REVIEW

Blind spots at oncological CT: lessons learned from PET/CT

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Date accepted for publication 28 May 2012

Abstract

Improved accuracy in oncological computed tomography (CT) could lead to a decrease in morbidity and improved survival for oncology patients. Visualization of metabolic activity using the glucose analogue [^{18}F]fluorodeoxyglucose (FDG) in combination with the high anatomic resolution of CT in an integrated positron emission tomography (PET)/CT examination has the highest sensitivity and specificity for the detection of primary and metastatic lesions. However, PET/CT costs are high and patient access is limited; thus CT remains the primary imaging modality in oncology patients. We have noted that subtle lesions are more easily detected on CT by radiologists with PET/CT experience. We aimed to provide a brief review of the literature with comparisons of multi-detector computed tomography (MDCT) and PET/CT in primary and metastatic disease with an emphasis on findings that may be overlooked on MDCT in cancer of the breast, lung, colon, and ovaries, and in melanoma, as well as thrombosis in oncology patients. We further reviewed our experience for illustrative comparisons of PET/CT and MDCT studies. Experience in interpreting conventional CT scans alongside PET/CT can help the reader develop an appreciation for the subtle appearance of some lesions on CT that might otherwise be missed. This could improve detection rates, reduce errors, and improve patient management.

Keywords: *Oncological imaging; neoplasms; diagnosis; computed tomography; positron emission tomography/computed tomography; diagnostic errors; prevention and control.*

Introduction

Imaging evaluation of patients with cancer makes up a substantial portion of the workload in radiology departments[1]. Discordant interpretations of computed tomography (CT) scans are common and have been reported in 31–37% of patients, while multicenter trials have reported changes in patient management due to discordant readings in up to 23% of patients[2,3]. In addition, since medical malpractice lawsuits filed against imaging specialists are related to missed diagnoses in 70% of cases, with cancer-related claims being the most frequent[4], improved accuracy in the interpretation of oncological CT studies could reduce legal challenges in radiology departments.

In a study of the variables influencing the accuracy of interpretation of abdominal CT studies, Loughrey et al.[5] found that the only contributing factor to reach statistical significance was the skill of the individual radiologist. Simultaneous supervision of interventional procedures, level of training of the assigned resident physician, and tumor type did not influence the error rate. Accuracy of interpretation of imaging studies in general is also improved when the interpreting physician has access to appropriate clinical findings, and when current studies are compared with previous examinations. Computer-

aided detection tools may also improve diagnostic accuracy in some clinical settings[4].

Suboptimal imaging techniques are also a signficant cause of error in oncologic CT. Standardization of imaging protocols that use intravenous and oral contrast material may thus also improve diagnostic accuracy[6].

Furthermore, images should be analyzed systematically. Particular attention should be paid to known problem areas and pitfalls specific to the underlying disease[6]. It is also important to carefully assess blind spots in patients with primary tumors and metastatic disease.

Over the past 15 years, visualization of metabolic activity using the glucose analogue [18F]fluorodeoxyglucose (FDG) in combination with the high anatomic resolution of CT in a single integrated positron emission tomography (PET)/CT examination has shown increasing importance in the diagnosis, staging and follow-up of a wide range of malignant diseases[7]. However, the cost of PET/CT remains high and patient access is limited. Radiologists who are familiar with the appearance of lesions on PET/CT may come to better appreciate how these subtle lesions appear on CT, as many of the areas that are easily missed are FDG avid. If these CT scans were being read without the added experience from PET/CT, these findings would probably not have been picked up on CT. Familiarity with PET/CT may thus improve detection rates and avoid errors.

In this article, we present regions of primary and metastatic disease that can be missed on multi-detector computed tomography (MDCT). In our experience, these blind spots and overlooked regions are more easily detected on CT by a reader who is experienced in reading PET/CT.

Figure 1   **A 55-year-old woman with breast cancer. (a) CT scan demonstrates a rounded soft tissue area seen in the lateral part of the right breast. (b) PET/CT demonstrates increased FDG uptake, compatible with breast cancer.**

Breast cancer

Breast cancer is the most common form of cancer and the second most common cause of cancer-related deaths in women. In 2009, approximately 190,000 new cases of breast cancer were diagnosed in the United States and over 40,000 women died of the disease[8]; the incidence in Europe is 94.3 per 100,000 women[9]. While mammography is the most efficient way to screen for primary breast cancers, the ability to spot primary breast lesions and metastases on routine CT scans is important, as this may lead to a diagnosis before the patient would have otherwise come to medical attention[10], and improve the accuracy of staging for patients with a breast cancer diagnosis.

CT scans may demonstrate incidental findings that must be identified as either pathologic or benign. Moyle et al.[11] reported a 30% rate of malignancy in patients referred to a breast clinic for assessment of incidental breast lesions detected on CT. Lesion spiculation and irregularity were strongly suggestive of malignancy, while calcification patterns did not aid in the diagnosis.
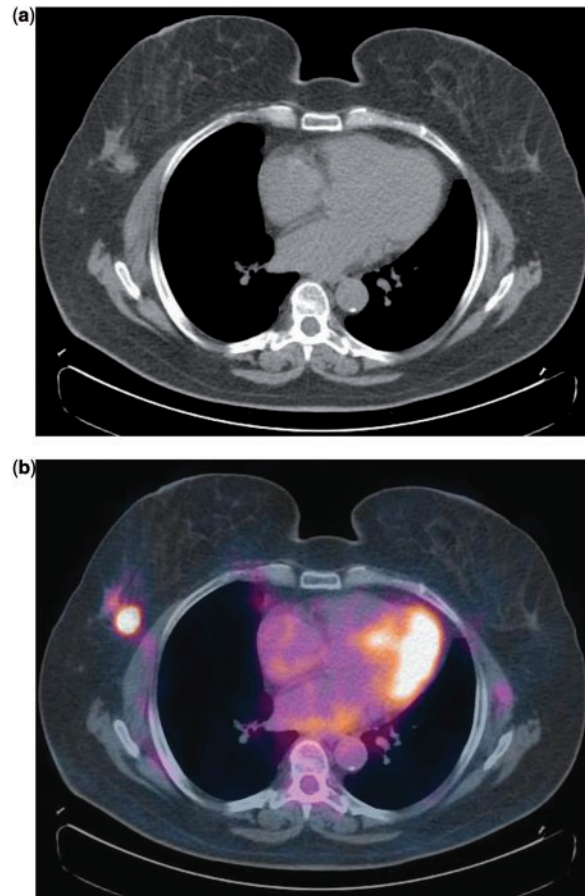
Malignant lesions were significantly larger than benign lesions.

Detecting breast malignancies on CT and differentiating them from normal breast parenchyma is challenging, and breast lesions can be missed. PET/CT has the ability to demonstrate primary breast tumors very clearly[12]. A side-by-side comparison of breast lesions on CT and fused PET/CT is presented in Fig. 1.

The presence of distant metastasis in patients with breast cancer is a key prognostic factor. CT is a useful modality for detecting metastases, with a sensitivity of 83% and a specificity of 85%, while PET has sensitivity and specificity of 87% and 83% respectively[13]. Although the diagnostic accuracy of the two modalities is similar, they are complementary. Combined PET/CT harnesses this complementary nature, and improves diagnostic accuracy[12]. Blind spots that are most often overlooked on CT are metastases to the bone and lymph nodes, especially internal mammary, retropectoral, mediastinal, and axillary lymph nodes[12]. Thus, special attention should be paid to these areas when reviewing CT scans
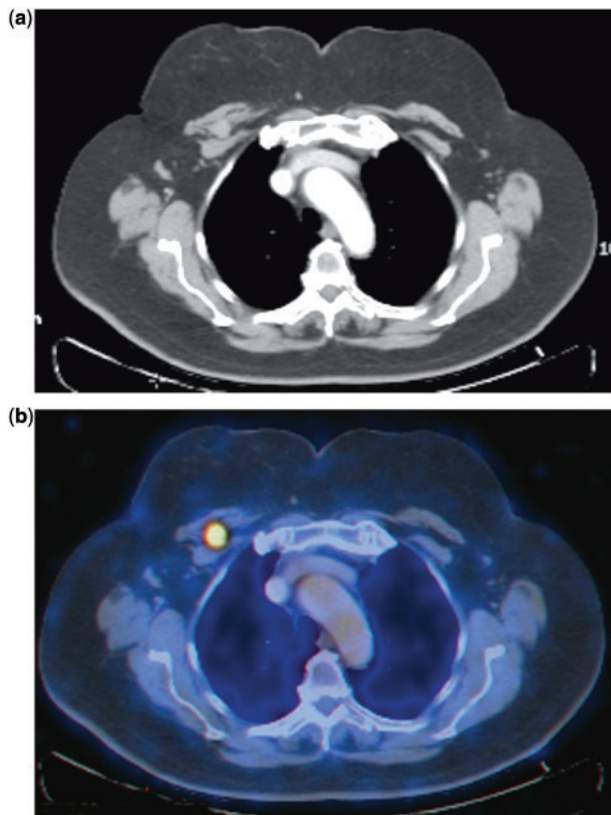
Figure 2 **A 53-year-old woman with breast cancer. (a) CT reveals an enlarged rounded lymph node secondary to breast cancer spread between the pectoralis muscles. (b) The lymph node is visible as an area of increased FDG uptake on PET/CT.**

of a breast cancer patient. PET/CT effectively demonstrates metastases in these regions (Figs. 2 and 3).

Lung cancer

In Europe and the United States, lung cancer is the second most frequently diagnosed primary malignancy and the leading cause of cancer-related mortality for both men and women. There were 220,000 new cases and 160,000 deaths in 2009 in the United States[8]. The incidence in Europe in 2006 was 75.3 and 18.3 per 100,000 in men and women, respectively[9]. In detecting primary lung cancer lesions on CT, certain areas are commonly overlooked. White et al.[14] studied the characteristics of 15 primary lung cancers that were overlooked in 14 patients. The missed tumors were primarily endobronchial and lower lobe lesions. Unrelated major abnormalities were also a factor in overlooked cases. Li et al.[15] reviewed the characteristics of 32 lung cancers missed on low-dose helical CT screening. The missed tumors were found in all lobes of the lungs, often in the central region, with some lesions overlapping with hilar structures. In many patients, there was
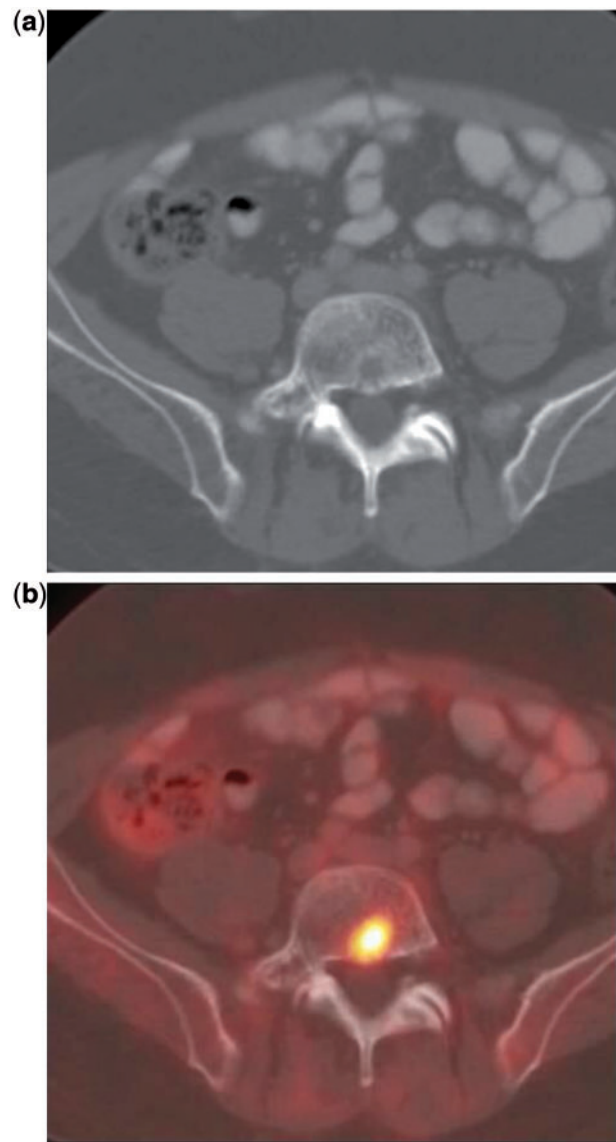

Figure 3 **A 62-year-old woman with breast cancer. (a) CT reveals a subtle bone metastasis causing disruption of the posterior border of the L5 body. (b) The lesion is illustrated clearly on PET/CT due to its increased FDG uptake.**

underlying lung disease, and other more obvious lesions were identified while the lung cancer was missed.

Small cell lung cancer is assumed to have metastasized at presentation, thus detection of metastases is less relevant to surgical decision making. However, determining whether non-small cell lung cancer has metastasized is central for treatment decisions and prognosis. In comparison with PET and CT individually, PET/CT was shown to improve the diagnostic accuracy of tumor, node, and distant metastasis (TNM) staging for non-small cell lung cancer. Antoch et al.[16] reported overall TNM staging accuracy in 96% of patients with PET/CT, 70% with CT alone, and 74% with PET alone. Assessment of
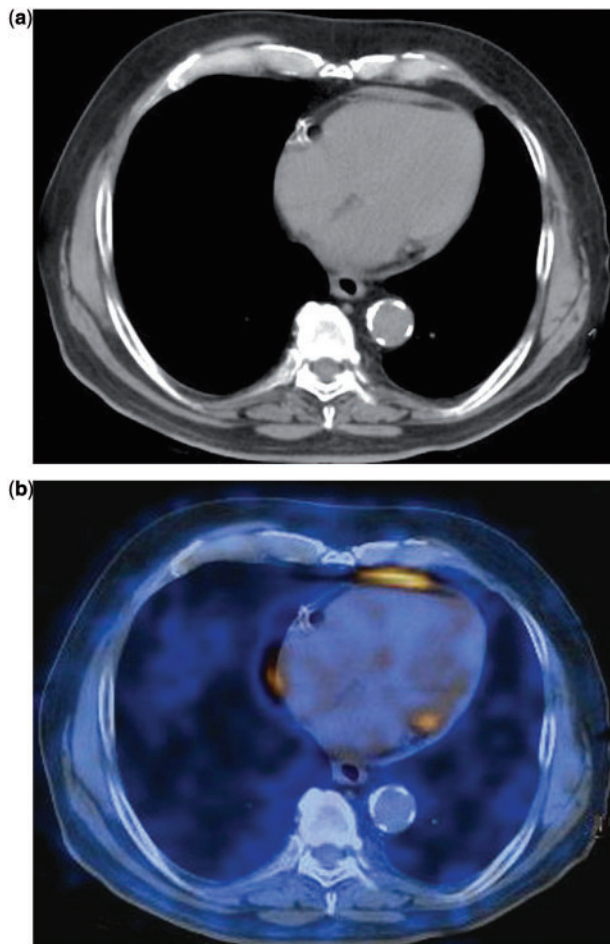
Figure 4 **A 59-year-old man with lung cancer. (a) CT demonstrates pericardial thickening. (b) PET/CT reveals increased FDG uptake, indicating that metastatic cancer is the cause of this thickening.**

mediastinal lymph node involvement had an accuracy of 93%, 63%, and 89%, respectively, for PET/CT, CT alone, and PET alone. Lardinois et al.[17] found correct and unequivocal classification of tumor extent in 88% with PET/CT versus 58% with CT and 40% with PET; lymph nodes were accurately staged in 81% with PET/CT versus 59% and 49% with CT and PET, respectively.

The heart or pericardium was involved in 17–31% of lung cancer patients in autopsy studies[18]. Tumor extension to the heart, pericardium, or great vessels may affect TNM classification and decisions on patient management. The differential diagnosis includes malignant pericardial effusion, inflammation, fibrosis due to radiation therapy, drug-induced pericarditis, infection, and other causes. Findings on CT may be subtle[19]. A comparison of classic presentation of pericardial thickening associated with tumor extension on CT and PET/CT is found in Fig. 4.

The lung pleura is another area where primary and metastatic lung tumors are found. Metastatic adenocarcinoma is the most common malignancy in the pleura,
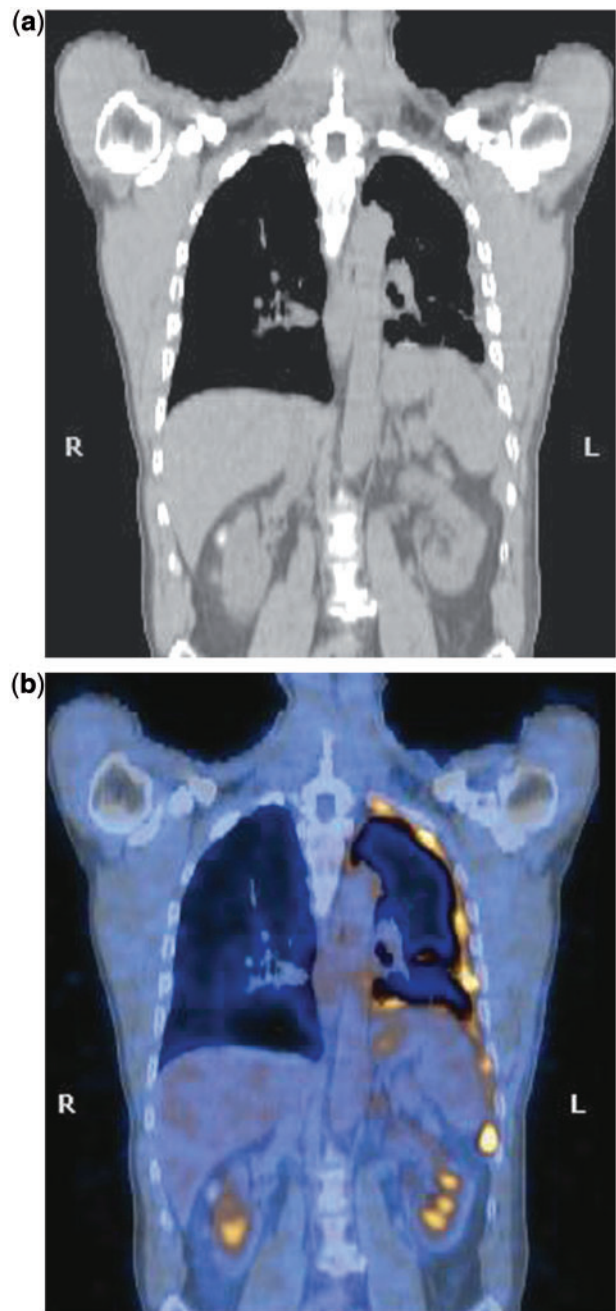

Figure 5 **A 47-year-old man with lung cancer. (a, c) CT reveals nodularity and thickening of the pleura. (b, d) Note increased uptake indicating malignancy on the PET/CT views.**

while mesothelioma is the more frequently diagnosed primary malignancy. CT can be used for the identification of these pleural masses, but radiological findings can be subtle[20]. There are several criteria that help differentiate between benign and malignant pleural disease on CT. These include circumferential or nodular pleural thickening, thickening greater than 1 mm, and mediastinal pleural involvement[21] (Fig. 5).
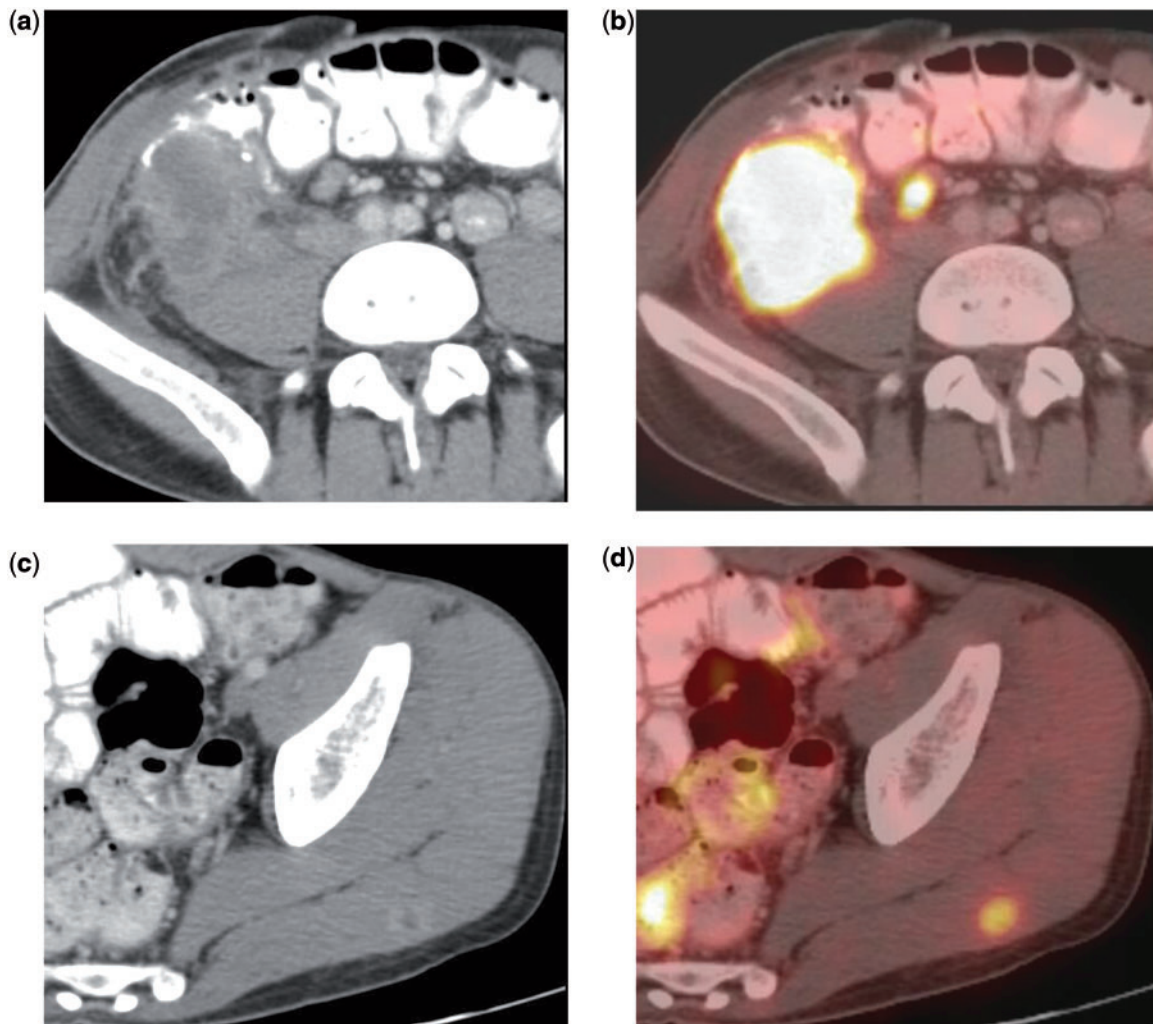
Figure 6 **A 62-year-old woman with locally advanced cancer of the right colon. (a, b) CT shows invasion of adjacent structures, which is depicted easily on PET/CT. (c, d) CT reveals a subtle skeletal mass with increased FDG uptake on PET/CT. Discovery of this metastasis led to restaging of the patient.**

Once integrated PET/CT becomes more widely available, it may become the optimal tool for non-invasive staging of non-small cell lung cancer. However, CT currently plays a significant role in staging and restaging, since it is more accessible and less expensive than PET and PET/CT. As such, an appreciation for lesions that are subtle on CT is important.

Colon cancer

The incidence of colorectal cancer in Europe is 55.4 per 100,000 in men, 34.6 per 100,000 in women[9]. In the United States, colorectal cancer is the third most common cancer in both men and women, with approximately 147,000 new cases diagnosed and 50,000 deaths in 2009[8]. With the exception of virtual colonoscopy, PET, CT, and PET/CT have limited roles in the primary diagnosis of colon cancer; however they have important roles in staging, assessing response to treatment, and detecting recurrence.

In a series of 38 patients, Kantorova et al.[22] reported CT and PET sensitivity for the detection of primary colorectal tumors at 49% and 95%, respectively, of lymph node involvement as 0% and 29%, and sensitivity for liver metastases as 67% and 78%. The authors provided no information regarding CT protocols. In an earlier study, CT sensitivity in the detection of liver metastases was 38% and specificity was 97%, versus sensitivity and specificity of 88% and 100% for PET[23].

Selzner et al.[24] compared findings for contrast-enhanced CT and PET/CT in 76 patients with metastatic colorectal cancer. They reported 53% and 93% sensitivity of CT and PET/CT, respectively, for detection of local recurrence at the primary colorectal site. CT and PET/CT had comparable sensitivity for detection of intrahepatic masses; however PET/CT was more successful in detecting intrahepatic recurrences following
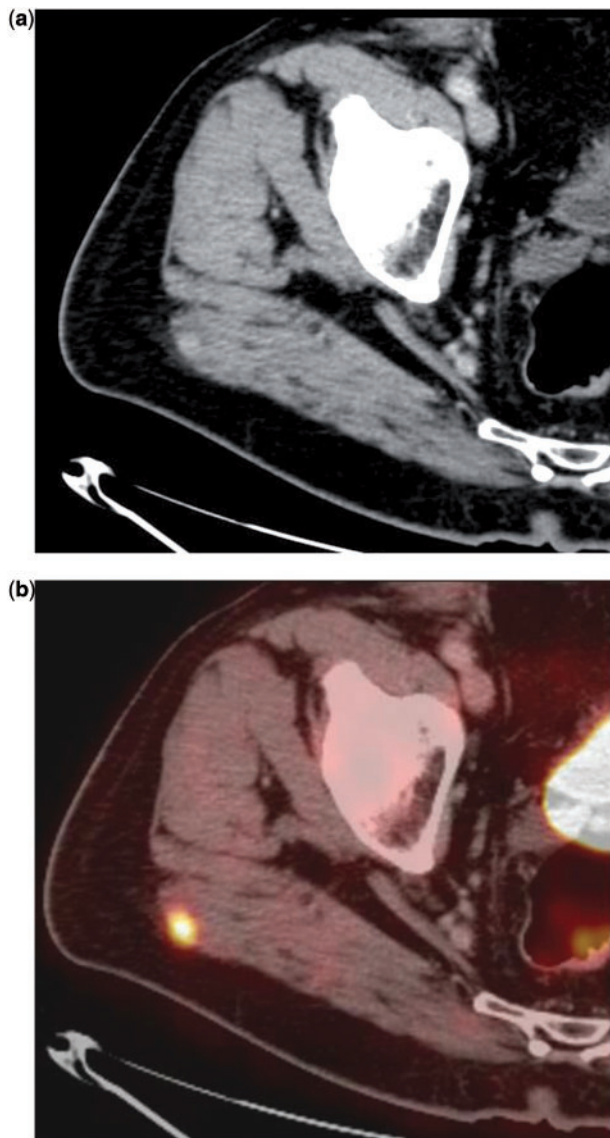
Figure 7 **A 45-year-old man with cancer of the colon. (a) Metastasis to the gluteal muscle is very subtle on CT. Muscular metastases are often seen as small enhancing nodules, only on retrospective analysis. (b) The lesion is more clearly demarcated on PET/CT.**

hepatectomy. Extrahepatic metastases in colorectal cancer patients were detected with 64% sensitivity by contract CT versus 89% sensitivity with PET/CT.

Picking up local invasion (Fig. 6a,b) as well as subtle metastases of colonic adenocarcinoma to lymph nodes, peritoneum, liver, lungs, skeleton (Fig. 6c,d) and soft tissue (Figs. 7, 8) is important, as their detection may upstage a diagnosis and alter patient management[22,24,25]. Metastases to the skeletal muscle characteristically present as rim-enhancing lesions with central hypoattenuation[26]. PET/CT has good sensitivity for the detection of soft tissue metastases, which may have prognostic implications and provide easily accessible biopsy sites[27].
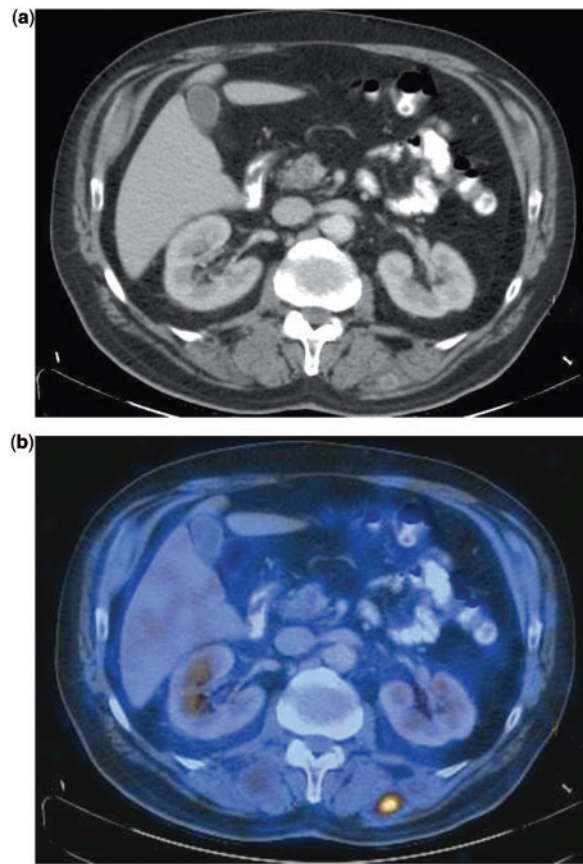

Figure 8 **A 53-year-old man with colon cancer. (a) A subtle metastasis to the lumbar muscle as seen on CT. (b) This lesion is easily visible on PET/CT.**

Ovarian cancer

About 21,500 women in the United States are diagnosed with ovarian cancer each year, with about 14,600 annual deaths from the disease. Most women are diagnosed at a late stage, causing the overall 5-year survival rate to be only 55%[8]. European incidence and mortality in 2008 were reported as 13.5 per 100,000 and 7.6 per 100,000, respectively[28]. Detection of metastases is important for prognosis assessment and treatment planning, as well as for patient follow-up, since 50% of ovarian cancer patients will present with recurrence after first line surgery and chemotherapy. Sebastian et al.[29] found consistently higher sensitivity and accuracy of PET/CT compared with CT for detection of metastases from ovarian tumors in the body, chest, and abdomen.

The most common route of ovarian metastasis is to the peritoneum, which leads to peritoneal carcinomatosis. Detection of carcinomatosis is important, as this may influence a decision to forego or delay surgery in favor of immediate systemic therapy in some patients. Coakley et al.[30] reported sensitivity for the detection of peritoneal implants on spiral CT as 85–93% overall, although sensitivity remained low at 25–50% for metastases 1 cm
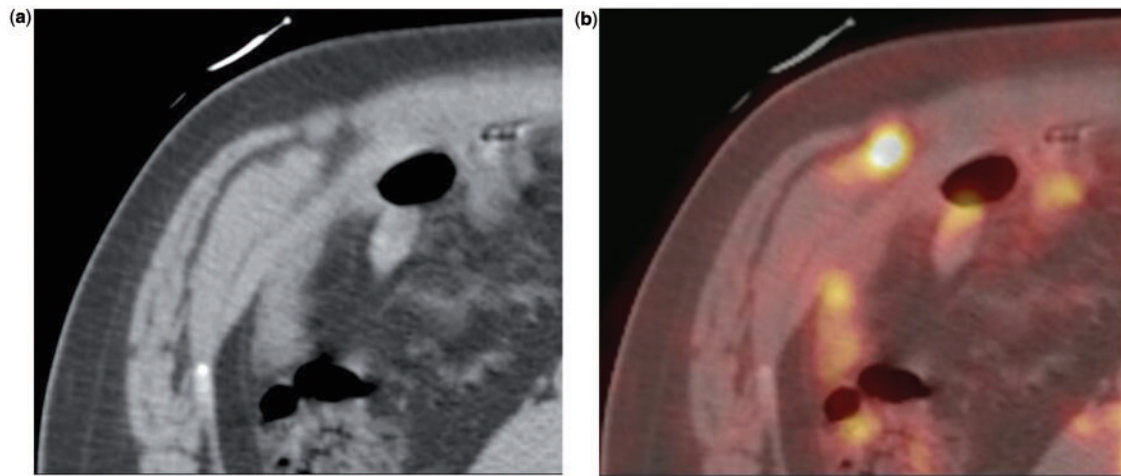
Figure 9 **A 39-year-old woman with ovarian cancer. (a) A very subtle peritoneal metastasis is seen on CT. (b) The lesion is well illustrated on PET/CT.**
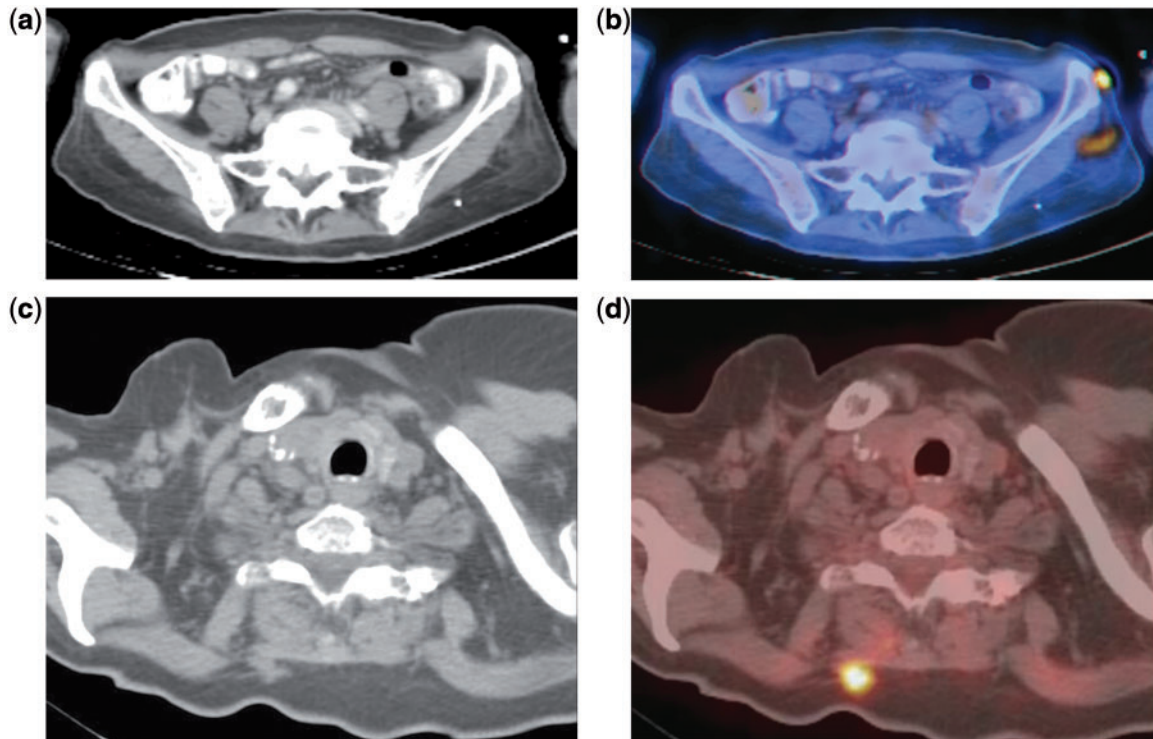

Figure 10 **A 51-year-old woman with melanoma. (a, c) CT reveals subcutaneous nodules that could easily be overlooked. (b, d) Increased FDG uptake on PET directs the reader to these blind spots.**

and smaller. Interobserver variability in detecting the smaller lesions was significant, showing the challenges inherent in accurate assessment of these patients with CT.

The best CT criteria for identification of peritoneal metastasis is the presence of a nodular, plaque-like, or infiltrative soft tissue lesion in the peritoneal fat or on the peritoneal surface[31]. The presence of ascites, parietal peritoneal thickening, or small bowel thickening may also indicate peritoneal metastases[32]. Fig. 9 illustrates the presentation of a subtle peritoneal metastasis on CT and PET/CT.
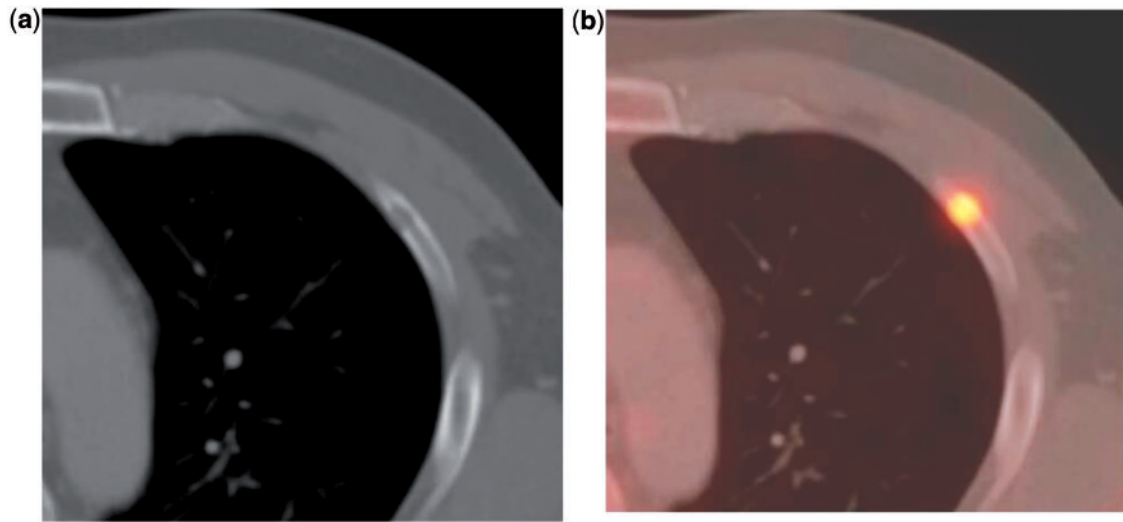
Figure 11 **A 63-year-old man with melanoma. (a) A tiny lytic lesion to the rib cage, consistent with melanoma metastasis, is seen on CT. (b) On PET/CT the lesion is clearly demonstrated.**

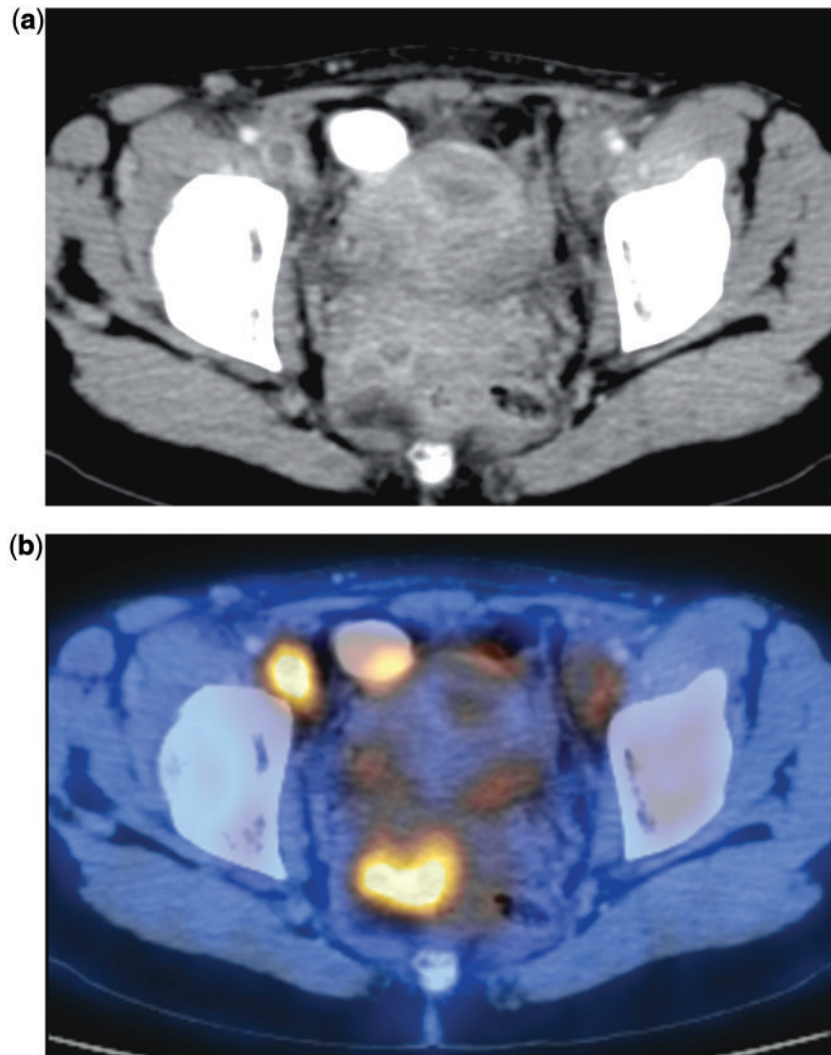
Figure 12 **A 32-year-old woman with advanced-stage melanoma. (a) CT demonstrates a deep vein thrombosis in the right common femoral vein. (b) On PET/CT this lesion is seen as an area of increased FDG uptake, indicating its malignant nature.**

Melanoma

European incidence for melanoma was reported as 11.3 per 100,000 in 2008[28]. The incidence in the United States is rising, with 69,000 new cases and 9000 deaths in 2009[8]. PET, PET/CT and CT imaging are not used for initial diagnosis, which is usually made clinically. Sentinel node biopsy remains the gold standard for assessment of regional spread in patients with stage I or II disease[33].

Patients with stage III or IV melanoma are at high risk for metastasis, which may be detected with CT, PET, or PET/CT. In earlier studies, CT sensitivity and specificity was reported as 55% and 83%, respectively, compared with 94% and 83% for PET[34]. In 2007, Mottaghy et al.[35] reported PET/CT sensitivity was 91%. PET/CT substantially improved lesion localization and characterization. In 13% of patients, this led to a change in clinical staging and oncological management. Fuster et al.[36] found PET alone to be more accurate than CT in detecting skin lesions, malignant lymph nodes, and metastases to the abdomen, liver, and bone.

However, as CT is more readily available and less expensive than PET and combined PET/CT, the ability to detect melanoma metastasis using this modality remains important. The liver, subcutaneous tissue, lymph nodes, and bone are regions where lesions can be especially subtle on CT scans[34,36]. Lesions in these regions are illustrated clearly on PET/CT (Figs. 10 and 11).

Thrombosis

Thrombosis is a significant cause of morbidity and mortality among oncology patients, especially patients with pancreatic and hepatocellular carcinoma[37]. In one report, thrombosis was present in 6.8% of oncologic staging CT scans[38], and another study found a 9% prevalence of pulmonary embolism among inpatients with malignant disease[39]. Certain features on CT suggest malignant versus benign thrombus. These include diameter, generalized enhancement, and neovascularization[40]. On PET/CT scans there is significantly higher FDG uptake in vessels containing thrombi[41], however care is required to distinguish between thrombotic and tumor emboli, and to rule out other potential causes of increased metabolic activity. A comparison of the CT and PET/CT appearance of deep vein thrombosis is shown in Fig. 12.

Conclusion

Experience in PET/CT reading may highlight blind spots when reading oncology CT. It is not our intent to underestimate the routine use of PET/CT in oncology patients, but rather to bring illustrative cases in which familiarity with the presentation of malignant lesions on PET/CT may improve the ability to detect subtle changes on MDCT when it is used as the sole imaging tool for staging or follow-up of oncology patients. Based on experience with PET/CT, radiologists can be better prepared to identify subtle and readily overlooked lesions when only CT is available, thus avoiding errors and helping to improve patient management.

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