^{18}F-FDG PET/CT: Normal Variants, Artefacts, and Pitfalls in Colorectal Cancer

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5.1 Introduction

Colorectal cancer is the third most common cancer worldwide and the second most common cancer in Europe. The role of ^{18}F-FDG (FDG) PET/CT in suspected recurrence, in patients with liver metastases eligible for surgical management, and in treatment response evaluation in colorectal carcinoma is now well established with more data emerging in initial staging of colorectal cancer [1]. FDG PET/CT can influence the management strategies in colorectal patient in up to 30% of the cases [2]. In this context, adequate understanding of the physiological variants, possible artefacts, as well as imaging pitfalls of FDG PET/CT in colorectal carcinoma patients is extremely important.

5.2 Physiological Variants

A thorough understanding of sites of physiological uptake in abdomen and pelvis (Fig. 5.1) is an essential prerequisite to interpret FDG PET/CT scans in colorectal carcinoma. Physiologically increased FDG uptake is seen in the diaphragmatic cruces in conditions of increased abdominal breathing effort (Fig. 5.2). Perhaps FDG uptake in the gastrointestinal tract is the most variable (Fig. 5.3) ranging from no

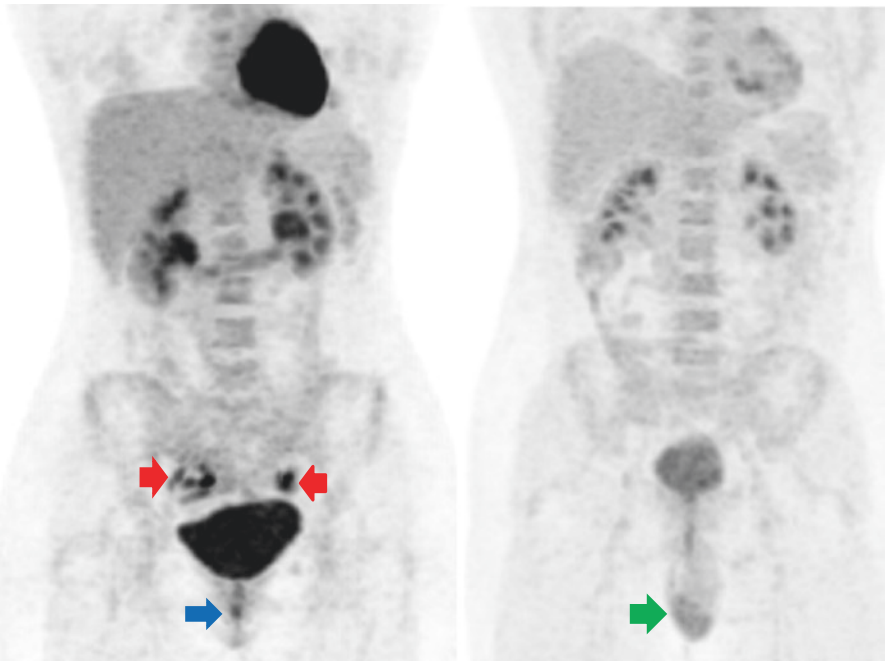

Fig. 5.1 Physiological FDG uptake in the abdomen and pelvis: Usually most intense FDG activity is noted in the pelvicalyceal system, ureters, and urinary bladder. Physiological but less intense FDG uptake is noted in the liver, spleen, bone marrow, and renal cortices. Physiological (variable) FDG uptake may be seen in the uterus and ovaries (*red arrows*) depending on the phase of menstrual cycle. Physiological (low to moderate grade) FDG uptake may be seen in the testes (*green arrow*). Focal FDG uptake at the anus (*blue arrow*) is due to sphincter activation or local inflammation

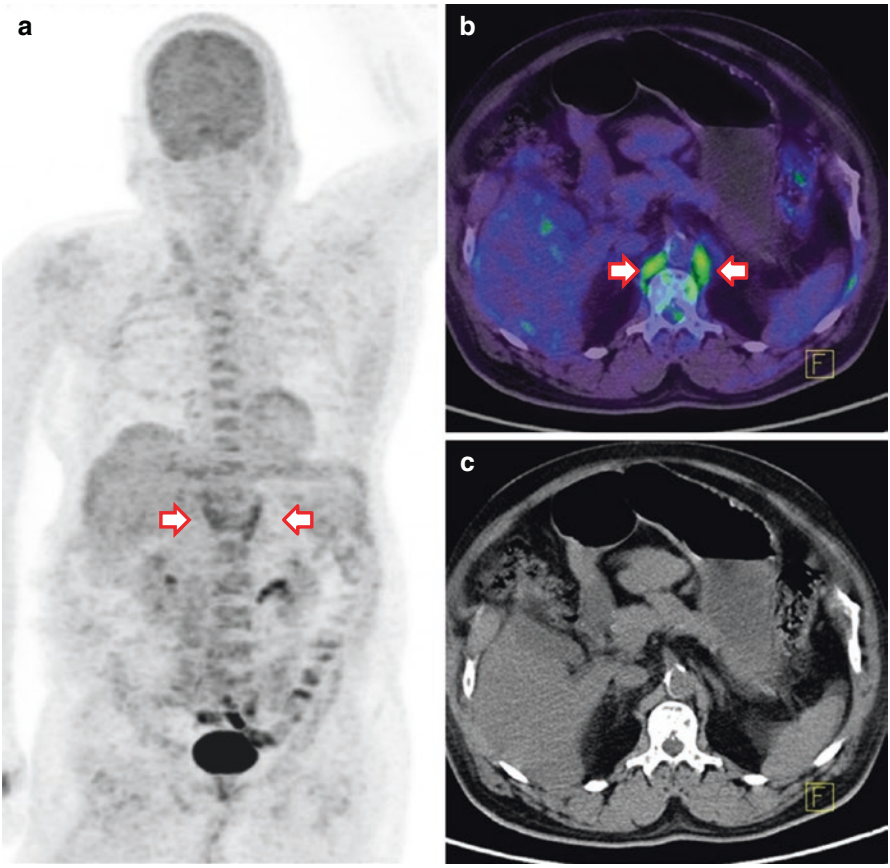

Fig. 5.2 FDG uptake in bilateral diaphragmatic cruses (**a - MIP**). Physiological nature of the uptake can be ascertained by the symmetrical nature of FDG uptake (**b**) and absence of any lesion in the CT part (**c**)

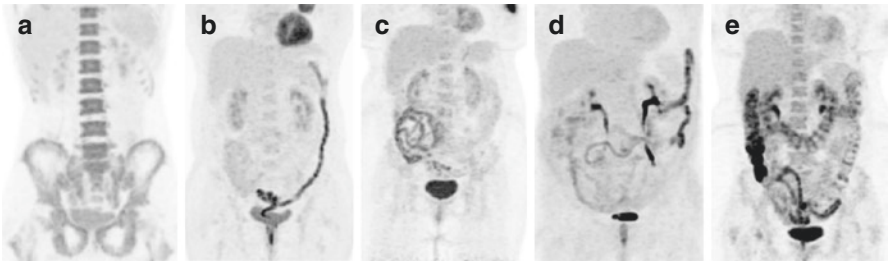

Fig. 5.3 Physiological uptake pattern in large and small bowel. It can range from absent uptake (**a**) to segmental (**b**, **c**), patchy (**d**), or diffuse uptake (**e**)

discernible uptake above background to diffuse intense FDG uptake [3] and may be affected by a number of factors ranging from smooth muscle contraction to mucosal metabolic activity [4].

5.3 Artefacts and Imaging Pitfalls

Potential artefacts and imaging pitfalls in the interpretation of FDG PET/CT in colorectal cancers are mostly related to abdomen and pelvic regions. They can be broadly grouped into technical: organ or pathology specific and treatment related.

5.4 Technical Artefacts

5.4.1 Misregistration

Misregistration is an incorrect superimposition of PET and CT data on a fused image, potentially resulting in an abnormality being ascribed to the wrong structure. It may be due to breathing, patient motion, bowel motility, or distension of the bladder and can result in both false-positive or false-negative PET findings if not identified and corrected appropriately [5]. Respiratory motion artefacts (Fig. 5.4) predominantly affect structures close to the diaphragm especially liver lesions and basal lung lesions. Review of PET alone images and identification of any associated CT abnormalities would be helpful. Patient motion and consequent artefacts are minimised by (a) placing the patient in a comfortable position, (b) instructing patient not to move during the study, and (c) having the patients empty their bladder before the start of the study. Acquisition of PET images from pelvis to head, after CT acquisition, also helps in reducing artefacts due to bladder filling (Fig. 5.5). Bowel peristalsis and positional changes also result in misregistration (Fig. 5.6),

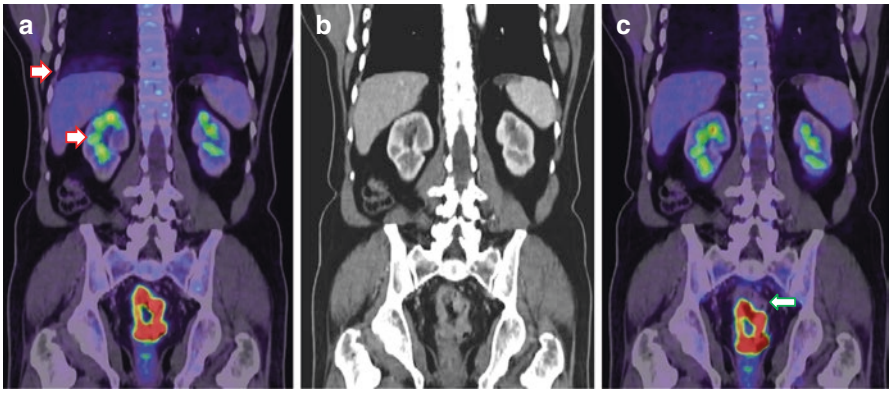

Fig. 5.4 Misregistration of liver and renal FDG uptake (**a - coronal fused PET/CT, b - corornal contrast enhanced CT**) due to respiratory movement (*red arrows*). (**c**) Images after manual correction for misregistration of liver and renal activity, but it induces misregistration at the site of pathological FDG uptake in the lesion in the rectum (*green arrow*). Care should be taken while interpreting images with misregistration

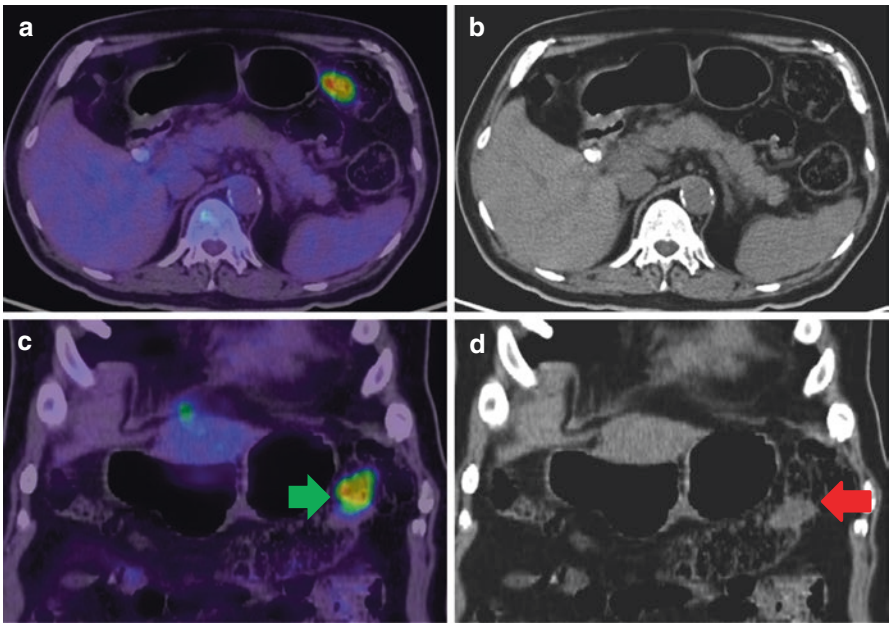

Fig. 5.5 Misregistration due to bowel movement. Intensely FDG concentration in the left third of the transverse colon (**a**) with no corresponding lesion seen in CT (**b**). Careful review of coronal images (**c - coronal fused PET/CT and d - coronal CT images**) reveals the misregistration (*green arrow*—FDG uptake and *red arrow*, lesion in CT)

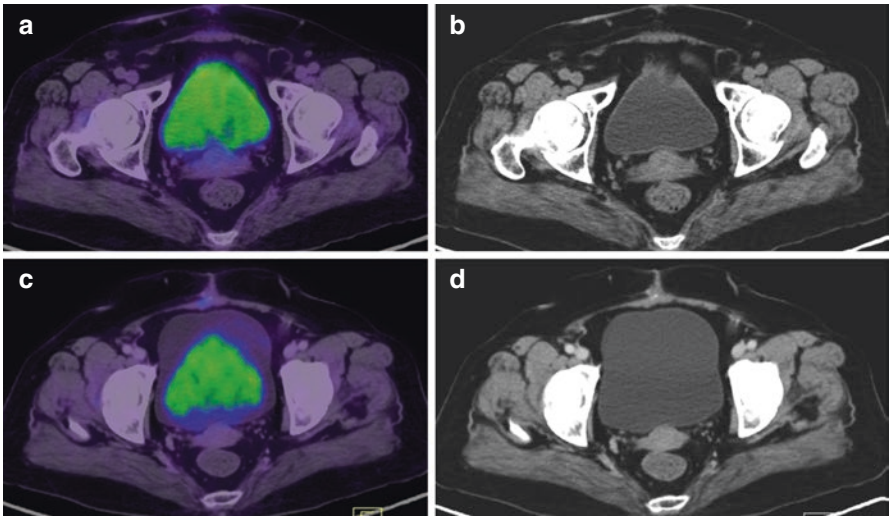

Fig. 5.6 Bladder misregistration—fused PET/CT (**a**) images and corresponding section of plain CT (**b**) used for fusion. Contrast-enhanced CT was acquired after plain CT without changing the patient position. Misregistered PET/CECT image (**c**) and corresponding section of contrasten-hanced CT (**d**) used for fusion

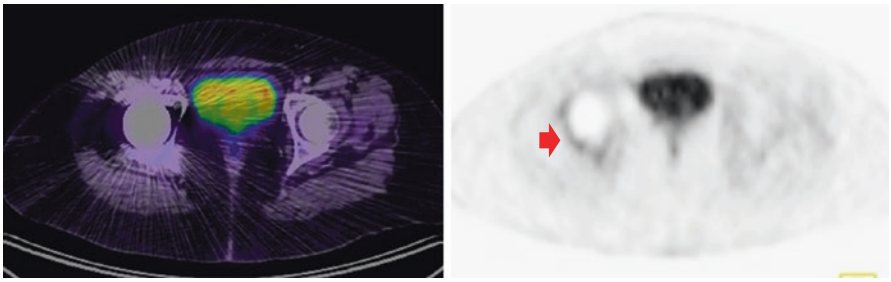

Fig. 5.7 Artefact due to metallic orthopaedic implant in the right femur. The CT-based attenuation map corrects (or overcorrects) photopenic areas adjacent to high-attenuation structures and makes them appear hypermetabolic on the attenuation-corrected PET images (*red arrow*). Review of PET images alone and attenuation noncorrected images would be helpful

particularly in the small bowel. Potential use of antiperistaltic agents like *N*-butylscopolamine exists but requires further studies and validation [6].

5.4.2 Partial Volume Effect

In PET scanners, spatial resolution effects can lead to underestimation of activity in small lesions with consequent pitfalls in assessing small moderately active lesions, where modest changes in apparent activity may influence interpretation [7].

5.4.3 Attenuation Correction Artefacts

It is seen in the presence of highly attenuating objects like metallic prostheses/stents, high-density drainage tubes, and dense intravenous contrast in the path of the CT beam (Fig. 5.7). These artefacts can easily be identified by comparing the attenuation-corrected images with the uncorrected images. [8].

5.4.4 Truncation Artefacts

Truncation artefacts in PET/CT are essentially due to the difference in size of the axial field of view between the CT (50 cm) and the PET (70 cm) tomographs. Modern scanners mitigate these effects by reconstructing attenuation correction maps to 70 cm using data extrapolation methods [9, 10].

5.5 Organ- and Pathology-Specific Pitfalls

5.5.1 Liver

Physiological FDG uptake is homogeneous/uniformly mottled and slightly greater than splenic uptake (Fig. 5.8). The significance of suspicious focus of FDG uptake in the liver can be ascertained by checking whether the uptake is distinctly

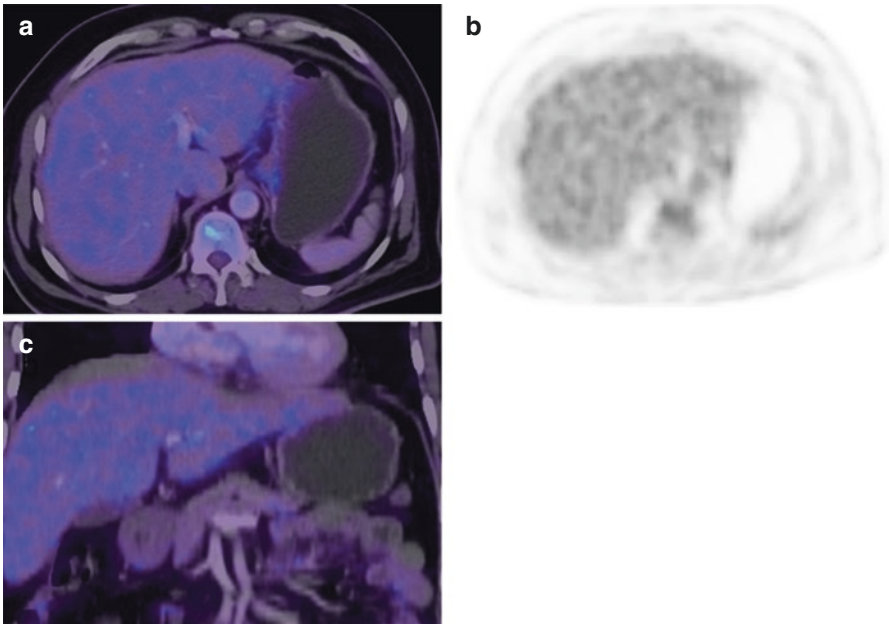

Fig. 5.8 Physiological FDG uptake in the liver (**a**, **c**). Fine mottled appearance of physiological FDG uptake in the liver made out in PET image

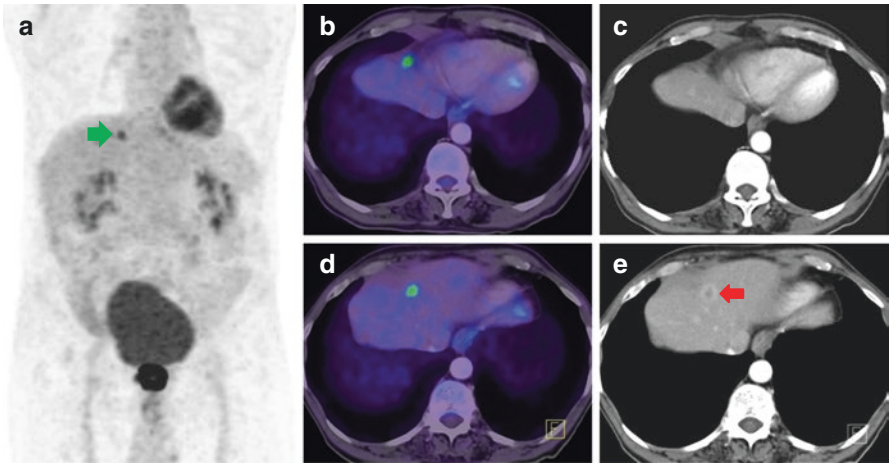

Fig. 5.9 Case of carcinoma of the rectum 18F-FDG PET/CT for initial staging reveals focal FDG uptake in the liver (**b**) with no corresponding lesion seen in CT part (**c**). Review of MIP shows the lesion to be significant (*green arrow*) (**a**). Movement misregistration is manually corrected, and corresponding CT image shows a peripherally contrast-enhancing lesion in segment VIII of the liver (*red arrow*) (**e**)

discernible in the maximum intensity projection image and whether there is a corresponding lesion in contrast-enhanced CT or MRI images (Fig. 5.9). False-positive and false-negative FDG uptake in the liver [11, 12] is described in Table 5.1.

Table 5.1 False-positive and false-negative FDG uptake in the liver with relevance to cases of colorectal malignancies

S. No.	False Negative	False positive
1	Lesions smaller than resolution of PET	Liver abscess
2	Necrotic and mucinous metastatic adenocarcinoma	Infarct
3	Post-chemotherapy	Granulomatous diseases
4	Coexistent hepatomas/infiltrative subtype of cholangiocarcinoma	Cholangitis (uptake along the biliary tree

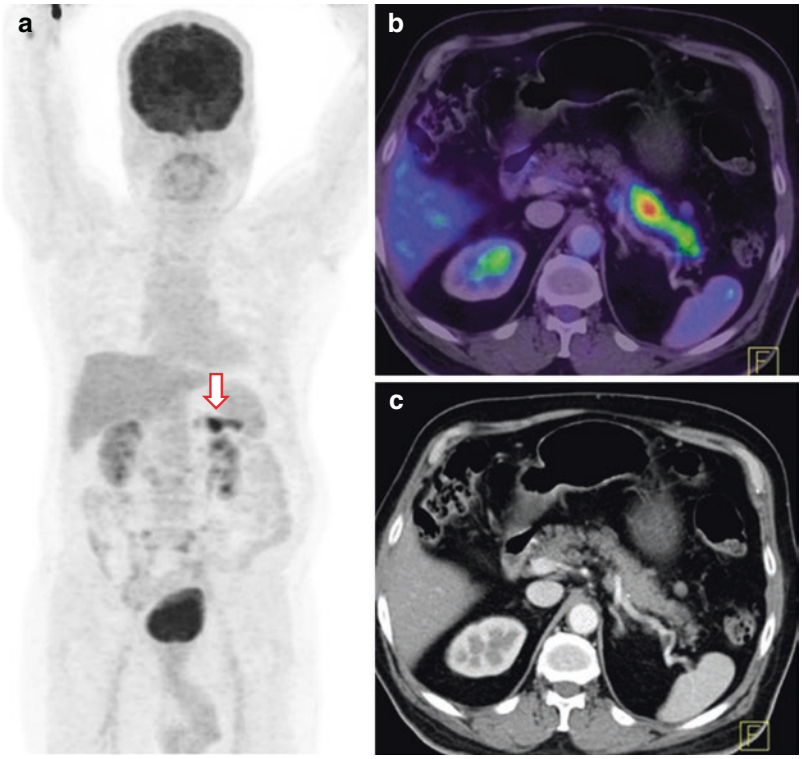

Fig. 5.10 A 73-year-old male patient who was a treated case of carcinoma of the rectum, on follow-up, mild rise in CEA levels was noted. 18F-FDG PET/CT (**a - MIP**) was done for suspected recurrence which showed abnormal intense FDG uptake on distal body and tail of pancreas (**b - axial fused PET/CT and c - axial contrast enhanced CT**) with no abnormal FDG avid lesions elsewhere in the body. CA19-9 levels were marked elevated. Distal pancreatectomy was done, and histopathology report revealed primary pancreatic adenocarcinoma

5.5.2 Spleen, Pancreas, and Adrenals

In general, splenic uptake greater than the liver is considered significant. Isolated focal increased FDG uptake in the pancreas in a case of colorectal malignancy is unlikely to be metastatic (Fig. 5.10). Increased FDG uptake (focal/diffusely increased) in the spleen [11], pancreas [13–14], and adrenals [15] is listed in Table 5.2.

Table 5.2 Causes of focal/diffusely increased FDG uptake in the spleen and pancreas

No.	Spleen	Pancreas	Adrenals
1.	Lymphoma	Primary pancreatic malignancy	Adenoma
2.	Myeloproliferative disorders	Pancreatitis	Hyperplasia
3.	Sarcoidosis	Post-radiation changes	Oncocytoma
4.	Infections—tuberculosis, kala-azar, malaria, infectious mononucleosis, etc.	Portal vein thrombus	Angiomyolipoma
5.	Chemotherapy	Haemorrhagic pseudocysts	Pheochromocytoma
6.	Exogenous marrow stimulation	Retroperitoneal fibrosis	Paraganglioma
7.	Metastasis	Metastasis	Metastasis

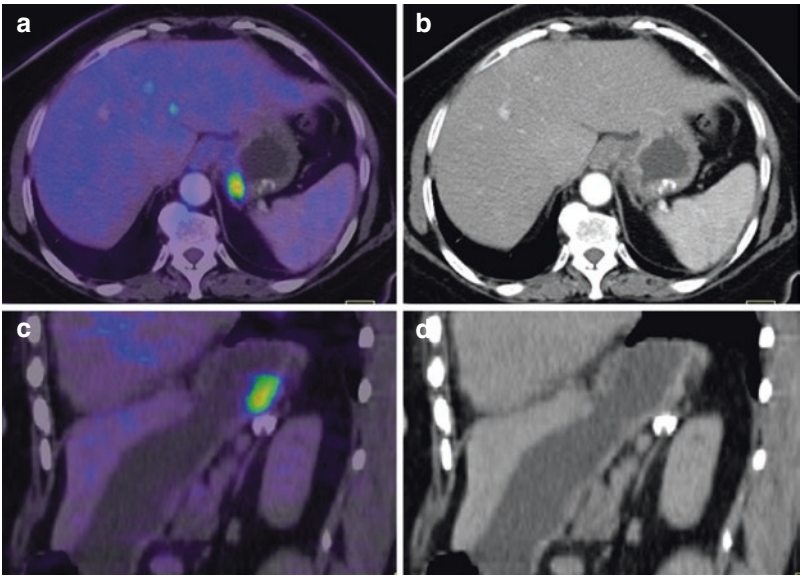

Fig. 5.11 IIncidentally detected FDG uptake in the posterior wall of cardia of the stomach (**a - axial fused PET/CT, b - axial contrast enhanced CT, c - coronal fused PET/CT and d - coronal contrast enhanced CT sections**). Upper GI endoscopy revealed a gastric ulcer, and biopsy was negative for malignancy

5.5.3 Stomach

Diffuse FDG uptake is often seen associated with gastritis. Focal FDG uptake in stomach if clinically significant can be further evaluated with endoscopy (Fig. 5.11).

5.5.4 Colon and Small Bowel

Oral contrast is particularly useful in characterising small bowel pathology and is routinely used in FDG PET/CT; however, rectal contrast is not routinely used.

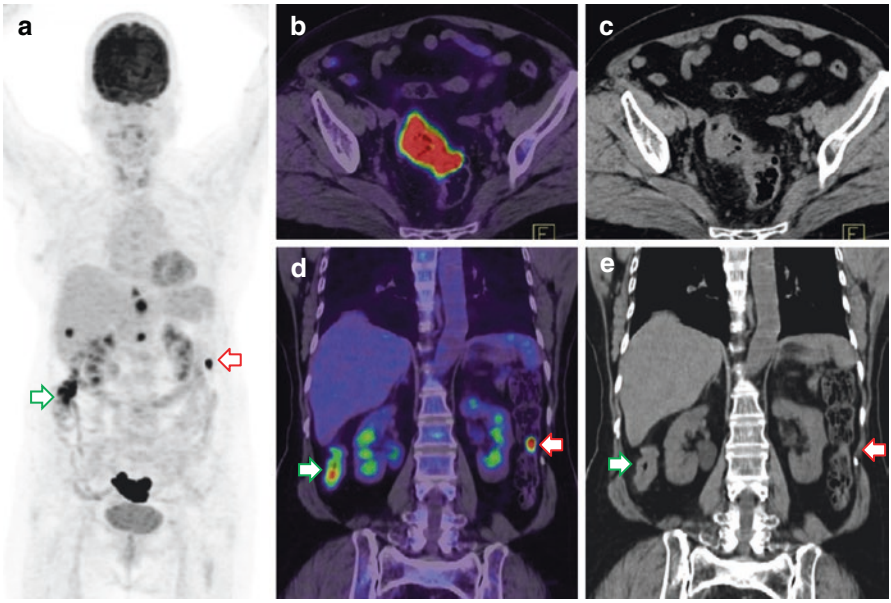

Fig. 5.12 A 71-year-old female with diagnosed carcinoma of the sigmoid colon, 18F-FDG PET/CT (**a - MIP**) for initial staging showed intense FDG uptake in the sigmoid colon (**b - fused PET/CT axial section, c - contrast enhanced CT axial section**). Focal abnormal intense FDG uptake (*red arrow*) was also noted in the middescending colon which turned out to be a neoplastic polyp (**d - coronal fused PET/CT, e - coronal contrast enhanced CT section**). A short segment of intense FDG uptake is noted in the ascending colon (*green arrow*) with apparent thickening in the unprepared bowel which did not correspond to any abnormality on colonoscopy. Significant FDG uptake in relatively long segments of the colon with no definite mural thickening on CT is often noted without any subsequent abnormality being identified

Careful correlation with adjunct CT findings is crucial in interpretation of FDG avidity in the colon (Fig. 5.12). Mostly characteristic CT findings help in identifying non-malignant causes of FDG uptake in the colon including appendicitis, diverticulitis, and focal abdominal or pelvic abscesses. Focal intense FDG activity in the colon (Fig. 5.13) may represent neoplastic lesion in up to 68% cases and hence warrants further evaluation with colonoscopy or CT colonography [16]. Intense large and small bowel uptake may be seen in diabetic patients on metformin (Fig. 5.14) [17].

5.5.5 Urinary Tract

Focal pooling of the tracer in the renal calyces or pelvis, dilated or redundant ureters, or bladder diverticula can mimic pelvic or retroperitoneal lymph node metastasis (Fig. 5.15). Careful review of the MIP image for the characteristic course of ureteric activity and search for coexistent anatomical lesion on CT part are helpful. The use of loop diuretics and delayed imaging helps to tackle the effects of radioactive urine in the urinary tract.

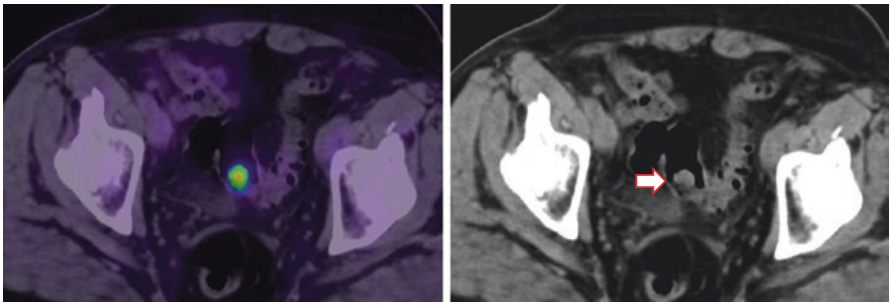

Fig. 5.13 Incidentally detected intense FDG uptake in a sigmoid polyp (*red arrow*), which on colonoscopy and biopsy was found to be malignant

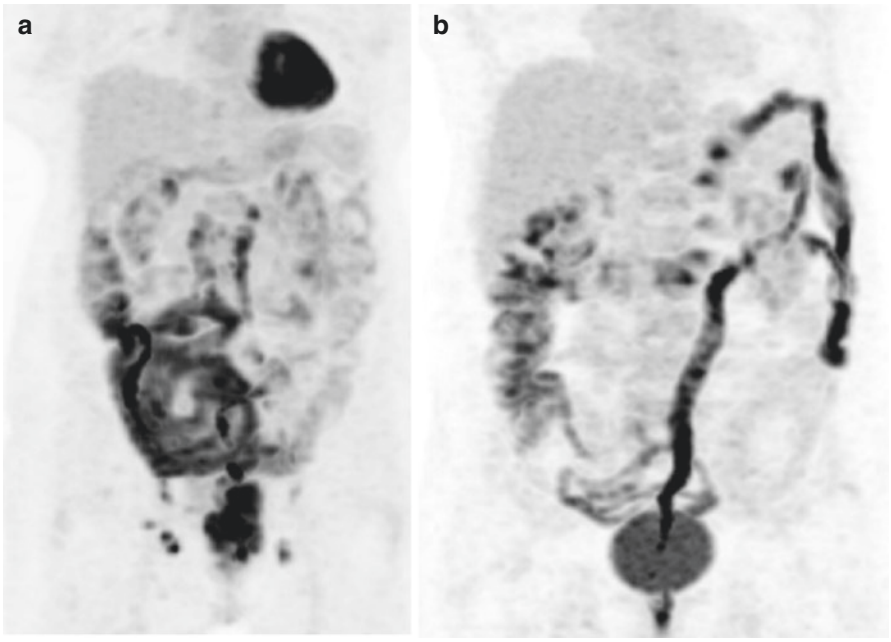

Fig. 5.14 High FDG uptake in bowel in patients on metformin

5.5.6 Reproductive System

In females, ovaries as well as uterus show variable physiological uptake depending on the phase of menstrual cycle. In males, prostate and testis may show variable physiological FDG uptake. Correlative anatomical imaging is helpful.

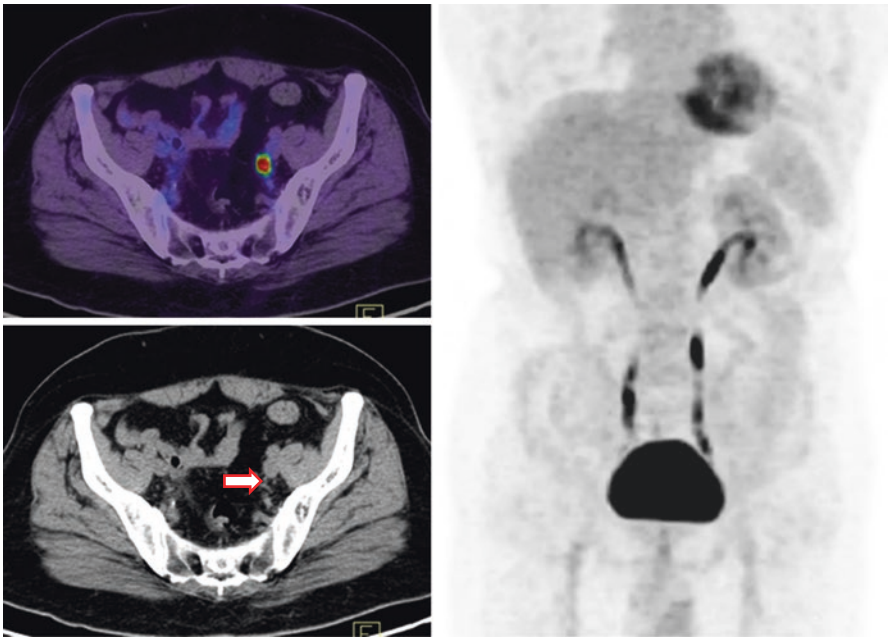

Fig. 5.15 Ureteric pooling of tracer mimicking FDG avid lymph node in fused PET/CT images. Review of CT images confirms the absence of lymph node (*red arrow*), and review of MIP images reveals the characteristic pattern of urinary activity in ureter on both sides

5.5.7 Bone

Bone lesions in the context of colorectal carcinoma have to be interpreted with caution. Sclerosis/lytic changes may not be obvious in CT; also benign mimickers with FDG uptake like Paget's disease (Fig. 5.16), fibrous dysplasia, and healing fracture exist. Diffuse increase in bone marrow activity is seen following chemotherapy and exogenous marrow stimulation which may make interpretation of bone lesions difficult. Diffuse marrow metastases, although rare, do exist (Fig. 5.17).

5.5.8 Muscle

Muscle metastases/deposits although rare have to be kept in mind (Fig. 5.18), and mimickers include abscess. Often tissue diagnosis is required in such cases especially in the context of cystic muscle metastases. Enthesitis can result in focal FDG uptake at the site of muscle insertion (Fig. 5.19).

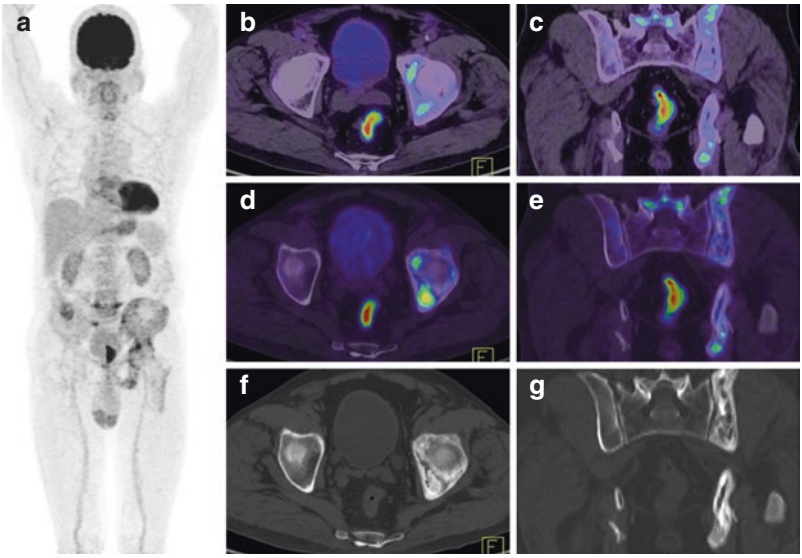

Fig. 5.16 A 68-year-old man with moderately differentiated adenocarcinoma of the rectum, 18FFDG PET/CT (**a - MIP**) for initial staging reveals intensely FDG-concentrating wall thickening in the rectum (**b**, **c**) with moderate patchy FDG uptake in diffuse sclerotic lesions (**d–g**) involving the left hemi pelvis and L5 vertebra. Biopsy from left iliac crest revealed it to be a Paget's disease

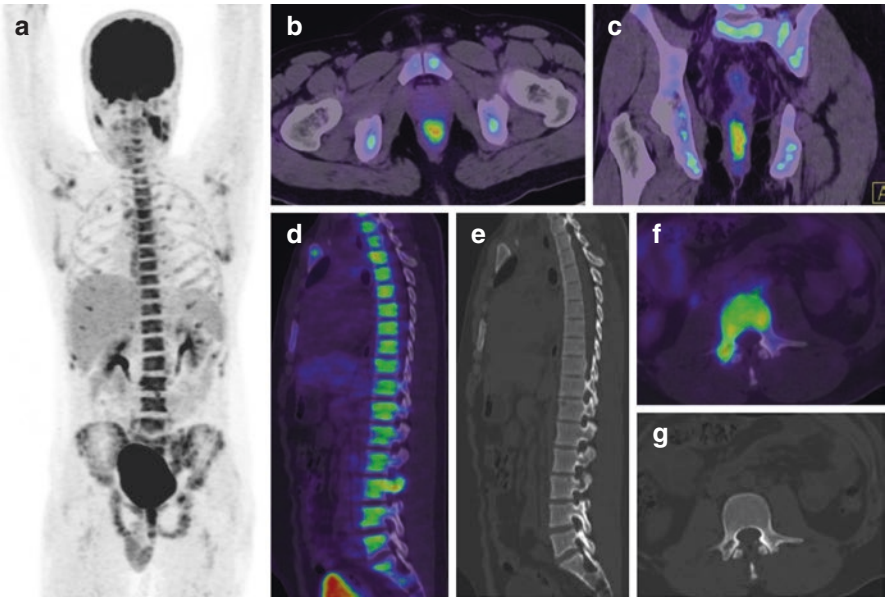

Fig. 5.17 A 28-year-old gentleman diagnosed with primary adenocarcinoma of the rectum, 18FFDG PET/CT (**a - MIP**) for initial staging showed intense FDG avid lesion in rectum (**b - axial fused PET/CT, c - coronal fused PET/CT**) with diffuse intense heterogeneous FDG uptake in the marrow (**d - sagittal fused PET/CT, e- sagittal CT section in bone window**). Heterogeneous FDG uptake in the marrow with involvement of the right pedicle of L3 vertebra (**f**, **g**), a bone marrow biopsy was done which confirmed marrow metastases from poorly differentiated adenocarcinoma

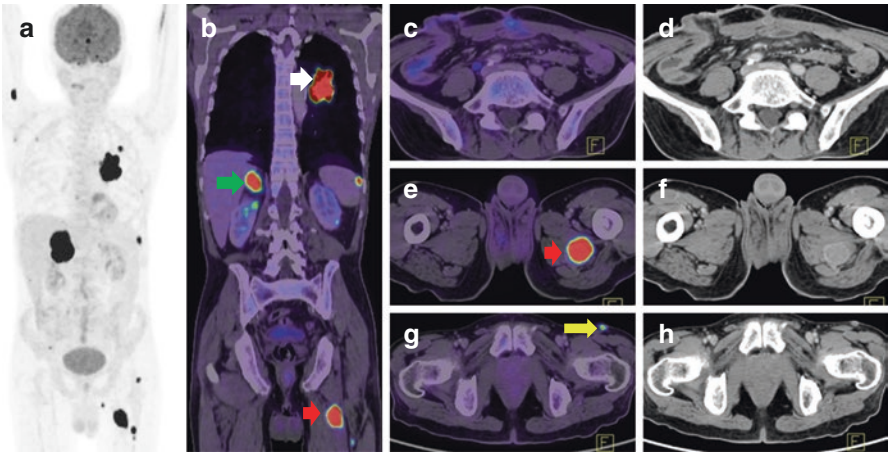

Fig. 5.18 A 64-year-old male patient diagnosed with adenocarcinoma of colon post-surgery and adjuvant chemotherapy, 18F-FDG PET/CT revealed no abnormal lesion in residual bowel (**c**,**d**); intensely FDG-concentrating mass lesion in the left hilar region (*white arrow*), right adrenal lesion (*green arrow*), skin nodule (*yellow arrow*), and muscle lesions (*red arrow*). Biopsy from the muscle lesion proved it to be metastatic adenocarcinoma, and second primary in the lung was later confirmed

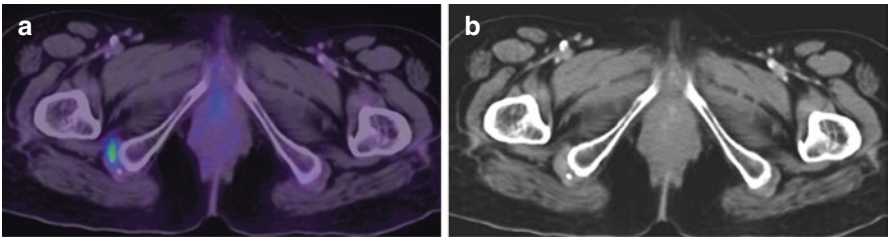

Fig. 5.19 Mild focal FDG uptake at the site of muscle attachment in the right ischium due to enthesitis

5.5.9 Lymph Nodes

An advantage of FDG PET is the ability to depict malignant neoplasms in lymph nodes when the nodes are not pathologically enlarged. False negatives include small-sized lymph nodes (smaller than the resolution of PET scanner), mucinous adenocarcinoma metastases, and post-chemotherapy. False positives include active granulomatous disease such as tuberculosis and sarcoidosis and infection or recent instrumentation resulting in high FDG uptake in involved nodes (Fig. 5.20) [11]. In cases of colorectal malignancies, isolated mediastinal/cervical lymph nodal FDG uptake in the absence of abdominal and pelvic disease should be considered as unrelated to colorectal malignancy unless otherwise proved (Fig. 5.21).

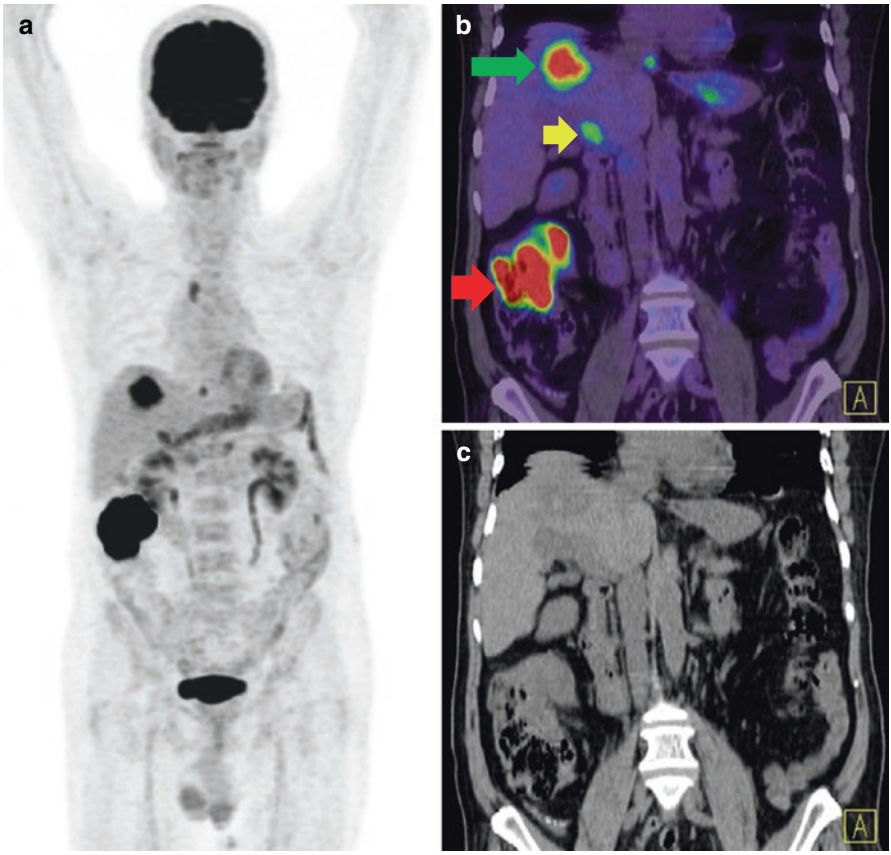

Fig. 5.20 A 75-year-old man with carcinoma in the ascending colon and suspected liver metastasis in segment VIII on contrast-enhanced CT abdomen underwent 18F-FDG PET/CT which showed intensely FDG-concentrating primary lesion in the ascending colon (*red arrow*), intensely FDG-concentrating lesion in segment VIII (*green arrow*), and moderately FDG-concentrating lesion in periportal lymph node (*yellow arrow*). Right hemicolectomy with metastasectomy of liver lesion and lymph nodal dissection was done, with final histopathology confirming adenocarcinoma of the ascending colon and with liver abscess and reactive periportal lymph node

5.5.10 Peritoneum

Increased FDG uptake is frequently seen in peritoneal metastases which appear either nodular or diffuse (Fig. 5.22). The peritoneal disease may not be associated with any abnormal FDG uptake in small-volume disease. False-positive FDG uptake may also be seen in the peritoneum postoperatively due to inflammation. Malignant ascites does not take up FDG.

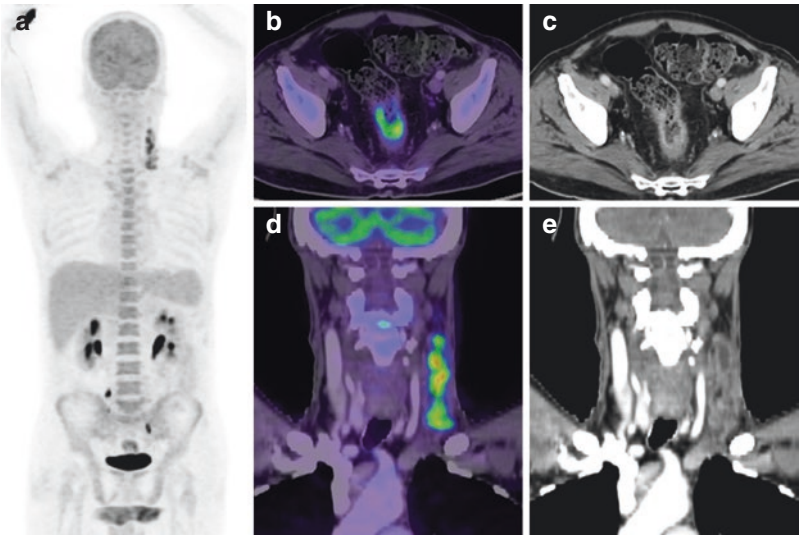

Fig. 5.21 A 53-year-old man diagnosed with carcinoma of the rectum, 18F-FDG PET/CT (**a - MIP**) for initial staging revealed intense FDG uptake in the primary lesion in rectum (**b**, **c**). There was no evidence of any pelvic or abdominal lymphadenopathy. Intensely FDG-concentrating necrotic left cervical lymph nodes were noted (**d**, **e**). Biopsy of the cervical lymph nodes confirmed it to be due to tuberculous lymphadenopathy

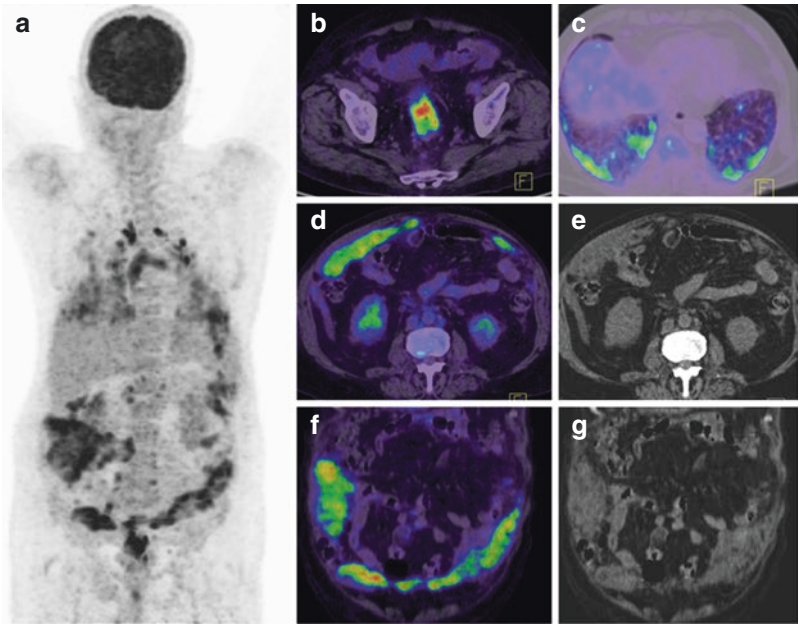

Fig. 5.22 A 66-year-old man with carcinoma of the rectosigmoid, 18F FDG PET/CT shows intense FDG avid primary site (**b**), extensive intensely FDG-avid omental nodules and omental thickening (**d**–**f**) with FDG avid lung lesions (**c**) and mediastinal lymph nodes

5.6 Treatment-Related Pitfalls

Surgery, radiation therapy, and chemotherapy forms an integral part of the treatment plan of colorectal malignancies. False-positive FDG uptake following surgery and radiation therapy can occur unless adequate time gap is given with the PET/CT. False negative (no uptake in scan with disease on histopathology) can be seen at primary site, lymph nodes, and liver lesions following chemotherapy. Postsurgical complications like haematoma and surgical abscesses can result in false-positive FDG uptake. Stoma/anastomotic sites can show diffuse or focal FDG uptake, and careful review of CT images for any abnormal thickening or mass lesions is required to clarify possibility of disease involvement (Fig. 5.23). Exogenous marrow stimulation or chemotherapy can result in increased FDG uptake in bone marrow which may make identification of skeletal lesions difficult (Fig. 5.24). Treatment for coexistent disease can also complicate interpretation of FDG avid lesions and requires judicial clinical judgement (Fig. 5.25).

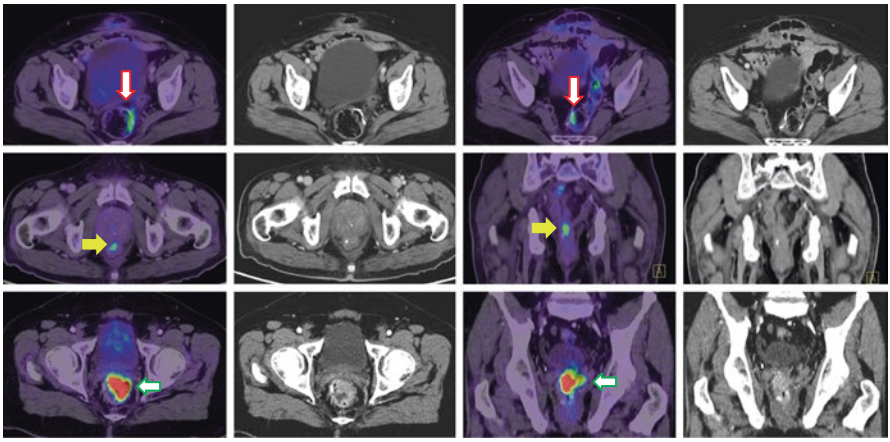

Fig. 5.23 Anastomotic site FDG uptake interpretation: Upper row images—FDG PET/CT scan done 4 weeks after surgery for restaging shows post-surgical inflammation (*red arrow*) with no abnormal wall thickening at the anastomotic site. Middle row images—FDG PET/CT scan done 2 years after surgery in a patient with rising CEA levels. Mild FDG uptake is noted at the anastomotic site with doubtful thickening (*yellow arrow*). Colonoscopy is suggested for further evaluation of the anastomotic site. Lower row images: FDG PET/CT scan done 1.5 years after surgery showing intensely FDG-concentrating definitive lesion at the anastomotic site (*green arrow*)

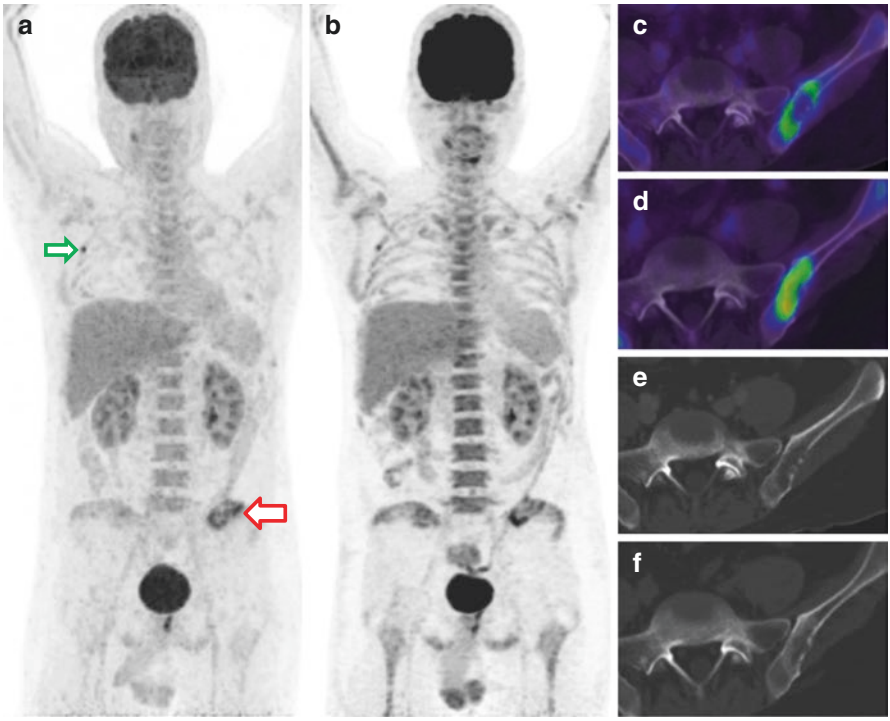

Fig. 5.24 A 56-year-old man who is a treated case of carcinoma of the rectum (surgery and adjuvant chemoradiation) on follow-up had rising CEA levels. 18F FDG PET/CT (**a - MIP**) for suspected recurrence evaluation revealed increased FDG uptake in the left iliac bone (*red arrow*) and right third rib (*green arrow*). Biopsy from left iliac bone confirmed the metastasis, and he underwent three cycles of chemotherapy. 18F-FDG PET/CT for response evaluation (**b**) shows diffuse FDG uptake in marrow due to reactive changes sparing the RT field in pelvis. Pretreatment FDG uptake in the left iliac bone (**c**), and corresponding lytic lesion (**e**) is noted. Careful observation and interpretation of findings are required as posttreatment FDG uptake is increased (**d**) with development of mild sclerotic changes in the left iliac bone lesion (**f**) and no new lesions are noted

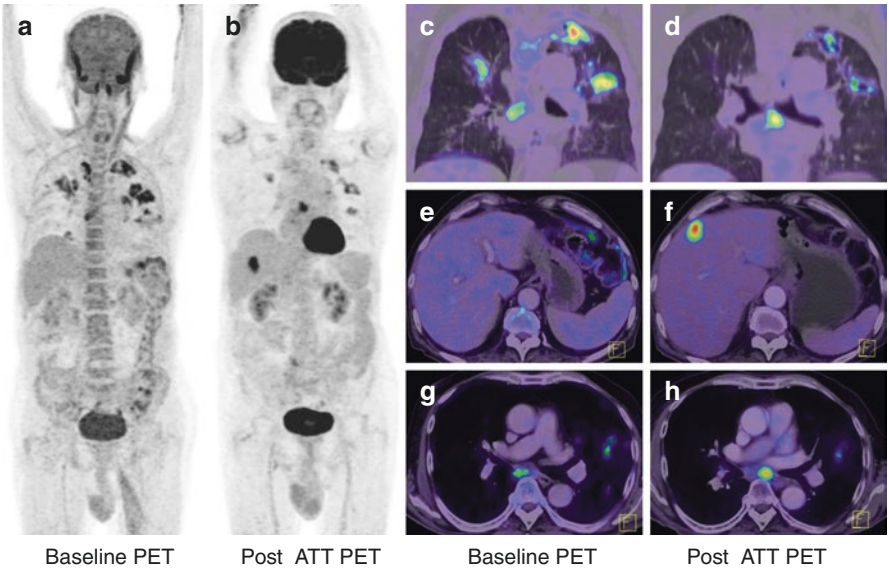

Fig. 5.25 A 66-year-old treated case of carcinoma of the rectum posttreatment on follow-up developed unexplained loss of weight and appetite with mild elevation of CEA levels. 18F-FDG PET/CT for suspected recurrence (**a - MIP**) revealed intensely FDG avid cavitary lesions in the upper lobe of both the lung fields (**c**) with FDG avid mediastinal lymph nodes (**g**). The presence of acid-fast bacilli was confirmed in bronchoalveolar lavage, and the patient was started on ATT. After completing 6 months of antitubercular treatment (ATT), 18F-FDG PET/CT (**b - MIP**) was repeated as the CEA levels rose significantly. Post-ATT PET showed reduction in FDG avidity in the lung lesions (**d**) and mediastinal lymph nodes except subcarinal lymph node which showed increase in FDG avidity (**h**). Intensely FDG-concentrating new lesion was noted in the liver (**e - baseline PET axial section with no liver lesion and f - corresponding section in follow up PET with liver lesion**) which was suspicious for liver metastasis and later on confirmed on biopsy and histopathology as metastasis

Conclusion

FDG PET/CT is a very useful tool in the management of colorectal malignancies. Careful elucidation of clinical history, minimising technical artefacts, and an adequate understanding of the physiological variants and imaging pitfalls of FDG PET/CT help in accurate reporting of FDG PET/CT in colorectal malignancies.

Key Points

- A thorough understanding of sites of physiological uptake in the abdomen and pelvis is an essential prerequisite to interpret FDG PET/CT scans in colorectal carcinoma.
- Respiratory motion artefacts predominantly affect structures close to the diaphragm especially liver lesions and basal lung lesions. Review of PET alone images and identification of any associated CT abnormalities would be helpful.
- Bowel peristalsis and positional changes also result in misregistration, particularly in the small bowel.
- Physiological FDG uptake in the liver is homogeneous/uniformly mottled and slightly greater than splenic uptake. The significance of suspicious focus of FDG uptake in the liver can be ascertained by checking whether the uptake is distinctly discernible in the maximum intensity projection image and whether there is a corresponding lesion in contrast-enhanced CT or MRI images.
- Diffuse FDG uptake is often seen associated with gastritis. Focal FDG uptake in the stomach if clinically significant can be further evaluated with endoscopy.
- Oral contrast is particularly useful in characterising small bowel pathology and is routinely used in FDG PET/CT; however, rectal contrast is not routinely used.
- Careful correlation with adjunct CT findings is crucial in interpretation of FDG avidity in the colon.
- Focal intense FDG activity in the colon may represent neoplastic lesion in up to 68% cases and hence warrants further evaluation with colonoscopy or CT colonography.
- Intense large and small bowel uptake may be seen in diabetic patients on metformin.
- Focal pooling of the tracer in the renal calyces or pelvis, dilated or redundant ureters, or bladder diverticula can mimic pelvic or retroperitoneal lymph node metastasis.
- Ovaries as well as uterus shows variable physiological uptake depending on the phase of menstrual cycle.
- False-positive FDG uptake following surgery and radiation therapy can occur unless adequate time gap is given with the PET/CT.

- False negative (no uptake in scan with disease on histopathology) can be seen at primary site, lymph nodes, and liver lesions following chemotherapy.
- Postsurgical complications like haematoma and surgical abscesses can result in false-positive FDG uptake.
- Stoma/anastomotic sites can show diffuse or focal FDG uptake, and careful review of CT images for any abnormal thickening or mass lesions is required to clarify possibility of disease involvement.

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