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Introduction to Correlative Imaging

What Radiologists and Nuclear Medicine Physicians Should Know on Hybrid Imaging

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Introduction

Correlation is defined as a connection or relationship between two or more things that are not caused by chance [1]. Medical research is naturally based on finding the relationship between the known and the unknown [2]. Correlation has been an integral part of medicine. A clinician correlates signs and symptoms with the results of medical imaging, pathology or laboratory investigations. A nuclear medicine physician or radiologist correlates findings of medical imaging with another imaging modality or laboratory investigation such as tumor marker levels, hormone levels etc. Correlative imaging comprises combining complimentary information provided by different imaging techniques for better interpretation of pathology.

In this chapter, our aim is to familiarize readers with the basics of correlative imaging, the strengths and shortcomings of various imaging modalities, and how the correlation among them leads to better understanding of pathologies. The main emphasis of this chapter will be on “fusion imaging”, which has proved to be the best available form of correlative imaging at present.

Correlative Imaging

Medical imaging has come a long way since Roentgen first discovered the X-ray in 1895 [3]. Today X-ray, fluoroscopy, computed tomography (CT), ultrasonography, single-photon emission tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), PET-CT, SPECT-CT, and PET-MRI form the gamut of medical

imaging. Table 1.1 provides a brief review of the different tomographic imaging modalities which form the crux of correlative imaging.

Each imaging modality has its own strengths and shortcomings. The utilization of an individual modality depends on multiple factors:

- 1) Patient-related factors: age of patient, organ of interest, claustrophobia, contrast allergy, pregnancy etc.
- 2) Modality-related factors: availability, radiation exposure, resolution, need of morphological versus functional information
- 3) Physician-related factors: expertise of radiologist/nuclear medicine physician or preference of referring physician
- 4) Miscellaneous: financial burden of examination, insurance coverage etc.

Depending on these multiple factors, an imaging modality is utilized as the investigation of choice during workup of a particular patient. However, it is not uncommon that imaging findings are nonspecific and rather than leading to a definitive diagnosis they lead to a spectrum of differential diagnoses. Through “fusion imaging” or “hybrid imaging” radiologists/nuclear physicians frequently utilize correlative imaging with the intent to narrow down the differentials and/or pinpoint the diagnosis.

Correlative imaging can be defined as “imaging the same sample (field of view [FOV] or subject) sequentially or simultaneously with different imaging modalities to obtain complimentary/additive information.”

Table 1.1 Overview of the salient attributes of important tomographic imaging modalities.

	PET	SPECT	CT	MRI
Principle	Three-dimensional distribution of positron-emitting labeled radiotracers	Computer-generated image of local radioactive tracer distribution in tissues produced through the detection of single-photon emissions from radionuclides introduced into the body in the form of SPECT radiotracers	Combined X-ray transmission source and detector system rotating around the subject to generate tomographic images	Strong magnetic field and radio waves to create detailed images of the organs and tissues within the body
The tracer/contrast used	Positron-emitting radio-pharmaceuticals	Gamma-ray-emitting radio-pharmaceuticals	Iodine-containing contrast medium	Gadolinium-based contrast agents
Resolution	++	+	+++	+++
Functional assessment	+++	++	+	++
Radiation exposure	++	+	+++	None
Allergy/acute side effects	No	No	Yes	Yes
Measurable parameter/quantification unit	PET tracer uptake/standardized uptake value	—	Attenuation value/Hounsfield unit	Apparent diffusion coefficient/mm ² /s

CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography; SPECT, single-photon emission tomography.

Correlative imaging has been in practice in the form of comparative imaging for many years, a typical example of this being the “hot spot” observed in bone scans interpreted as metastatic or degenerative based on comparing it with MRI or CT of the same bone. However, now fusion imaging techniques such as SPECT-CT, PET-CT, and PET-MRI have emerged as most widely accepted form of correlative imaging. Conventionally, SPECT and PET had been domains of nuclear physicians while CT and MR had been the radiologist’s forte. With the advent and rapid success of fusion imaging there is a need for combined knowledge of both nuclear medicine and radiology for accurate interpretation of fusion imaging findings. In the next section, we aim to familiarize nuclear physicians and radiologists with the basic principles of tomographic techniques utilized in correlative/fusion imaging.

Positron Emission Tomography–Computed Tomography

PET-CT: What a Radiologist Should Know about PET

Basics of PET-CT

Positron Emission Tomography

PET is a tomographic technique that measures the three-dimensional distribution of positron-emitter labeled radiotracers. PET allows noninvasive quantitative assessment of biochemical and functional processes. The most commonly

used tracer at present is the ¹⁸F-labeled glucose analogue fluorodeoxyglucose (FDG), and it is the workhorse of PET-CT imaging at present.

Though most commonly utilized in oncological imaging, FDG-PET has many other nononcological applications now: dementia, myocardial viability, and infection imaging to name a few. Hence FDG is utilized here as example to demonstrate PET tracer characteristics to radiologists.

• Principle of FDG PET imaging

Enhanced glucose metabolism of cancer cells (primarily dependent on anaerobic glycolysis or the Warburg effect) forms the fundamental basis of FDG PET/CT imaging of malignancies. The increased glucose utilization by the malignant cells is characterized by high expression of glucose transporters (GLUTs, namely GLUT1 and GLUT3) and upregulation of hexokinase activity [4].

Glucose is taken up by tumor cells by facilitated transport (via GLUT) and then undergoes glycolysis with the formation of pyruvate under aerobic conditions. However, under hypoxic conditions (such as in a necrotic tumor), glucose is metabolized under anaerobic conditions with resultant increased tumor lactate levels. FDG is a radiopharmaceutical (RP) analog of glucose that is taken up by metabolically active tumor cells using facilitated transport similar to that used by glucose (Figure 1.1). Despite the chemical differences, cellular uptake of FDG is similar to that for glucose. FDG passes the cellular membrane through facilitated transport mediated by the GLUTs, of which more than 14

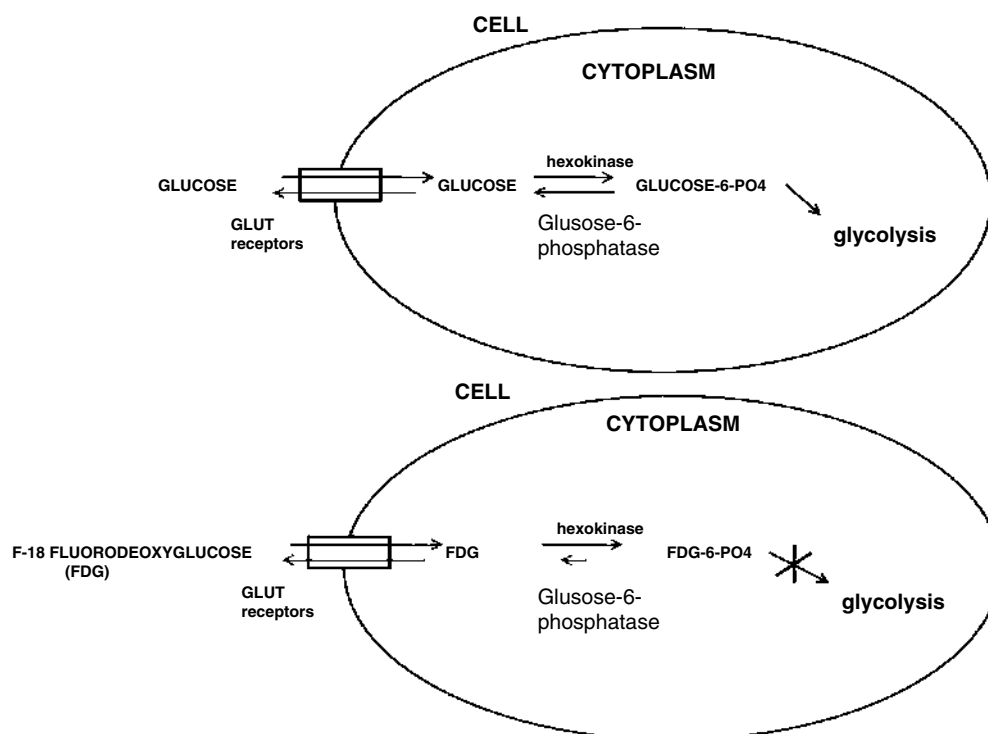


Figure 1.1 Mechanism of FDG uptake and metabolic trapping inside the cell.

different isoforms have been identified in humans, differing in their tissue distribution and affinity for glucose. GLUT1 is the most common glucose transporter in humans and is, together with GLUT3, overexpressed in many tumors [5–7]. Like glucose, it undergoes phosphorylation to form FDG-6-phosphate; however, unlike glucose, it does not undergo further metabolism. At the same time, expression of the enzyme glucose-6-phosphatase is usually significantly decreased in the malignant cells, and FDG-6-phosphate thus undergoes only minimal dephosphorylation, hence becoming “metabolically trapped” in cancer cells [8]. The distribution of FDG in normal organs and pathological lesions is detected by PET scanners.

• Preparation for FDG-PET and scan acquisition

Patients are advised to fast and not consume beverages, except for water, for at least 4–6 hours before the administration of FDG to decrease physiologic glucose levels and to reduce serum insulin levels to near basal levels. Oral hydration with water is encouraged. Intravenous fluids containing dextrose or parenteral feedings also should be withheld for 4–6 hours [9]. FDG is injected intravenously and the PET scan is typically acquired 50–90 minutes after FDG injection.

• Normal biodistribution and physiological variants

Physiological FDG uptake is seen in the brain, myocardium, liver, spleen, stomach, intestines, kidneys and

urine, lymphoid tissue, bone marrow, salivary glands, and testes (Figure 1.2). Breast, uterus, ovary, and thymus can show variable FDG uptake.

Causes of Physiological FDG Uptake and Normal Variants Mimicking Pathology

As increased FDG uptake is not limited to malignant tissues alone, for the appropriate interpretation of FDG PET-CT imaging the interpreting radiologist needs to be aware of the physiological causes of FDG uptake as well as commonly encountered physiological variants [10–15].

Table 1.2 summarizes and enumerates the different physiological causes and sites of FDG uptake that can mimic disease and the suggested interventions to reduce them.

• Quantification of FDG uptake and SUV

While interpreting a PET-CT scan, it is the relative tissue uptake of FDG (or any other PET RP) that is of interest to the reporting physician. Visual analysis is sufficient in most cases, but the standardized uptake value (SUV) is a commonly used measure of FDG uptake and it is routinely mentioned in PET-CT reports. The basic expression for SUV is [16]

$$\text{SUV} = \frac{r}{(a \times w)}$$

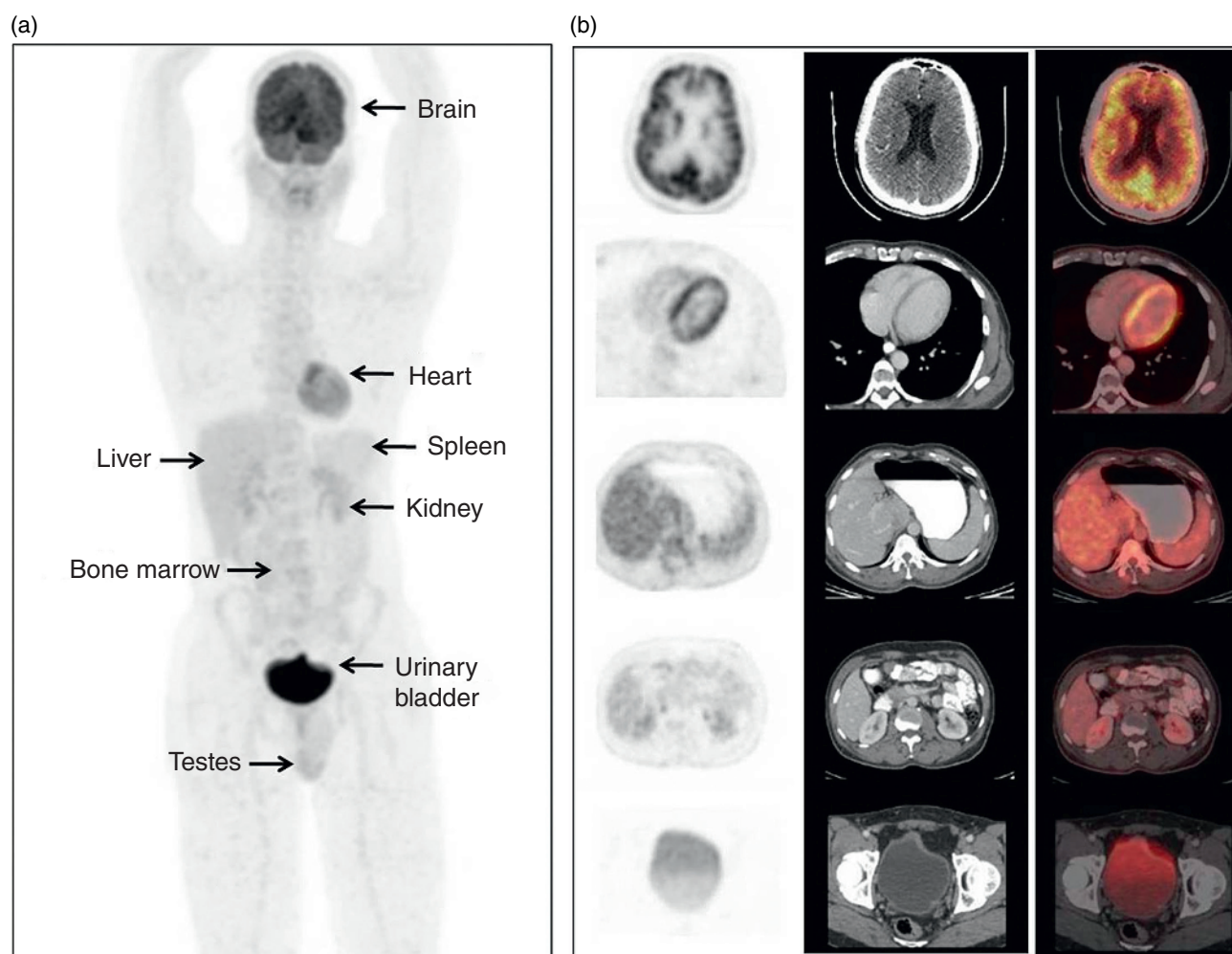


Figure 1.2 A typical example of the physiological distribution of FDG uptake in a conventional vertex-to-mid thigh whole-body PET study. (a) Maximum intensity projection (MIP) image of a PET scan. (b) Three columns depicting (left to right) trans-axial PET only, trans-axial CT only, and trans-axial fused PET-CT images of physiological distribution.

where r is the radioactivity activity concentration (kBq/ml) measured by the PET scanner within a region of interest (ROI), a is the decay-corrected amount of injected radiolabeled FDG (kBq), and w is the weight of the patient (g), which is used as a surrogate for distribution volume of tracer. If all the injected FDG is retained and uniformly distributed throughout the body, the SUV everywhere will be 1 g/ml regardless of the amount of FDG injected or patient size [17, 18]. Commonly SUVmax of lesions (maximum SUV) is provided in reports, which is the SUV of most avid voxel in ROI.

The reproducibility of SUV measurements depends on the reproducibility of clinical protocols, for example dose infiltration, time of imaging after ^{18}F -FDG administration, type of reconstruction algorithms, type of attenuation maps, size of the ROI, and changes in uptake by organs other than the tumor [9]. SUV or SUVmax values are often

utilized as a marker of change in the metabolic activity of pathology and hence it is important to reproduce the scan conditions during the follow-up PET-CT scan performed for response evaluation.

What Nuclear Medicine Physicians Need to Know about CT

PET alone is limited by poor anatomic detail, and correlation with some other form of imaging, such as CT, is desirable for differentiating normal from abnormal radiotracer uptake [8]. Hence PET-CT morpho-metabolic imaging emerged as an ideal single investigation for oncology practice. However, this also mandates the nuclear physician to have adequate knowledge of the CT component of imaging as well as the various interventions employed in CT acquisition.

Table 1.2 Characteristics and causes of physiological uptake of FDG and methods to circumvent them.

Causes/sites of FDG uptake	Physiology behind FDG uptake	PET-CT appearance	Interventions to reduce uptake
Brown adipose tissue (BAT)	Nonshivering thermogenesis requires glucose for glycolysis as a source of adenosine triphosphate, which in turn is utilized in fatty acid oxidation BAT is innervated by the sympathetic nervous system and expresses beta-adrenergic receptors, which are stimulated by cold	FDG uptake in fat density (–150 to –50 HU) in neck, shoulder, and paraspinal regions (Figure 1.3) Less common in perirenal, perigastric regions FDG uptake in BAT is more common in younger patients, females > males	Making patients wear warm clothing and providing a blanket in the waiting suite to avoid cold-induced BAT activation. Premedication with beta-blockers or diazepam
Vocal cords	Phonation-related laryngeal muscle contraction	Symmetrically increased FDG uptake in both vocal cords (Figure 1.4)	If the region of interest is the larynx, the patient should be instructed to avoid talking after FDG injection
Myocardium	Glucose as substrate for energy (GLUT1 and insulin-sensitive GLUT4)	Variable, focal or diffuse without corresponding morphologic abnormality on CT	Fasting before FDG PET-CT (4–12 hours) High-fat, low-carbohydrate diet before scan Premedication with unfractionated heparin before FDG injection
Thymus	Physiological uptake in pediatric patients (especially in postchemotherapy setting, known as “thymic rebound”)	Inverted V-shaped/butterfly pattern of anterior mediastinal uptake on the transaxial view and absence of lesion on corresponding CT (Figure 1.5)	The uptake has a diffuse characteristic pattern: no specific intervention
Lactating breasts	Due to secretory hyperplasia and the increased expression of GLUT-1	Bilateral breast reveal diffuse FDG uptake, but if infant is suckling unilateral breast only that side can show diffuse FDG uptake (Figure 1.6)	The uptake has a diffuse characteristic pattern: no specific intervention
Urinary system	FDG excretion in urine	Usually does not affect scan interpretation Focal retention in kidneys/ureter/urinary bladder can mimic pathology	Dual point/delayed postvoid imaging with or without diuretic intervention
Ovary	FDG uptake in corpus luteal cyst	Ovoid FDG uptake with smooth margins or a rim of FDG uptake with a photopenic center (Figure 1.7)	Correlation with menstrual history
Endometrium	FDG in menstrual flow	FDG uptake in endometrium in a diffuse uniform pattern (Figure 1.8)	If being evaluated for gynecological pathology, PET-CT scan should be scheduled in the postmenstrual phase
Colon	Related to bowel motility The uptake in cecum and right colon could be result of higher lymphocytes in these regions	Typically heterogeneous and can vary in distribution from mild focal to diffuse uptake Often, there is higher uptake within the cecum and right colon	Uptake pattern: no interventions

(Continued)

Table 1.2 (Continued)

Causes/sites of FDG uptake	Physiology behind FDG uptake	PET-CT appearance	Interventions to reduce uptake
Spinal cord	Inadequate clearance of FDG from the artery of Adamkiewicz, which originates on the left side of the aorta between the T9 and T11 vertebral segments Increased cross-sectional area of the spinal cord	The physiological FDG uptake is visualized in the cervical spinal cord peaking at C4 level, and in the lower thoracic spinal cord peaking at the T11–T12 segments (Figure 1.9)	
Skeletal muscles	Exercise induces glucose uptake in skeletal muscles Labored breathing can increase FDG uptake in intercostal muscles and diaphragm In postmeal state, insulin increases GLUT (GLUT-4) mediated skeletal muscle glucose uptake	If related to exercise, usually symmetrical FDG uptake in muscles with no abnormal enhancement or lesion on CT If related to meal/insulin diffuse FDG uptake in skeletal muscles (usually also accompanied with cardiac FDG uptake) If related to labored breathing, intercostal muscles and diaphragm reveal symmetrical increased FDG uptake (Figure 1.10)	Patients should avoid strenuous exercise for 48–72 hours before scheduled scan Fasting status should be confirmed before FDG injection

BAT, brown adipose tissue; FDG, fluorodeoxyglucose; GLUT1, glucose transporter 1; GLUT4, glucose transporter 4; PET-CT, positron emission tomography/computed tomography.

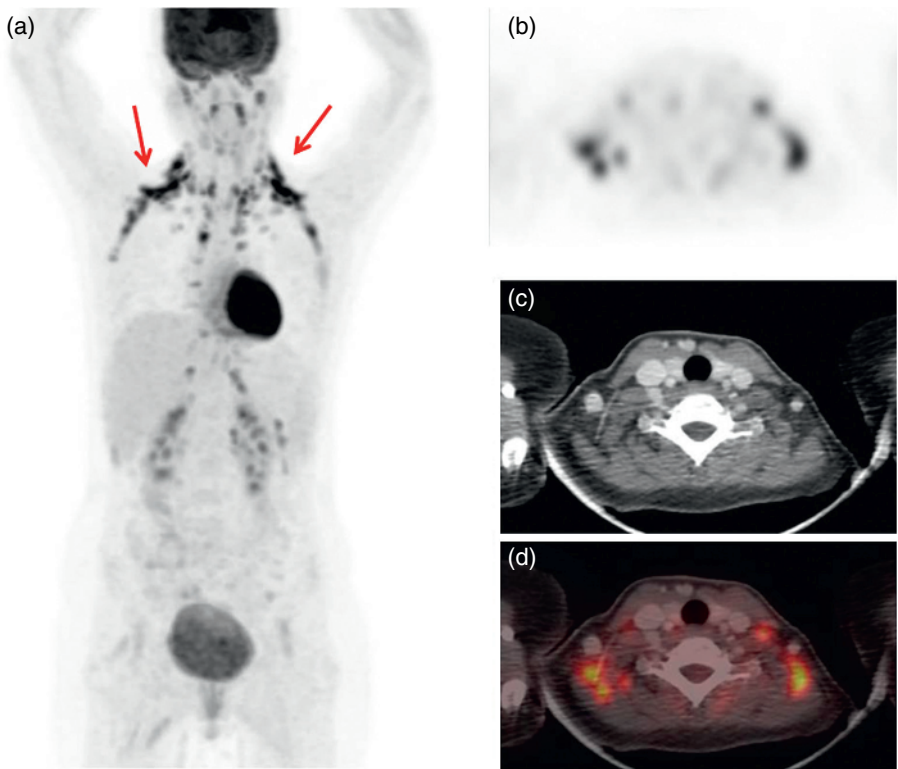


Figure 1.3 (a) FDG uptake in brown adipose tissue in bilateral cervical (red arrows), paraspinal, and perirenal regions as shown in MIP image, (b) transaxial PET-only image of the neck region, (c) transaxial CT-only image, and (d) fused PET-CT image.

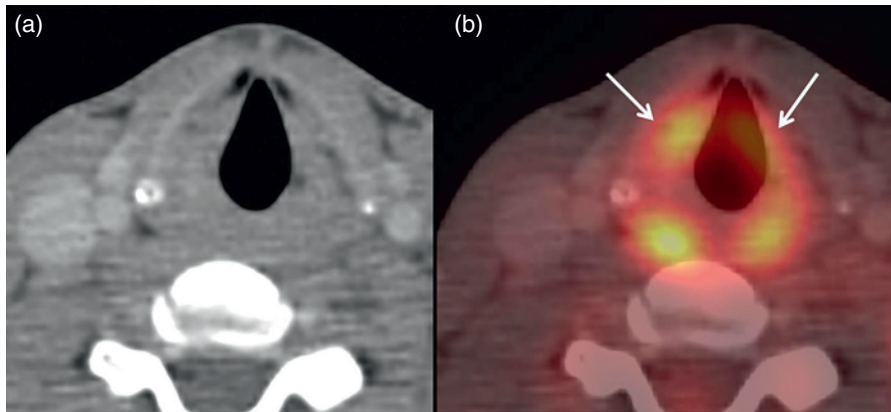


Figure 1.4 (a) Transaxial CT-only image of vocal cords. (b) The fused PET-CT image of the same region shows symmetrical increased FDG uptake in bilateral vocal cords (arrows). This patient was groaning due to painful skeletal secondaries, resulting in hypermetabolism in the vocal cords.

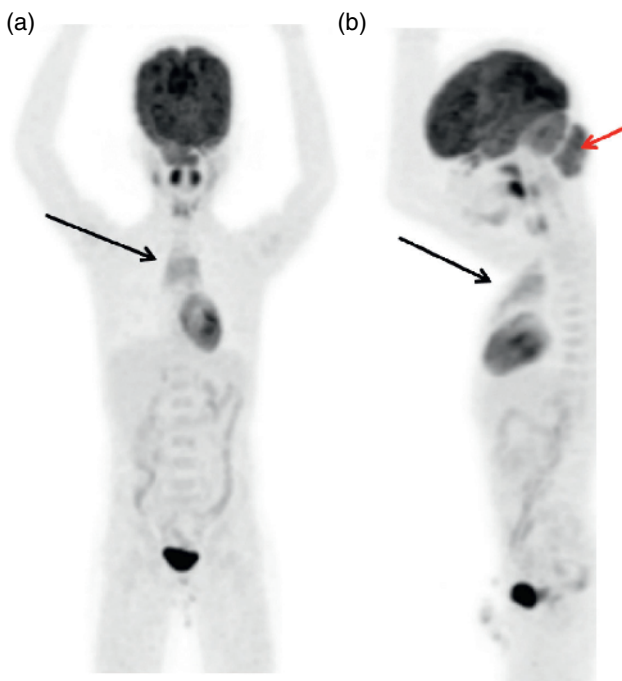


Figure 1.5 (a) MIP image of PET-CT of a 10-year-old boy showing physiological FDG uptake in the thymus (black arrows). (b) Hypermetabolism in the soft tissue neoplasm in the occipital region (red arrow).

Computed Tomography

Although the potential applications of X-rays in medical imaging diagnosis were clear from the beginning, the implementation of the first X-ray CT system was made in 1972 by Godfrey Newbold Hounsfield (Nobel prize winner in 1979 for Physiology and Medicine), who constructed the prototype of the first medical CT scanner and is considered the father of CT. After this, CT was immediately welcomed by the medical community and has often been referred to

as the most important invention in radiological diagnosis since the discovery of X-rays [19, 20].

Principle of CT

The CT scanner creates cross-sectional images by projecting a beam of X-rays through one plane of an object (patient) from defined angle positions performing one revolution. These X-rays are generated by a rotating X-ray tube (Figure 1.11). As the X-rays pass through the patient, some of them are absorbed, while some are scattered and others are transmitted. The process of X-ray attenuation refers to the intensity reduction involving those X-rays which are scattered or absorbed. X-rays which are attenuated due to the interactions with the object do not reach the X-ray detector. Photons transmitted through the object at each angle are collected on the detector and visualized by computer, creating a complete reconstruction of the patient. The three-dimensional (3D) gray value data structure gained in this way represents the electron density distribution in the area of interest [19].

The ability of matter to attenuate X-rays is measured in Hounsfield units (HU). By definition, water is assigned a density value of 0HU and air a value of -1000 HU. Attenuation values for most soft tissues fall within 30–100 HU. Notable exceptions are lungs, with attenuation values approaching -1000 HU (due to high air content), and mineralized tissues such as bone, with attenuation values of approximately 1000 HU [21].

Intravenous and Oral Contrast in CT Scanning

Intravenous Contrast

Differences in the CT attenuation of healthy tissue and pathology can improve the quality of the images

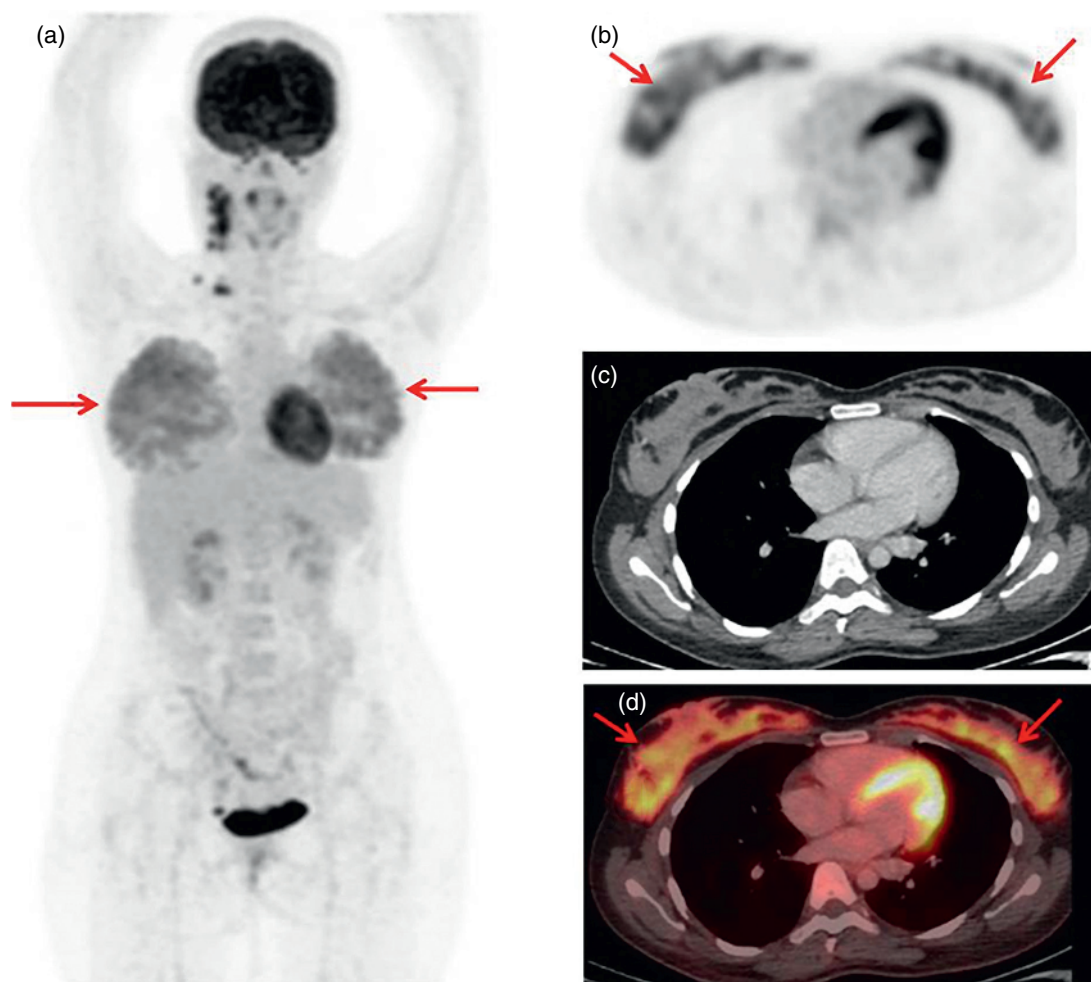


Figure 1.6 (a) MIP image of PET-CT showing FDG uptake in bilateral breasts of a nursing mother (red arrows), (b) transaxial FDG PET of breast region, (c) CT of breast region and (d) fused PET-CT of breast region.

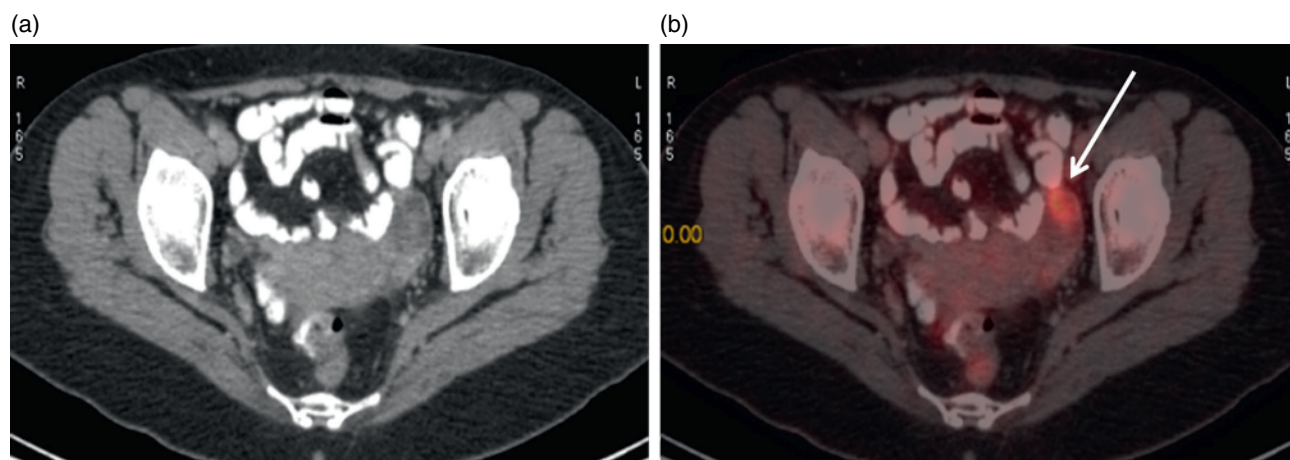


Figure 1.7 (a) CT image of pelvic region and (b) fused PET-CT of same region showing increased FDG uptake in a corpus luteal cyst in the left adnexal region (arrow).

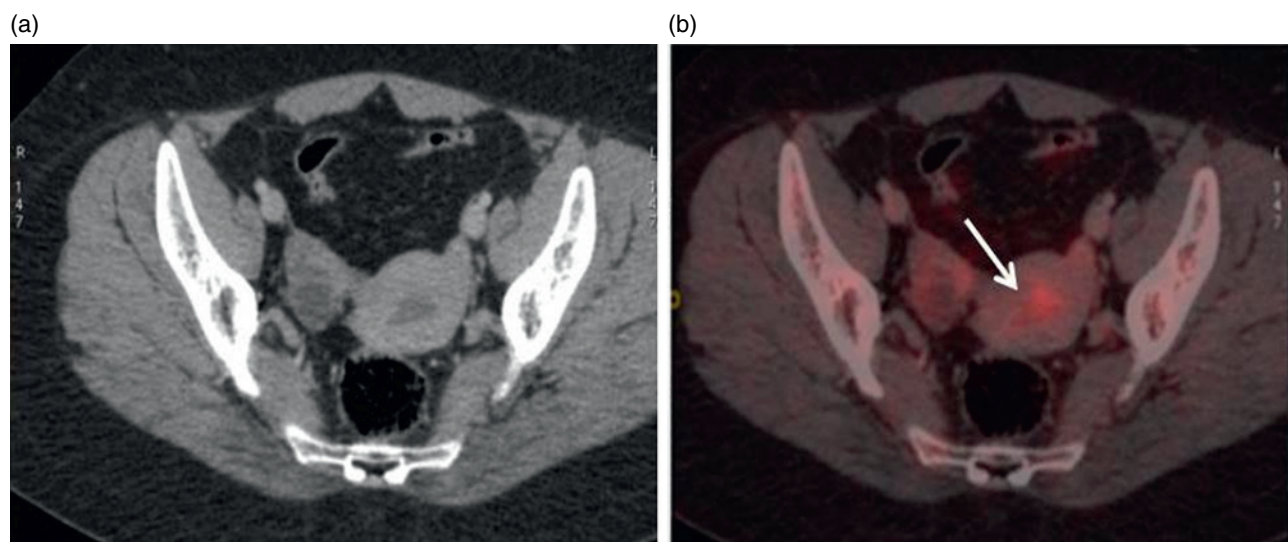


Figure 1.8 FDG PET-CT of a 27-year-old female. (a) Transaxial CT of pelvic region and (b) fused PET-CT image of pelvic region revealing FDG uptake in fluid in the endometrial cavity (arrow) corresponding to menstruation.

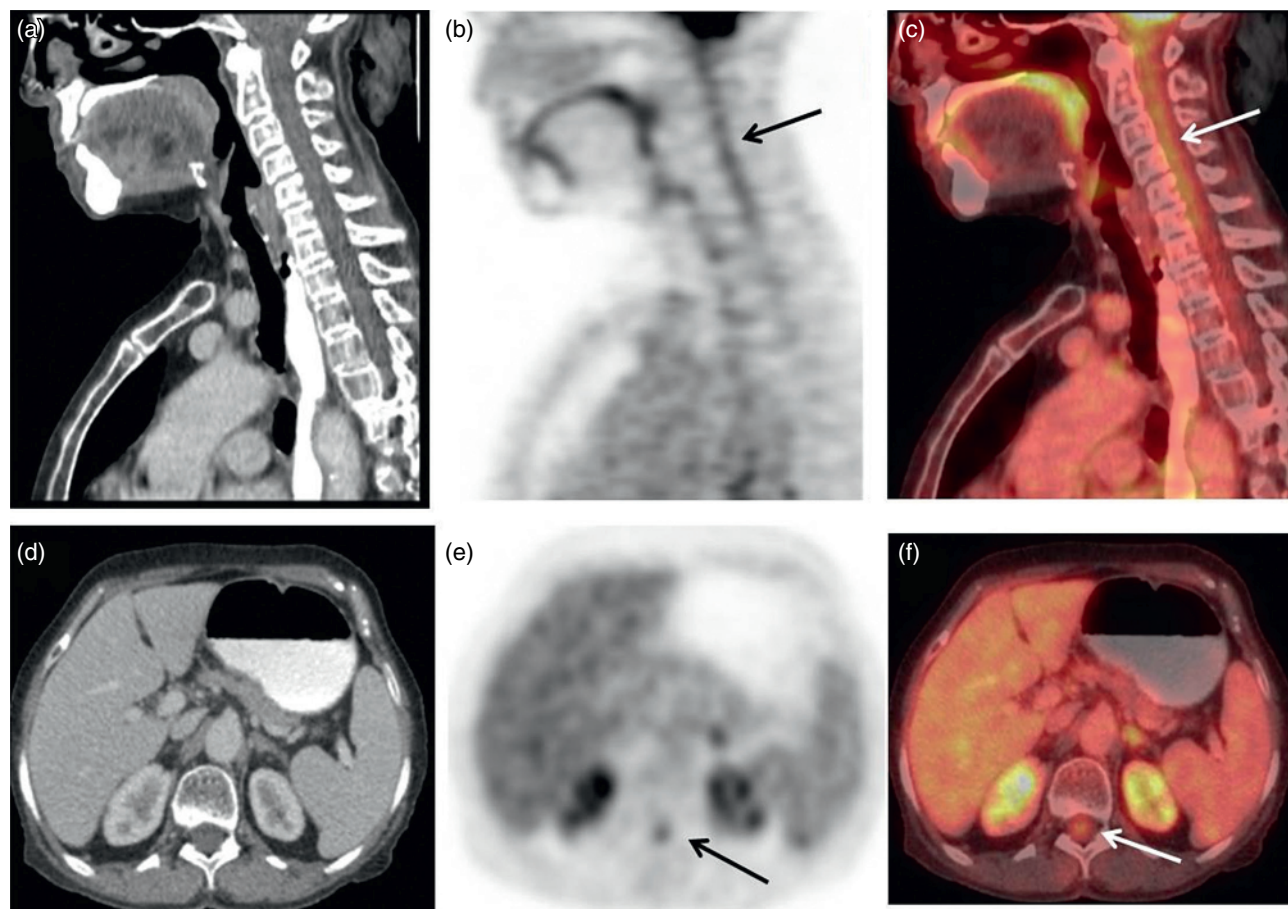


Figure 1.9 (a) Sagittal CT, (b) PET, and (c) fused PET-CT images revealing physiological FDG uptake in the cervical spinal cord (arrows). (d) Transaxial CT, (e) PET, and (f) fused PET-CT images showing focal FDG uptake at the T11-T12 level in the spinal cord (arrows).

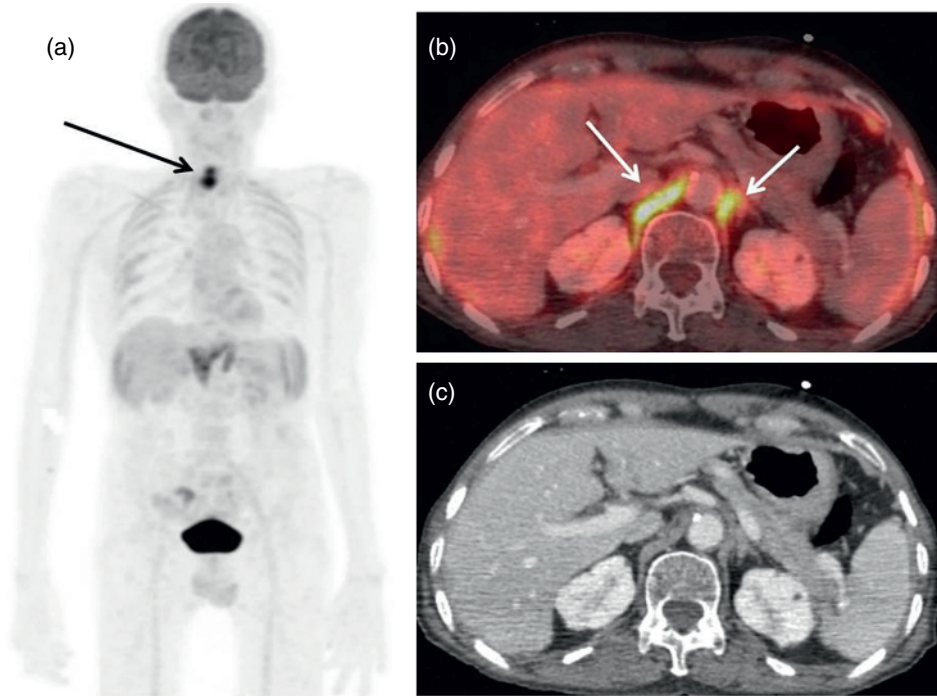


Figure 1.10 (a) In a carcinoma larynx patient, the MIP image of FDG PET-CT reveals a hypermetabolic lesion in the neck corresponding to the site of primary malignancy (black arrow). (b) Fused PET-CT image shows increased FDG uptake in the intercostal muscles and diaphragmatic crura (white arrows). (c) Transaxial CT of the same region. The augmented FDG uptake in these muscles of respiration was the result of labored breathing due to narrowing of the airway caused by the laryngeal malignancy.

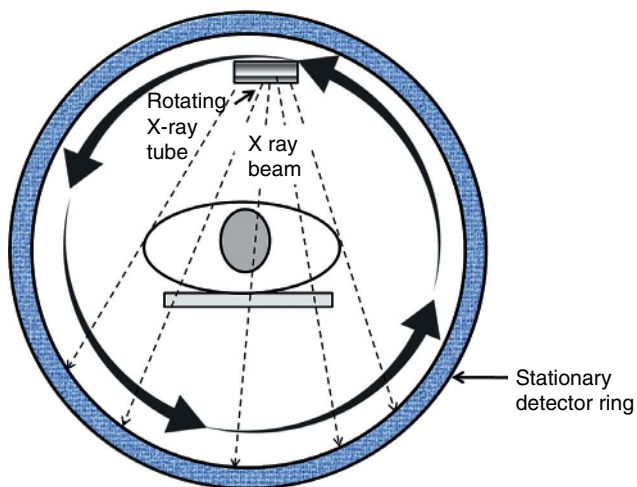


Figure 1.11 Basic principles of a CT scan.

(i.e. greater signal-to-noise and contrast to noise ratios) and hence facilitate detection of abnormality. Hence, contrast imaging agents are often used for better visualization of the tissue of interest by CT [21, 22].

Today, a wide range of ionic and nonionic contrast agents is available and effective diagnostic dose of a contrast agent

for CT imaging is in the molar concentration range. Since use of intravenous contrast is known to be associated with adverse effects in susceptible population and allergies, caution needs to be exercised during their use. When diagnostic contrast-enhanced CT with intravenous contrast media is to be performed (after the PET/CT examination), indications, contraindications, and restrictions have to be assessed by a qualified physician/radiologist. Medication that interacts with intravenous contrast (e.g. metformin for the treatment of diabetes) and relevant medical history, especially compromised renal function, have to be taken into consideration [23].

Gastrointestinal Contrast Agent

Depending on the ROI, gastrointestinal luminal contrast agent may be administered to improve the visualization of the gastrointestinal tract in CT (unless it is not necessary for the clinical indication or it is medically contraindicated). This is more commonly done via oral administration and less commonly by the rectal enema route for evaluation of colonic pathologies.

It should be noted that the contrast agents alter the attenuation caused by tissues and hence result in overestimation of SUV values used in PET quantification (more so with IV contrast as compared to gastrointestinal) [24].

CT Protocols in PET-CT

After the advent of PET-CT in the 1990s, the initial PET-CT acquisition protocols utilized CT as a fast transmission source for attenuation correction, with little additional information for anatomic localization. However, these CT protocols could not generate diagnostic quality CT images. These protocols can be largely considered as low-dose CT scans. The effective dose due to CT procedures in such low-dose CT scans is typically 3–6 mSv [25].

However, after realizing the logistic advantages of a single examination for functional (PET) and morphological (CT) information, CT is now being utilized as a fast transmission source as well as a state-of-the-art diagnostic tool to maximize image quality. This protocol involves optimal acquisition parameters together with oral and intravenous contrast agents. These protocols can be largely considered as diagnostic CT scans. The effective dose due to CT procedures in such diagnostic CT scans is typically 11–20 mSv.

There are numerous variations in CT protocols and they are discussed in detail in FDG PET-CT guidelines [23, 26]. The representative two approaches are shown in Figure 1.12.

Display of Fused PET-CT Images

In PET-CT scanners (prototype shown in Figure 1.13), the patient lies still on a bed which is then translated through fixed mechanically aligned coaxial CT and PET gantries so that the data acquired are precisely co-registered in

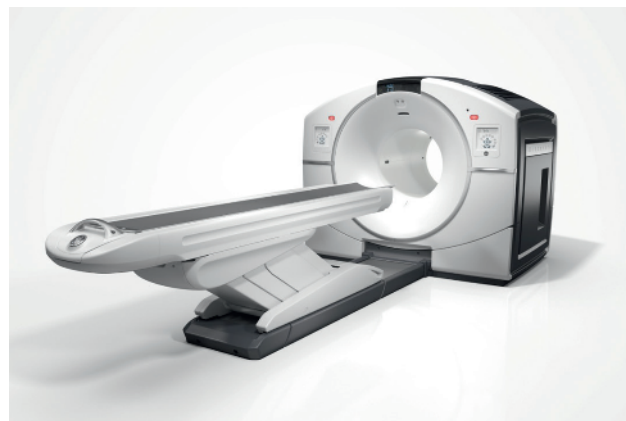


Figure 1.13 Prototype of a PET-CT scanner available in clinical practice, the GE Discovery IQ Gen2 PET-CT scanner.

space [27]. The PET acquisition typically occurs immediately after the CT acquisition to minimize the effects of patient motion.

After reconstruction, the high-resolution anatomical images (from CT) are overlaid with the functional images (from PET) to provide the precise localization of hyper-metabolic regions. The images consist of PET only, CT only, and fused PET-CT, which are viewed in the transaxial, coronal, and sagittal planes. Additionally, a cine maximum intensity projection (MIP) image provides a specific type of rendering in which the brightest voxel (the voxel with maximum FDG uptake) is projected into the 3D image. This MIP image enables a “gestalt” impression of the study [28]. An example of a typical display is shown in Figure 1.14.

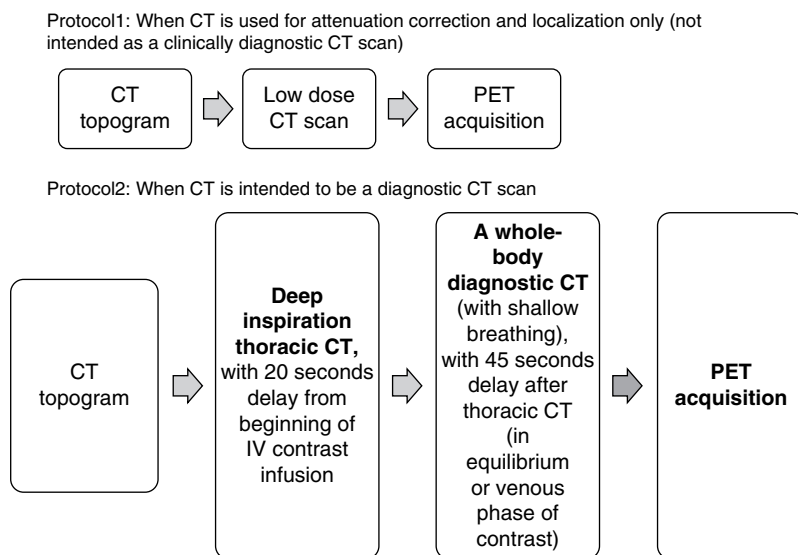


Figure 1.12 Schematic representation of representative PET-CT acquisition protocols.

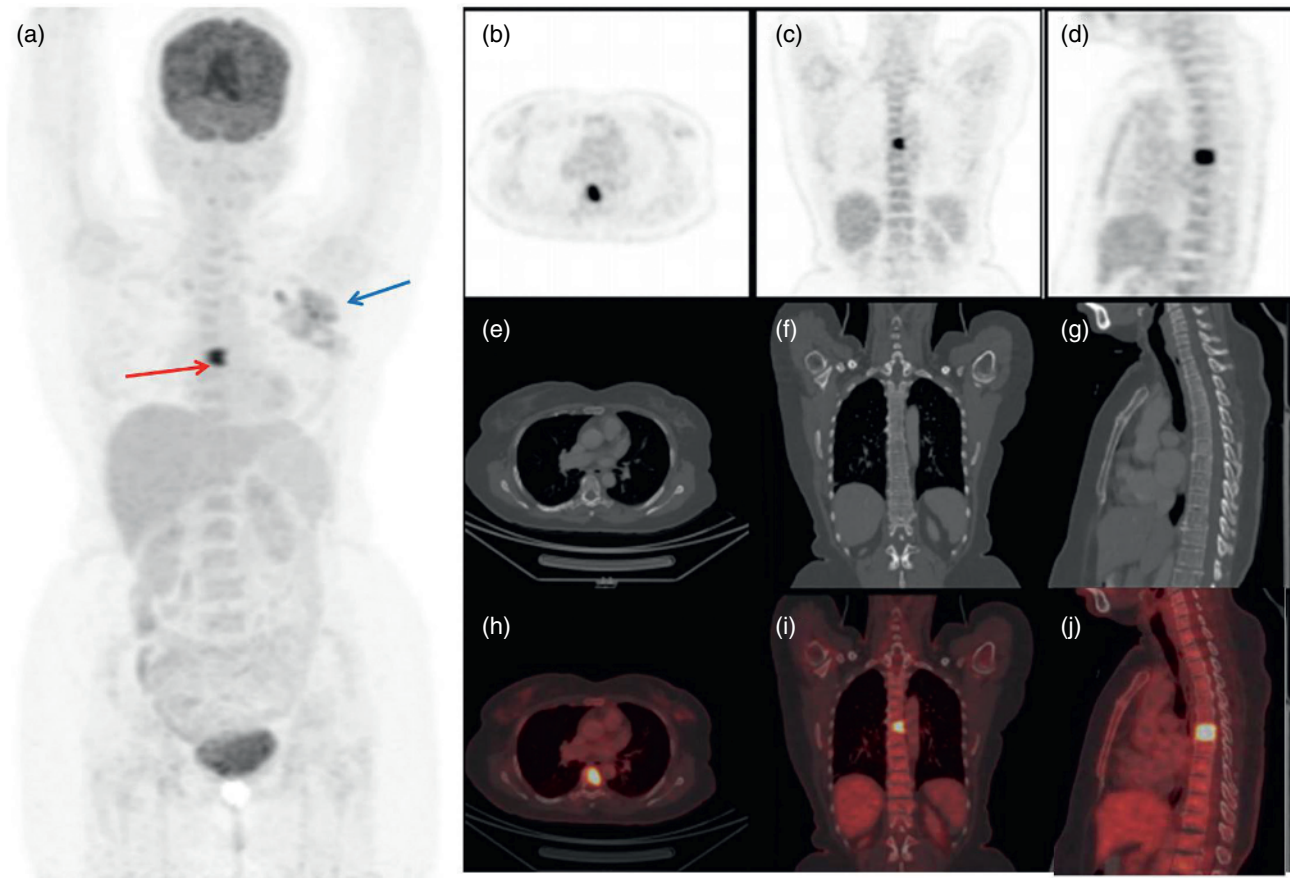


Figure 1.14 Staging FDG PET-CT of a 53-year-old female diagnosed with locally advanced carcinoma of the left breast (blue arrow) with metastatic lesion in body of D7 vertebra (red arrow). The following components of PET-CT are seen: (a) maximum intensity projection (MIP) image, (b) trans-axial PET only image, (c) coronal PET only image, (d) sagittal PET only image, (e) trans-axial CT only image, (f) coronal CT only image, (g) sagittal CT only image, (h) trans-axial PET-CT fusion image, (i) coronal PET-CT fusion image, (j) sagittal PET-CT fusion image

Artifacts in PET-CT Fusion

Recent PET-CT scanners allow excellent fusion of the PET and CT images and thus improve lesion localization and interpretation accuracy. Moreover, the employment of the CT data for attenuation correction has led to high patient throughput [29]. Although PET-CT imaging offers many advantages, this dual-modality imaging also poses some technical challenges due to a few artifacts. The reader interpreting PET-CT scans needs to be aware of these limitations.

The artifacts can be broadly divided into following categories:

1) *Motion artifacts (respiratory or patient related)*: Although the CT and PET acquisitions are performed without changing the patient position, voluntary or involuntary movements of patient can result in misregistration of PET and CT images. Most commonly such misregistration artifacts are observed in lesions of the lungs and liver. An example is shown in Figure 1.15.

Efforts have been made to minimize such image degradation by the generation of a respiratory motion corrected or four-dimensional PET-CT during which the PET data are acquired in synchronization with respiratory motion [30].

- 2) *Attenuation correction artifacts*: The presence of high-density material in the patient's body either in the form of high-density material like bone cement or venous pooling of intravenous contrast/barium from previous studies in bowel loops can result in artifactual FDG uptake due to exaggerated attenuation correction at these sites. A clinical example is shown in Figure 1.16.
- 3) *Beam hardening artifact*: This artifact appears as multiple linear bands of abnormal attenuation traversing a body part adjacent to high-attenuation objects, such as metal prosthesis, dental fillings, chemo ports, and pacemakers. Patients need to be instructed to remove metallic objects before scan acquisition and a note should be made of fixed/in situ metallic prosthesis/implants. An example is shown Figure 1.17. Some implants/prosthesis can result

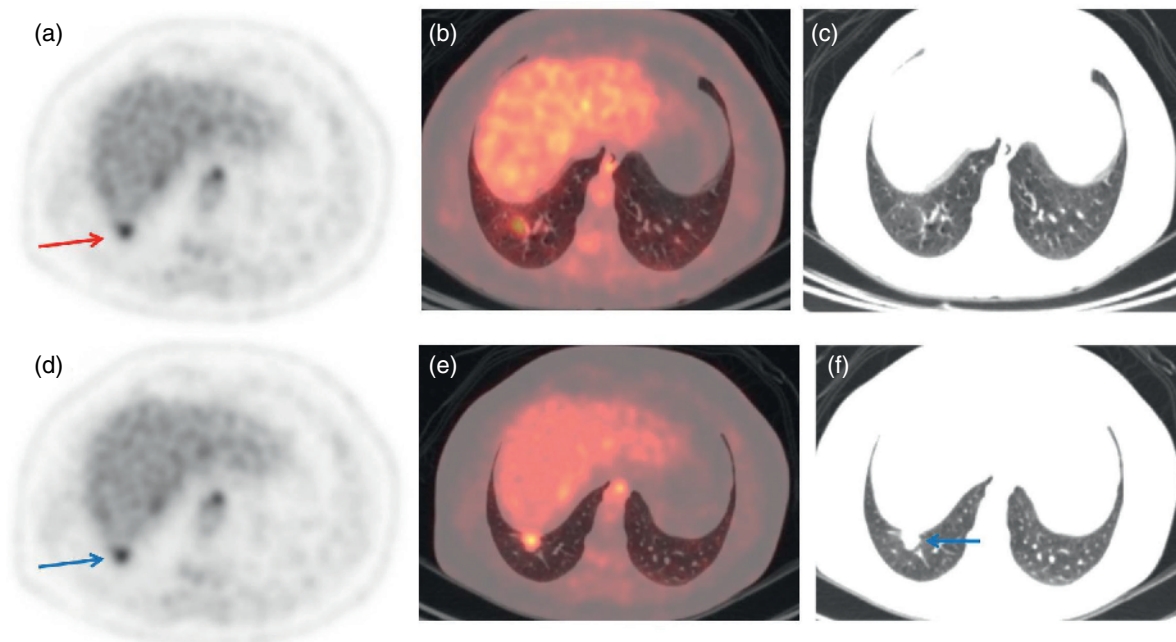


Figure 1.15 50-year-old male, known smoker, referred for characterization of a solitary pulmonary nodule in the basal region of the lower lobe of the right lung. (a) A focus of increased FDG uptake is noted (red arrow), which does not correspond to any morphological abnormality in fused PET-CT (b) and CT only (c). The acquisitions were repeated with shallow breathing to minimize the lung motion and the second set of images (d)–(f) reveal focal FDG uptake in a 14×14 mm sized nodule in the basal region of the lower lobe of the right lung (blue arrow), suspicious of neoplastic pathology.

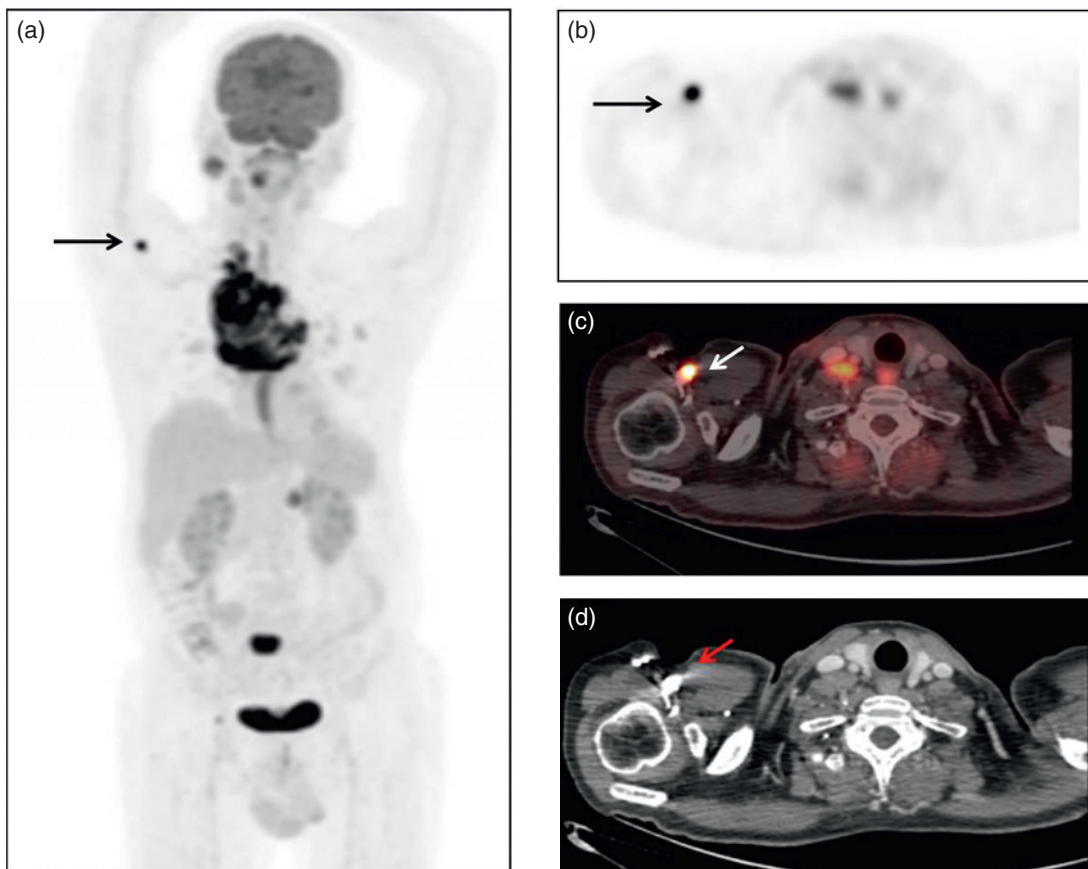


Figure 1.16 MIP image of FDG PET-CT of a 36-year-old female for staging lymphoma. The focal uptake observed in the right axillary region (black arrows in (a) and (b), and white arrow in (c)) was artifactual due to pooling of intravenous contrast material in the right subclavian vein. The high density of contrast (red arrow in (d)) resulted in high attenuation correction and resultant artifactual FDG uptake in the PET image.

in false-positive PET findings due to changes in attenuation correction factors.

A similar artifact can be seen when the PET-CT scan is acquired with the hands on the sides of the trunk and hence the easiest way to prevent this artifact is to perform the scan with arms up or down, depending on clinical indication.

- 4) **Truncation artifact:** Truncation artifacts in PET-CT are due to the difference in size of the FOV between the CT (50 cm) and PET (70 cm) tomographs [31]. These artifacts are frequently seen in large patients or patients scanned

with arms down, such as in the case of head and neck malignancy. When a patient extends beyond the CT FOV, the extended part of the anatomy is truncated and consequently is not represented in the reconstructed CT image. Truncation also produces streaking artifacts at the edge of the CT image, resulting in an overestimation of the attenuation coefficients used to correct the PET data. This increase in attenuation coefficients creates a rim of high activity at the truncation edge (see the example in Figure 1.18), potentially resulting in misinterpretation of the PET scan [32]. Therefore, in PET-CT imaging, it is

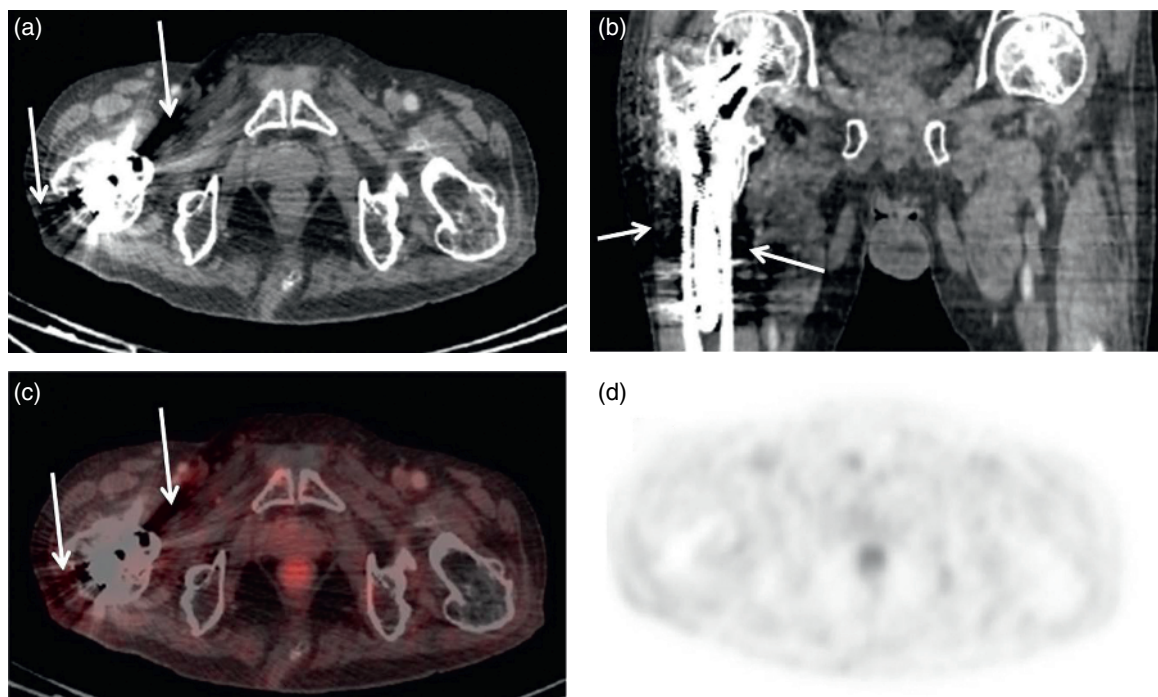


Figure 1.17 Beam hardening artifact caused by a metallic implant in the right femur, seen as linear bands of abnormal attenuation (arrows in (a)–(c)). No artifact is noted in the PET-only image (d).

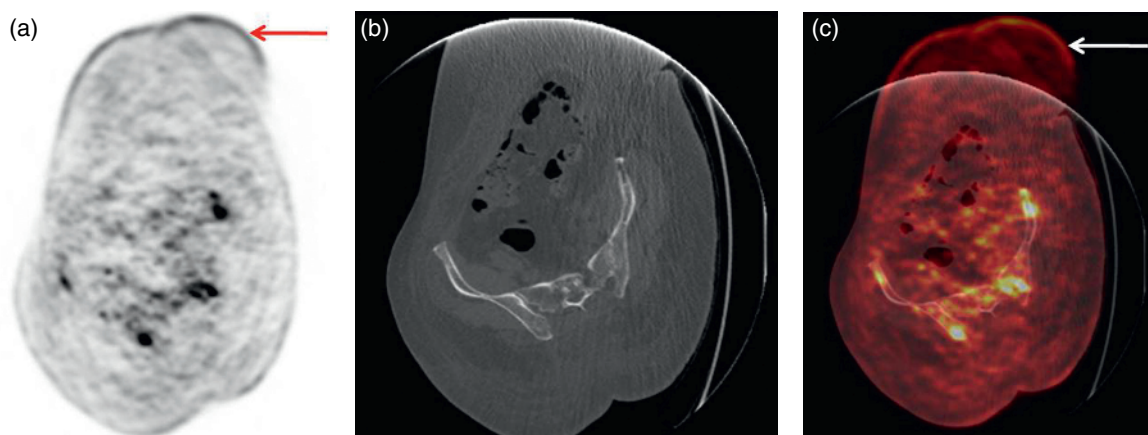


Figure 1.18 Truncation artifact in a large patient resulting in the rim of FDG uptake in PET image (a, arrow), loss of information in CT only image (b), and FDG uptake without morphological data in fused PET-CT (c, arrow).

crucial that technologists carefully position the patient at the center of the FOV and with arms above the head to reduce truncation artifacts [29].

- 5) *Radiopharmaceutical related*: Although relatively rare, focal FDG uptake (or other PET radiotracer uptake) without any CT demonstrable lesion needs to be interpreted with caution, especially in lung paren-

chyma (see the example in Figure 1.19). Such uptake can be the result of iatrogenic FDG micro-embolus at the time of injection [33] and when such a finding can affect management of a patient, a follow-up scan can be performed to avoid false-positive interpretation. In the next section, few clinical case examples present (Figures 1.20–1.22).

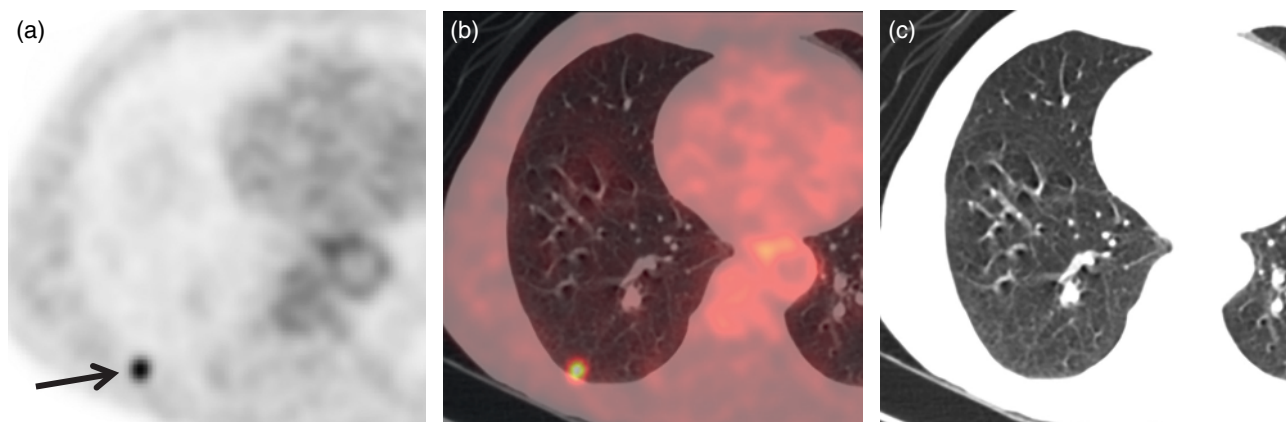


Figure 1.19 Focal FDG uptake seen in the PET image (a, arrow) and fused PET-CT (b) does not correspond to any nodule/lesion in the corresponding CT trans-axial slice of the right lung (c). Such a pattern can be the result of an iatrogenic micro-embolus of FDG caused during injection.

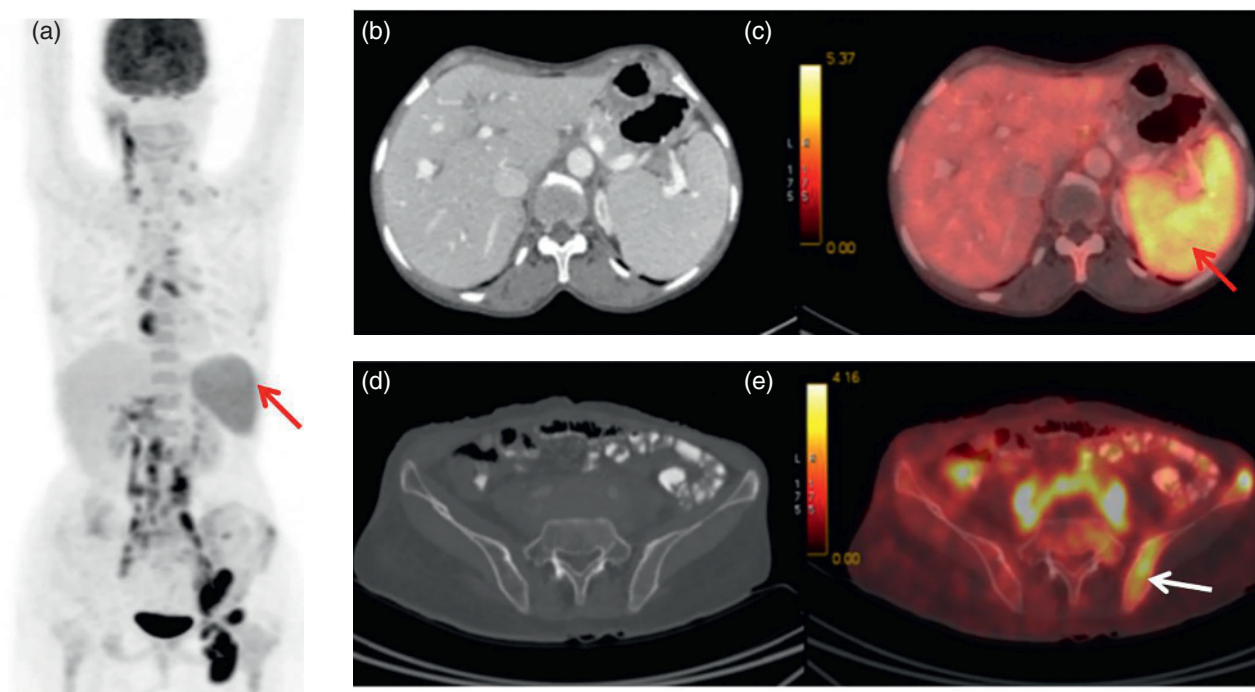


Figure 1.20 A 28-year-old male recently diagnosed with non-Hodgkin's lymphoma for staging FDG PET-CT evaluation. The supra-diaphragmatic and infra-diaphragmatic lymphadenopathy was apparent on CT and was suggestive of stage III NHL. However, the hypermetabolism in spleen (a and c, arrow) and left iliac bone (e, arrow) could be appreciated in PET and fused PET-CT images and hence indicated splenic as well as bone marrow involvement, upstaging disease to stage IV. Note that in the CT-only images (b) and (d) the spleen and left iliac bone appear unremarkable.

FDG PET-CT Clinical Examples

The following section consists of the pictorial demonstration of clinical case examples (Figures 1.20–1.22) where fusion imaging of FDG PET and CT resulted in accurate diagnosis of pathology and its extent that would have been otherwise difficult to reach.

PET-CT Tracers Beyond FDG

Although 18-F-FDG is the most widely used tracer in fusion imaging in the form of PET-CT, many other RPs have made a significant impact in patient management and have become part of routine patient management. The list of such RPs is exhaustive and beyond the scope of this chapter; a few common ones are listed in Table 1.3 [34–38] with case examples shown in Figures 1.23–1.25.

Table 1.3 PET beyond FDG: the important contemporary tracers and their clinical applications.

PET radiopharmaceutical	Mechanism of uptake	Clinical use
Gallium-68 and F-18 PSMA labeled PSMA targeted ligands (small-molecule PSMA inhibitors)	Binding to PSMA	Prostate carcinoma: biochemical recurrence, staging high-risk cases, and treatment planning for peptide receptor radioligand therapy
Gallium-68 DOTANOC/ DOTATOC/DOTATATE (DOTA-conjugated peptides)	Binding with somatostatin receptors expressed in neuroendocrine tumor cells	Neuroendocrine tumor imaging and treatment planning for peptide receptor radionuclide therapy
Fluorine-18 fluoro-dopamine	Analog of L-DOPA, to trace the dopaminergic pathway and to evaluate striatal dopaminergic presynaptic function	Evaluation of movement disorders Evaluation of congenital hyperinsulinemia
Fluorine-18 sodium fluoride	¹⁸ F is substituted for hydroxyl groups in hydroxyapatite and covalently bonds to the surface of new bone	Diagnosis of skeletal metastases

DOPA, dihydroxyphenylalanine [2-amino-3-(3,4-dihydroxyphenyl) propanoic acid; DOTA, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; DOTANOC, DOTA-Nal³-octreotide; DOTATOC, DOTA-Tyr³-octreotide; DOTATATE, DOTA-Tyr³-octreotate; FDG, fluorodeoxyglucose; PET, positron emission tomography; PSMA, prostate specific membrane antigen.

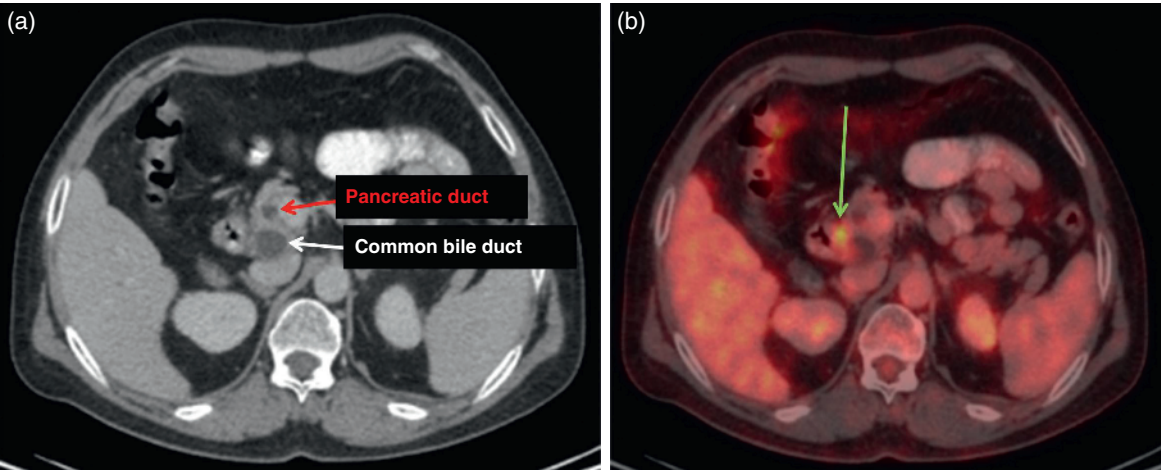


Figure 1.21 A 56-year-old male complained of chronic, intermittent abdominal pain and recent onset jaundice, nausea. Ultrasonography revealed an overdistended gall bladder without any calculus. FDG PET-CT was performed with suspicion of pancreatobiliary neoplastic pathology. (a) The contrast-enhanced CT revealed a dilated pancreatic duct and common bile duct, the “double duct sign” (white arrow), indicating pathology in ampullary region. However, on contrast-enhanced CT alone no obvious morphological lesion could be identified in the ampullary/duodenal region. However, in the FDG PET images, focal hypermetabolism is seen in the right lumbar region of the abdomen. When the PET and CT images are fused (b), the hypermetabolism corresponds to the ampullary region of the duodenum (green arrow) and indicates an ampullary lesion obstructing the pancreatic and common bile ducts. On endoscopy, an ulcerated lesion was found in the second part of the duodenum, which revealed ampullary carcinoma on histopathology.

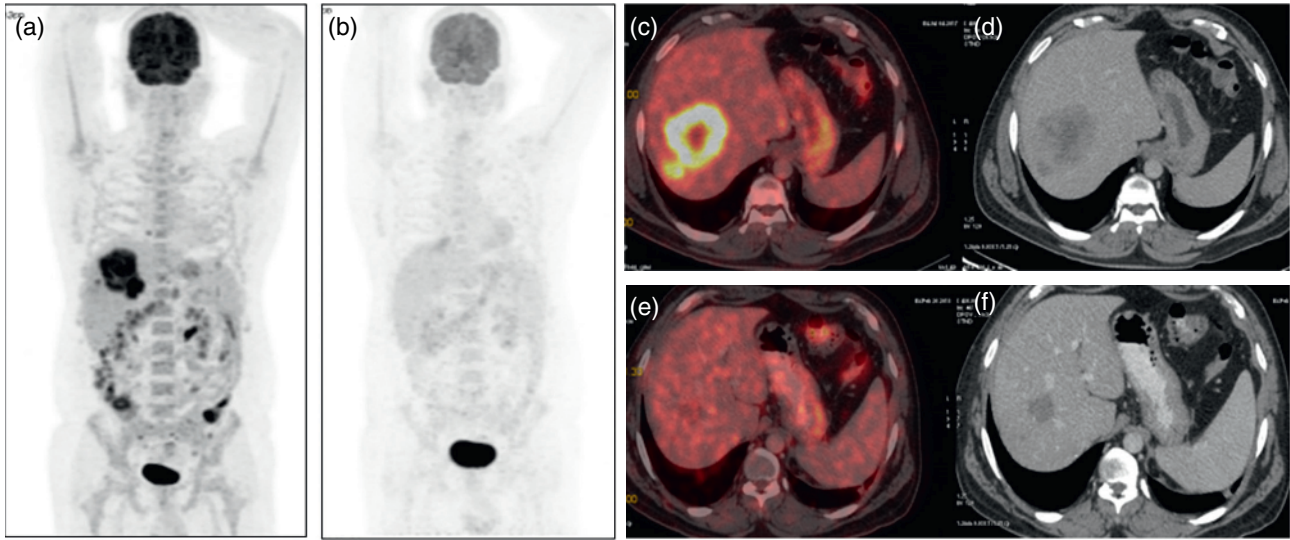


Figure 1.22 Pre- and postchemotherapy FDG PET-CTs of a metastatic carcinoma rectum. The pretherapy PET-CT MIP (a), fused PET-CT (c), and CT-only (d) images reveal FDG avid hepatic metastasis. Posttreatment images (b), (e), and (f) reveal complete metabolic response, as seen by resolution of FDG uptake and partial morphological regression, as seen by the reduction in the size of the lesion.

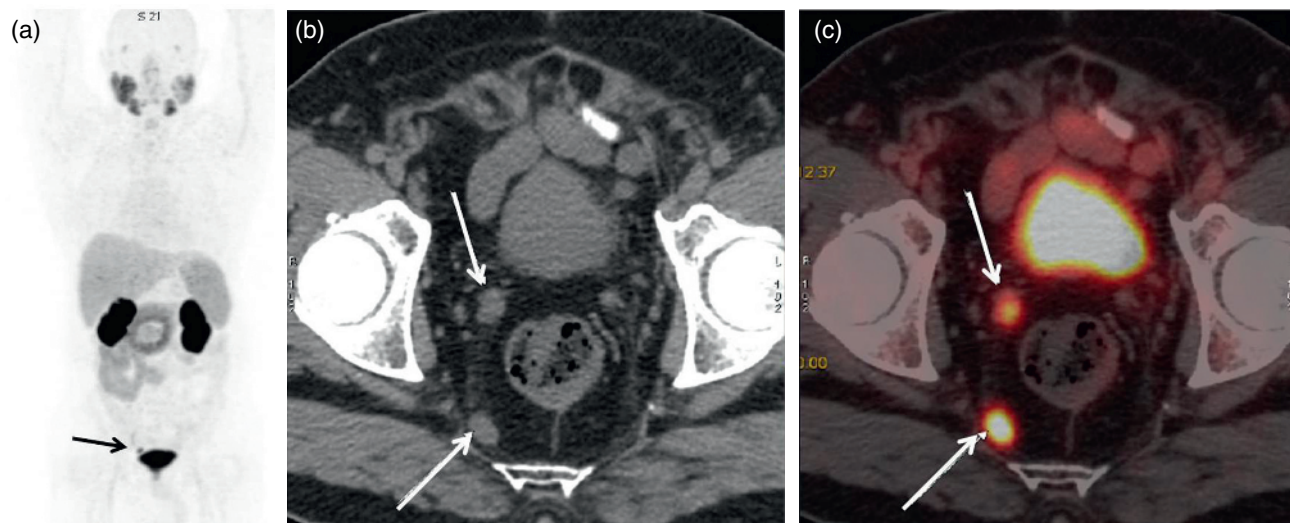


Figure 1.23 MIP image of ^{68}Ga -PSMA-11 PET-CT for evaluation of biochemical recurrence of prostate carcinoma in a 61-year-old male. Increased PSMA expression seen in pelvic region (a, black arrow). (b) CT and fused PET-CT reveal increased PSMA expression in perirectal lymph nodes (white arrows). (d) Scan pattern suggests metastatic lymphadenopathy as a cause of rising PSA levels.

SPECT-CT Imaging

Introduction

Among the fusion or correlative imaging modalities, PET-CT is the often discussed modality, mainly due to its widespread clinical and research applications, although we must emphasize the potential and increasing applications of SPECT-CT, which is often underestimated and may be

another powerful correlative imaging tool in the future. Gamma camera (Figure 1.26) has been in use for getting functional information on the physiological, biochemical, and metabolic processes in the various organs in the body. The tracer used in gamma camera imaging is usually specifically targeted to obtain information from a particular organ system. Hence, once administered into the patient's body, the tracer accumulates in the target organ system. The more specific the tracer, the more information from

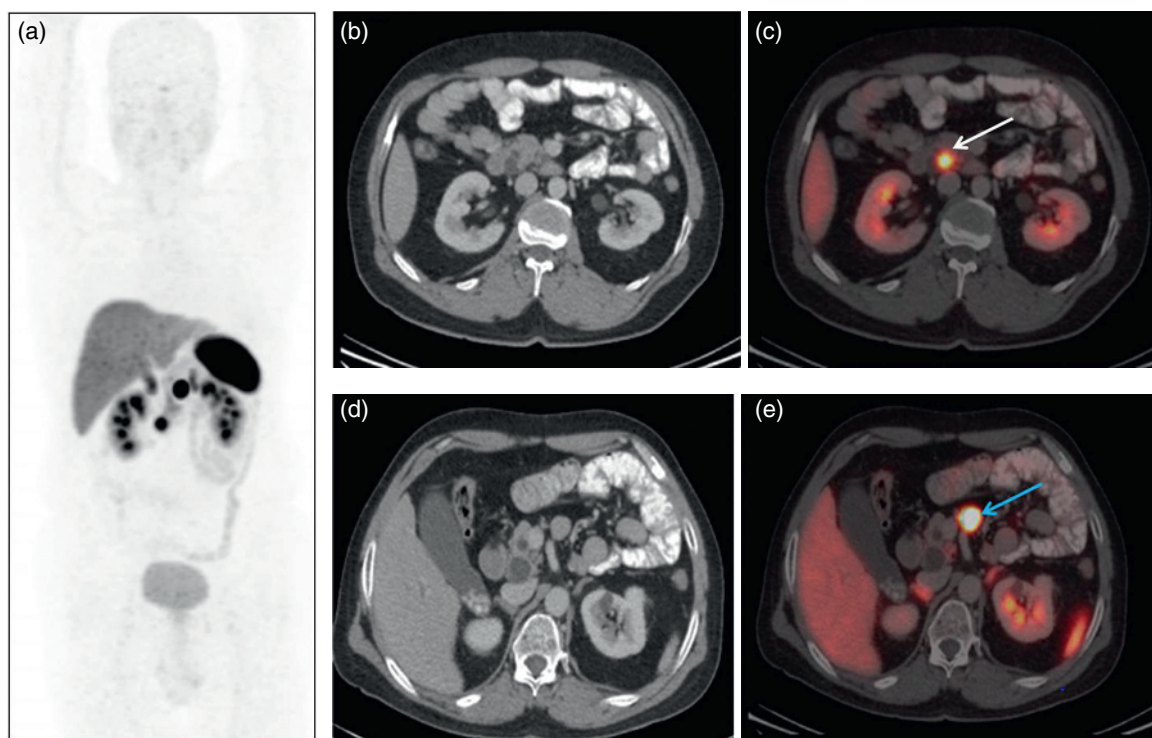


Figure 1.24 MIP image of ^{68}Ga -DOTA-NaI³-octreotide PET-CT images of a 51-year-old male patient with clinical suspicion of neuroendocrine tumor. He complained of recurrent vomiting and abdominal pain, and was found to have substantially elevated serum chromogranin A levels. (b) Transaxial CT image and (c) fused PET-CT revealed increased somatostatin receptor expression in a small nodular lesion in the second part of the duodenum (white arrow). (d) Transaxial CT revealed enlarged perilesional lymph node. (e) Increased somatostatin expression was seen in the enlarged perilesional lymph node (blue arrow). Biopsy of the duodenal lesion revealed grade 1 neuroendocrine tumor.

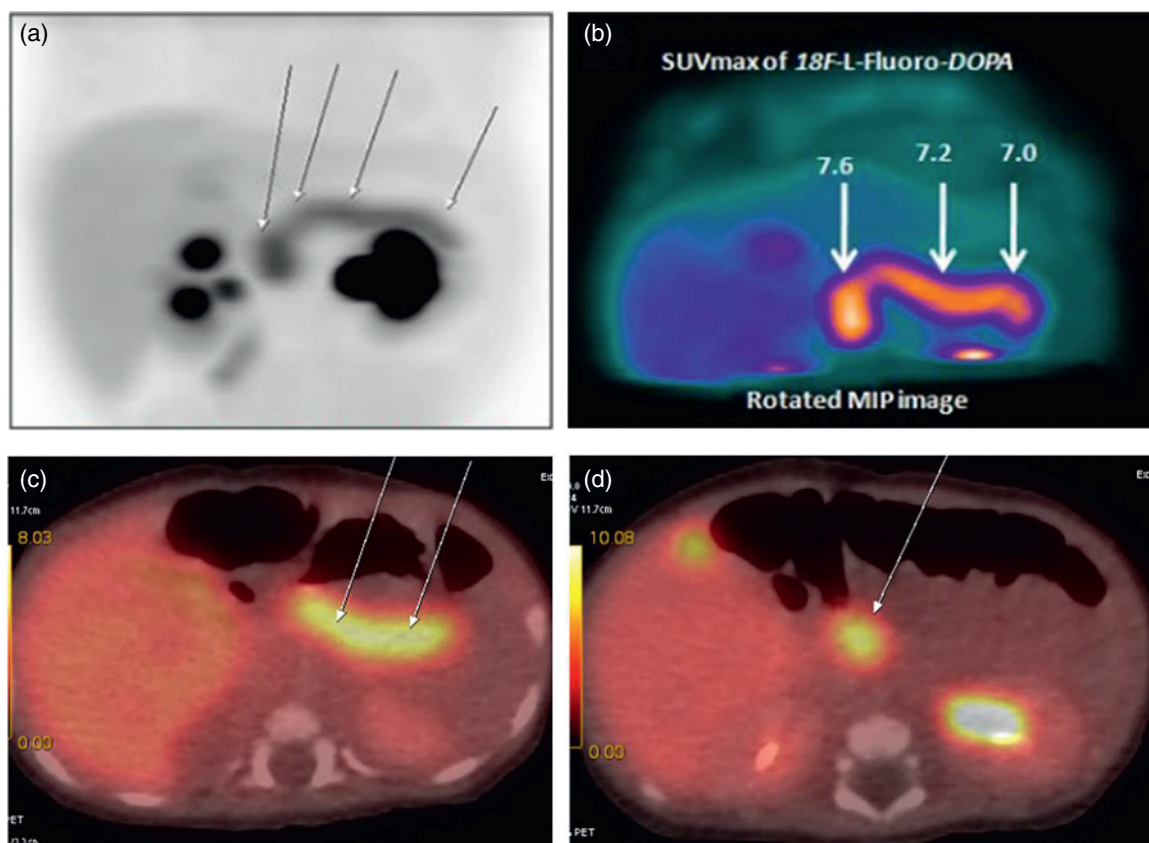
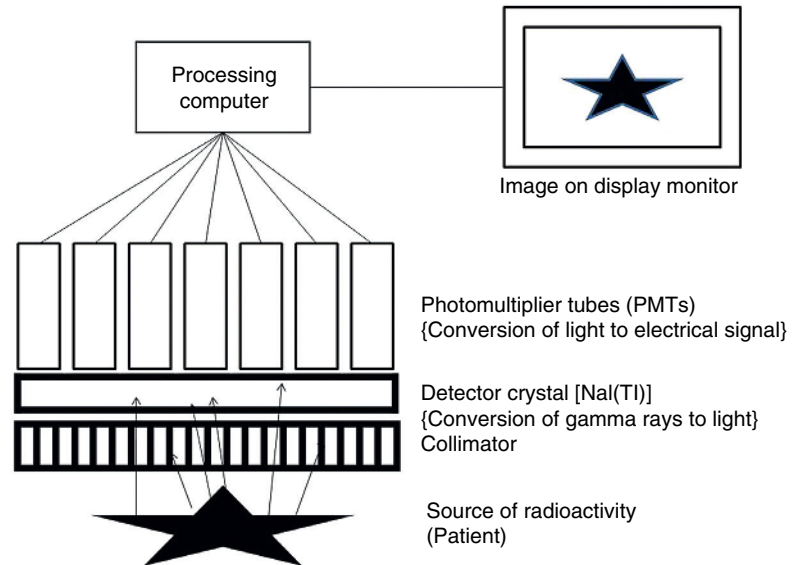


Figure 1.25 (a) and (b) MIP images of ^{18}F -fluoro-DOPA PET-CT of a 1-month-old baby with recurrent severe hypoglycemia due to congenital hyperinsulinism. This rare and grave condition is the result of islet cell hyperplasia, which can be either focal or diffuse. (c) and (d) Transaxial fused PET-CT images reveal diffuse radioactive dopamine uptake was noted in the pancreas, marked with arrows, suggestive of diffuse islet cell hyperplasia. In the focal type only partial pancreatectomy of the hyperfunctioning focus is performed, while in the diffuse type a near-total pancreatectomy may be required.

Figure 1.26 Schematic representation of gamma camera.



the target organ may be collected about a particular pathophysiological process. However, at the same time, whatever little morphological information is obtained by background tracer activity diminishes significantly. Hence nuclear medicine techniques often lack anatomical landmarks. Also, there is definite loss of data in the planar imaging due to the attenuation of gamma rays coming from organs deep inside the body.

SPECT entails 3D reconstruction of tracer distribution within the patient body with the help of data collected by rotating detectors around the patient body. This helps to achieve better anatomical information, for example in the case of bone scan or myocardial perfusion imaging. CT scanning, on the other hand, is a 3D reconstruction of X-ray attenuation value maps providing morphological details like size, shape, and location. Use of contrast agent in CT primarily provides information about perfusion and the changes in perfusion pattern occurring in various disease processes. However, CT often does not provide any information on the functional or metabolic status of organs in the body. Many disease processes show pathophysiological changes much before morphological changes are manifested. Also, in presence of anatomical distortions secondary to various treatments, anatomical imaging interpretations are difficult and often uncertain because of changes in symmetry and perfusion pattern.

Hence it is of vital importance to understand that nuclear medicine (SPECT) and anatomical imaging (CT) are not competitive to each other, but in fact complementary in nature. The fundamental advantages of this are as follows:

- i) Combined SPECT-CT images have the best of both worlds. They have all the anatomical information lacking in SPECT images and functional information lacking in CT images. CT also helps in proper localization of tracer uptake to ultimately help in correct diagnosis and treatment.
- ii) Not only this, CT attenuation maps are used for attenuation correction and this improves the quality of SPECT images. There are many applications of SPECT-CT that are well established clinically. As new advanced systems are becoming widely available, further improving the accuracy of image fusion and shortening acquisition times, the newer applications are becoming more evident. Apart from applications in oncology, interesting uses of SPECT-CT are seen in the areas of minimally invasive surgery and cardiology. We shall start our treatise with some technical information about these systems before going into the clinical applications.

SPECT-CT System Information

Combining SPECT and CT images acquired from different standalone machines has often been challenging. This is because usually the studies are acquired on different dates, on different machines by different operators using different protocols. This creates differences in the position of the patient body, extremities as well as spinal curvatures, as table positions may differ with different systems. Furthermore, it is not possible to match respiratory, cardiac motion, and position of stomach, intestines,

and urinary system at different time frames. Software fusion techniques have been developed which can register and fuse images from multiple sources [39, 40], but they are best suited for correlating images from rigid structures such as the brain [41] and skeleton [42, 43]. However, for thorax and abdomen, due to inherent movement of internal organs, software fusion has remained challenging. Data sets from two fundamentally different imaging modalities with different spatial resolution and with few common landmarks make it further complicated. A system offering same geometry for acquisition of SPECT and CT images almost simultaneously, such as SPECT-CT scanning, offers much better data sets for fusion. Here the patient remains on the same table and in the same position while undergoing SPECT and CT acquisitions separated by a few minutes.

The practical advantages of SPECT-CT fusion imaging are multifold:

- i) These systems are able to superimpose functional information from nuclear medicine data sets onto anatomical information from CT scans, greatly improving the confidence of the reporting diagnostician.
- ii) These systems are able to facilitate attenuation correction of SPECT data with patient-specific attenuation maps acquired from CT [44, 45]. Because of this, there is improvement in the spatial resolution, contrast, and signal-to-noise ratio of the image.
- iii) There is improvement in the functional data quality aided by CT, which shows great promise in quantification of RP uptake [46, 47]. This is very useful for (i) better radiation dosimetry [48, 49] and (ii) monitoring response to therapy.

The concept of combining structural and functional information was conceived and implemented in prototype

form at the very beginning of emission and transmission CT, most notably the work by Kuhl, Hale, and Eaton, who obtained the first trans-axial transmission CT scan of a patient's thorax using their Mark II brain SPECT scanner in the mid-1960s [50]. However, use of transmission imaging with an external radionuclide transmission source was introduced for attenuation correction in SPECT [51, 52] and PET [53, 54] only in the 1980s. In this system, external transmission scanning was used with SPECT to perform both attenuation correction and anatomical localization. However, a transmission scan provides poor quality anatomical details and contrast resolution, hence these systems never grew into routine applications. Over the last decade or so, combined SPECT-CT scanners have become commercially available which acquire data from SPECT and CT on the same gantry. The patient remains in same position and on the same table, which is then sequentially moved from one modality to another. The final data acquired is then transferred to a single computer which does data correction, image reconstruction, integration, and display and allows analysis for better diagnosis.

The early SPECT-CT systems tried simultaneous acquisition of SPECT and CT data [55, 56], but the problem with a simultaneous SPECT-CT acquisition system was in designing a common detector with sufficient temporal and energy resolution to discriminate the primary radionuclide photons from both the X-ray signal and the scatter of the radionuclide photons. This problem remains unsolved. The “modern” SPECT-CT system was originally developed by Hasegawa et al. at the University of California, San Francisco in the mid-1990s [45]. These systems have SPECT and CT gantries in tandem (in-line) which can acquire patient data sequentially and send it to the same computer for further fusion and processing (Figure 1.27).

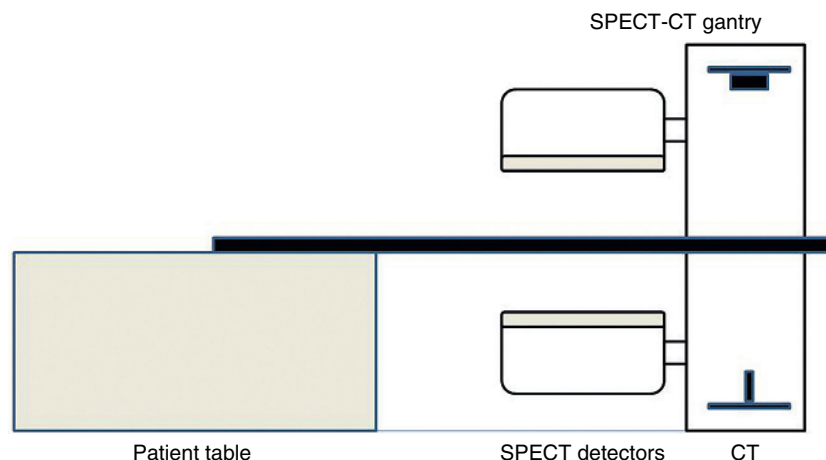


Figure 1.27 Schematic diagram of the modern SPECT-CT system.

General SPECT-CT Protocols

The first commercial SPECT-CT combination that was designed as a single unit was the GE Millenium™ hybrid SPECT/PET/CT camera equipped with a HawkEye™ single-slice CT (GE Healthcare, Haifa, Israel). The CT produced images with a slice thickness of 1 cm and a 256×256 matrix size with a spatial resolution of about 3.5 mm. Because of its coarse resolution, the CT was not regarded as a diagnostic CT. Reconstruction was performed using filtered back projection. The system was also offered with a 1-in. crystal and a coincidence unit for PET imaging. This system was the commercial implementation of the very successful research by the late Hasegawa et al. [57].

Almost all current SPECT-CT systems offer high-resolution diagnostic CT units as part of their SPECT-CT systems. One of the manufacturers (Mediso) even offers a complete SPECT/CT/PET with high-resolution lutetium-yttrium oxyorthosilicate (LYSO) detector technology as part of their AnyScan family of systems. The CT scan in these devices is a diagnostic CT scan which is used for attenuation correction based on individual patient-based tissue density data. The SPECT-CT workstations allow image reconstruction, and three-plane (transaxial, coronal, sagittal) and 3D display, including MIP and surface volume rendering. SPECT, CT, and fused images are shown on the same screen, and an interconnected pointer is available to exactly colocalize the morphological and functional areas of interest identified in either one of the two study components.

The cost of SPECT-CT systems is considerably higher than that of a conventional gamma camera, especially for devices including a full diagnostic capability CT. Higher cost has constrained the availability of this technology to places with limited financial resources. New SPECT devices have recently been developed using CdTe/CdZnTe semiconductors instead of the classic NaI (Tl) scintillation crystals. Such newer systems are smaller, and have higher sensitivity and intrinsic resolution than conventional cameras.

SPECT-CT Acquisition

Most clinical SPECT systems still rely on the Anger camera principle discussed earlier, where the location of a photon interaction (i.e. scintillation) site in the body is calculated as the center of gravity of the position-dependent energy signals from a two-dimensional (2D) array of photomultiplier tubes (PMTs) attached to the back of the scintillation crystal [58]. The available NaI (Tl) crystal thicknesses vary

between 3/8 and 3/4 in. (9.5 and 19 mm) depending on the intended usage for radionuclides emitting lower energy photons (e.g. ^{99m}Tc) and/or higher energy photons (e.g. ^{131}I). Thicker crystals improve the photo-peak efficiency but degrade the intrinsic spatial resolution.

Acquisition on SPECT-CT systems is performed in a sequential mode. The SPECT-CT systems using a diagnostic CT component have higher spatial resolution and faster scanning time. However, diagnostic CT delivers higher radiation doses. The SPECT component is acquired by a rotating, dual-head, variable angle sodium-iodide scintillation camera. SPECT acquisition currently requires a routine scanning time of approximately 20–30 minutes, depending on the radiotracer and the axial length of the body area scanned. CT is usually acquired in matrices of 512×512 with the newest CT scanners or 256×256 in older scanners, and has to be resized into slices with the same pixel format and slice width as SPECT. SPECT is reconstructed using iterative methods incorporating photon attenuation correction based on the X-ray transmission map and scatter correction. Since X-ray and radionuclide data are not acquired simultaneously, the SPECT images are not contaminated by scatter radiation generated during the X-ray image acquisition. Also, since the patient is not removed from the table, both imaging components are acquired with a consistent and identical patient position, allowing accurate image registration if we assume that the patient has not moved during the entire duration of the SPECT-CT study.

The current SPECT systems are equipped with detection devices or sensors to automatically calculate noncircular orbits: the detection methods can be based on optical detection using light-emitting diodes. Aside from the safety aspect, noncircular orbits ensure closer distances to the patient for each of the SPECT projections as well as easy setup procedures, which together reduce the overall time that the patient spends on the imaging table. Companies now offer advanced and integrated diagnostic SPECT-CT solutions with 2-, 6-, or 16-slice diagnostic CTs. Basically, the SPECT-CT is a hybrid or a combination of each of the two systems that have the same characteristics as the respective standalone devices.

Image Reconstruction

Most of the newer SPECT systems use statistical iterative reconstruction for creating images [59, 60]. An iterative procedure includes some kind of model of how the images are formed by the acquisition system. For a SPECT system, an image is formed by the collimation of emitted photons such that only those photons parallel to the collimator hole will interact with the crystal and produce scintillation

events. Hence, these so-called projections are created as 2D representations of all photons detected along the projection lines and this gives rise to a distance-dependent resolution. The greater the distance of the camera head from the radioactive source, the poorer the resolution. There is no information about source depth in the 2D projections. The purpose of the reconstruction algorithm is therefore to create an estimate of the source distribution in 3D. From the CT in SPECT-CT systems, attenuation maps are generated and incorporated in the image formation model.

In an iterative reconstruction algorithm, one starts with an initial estimate of the internal and unknown radionuclide distribution. This estimate is usually an image set with equal and constant voxel values. SPECT projections are then calculated from the initial estimate using a computer model of the imaging system. The underlying assumption is that if the calculated projections match the measured projections, then the internal unknown activity distribution in the patient matches the estimate. Initially, these are most likely nonagreeing, so the initial estimate needs to be modified. Therefore, updates are made in the estimate based on a comparison between calculated projections of the estimate using the physics of the imaging process and the measured projections. By back projection, the deviations between these two projection sets finally form an error image of weighting factors that is used to update the initial image estimate. This procedure is placed in an iterative loop in which the calculated and measured projections are compared until the deviation is smaller than a selected criterion (convergence has been reached). Hence, when this happens, the reconstruction loop is stopped. However, in actual practice, as projection data is noisy, the iterative reconstruction procedures are stopped after only a small number of iterations because the noise in the final image goes on increasing for a large number of iterations. The most popular iterative reconstruction algorithm implemented is ordered subset expectation maximization (OS-EM) [61] due to the speed with which it reaches a good estimate of the activity distribution.

However, there are many other factors, such as nonhomogeneous photon attenuation, contribution from scattered photons, and blurring due to the collimator response, which need to be accounted for during reconstruction of the image. The compensation for these factors is relatively easy in iterative reconstruction, but there are still some issues when combining these two systems. It should be remembered that a SPECT acquisition is averaged over many respiratory cycles, which blurs the image, while rapidly acquired CT images are instantaneous images and may not match with the averaged SPECT image. The spatial resolution of the SPECT system is also far lower than that of CT. Hence, if high-resolution CT images are used for

attenuation correction, there is a possibility that artifacts may appear at boundaries between different attenuating tissues because of the spill-out of events. Often this effect is reduced by smoothing the CT images with a Gaussian kernel that results in a spatial resolution of the CT images comparable with the spatial resolution of the SPECT images. Also, depending on the acquisition parameters (voltage and mAs), the CT image may not be optimal for attenuation correction and the scaling from the X-ray bremsstrahlung spectra to the specific photon energy used in SPECT may not be optimal. Hence, when using CT only for attenuation correction, so-called low-dose protocols can be used which are optimized, such as a longer scanning time to average the respiratory movements and matched spatial resolutions [62].

The problem of scatter correction has been taken care of by various methods. Siemens and GE have implemented some form of the dual-energy window method based on the estimation of scatter from additional energy windows for subtraction from projection data or used within iterative reconstruction methods as an additive term [63]. However, it is generally known that the distribution of scatter in additional lower scatter windows does not reproduce the scatter distribution in the main photo-peak energy window. Alternatively, model-based scatter compensation has been used that does not rely on additional energy window data collection. Instead, it models the scatter in the main photo-peak energy window by using pre-calculated scatter kernels or in real-time calculates the scatter based on theoretical cross-sections of first-order scattering. Philips has implemented a version of the effective scatter source estimator method, originally developed by Frey and Tsui [64].

There is also a need for some compensation for the limited spatial resolution due to the collimator design. This is generally implemented in the iterative reconstruction algorithm, modeling the depth-dependent blurring caused by photons that reach the detectors. The effect of partial volume is an apparent reduction of the radioactive count density/X-ray density that occurs when an organ/tumor/defect only partially resides within the “sensitive volume of the imaging instrument (in space or time)” [65–68]. From the review of Erlandsson et al. [68] it is clear that an extensive body of work exists in an effort to minimize the partial volume effect. The main aim of partial volume correction (as well as resolution correction) is to improve the quantitative accuracy of the structure under investigation. CT can be used for correction of partial volume in SPECT images owing to its high sampling frequency.

Patient body movement can occur during both the SPECT and CT portions of the study. The acquisition times for conventional SPECT-CT systems can vary from 10 minutes to more than 30 minutes depending on area scanned and

count rate. During acquisition, SPECT typically takes much more time than CT. All manufacturers offer registration tools to manually or automatically register SPECT and CT in case movement occurs between those two scans. The motion during the CT portion of the acquisition is usually minimized owing to short scan times as well as breath-holding by the patient for diagnostic CT scan. All manufacturers have some form of motion correction for SPECT itself using the consistency of the projections. These algorithms usually work best for small and simple motions. However, for excessive and complex motions, the SPECT-CT acquisition needs to be repeated.

New SPECT-CT Scanners with Solid-state Detectors

The most common scintillation material used in gamma camera is NaI(Tl). It is readily available and cost-effective. If we review the principal characteristic of gamma cameras, then the absorbed photon energy is converted to visible light in proportion to the deposited energy and this light is then detected by PMTs. PMTs convert this light to electrons at the cathode surface of the PMTs and the signal is amplified using a sequence of dynodes to create an electrical signal. This signal is then processed to get information about the energy and position of the original gamma rays. Because there are many steps involved, the uncertainty in the measured energy signal is quite large, resulting in an energy resolution in the order of 10% full width at half maximum at 140 keV. Furthermore, a large number of PMTs are required to determine the location of the interaction. That is why the size of the scintillation camera head is quite large and requires sophisticated tuning methods so that all PMTs provide similar amplitude signals for the same imparted energy.

Recently, commercial SPECT systems based on cadmium-zinc-telluride (CdZnTe or simply CZT) have been introduced. CZT is a solid-state detector material that generates signals from the collection of induced charge created by the ionizations from photoelectric interactions or Compton scattering. Here each photon is directly converted into an electrical signal. The major advantages of these new CZT modules are their small size and the absence of PMTs, which allows for a compact camera. It also increases the overall system sensitivity significantly. The improvement in sensitivity can either be used to reduce the acquisition time of a given administered activity or reduce the radioactivity administered for the same acquisition time. The major contrasting points between a conventional gamma camera and the CZT-based SPECT-CT system are given in Table 1.4. The GE Healthcare full-size

Table 1.4 The major contrasting points between conventional (NaI-based) gamma cameras and a cadmium-zinc-telluride (CZT)-based SPECT-CT system.

Attributes	Conventional gamma camera (NaI)	CZT-based gamma camera
Type of crystal	Scintillation	Semiconductor
Interaction of gamma rays	Produces light	Produces electron-hole pair
Photomultiplier tube	Necessary to convert light signal to electrical signal and amplify it	Not required
Detector assembly	Bulky	Sleek
Sensitivity	+	+++
Spatial resolution	+	+++
Energy resolution	+	+++
Image contrast	+	+++
Image quality	+	+++
Acquisition time	+++	+
Radiation exposure	+++	+
Available field of view	++	+++
Cost	+	+++

CZT based SPECT-CT system (Discovery NM/CT 870 CZT) provides up to 75% reduction in injected dose or scan time, improved system spatial resolution, from 4.3 to 2.8 mm, and exceptional energy resolution, 6.3% compared to 9.5%, according to data provided by them. They also claim greater than 40% improvement in SPECT contrast-to-noise ratio, 67% reduction in detector frame size, from 7.5 to 2.5 cm, and 25% greater optimal FOV than NaI [69]. There are newer CZT systems, such as the VERITON CZT camera (Spectrum Dynamics, Caesarea, Israel), which are similar to PET-CT cameras in architecture with detectors arranged in a ring configuration around the patient [70].

Clinical Examples of SPECT-CT

As there are chapters dedicated to the clinical applications of SPECT-CT system later in the book, we restrict ourselves to a few clinical examples. The selected clinical examples of SPECT-CT acquisitions shown in Figures 1.28–1.32 are such that, if not for combined imaging, the diagnosis might have been missed or delayed.

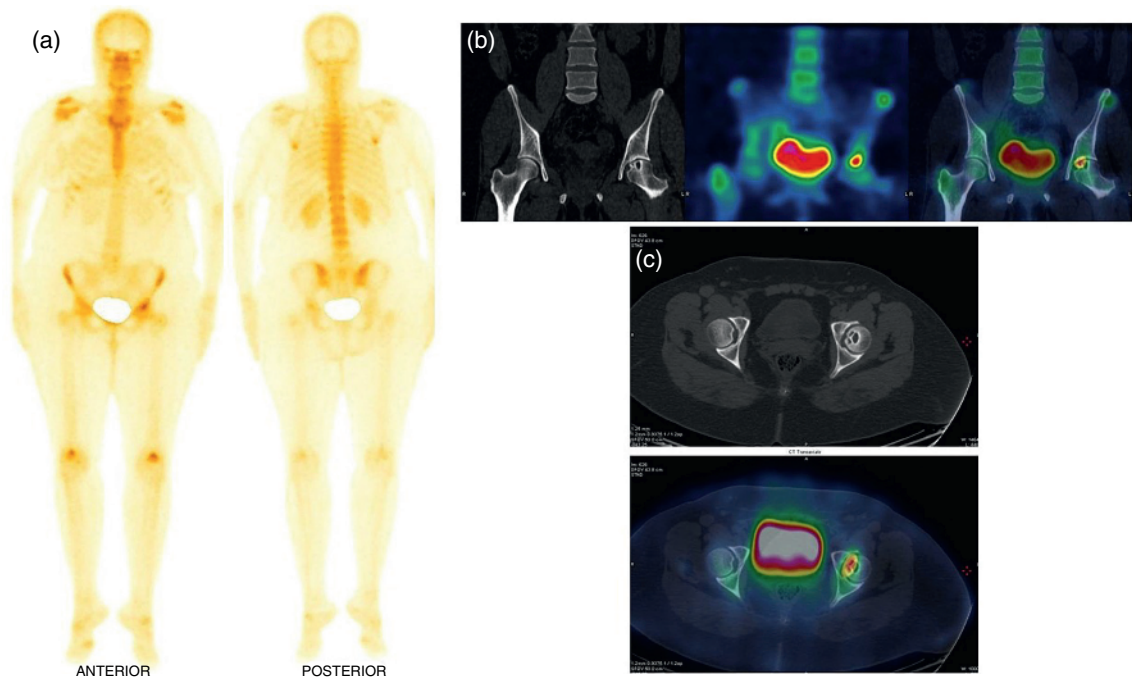


Figure 1.28 A 51-year-old female with a presenting complaint of left hip joint pain. (a) The bone scan showed increased tracer uptake in the upper part of the left hip joint. (b) and (c) The SPECT-CT scan of the pelvis showed subchondral cysts in the head of the left femur, suggestive of osteoarthritis. In this case the bone scan helped to find the active osteoblastic reaction in the left hip joint region as cause of pain and the CT component helped to localize abnormal tracer uptake. The morphological findings of osteoarthritis on CT added specificity to bone SPECT findings.

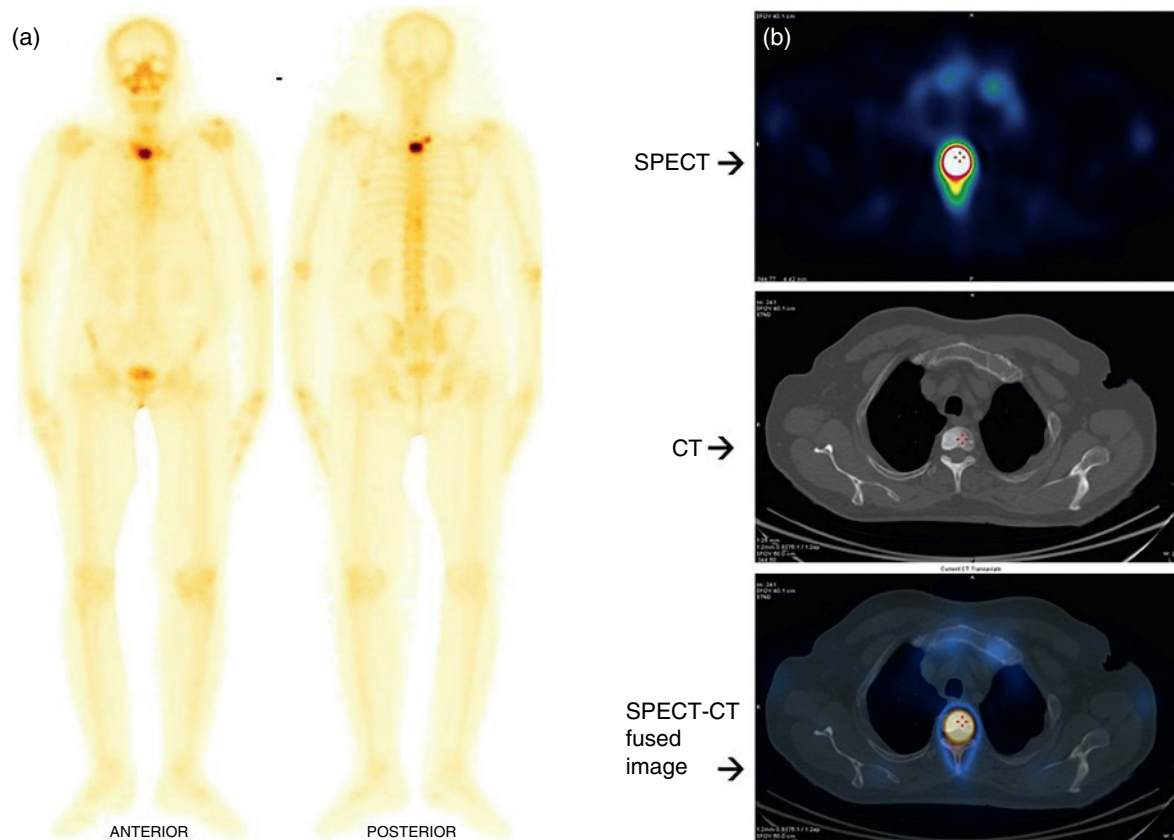


Figure 1.29 A 70-year-old male with diagnosed carcinoma of prostate. His serum PSA level was 34 ng/mL. (a) The whole-body bone scan shows focal increased tracer uptake in the upper dorsal vertebra. (b) The SPECT-CT scan of the thorax shows increased tracer uptake corresponding to sclerotic lesion involving the D2 vertebral body consistent with solitary skeletal metastasis. In this case, the bone scan detected a solitary osteoblastic lesion in the upper dorsal vertebra and CT localized it to the D2 vertebra showing sclerosis, hence confirming metastatic disease.

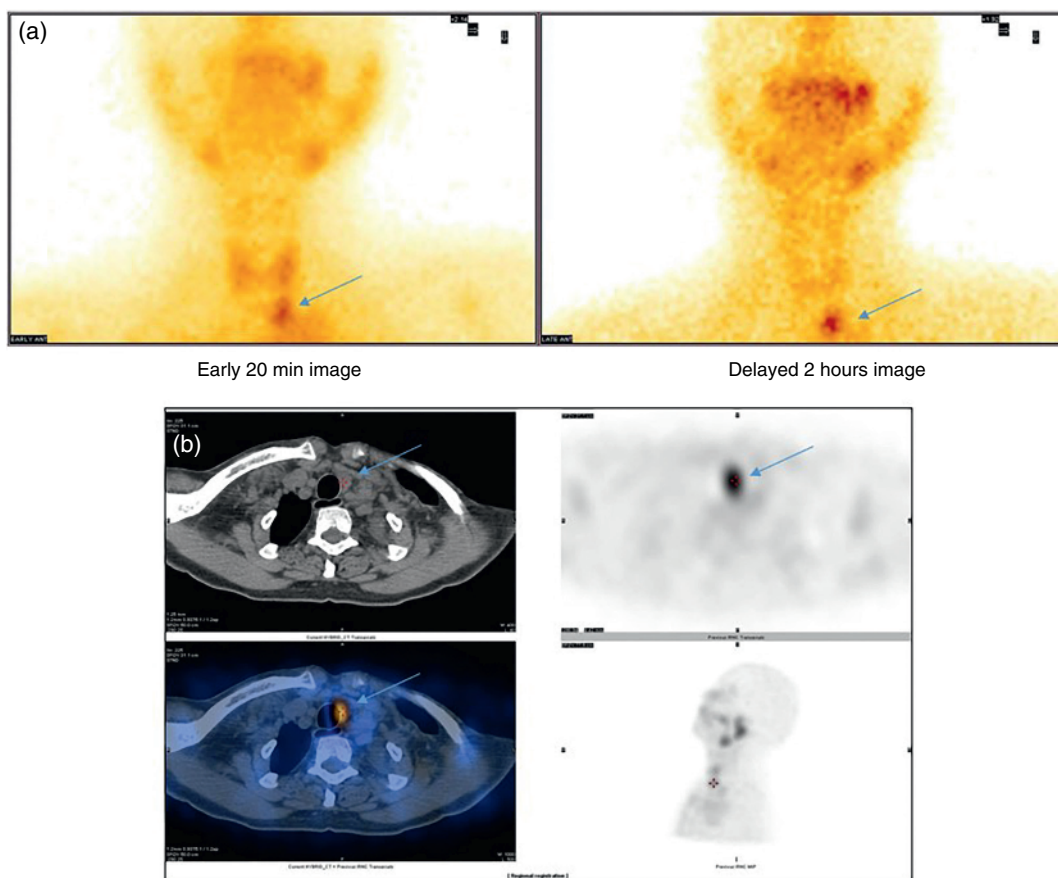


Figure 1.30 A 35-year-old male with recurrent pancreatitis. He was found to have elevated serum parathyroid hormone levels during evaluation and was referred for a ^{99m}Tc -MIBI parathyroid scan. (a) Dual phase parathyroid scintigraphy in anterior static images showing focal abnormal tracer uptake near the lower pole of the left lobe of the thyroid gland (blue arrow) with focal tracer retention seen in the delayed image. (b) SPECT-CT of the neck showing abnormal tracer uptake corresponding to a 14×14 mm nodule in the left upper paratracheal region inferior to the lower pole of the left lobe of the thyroid gland suggestive of parathyroid adenoma. The SPECT-CT scan helped in the exact localization of the parathyroid lesion and aided with better surgical planning.

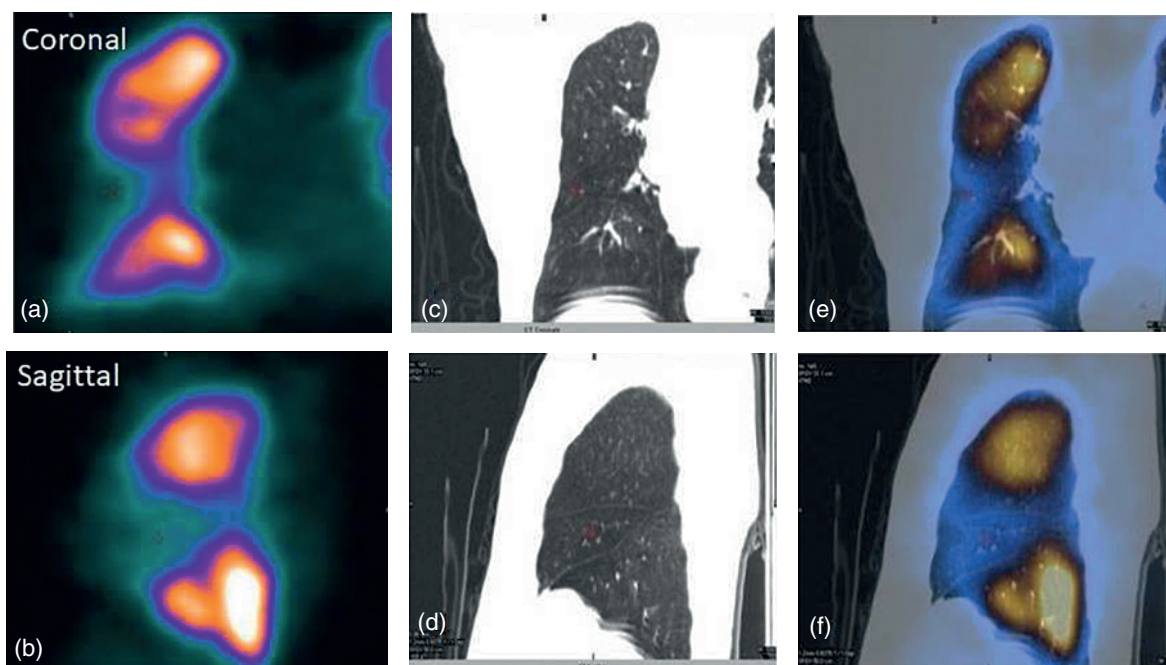


Figure 1.31 A 70-year-old male with chronic kidney disease and suspected pulmonary thromboembolism. The ^{99m}Tc -macroaggregated albumin lung perfusion scan (a, b) showed a perfusion defect in the right middle lobe. The SPECT-CT scan (e, f) showed a large perfusion defect in the middle lobe of the right lung with no morphological abnormality, such as a space-occupying lesion, consolidation or fluid accumulation on the CT scan. The CT scan (c, d) showed well-aerated lung parenchyma in the region of the perfusion defect, potentially eliminating the need for a ventilation scan to diagnose pulmonary thromboembolism.

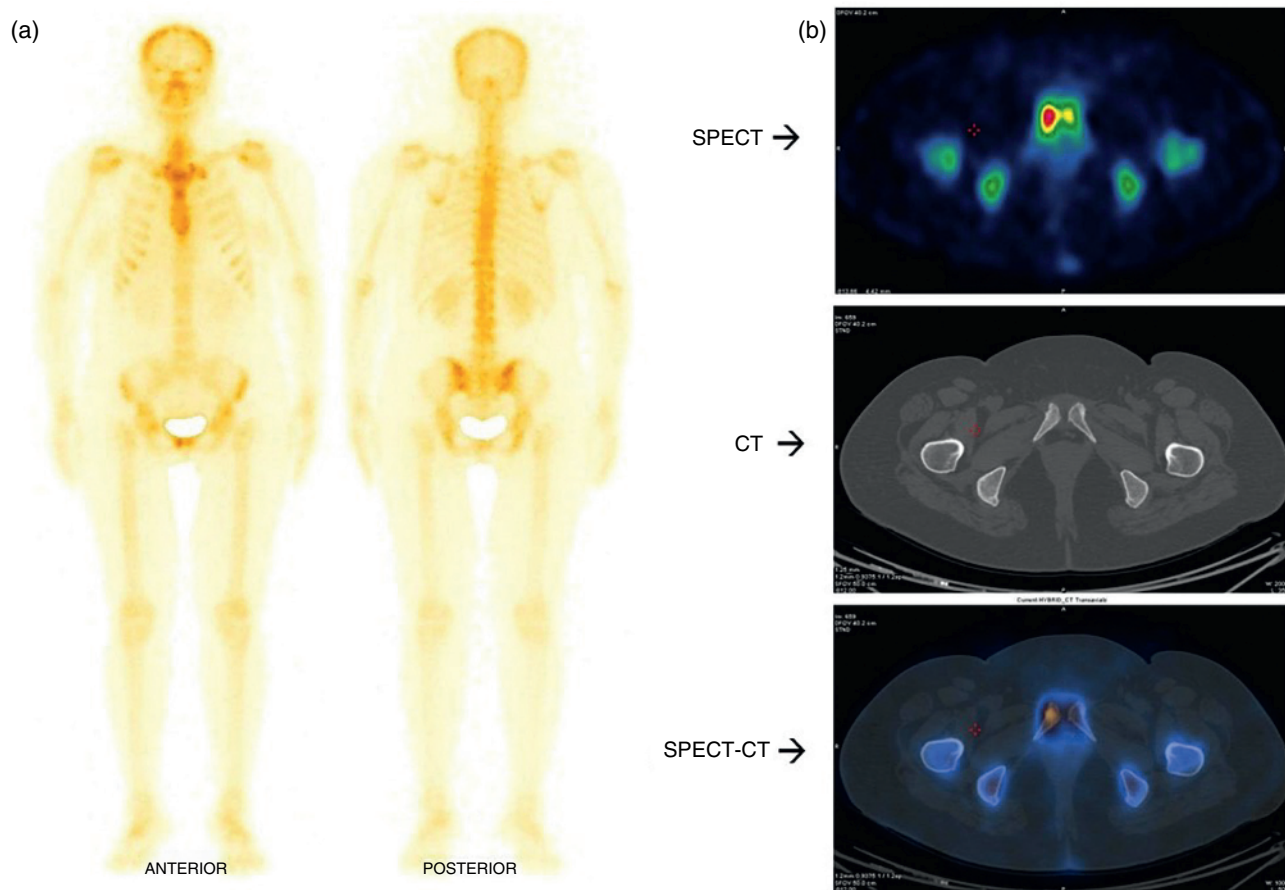


Figure 1.32 A 30-year-old female who delivered a baby 2 years previously. She presented with complaints of pubic region pain. Her whole-body bone scan (a) showed mildly increased tracer uptake in the pubic bones (right > left). (b) The SPECT-CT scan of the pelvic region showed foci of increased tracer uptake in bilateral pubic bones (Rt > Lt) along with widened pubic symphysis joint space and subtle erosions of the right pubic bone suggestive of osteitis pubis. In this example, the whole-body bone scan and SPECT scan were able to pinpoint the possible site of pathology, while the CT scan confirmed the diagnosis of osteitis pubis with characteristic morphological features.

Conclusion

In summary, in this treatise we have elaborated on the fundamental principles, imaging protocol, and clinical applications of the hybrid imaging modalities PET-CT and SPECT-CT to provide the readers with a comprehensive working knowledge on the subject. A plethora of illustrative clinical case examples have been provided deliberating on (i) the normal physiological variants and benign pathologies

mimicking malignancy, (ii) the enumeration and depiction of artifacts in PET-CT fusion imaging, and (iii) the value of combined imaging, where the PET-CT and SPECT-CT fusion imaging resulted in accurate diagnosis of pathology. With a number clinical and research applications continuing to evolve, it is expected the correlative anatomical-functional approach would play an important role in clinical decision-making for both oncological and nononcological applications.

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