Review Article

A Review on the Usage of Bone Single-Photon Emission Computed Tomography/Computed Tomography in Detecting Skeletal Metastases in the Post-COVID-19 Era: Is it Time to Ditch Planar and Single-Photon Emission Computed Tomography only Gamma Camera Systems?

Abstract

Planar whole-body bone scanning (WBS) is widely used to evaluate skeletal lesions seen in cancer and noncancer cases. Frequently, degenerative, or other benign bony changes may give rise to indeterminate lesions that mimic bone metastases. In the post-COVID-19 era, there is an evolutionary phase that puts importance on global development and adaptability, which encompasses to include nuclear medicine practices worldwide. Single-photon emission computed tomography/computed tomography (SPECT/CT) can be used to improve the characterization of these lesions and help to resolve the diagnostic conundrum while reducing the need for patients to undergo multiple different examinations at various imaging departments. The fusion of SPECT and CT allows morphological characterization of functional abnormality detected by focal tracer uptake on planar scintigraphy, which provides a one-stop center imaging in nuclear medicine departments. The objective of this study was to review the diagnostic accuracy of SPECT/CT in diagnosing bone metastases in a variety of oncology and nononcology cases and to determine the feasibility of performing bone SPECT/CT in all suspected cancer cases, including cases of bone infection instead of planar imaging alone. The utilization of hybrid SPECT/CT in indeterminate bone lesions detected on planar WBS can significantly increase the diagnostic confidence and accuracy of image interpretation. Recognition of patterns of disease identified using hybrid imaging can improve the management of patients with potentially lower costs in the long term. Currently, hybrid SPECT/CT machines are becoming a norm in nuclear medicine departments, thus potentially making single planar application machines obsolete in the near future. We hypothesize that in the interest of providing a meaningful interpretation of isotope bone scans, the default protocol should involve the option of acquiring SPECT/CT images rather than relying on whole-body scans only. Departments choosing to upgrade existing equipment or those choosing to invest in only one gamma camera should proactively opt for hybrid SPECT/CT systems.

Keywords: *Bone metastasis, cancer imaging, diagnostic performance, oncology, single-photon emission computed tomography*

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Introduction

Planar whole-body bone scanning (WBS) is widely used to evaluate skeletal lesions seen in cancer patients and for the staging of disease. Bone-seeking radiotracers such as technetium-99 m methylene diphosphonate (^{99m}Tc-MDP) and technetium-99 m hydroxy MDP (^{99m}Tc-HDP) are routinely used for WBS diagnostic imaging to target metastases. WBS can help to noninvasively detect bone metastasis, which is a common sequela in advanced cancers, particularly solid tumors such as prostate, breast, and lung cancers.[1] However, degenerative and benign bony conditions may give rise to indeterminate bone lesions (IBL) that mimic bone metastases.[2] Single-photon emission computed tomography/computed tomography (SPECT/CT) can be used to improve the characterization of these lesions and help to resolve the diagnostic conundrum. SPECT/CT can be utilized to evaluate the tumor microenvironment (TME) in bone metastases as it enables the evaluation of multiple sites in the body suspected to have cancer spread, facilitates the serial assessment of the same bone site, and prevents the need to perform a biopsy.[3]

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It was initially predicted that the rapid development of positron emission tomography/CT (PET/CT) technology would ultimately make tomographic and SPECT imaging obsolete.[4] Despite this, advances in hybrid imaging saw a revival of interest in SPECT imaging, particularly with the advent of hybrid SPECT/CT machines. The full synergism of this hybrid imaging modality has been predicted to be able to bring great advantages to clinical workflow and patient management in nuclear medicine departments.

Planar WBS can be utilized to evaluate the whole body in one imaging procedure. This enables the characterization of the metabolic activity of bone lesions, to assess for the extent of metastases for cancer staging, and for the assessment of treatment response. WBS is a common procedure in nuclear medicine departments because it provides a relatively high sensitivity for the detection of bone metastases, albeit its relatively low specificity that can lead to false-positive findings. False-positive findings are often caused by IBL that have increased tracer uptake giving rise to hot spots on WBS, which can occur in degenerative joint disease (DJD), infection/inflammation in the bones, traumatic bone injury, and benign bone conditions.[1]

In the past decade, many centers have been advocating the use of SPECT/CT imaging to complement planar WBS, as it carries the promise of improved diagnostic accuracy. Some systematic reviews have evaluated the role of various other diagnostic imaging modalities such as magnetic resonance imaging (MRI) and PET/CT.[5] Meanwhile, there have been other studies that have reviewed the quantification method in evaluating metastatic bone disease using SPECT/CT.[1,6,7] To date, there is a lack of summarized information pertaining to the standardization of SPECT/CT imaging techniques, image interpretation, and diagnostic accuracy of this examination. Thus, we aimed to review the role, techniques of interpretation, and potential pitfalls pertaining to the use of SPECT/CT in making the diagnosis of bone metastases in a variety of oncology cases. We also aimed to determine the feasibility of performing bone SPECT/CT compared to other diagnostic imaging modalities in specific cancer types, discuss various other SPECT radiotracers for whole-body imaging, and highlight the technological developments that have enabled absolute radioactivity quantification using SPECT, which may improve prediction of bone metastases therapy response. Finally, we make practical recommendations for the utility of bone SPECT/CT imaging in a general nuclear medicine setting.

Role of Single-Photon Emission Computed Tomography/Computed Tomography in Detecting Bone Metastases in Oncological Cases

SPECT/CT is useful for evaluating bone metastases in a wide range of cancers. Bone metastases can occur in as high as 70% of patients suffering from advanced prostate and breast cancers.[8] Hence, the majority of cases referred for WBS and subsequently undergoing SPECT/CT are patients with prostate or breast cancer. SPECT/CT can guide the accurate localization of bone lesions as well as aid in the differentiation between benign and malignant lesions.[9] To comprehend the interpretation of abnormal tracer uptake detected on WBSs and ultimately diagnose early bone metastases, it is crucial to elucidate the pathophysiology of bone metastasis. Moreover, although the metastatic bone disease is broadly categorized as osteoblastic and osteolytic, there is a wide spectrum of overlapping patterns of the condition between the two extremes.

The "seed and soil" theory of metastasis, introduced by Paget in 1889, states that tumor cells will propagate to and proliferate in a site that has permissive TME for its growth.[10] Patients with advanced solid tumors often develop bone metastases due to the favorable TME in the bone marrow, which acts as a niche for distant seeding of disseminated tumor cells (DTC).[11] Osteolytic bone metastasis occurs as a result of paracrine interactions between parathyroid hormone-related protein and transforming growth factor-beta, which result in activation of the receptor activator of nuclear factor kappa B ligand and deactivation of osteoprotegerin factor (RANKL-RANK-OPG system) that acts as a catalyst for osteoclastogenesis.[12] This cascade of events commonly occurs in breast and renal cancers; hence the lesions will appear osteopenic on WBS and demonstrate corresponding lytic areas on the contemporaneous CT scan. Whereas endothelin-1, Dickkopf homolog-1 and vascular endothelial growth factor regulations propagate the development of osteoblastic bone metastases by stimulating osteoblastic activity.[12] This pathway is commonly activated in prostate cancer, which demonstrates areas of increased tracer uptake on WBS with corresponding sclerotic lesions on the contemporaneous CT scan.

Prostate Cancer

The cumulative incidence of bone metastases has an exponential rise within the 1st 2 years of diagnosing solid tumor cancers, including prostate cancer, with the meantime to detecting bone metastasis after index solid tumor diagnosis being 1.1 years.[13] A meta-analysis comparing the diagnostic performance of WBS, bone SPECT, and 18 F-choline in detecting prostate cancer bone metastases revealed that the pooled sensitivity based on per-lesion analysis were 0.59 (95% confidence interval [CI]: 0.55–0.63), 0.90 (95% CI: 0.86–0.93), and 0.84 (95% CI: 0.81–0.87), respectively, whereas the pooled specificities were 0.75 (95% CI: 0.71–0.79), 0.85 (95% CI: 0.80–0.90), and 0.93 (95% CI: 0.89–0.96), respectively.[14] Another study regarding the diagnostic accuracy of SPECT/CT stated that the pooled sensitivity and specificity for characterizing IBL were 93.0% (95% CI: 0.91–0.95) and 96.0% (95% CI: 0.94–0.97), respectively.[1]

Elevated serum prostate-specific antigen (PSA) stimulates the expression of OPG and RANKL, subsequently deactivating osteoclastic activity and increasing the osteoblastic features in metastatic prostate cancer.[15] Furthermore, the expression of androgen receptors is an important factor in the regulation of prostate cancer cell growth and development at an early stage of the disease.[15] A serum PSA value of <20 ng/ml has a high negative predictive value (NPV) and can commonly rule out the possibility of detecting bone metastasis on WBS.[16] Moreover, serum PSA has a reasonably high sensitivity of 86.5% and NPV of 80% but has low specificity of 54.5% and a low positive predictive value (PPV) of 69.7% for demonstrating bone metastases on WBS. In addition, asymptomatic patients with Gleason's score of <8 are not routinely recommended for a staging bone scan.[17] In treatment-naive patients with raised serum PSA, a WBS can be utilized to exclude bone metastases, whereas, during posttreatment follow-up, a normal serum PSA level may obviate the need for "routine" bone scan.[18] Paradoxically, WBS can also worsen, giving rise to the "flare phenomenon" that occurs as a response within 6 weeks of commencing treatment, leading to increased false-positive findings.[17,19] In advanced prostate cancer, extensive skeletal metastasis can give rise to a "superscan," as evidenced by markedly increased skeletal uptake on WBS relative to the soft tissue uptake as well as faintly outlined kidneys or even absence of visualized uptake in the kidneys. In addition, bone scan index (BSI) has become increasingly utilized in the evaluation of prostate cancer to determine the disease prognosis. BSI is designed to represent tumor burden in a WBS and is calculated based on the cumulative percentage of the total skeletal mass involved by tumor.[20] As of late efforts have been underway to make this process automated by employing artificial intelligence platforms.[21]

Although commonly associated with sclerotic or osteoblastic bone metastasis, prostate cancer may also be present with mixed lesions. SPECT/CT can accurately characterize abnormal tracer uptake on WBS by identifying sclerotic or destructive lytic bone lesions [Figure 1].

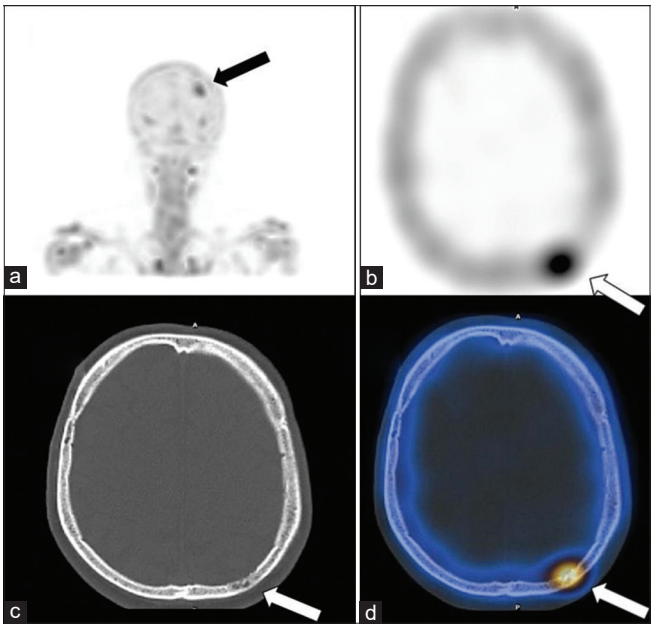

Figure 1: A 67-year-old man was diagnosed to have prostate adenocarcinoma (Gleason 7), with recent PSA level of 30.82 ng/mL. (a) Planar WBS and (b) SPECT imaging showed focal increased tracer uptake in the left posterior parietal skull bone (black arrow), (c) plain CT scan of the skull showed corresponding mixed lytic-sclerotic bone lesion (white arrow). (d) Fused SPECT/CT image localizing the radiotracer avid lesion at the left posterior parietal skull bone (white arrow), likely a bone metastasis. WBS: Whole-body bone scanning, PSA: prostate specific antigen, SPECT/CT: Single photon emission computed tomography/computed tomography

Breast Cancer

At diagnosis, bone metastases that occur in breast cancer patients are primarily osteolytic and driven by a vicious paracrine crosstalk between the DTC and osteoclasts.[11] Hence, the predominantly lytic bone lesions occurring in breast cancer are difficult to detect by WBS, making SPECT/CT an indispensable modality for improved visualization of destructive bone lesions and soft-tissue invasion.[22] Furthermore, improved diagnostic accuracy has been achieved by utilizing SPECT/CT to stage breast cancer, which has led to the reduced number of downstream radiological studies being performed.[23] A large-scale study of patients with breast cancer by Palmedo *et al*. 2014, it was revealed that the sensitivities, specificities, NPV and PPV of (i) WBS, (ii) SPECT alone, and (iii) SPECT/CT were, (i) 93%, 78%, 95%, and 59%; (ii) 94%, 71%, 97%, and 53%; and (iii) 97%, 94%, 97%, and 88%, respectively.[24] In particular, follow-up scans within 12 months can help improve diagnostic confidence by comparing the pattern and intensity of radiotracer uptake in IBL.[24] SPECT/CT can accurately characterize abnormal tracer uptake on WBS to differentiate benign or malignant lesions, hence preventing incorrect upstaging or downstaging of disease [Figure 2].

Lung Cancer

Skeletal metastases occur in as high as 20%–30% of lung cancer patients at initial diagnosis, and in up to 66% at autopsy.[25] The bone metastases from lung cancer are predominantly osteolytic, making WBS less accurate in detecting bone involvement. Considering there is a high incidence of bone metastases that occurs in lung cancer, careful evaluation of planar imaging and prudent use of SPECT/CT hybrid imaging improve the detection of both lytic and sclerotic lesions.[26] The tumor type and stage of the disease are important factors that influence the probability for detecting bone metastases. Compared to F18-sodium fluoride PET/CT (F18-NaF PET/CT), WBS has low sensitivity for detecting spinal metastases (40%) but relatively higher sensitivity for detecting metastases to the skull, thorax, and extremities (80%–90%).[25] In general, osteolytic bone metastases from lung cancer tend

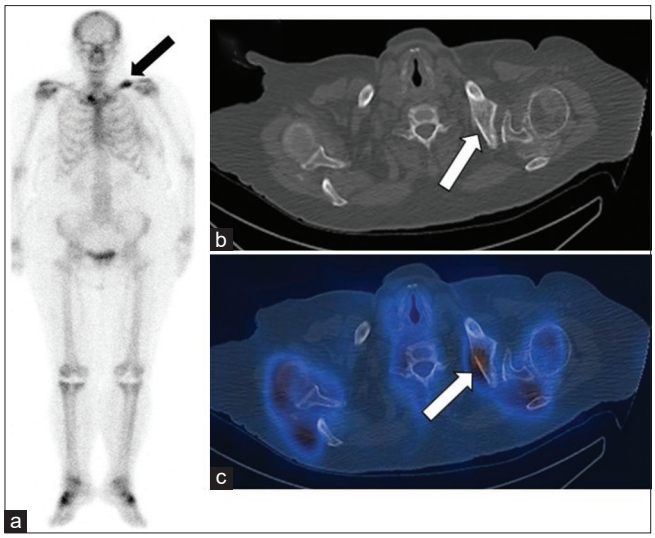

Figure 2: A 74-year-old woman with left breast carcinoma (T2N1aMx). (a) Planar WBS in frontal view showed increased tracer uptake at the left clavicle (black arrow). (b) CT scan showed break in the cortex at the left mid clavicle (white arrow) with no significant suspicious bony changes. (c) Fused SPECT/CT image localised the avid radiotracer uptake at the left clavicle, likely to represent a recent fracture. Hence, SPECT/CT helps to differentiate between benign and malignant processes, WBS: Whole-body bone scanning, SPECT/CT: Single photon emission computed tomography/ computed tomography

to be aggressive and demonstrate cortical destruction on CT. Hence, 18F- fludeoxyglucose (FDG) PET/CT is the modality of choice for the staging of lung cancers, particularly nonsmall cell lung cancers (NSCLC), as it can also be used to accurately assess treatment response.[27,28]

Renal Cell Cancer

The majority of renal cancers tend to be renal cell carcinoma (RCC), having predominantly three histological subtypes, i.e. clear cell, papillary, and chromophobe RCC, with the clear cell RCC being a significant predictor of metastasis.[29] European Association of Nuclear Medicine procedure guidelines recommend that in patients undergoing renal replacement therapy, hemodialysis should be performed within 5 h of radiotracer injection for bone scan to significantly reduce the blood pool and soft-tissue tracer activity.[20] WBS may be useful in detecting metastases, particularly in symptomatic patients having pain due to nerve root compression, pain due to impending pathological fracture, or symptoms of hypercalcemia. Furthermore, at an advanced stage, there can be the compensatory osteoblastic activity that leads to the identification of hot spots of WBS.[30] Although more expensive, 18F-FDG PET/CT is preferred for staging RCCs.[30]

Bladder Cancer

Baseline WBS carries minimal impact on bladder cancer patient management and further oncological therapy, thus should not be routinely performed for staging.[31] This is due to the low propensity of bladder cancers, including cervical, endometrial, and gastrointestinal tract tumors to develop skeletal metastases caused by the lack of affinity of these cancer lines with the bone matrix resulting in reduced ability to flourish in the bone marrow microenvironment.[32] Nevertheless, in patients who did not undergo radical cystectomy, there was a 25% risk of detecting bone metastases on WBS compared to a 13% risk in patients who had undergone radical cystectomy.[31]

Planar WBS and SPECT/CT are being used to evaluate IBL detected in a patient with bladder cancer [Figure 3]. However, it is important to note that lytic bone lesions may have variable tracer activity with nil to low-grade tracer uptake [Figure 4].

Hepatocellular Carcinoma

Bone metastases in hepatocellular carcinoma (HCC) are predominantly osteolytic, making WBS less sensitive to detecting bone metastases compared to PET/CT imaging. Moreover, bone metastases from HCC generally do not demonstrate hypermetabolism on 18F-FDG PET/CT scans.[3] Interestingly, patients having HCC who undergo treatment with high-intensity focused ultrasound often demonstrate photopenic areas in the anterior right-sided ribs, which occurs as a result of tissue damage along the path of the ultrasound beam.[33]

Testicular Cancer

The incidence of testicular cancers is relatively rare. Nevertheless, there are certain features on bone SPECT/CT imaging that should highlight the possibility of testicular tumors, such as predominantly iliac bone involvement of bone metastasis.[34] This occurs because of the lymphatic drainage route of testicular cancers that spread along the iliac lymph node chain. Interestingly, it has been reported that staging WBS with complementary SPECT/CT for testicular tumors can identify extraosseus radiotracer uptake arising from calcified metastatic paraaortic lymph nodes.[35]

Common Pitfalls in Whole-Body Bone Scanning Interpretation that are Mimickers of Bone Metastasis

The relatively low specificity of WBS leads to a substantial number of false-positive findings. The common pitfalls of WBS occur when diagnosing abnormal radiotracer uptake occurs in the spine. Nevertheless, with the utility of SPECT/CT, features of DJD such as end plate sclerosis, anterior osteophytes, and subchondral cysts, are identified. Furthermore, a diagnostic dilemma can occur when diagnosing focal hot spots detected within the vertebral bodies, which can occur in the presence of intraosseous hemangiomas. However, this can be resolved by a SPECT/CT scan

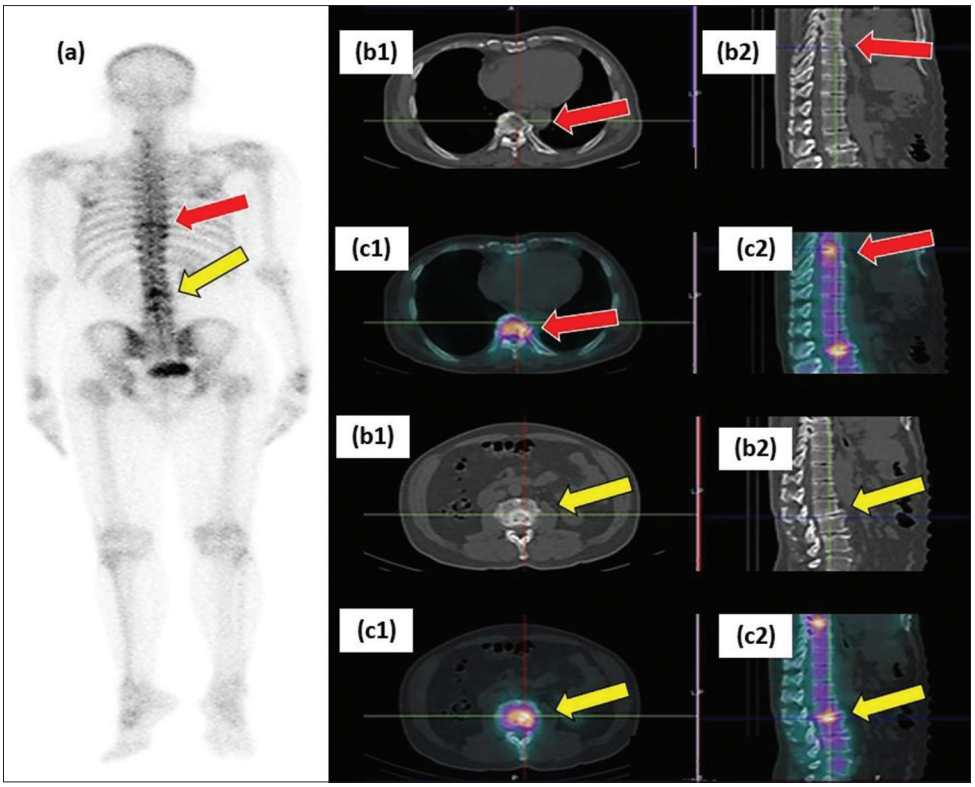

Figure 3: A 64-year-old man with lumbar pain and underlying bladder carcinoma. (a) Planar WBS revealed foci of increased tracer uptake at T8/T9 (red arrow), L2/L3 (yellow arrow) and L3/L4 vertebrae, corresponding to spinal osteoporotic DJD as seen on CT (b1, b2).(c1, c2) Fused SPECT/CT images demonstrating the DJD at T8/T9 (red arrow) and L2/L3 (yellow arrow), respectively. WBS: Whole-body bone scanning, SPECT/CT: Single photon emission computed tomography/computed tomography, DJD: Degenerative joint disease

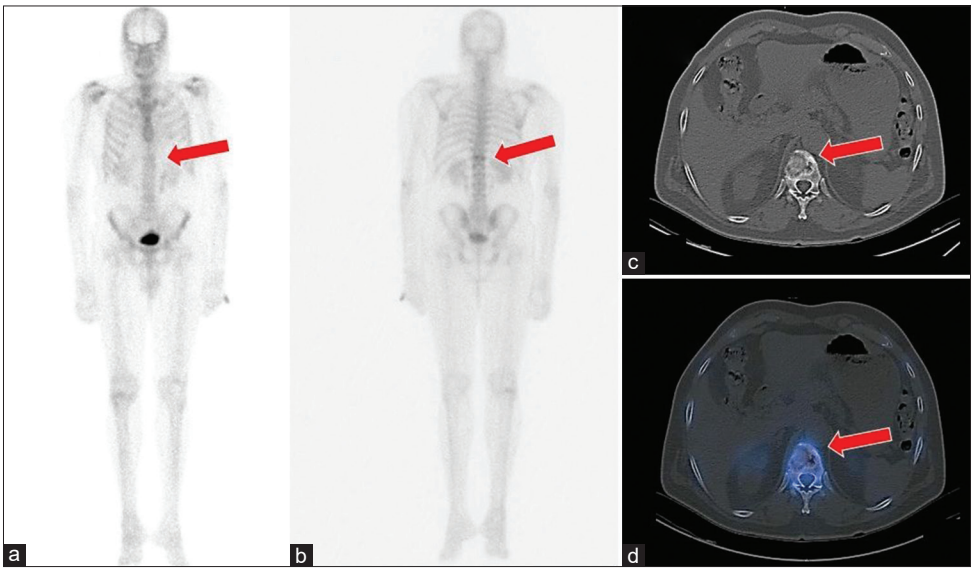

Figure 4: A 73-year-old man with bladder carcinoma, postchemotherapy. (a) Anterior and (b) posterior planar WBS revealed very subtle tracer uptake at the T12 vertebra (red arrow). (c) Plain CT, (d) Fused SPECT/CT images revealed subtle, low-grade tracer uptake of a pathological compression fracture at T12 vertebral body, with the associated lytic bone lesion (N. B. Bone scan is less sensitive in evaluating lytic bone lesions.). WBS: Whole-body bone scanning, SPECT/CT: Single-photon emission computed tomography/computed tomography

that is able to detect characteristics "polka dot," "spoke wheel," or "corduroy sign," on the contemporaneous CT scan.[36] On the other hand, diffuse tracer uptake in the lumbar vertebrae, especially at level L1–L4 may appear suspicious on WBS; however, these are likely to indicate osteoporotic fractures. These fractures result in the degenerative collapse of the vertebral bodies and often demonstrate a "vacuum phenomenon," which can be distinguished from metastases by reviewing the sagittal view of the SPECT/CT images.

The pelvic bones, although being a common site for bone metastases, is also where IBLs are frequently detected, hence may lead to a pitfall for misdiagnosing bone metastases. Sacral insufficiency fractures and osteitis condensans ilii are among some benign conditions that can give rise to indeterminate hot spots on WBS.

It is a known fact that multiple foci of radiotracer uptake on WBS in the axial and proximal appendicular skeleton (the sites with red marrow that are favorable TME for the seeding of cancer cells) give a clear-cut diagnosis of bone metastasis [Figure 5]. Occasionally, focal hot spots can be detected in a site distant from primary cancer, such as in the skull, which leads to a diagnostic conundrum, particularly when there are no other hot spots detected elsewhere on the WBS. Such findings can be resolved by SPECT/CT, which may identify physiological or benign conditions such as the uptake at the confluence of sutures, sutural foramina, enlarged Pacchionian granulations, hyperostosis frontalis interna, osteoid osteomas, meningiomas, skull hemangiomas, and fibrous dysplasia, among others.[37]

The presence of enthesopathy is another cause for false-positive findings on WBS. Frequent sites involved include the tuberosity of the humerus, olecranon, patella of the knees, the greater and lesser trochanters of the femora, pelvis bones, and calcaneum.[36] SPECT/CT can usually distinguish the features of degenerative changes from bone metastases by identifying subchondral bone erosion, subchondral sclerosis, and crystal deposition at the joints and along the tendon attachment sites.

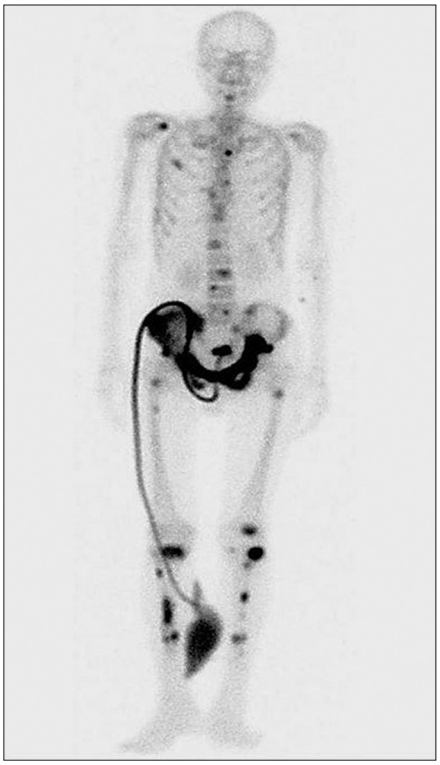

Figure 5: A 74-year-old man with newly diagnosed prostate carcinoma (Gleason 8 and PSA 2300 ng/mL). Planar WBS showed multiple tracer-avid bone metastases in the axial and appendicular skeleton. The urinary catheter was noted *in situ*. In cases of extensive bone metastases, SPECT/CT may not be required. WBS: Whole-body bone scanning, PSA: prostate-specific antigen, SPECT/CT: Single-photon emission computed tomography/computed tomography

Comparison of the Performance of Single-Photon Emission Computed Tomography/Computed Tomography with other Diagnostic Imaging Modalities

SPECT/CT remains as a cost-effective and immediate solution to resolve IBL detected on WBS. MRI is often utilized to characterize the soft-tissue component of lesions. Although MRI does not involve using ionizing, the examination is more costly and takes a relatively longer time to perform. Furthermore, MRI may be contraindicated in certain instances, in which the patients may have a nonremovable electronic or metallic implant within the body. A meta-analysis of 45 studies revealed that Ga68-prostate-specific membrane antigen (Ga-68 PSMA) PET/CT scan was the modality of choice for detecting metastases from prostate cancer, yielding a sensitivity of 91% and specificity of 99%, respectively.[38] The diagnostic accuracy for detecting metastasis was also good using 18F-NaF, 11C-choline, 18F-choline, 18F-FDG, and 18F-Fluciclovine PET/CT, but less superior compared to Ga-68 PSMA scans.[38]

Other Single-Photon Emission Computed Tomography Radiotracers used to Rule out Bone Metastases

Apart from bone-seeking agents, other WBS and SPECT compatible radiotracers have been investigated and subsequently adopted into mainstream nuclear imaging to detect bone metastasis and stage cancers. One such radiopharmaceutical is I-131 that is used to perform whole-body scans which has been historically applied for the staging of differentiated thyroid cancers. Another radiopharmaceutical that is disease specific is I-131 meta-iodobenzylguanidine (I131-MIBG) which selectively targets tumors arising from the sympathetic nervous system. Thus, I131-MIBG is used to stage neuroblastomas, paragangliomas, etc., as well as calculate dosimetry and deliver therapy.[39] Recently, Tc99 m-PSMA has been introduced as a novel radiopharmaceutical to stage prostate cancers.[40] In addition, the introduction of the radiopharmaceutical fibroblast activation protein inhibitor (Tc99 m) holds promise to become a mainstream contender that can be an alternative to 18F-FDG PET/CT for oncology imaging.[41,42]

Quantification of Single-Photon Emission Computed Tomography/Computed Tomography

Quantification of SPECT/CT provides the added value of improved diagnostic accuracy in differentiating bone

metastases from DJD. The maximum standardized uptake value (SUV_{max}) is measured for quantification by drawing a volume of interest around hot spots detected on WBS, followed by a calculation of the voxel activity concentration factored to the patient's weight and divided by the decay corrected injection activity as denoted by the SUV of the adjacent normal-looking tissue, which represented the background activity.[43] Before this, calibration of the scanner needs to be performed by using a standardized PECT/CT phantom, which aids in the conversion of the reconstructed counts into units of activity concentration.[43] SUV_{max} was noted to be significantly higher in bone metastases compared to DJD.[44] Tabotta *et al*. achieved sensitivity, specificity, PPV, and NPV of 87%, 92%, 99%, and 49%, respectively, for detecting bone metastases in prostate cancer by using a SUV_{max} cutoff of 19.5 g/mL.[6]

Recommendations for Single-Photon Emission Computed Tomography/Computed Tomography usage and Points for Consideration

In the aftermath of COVID-19 infection, there has been a global call for heightened infection protection that involves reduced exposure of the at-risk public to the hospital environment, as well as prioritization of the continuity of essential services.[45] WBS and SPECT/CT are cost-effective diagnostic tools that aid in the diagnosis of bone metastases and help stage certain cancers. The hybrid application of SPECT/CT is relatively easily and widely available in most countries worldwide, making it the preferred adjunct investigation for staging certain cancers. A recent meta-analysis reported that the pooled sensitivity and specificity of SPECT/CT were 93.0% (95% CI: 0.91–0.95) and 96.0% (95% CI: 0.94–0.97), respectively, for correctly diagnosing bone metastasis in IBL.[1]

In a study by Sharma *et al*.,[46] it was found that SPECT/CT is superior compared to planar scintigraphy and SPECT alone in characterizing indeterminate lesions on bone scintigraphy. SPECT/CT was noted to have a significant impact on patient management in about 66% of patients compared to planar scans only, and in approximately 20% of patients compared to SPECT alone. Similar findings were also seen by Jambor *et al*.[47] with SPECT/CT recording a smaller number of equivocal lesions compared to planar-only imaging.

A matter of arising concern is the increased exposure to ionizing radiation, which has resulted from the addition of CT scan imaging to acquire anatomical information to complement functional imaging. The additional radiation dose from the CT portion in SPECT/CT is variable and can range from <1 mSv for CT attenuation correction to 8 mSv for a diagnostic CT.[19] The average effective dose value of SPECT/CT is estimated at 3.8 mSv.[48] This variation has also been mainly attributed to the diversity in the length of the scans involving whole-body versus region of interest imaging.[49] Hence, there is a future need for dose optimization in SPECT/CT, especially in the determination of the optimal scan length.[49]

In addition, there is also a need to balance the use of CT for anatomical correlation and exposing patients to additional radiation with careful consideration being implemented on the risks and benefits of SPECT/CT compared to SPECT only study. It is of utmost importance to be able to adapt good practices in optimizing the increased radiation dose incurred by adding on the CT component in the scans, thus ensuring the exposure levels do not exceed the recommended diagnostic reference levels.[50]

There are different approaches in incorporating bone SPECT/CT in oncology patients. This entails a targeted SPECT/CT for indeterminate bone uptake[51] and a whole-body SPECT/CT.[52] Whole-body SPECT/CT, however, results in higher radiation dosimetry with a longer scan acquisition time.[52] It has been shown that a two-bed systematic SPECT/CT has limited incremental value on the initial staging diagnosis in terms of disease certainty and specificity compared to a single-bed targeted SPECT/CT.[52] Although whole-body SPECT/CT is more sensitive compared to targeted SPECT/CT, there were no significant differences in terms of specificity.[52,53] From a practical point of view, the use of targeted SPECT/CT has been applied in many centers, with its usage being reported in approximately 15% of cases.[51] A focused SPECT/CT is more efficient and enables optimal utilization of reporting and imaging capacity, which obviates the need for follow-up imaging, especially in inconclusive bone lesions seen on planar imaging.[51] Furthermore, selective use of SPECT/CT is essential, especially in indeterminate skeletal lesions, to maximize and enhance patient throughput. The consensus is that certain conditions do not necessitate the addition of SPECT/CT, for example, a normal planar bone scan, scans with multiple foci of metastatic disease, scans having tracer uptake at the joints that is suggestive of arthropathy, scans having uptake pattern that is characteristic of benign pathology, and the availability of recent correlative cross-sectional imaging.[51] In fact, the addition of SPECT/CT by technologists when doctors are not readily available in the department should be conducted with prudence as many a times, SPECT/CT can be omitted after proper image assessment and a correlation is made with the clinical history.

The spatial resolution of planar bone scintigraphy is low and measures roughly 1 cm,[19] which poses difficulty in characterizing bone lesions that are small. Nonetheless, SPECT offers better spatial resolution at 8 mm, while PET bone imaging with NaF offers superior spatial resolution at 4 mm,[19] which aids in the detection of small bone lesions. The recent advances of SPECT reconstruction algorithm have led to greater resolution of SPECT/CT images. The

xSPECT/CT integrates the info from CT into the raw data acquired from SPECT/CT before image reconstruction, producing high-quality skeletal SPECT/CT imaging.[54] In a prospective study involving 200 patients by Ian Duncan and Nicholas Ingold,[54] compared to the conventional SPECT/CT, xSPECT/CT demonstrates more diagnostic information in 71.1% of cases, detects additional lesions with an average of 2.4 lesions per case with 39% of the lesions measuring <6 mm, and a change of diagnosis were observed in 20% of cases after review of the xSPECT/CT images.[54] However, there is currently no study which compares the sensitivity and specificity in disease detection between xSPECT/CT and NaF PET/CT. As both imaging modalities can quantify the uptake intensity with SUV, it would be interesting to know if xSPECT/CT performance would be comparable to that of NaF PET/CT imaging.

Next, the quantification of WBS using the BSI as well as SUV assessment has become an essential component for staging prostate cancers. These techniques facilitate standardized reporting and are instrumental in the development of automated software that aids in diagnosing bone metastases. Nevertheless, it is crucial to be prudent in selecting patients who will ultimately benefit from SPECT/CT. Points for consideration when deciding on any additional imaging include the type of primary cancer, the level of detected tumor markers, the number, site, and pattern of distribution of hot spots that are detected on WBS, as well as any history of recent chemoradiotherapy.

Last but not least is the issue of cost. The additional cost of upgrading a SPECT gamma camera to a SPECT/CT scanner includes building and engineering alteration, additional shielding, and electrical upgrading. Currently, there is yet a study which highlights the cost-effectiveness or the economic value of bone SPECT/CT in oncology patients and its impact on subsequent patient management. In a study by Wyngaert *et al*.,[55] it was found that diagnostic bone SPECT/CT scan resulted in cost saving of $622.6/patient per year compared to conventional CT and $574.5 per patient per year compared to metal artifact reduction sequence MRI in post knee arthroplasty patients who presented with moderate-to-severe pain postsurgery. In another study by Romsa *et al*.,[56] lung perfusion study with SPECT/CT was found to be highly cost-effective and enabled a more definite assessment of lobar perfusion function, leading to an accurate ppoFEV_1 in the presurgical planning of NSCLC patients compared to planar scintigraphy. It constitutes a change to surgery in 1.3% of patients who were deemed nonoperable, and in 3.3% of surgical patients, an aggressive therapy was given. Similarly, SPECT/CT was found to have superior economic value in the diagnosis of pulmonary embolism compared to computed tomography pulmonary angiography, planar scintigraphy and SPECT with better sensitivity and specificity, resulting in lower hospitalization cost for false-positive cases.[57]

Conclusion

Hybrid imaging using SPECT/CT is an indispensable adjunct investigation in most nuclear medicine departments worldwide. Current advances in technology avail the safe use of this modality, thus potentially making the single planar application machines obsolete in the near future. We recommend that SPECT/CT be utilized when there is an indeterminate or equivocal lesion detected on WBS. The evidence is strong in support of performing SPECT/CT, which is more cost-effective because it facilitates faster clinical decision-making and reduces the need for follow-up scans. Consequently, there will be reduction in the number of referrals for additional radiological imaging, which will incur more cost, traveling time, and delays in the time taken to treat cancers.

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Conflicts of interest

There are no conflicts of interest.

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