and visual inspection. - Pixel value-based programs may miss finer structures or patterns, leading to incorrect assessment of image uniformity. - Alternative evaluation methods, including region of interest (ROI) analysis and calculation of SNR and contrast, have been proposed. - Formulas that can be used to calculate the SNR and contrast have been discussed.	Lofton (2010), Bushberg (2012), Cherry et al. (2012), Pandey et al. (2017), Abdulla and Clarke (2020), Baldelli et al. (2020), Noori-Asl (2020), Sayed (2021)

CHAPTER 3

METHODOLOGY

3.1 Study Design

The chosen study design is quantitative and qualitative, consisting of a combination of experimental studies (extrinsic and intrinsic uniformity testing) and clinical studies (interpreting any detected artifacts on selected clinical bone images). The clinical study is a retrospective approach, which clarifies that the study does not involve performing whole-body bone scans on new patients. Instead, it focuses on analysing existing clinical bone images to interpret detected artifacts on selected images. It is important to note that this study will not influence the interpretation of the existing clinical bone images of the patients.

3.2 Study Location

The study area for this research is the Department of Nuclear Medicine at Hospital Universiti Sains Malaysia (HUSM) in Kubang Kerian, Kota Bharu, Kelantan. This department is equipped with a SPECT-CT scanner (GE Healthcare Discovery NM/CT 670 Pro) with gamma camera detectors for medical imaging. Various radiopharmaceuticals are available within the department, including Cobalt-57 (Co-57) flood source and Technetium-99m (Tc-99m), both of which will be used in my study. Besides, the treatment provided by this department includes whole-body bone scan, which is helpful in collecting data for my study.

3.3 Study Population for Clinical Study

1. Target population: Existing patients who had received a whole-body bone scan in Kelantan.