

# Management of Incidental Breast Lesions Detected at Nuclear Medicine Examinations

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Nuclear medicine studies are often performed in patients with breast cancer; however, incidental radiotracer uptake in the breasts can be observed in patients with nonbreast malignancies. Benign and malignant lesions can be identified on planar, SPECT, and PET scans. This review will outline the molecular and radiographic imaging appearance of benign and malignant breast lesions on sestamibi scans, bone scans, radioiodine studies, as well as PET studies using fluorine 18 ( $^{18}\text{F}$ ) fluorodeoxyglucose, gallium 68 ( $^{68}\text{Ga}$ ) tetraazacyclododecane tetraacetic acid octreotate (or DOTATATE),  $^{68}\text{Ga}$  prostate-specific membrane antigen, and  $^{18}\text{F}$ -fluciclovine radiotracers. Recognizing these lesions at molecular and anatomic imaging is important to ensure accurate diagnosis and appropriate management.

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Nuclear medicine studies such as bone scan, lymphoscintigraphy, and fluorine 18 ( $^{18}\text{F}$ ) fluorodeoxyglucose (FDG) PET/CT may be performed in patients with breast cancer for staging and treatment planning. Focal or diffuse radiotracer uptake can also be incidentally found within the breast in patients without breast cancer. These findings may be clinically relevant and could correlate with mammogram or breast US to help confirm a suspected diagnosis, which may save the patient additional workup and anxiety. Certain lesions may demonstrate avid uptake of one radiotracer but fail to have any uptake of another. Familiarity with the expected level of radiotracer uptake of specific breast lesions may also aid in making the correct diagnosis. There are PET radiotracers including gallium 68 ( $^{68}\text{Ga}$ ) tetraazacyclododecane tetraacetic acid octreotate (DOTATATE),  $^{18}\text{F}$ -fluciclovine, and  $^{68}\text{Ga}$ -prostate-specific membrane antigen (PSMA) that may also demonstrate incidental breast uptake. Reviewing pathologic correlation of these incidental lesions can be helpful in future imaging interpretation.

The goals of this review are to demonstrate the spectrum of breast lesions that can be detected on various molecular imaging studies, present relevant features on correlative anatomic imaging, and help the reader obtain additional imaging when warranted. This institutional review board–approved, Health Insurance Portability and Accountability Act–compliant pictorial essay will provide an overview of various planar, SPECT, and PET nuclear medicine studies and the breast lesions that can be detected at each.

## Planar and SPECT Scintigraphy

### Technetium 99m–Sestamibi

Technetium 99m ( $^{99\text{m}}\text{Tc}$ )–sestamibi is used for myocardial perfusion imaging and localization of parathyroid adenomas in the evaluation of hyperparathyroidism. It is lipophilic and localizes to the mitochondria via passive

cellular diffusion (1). In myocardial perfusion imaging,  $^{99\text{m}}\text{Tc}$ -sestamibi diffuses from the blood into myocardial cells and is retained in the mitochondria. The extraction rate of the radiotracer is proportional to coronary blood flow, making it useful in the evaluation of myocardial perfusion and detection of coronary artery disease (1). In endocrine imaging, normal parathyroid glands do not have increased uptake of sestamibi, but parathyroid adenomas possess oxyphil cells that contain many mitochondria that have high uptake and slow release of sestamibi.

Many tumors, including breast cancers, take up  $^{99\text{m}}\text{Tc}$ -sestamibi, which may be incidentally detected on scans for myocardial perfusion or hyperparathyroidism. Intraductal carcinoma, ductal carcinoma in situ, and infiltrating lobular carcinoma can have increased uptake on sestamibi studies (2). In fact,  $^{99\text{m}}\text{Tc}$ -sestamibi is approved by the United States Food and Drug Administration for the detection of breast cancers. These studies are also known as molecular breast imaging or breast-specific gamma imaging, which have reported sensitivity as high as 95% and specificity up to 80% (3). There is variability in breast cancer sestamibi uptake, and cancers without increased uptake can result in a false-negative study (2). Recurrent or metastatic breast cancer in the axilla may also be detected; therefore, it is important to evaluate all aspects of the image (Fig 1). Furthermore, a new focal breast mass at correlative CT from a SPECT/CT scan warrants further workup, even in the absence of increased tracer uptake. Some benign masses, such as myofibroblastoma, do not have increased sestamibi uptake but present as a discrete breast mass at CT (Fig 2).

Benign breast lesions such as fibroadenomas and fibrocystic disease may also be identified on  $^{99\text{m}}\text{Tc}$ -sestamibi scans, although they may demonstrate variable uptake (2). Intraductal papillomas can demonstrate absence of uptake, and sclerosing adenosis can have false-positive uptake (2). Because the leading differential for a breast mass with increased sestamibi uptake is breast cancer, such a lesion

## Abbreviations

FDG = fluorodeoxyglucose, DOTATATE = tetraazacyclododecane tetraacetic acid octreotate, MDP = methylene diphosphonate, PSMA = prostate-specific membrane protein, SUV = standardized uptake value,  $SUV_{max}$  = maximum SUV

## Summary

This review outlines the molecular and radiographic imaging appearance of benign and malignant breast lesions on sestamibi scans, bone scans, radioiodine studies, as well as PET studies using fluorine 18 ( $^{18}F$ ) fluorodeoxyglucose, gallium 68 ( $^{68}Ga$ ) tetraazacyclododecane tetraacetic acid octreotate (or DOTATATE),  $^{68}Ga$  prostate-specific membrane antigen, and  $^{18}F$ -fluciclovine radiotracers.

## Essentials

- Breast lesions can be incidentally detected in patients who are undergoing imaging for different types of disease states, and these lesions should be carefully assessed for proper diagnosis.
- There can be variable uptake of different radiotracers within malignant and benign breast lesions, which may warrant further diagnostic testing.

warrants additional evaluation with breast imaging. Some authors have attempted to use semiquantitative methods to differentiate benign from malignant lesions in the breast. The mean relative uptake factor of  $^{99m}Tc$ -sestamibi, defined as the ratio of the maximal counts of the breast lesion to maximal counts of the background parenchyma, has been shown to be 2.37 for benign lesions and 4.27 for cancers (4). Other studies have suggested using an early phase lesion-to-background ratio of 3.13 to differentiate benign from malignant lesions (5).

## $^{99m}Tc$ -Methylene Diphosphonate Bone Scan

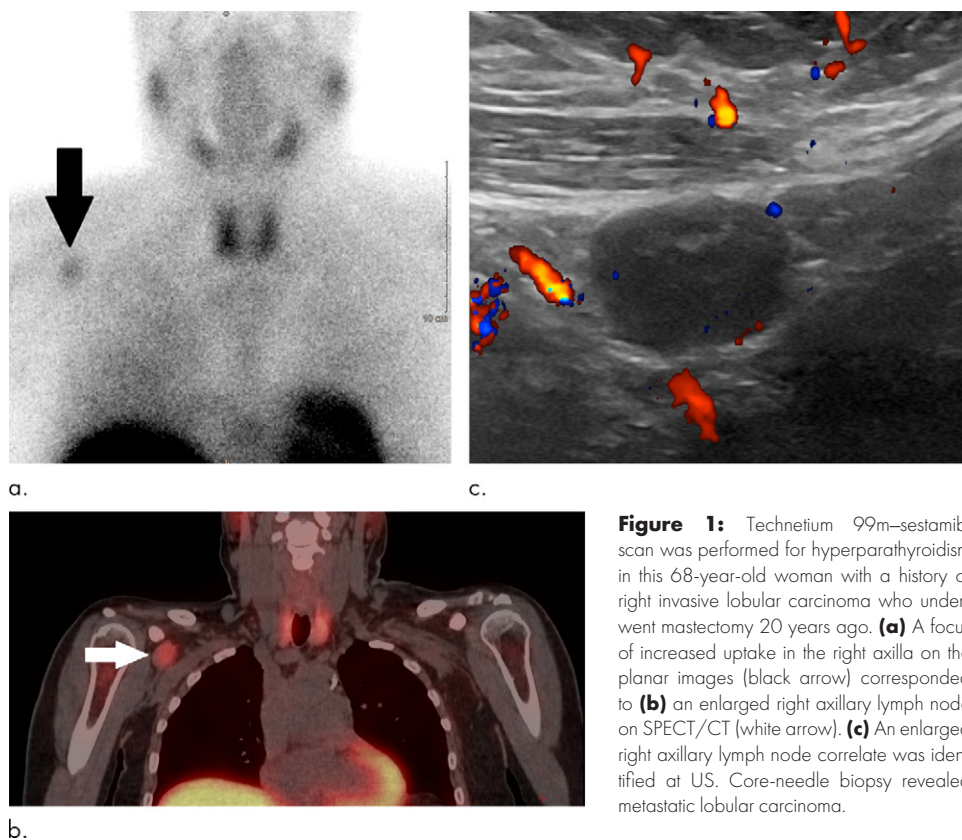
The bone scan is one of the most common nuclear medicine studies performed for evaluation of metastatic disease, tumors, infection, and trauma.  $^{99m}Tc$ -methylene diphosphonate (MDP) is injected intravenously, and imaging may be performed 2–4 hours after injection for a single-phase study. Accumulation of  $^{99m}Tc$ -MDP increases with increasing blood flow and osteoblastic activity, where there is increased bone formation or repair.  $^{99m}Tc$ -MDP binds to bone by chemisorption to hydroxyapatite in the osseous matrix (1). It can also bind to amorphous calcium phosphate in soft-tissue calcification or ossification.

Patients with breast cancer may undergo a bone scan as part

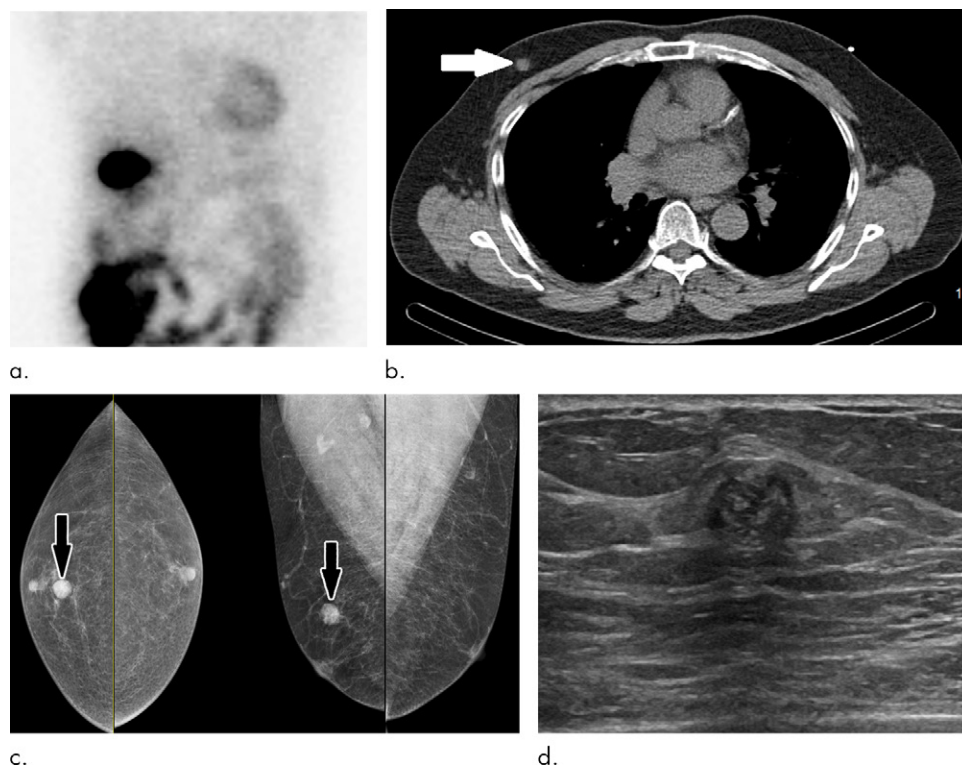
of their metastatic workup. Uptake can be seen in the breast cancer itself, which may be due to  $^{99m}Tc$ -MDP binding to calcifications in soft tissue or necrotic tumor (Fig 3). More classically, patients with diffuse osseous metastatic disease demonstrate multiple focal areas of increased uptake throughout the skeleton.

Primary sarcoma in the breast can also demonstrate increased uptake on bone scan, possibly related to the presence of microscopic calcification (6). Primary or metastatic osteosarcoma, a bone-forming tumor in the breast, can also demonstrate intensely increased uptake (7,8). Although a rare site of metastasis, metastases from the gastrointestinal tract, lung, kidney, thyroid, and skin have been identified in the breast (7).

Benign processes such as fibroadenomas, fibrocystic disease, lactational change, gynecomastia, breast implants, hematomas, and fat necrosis have also been reported to demonstrate increased uptake on bone scan (9). These are rare causes of MDP accumulation and may be related to local metabolic conditions, inflammation, collagen deposition, and/or increased blood flow (9). One study found that following injection of  $^{99m}Tc$ -MDP, background breast parenchymal uptake remained constant; however, uptake in breast cancers peaked at 10–20 minutes following injection, with a mean tumor-to-background ratio of 3.8 (10). Ninety-three percent of benign lesions demonstrated no uptake, and fibroadenomas demonstrated significantly lower uptake than malignancy (10). If focal breast uptake on a bone scan cannot be explained by a known breast cancer, comparison with prior studies and additional imaging with SPECT/CT would be appropriate. Any new breast mass warrants additional workup with breast imaging.



**Figure 1:** Technetium  $^{99m}$ -sestamibi scan was performed for hyperparathyroidism in this 68-year-old woman with a history of right invasive lobular carcinoma who underwent mastectomy 20 years ago. **(a)** A focus of increased uptake in the right axilla on the planar images (black arrow) corresponded to **(b)** an enlarged right axillary lymph node on SPECT/CT (white arrow). **(c)** An enlarged right axillary lymph node correlate was identified at US. Core-needle biopsy revealed metastatic lobular carcinoma.



**Figure 2:** A 61-year-old man with coronary artery disease underwent technetium 99m-sestamibi myocardial perfusion scan with an attenuation correction CT. **(a)** There was no increased sestamibi uptake in the breast or chest wall. **(b)** At CT, there was an incidental 1-cm soft-tissue nodule in the right breast (white arrow). **(c)** A mammogram and **(d)** US confirmed a 1.1-cm round, circumscribed mass in the right upper central breast at 12:00 o'clock (black arrows). Core-needle biopsy and subsequent surgical excision of the mass revealed a myofibroblastoma, a benign mass often seen in men.

### Radioiodine Scans

There are several radioactive isotopes of iodine, the most commonly used being iodine 131 ( $^{131}\text{I}$ ) and iodine 124 ( $^{124}\text{I}$ ). Iodine is an essential element used by the thyroid gland to produce thyroid hormone (11). Iodine enters the thyroid follicular cells from the blood stream through the sodium-iodine transporter on the cell surface. The iodine is then oxidized and organified with thyroglobulin molecules (11). Other organs may require iodine for metabolism or excretion and are also able to take up iodine by expressing the sodium-iodine transporter.

The lactating breast expresses the sodium-iodine transporter and often demonstrates increased radioiodine uptake, which can appear symmetric, asymmetric, crescentic, or irregular (Fig 4) (12). Hyperprolactinemia from a pituitary microadenoma can also result in diffusely increased breast uptake as prolactin mediates increased expression of the sodium-iodine transporter (13).

Increased  $^{131}\text{I}$  breast uptake is seen in 6% of nonlactating women, and the cause is often poorly understood, but it can be related to fat necrosis, gynecomastia, supernumerary breasts, lactational duct cysts, or galactoceles (13). In the case of fat necrosis, the increased  $^{131}\text{I}$  uptake may be related to inflammation and scarring (13). Benign masses, such as fibroadenomas, can have increased  $^{131}\text{I}$  uptake due to increased expression of the sodium-iodine transporter (11). Breast cancers also express the sodium-iodine transporter but may not concentrate iodine to the same degree as the thyroid gland (11). The mean background breast parenchymal 24-hour uptake of  $^{131}\text{I}$  is 3.5% and usually less than

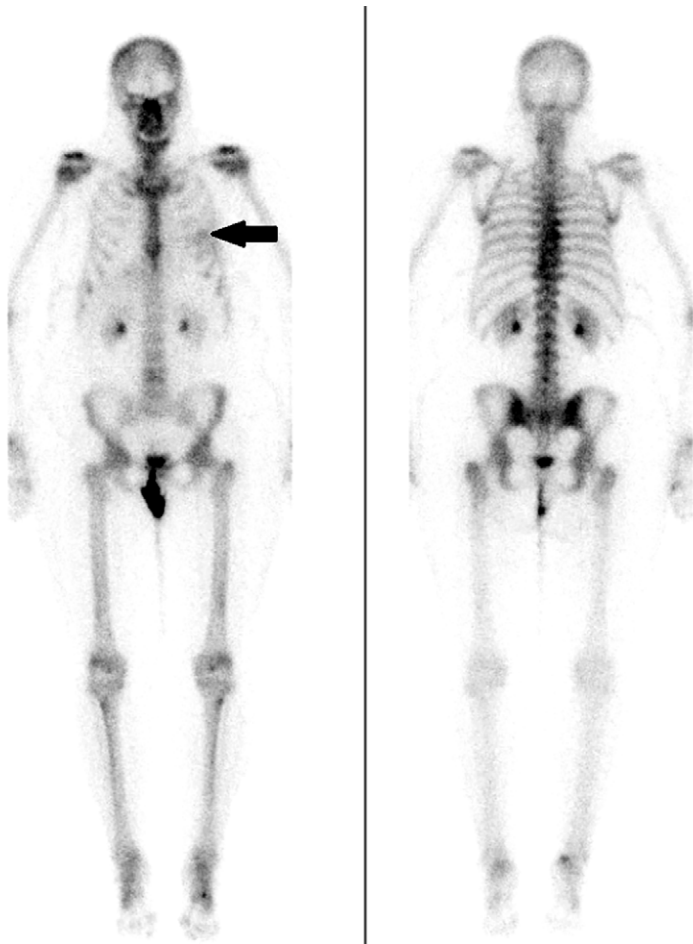
10% (14). Benign and malignant breast lesions can demonstrate 36% higher uptake than background, but the overlap between benign and malignant lesions is too great to be able to differentiate them (14). Focal or asymmetric radioiodine uptake in the breast that cannot be explained by lactation or another benign cause warrants further investigation.

### Positron Emission Tomography

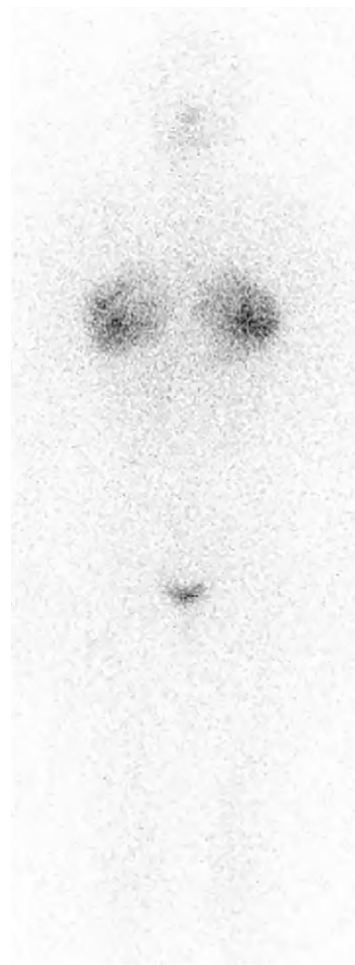
#### $^{18}\text{F}$ -FDG Imaging

$^{18}\text{F}$ -FDG, a glucose analog, is commonly used for the evaluation of various malignancies. Cancer cells demonstrate increased rates of glucose metabolism compared with normal tissue, which allows them to take up greater amounts of  $^{18}\text{F}$ -FDG (15). After intravenous injection,  $^{18}\text{F}$ -FDG enters the cell through glucose transporter membrane proteins (glucose transporter 1 [GLUT1]) and undergoes phosphorylation by the enzyme hexokinase. Normal phosphorylated dietary glucose is further metabolized through glycolysis or glycogen formation; however, phosphorylated  $^{18}\text{F}$ -FDG cannot undergo further metabolism and becomes trapped within the cancer cells (16,17).

Breast cancers may have increased  $^{18}\text{F}$ -FDG uptake depending on expression of the GLUT1 transporter and hexokinase, number of viable tumor cells, histologic subtype, tumor vascularity, cell proliferation, and presence of inflammatory cells (18). Breast cancers tend to have higher  $^{18}\text{F}$ -FDG uptake when they



**Figure 3:** A 51-year-old woman with breast cancer underwent bone scan to evaluate for osseous metastatic disease. There was no metastatic disease; however, there was increased uptake in the left breast at the site of primary malignancy (black arrow). Urine contamination containing excreted radiotracer is present overlying the pelvis.



**Figure 4:** A 34-year-old woman with papillary thyroid cancer after total thyroidectomy and radioiodine treatment underwent a thyrogen-stimulated iodine 131 whole-body scan. Bilateral diffuse uptake in the breasts was consistent with lactational changes. (Image courtesy of Dr Anca Avram.)

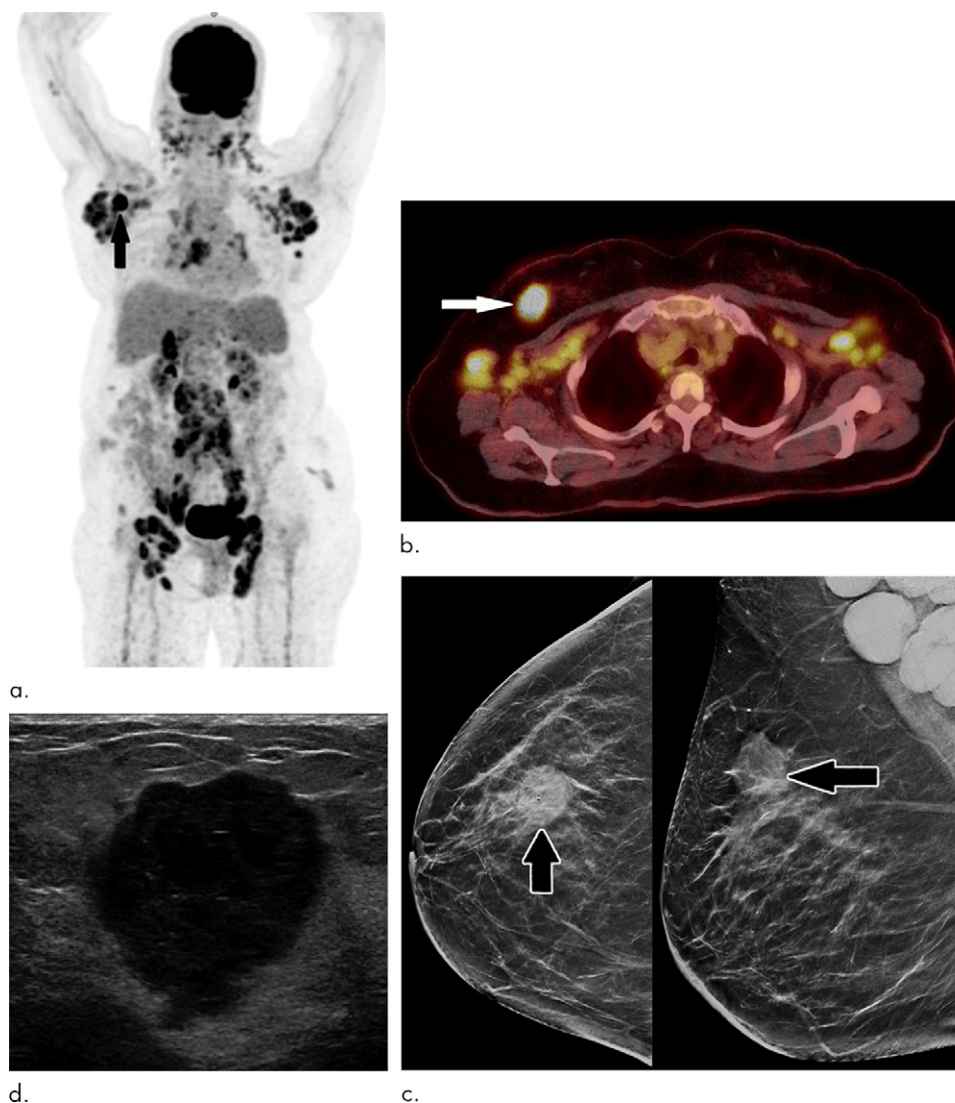
are larger in size, high grade, triple negative, or estrogen receptor negative (18). Higher  $^{18}\text{F}$ -FDG uptake in breast cancers is associated with a higher rate of recurrence and poorer prognosis (19).  $^{18}\text{F}$ -FDG uptake is also noted to be lower in infiltrating lobular carcinoma and ductal carcinoma in situ compared with intraductal carcinoma (19).

$^{18}\text{F}$ -FDG PET/CT can be used for breast cancer staging and monitoring response to therapy. The National Comprehensive Cancer Network recommends patients with early stage I or II breast cancer be evaluated with bone scan and CT of the chest, abdomen, and pelvis.  $^{18}\text{F}$ -FDG PET/CT is not routinely indicated in patients with stage I, II, or operable stage III breast cancer. For patients with stage IIIA disease or higher,  $^{18}\text{F}$ -FDG PET/CT is optional (20). Ultimately,  $^{18}\text{F}$ -FDG PET/CT is not a replacement for contrast-enhanced diagnostic CT for routine staging of patients with breast cancer (21).

Breast cancers with increased uptake can be incidentally detected at  $^{18}\text{F}$ -FDG PET/CT performed for other indications (Figs 5, 6). When  $^{18}\text{F}$ -FDG PET/CT is performed for a nonbreast malignancy, a hypermetabolic breast mass could represent a second breast primary, which may affect

treatment plans and should undergo dedicated breast imaging. Hypermetabolic breast lesions are also a potential blind spot in patients with active lymphoma. Attention should be directed to morphology and FDG avidity. Spiculated or irregular breast masses with a metabolic signature different than the primary tumor may warrant biopsy to rule out a primary breast cancer.

Benign and inflammatory breast lesions can demonstrate increased uptake on  $^{18}\text{F}$ -FDG PET/CT. Fat necrosis (Fig 7) is a sterile inflammatory process that may have increased FDG uptake due to metabolically active inflammatory cells (22). At mammography, it can appear as lipid cysts, calcifications, or a mass (22,23). At US, fat necrosis has variable appearances but may appear as a hyperechoic mass. Fat necrosis is in the differential diagnosis for a hypermetabolic breast mass, especially with history of prior breast intervention or trauma. Reactive changes to silicone and silicone adenitis (Fig 8) can be FDG avid, and correlation with history and anatomic imaging can lead to a specific diagnosis. If classic diagnoses of



**Figure 5:** A 72-year-old woman with lymphoma underwent fluorine 18 fluorodeoxyglucose (FDG) PET/CT which (a) demonstrated enlarged, intensely FDG-avid lymph nodes in the neck, chest, abdomen, and pelvis. (b) There was also a hypermetabolic right breast mass (black and white arrows), which correlated at (c) mammography with a 3.1-cm irregular mass at 12 o'clock. There was also marked right axillary lymphadenopathy on mammogram (right image in c, mediolateral oblique view). (d) US image demonstrates an irregular hypoechoic right breast mass. Core-biopsy of the mass revealed invasive ductal carcinoma.

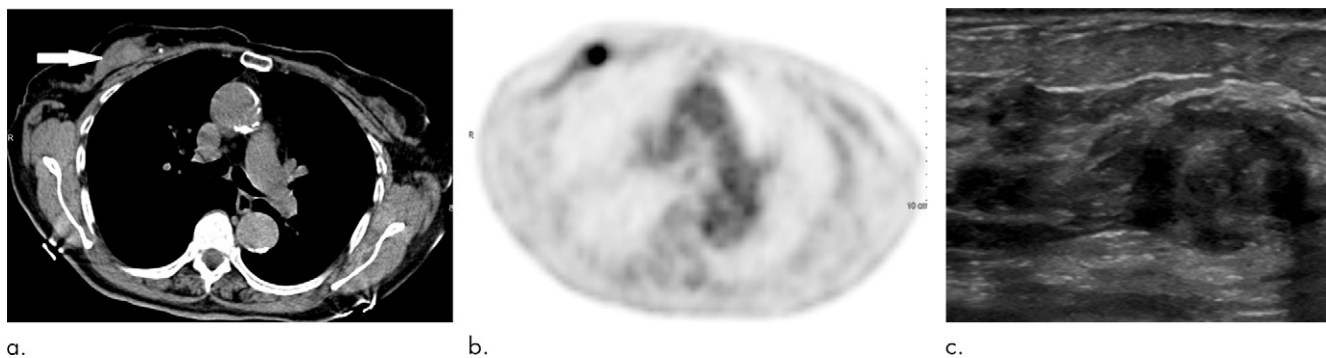
fat necrosis or silicone adenitis cannot be definitively made from a PET scan, the patient should be referred for dedicated breast imaging.

Other benign causes of increased breast uptake on  $^{18}\text{F}$ -FDG PET/CT scans include mastitis, fibroadenomas, and gynecomastia (18). Mastitis will have diffuse uptake in the areas involved. Fibroadenomas typically demonstrate mild or no FDG uptake; however, they can demonstrate increased FDG uptake mimicking a malignancy. Similarly, gynecomastia generally presents as increased breast tissue at CT and has FDG uptake equal to or less than that of liver, but asymmetric or nodular appearances can mimic breast cancer (18). Breast malignancies have a median standardized uptake value (SUV) of 2.4 and mean maximum SUV ( $\text{SUV}_{\text{max}}$ ) of 3.1 compared with median SUV of 1.5 and mean  $\text{SUV}_{\text{max}}$  1.9 for benign lesions (24,25).

### $^{68}\text{Ga}$ -DOTATATE Imaging

$^{68}\text{Ga}$ -DOTATATE is a relatively new PET radiotracer used for imaging neuroendocrine tumors such as pheochromocytomas, paragangliomas, and meningiomas (26).  $^{68}\text{Ga}$ -DOTATATE binds to somatostatin receptors on the cell surface of neuroendocrine tumor cells, like indium 111 ( $^{111}\text{In}$ )-octreotide, which has been traditionally used in imaging of neuroendocrine tumors (26). Compared with  $^{111}\text{In}$ -octreotide,  $^{68}\text{Ga}$ -DOTATATE has faster uptake, superior resolution, and a lower radiation dose (26). False-positive or physiologic uptake of  $^{68}\text{Ga}$ -DOTATATE can be seen in the pancreatic uncinuate process, inflammation, osteoblastic activity, and splenosis (26).

Up to 50% of breast tumors and other nonneuroendocrine malignancies including papillary thyroid cancer, follicular thyroid adenoma, non-Hodgkin lymphoma, and meningioma



**Figure 6:** A 76-year-old woman underwent fluorine 18 fluorodeoxyglucose PET/CT for evaluation of a pulmonary nodule that **(a, b)** revealed an incidental hypermetabolic right breast mass (arrow). Mammogram revealed extremely dense breasts and a correlate was not identified. **(c)** US image reveals a suspicious 2.0-cm solid, heterogeneous mass. The patient ultimately underwent surgical excision, and pathologic findings revealed right breast metaplastic carcinoma and right lung adenocarcinoma.

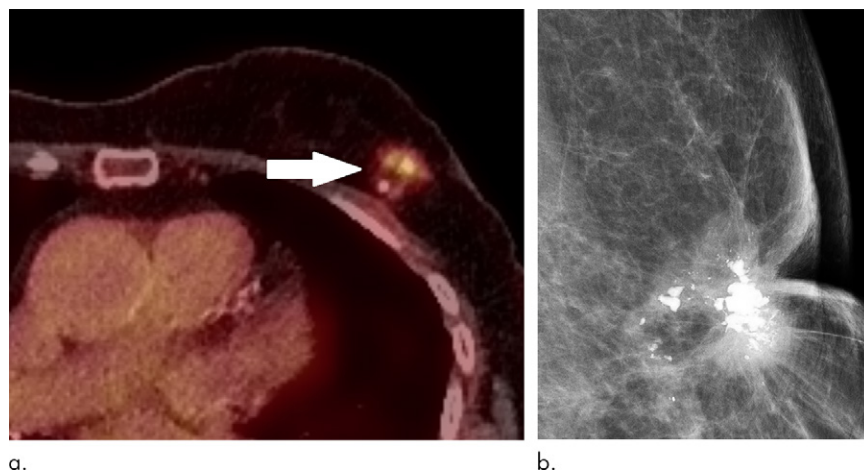
demonstrate increased  $^{68}\text{Ga}$ -DOT-ATATE uptake (27). Metastatic neuroendocrine tumors to the breast can also present as a mass with focally increased  $^{68}\text{Ga}$ -DOTATATE uptake (28). When focal breast uptake is identified, it is important to differentiate a primary breast cancer from a neuroendocrine tumor metastasis for treatment planning purposes (28). An incidentally detected breast cancer at  $^{68}\text{Ga}$ -DOTA-NOC (DOTA 1-Nal3-octreotide) PET/CT, a similar radiotracer analog, may demonstrate  $\text{SUV}_{\text{max}}$  of 3.3, and accompanying metastatic axillary lymph nodes may have an  $\text{SUV}_{\text{max}}$  of 2.8 (29).

Benign breast lesions, such as fibroadenomas, can also demonstrate increased uptake on  $^{68}\text{Ga}$ -DOTATATE scans (Fig 9). Increased uptake in fibroadenomas suggests they express the somatostatin receptor 2, which is targeted by  $^{68}\text{Ga}$ -DOT-ATATE (30). At  $^{68}\text{Ga}$ -DOTATATE PET/CT, these lesions can mimic a primary breast cancer or a neuroendocrine tumor metastasis. If such lesions are identified, correlation with history and imaging is important to avoid unnecessary workup of previously characterized or biopsied masses. Reviewing prior US may help to confirm the typical appearance of a circumscribed, homogeneously hypoechoic mass.

$^{68}\text{Ga}$ -DOTATATE can accumulate in the breasts of lactating women and is then excreted in breast milk. Lactational changes typically appear as diffusely increased mild radiotracer uptake (31). To limit the amount of radiation exposure to the child of a lactating woman undergoing  $^{68}\text{Ga}$ -DOTATATE PET/CT, it is recommended that the patient stop breastfeeding for 4 hours after the study, then express and discard any breast milk prior to resuming breastfeeding (31).

### $^{68}\text{Ga}$ -PSMA Imaging

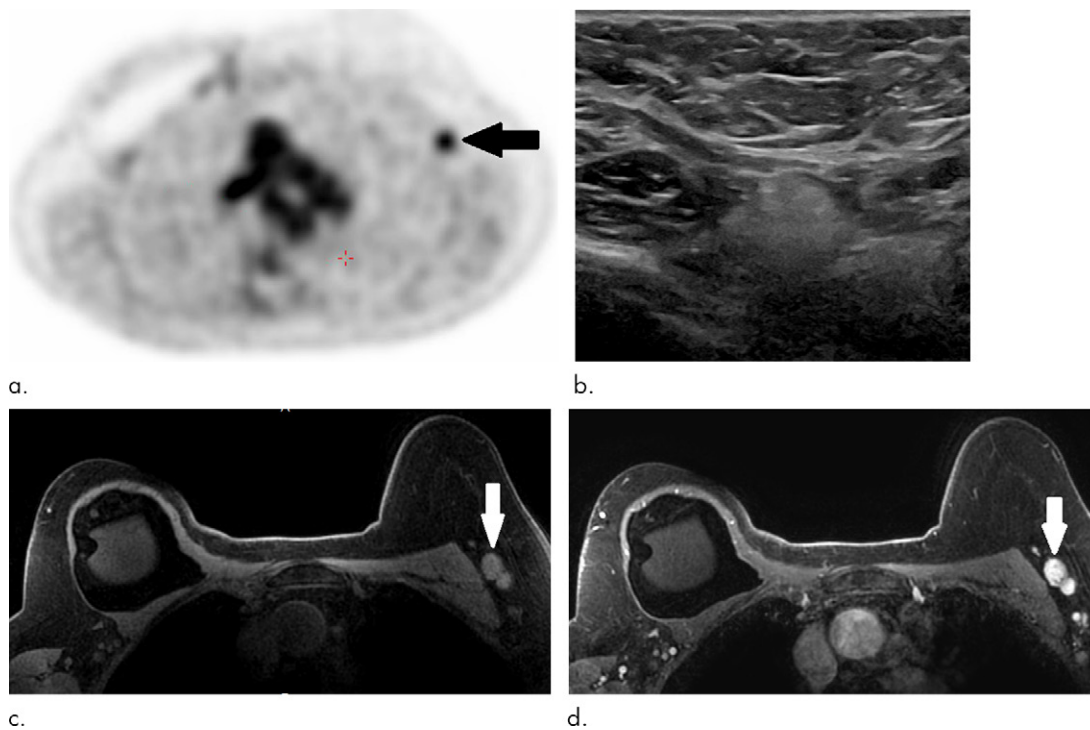
$^{68}\text{Ga}$ -PSMA is another relatively new PET radiotracer that binds to PSMA, expressed on cell membranes of prostate cells.  $^{68}\text{Ga}$ -PSMA demonstrates physiologic uptake in the lacrimal and salivary glands, liver, spleen, small and large bowel,



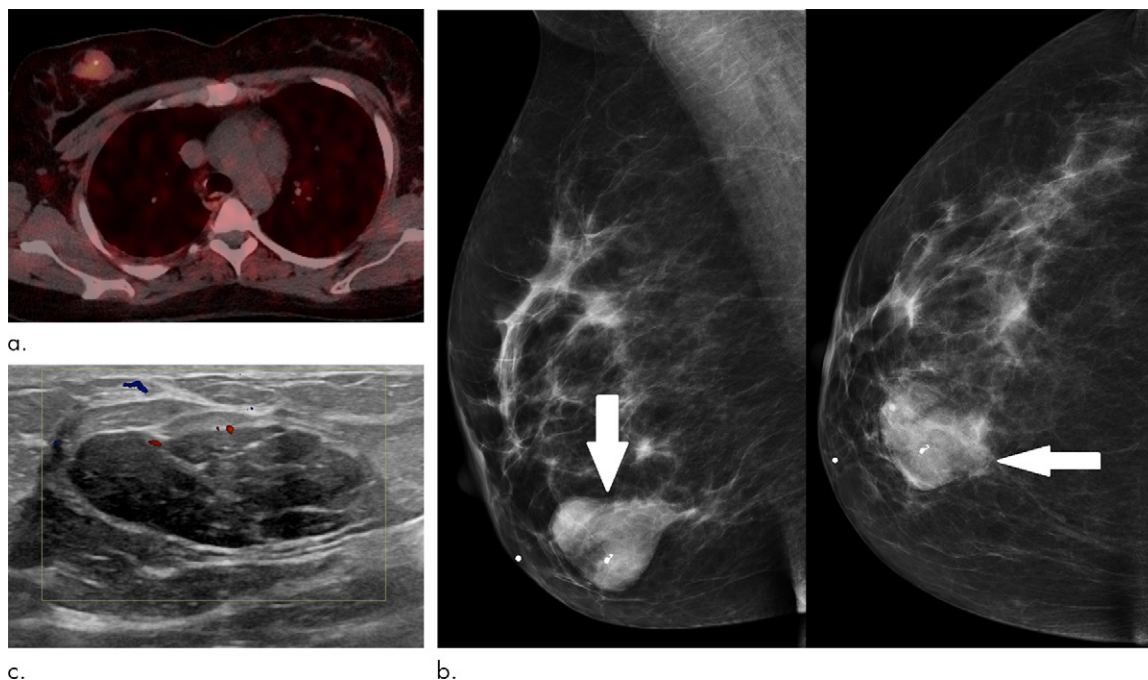
**Figure 7:** A 91-year-old woman with a pulmonary nodule underwent fluorine 18 fluorodeoxyglucose PET/CT that **(a)** demonstrated a hypermetabolic left breast mass (arrow) containing fat and calcifications. **(b)** Further mammographic evaluation demonstrated fat necrosis at a prior lumpectomy site.

and kidney. There is increased expression of PSMA in primary and metastatic prostate cancer (32); however, increased expression can also be found in cancers of the colon, esophagus, thyroid, and lung, as well as renal cell carcinoma and brain tumors (32).  $^{68}\text{Ga}$ -PSMA can also bind to breast cancer and its metastases (33,34). Breast cancer metastases may demonstrate greater uptake of  $^{68}\text{Ga}$ -PSMA compared with the primary tumor (33,34). There is variability in the degree of  $^{68}\text{Ga}$ -PSMA uptake in breast cancers of different patients and among different lesions in the same patient (33,34). As of now, this radiotracer has not yet been approved by the United States Food and Drug Administration and is currently being utilized as part of a clinical trial.

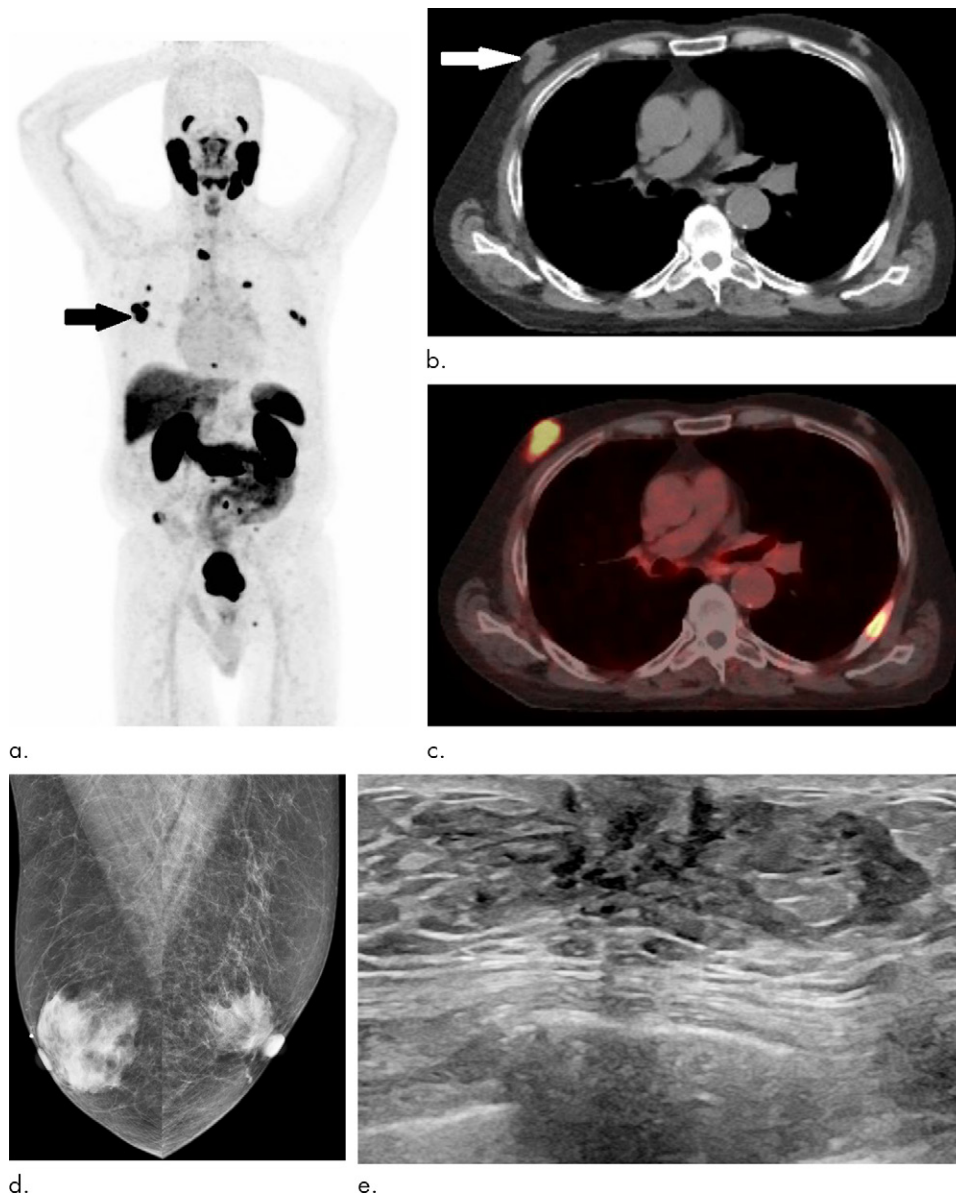
PSMA expression has also been reported in benign conditions such as sarcoidosis, Paget disease of the bone, schwannoma, thyroid adenoma, benign breast tissue, gynecomastia (Fig 10), and pseudoangiomatous stromal hyperplasia (34–36). Gynecomastia is seen in up to 75% of men with prostate cancer undergoing antiandrogen therapy, due to relatively increased amounts of estrogen compared with testosterone, and these patients are often imaged with  $^{68}\text{Ga}$ -PSMA (36). The typical presentation of gynecomastia is bilateral diffuse breast tissue enlargement with moderate uptake of  $^{68}\text{Ga}$ -PSMA (36). To avoid misinterpreting a



**Figure 8:** A 65-year-old woman underwent evaluation for cardiac sarcoidosis with fluorine 18 fluorodeoxyglucose (FDG) PET/CT **(a)** which revealed an FDG-avid left axillary lymph node (black arrow). **(b)** A pacemaker obscured imaging with mammography; however, US demonstrated a 1.5-cm oval hyperechoic mass with snowstorm appearance in the left axilla. **(c)** Comparison with a prior breast MRI from several years ago on T2-weighted with fat saturation and **(d)** T1-weighted with fat saturation postcontrast images demonstrated a stable 1.7-cm left axillary lymph node conglomerate (white arrow). The patient had a silicone-containing double-lumen right breast implant and history of a left silicone breast implant that had been removed. FDG avidity in the left axillary lymph node containing silicone is compatible with silicone adenitis.



**Figure 9:** A 42-year-old woman underwent gallium 68 DOTATATE PET/CT to evaluate for carcinoid. **(a)** No carcinoid tumor was identified; however, a 3.2-cm lobulated right breast mass with increased radiotracer uptake and central high density was identified. **(b)** A prior two-view mammogram demonstrated a well-circumscribed mass containing a clip (arrow), consistent with a biopsy-proven fibroadenoma, stable for 2 years. **(c)** Comparison with prior US confirmed the findings.



**Figure 10:** A 70-year-old man with recurrent prostate cancer and rising prostate-specific antigen level underwent gallium 68–prostate-specific membrane antigen PET/CT to identify metastatic disease. **(a)** Whole-body maximum intensity projection image demonstrates diffuse metastatic disease with increased uptake in the chest, abdomen, and pelvis. **(a, b)** A mass in the right breast (arrow) was found to have intensely increased uptake **(c)**. The patient underwent breast imaging with **(d)** mammography and **(e)** US, which revealed benign asymmetric gynecomastia.

benign breast mass with increased  $^{68}\text{Ga}$ -PSMA uptake as malignant, the lesion should undergo histologic sampling (35).

### $^{18}\text{F}$ -Fluciclovine Imaging

Anti-1-amino-3- $^{18}\text{F}$ -fluorocyclobutane-1-carboxylic acid ( $^{18}\text{F}$ -FACBC) also known as  $^{18}\text{F}$ -fluciclovine (Axumin; Blue Earth Diagnostics, Burlington, Mass) is another relatively new PET radiolabeled amino acid tracer used most commonly for prostate cancer (37). It is taken up by cells through sodium-dependent amino acid transporters. Normal biodistribution demonstrates intense uptake in the liver and pancreas, moderate salivary and pituitary uptake, and variable mild-to-moderate bowel activity (37). Moderate bone marrow and mild muscle activity are present on early images, with decreasing marrow

activity and increasing muscle activity with time (37).  $^{18}\text{F}$ -fluciclovine uptake can occur in benign processes such as infection, inflammation, prostatic hyperplasia, and metabolically active benign bone lesions such as osteoid osteoma (37).

$^{18}\text{F}$ -fluciclovine has also been studied for imaging cerebral gliomas, breast, lung, and head and neck cancers (37). Breast cancer can occur synchronously in patients with recurrent prostate cancer; however, they have different degrees of  $^{18}\text{F}$ -fluciclovine uptake (38). Breast cancers demonstrate significantly increased  $^{18}\text{F}$ -fluciclovine uptake compared with benign lesions such as scarring after therapy, fibroadipose tissue, and fibrocystic change (39,40). Aggressive breast cancers may demonstrate relatively increased uptake and histologic subtypes such as invasive lobular carcinoma may demonstrate increased uptake with  $^{18}\text{F}$ -fluciclovine as



compared with  $^{18}\text{F}$ -FDG (39).  $^{18}\text{F}$ -fluciclovine can detect uptake in nodal and skeletal metastases but is limited in evaluating hepatic metastases due to the high physiologic background uptake (39).

## Conclusion

Many benign and malignant breast lesions may be incidentally detected on scintigraphic and PET nuclear medicine studies. Many new PET radiotracers are being introduced for clinical use which may lead to an increase in the number of incidentally detected breast lesions. Differentiating benign from malignant uptake in the breast and primary breast neoplasms from metastatic lesions is important in guiding clinical management. Familiarity with the imaging appearances of breast lesions on various modalities can help the radiologist make an accurate diagnosis, avoid unnecessary follow-up, and recommend dedicated breast imaging, when appropriate.

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## References

- Ziessman HA, O'Malley JP, Thrall JH. Nuclear medicine: the requisites. Requisites in radiology. 3rd ed. Philadelphia, Pa: Mosby Elsevier, 2006.
- Khalkhali I, Cutrone J, Mena I, et al. Technetium-99m-sestamibi scintimammography of breast lesions: clinical and pathological follow-up. *J Nucl Med* 1995;36(10):1784–1789.
- American College of Radiology. ACR Practice Parameter for the Performance of Molecular Breast Imaging (MBI) Using a Dedicated Gamma Camera. Reston, Va: American College of Radiology, 2017.
- Meissnitzer T, Seymer A, Keinrath P, et al. Added value of semi-quantitative breast-specific gamma imaging in the work-up of suspicious breast lesions compared to mammography, ultrasound and 3-T MRI. *Br J Radiol* 2015;88(1051):20150147.
- Lee JS, Kim SJ, Kim IJ, et al. Characterization of breast lesion using double phase Tc-99m Tetrofosmin scintimammography: comparison of visual and quantitative analyses. *Eur J Radiol* 2006;57(1):76–80.
- Shen YY, Wu YC, Kao CH, Hsieh TC. Huge primary soft tissue sarcoma of the breast on bone scan. *Clin Nucl Med* 2014;39(1):99–101.
- Basu S, Moghe SH, Shet T. Metastasis of humeral osteosarcoma to the contralateral breast detected by 99mTc-MDP skeletal scintigraphy. *Jpn J Radiol* 2009;27(10):455–457.
- Momoi H, Wada Y, Sarumaru S, et al. Primary osteosarcoma of the breast. *Breast Cancer* 2004;11(4):396–400.
- Burnett KR, Lyons KP, Brown WT. Uptake of osteotropic radionuclides in the breast. *Semin Nucl Med* 1984;14(1):48–49.
- Piccolo S, Lastoria S, Mainolfi C, Muto P, Bazzicalupo L, Salvatore M. Technetium-99m-methylene diphosphonate scintimammography to image primary breast cancer. *J Nucl Med* 1995;36(5):718–724.
- Oh JR, Ahn BC. False-positive uptake on radioiodine whole-body scintigraphy: physiologic and pathologic variants unrelated to thyroid cancer. *Am J Nucl Med Mol Imaging* 2012;2(3):362–385.
- Bakheet SM, Hammami MM. Patterns of radioiodine uptake by the lactating breast. *Eur J Nucl Med* 1994;21(7):604–608.
- Itani M, Lewis DH. I-131 uptake in fat necrosis of the breast. *Radiol Case Rep* 2016;12(1):161–167.
- Eskin BA, Parker JA, Bassett JG, George DL. Human breast uptake of radioactive iodine. *Obstet Gynecol* 1974;44(3):398–402.
- Annibaldi A, Widmann C. Glucose metabolism in cancer cells. *Curr Opin Clin Nutr Metab Care* 2010;13(4):466–470.
- Gallagher BM, Fowler JS, Gutterson NI, MacGregor RR, Wan CN, Wolf AP. Metabolic trapping as a principle of oradiopharmaceutical design: some factors responsible for the biodistribution of [18F] 2-deoxy-2-fluoro-D-glucose. *J Nucl Med* 1978;19(10):1154–1161.
- Smith TA. FDG uptake, tumour characteristics and response to therapy: a review. *Nucl Med Commun* 1998;19(2):97–105.
- Dong A, Wang Y, Lu J, Zuo C. Spectrum of the Breast Lesions With Increased  $^{18}\text{F}$ -FDG Uptake on PET/CT. *Clin Nucl Med* 2016;41(7):543–557.
- Berg WA. Nuclear Breast Imaging: Clinical Results and Future Directions. *J Nucl Med* 2016;57(Suppl 1):46S–52S.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Plymouth Meeting, Pa: National Comprehensive Cancer Network, 2018.
- Rosen EL, Eubank WB, Mankoff DA. FDG PET, PET/CT, and breast cancer imaging. *RadioGraphics* 2007;27(Suppl 1):S215–S229.
- Adejolu M, Huo L, Rohren E, Santiago L, Yang WT. False-positive lesions mimicking breast cancer on FDG PET and PET/CT. *AJR Am J Roentgenol* 2012;198(3):W304–W314.
- Taboada JL, Stephens TW, Krishnamurthy S, Brandt KR, Whitman GJ. The many faces of fat necrosis in the breast. *AJR Am J Roentgenol* 2009;192(3):815–825.
- Beatty JS, Williams HT, Gucwa AL, et al. The predictive value of incidental PET/CT findings suspicious for breast cancer in women with non-breast malignancies. *Am J Surg* 2009;198(4):495–499.
- Litmanovich D, Gourevich K, Israel O, Gallimidi Z. Unexpected foci of  $^{18}\text{F}$ -FDG uptake in the breast detected by PET/CT: incidence and clinical significance. *Eur J Nucl Med Mol Imaging* 2009;36(10):1558–1564.
- Hofman MS, Lau WF, Hicks RJ. Somatostatin receptor imaging with 68Ga DOTATATE PET/CT: clinical utility, normal patterns, pearls, and pitfalls in interpretation. *RadioGraphics* 2015;35(2):500–516.
- Yamaga LYL, Wagner J, Funari MBG. 68Ga-DOTATATE PET/CT in Non-neuroendocrine Tumors: A Pictorial Essay. *Clin Nucl Med* 2017;42(6):e313–e316.
- Acar E, Durak H, Kabukcuoğlu S, İşiksoy S, Kaya GÇ. Retro-orbital, Breast, Cardiac, Skin, and Subcutaneous Metastases of Neuroendocrine Tumor From a Tail Gut Cyst on 68Ga-DOTATATE PET/CT Imaging. *Clin Nucl Med* 2017;42(5):364–367.
- Sampaio Vieira T, Borges Faria D, Souto Moura C, Francisco E, Barroso S, Pereira de Oliveira J. Incidental finding of a breast carcinoma on Ga-68-DOTA-1-Nal3-octreotide positron emission tomography/computed tomography performed for the evaluation of a pancreatic neuroendocrine tumor: A case report. *Medicine (Baltimore)* 2018;97(36):e11878.
- Papadakis GZ, Millo C, Sadowski SM, Karantanas AH, Bagci U, Patronas NJ. Breast Fibroadenoma With Increased Activity on 68Ga DOTATATE PET/CT. *Clin Nucl Med* 2017;42(2):145–146.
- Forwood NJ, Kanthan GL, Bailey DL, Chan DL, Schembri GP. 68Ga-DOTATATE Breast Uptake and Expression in Breast Milk. *Clin Nucl Med* 2016;41(8):654–655.
- Fendler WP, Eiber M, Beheshti M, et al. 68Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0. *Eur J Nucl Med Mol Imaging* 2017;44(6):1014–1024.
- Satheke M, Lengana T, Modiselle M, et al. 68Ga-PSMA-HBED-CC PET imaging in breast carcinoma patients. *Eur J Nucl Med Mol Imaging* 2017;44(4):689–694.
- Kasoha M, Unger C, Solomayer EF, et al. Prostate-specific membrane antigen (PSMA) expression in breast cancer and its metastases. *Clin Exp Metastasis* 2017;34(8):479–490.
- Malik D, Basher RK, Mittal BR, Jain TK, Bal A, Singh SK. 68Ga-PSMA Expression in Pseudoangiomatous Stromal Hyperplasia of the Breast. *Clin Nucl Med* 2017;42(1):58–60.
- Sasikumar A, Joy A, Nair BP, Pillai MRA, Madhavan J. False Positive Uptake in Bilateral Gynecomastia on 68Ga-PSMA PET/CT Scan. *Clin Nucl Med* 2017;42(9):e412–e414.
- Schuster DM, Nanni C, Fanti S, et al. Anti-1-amino-3- $^{18}\text{F}$ -fluorocyclobutane-1-carboxylic acid: physiologic uptake patterns, incidental findings, and variants that may simulate disease. *J Nucl Med* 2014;55(12):1986–1992.
- Gill HS, Tade F, Greenwald DT, Yonover PM, Savir-Baruch B. Metastatic Male Breast Cancer With Increased Uptake on  $^{18}\text{F}$ -Fluciclovine PET/CT Scan. *Clin Nucl Med* 2018;43(1):23–24.
- McConathy J.  $^{18}\text{F}$ -Fluciclovine (FACBC) and Its Potential Use for Breast Cancer Imaging. *J Nucl Med* 2016;57(9):1329–1330.
- Tade FI, Cohen MA, Sryblo TM, et al. Anti-3- $^{18}\text{F}$ -FACBC ( $^{18}\text{F}$ -Fluciclovine) PET/CT of Breast Cancer: An Exploratory Study. *J Nucl Med* 2016;57(9):1357–1363.