SPECT/CT Imaging: Clinical Utility of an Emerging Technology

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Single-photon emission computed tomography (SPECT) has been a mainstay of nuclear medicine practice for several decades. More recently, combining the functional imaging available with SPECT and the anatomic imaging of computed tomography (CT) has gained more acceptance and proved useful in many clinical situations. Most vendors now offer integrated SPECT/CT systems that can perform both functions on one gantry and provide fused functional and anatomic data in a single imaging session. In addition to allowing anatomic localization of nuclear imaging findings, SPECT/CT also enables accurate and rapid attenuation correction of SPECT studies. These attributes have proved useful in many cardiac, general nuclear medicine, oncologic, and neurologic applications in which the SPECT results alone were inconclusive. Optimal clinical use of this rapidly emerging imaging modality requires an understanding of the fundamental principles of SPECT/CT, including quality control issues as well as potential pitfalls and limitations. The long-term clinical and economic effects of this technology have yet to be established.

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Introduction

Single-photon-emission computed tomography (SPECT) has been used in general nuclear medicine, nuclear cardiology, and nuclear neurology for several decades to provide three-dimensional images of radiotracer distribution (1). Although SPECT data, in general, have proved superior to those of planar imaging, use of SPECT data has occasionally been less than optimal because of an inability to provide accurate anatomic localization of an identified abnormality. By combining SPECT with an anatomic imaging modality such as computed tomography (CT), it is now feasible to address this limitation. Although SPECT/CT was explored by Hasegawa et al (2) in the early 1990s, only in the past few years with the success of combined positron emission tomography (PET) and CT systems has there been a significant commercial interest in developing and promoting a similar hybrid system for SPECT.

The advantages of SPECT/CT parallel those of PET/CT in many ways. First, while anatomic imaging techniques allow accurate detection and localization of morphologic abnormalities, nuclear medicine studies reflect the pathophysiologic status of the disease process. However, both methods also have their limitations. Using a combined system, one can now sequentially acquire both anatomic and functional information that is very accurately fused in a single examination (3). A second important feature of SPECT/CT imaging is the ability to correct the nuclear emission images for attenuation and photon scatter to obtain more accurate image data. This should improve the ability of the nuclear medicine physician or radiologist to identify abnormalities in organs that exhibit homogeneous but abnormal tracer uptake, and to provide a more reliable determination of the response to medical or surgical intervention.

In this article, we focus on the principles and basic science of SPECT/CT instrumentation (3) and imaging. We then highlight the potential limitations of this imaging technique (4) and its clinical utility in cardiology, musculoskeletal applications, infection, oncology, general nuclear medicine, and neurology.

Basic Science

SPECT is defined as tomographic scintigraphy where computer-generated three-dimensional images of radioactive tracer distribution are produced by detection of single photons from acquired multiple-planar images. By contrast, CT is tomographic imaging performed with an external x-ray source to derive three-dimensional anatomic image data.

Software algorithms for coregistration of anatomic and physiologic images were developed in the 1980s and achieved variable success, starting with fusion of brain images by using external markers. More recently, automated software for image coregistration, such as software based on the mutual information algorithm, has become commercially available and has shown much success in fusing brain images. Coregistration of neck, chest, and abdominal images has proved to be more problematic because of the lack of anatomic reference points on the nuclear medicine images. Also, the regions are not rigid structures, and differences in patient positioning and respiratory motion can easily result in misalignment of the SPECT and CT images. Finally, when imaging studies are performed at different times, positional differences in certain structures, such as the intestinal tract, can adversely affect coregistration.

Hasegawa and his colleagues (2) attempted to devise a system capable of performing simultaneous CT and SPECT studies, which formed the basis for the development of hybrid SPECT/CT systems for clinical use. The first commercial system, called the Hawkeye, was developed by General Electric in 1999. This system mounted an x-ray tube on a ring gantry opposite cadmium tungstate detectors. Although the primary purpose of the CT was to provide a high-quality attenuation map, it also provided fair anatomic images. Other benefits of this compact system were a lower radiation dose to the patient and a reduction in necessary room shielding compared with those of conventional CT. More recently, other vendors have chosen to develop SPECT/CT systems more similar to PET/CT systems. The hybrid cameras from Philips Medical Systems (Precedence) and Siemens Medical Solutions (Symbia) both use a dedicated CT unit. This reduces the time of scanning while providing high-quality CT images but necessitates greater space and shielding requirements.

To correct for attenuation, it is necessary to produce an attenuation map of the spatial distribution of attenuation coefficients for each patient. The attenuation map is then used by an iterative reconstruction algorithm to perform attenuation correction for the emission data. In the past, this attenuation correction was performed with radionuclide-based transmission images but rarely used clinically. Currently, CT-based attenuation correction has become the standard for PET and is rapidly emerging as the standard for SPECT. CT Hounsfield units are converted to attenuation
coefficients at the energy of the SPECT radionuclide. This conversion of a CT image to an attenuation map can be performed with a segmentation, scaling, or hybrid technique. The CT image matrix size and filter are also modified to match the resolution of the SPECT data (3).

The benefits of using CT for attenuation correction as opposed to a radionuclide transmission source include less noise, faster acquisition, no influence on CT data by the SPECT radionuclide, and no need to replace decayed transmission sources (5). Unfortunately, a potential disadvantage is that there is sequential acquisition of CT data and then SPECT data; therefore, misregistration can occur, with patient movement leading to an artifact on the corrected scintigraphic images.

In addition to improved attenuation correction, SPECT/CT provides additional value by producing coregistered anatomic images that are obtained in the same study (6,7). This allows more efficient access to both sets of images with an ability to control patient position, as well as a patient benefit of convenience. Current specifications suggest that the coregistration accuracy of SPECT and CT images may be 3 mm or better on the basis of our own phantom studies.

**Challenges for SPECT/CT Imaging**

Challenges associated with the implementation of SPECT/CT include higher equipment costs (especially if one obtains a 16- or 64-detector row CT unit needed for cardiac CT angiography) and ancillary items such as room renovation; lead shielding; increased space, power, and cooling requirements; and high SPECT/CT camera weight. Some of these issues are minimized with the non–multidetector CT scanner system. Consideration must be given to whether the additional radiation burden associated with the CT component, which can vary from 2 to 80 mSv depending on the system and protocol used, is justified especially with pediatric patients (4).

Several artifacts can be encountered with SPECT/CT. Patient movement between acquisition of the SPECT and CT images will lead to misregistration (8), which not only affects anatomic localization but also produces an incorrect attenuation map, causing defects on the attenuation-corrected images (Fig 1). Movement can result from respiratory (9) and cardiac motion, sagging...
of the emission table, and patient motion between SPECT and CT acquisitions. It is essential that any SPECT/CT system use a coregistration program and associated quality control phantom on a regular basis to ensure correct alignment between the SPECT and CT scanners, in addition to routine quality control for both SPECT and CT. It is also beneficial to have a quality control program to realign the SPECT/CT data before attenuation-corrected SPECT image reconstruction, to correct for patient motion.

Other sources of error include CT truncation, metal artifact, and beam-hardening artifact. Truncation, which occurs because the smaller CT field of view compared with that of SPECT may not account for part of the patient beyond the field of view, can result in an inaccurate attenuation correction map and reduce image quality, particularly in large patients. Artifacts from metal or beam hardening can also affect CT image quality and may lead to artifactual focal uptake on attenuation-corrected SPECT images, which is caused by incorrect scaling of the Hounsfield units into the SPECT attenuation map.

Training and credentialing of nuclear medicine technologists and physicians involved with both components of PET/CT or SPECT/CT is an area of controversy. Nuclear medicine physicians who routinely interpret results of nuclear medicine studies may require additional training in evaluating the CT component of the study and vice versa. Some states do not allow nuclear medicine technologists to operate CT scanners. At present, no consensus has been reached as to who is permitted to perform these studies and interpret their results and the amount of training required before one is considered competent. Finally, because of the breadth of SPECT/CT studies demonstrating possible usefulness, one other potential issue is the difficulty of optimizing work flows and scheduling studies to maximally provide patient benefit, as opposed to performing conventional SPECT alone.

**Clinical Applications**

**Cardiology**

Noninvasive cardiac imaging, and specifically SPECT myocardial perfusion imaging, is a cornerstone of clinical management of established or suspected coronary atherosclerotic disease. Use of SPECT/CT for attenuation correction has been recommended by the American Society of Nuclear Cardiology as an adjunct to myocardial perfusion imaging studies when feasible (10). Although transmission source attenuation correction has been available for several years, it has not gained widespread clinical acceptance. The greater interest in SPECT/CT may lead to greater use of attenuation correction in cardiac SPECT. Myocardial perfusion SPECT images are susceptible to attenuation artifact from the breast and dia-
phragm; these artifacts can be confused with true perfusion defects and can obscure real coronary disease (Fig 2). Attenuation correction should increase the specificity of the test (11).

Recently, there has been an emergence of use of CT to evaluate coronary artery calcification and for coronary angiography. Some have suggested combining the functional SPECT data with the anatomic CT information to potentially improve the current standard of practice (12–14). Although there are only limited data to support this idea, it is likely that these imaging technologies will be complementary, especially in predominantly asymptomatic patient populations in whom the diagnosis of coronary artery disease is not established. However, as these testing algorithms are considered for use in various patient populations, it is important to appreciate the radiation burden that the patient sustains, which is substantial (15).

In addition, occasionally abnormal noncardiac uptake of the perfusion tracer is noted on the cardiac images. With concurrent CT imaging, one can efficiently localize the abnormal extracardiac uptake and differentiate between a true abnormality and a false-positive finding (Fig 3). Abnormalities seen at CT can also be evaluated with the functional study (16).
Figure 4. Demonstration of the extent of malignancy in a young male patient with sarcoma. (a) Anterior whole-body scan shows definite involvement of the medial soft tissue in the lower right thigh. However, the presence of bone involvement is less certain. (b, c) Anterior (b) and lateral (c) fused SPECT/CT images show the soft-tissue involvement (arrowhead) along with osseous disease (arrow). Although bone scanning is typically a sensitive examination, there may be issues with specificity or localization of lesions.

Figure 5. Localization of gallium uptake with SPECT/CT in a patient suspected to have a spine infection. (a) Planar image shows findings indicative of a spine infection (arrow). However, the location of the infection is not clear. (b–d) CT (b), SPECT (c), and fusion (d) images show clear correspondence between the abnormal scintigraphic findings and the defects seen at CT (arrow in d). The diagnosis of discitis with associated bone involvement was made by using both modalities.
Musculoskeletal Imaging
Bone scintigraphy has been a mainstay in the noninvasive evaluation of bone disease for decades. Although other imaging modalities have emerged, bone scanning continues to be widely used. It is generally thought to be a sensitive but nonspecific examination. Although SPECT bone scintigraphy provides better evaluation of abnormal tracer uptake, it still produces less than ideal anatomic localization. Review of the results of two separate studies, either side by side or as fused images, can be helpful but in some situations can be unsatisfactory or very time-consuming. SPECT/CT should increase specificity in most cases.

Several potential applications for SPECT/CT have been described for nononcologic bone scanning (17,18). These include localization of infection or inflammation (discussed in the next section), evaluation of bone trauma such as suspected spondylolysis, and differentiating degenerative changes from more malignant processes (19). Identification of benign skeletal abnormalities is enhanced with SPECT/CT; in equivocal cases of malignancy, SPECT/CT may be necessary to make the correct diagnosis (20–22). Finally, the extent of disease may be determined only with anatomic imaging (Fig 4).

Imaging of Infection
Gallium imaging and white blood cell imaging have long been used clinically to evaluate infection and inflammation. Other newer agents are becoming more common. All of these studies reflect mainly functional data, although some gross anatomic detail is often possible. In some cases, the ability to define fine anatomic detail may be critical in discriminating between pathologic and physiologic uptake (Fig 5). Several studies have shown the benefit of hybrid imaging of infection in relatively low numbers of patients (23–27). In aggregate, these early reports indicate that SPECT/CT increases specificity and may significantly affect disease management.

Oncology
Use of radiolabeled monoclonal antibodies such as ProstaScint (indium 111 [111In] capromab pendetide; Cytogen, Princeton, NJ) (Fig 6) or other oncologic imaging agents for the assessment of malignant disease is frequently limited because of poor spatial resolution and a poor signal-to-noise ratio. SPECT/CT imaging provides value to the clinician by allowing accurate
**Figure 7.** Evaluation of uptake with SPECT/CT in a patient suspected to have a left-sided paraganglioma and a left renal mass at CT. Planar imaging showed a focus of uptake in the left abdomen, but there was uncertainty whether the focus correlated with the renal mass or the paraganglioma. SPECT/CT images show that the focus of uptake corresponds to the paraganglioma (arrowhead in a) with no uptake in the renal mass (arrowhead in b), which proved to be a renal cell carcinoma at biopsy.

**Figure 8.** Localization of an incidental finding and improved confidence for reporting a known lesion in a patient with a history of thyroid cancer. An octreotide study of a left temporal intraventricular lesion was performed to evaluate for a possible meningioma. (a, b) Planar images show an unexpected finding in the neck (arrow in a) and faint uptake in the head (arrow in b). (c) SPECT/CT image shows the neck lesion (arrow), which was found to be recurrent Hürthle cell cancer at histologic analysis. (d) SPECT/CT image shows a somatostatin-positive lesion (arrow) at the site of the CT finding, an appearance consistent with a meningioma or less likely metastatic thyroid cancer.
 localization of radiopharmaceutical accumulations, detection of occult disease sites, characterization of metabolically active areas of known lesions, and potentially by providing a means of quantifying tracer uptake (28–32). Quantitative serial determinations of tracer uptake at known malignant sites can provide an objective means of measuring the tumor response to therapy; in some instances, they may allow prediction prior to treatment of whether the proposed therapy is likely to be efficacious.

Most neuroendocrine tumors secrete metabolically active substances that are similar to the analogs used for imaging (metaiodobenzylguanidine) or related to their receptor expression (somatostatin or octreotide). Despite the high sensitivity of most neuroendocrine tumors at somatostatin receptor scintigraphy, this technique is limited by small tumor size and lack of anatomic localization. Specificity is reduced because of the normal biodistribution of radiolabeled octreotide. Metaiodobenzylguanidine imaging poses similar challenges. SPECT/CT enhances detection of primary or metastatic disease, provides better delineation of the extent of disease, and permits confirmation of absent uptake at sites of concern with anatomic imaging (33–36) (Fig 7). It may also allow identification of unsuspected concurrent malignancy (Fig 8).

An important recent advance in surgical oncology is use of lymphoscintigraphy for presurgical localization of sentinel lymph nodes, most commonly in breast cancer and melanoma patients. If imaging is requested, the scintigraphy alone is limited because of a lack of anatomic detail. For patients with lesions in the head and neck or pelvis, SPECT/CT imaging provides better localization of sentinel nodes and allows one to minimize the extent of surgical intervention (Fig 9) while avoiding incomplete removal of the sentinel lymph nodes (37–44).

Figure 9. Location of sentinel lymph nodes with SPECT/CT in a patient with a melanoma of the left ear. (a) Image from sentinel lymphoscintigraphy shows the injection site in the left ear region (arrow). (b, c) Coronal fused SPECT/CT images show the locations of proximal (arrow in b) and more distal (arrow in c) sentinel lymph nodes. Although detection of sentinel lymph nodes can be performed with planar imaging alone, the addition of CT helps identify the sentinel lymph node sites in an anatomic manner, which greatly aids the surgeon in planning the operation and locating these lymph nodes intraoperatively.
salivary glands, gastric mucosa, intestinal tract, and urinary bladder. Image fusion with CT provides incremental information (45). Differentiation of focal uptake between malignant and benign causes (Figs 10, 11) can have an enormous effect on clinical management. Tharp et al (45) showed that SPECT/CT provided incremental value in 57% of their patients. Others have reported similar results (46,47).
include shorter surgical times and hospital stays. For these minimally invasive surgical techniques to be feasible, preoperative localization of the parathyroid adenoma must be effective. $^{99m}$Tc sestamibi imaging plays a major role in diagnosis, and in combination with neck ultrasonography

Figure 11. Differentiation between malignancy and benign changes with SPECT/CT in a patient with thyroid cancer who underwent whole-body $^{131}$I scanning to assess for residual recurrent disease. (a, b) Anterior (a) and posterior (b) $^{131}$I scans show focal activity in the right suprarenal region. (c, d) Coronal (c) and axial (d) SPECT/CT images show that the uptake is located in the renal collecting system (arrow), a finding consistent with physiologic urinary activity.

**General Nuclear Imaging**

The use of more minimally invasive surgical procedures in patients with primary hyperparathyroidism caused by a solitary adenoma is increasing because of a concern for potentially avoidable hypoparathyroidism and recurrent laryngeal nerve injury with bilateral neck dissection. Additional benefits of minimally invasive surgery
it is the strategy of choice. SPECT imaging increases the sensitivity for detection of parathyroid adenomas, and SPECT/CT is helpful not only for localization of the abnormality and for finding ectopic foci but also for increasing the specificity by demonstrating potential false-positive findings such as thyroid nodules (Fig 12) and brown adipose tissue (48–52).

Several nononcologic nuclear medicine studies in the abdomen potentially can be improved by fusing them with corresponding CT images (53). Studies for evaluation of hepatic hemangiomas (54,55), splenosis (56), inflammatory bowel disease (27), gastrointestinal bleeding, Meckel diverticula (57), and biliary leak (58) have been performed. In a patient suspected to have a post–renal transplantation leak (Fig 13), SPECT/CT imaging was immensely helpful in localizing the urinary leak, resulting in modification of the surgical procedure (59).

Another potential use for SPECT/CT imaging described in the literature is with ventilation-perfusion lung scanning. This technique has been described for cases of pulmonary thromboembolism detection to better correlate perfusion and CT defects (60) and for pre- and postoperative...
The major limitation of brain SPECT study is the attenuation by the skull. The commonly used Chang method of attenuation correction is based on a simple mathematical formula, which is susceptible to technical variation. In diagnosis of dementia with SPECT, it can be difficult to separate the real defect from the attenuation artifact. Variation between images owing to the Chang attenuation correction may generate artifact when ictal-interictal subtraction SPECT scans are used for seizure localization. SPECT/CT will provide more accurate attenuation correction and diagnostic results.

Another useful clinical indication is in patients suspected of having cerebrospinal fluid leaks (63). Localization of the leak is often difficult because of the lack of anatomic detail on the assessment of lung function where more precise evaluation of regional pulmonary function and prediction of postoperative lung function may be possible (61).

**Neurology**

CT and magnetic resonance (MR) imaging are essential for brain assessment, but functional imaging does provide additional important information in many patients. CT will provide anatomic information for brain SPECT images when MR imaging is not feasible. In the assessment of brain tumors with SPECT, particularly after treatment when anatomic imaging studies may not allow differentiation between post–radiation therapy necrosis and residual tumor, SPECT/CT has demonstrated improved diagnostic accuracy with a positive effect on clinical decision making over SPECT alone (62).

**Figure 13.** Localization of a urinary leak after renal transplantation. Shortly after transplantation, fluid leakage into the anterior dressings was seen, raising concern about a possible urine leak. Axial images from a $^{99m}$Tc mercaptoacetyltriglycine study (displayed from superior [a] to inferior [d]) show a urine leak (arrow in d). The imaging findings guided the surgeons to the exact location of the leak site. A bladder diverticulum on the left side is incidentally noted (arrow in c).
therapy planning should be feasible (64–68). Use for hepatic infusion chemotherapy (69,70), after beta-emitter therapy (71), for quantitation in order to develop a measurement similar to the standardized uptake value in PET, and in guided biopsy (to have fused images for defining sites of functional importance) (72) has been described in the literature. In cardiology, a variety of imaging protocols are possible (73). Because the main benefit for SPECT/CT would be attenuation correction and anatomic image fusion, except for possibly cardiac studies, the development of 64- and even 256-detector row CT is unlikely to affect SPECT/CT in most applications.

**Figure 14.** Detection of a cerebrospinal fluid leak with SPECT/CT in a patient with a lumboperitoneal shunt for pseudotumor cerebri who experienced headaches. There was clinical suspicion of a cerebrospinal fluid leak. Axial (a, b) and sagittal (c, d) images from CT (a, c) and scintigraphy (b, d) show a cerebrospinal fluid leak (arrow in b, arrowhead in d), which is not at the site of radiotracer injection and extends posteriorly at the lower lumbar spine level.
Conclusions

SPECT/CT is rapidly emerging as an important clinical imaging method with distinct advantages for patients undergoing differing types of nuclear imaging procedures. The additional anatomic localization provided by SPECT/CT imaging has proven beneficial in situations in which SPECT results alone were inconclusive. With appropriately performed attenuation and scatter correction, measurements of tissue tracer uptake can be obtained from the SPECT/CT images and used to quantitatively determine the response to medical intervention. As is true for any advanced imaging procedure, a thorough understanding of the strengths and limitations of the technique is necessary to achieve an optimal clinical benefit. At present, the long-term clinical and economic effects of the technology, although promising, are still to be determined.

References


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Pages 1098
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