

Original Article

The Role of Routine Whole Volume SPECT Reconstruction in Comparison to Cine Raw Data in the Detection of Extracardiac Uptake on Myocardial Perfusion Scans

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Abstract

The objective of this study was to determine the role of routine whole volume reconstructed single-photon emission tomography (rSPECT) compared to cine raw data to detect extracardiac uptake of Sestamibi (MIBI). In a retrospective study, the myocardial perfusion studies of 426 patients were inspected separately for extracardiac uptake on cine raw data and rSPECT. The acquisition parameters for all the images were done according to departmental protocol. The whole volume SPECT data was selected and processed by HOSEM iterative reconstruction using the HERMES computer software system. The images were assessed by two observers, a student in training and a senior consultant nuclear medicine physician. The overall mean age and standard deviation of the 426 patients at the time of the study was 60 ± 12 years. Statistical analysis was performed using the Kappa and McNemars tests. The clinical significance of the extracardiac uptake was evaluated using hospital folders and /or laboratory results after viewing images. rSPECT detected 25 patients (5.9%) and cine raw data identified 18 patients (4.2%) with extracardiac uptake. All the areas of extracardiac uptake noted on cine raw data were seen on the rSPECT images. Only 21 of the 25 patients had complete 5-year clinical follow-up. The value of the clinical significance of the extracardiac uptake was limited due to the study being retrospective. The proportion of positives identified by rSPECT was significantly larger than those identified by cine raw data ($P = 0.0082$). Although our study demonstrates that rSPECT is more sensitive than cine raw data in detecting extracardiac uptake, it also shows that there is no benefit in routine whole volume rSPECT in daily clinical practice.

Keywords: Cine raw data, extracardiac uptake, myocardial perfusion single-photon emission tomography, Sestamibi

Introduction

Myocardial perfusion single-photon emission tomography (MPSPECT) imaging is a validated diagnostic technique, routinely used to evaluate myocardial perfusion in patients with suspected coronary artery disease. Three myocardial perfusion agents are commercially available and in widespread

use: Thallium ²⁰¹Tl chloride, ^{99m}Tc SestaMIBI (Cardiolite, Lantheus Medical Imaging, N. Billerica, MA, USA), and ^{99m}Tc Tetrofosmin (Myoview, GE Healthcare, Amersham, UK).^[1] ^{99m}Tc SestaMIBI (MIBI) is used in the Department of Nuclear Medicine at Tygerberg Hospital.

Sestamibi was first described in 1984 by Jones *et al.* as a myocardial perfusion tracer.^[2] In 1990, Delmon-Moingeon *et al.* described Sestamibi as an *in vivo* tumor imaging agent.^[3] Although the exact uptake mechanisms into the myocardial and tumor cells are not well understood, it is postulated to be related to blood flow, blood residence time, and the cellular uptake due to passive influx of the lipophilic cation, driven by the plasma and mitochondrial membrane potentials generated in living cells. Elevated potentials are directly related to metabolic state.^[4] MIBI is physiologically taken

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up by the salivary glands, thyroid, heart, liver, spleen, and skeletal muscle. There is physiological hepatobiliary and renal clearance. The advantages include a readily available kit which is easy to prepare and cost-effective for a large patient-base, and reasonable radiation dosimetry with good quality images from the 140-keV single gamma photon energy of ^{99m}Tc .

There is a relationship of the increased incidence for tumor risk with increasing age.^[5] It is not surprising that the incidence for detection of malignant lesions will increase on a MPSPECT corresponding to the increasing age at which the prevalence of cardiac diseases exists.

As the ultimate goal is the well-being of the patient, any available information should be examined and interpreted.^[6,7] MIBI has fortuitously been observed to show uptake in benign and malignant tumors including the lung, thyroid, brain, lymph node metastasis, bone and in breast cancer.^[8-21]

The routine evaluation of myocardial perfusion scans includes the reconstructed SPECT images localized just to the myocardium. The routine protocol for the evaluation of myocardial perfusion scans includes the inspection of the planar, cine raw data and the reconstructed SPECT images limited just to the myocardium. The reviewing of cinematic projections in order to detect extracardiac uptake has been recommended.^[6,20-22] Previously, whole volume reconstruction was only done when extracardiac uptake was noted on the planar or cine raw data images.

Materials and Methods

The aim of the study was to determine the role of routine whole volume reconstructed single-photon emission tomography (rSPECT) compared to cine raw data to detect extracardiac uptake of Sestamibi (MIBI). This retrospective study was approved by the Ethics Committee of the Division of Research Development and Support at Stellenbosch University. A 1-day protocol was used in this department. The dose for the resting study was approximately two thirds more than the dose injected for the stress (dose range 740–1000 MBq). The resting study was performed approximately 3 hours after the stress study. The resting study images were only used due to the higher dose giving better image quality. The resting studies done from January 2002 to December 2002 in the Division of nuclear medicine were reviewed.

The departmental acquisition protocol was followed. The injection of MIBI was followed by a minimum waiting period of 60 minutes. The myocardial perfusion SPECT imaging was acquired using a dual-headed gamma camera (Elscont Helix Apex SPX) equipped with a

low-energy, all-purpose, parallel-hole collimator. The SPECT data was acquired in list mode with 180° arc, either supine with a starting angle of 90° or prone with a starting angle of 270°. The cine raw data images were viewed in a thermal color scale.

The cine raw SPECT data of the resting MIBI scans were processed using HOSEM iterative reconstruction on the HERMES software system. The entire field of view of 40 cm by 50 cm was selected for reconstruction and a predefined reconstruction protocol was applied. The protocol was defined using 30 iterations and 4 subsets and the Butterworth filter was used with 0.900 cycles/cm and an order of 5. The rSPECT images were displayed in a gray color scale. The images were evaluated using three-dimensional localization with standard tomographic sections of the body (sagittal, coronal and transaxial) and then displayed in static transverse slices for further assessment.

The images were assessed by two observers, a student in training and a senior consultant nuclear medicine physician. The cine raw data and the rSPECT images were viewed separately to eliminate bias. Extracardiac uptake not as a result of normal biodistribution was considered abnormal. Statistical analyses were performed in consultation with the Centre for Statistical Consultation at the University of Stellenbosch. Analysis of the primary outcome variable was achieved by means of the Kappa statistic (tests for significance) for agreement and McNemar's test. Hospital folders and/or laboratory results of the patients found with extracardiac uptake were reviewed in order to evaluate the clinical significance of the extracardiac uptake. All identifying details such as the name and hospital number were not recorded on a data capture sheet or directly linked to the data set, maintaining patient confidentiality.

Results

A total of 427 resting studies were assessed for extracardiac uptake. On completion of data collection and reconstruction, there were 426 cine raw data and 426 rSPECT images. One study was uninterpretable and excluded from the study. The study group of 426 patients had a mean age \pm standard deviation of 60 ± 12 years. After reviewing all the images in the study group, only 25 patients were found to have extracardiac uptake. The mean age and standard deviation of the 25 patients were 60 ± 12 years.

Further analyses revealed that rSPECT detected 25 patients (5.9%) and cine raw data identified 18 patients (4.2%) with extracardiac uptake. The entire extracardiac uptake noted on cine raw data was seen on the rSPECT images.

A descriptive analysis of the 25 sites of extracardiac uptake was done. Focal uptake was seen in the left axilla (8 patients), right axilla (6 patients), retrosternal area (1 patient), in the region of the suprasternal notch (1 patient), in the left lung upper lobe (1 patient) and the thyroid (6 patients) [Table 1]. There was generalized inhomogeneous bone marrow uptake in two patients. A Kappa value of 0.8288 was observed, indicating a relatively strong agreement between the two methods with a *P*-value <0.0001. According to the McNemar's method, the proportion of positives identified by rSPECT was significantly larger than the proportion of positives identified by cine raw data (*P* = 0.0082).

Hospital folders and/or laboratory results of the patients found with extracardiac uptake were reviewed in order to assess the clinical significance of those extracardiac uptake findings. Folders and follow-up were not available in three patients and another patient died of cardiac complications soon after the study in 2002. These patients had focal uptake in the thyroid (1), left lung upper lobe (1), right (1) and left (1) axillae [Table 2].

There were seven patients with extracardiac uptake identified only on rSPECT. One patient with a focus in the thyroid had a history of squamous cell carcinoma (the same year as the study) and basal cell carcinoma (2 years after the study). A second patient with a focus in the retrosternal region was diagnosed with pulmonary tuberculosis (PTB) in the left lung (a year after the study) with no complications. In three patients with uptake in

the thyroid, left axilla and suprasternal notch area, the clinical follow-up did not reveal any malignancies or significant clinical illnesses, which would explain the extracardiac uptake. The remaining two patients were lost to follow-up.

Overall, the review of the clinical records, laboratory and histopathological findings in 21 patients revealed that 6 out of these 21 patients were diagnosed with malignancies over a 5-year period, following their cardiac examinations, revealing extracardiac uptake of Sestamibi. The sites of extracardiac uptake in these six patients included thyroid (*n* = 1), right axilla (*n* = 3) and bone marrow (*n* = 2). Except for one patient diagnosed with PTB diagnosed within a year of the study, the remaining 14 patients had no significant clinical incidences during the 5-year follow-up period.

Discussion

Extracardiac uptake may be infrequent and incidentally detected when routinely assessing myocardial perfusion studies. The reported incidence for detection of extracardiac uptake on cine raw data was 1.2 and <1%

Table 2: Imaging and sites of extracardiac uptake with no clinical follow-up (*n* = 4)

Cine raw data	rSPECT
Negative	Left lung upper lobe
Right axilla	Right axilla
Left axilla	Left axilla
Negative	Thyroid

Table 1: Imaging, sites of extracardiac uptake and clinical findings (*n* = 21)

Cine raw data	rSPECT	Clinical findings
Negative	Thyroid	Squamous cell cancer (Ca) was diagnosed the same year and basal cell Ca was diagnosed 2 years after the study
Negative	Retrosternal area	PTB in the left lung was diagnosed a year after the study
Right axilla	Right axilla	Tubular adenoma of the colon (diagnosed 2 years after the study)
Right axilla	Right axilla	Negative*
Left axilla	Left axilla	Negative*
Bone marrow	Bone marrow	Laryngeal Ca (squamous cell) was diagnosed in the same year as the study
Bone marrow	Bone marrow	Prostate Ca was diagnosed 2 years after the study
Right axilla	Right axilla	Gastric Ca was diagnosed 2 years after the study
Right axilla	Right axilla	Cervical Ca was diagnosed 2 years after the study
Negative	Suprasternal notch	Negative*
Left axilla	Left axilla	Negative*
Left axilla	Left axilla	Negative*
Negative	Thyroid	Negative*
Negative	Left axilla	Negative*
Left axilla	Left axilla	Negative*
Left axilla	Left axilla	Negative*
Left axilla	Left axilla	Negative*
Right axilla	Right axilla	Negative*
Thyroid	Thyroid	Negative*
Thyroid	Thyroid	Negative*
Thyroid	Thyroid	Negative*

*Negative: no malignancies or significant clinical findings

according to the data published by Gedik^[21] and Jones,^[22] respectively. This study shows a higher incidence of extracardiac uptake of 4.2% on cine raw data and 5.9% on rSPECT.

Our study, like that of Gedik,^[21] demonstrates that rSPECT provides more detailed anatomical correlation and better characterization of lesions, helping in defining the abnormality seen on cine raw data, and thereby obviating potential false-positive results. In our study, such areas included uptake around the mediastinum, particularly in regions occupied by the right atrium and ventricle as well as the great vessels. Other areas included variations in intensity of the salivary and thyroid glands due to asymmetrical positioning of the head and neck, increased activity in the left scapula due to the SPECT data being acquired from left posterior oblique (LPO) to right anterior oblique (RAO), and the injection site frequently resulting in prominent vessel visualization. In review of the patients' folders with axillary uptake, none were related to the injection site.

Six patients were diagnosed with malignancies during the 5-year follow-up. One patient had basal and squamous cell carcinomas, which were diagnosed in 2002 and 2004, respectively, both involving the left ear. This patient was treated with local radiotherapy and had no history of lymph nodes or spread of disease. This patient had uptake below the left thyroid lobe, only seen on rSPECT. A second patient had cervical carcinoma diagnosed in 2004, with uptake in the right axilla, seen on both images. A third patient was diagnosed with gastric carcinoma in 2004, had uptake in the right axilla, also seen on both images. A fourth patient had tubular adenoma of the colon, diagnosed in 2004, with uptake in the right axilla, seen on both images. Reviewing the patients' folders, it appears that the extracardiac uptake noted in the four patients mentioned above was unrelated to the patients' underlying pathology. A fifth patient had prostate carcinoma diagnosed in 2002 and a sixth patient was diagnosed with laryngeal carcinoma in 2004; both had uptake in the bone marrow, seen on both images. Despite the bone marrow uptake being seen on both cine raw data and rSPECT, it was visualized more clearly on rSPECT. In 2002, Wakasugi^[23] found that MIBI accumulation attributed to bone marrow metastases may occur at an early stage, before the bone remodeling process in the surrounding bone can be detected on conventional bone scans, supporting the importance of our findings.

There are several limitations in this retrospective study. These are as follows: 1) the study being retrospective; 2) in review of the patients' folders, none of the 25 areas of extracardiac uptake were reported previously, as images were displayed and viewed on emulsion films; 3) immediate clinical workup of these

patients could not be done; 4) the lack of follow-up of four patients, and the clinical significance could not be determined; and 5) physiological hepatobiliary excretion precluded the detection of abnormal uptake below the diaphragm.

Although not done in our study, it could be recommended that SPECT/CT has a potential role in localizing and characterizing possible abnormal uptake above and below the diaphragm. In view of the limited number of lesions detected in the study group, similar studies are needed to verify or corroborate this study.

Conclusion

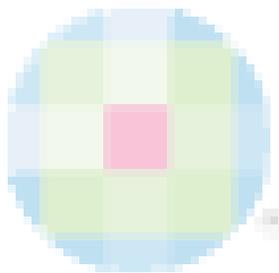
Although our study demonstrates that rSPECT is more sensitive than cine raw data in detecting extracardiac uptake, there is no benefit of routine whole volume rSPECT in daily clinical practice.

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