Final Submission of Research Report

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June 2016

MMed Nuclear Medicine

DETECTING SPINAL BONE METASTASES – SHOULD SPECT/CT IMAGES OF THE SPINE REPLACE SPECT AND PLANAR BONE SCAN IMAGING?

LIST OF CORRECTIONS

1. Cover page: Date changed to June 2016
2. Pages v and vi: Abstract shortened
3. Page 2
    - P1: SPECT imaging is performed by acquiring multiple two dimensional images, or projections, from multiple angles in a 360° arc around the patient. Tomographic reconstruction is then done on a computer by using special tomographic reconstruction algorithms to yield a three dimensional data set that can be viewed in transaxial, sagittal or coronal views, similar to three dimensional radiology studies such as computed tomography (CT) or magnetic resonance imaging (MRI).[3,4]
4. Page 13
    - P4: The above discussed literature describe a clear advantage of SPECT/CT imaging over SPECT imaging alone, most noticeable because of the increased accuracy it offers. However, the increased accuracy rests not only upon the improved lesion location, but also on the diagnostic information obtained from the underlying CT changes.
5. Page 14
    - P1: Despite all the clear diagnostic advantages of a hybrid SPECT/CT system for detecting the presence of bone metastases, its use in everyday practice has still not been established, especially in resource limited settings such as our own, as these hybrid systems are costly and radiologists are not readily available to evaluate the CT changes.
    - P2: This retrospective study was undertaken to evaluate the additional diagnostic value of SPECT/CT imaging of the spine in our environment where the CT component is not co-read with a radiologist. The additional value of SPECT/CT was compared to planar and SPECT images in patients with known solid tumour malignancies in order to validate its use in a resource constrained environment such as ours.
    - P3: In addition, the correlation between back pain and abnormal findings on the bone scan was evaluated, as well as the correlation between spinal kyphoscoliosis, back pain and lesions seen on bone scan.

- P4: Patients with haematological malignancies were excluded, as metastases from such malignancies typically originate in the bone marrow and often elicit osteolytic metastases, which are poorly visualized on bone scan.[1]

6. Page 16
    - P1: (Objectives) If any correlation could be found between back pain and the presence of spinal metastases
    - P2: (Objectives) If any correlation could be found between the presence of back pain and spinal kyphoscoliosis
    - P6: Inclusion and exclusion criteria are outlined in Table 1 below.
7. Page 18
    - P3: Planar images (Modality 1), SPECT reconstructed images without CT attenuation correction (Modality 2), SPECT reconstructed images with CT attenuation correction (Modality 3) as well as fused SPECT/CT images (Modality 4) were evaluated randomly and anonymously on different days and compared.
8. Page 27
    - Table 3 moved down to follow graph 1.
9. Page 40
    - P1 and 2 removed
10. Page 41
    - P3: This most likely reflects the increase in specificity that is gained by the use of SPECT/CT and is in keeping with previous literature.
11. Page 43
    - P3: The CT appearance of lesions were not included in the classification of lesions as benign or malignant. This could potentially lead to an underestimation of the value of SPECT/CT.
    - P4: The fate of individual lesions was not followed. As such the changes between modalities with regards to total lesions and total malignant lesions were a combination of upstaged and downstaged lesions which does not truly reflect the change in each individual patient.
    - P5: Our findings support a benefit of SPECT/CT as opposed to SPECT imaging of the spine. The additional value of SPECT/CT to SPECT and planar imaging of the spine lies primarily in the down-staging of one in every ten patients.
    - P6: The impact of the use of SPECT/CT in individual patients as opposed to the group as a whole was not maximally explored. As such the per patient impact of SPECT/CT may potentially be underestimated. However, a post hoc analysis of the available data can be done to address this specific matter.
12. Page 44
    - P2: In resource limited settings SPECT still offers good sensitivity in the detection of malignant lesions and may suffice for the overall diagnosis of spinal metastases. However, additional costs will have to be considered with regards to radiological correlation of indeterminate lesions as well as the impact of delayed accurate staging of the patient. These costs and impact to the patient has to be weighed carefully against the higher cost of a SPECT/CT camera.

DETECTING SPINAL BONE METASTASES – SHOULD SPECT/CT IMAGES OF THE SPINE REPLACE SPECT AND PLANAR BONE SCAN IMAGING?

Dr. Lizette Louw

Student number 0113415w

A Research Report submitted to the Faculty of Health Sciences,

University of the Witwatersrand,

in partial fulfillment of the requirements for the degree of

Master of Medicine

in the branch of Nuclear Medicine

Johannesburg

JUNE 2016

Candidate's declaration

I, Lizette Louw, declare that this research report is my own work. This research report is being submitted for the degree of Master of Medicine in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

Dr. Lizette Louw

June 2016

Master of Medicine in the branch of Nuclear Medicine

June 2016

To whom it may concern:

Re: Dr. Lizette Louw
Student number 0113415W
Staff number: 00100128
MMed Nuclear Medicine

This letter is to certify that dr. Lizette Louw has done her research in Nuclear Medicine. Her topic is **"Detecting spinal bone metastases – should SPECT/CT images of the spine replace SPECT and planar bone scan imaging?"** She compiled and analyzed the data herself with the assistance of a statistician and followed the protocol for her study accordingly.

The research report was entirely written by herself with assistance from her supervisor.

Kind regards,

Prof MDTHW Vangu
Head: Radiation Services Disciplines
Head: Department of Nuclear Medicine

Dedication

My parents, Kobus and Joan Smit: Thank you for your support and numerous sacrifices throughout my life. Amongst numerous other valuable lessons, you taught me to persevere and work hard.

My children, Levann and Theo: You are my sunshine! You make me happy when skies are blue... Thank you for your pure, unconditional and uplifting love.

My cousin, Franzel: I will always have a tear for you in my heart. Thank you for your short life that propelled me into the field of medicine.

Acknowledgements

- My gratitude towards the staff at the Nuclear Medicine Department at Chris Hani Baragwanath Academic Hospital for their assistance in retrieving archived data.

- A special thank you to Lebo Tawane for her assistance with the statistical analysis.

- Last, but definitely not least, my gratitude towards my supervisor, professor Vangu, for his valuable input and guidance, not only with this project, but throughout my career.

Abstract

Bone scan is a highly sensitive tool for the early identification of osteoblastic metastases. The specificity can be improved by more precise localization of lesions on bone scan with the use of SPECT or SPECT/CT, while also improving diagnostic accuracy and reporter confidence.

Considering the cost of imaging equipment, and specifically the two to three-fold higher cost of a SPECT/CT gamma camera compared to a SPECT gamma camera, it is of vital importance to validate the additional value of SPECT/CT in the diagnosis of metastatic disease prior to advocating the use of this expensive modality.

This retrospective study was undertaken to evaluate the additional diagnostic value of SPECT/CT imaging of the spine as compared to planar and SPECT imaging in a resource constrained environment, in patients with known solid tumour malignancies. A total of 192 patients (131 males and 61 females), aged 19 – 89 years were included for data analysis. Planar images (Modality 1), SPECT reconstructed images without CT attenuation correction (Modality 2), SPECT reconstructed images with CT attenuation correction (Modality 3) as well as fused SPECT/CT images (Modality 4) were evaluated and compared.

In keeping with literature, our results confirmed a significant benefit in the addition of any SPECT modality to planar bone scan imaging, with a change to diagnosis of metastatic disease in a third of patients. The impact of additional SPECT imaging lay mainly in up-staging patients.

The further addition of SPECT/CT images altered the final diagnosis of metastatic disease in about one out of every six patients, with the main impact on down-staging these patients.

Our study confirms the benefit of SPECT imaging to planar imaging of the spine in the evaluation of metastatic disease in patients with known malignancies. Our findings also support a benefit of SPECT/CT as opposed to SPECT imaging of the spine. The additional value of SPECT/CT to SPECT and planar imaging of the spine lies primarily in the down-staging of one in every ten patients.

In resource limited settings SPECT still offers good sensitivity in the detection of malignant lesions and may suffice for the overall diagnosis of spinal metastases. However, additional costs will have to be considered with regards to radiological correlation of indeterminate lesions as well as the impact of delayed accurate staging of the patient. These costs and impact to the patient has to be weighed carefully against the higher cost of a SPECT/CT camera.

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Nomenclature and Abbreviations

^{99m}Tc	^{99m}Technetium
MDP	Methylene Diphosphonate
SPECT	Single photon emission computed tomography
CT	Computed tomography
SPECT/CT	Fused SPECT and CT images
LEHR	Low energy high resolution collimator

R14/49 Dr Lizette Louw

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150650

NAME: (Principal Investigator)	Dr Lizette Louw
DEPARTMENT:	Nuclear Medicine Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Detecting Spinal Bone Metastases - Should Spect/CT Images of the Spine Replace Spect and Planar Bone Scan Imaging?
DATE CONSIDERED:	26/06/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Mboyo-Di-Tamba Vangu
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	09/09/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature ____________ Date ____________

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

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CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PA TO THE CEO
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To : Dr. Lizette Louw
M150650

From : Dr. Sandile Mfenyana
CEO: CHBA hospital

Date : 27 August 2015

Re : Application for Permission to Conduct a study in Detecting Spinal Bone Metastases/CT Images of the Spine Replace Spect and Planar Bone Scan Imaging

Your application for permission to conduct study in the Nuclear Medicine For Detecting Spinal bone Metastases –Should Spect/CT images of the Spine Replace Spect and Planar Bone Scan Imaging at Chris Hani Baragwanath Academic Hospital has been approved by the CEO: Dr. Sandile Mfenyana.

Hoping that the Institution (CHBAH) will meet the requirements of the study concerned.

Wishing you well in your future endeavors

Regards,

Dr.SCB Mfenyana
CEO : CHBAH 15.08.27

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CHAPTER 1

INTRODUCTION

Radionuclide bone scintigraphy (bone scan) is a highly sensitive tool to identify areas of increased bone metabolism. As such it is commonly used in the assessment of patients with malignancies for the early identification of osteoblastic metastases.

The typically used tracers are ^{99m}Technetium (^{99m}Tc) labeled phosphonates such as ^{99m}Tc-methylene diphosphonate (^{99m}Tc MDP). These radiopharmaceuticals incorporate into the hydroxyapatite crystal matrix of new bone. Malignant metastases that produce an osteoblastic response is thus best visualized on bone scan.[1]

Bone metastases occur in the red marrow where it causes a cortical response, mediated by osteoblasts, when it grows. This osteoblastic response to micro-metastases can be detected on a bone scan 2-18 months before metastatic lesions can be detected on plain film radiographs, because considerable bone destruction of 30 – 70% demineralization is required before metastatic lesions can be detected on plain film radiographs.[1,2]

Although bone scans have a high sensitivity in the detection of an osteoblastic response, the specificity is compromised due to benign processes that also cause osteoblastic, most often degenerative disease in the age group of patients affected by malignant disease. More precise localization of a lesion on bone scan can improve the specificity of the findings. Malignant lesions in the spine usually involve the vertebral body or pedicles, whereas benign disease involves the vertebral end plates, facet joints, transverse or spinous processes, or extend outside the normal vertebral body outline.[1]

It is well known that the diagnostic accuracy of bone scans in patients with the clinical suspicion of spinal metastases is improved by the addition of single photon emission computed tomography (SPECT) imaging of the spine to planar images, especially if the planar scan was normal or borderline abnormal.[3] SPECT imaging is performed by acquiring multiple two dimensional images, or projections, from multiple angles in a 360° arc around the patient. Tomographic reconstruction is then done on a computer by using special tomographic reconstruction algorithms to yield a three dimensional data set that can be viewed in transaxial, sagittal or coronal views, similar to three dimensional radiology studies such as computed tomography (CT) or magnetic resonance imaging (MRI).[3,4]

With SPECT imaging the lesion-to-background contrast is improved, which then results in improved sensitivity.[4] The more precise localization of lesions with increased tracer uptake also improves specificity, as malignant lesions in the spine can be distinguished from benign lesions based of their location.[1,5]

The findings that are considered equivocal on bone scan require correlation with anatomical imaging, with plain film radiographs usually the initial choice.[1,6] However, normal radiographs would require further radiological correlation with X-ray computed tomography (CT) and / or magnetic resonance imaging (MRI), as many lesions are poorly visualized or even missed on plain radiographs.[1,2]

Fusion of SPECT and CT images (SPECT/CT), can potentially not only improve the localization of lesions as compared to SPECT alone, but also add structural and diagnostic information, depending on the resolution of the CT component. As such the diagnostic accuracy of bone scan imaging can be further improved and additional radiological imaging avoided, thereby saving cost and obviate additional radiation exposure. In fact, SPECT/CT has been found to significantly reduce the number of lesions, and patients, regarded as equivocal on SPECT images alone.[6-8]

In the evolution of SPECT image interpretation and anatomical correlation, findings on SPECT images were initially correlated with side-by-side visual comparison between separately acquired diagnostic CT and SPECT images. Subsequently developed software that fuse and co-register separately acquired CT and SPECT images proved superior to such side-by-side visual comparison.[9,10] Co-registration of images in the chest and abdomen is not always easy, especially when the images were acquired on different days with different systems and using different protocols. Because the chest and abdomen are not rigid structures, alignment of CT and SPECT images is challenging in the presence of different patient positioning. Respiratory motion and movement of internal organs also contribute to these problems.[11-13]

Hybrid SPECT/CT systems integrate a dual head gamma camera with a CT scanner in the same gantry and have been commercially available for almost 15 years. The CT component was mainly developed and designed for the purpose of attenuation correction and more precise lesion localization and not for diagnostic radiology interpretation. SPECT and CT imaging of the patient with such a hybrid system ensures virtually no changes in patient position, as there is an almost negligent delay between the acquisitions of each.

Today there are many different hybrid SPECT/CT systems available commercially as these systems continue to gain widespread popularity. The main difference between these systems lies in the quality of the CT component. The most basic CT component includes single slice CT with low resolution, with more sophisticated systems becoming available that incorporate spiral CT or even multislice CT in an attempt to optimize resolution of the CT component in order to enable morphological characterization of lesions in addition to anatomical localization.[14,15,16] Although the added CT comes at the expense of an increase in the radiation dose to the patient, the effective dose for the additional CT component is still less than the dose the patient would receive with conventional diagnostic CT examinations of the same region.[17]

Interpretation of SPECT/CT images obtained with a hybrid system has shown higher diagnostic accuracy in soft tissue pathologies such as tumours (benign or malignant) and infection, mainly because of more accurate localization of tracer uptake.[18] There is also documented improved reporter confidence.[8,18,19]

To maximize the benefit to the patient and find a balance between the additional diagnostic information obtained versus the additional time, cost and radiation exposure, the use of SPECT/CT in various clinical scenarios should be clearly defined.

1.1 Background

Bone is made up of a crystalline lattice, which is composed of calcium, phosphate and hydroxyl ions.[20,21,22,23] These ions form the inorganic mineral hydroxyapatite. Other constituents of bone include collagen, other minerals and ground substance.[1,2,20,21,22,23]

Each vertebra consists of a vertebral body made up of spongy bone occupied by red marrow, with superior and inferior surfaces. The individual vertebral bodies are separated by intervertebral discs, which forms the articulating surfaces and allows movement between adjacent vertebrae. Posterior to the vertebral body lies the vertebral arch, forming the vertebral foramen between the arch and the vertebral body through which the spinal cord passes. At the junction of the vertebral arch and the vertebral body lies the pedicles; one on each side. From the vertebral arch the spinous process projects posteriorly and two transverse processes project laterally. On the superior and inferior surfaces two articular processes project on each side, forming four facet joints. Facet joints are synovial joints, which allow gliding movements between vertebrae. Ribs articulate with the thoracic vertebrae at the costovertebral and costotransverse joints. Costovertebral joints are formed between the head of the rib, two consecutive thoracic vertebrae and the intervertebral disc between the vertebrae. These joints lie on the posterolateral aspect of the vertebral body, lateral to the pedicles. The costotransverse joints are formed between the tubercle of a rib and the anterior surface of the transverse process. These joints lie posterior and lateral to the pedicles [Figures 1, 2, 3 and 4].[24,25]

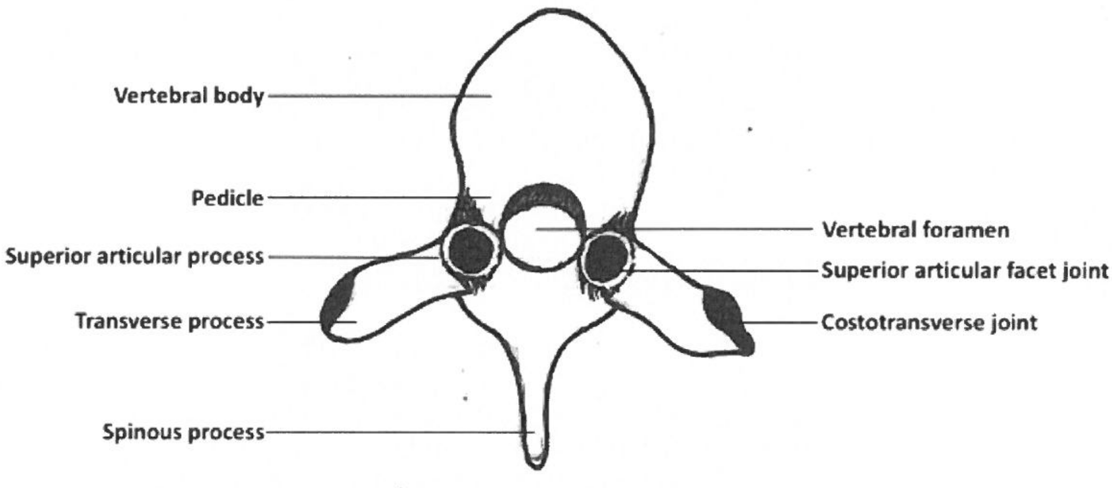


Figure 1. Superior view of a thoracic vertebra

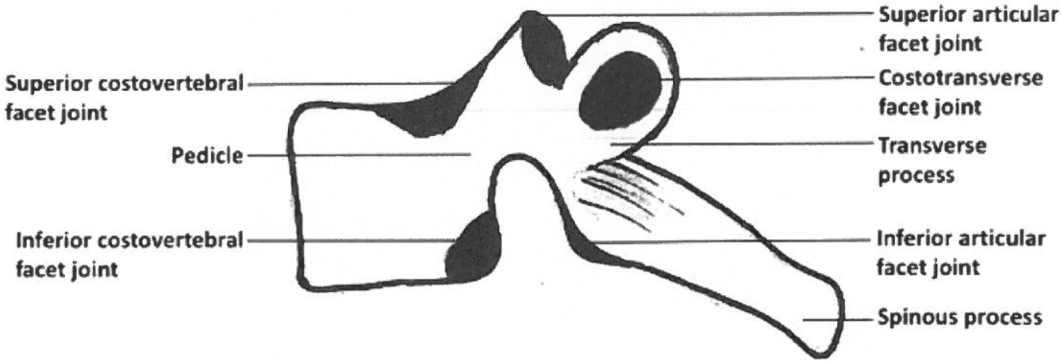


Figure 2. Lateral view of a thoracic vertebra

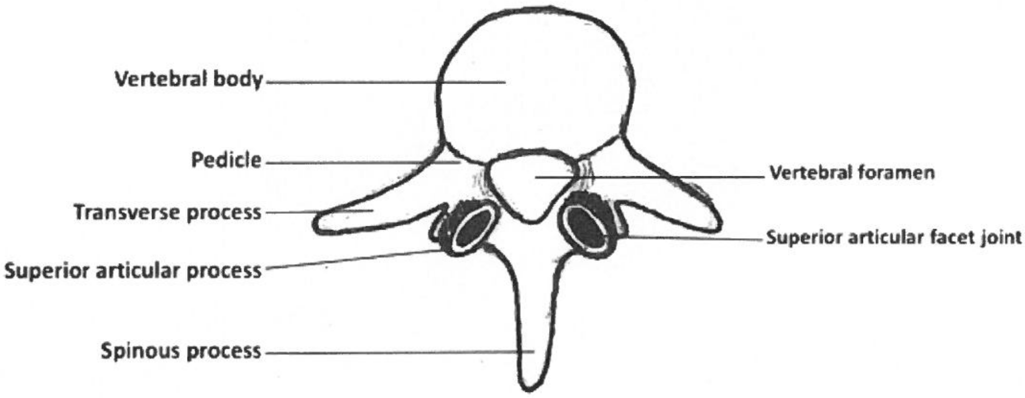


Figure 3. Superior view of a lumbar vertebra

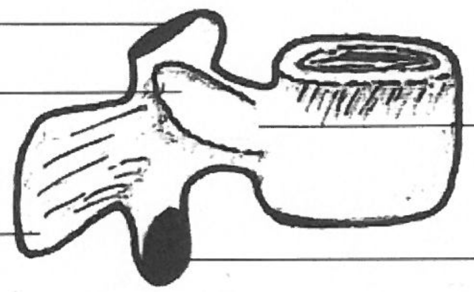


Figure 4. Lateral view of a lumbar vertebra

Bone seeking radiopharmaceuticals are analogs of either calcium, phosphate or the hydroxyl groups.[26] Various ^{99m}Tc labelled diphosphonates are commercially available for bone imaging, but in South Africa the only available bone scan tracer is ^{99m}Tc labelled methylene diphosphonate (MDP). Initial accumulation of MDP in bone is mainly related to blood supply, with capillary permeability, local acid-base homeostasis, hormones, vitamins and bone turnover playing a lesser role.[20,21] Subsequent retention of MDP in bone is attributed to a process called chemisorption, where the MDP concentrates in the mineral phase of bone, binds to the hydroxyapatite crystals and reflect osteoblastic activity.[20-23, 26]

In the absence of significant renal pathology, there is rapid excretion of MDP through the kidneys with a high target-to-background ratio obtained within 2-3 hours post tracer injection. Image acquisition is thus commenced 3-4 hours post tracer injection, after the patient has emptied the urinary bladder.[20-23, 26]

Bone metastases affects about two thirds of patients with cancer, with metastatic spread to bone predominantly seen in malignancies of the breast, prostate, lung, thyroid and kidney.[2,27,28]

It is postulated that the following sequence of events are required for metastatic spread of tumor to occur:[23,29]

- Separation of tumor cells from the primary tumor
- Separated tumor cells gain access to an efficient blood capillary or lymphatic channel
- The cells survive the transport to subsequently attach to a distant capillary bed endothelium and exit the capillary vessel
- A new, supporting blood supply develops successfully.

In extraskeletal malignancies, hematogenous metastatic spread is the most important mechanism underlying bone metastases, and these metastases may spread via either the arterial or venous system.[1,20,22,23,29] Batson's venous plexus plays a major role in tumor spread via the venous system. It is a prevertebral venous plexus consisting of thin-walled veins that form an intercommunicating system with low intraluminal pressure. From this plexus there is extensive communication with the venous systems in the spinal canal as well as the caval, portal, intercostal, pulmonary and renal systems.[1,2,23] Metastatic spread via this venous plexus explains the well known pattern of metastatic spread from various sites in the body to the axial skeleton.[1,2,20,22,23,30,31,32]

Bone metastases that occur via the hematogenous route seed and start in the medullary cavity of the bone before involving the cortex.[1,2,29,32] Bone usually responds in one of two ways to metastases:[33]

1. Increased bone resorption, primarily related to the action of osteoclasts;
2. Increased bone formation by either stromal bone formation (less important and occurs mainly in prostate carcinoma) or reactive bone formation as a response to bone destruction.

In the latter, there is deposition of immature woven bone, which is then converted to lamellar bone.

The axial skeleton is rich in red bone marrow and commonly involved in metastatic disease.[1,2,29,30,34,35] Red bone marrow is predominantly involved due to the large capillary network which has a sluggish blood flow and higher overall blood flow as compared to cortical bone.[1,2,30] Within the axial skeleton, the vertebral bodies are the most common site for metastases.[30,34,35] This is related to the large amount of bone mass in the vertebral column as well as red bone marrow located in the vertebral body. Perhaps the most important contributing factor to vertebral metastatic involvement is the Batson's venous plexus that provide direct communication from various locations within the body to the spine.[1,2,20,21,23,30,31,32,35]

Within the vertebrae, metastases are more common in the posterior aspect of the vertebral body as well as the pedicles.[32] Uptake of tracer along the lateral aspects and anterior edge of the vertebral body, as well as the posterior elements is generally related to benign disease, most often degenerative changes [Figure 5].[1,3,4,8,32,36,37]

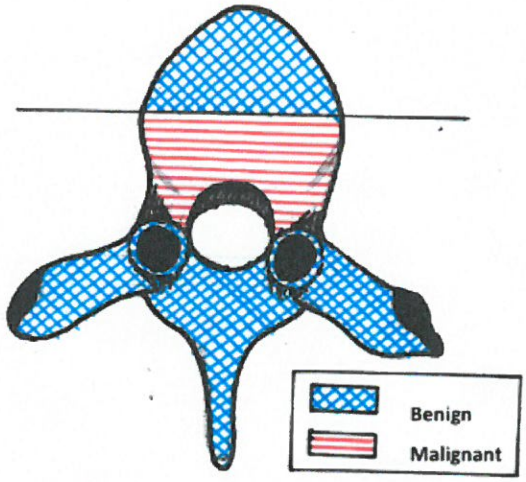


Figure 5. Location of expected benign and malignant lesions in the vertebrae

The most common indications for a bone scan in patients with a known malignancy are to assess the extent of bone involvement in order to plan appropriate therapy, in the assessment of bone pain and lastly to assess the response of metastatic burden to therapy.[1,31]

1.2 Literature review

Despite developments in structural imaging, bone scanning with ^{99m}Tc MDP remains the most frequently used procedure to evaluate for metastatic bone disease in patients with cancer, especially osteoblastic, or sclerotic, bone metastases.

In the evaluation of spinal lesions, SPECT/CT improves the localization of lesions as compared to SPECT alone, and may even add structural and diagnostic information.[14,15,16] As such the diagnostic accuracy of bone scan imaging can be improved to the extent that additional radiological imaging may be avoided, thereby saving cost as well as avoiding additional radiation exposure. Compared to SPECT images of the spine, SPECT/CT has been found to significantly reduce the number of lesions and patients regarded as equivocal.[4-8]

Horger et al evaluated 47 patients with 104 lesions considered as equivocal on bone scan. Using histological confirmation or long term follow-up as a gold standard, they found the accuracy of SPECT/CT to be 85% in classifying lesions as benign or malignant, with the highest accuracy in lesions of the skull, sternum, ribs and spine.[38]

Palmedo et al used clinical follow-up as the gold standard in their prospective study of 308 patients with either breast or prostate carcinoma to evaluate the diagnostic value of SPECT/CT and impact on patient management, as compared to planar and SPECT imaging. The specificity and positive predictive value was significantly better for SPECT/CT imaging than for planar or SPECT imaging. The greatest impact on patient management was on disease down-staging which affected about a third of the patients.[39] Specifically in patients with prostate or breast cancer, SPECT/CT imaging has been shown to have a significant impact on patient staging and management.[40,41] Fused SPECT/CT images not only improves the diagnostic accuracy, but also improves confidence of those interpreting the studies.[8,10,18,19]

The spine is a common site for skeletal metastases. Patients affected by cancer are often older than 50 years of age and this age group may also have symptomatic or asymptomatic degenerative pathology in the spine.[42,43] Degenerative changes in the spine may cause back pain, which can often not be clinically distinguished from malignant involvement. Bone scan, and specifically SPECT or SPECT/CT imaging of the spine, plays an important role in distinguishing these two entities.[6,37,38] Similarly, in patients with previous spinal surgery with orthopaedic hardware in situ, the increased accuracy of SPECT or SPECT/CT imaging of the spine reduces the number of lesions considered as equivocal for malignant involvement.[44-46]

Solitary lesions in the spine carry a high risk for malignant involvement in a patient with known malignancy, but the finding is still non-specific and requires further radiological correlation to exclude a compression fracture or other benign pathology as a cause. In this scenario SPECT/CT imaging of the spine has also proven to be superior to planar or SPECT imaging.[47,48]

This seemingly optimal imaging modality has its limitations and pitfalls as well. Artifacts may be caused by patient, technical or instrumentation related factors.[49] Defective instrumentation such as photomultiplier tube defects can create apparent photon deficient areas, which may be interpreted as possible lytic bone lesions. The majority of patient or technical related artifacts will however be eliminated with SPECT imaging, due to the improved spatial resolution.[49,50]

Accurate co-registration of the SPECT and CT data is crucial for accurate localization of tracer uptake. The most important factor affecting co-registration is patient motion. Neither patient movement nor organ motion can be completely eliminated, even with the use of motion correction software and co-registration software.[11,12,13,49,50] Ongoing research is aimed on minimizing the acquisition time or use alternative reconstruction methods in order to reduce the impact of patient motion.[51,52] To minimize the chances of voluntary patient motion, it is vital to ensure that the patient is as comfortable as possible and understands the importance of lying still.

An important factor to consider in SPECT imaging is attenuation correction. Photons originating from the center of the object or patient interact with surrounding soft tissue mainly through the Compton effect.[54] The result of this is underestimation of the intensity of tracer uptake in areas with high uptake towards the center of the object or body due to attenuation, and possible overestimation of tracer intensity in areas with low uptake due to photon scatter.[55] Data derived from CT acquisition can be used to correct photon attenuation and scatter by using the Hounsfield Units to create an attenuation map. This map calculates the levels of attenuation that a photon beam encounters from the point of emission to the point of detection, via a specific trajectory pathway.[47,55,56] This CT based attenuation correction can be incorporated in the iterative reconstruction algorithms,[57,58] and a CT based attenuation correction map can also be used to correct for scatter photons.[50,56]

Attenuating materials such as metal objects or orthopaedic hardware can generate artifacts on the CT data images and thus affect the CT based attenuation map.[50]

The above discussed literature describe a clear advantage of SPECT/CT imaging over SPECT imaging alone, most noticeable because of the increased accuracy it offers. However, the increased accuracy rests not only upon the improved lesion location, but also on the diagnostic information obtained from the underlying CT changes. Despite all the clear diagnostic advantages of a hybrid SPECT/CT system for detecting the presence of bone metastases, its use in everyday practice has still not been established, especially in resource limited settings such as our own, as these hybrid systems are costly and radiologists are not readily available to evaluate the CT changes.

This retrospective study was undertaken to evaluate the additional diagnostic value of SPECT/CT imaging of the spine in our environment where the CT component is not co-read with a radiologist. The additional value of SPECT/CT was compared to planar and SPECT images in patients with known solid tumour malignancies in order to validate its use in a resource constrained environment such as ours.

In addition, the correlation between back pain and abnormal findings on the bone scan was evaluated, as well as the correlation between spinal kyphoscoliosis, back pain and lesions seen on bone scan.

Patients with haematological malignancies were excluded, as metastases from such malignancies typically originate in the bone marrow and often elicit osteolytic metastases, which are poorly visualized on bone scan.[1]

CHAPTER 2

MATERIALS AND METHODS

Ethics clearance was obtained from the University of Witwatersrand's Human Research Ethics Committee (HREC), ethics clearance number M150650 (Appendix 1).

Permission was obtained from the CEO of Chris Hani Baragwanath Academic Hospital for the use of hospital patients' information (Appendix 2).

2.1 Study design

Bone scan is the most frequent diagnostic procedure in the evaluation of malignant metastatic disease. Despite the well-documented benefit of additional SPECT imaging of the spine, there are no clear recommendations for the use of SPECT/CT, especially in financial resource limited areas.

This was a retrospective study that aimed to evaluate the additional diagnostic value of SPECT/CT imaging of the spine with ^{99m}Tc MDP as compared to planar and SPECT imaging in a resource constrained environment. The additional value was assessed on a lesion-base as well as on a patient-base.

2.2 Objectives

The aim of this study was to determine

- the additional value of SPECT/CT as compared to SPECT and planar bone scan images in the diagnosis of spinal metastases in patients with a known malignancy
- if the use of CT for attenuation correction improves the diagnostic accuracy of SPECT images

- If any correlation could be found between back pain and the presence of spinal metastases
- If any correlation could be found between the presence of back pain and spinal kyphoscoliosis

2.3 Population

All patients with known solid tumour malignancies referred to Chris Hani Baragwanath Academic Hospital Nuclear Medicine department from January 2013 – May 2015 for a bone scan, and in whom SPECT/CT of the spine were done, were enrolled in the study.

All age ranges of the adult population (> 18 years old) were included.

A total of 192 patients (131 males and 61 females), aged 19 – 89 years were included for data analysis.

Inclusion and exclusion criteria are outlined in Table 1 below.

Table 1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• Patients older than 18 years • Patients with a known solid tumour malignancy referred for bone scan	• Patients with haematological malignancies • Patients with a known solid tumour malignancy who had a bone scan, but no SPECT/CT imaging of the spine was done

2.4 Imaging protocol, data processing and data collection

The sample population was derived from a database kept in the department of all bone scan studies done. These were accessed retrospectively. The original study request form was reviewed to extract information such as gender, age, type of malignancy and presence / absence of back pain.

Patients were imaged according to existing departmental imaging protocols. According to these protocols, patients were injected with 20mCi of ^{99m}Tc MDP intravenously. Planar images of the whole body were acquired at 3 - 4 hours post tracer injection. Optional additional static images of specific regions of interest were acquired in individual cases. SPECT/CT reconstructed images of the spine were acquired if there was abnormal uptake in the spine seen on the planar images that required more accurate localization, or if there was a history of back pain but the planar images appeared unremarkable.

All the planar images were acquired on a gamma camera equipped with a low energy high resolution (LEHR) collimator. SPECT/CT images were acquired with a double head, rotating large field of view gamma camera (Philips Brightview XCT) equipped with a LEHR collimator. The SPECT images were acquired on a 64 x 64 matrix with a total of 64 images of 20 seconds each obtained over a circular arch of 360°. The following parameters were used for CT data acquisition: 2.0mm slices, 120kV, 80mA and 256 x 256 matrix.

For modality 2, the SPECT data was reconstructed with no applied attenuation correction, using the Astonish iterative reconstruction with 3 iterations and 8 subsets. No pre- or post filter was applied.

For modalities 3 and 4, the SPECT data was reconstructed with CT attenuation correction, using the same iterative reconstruction parameters as for modality 2. No pre- or post filter was applied.

The CT data was reconstructed with iterative reconstruction.

2.5 Data analysis

All images were processed and viewed by two experienced Nuclear Physicians. Planar images (Modality 1), SPECT reconstructed images without CT attenuation correction (Modality 2), SPECT reconstructed images with CT attenuation correction (Modality 3) as well as fused SPECT/CT images (Modality 4) were evaluated randomly and anonymously on different days and compared. The two readers evaluating the images were blinded to the clinical information as well as the findings from the various modalities in the same patient. In isolated cases of disagreement, consensus was reached.

The system of reviewing comprised of the visual analysis of lesions on the following reviewing levels:

Modality 1 (M1)

- Localization of the vertebra / vertebrae involved
- Region of vertebra involvement
  - Midline [Figure 6]
  - Edge [Figure 7]
  - Lateral aspect, extending towards the midline [Figure 8]
  - Entire vertebral body, linear uptake [Figure 9]

- Entire vertebral body, irregular uptake [Figure 10]

Figure 6. Uptake in the midline of the vertebrae on planar images

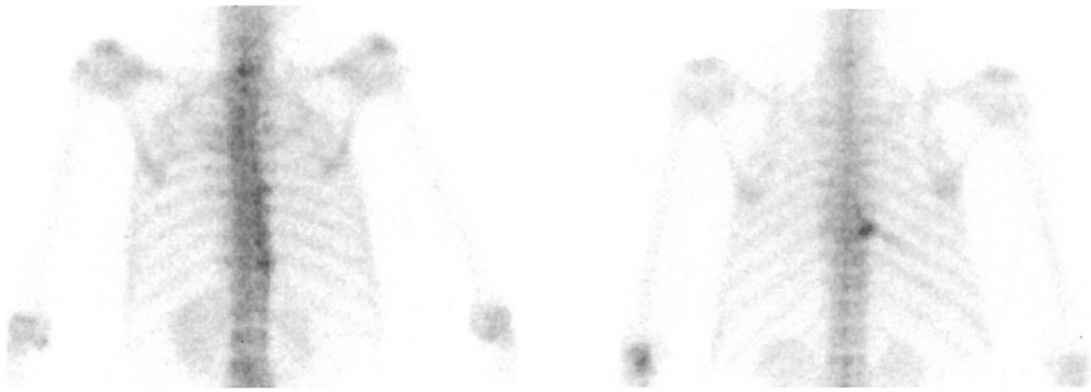


Figure 7a and 7b. Uptake on the edge of the vertebrae on planar images

Figure 8a and 8b. Uptake in the lateral aspect of the vertebra, extending towards the midline on planar images

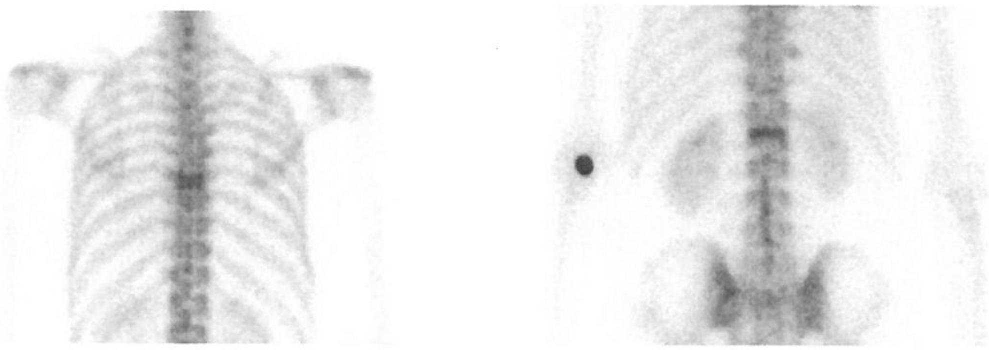


Figure 9a and 9b. Linear uptake in the vertebral body on planar images

Figure 10. Irregular uptake in the vertebral body on planar images

Modalities 2, 3 and 4 (M2, M3, M4)

- Localization of the vertebra / vertebrae involved
- Region of vertebra involvement
    - Anterior vertebral body [Figure 11]
    - Vertebral body, diffuse uptake throughout [Figure 12]
    - Lateral aspect of the vertebral body [Figure 13]
    - Posterior aspect of the vertebral body [Figure 14]
    - Pedicle [Figure 15]

- Facet joint [Figure 16]
- Spinous process [Figure 17]

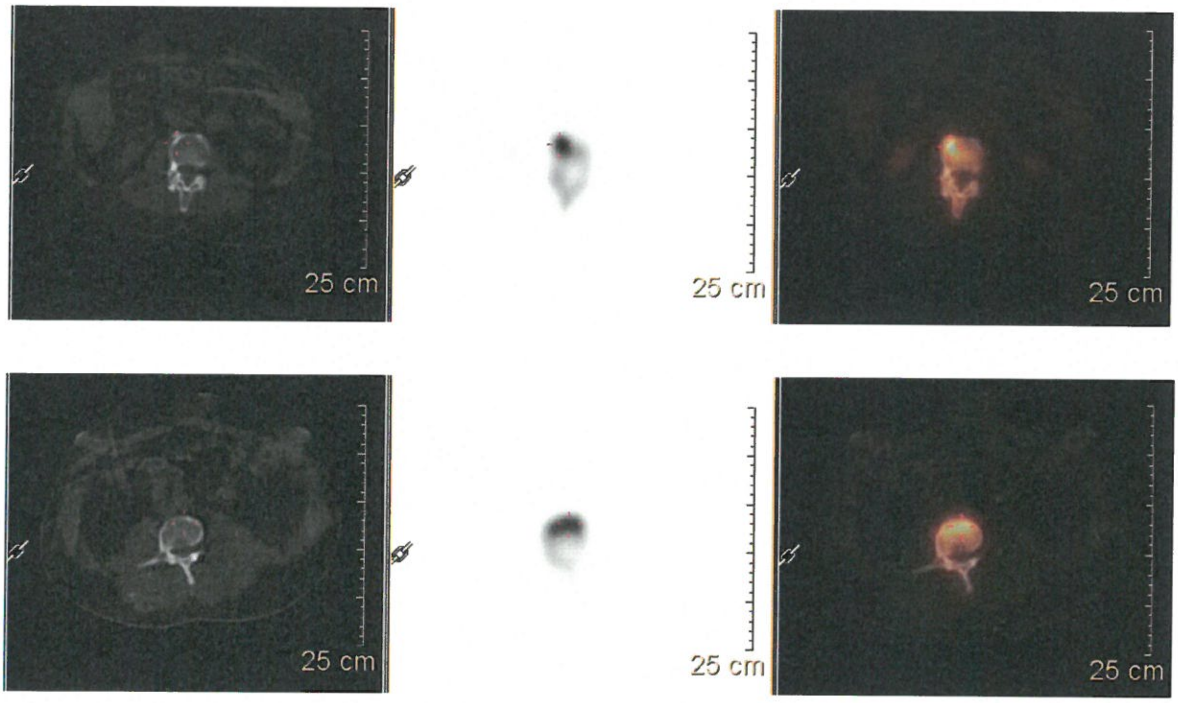


Figure 11a and 11b. Uptake in the anterior aspect of the vertebral body on SPECT or SPECT/CT

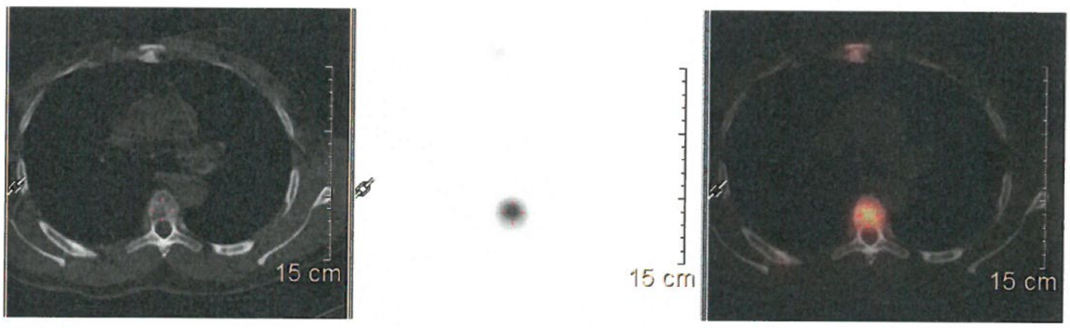


Figure 12. Diffuse uptake in the vertebral body on SPECT or SPECT/CT

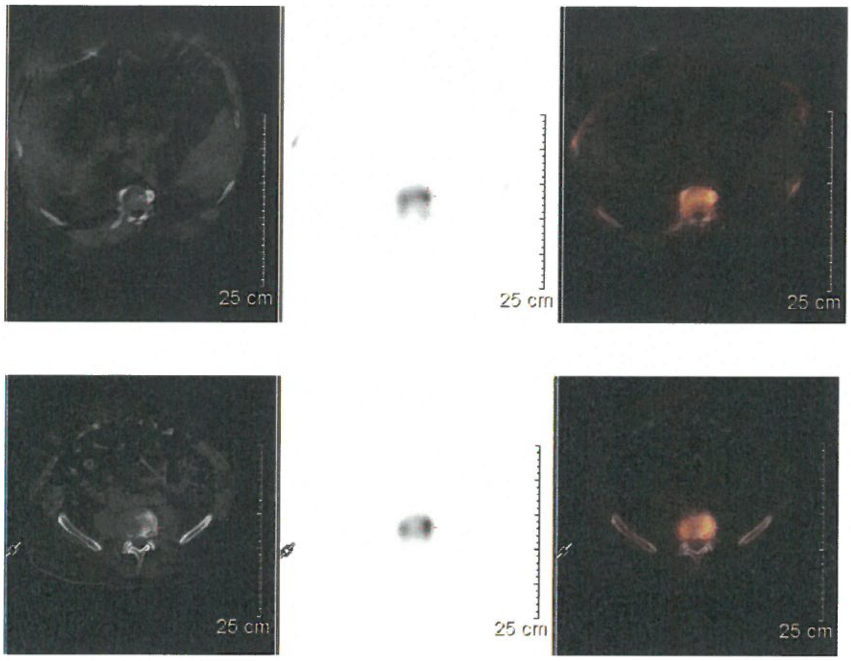


Figure 13a and 13b. Uptake in the lateral aspect of the vertebral body on SPECT or SPECT/CT

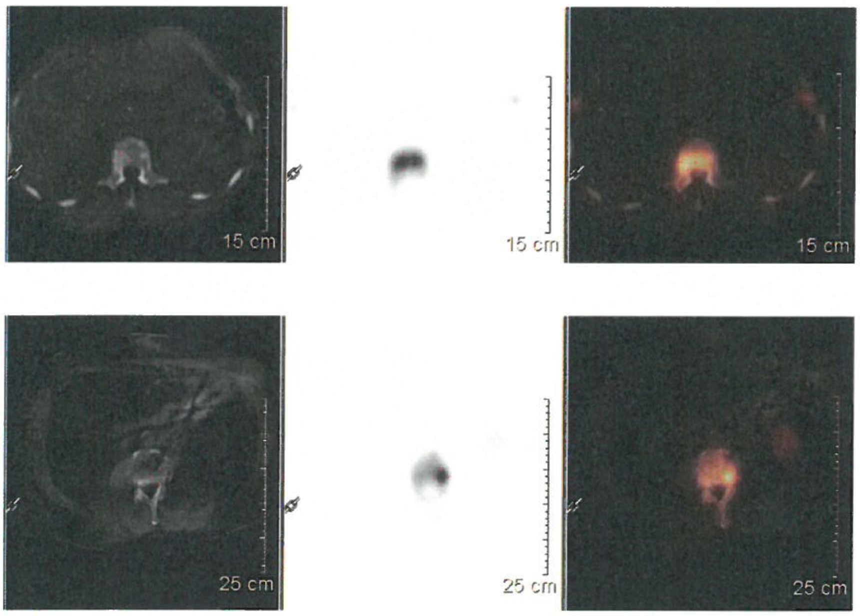


Figure 14a and 14b. Uptake in the posterior aspect of the vertebral body on SPECT or SPECT/CT

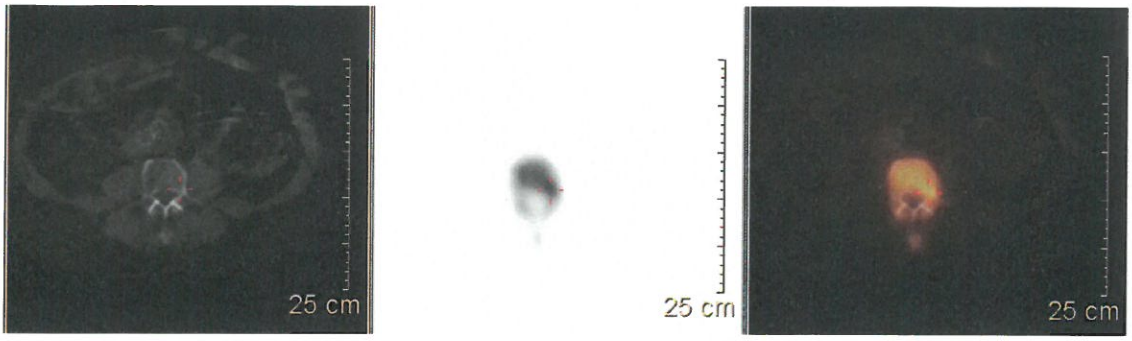


Figure 15. Uptake in the pedicle of the vertebral body on SPECT or SPECT/CT

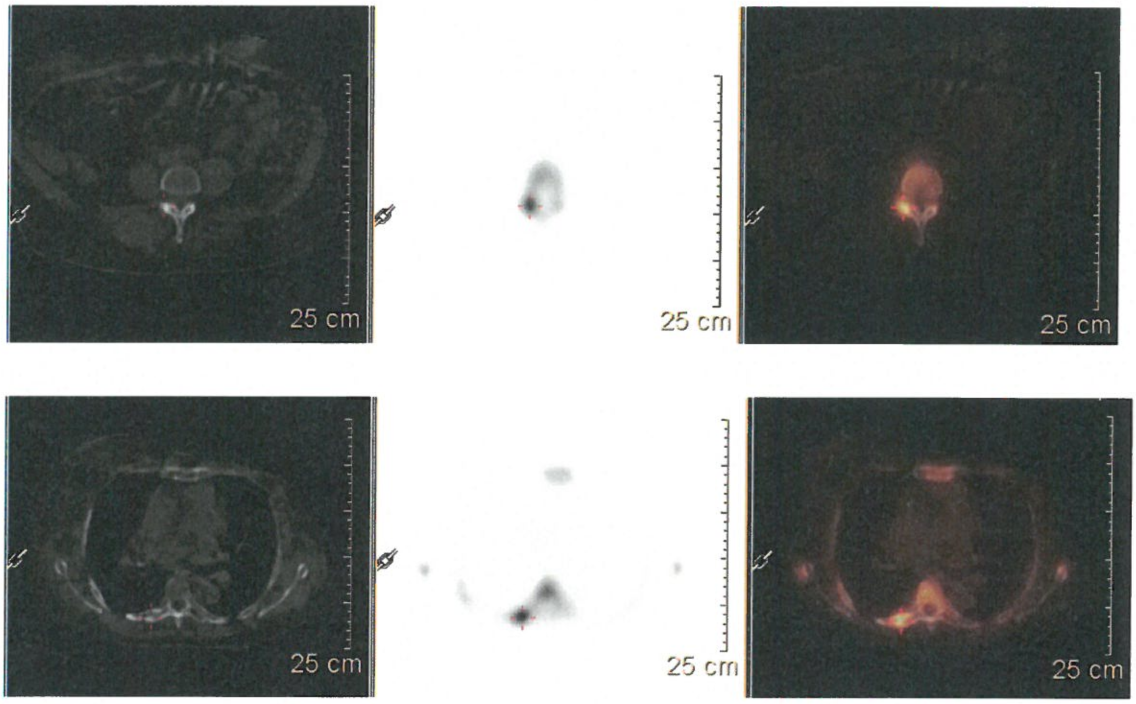


Figure 16. Uptake in the facet joints of the vertebrae on SPECT or SPECT/CT

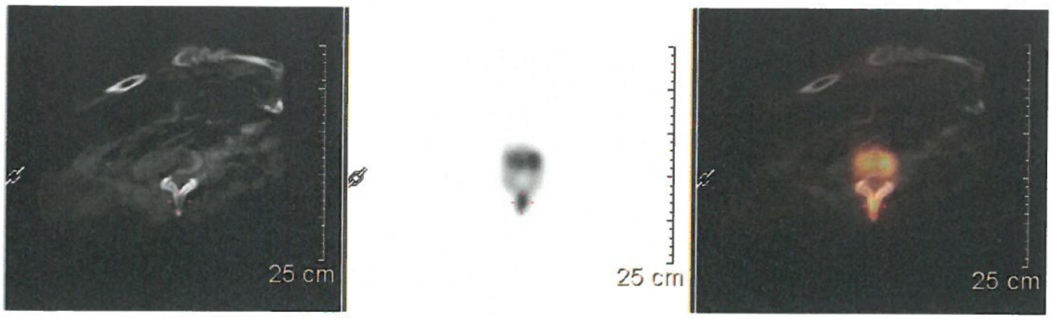


Figure 17. Uptake in the spinous process of the vertebral body on SPECT or SPECT/CT

Each lesion was graded on a 2-point diagnostic scale for each group:

1. Likely benign, if the lesion was located in the anterior vertebral body, lateral aspect of the vertebral body, facet joint or spinous process

2. Likely malignant, if the lesion was located in the posterior aspect of the vertebral body, pedicle, or diffusely involved the vertebral body

Finally, the overall diagnosis of the presence or absence of metastatic disease in each patient was compared between the 4 modalities.

2.6 Statistical analysis

Data were analyzed using the IBM SPSS statistical analysis package, version 22.

For continuous variables the descriptive results were presented as medians and range (normal or not normally distributed). Categorical variables were summarized as frequencies and percentages.

Correlation between specific aspects of the groups was measured using the t-test and Chi-square method. A p-value below 0.05 was considered to be significant.

The strength of agreement of interpretation of the sets of qualitative images was assessed with kappa coefficient.

A one-way repeated measures ANOVA was performed to determine the increment of findings among the groups.

CHAPTER 3

RESULTS

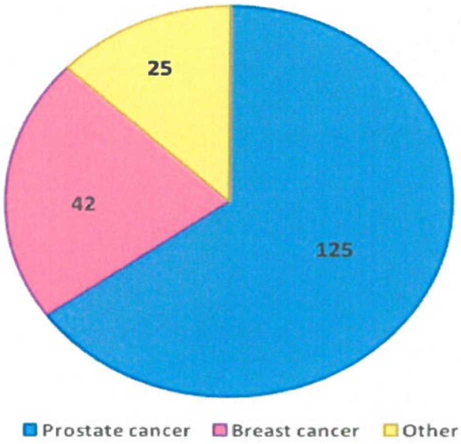
Studies from a total of 192 patients were analyzed. The original bone scan request forms were reviewed to determine the tumour type as well as the presence of absence of back pain. The images were assessed to determine the presence of spinal kyphoscoliosis, involving the thoracic and/or the lumbar spine [Tables 2 and 3]. The majority of patients had prostate cancer (65.1%) or breast cancer (21.9%), as demonstrated in graph 1.

Table 2: Patient characteristics

Characteristic	Total
N	192
Age (year) [a]	63.53 ± 12.47
Median	66
Gender [b]	
Male	131 (68.2)
Female	61 (31.8)
Back pain [b]	
Yes	116 (60.4)
No	39 (20.3)
Not documented	37 (19.3)
Kyphoscoliosis [b]	
Total	45 (23.4)
Thoracic spine only	14
Lumbar spine only	21
Thoracolumbar spine	10

[a]: Mean age and standard deviation

[b]: Frequencies (percentages)



Graph 1. Distribution of prostate cancer, breast cancer and other tumour types.

Table 3: Tumour types

Tumour type[a]	Total
Prostate carcinoma	125 (65.1)
Breast carcinoma	42 (21.9)
Colorectal carcinoma	3 (1.6)
Bladder carcinoma	4 (2.1)
Cervix carcinoma	3 (1.6)
Sarcoma	1 (0.5)
Leiomyosarcoma	1 (0.5)
Lung carcinoma	2 (1.0)
Vulva carcinoma	1 (0.5)
Endometrial carcinoma	1 (0.5)
Ovarian carcinoma	1 (0.5)
Head & neck malignancies	3 (1.6)
Renal cell carcinoma	2 (1.0)
Squamous cell carcinoma (skin)	1 (0.5)
Pancreatic carcinoma	1 (0.5)
Well differentiated thyroid carcinoma	1 (0.5)

[a]: Frequencies (percentages)

The total number of lesions identified in M1, M2, M3 and M4 were calculated [Table 4]. These results were then compared between the different groups. When evaluating the entire thoracolumbar spine, a significant difference was found between all modalities, except between non-attenuation corrected SPECT and SPECT/CT. However, when the thoracic and lumbar spine was evaluated separately, a significant difference remained only between planar imaging and any of the SPECT modalities (M2, M3 and M4) for the thoracic spine. For the lumbar spine a significant difference remained between all modalities, except between attenuation corrected SPECT and SPECT/CT [Table 5].

Table 4: Total number of lesions identified

	Thoracolumbar spine	**Thoracic spine**	**Lumbar spine**
Modality 1[a]	549	261	288
Modality 2[a]	1242	602	640
Modality 3[a]	1186	606	580
Modality 4[a]	1181	600	581

[a]: Frequencies

The increment between the different modalities was determined for the total number of lesions. With regards to the entire thoracolumbar spine, the increment was significant between all modalities, except between non-attenuation corrected SPECT and SPECT/CT. However, evaluating the increment in the thoracic spine, a significant increment was found only between planar imaging and any of the various SPECT modalities. In the lumbar spine the increment remained significant between all modalities, except between attenuation corrected SPECT and SPECT/CT [Table 6].

Table 5: Total lesions, comparison between modalities

	Thoracolumbar spine	Thoracic spine	Lumbar spine
M1:M2	p=0.000	p=0.000	p=0.000
M1:M3	p=0.003	p=0.000	p=0.000
M1:M4	p=0.000	p=0.000	p=0.000
M2:M3	p=0.000	p=0.860[a]	p=0.003
M2:M4	p=0.054[a]	p=0.929[a]	p=0.004
M3:M4	p=0.000	p=0.083[a]	p=0.594[a]

[a]: p>0.05 = not significant

The total number of lesions considered as malignant or potentially malignant in each group were calculated [Table 7]. The results are expressed as a percentage of the total lesions seen in each modality for the thoracolumbar spine in graph 2. The numbers from the different modalities were compared to each other. When evaluating either the entire thoracolumbar spine, or the thoracic and lumbar spine separately, a significant difference was found only between planar imaging and any of the various SPECT modalities [Table 8].

Table 6: Increment of total lesions detected between modalities

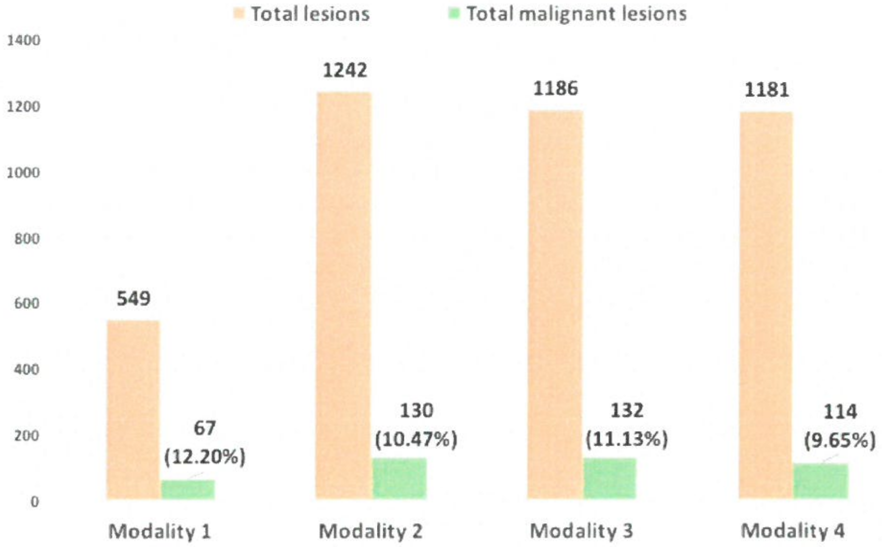
	Thoracolumbar spine	Thoracic spine	Lumbar spine
M1 to M2	p=0.000	p=0.000	p=0.000
M1 to M3	p=0.016	p=0.000	p=0.000
M1 to M4	p=0.000	p=0.000	p=0.000
M2 to M3	p=0.000	p=1.0[a]	p=0.017
M2 to M4	p=0.326[a]	p=1.0[a]	p=0.026
M3 to M4	p=0.000	p=0.5[a]	p=1.0[a]

[a]: $p>0.05$ = not significant

Table 7: Total number of lesions suspicious for malignant involvement

	Thoracic spine	Lumbar spine
Modality 1[a]	34 (13.03)	33 (11.45)
Modality 2[a]	76 (12.62)	54 (8.44)
Modality 3[a]	79 (13.04)	53 (9.14)
Modality 4[a]	68 (11.33)	46 (7.92)

[a]: Frequencies (percentages of total lesions in each anatomical region)



Graph 2. Malignant or potentially malignant lesions compared to the total number of lesions detected in each modality

Table 8: Potential malignant lesions, comparison between modalities

	Thoracolumbar spine	**Thoracic spine**	**Lumbar spine**
M1:M2	p=0.000	p=0.000	p=0.036
M1:M3	p=0.000	p=0.000	p=0.039
M1:M4	p=0.002	p=0.001	p=0.201[a]
M2:M3	p=0.828[a]	p=0.656[a]	p=0.862[a]
M2:M4	p=0.261[a]	p=0.378[a]	p=0.416[a]
M3:M4	p=0.171[a]	p=0.223[a]	p=0.414[a]

[a]: p>0.05 = not significant

The increment between the different modalities was determined for the number of lesions considered to be malignant or potentially malignant. With regards to the thoracolumbar spine as a whole, the increment was found to be significant only between planar imaging and any of the SPECT modalities. This pattern remained when evaluating only the thoracic spine, but in the lumbar spine the increment was not significant between any of the modalities [Table 9].

Table 9: Increment of malignant or potentially malignant lesions detected between modalities

	Thoracolumbar spine	Thoracic spine	Lumbar spine
M1 to M2	p=0.000	p=0.000	p=0.218[a]
M1 to M3	p=0.001	p=0.000	p=0.233[a]
M1 to M4	p=0.003	p=0.012	p=1.0[a]
M2 to M3	p=1.0[a]	p=1.0[a]	p=1.0[a]
M2 to M4	p=1.0[a]	p=1.0[a]	p=1.0[a]
M3 to M4	p=1.0[a]	p=1.0[a]	p=1.0[a]

[a]: p>0.05 = not significant

The distribution of lesion locations on the various SPECT modalities was assessed [Table 10]. The data from the different SPECT modalities (M2, M3 and M4) were reviewed to determine what percentage of lesions changed location [Table 11]. The greatest change was seen with the addition of CT.

Table 10: Distribution of lesion locations

	Modality 2	Modality 3	Modality 4
Anterior vertebral body[a]	360	365	355
Vertebral body, diffuse uptake throughout[a]	34	38	29
Lateral aspect of the vertebral body[a]	134	141	162
Posterior aspect of the vertebral body[a]	52	58	61
Pedicle[a]	48	36	25
Facet joint[a]	555	496	497
Spinous process[a]	59	52	52

[a]: Frequencies

Table 11: Change in lesion location

M1 to M2	M1 to M3	M2 to M3
5.71%	12.56%	9.44%

Using the CT component of the SPECT/CT images as reference, the data from M1, M2 and M3 were reviewed to determine what percentage of vertebrae changed location [Table 12]. The greatest change occurred in modality 1.

Table 12: Change in vertebral location

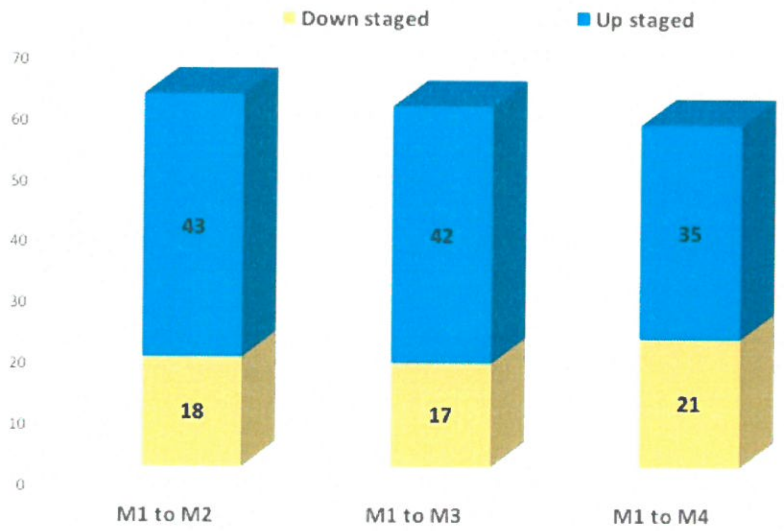
Modality 1	Modality 2	Modality 3
10.39%	2.5%	0.8%

Each patient was individually reviewed to determine how the diagnosis of probable metastatic disease changed between the different modalities [Table 13]. When comparing planar images to any of the SPECT modalities, the diagnosis changed in about a third of the patients, with the greatest impact being on up staging these patients from "no metastatic disease" to "probable or definite metastatic disease" [Graph 3]. Within the SPECT modalities the change in diagnosis was more pronounced when comparing either non-attenuation corrected or attenuation corrected SPECT to SPECT/CT, with the greatest impact now on down staging patients from "probable or definite metastatic disease" to "no metastatic disease" [Graphs 4 and 5].

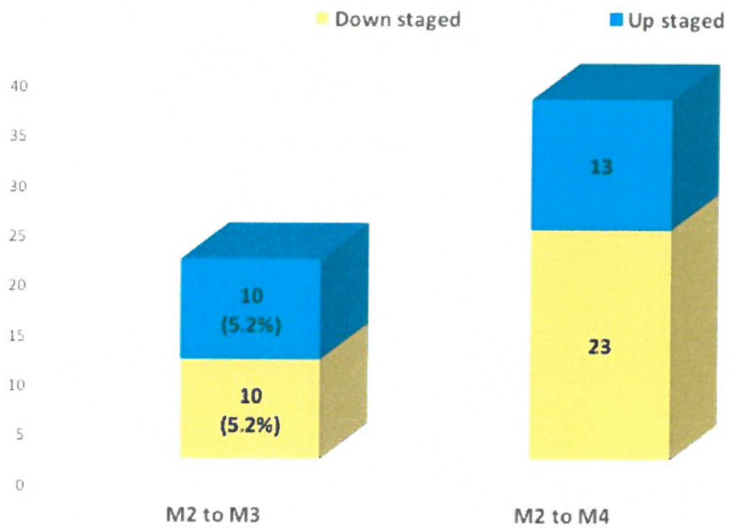
Table 13: Change in diagnosis of probable metastatic disease

	Total	Down staged	Up staged
M1 to M2[a]	61 (31,77)	18 (9,38)	43 (22,40)
M1 to M3[a]	59 (30,73)	17 (8,85)	42 (21,88)
M1 to M4[a]	56 (29,17)	21 (10,94)	35 (18,23)
M2 to M3[a]	20 (10,42)	10 (5,2)	10 (5,2)
M2 to M4[a]	36 (18,75)	23 (12,0)	13 (6,78)
M3 to M4[a]	29 (15,10)	20 (10,42)	9 (4,69)

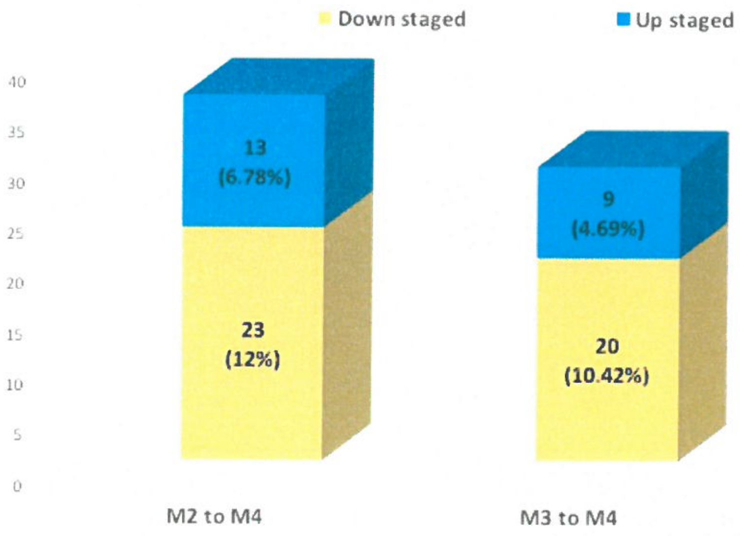
[a]: Frequencies (percentages)



Graph 3. Change in diagnosis of probable malignant disease from planar images (M1) to the various SPECT modalities (M2, M3 and M4)



Graph 4. Change in diagnosis of probable malignant disease from non-attenuation corrected SPECT (M2) to attenuation corrected SPECT (M3) and SPECT/CT (M4)



Graph 5. Change in diagnosis of probable malignant disease from non-attenuation corrected SPECT (M2) to SPECT/CT (M4), and attenuation corrected SPECT (M3) to SPECT/CT (M4)

No correlation was found between the presence of back pain and the two most frequent tumour types, prostate carcinoma and breast carcinoma (p=0.127). Within the 155 patients where the presence or absence of back pain was documented, 34 patients also had spinal kyphoscoliosis. The incidence of back pain in the patients with spinal kyphoscoliosis was 76.47% and in the patients without spinal kyphoscoliosis the incidence was almost similar at 74.38%. No statistical significant correlation was found between the presence of back pain and spinal kyphoscoliosis (p=0.804), even if separated into thoracic spine (p=0.569) and lumbar spine (p=0.776) involvement.

The presence of back pain was further correlated with the total number of lesions found in each modality for the thoracic and lumbar spine, but no significant correlation was found. However, a trend was seen between the presence of back pain and the total number of lesions in the lumbar spine, regardless of the modality [Table 14].

Table 14: Correlation between back pain and total lesion number

	Thoracic spine	**Lumbar spine**
Modality 1	p=0.519[a]	p=0.074[b]
Modality 2	p=0.308[a]	p=0.079[b]
Modality 3	p=0.498[a]	p=0.086[b]
Modality 4	p=0.459[a]	p=0.071[b]

[a]: p>0.05 = not significant; [b]: trend (p<0.09)

Documented back pain was then correlated with the total number of potentially malignant lesions found in each modality for the thoracic and lumbar spine, but no significant correlation was found [Table 15].

Table 15: Correlation between presence of back pain and number of potential malignant lesions

	Thoracic spine	**Lumbar spine**
Modality 1	p=0.535[a]	p=0.268[a]
Modality 2	p=0.474[a]	p=0.188[a]
Modality 3	p=0.753[a]	p=0.096[a]
Modality 4	p=0.415[a]	p=0.156[a]

[a]: p>0.05 = not significant

Lastly, each of the locations on the SPECT modalities was correlated with the presence of back pain. Significant correlation was found not to be consistent between the various modalities [Table 16]. No significant correlation was found between the presence of back pain and any of the various locations on planar images.

Of the 116 patients who complained of back pain, the planar images were considered normal in 24 of them (21%). Of these 24 patients, one or more abnormalities were detected on any of the SPECT modalities in 18 (75%).

Table 16: Correlation of back pain with selected lesion locations

	Modality 2	**Modality 3**	**Modality 4**
Thoracic spine Vertebral body, anterior aspect/edge	p=0.189[a]	p=0.004	p=0.027
Thoracic spine Vertebral body, diffuse uptake	p=0.049	p=0.071[a]	p=0.058[a]
Lumbar spine Vertebral body, lateral aspect	p=0.849[a]	p=0.762[a]	p=0.014
Lumbar spine Facet joint	p=0.052[a]	p=0.087[a]	p=0.184[a]

[a]: p>0.05 = not significant

CHAPTER 4

DISCUSSION AND CONCLUSION

Bone scan is a highly sensitive tool for the early identification of osteoblastic metastases.[1,2] Coexisting benign processes that also stimulate an osteoblastic response compromises the specificity. However, the specificity can be improved by more precise localization of lesions on bone scan with the use of SPECT or SPECT/CT,[1,3-8] while also improving on diagnostic accuracy[18] and reporter confidence.[8,18,19] This impact on diagnostic accuracy and reporter confidence is well documented in the evaluation of spinal lesions.[4-8,14-16]

In countries with limited resources for health, such as South Africa, careful consideration has to be given not only to cost-effective investigation of patients, but also to the most appropriate and cost-effective treatment. In order to achieve this goal, optimizing the diagnostic accuracy of relevant imaging modalities such as bone scans, is of paramount importance.

Considering the cost of imaging equipment, and specifically the two to three-fold higher cost of a SPECT/CT gamma camera compared to a SPECT gamma camera, it is of vital importance to validate the additional value of SPECT/CT in the diagnosis of metastatic disease prior to advocating the use of this expensive modality.

It is well known that the addition of SPECT to planar imaging increases the sensitivity of nuclear images, detecting more lesions on SPECT images than on planar images. Also, SPECT images increase the diagnostic accuracy through the well documented increased specificity.[3,4,5,8,36,37]

In keeping with previous literature, our results confirmed a significant benefit in the addition of any SPECT modality to planar bone scan imaging in both the total number of lesions detected and the number of potentially malignant lesions detected. The type of SPECT modality used did not make a difference in the evaluation of the thoracic spine. In the lumbar spine there was an additional benefit in the use of either attenuation corrected SPECT or SPECT/CT rather than only non-attenuation corrected SPECT when assessing the total number of lesions detected, but not when assessing the number of malignant or potentially malignant lesions. Other studies comparing the role of non-attenuation corrected SPECT versus attenuation corrected SPECT or SPECT/CT in the evaluation of the spine on bone scan could not be found in literature.

These findings imply that additional benign lesions may be identified in the lumbar spine with the additional use of attenuation corrected SPECT or SPECT/CT, but when the main purpose of the bone scan is to identify malignant or potentially malignant lesions, there is no significant added benefit in the detection of metastatic disease.

With the addition of SPECT to planar imaging, the diagnosis of metastatic disease changed in a third of patients, regardless of the type of SPECT modality, with the impact mainly on up-staging patients.

In keeping with the findings of Palmedo et al, the further addition of SPECT/CT images to either attenuation corrected or uncorrected SPECT altered the final diagnosis of metastatic disease in about one out of every six patients, with the main impact on down-staging these patients.[39] This most likely reflects the increase in specificity that is gained by the use of SPECT/CT and is in keeping with previous literature.

This increase in specificity and accuracy with the use of SPECT/CT is also seen in the amount of lesions that changed location between the different SPECT modalities and is most clearly seen when comparing SPECT/CT to non-attenuation corrected SPECT. With regards to the accurate location of the exact vertebra involved, the main impact of SPECT/CT is again on the additional value to planar imaging alone.

The use of attenuation corrected SPECT does not appear to be significantly superior to the use of non-attenuation corrected SPECT in the evaluation of the thoracic spine, but has superior performance in the evaluation of the lumbar spine. This may be related to the variable soft tissue attenuation from abdominal organs as compared to the more uniform attenuation from the lungs in the thoracic region.

The incidence of back pain is reported in the literature to be similar in patients with and without scoliosis.[59,60] In our results we also found no significant correlation with the incidence of scoliosis amongst the patients who reported having back pain. Furthermore, no significant correlation was found between reported back pain and number of lesions detected, nor with the number of malignant lesions detected. In our study back pain was therefore a poor predictor of malignant disease.

With regards to the lumbar spine, a trend was noticed between the presence of back pain and the number of lesions detected, but not with the number of potentially malignant lesions. This suggests that back pain may be a more common complaint in patients with increasing extent of degenerative changes in the lumbar spine, regardless of the extent of malignant involvement.

Of the 116 patients with a documented complaint of back pain, the planar images were normal in 24. In 18 of these 24 (75%), abnormalities were detected with SPECT imaging, again reflecting the increased sensitivity of SPECT imaging as compared to planar imaging.

Limitations:

This was a retrospective study on a patient population with a wide range of different malignancies, all with different metastatic potential and patterns of metastatic spread.

The accuracy of our findings of the presence or absence of malignant disease was not validated against further clinical follow-up, histological or imaging correlation.

In order to mimic everyday practice and ways of reporting in our environment, the transmission images were not evaluated by a specialist radiologist. The CT appearance of lesions were not included in the classification of lesions as benign or malignant. This could potentially lead to an underestimation of the value of SPECT/CT.

The fate of individual lesions was not followed. As such the changes between modalities with regards to total lesions and total malignant lesions were a combination of upstaged and downstaged lesions which does not truly reflect the change in each individual patient.

The impact of the use of SPECT/CT in individual patients as opposed to the group as a whole was not maximally explored. As such the per patient impact of SPECT/CT may potentially be underestimated. However, a post hoc analysis of the available data can be done to address this specific matter.

Conclusion:

Our study confirms the benefit of SPECT imaging to planar imaging of the spine in the evaluation of metastatic disease in patients with known malignancies. Our findings support a benefit of SPECT/CT as opposed to SPECT imaging of the spine. The additional value of SPECT/CT to SPECT and planar imaging of the spine lies primarily in the down-staging of one in every ten patients.

In resource limited settings SPECT still offers good sensitivity in the detection of malignant lesions and may suffice for the overall diagnosis of spinal metastases. However, additional costs will have to be considered with regards to radiological correlation of indeterminate lesions as well as the impact of delayed accurate staging of the patient. These costs and impact to the patient has to be weighed carefully against the higher cost of a SPECT/CT camera.

Non-attenuation corrected SPECT consistently performed poorer than attenuation corrected SPECT in the accurate localization of lesions and numbering of vertebra. Especially in the evaluation of the lumbar spine there appears to be a significant benefit of attenuation corrected SPECT over non-attenuation corrected SPECT. Furthermore, additional lesions were found on the non-attenuation corrected SPECT images that were not confirmed on the other modalities. These lesions were likely artifacts and corrected with the application of attenuation correction. When possible, and available, the use of attenuation corrected SPECT is thus superior to the use of non-attenuation corrected SPECT. Such attenuation correction may be achieved by various methods other than with the additional use of a transmission CT scan, such as used in our study.

Back pain was found to be a poor independent predictor for the presence of metastatic malignant disease.

Although we did not measure reporter confidence in our study, it is the subjective opinion of the author that there was a significant improvement in reporter confidence with the use of SPECT/CT, which would ultimately improve the quality of the final report sent out to the referring clinician.

Recommendations:

There is a need for a prospective study on the diagnostic accuracy of attenuation corrected SPECT as compared to non-attenuation corrected SPECT in the evaluation of spinal lesions, as well as a comparison between different attenuation correction techniques. Findings should be correlated with either CT images read by a radiologist, or histological and / or clinical long term follow up. It would be best for such a prospective study to be done on a more uniform population by limiting the tumour type being studied, such as prostate and/or breast cancer only.

Furthermore, the impact of the additional CT component to SPECT imaging should be correlated with the anticipated decreased need for additional correlative anatomical imaging when SPECT images are viewed in the absence of the CT component, to obtain a more comprehensive view on the true cost-effectiveness of this modality.

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