SPECT/CT in oncology

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Dr Fraser Hendry
Radiology registrar

Dr Sai Han
Consultant nuclear medicine physician
Nuclear medicine department, Glasgow Royal Infirmary, West of Scotland PET Centre, Gartnavel General Hospital, Glasgow
drsaihan1@gmail.com

Introduction
Radionuclide imaging can demonstrate whole body functional/metabolic information and plays an important role in oncology clinical and research practice. It is integral to many clinical pathways, assisting in diagnosis and staging, pre-operative localisation, monitoring response and detecting recurrence. However, planar scintigraphy and SPECT lack anatomical and structural details resulting in low specificity and sensitivity with inconclusive reports often requiring further imaging correlation. To overcome these limitations hybrid SPECT/CT was introduced to clinical practice in 1999 and it has become a commonly used imaging modality. By combining the functional map of radionuclide imaging with the anatomical detail of CT, it allows accurate localisation, attenuation correction and characterisation of lesions in the same session. The result is improved specificity, sensitivity and diagnostic confidence leading to earlier diagnosis and shorter time to treatment. Potential issues of SPECT/CT include additional radiation, time for scanning and reporting, staff training and incidentalomas.

New radiotracers, advances in hardware and improved software have all led to a number of exciting developments in SPECT/CT in recent years. Despite rapid advances in other modalities such as CT, MRI, PETCT and PETFMI, radionuclide SPECT/CT continues to play an important role in clinical practice.

SPECT/CT in skeletal malignancy
Isotope bone scans with 99mTc-MDP allow whole body screening for skeletal metastases, especially for osteoblastic metastases that are common in cancers such as prostate and breast. By adding CT localisation and characterisation of hot spots, SPECT/CT can help identify artefacts, differentiate between bone, joint, and soft tissue uptake, and benign from malignant processes. This gives major benefit to radionuclide oncology imaging as many common benign conditions such as degenerative change and fractures can have high uptake. These may be interpreted as malignant or inconclusive lesions on planar and SPECT imaging but are more readily appreciated on SPECT/CT. The CT component can show important structural abnormalities such as sclerotic lesions, lytic lesions (which can be falsely negative on scintigraphy) and aggressive lesions. In our experience adding targeted SPECT/CT to planar bone scans has significantly reduced the inconclusive results in assessing suspected bone metastases in breast cancer.

Moreover, critical conditions such as impending pathological fracture and spinal canal compromise may also be detected on SPECT/CT and the clinical team can be alerted for urgent assessment and intervention. It is debatable whether targeted or routine SPECT/CT should be performed. Common practice is a targeted SPECT/CT of the inconclusive planar image findings.

We suggest significant clinical symptoms such as local pain should also be considered, given the potential for false negative planar imaging due to lytic and soft tissue lesions (figure 1).

Recent improvements in scanner technology have resulted in whole body SPECT/CT being practicable for the first time. Rager et al found whole body SPECT/CT to be more sensitive than targeted SPECT/CT for detecting bone metastases.

SPECT/CT in neuroendocrine tumours
Neuroendocrine tumours (NET) are often small and difficult to identify on CT and MRI. Established radionuclide imaging includes 111In pentetreotide (Octreoscan) as a somatostatin receptor imaging (SSRI) agent for differentiated NETs and 123I MIBG for pheochromocytoma, paraganglioma and neuroblastoma etc. These play a key role in staging as well as diagnosis, prognosis, planning treatment, monitoring response and detecting recurrence. SPECT/CT provides accurate localisation and attenuation correction and has been shown to be superior to planar scintigraphy and SPECT in detecting NETs.

SPECT/CT can also reduce false positive planar scans such as meningioma, granuloma and infections. Until recently 111In pentetreotide (Octreoscan) was the most commonly used SSRI agent. Its limitations include a relatively high radiation dose and a two-day procedure. The recent introduction of 99mTc-EDDA/HYNIC-Ty3-octreotide (Tektrotyd) has been a significant step forward. 99mTc has advantages of better image quality, one-day procedure and lower radiation exposure. Although there are few studies directly comparing Octreoscan and Tektrotyd, the limited data available along with anecdotal evidence suggests that the latter provides superior image quality and sensitivity in tumour detection.

While 68Ga-DOTA PETCT has been shown to be superior to octreotide SPECT/CT for somatostatin receptor positive NETs, it is not yet widely available. It is therefore likely that SPECT/CT will remain the first-line SSRI for the foreseeable future.

MIBG SPECT/CT has been shown to improve diagnostic accuracy and diagnostic confidence in neural crest tumours.

Figure 1
A patient with previous lung cancer and right upper lobectomy was referred for bone scan with a two-month history of back pain and negative CT chest and abdomen. (A) Planar whole body bone scan was unremarkable but (B) SPECT/CT of painful and tender upper thoracic spine revealed soft tissue mass at previous resection site with lytic destruction of T3 and some infiltration into the spinal canal. The patient was urgently assessed and given radiotherapy. SPECT/CT improves diagnostic accuracy as well as highlighting critical conditions for urgent action.
SPECT/CT allows accurate localisation of MIBG activity to soft tissue and bone, and better characterisation of small lesions especially in the areas of high physiological MIBG uptake such as liver and urinary bladder.

**SPECT/CT in differentiated thyroid cancer**

Radioiodine is utilised for both the imaging (123I and 131I) and treatment of differentiated thyroid cancer (131I). Whole body planar scintigraphy can typically be performed following 131I radioiodine remnant ablation or adjuvant therapy, and for suspected relapse. Planar scintigraphy is limited by nonspecific physiological iodine uptake and lack of anatomical detail, and the incremental role of SPECT/CT is now well established. SPECT/CT can reveal physiological activity and malignant foci that often lie in close proximity especially following thyroidectomy +/- nodal dissection where normal anatomical landmarks are lost. SPECT/CT has been shown to positively influence staging, risk stratification and clinical management as well as increasing reporter confidence. Post-radioiodine SPECT/CT in differentiated thyroid cancer has been shown to have 78% sensitivity and 100% specificity for persistent/recurrent disease. Routine neck/ chest SPECT/CT identified non-iodine avid lesions, and reduced the need for routine cross-sectional imaging in 20%.10 As current thyroid cancer guidelines promote a more measured approach to surgery and radioiodine in low risk patients, the role of SPECT/CT in accurate risk stratification is vital.11

**SPECT/CT in sentinel lymph node imaging**

The sentinel lymph node (SLN) marks the first draining node from a primary tumour. Accurate identification of SLNs is crucial, as metastatic free SLNs imply that subsequent nodes are also disease free and extensive nodal dissection with potential complications may be avoided. Although SLN localisation techniques are evolving, with some variable practices among different centres, radionuclide SLN localisation is widely used, especially in breast cancer and melanoma. It has also been shown to be beneficial in other tumours such as head and neck, penile and gynaecological malignancies.

SLN imaging typically uses 99mTc nanocolloid injected intradermally near the primary tumour site. The lymphatic drainage pattern can then be imaged. SPECT/CT has been shown to be superior to planar scintigraphy particularly when the SLNs are not in the expected anatomical location.12,13 Planar scan false positive foci such as skin folds, lymphatic tracts and other tissues; and false negative nodes such as nodes close to the injection site and non- tracer avid metastatic nodes, may be revealed by SPECT/CT.

SPECT/CT can locate SLN to standard nodal stations (eg neck) and can provide better 3D image display, which may be beneficial to surgical planning.

**Other applications in oncology**

SPECT/CT plays an important role in the work-up for 90Y microsphere selective internal radiation therapy (SIRT) of liver malignancies by identifying extrahepatic shunts and guiding dosimetry. Pre-therapy SPECT/CT following transarterial 90Y-Tc MAA injection can detect potential off-targets such as lung, gall bladder and gastro-duodenal uptake, which can affect the treatment plan (eg reducing 90Y dose to acceptable lung level; adjusting hepatic artery catheter position; coiling the collaterals; adding gastroprotective medication etc). SPECT/CT based voluming of liver lobes is complimentary to conventional CT based assessment. Post-therapy Bremsstrahlung SPECT/CT can also reveal extrahepatic deposition.

SPECT/CT is also useful in the regional lung function assessment, which may be used in preoperative fitness assessment for lobectomy /pneumonectomy in radically treatable lung cancers. Historically, planar VQ scan has been quantified to provide regional lung functions (perfusion of different lung zones) to calculate the predictive post-operative lung function but zonal VQ does not accurately reflect the lobe(s) that are to be resected. Hybrid SPECT/CT VQ imaging can now localise the fissures and lobes and provide more accurate lobar function using dedicated lobar quantification software.

Evolving technology includes whole body SPECT/CT as mentioned earlier in the skeletal section. It can potentially

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**Figure 2**
Whole body bone scan staging of a patient with prostate cancer showed two foci of increased tracer uptake in left femoral neck and left posterior iliac region. (A) SPECT/CT clarifies the left femoral neck focus is an irregular sclerotic lesion with chondroid calcification consistent with benign enchondroma. (B) SPECT/CT confirms the left iliac lesion is a sclerotic metastasis.

**Figure 3**
Post-radioiodine diagnostic 123I imaging shows focal intense uptake in the midline anterior neck, which could be interpreted as residual thyroid lesion. However, SPECT/CT confirms it is at the tip of the thyroid cartilage without CT mass lesion and consistent with a remnant thyroglossal duct.
deliver a one-stop nuclear medicine and cross-sectional imaging service but the increased radiation, costs, scanning and reporting time, and incidentailoma rate may limit routine use. Another development is SPECT/CT quantification including standardised uptake value (SUV) with diagnostic and prognostic potentials. One of the strengths of SPECT/CT is its ability to scan a variety of radiotracers. An emerging tracer, prostate-specific membrane antigen (PSMA) PET is rapidly progressing to be a key imaging tool for prostate cancer theranostics but is not widely available yet. \(^99m\)Tc PSMA SPECT/CT has been shown to be superior to \(^99m\)Tc MDP bone scans in detecting metastases in biochemically relapsed prostate cancer.\(^{14}\) However, when compared to \(^{68}\)Ga-PSMA PETCT results have been mixed.\(^{15,16}\) It remains to be seen if \(^99m\)Tc PSMA SPECT/CT can fill the gaps of PETCT.

**Conclusion**

SPECT/CT has an important and varied role in oncology. Its ability to image a wide range of metabolic tracers, including simultaneous multiple tracer imaging, and to combine functional and anatomical details in the same session gives SPECT/CT a unique advantage over other imaging modalities. Recent advances in radiotracers, hardware and software ensure it will remain important and relevant within oncology for years to come.

**References**

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**Figure 4**

\(^{99m}\)Tc Tektrotyd SPECT/CT showing a solitary intensely octreotide avid endobronchial nodule in the left main bronchus. No octreotide avid nodal or distant disease. Pathology confirmed a typical carcinoid.

**Figure 5**

Sentinel node imaging with \(^{99m}\)Tc nanoocolloid injected around the site of melanoma in the posterior neck. Planar imaging (A,B) shows focal increased uptake inferolateral to the injection site. SPECT/CT confirms a 5x12mm sentinel node in the right neck level Va.