PET/CT in Colorectal Caner

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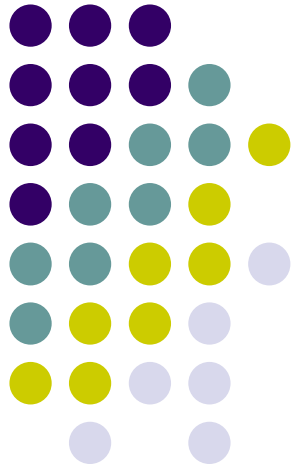


- Colorectal cancer (CRC) is overall the third most common type of malignancy worldwide (8% of all cancers)
- CRC is the third most common cancer-related leading cause of death in the United States
- There is a higher prevalence in men and in patients >60 years • Early clinical symptoms include:

- According to evidence-based data, FDG PET/CT is appropriate for staging of stage IV disease, ruling out or detecting synchronous metastases, and restaging of patients, especially in cases of rising tumor markers or clinical suspicion of recurrence but equivocal findings on onventional imaging modalities

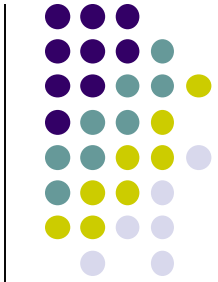
- Early clinical symptoms include:
- Hematochezia/melena, abdominal pain, anemia, bowel habit alteration
- Colonoscopy is the most accurate and preferred primary diagnostic procedure. CT colonography is an alternative method
- Metastatic disease is seen at first presentation in 20% of patients
- Surgery is the standard treatment, with or without chemoradiation and/or targeted therapy:

- Stage 0: Local surgical excision, occasional colectomy for very large tumors
- Stage I: Partial colectomy and regional lymph node dissection
- Stage II: Partial colectomy ± adjuvant chemotherapy or radiation therapy
- Stage III: Partial colectomy + regional lymph node dissection + chemotherapy ± radiation therapy
- Stage IV: Colectomy + neoadjuvant/adjuvant chemotherapy and/or targeted therapy + radiation therapy (in advanced cases)

Five-Year Survival

• Stage I	(T1 or T2, N0, M0)	94%
• Stage II	(T3-4, N0, M0)	82%
• Stage III	(any T, N1-3, M0)	67%
• Stage IV	(any T, any N, M1)	11%

Prognostic Factors



- Preoperative carcinoembryonic antigen (CEA)
- Tumor deposits
- Circumferential resection margin
- Perineural invasion
- Tumor regression grade after neoadjuvant therapy
- K-ras, BRAF, and DCC mutations
- Tumor stage
- Lymphovascular invasion

Histopathology

- Adenocarcinoma >90%
- Neuroendocrine, squamous cell, adenosquamous, spindle cell, undifferentiated <10%

Cancer Distribution

• Anorectal	29%
• Appendix, cecum, and ascending colon	23%
• Descending and sigmoid colon	23%
• Transverse colon	10%

Common Pattern of Spread

- Ascending and transverse colon: pericolic, right colic, middle colic

- Descending colon: pericolic, left colic, inferior mesenteric, middle colic, sigmoidal
- Rectosigmoid: pericolic, inferior mesenteric, left colic, superior and middle rectal (hemorrhoidal), perirectal, sigmoid mesenteric,sigmoidal

- Rectum: perirectal; sigmoid mesenteric; inferior mesenteric; lateral and presacral; sacral promontory; internal iliac; superior, middle, and inferior rectal (hemorrhoidal)

Cost-Effectiveness

- FDG PET/CT is cost-effective in the preoperative staging of
- recurrent colon and rectal cancers, as well as in the staging of
- metastatic disease, but not primary colon or rectal cancer

Primary Staging

- The primary decisive information in newly diagnosed CRC is the extent of disease to differentiate between:
- a. Stages I-III (i.e., absence of metastatic disease beyond regional lymph nodes)
- b. Stage IV (i.e., metastatic disease)
- Patients with stage I-III disease are candidates for primary resection with curative potential, whereas patients with stage IV disease can or should be spared resection of the primary in the absence of stenosis, because surgical treatment may provide no clinical benefit in this setting

Follow-Up After Surgery

- a. Patients with elevated tumor marker (i.e., CEA): defining the presence of recurrent disease in terms of (1) localization and (2) extent of disease to assess the possibility of potential reoperation,i.e., localized or operable recurrence versus diffusely metastatic disease
- b. Rectal cancer: differentiation between posttherapeutic scar tissue and viable tumors

Metastatic Disease

- a. Before initiation of therapy: differentiation between potentially operable and palliative situations

- b. Response assessment: Currently, systemic therapies including novel antibodies (e.g., anti–vascular endothelial growth factor or anti–epidermal growth factor receptor) and chemotherapies, such as irinotecan, oxaliplatin,and fluoropyrimidines, show promise regarding response rates and survival(increased toxicities and costs)

Pattern of Distant Metastasis

• 20% at presentation	
• Most common sites:	
• Liver	50%
• Peritoneum	25%
• Lung	10%–20%

Colorectal Cancer TNM Staging Guidelines

Primary Tumor (T)	Regional Lymph Nodes (N)	Distant Metastasis (M)
T0: No evidence of primary tumor **Tis:** Carcinoma in situ: intraepithelial or invasion of lamina propria **T1:** Tumor invades submucosa **T2:** Tumor invades muscularis propria **T3:** Tumor invades through the muscularis propria into pericolorectal tissues **T4a:** Tumor penetrates to the surface of the visceral peritoneum **T4b:** Tumor directly invades or is adherent to other organs or structures	**N0:** No regional lymph node metastasis **N1:** Metastasis in 1 to 3 regional lymph nodes **N1a:** Metastasis in 1 regional lymph node **N1b:** Metastasis in 2 to 3 regional lymph nodes **N1c:** Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis **N2:** Metastasis in 4 or more regional lymph nodes **N2a:** Metastasis in 4 to 6 regional lymph nodes **N2b:** Metastasis in 7 or more regional lymph nodes	**M0:** No distant metastasis **M1:** Distant metastasis **M1a:** Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node) **M1b:** Metastases in more than one organ/site or the peritoneum

- FDG PET/CT detects small lymph nodes that are not suspicious for metastases based on CT criteria, which have clinical relevance in the application of neoadjuvant treatment
- It may help in better planning of external beam radiation
- Eccentric primary tumor proliferation in the gastrointestinal tract may be missed by endoscopic evaluation, and FDG PET/CT imaging seems to provide more diagnostic accuracy in such cases

Pitfalls

False Positive:

- Physiologic FDG uptake within the colon may be intense, specifically in the cecum, ascending colon, and rectal region
- Physiologic FDG uptake in postoperatively posteriorly displaced pelvic organs may mimic rectal cancer recurrence. The falsepositive interpretation rate is reduced by the anatomic coregistration of the CT component in modern PET/CT scanners
- Hyperplastic and adenomatous polyps may have high FDG uptake
- Fistula and sinus tracts, as well as abscesses, can have intense FDG uptake; correlation with the CT scan is helpful
- Crohn disease, ulcerative colitis, typhlitis, and diverticulitis may represent false-positive FDG findings

Pitfalls

False Negative

- Mucinous adenocarcinoma
- Within 4 weeks of chemotherapy (PET should be performed at least 4 weeks after initiating therapy as false-positive results from inflammation can be seen in the first 2 weeks of treatment)
- Small tumor and/or lymph node metastasis (<8 mm)
- Metformin consumption (It may cause a diffuse colonic FDG uptake and obscure the underlying malignancy)
- Common false-negative results for all cancers: early-stage malignancy, hyperglycemic state, small lesions (<8 mm)

Primary Staging/Restaging

- According to clinical guidelines, CT and MRI are suggested as standard imaging modalities for the assessment of patients with CRC

- The staging accuracy of CT is about 50%–70% for colon cancer, which is almost similar to that of MRI

- Corresponding accuracies for the detection of lymph node (N) improvement are similar for both modalities, with approximately 85% accuracy. However, MRI is slightly superior to CT in detecting liver metastases

Primary Staging/Restaging

- FDG PET/CT has become an essential diagnostic procedure in evaluating most of the cancers before or after the treatment

- There are no sufficient data to support the use of FDG PET/CT in the preoperative staging of primary, recurrent, and metastatic CRC. This is mainly because FDG PET/CT seems to have no significant impact on decision making for therapy

- FDG PET/CT has an impact on the treatment approach by upstaging 50% and downstaging 21% of patients with lower rectal malignancies

- The use of FDG PET/CT could be considered in the case of inconclusive CT and/or MRI findings to rule out or confirm metastasis

- If the CEA level is elevated after therapy, contrast-enhanced CT is the diagnostic procedure of choice

- However, FDG PET/CT is recommended if CT fails to detect the location of disease recurrence or metastasis

- FDG PET/CT demonstrated a significantly higher sensitivity than CT scan for the detection of liver metastases from CRC (94% vs.84%)
- Sensitivity and accuracy of 95% and 97% for FDG PET/CT in the detection of intrahepatic and extrahepatic metastases vs. 97% and 94 for CT scan respectively
- Because of the limited spatial resolution of FDG PET/CT, MRI is still superior in the evaluation of liver lesions smaller than 1 cm

Recurrent Disease

- FDG PET/CT is recommended by the Royal College of Radiologists for patients with increasing tumor markers and/or clinical suspicion of recurrence but equivocal findings on other imaging modalities

- Serial CEA measurements are used after surgery to detect cancer recurrence (sensitivity about 80% , specificity about 70%)
- In cases of elevated CEA:
- Contrast-enhanced multidetector CT (sensitivity for detection of recurrent disease= 70% , specificity= 94%)
- FDG PET/CT (sensitivity for detection of recurrent disease= 97%, specificity=94%)

Therapy Monitoring & Prognostic value

- FDG PET/CT seems to be the superior prognosticator compared with conventional imaging
- Some investigators performed 18F-FDG PET/CT in patients with CRC before surgery and concluded that the patients with high total lesion glycolysis (TLG) and tumor metabolic volume have a poorer prognosis
- Other studies evaluated the metabolic activity of metastatic lesions from CRC and concluded that the lesions' standardized uptake value (SUV) is a prognosticator for overall survival independent of the consecutive therapy:
- SUV < 4.26 ⇒ median survival= 32 months
- SUV > 4.26 ⇒ median survival= 19 months

- patients with high total lesion glycolysis (TLG) and tumor metabolic volume have a poorer prognosis

- Significant decline in size and radiotracer uptake in tumor is an indicator for good prognosis

- PET can be used to monitor the results of minimally invasive therapies such as radiofrequency ablation (RFA) and interarterial 90Ymicrospherer radioembolization
- PET is more accurate than contrast-enhanced CT for evaluation of treatment success after RFA, and also more cost-effective
- local tumor progression secondary to residual tumor is most common in tumors greater than 3 cm

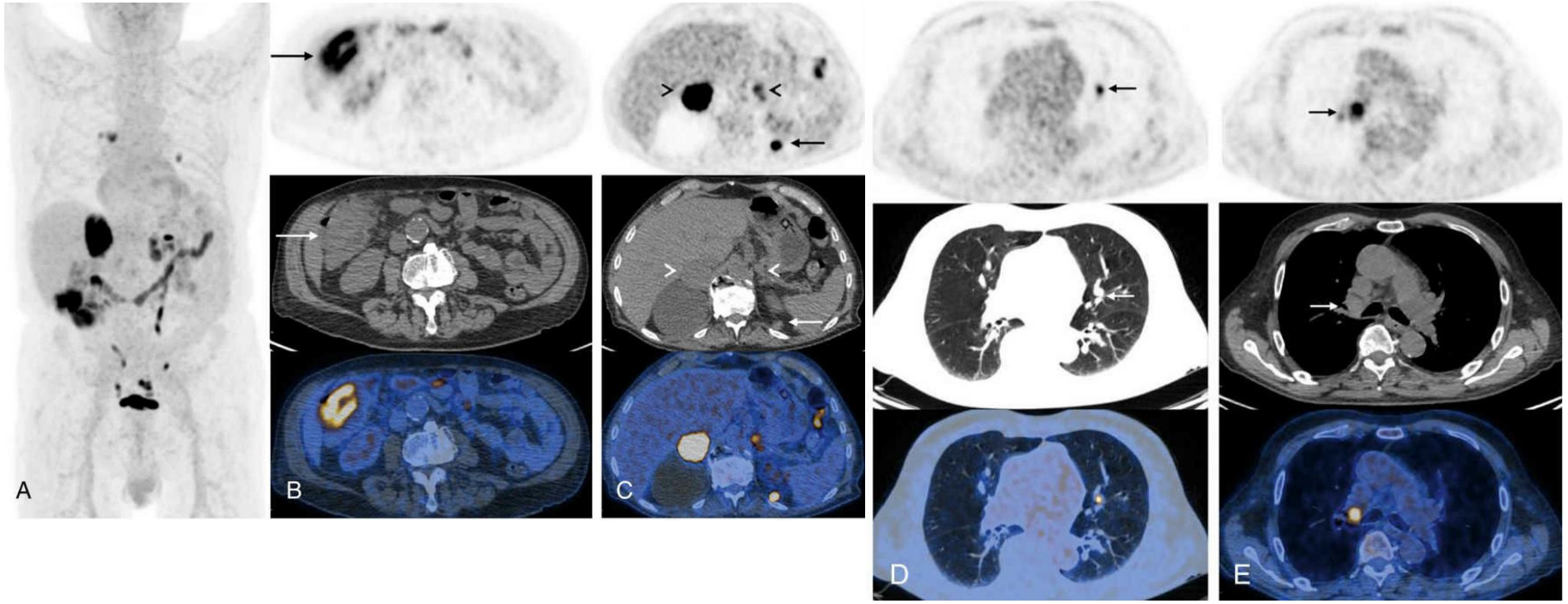
Conclusion

- FDG PET/CT seems to have no significant role in the primary staging of CRC, except in stage IV disease with distant metastases at presentation

- FDG PET/CT is useful for restaging or evaluation of recurrence, as well as in patients who are presenting with distant metastatic disease

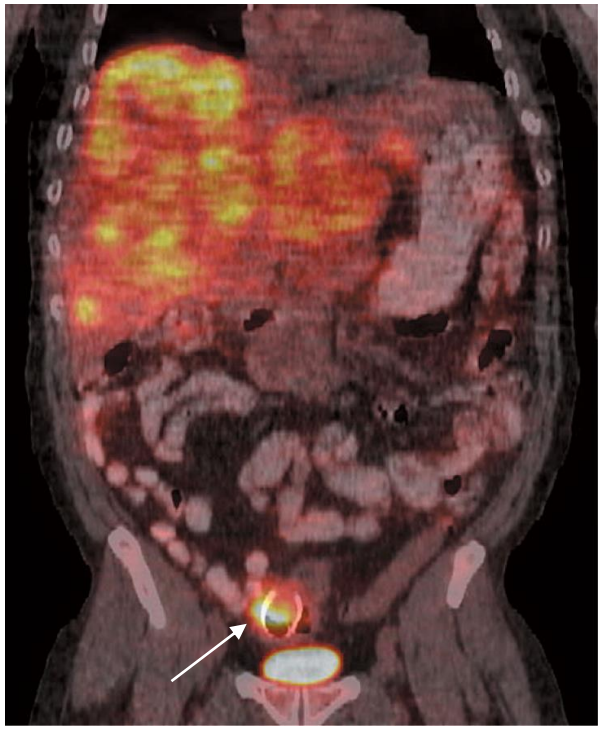
- FDG PET/CT is capable of predicting the patients' survival and prognosis, evaluating tumor response to therapy, and affecting patients' management

Staging Colon Cancer, Distant Metastasis



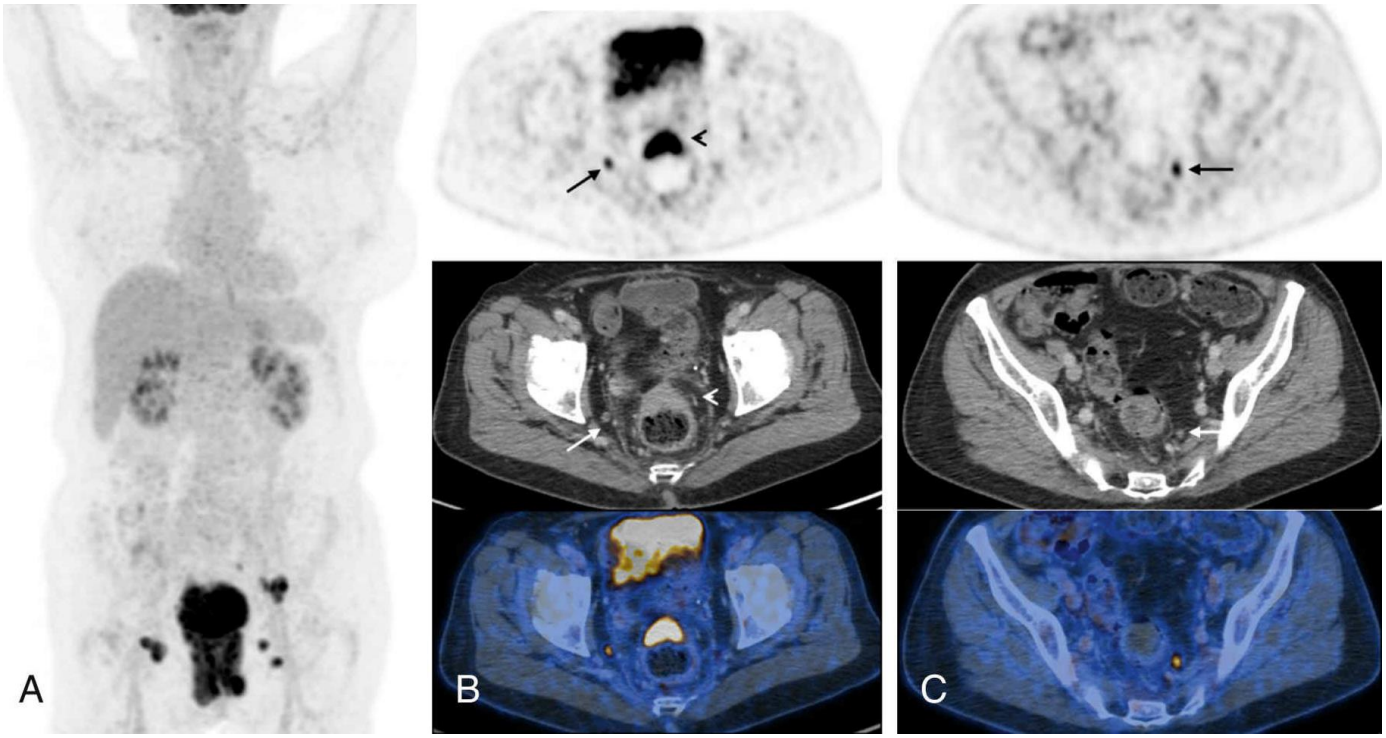
FDG PET/CT demonstrating a primary tumor in the ascending colon (B, *arrow*). FDG-avid bilateral adrenal (C, *arrowhead*), peritoneal (C, *arrow*), left pulmonary (D, *arrow*), and right hilar (E, *arrow*) metastases are noted

Metastatic Primary Colon Cancer



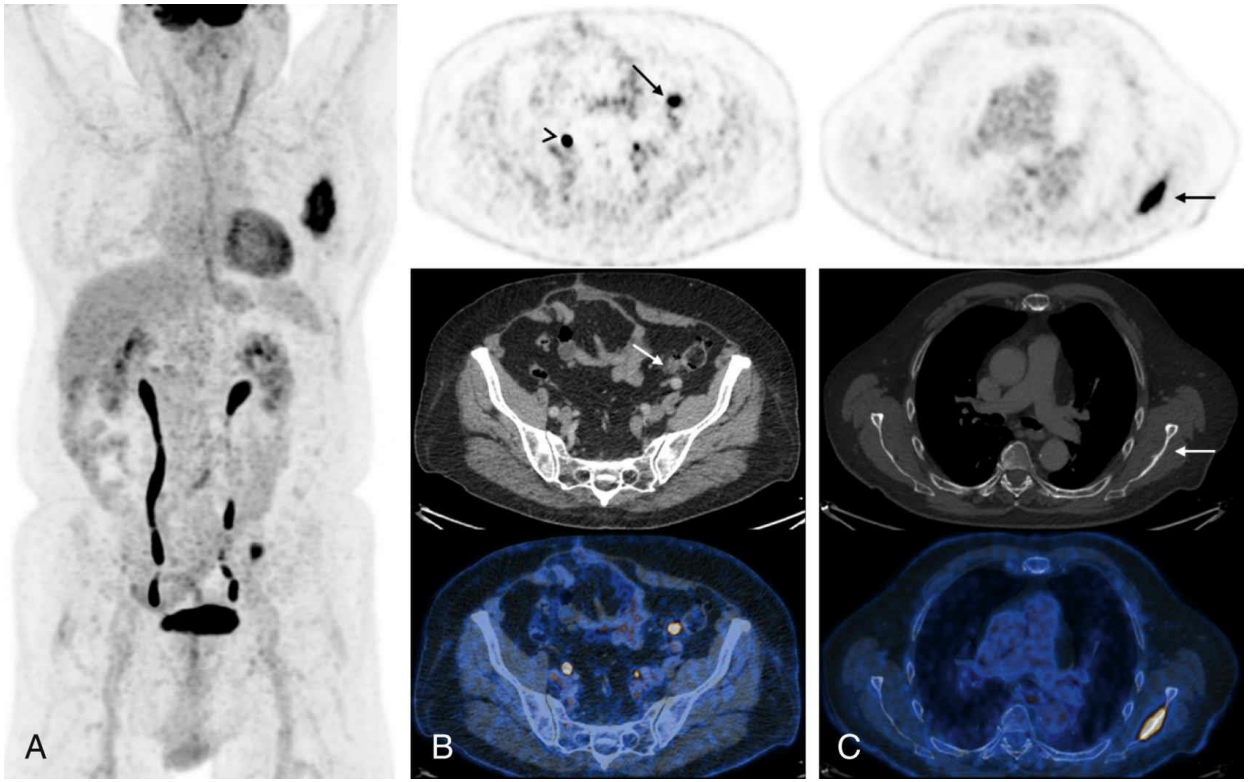
Metastatic primary colon cancer. Coronal PET/CT demonstrates a primary sigmoid colon cancer (arrow) with extensive hepatic metastases. A stent has been placed in the region of the tumor to relieve obstruction

Rectal Cancer, Radiotherapy Planning



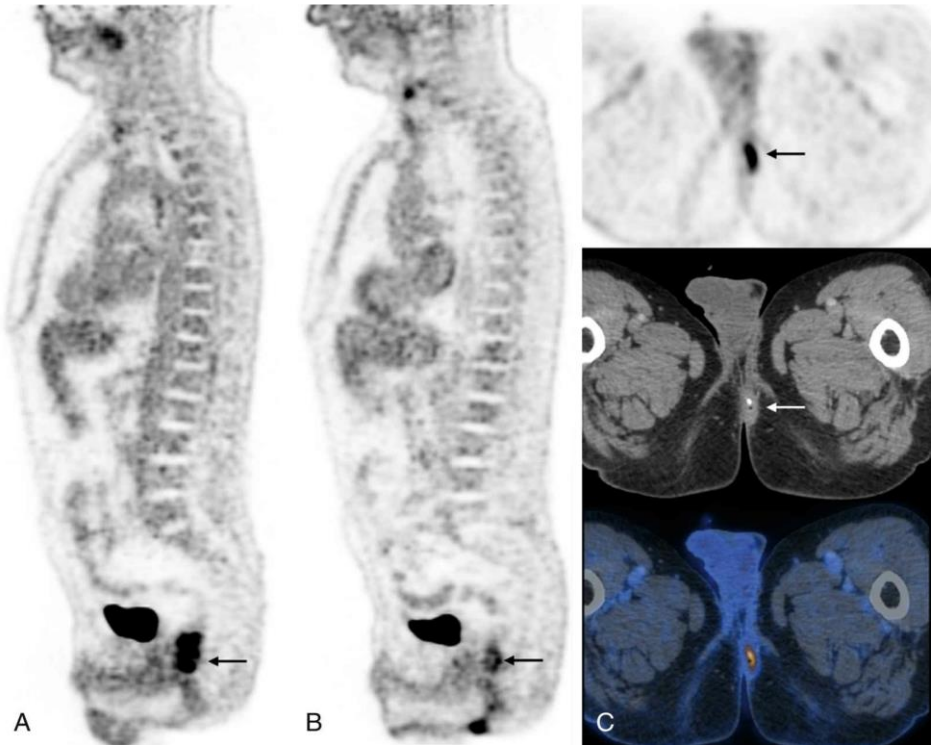
FDG PET/CT showing FDG-avid rectal wall thickening (B, *arrowhead*), representing the patient's known primary tumors. There are several tiny non-FDG-avid pelvic lymph nodes (B, *arrows*). An FDG avid right pulmonary metastatic nodule is also evident (C, *arrow*). A, FDG PET MIP image

Sigmoid Colon Cancer, Atypical Metastases



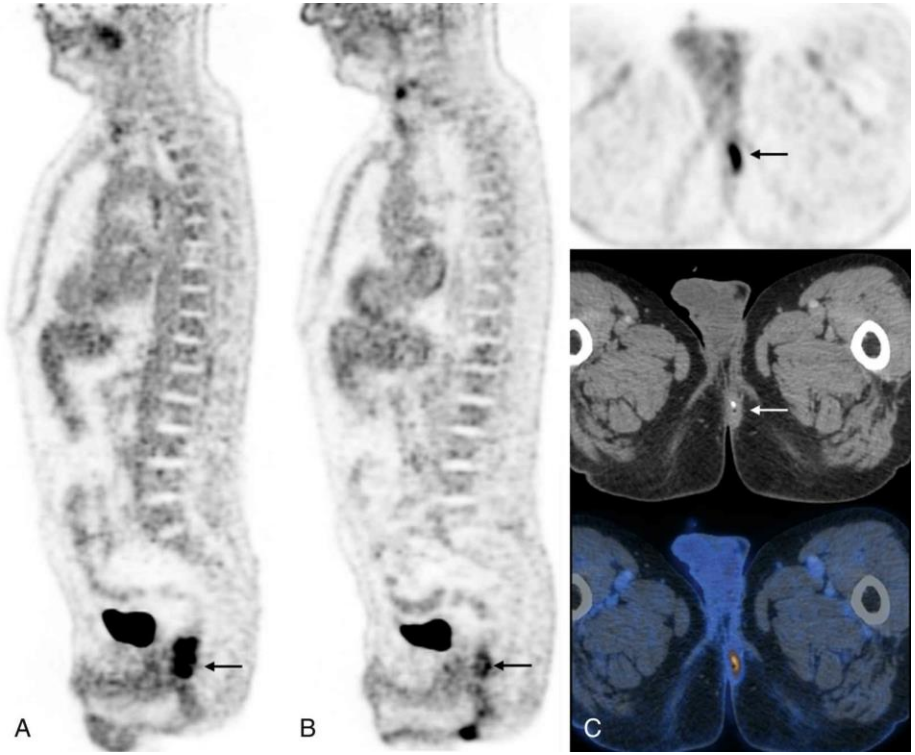
FDG PET/CT showing a small FDG-avid eccentric sigmoid wall thickening (B, *arrow*), which was confirmed as colon adenocarcinoma in pathology. An extensive FDG-avid lesion is evident on the left scapula, which is proved as metastasis by biopsy (C,*arrow*)

Staging Rectal Cancer, Pulmonary Metastasis



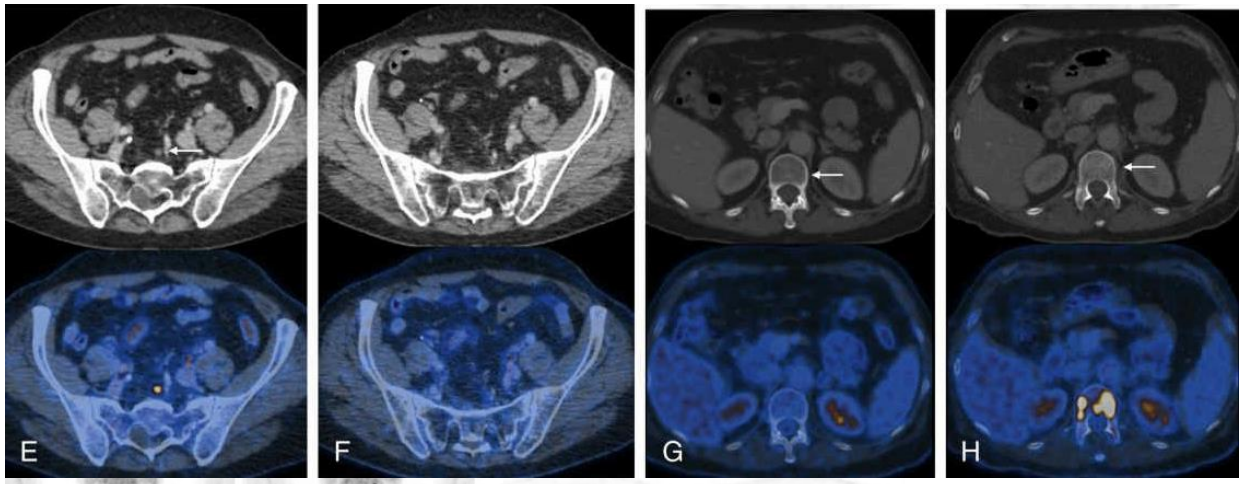
FDG PET/CT showing FDG-avid rectal wall thickening (B, *arrowhead*), representing the patient's known primary tumors. There are several tiny non-FDG-avid pelvic lymph nodes (B, *arrows*). An FDG avid right pulmonary metastatic nodule is also evident (C, *arrow*). A, FDG PET MIP image

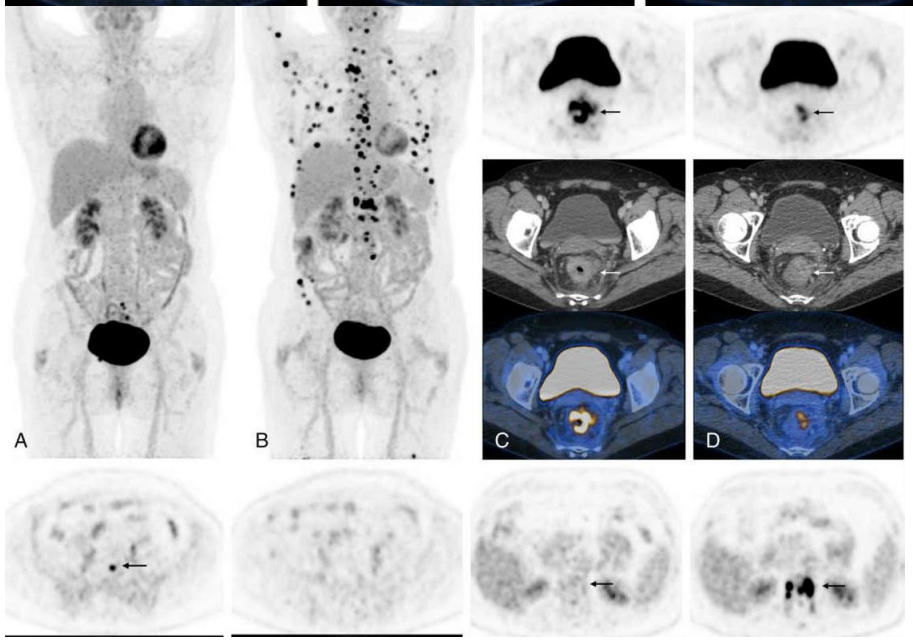
Rectal Cancer, Treatment Evaluation



FDG PET/CT showing an FDG-avid primary tumor (A, *arrow*) with an excellent metabolic response to neoadjuvant chemoradiation therapy (B, *arrow*). An increased focal FDG uptake is noted in the anal region on follow-up images (C, *arrow*), suggestive of inflammatory process caused by fistula formation after radiotherapy

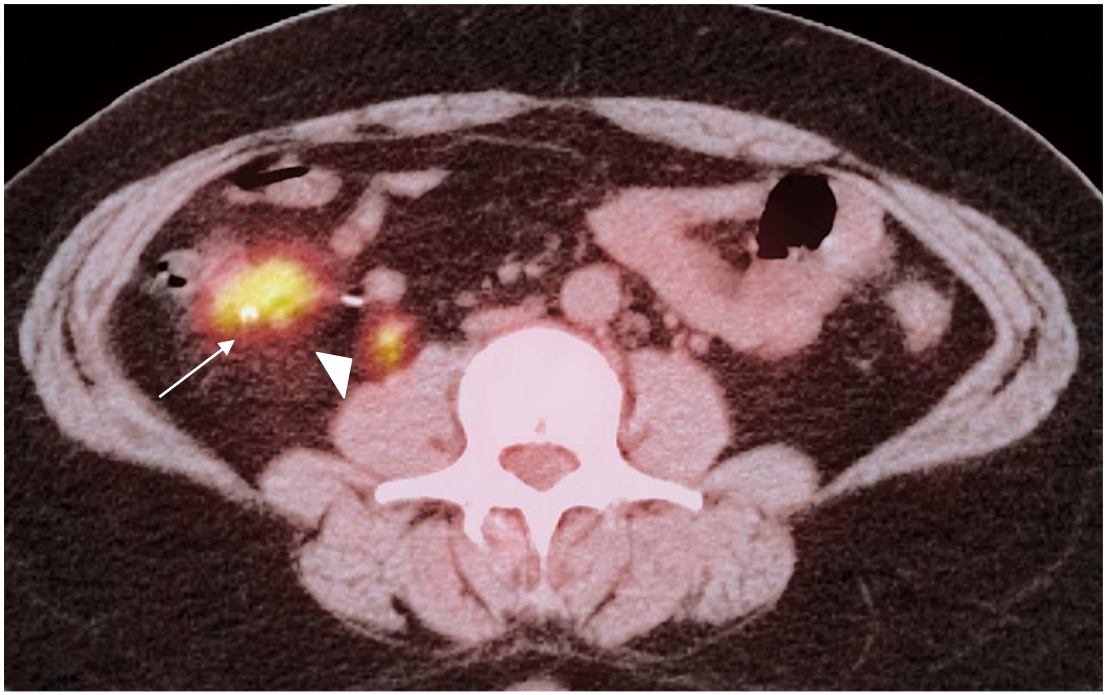
Restaging Rectal Cancer, Treatment Evaluation—Flip-Flop Response





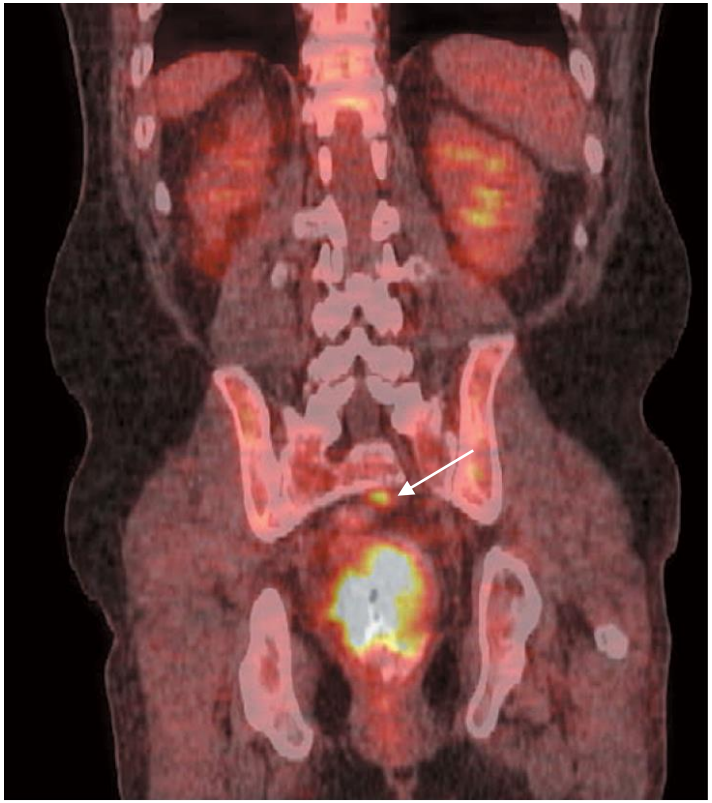
FDG PET/CT showing tracer-avid primary rectal malignancy (C, *arrow*) with excellent metabolic response to radiation therapy (D, *arrow*). A very small FDG-avid presacral metastatic lymph node is noted on PET without suspicious finding on CT (E, *arrow*). It responded to radiotherapy (F). The follow-up scan demonstrates extensive FDG-avid bone marrow metastases (B), with no prominent corresponding morphologic changes on CT (G, *arrow*, primary staging; H, *arrow*, restaging)

Recurrent Colon Cancer



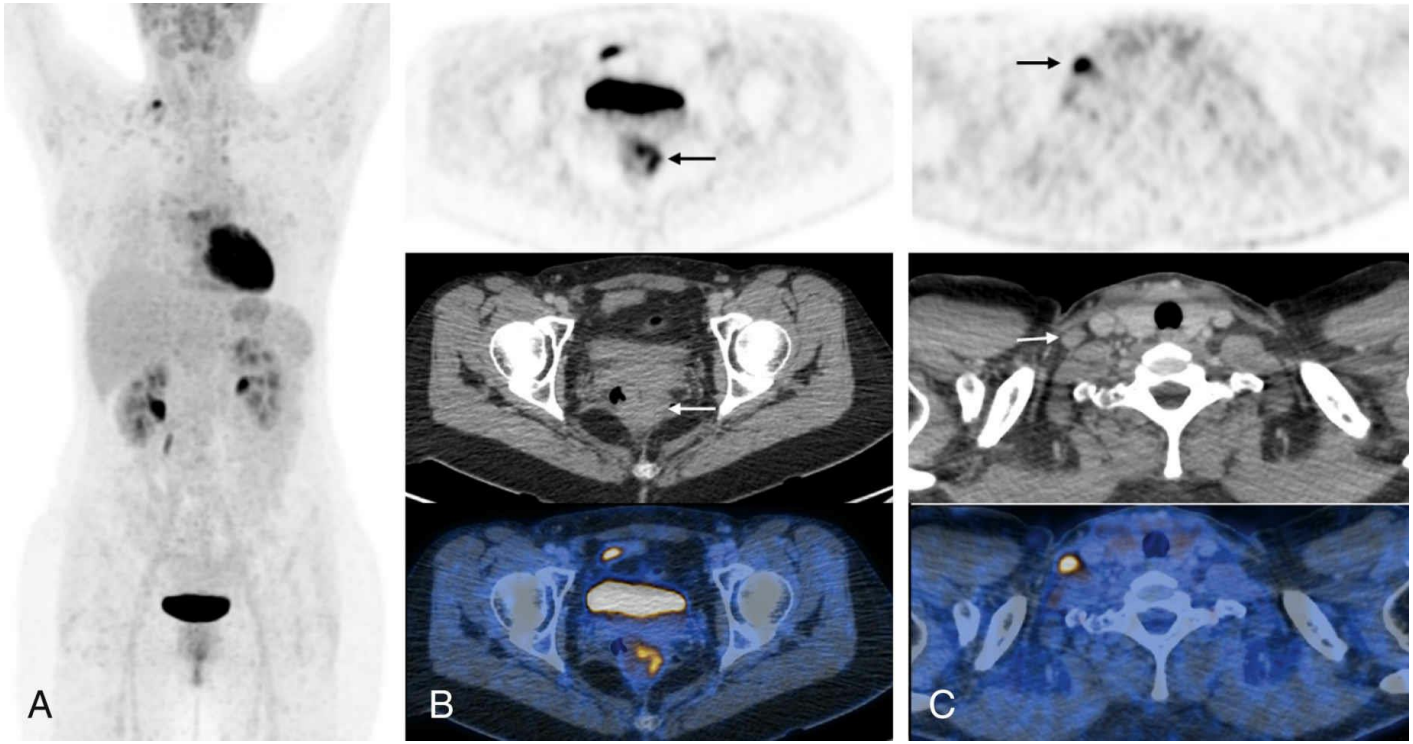
Recurrent colon cancer. Axial PET/CT scan in a patient with colon cancer demonstrates recurrent disease (arrow) near an anastomosis. A small medial focus of activity (arrowhead) is in the ureter

Recurrent Rectal Cancer



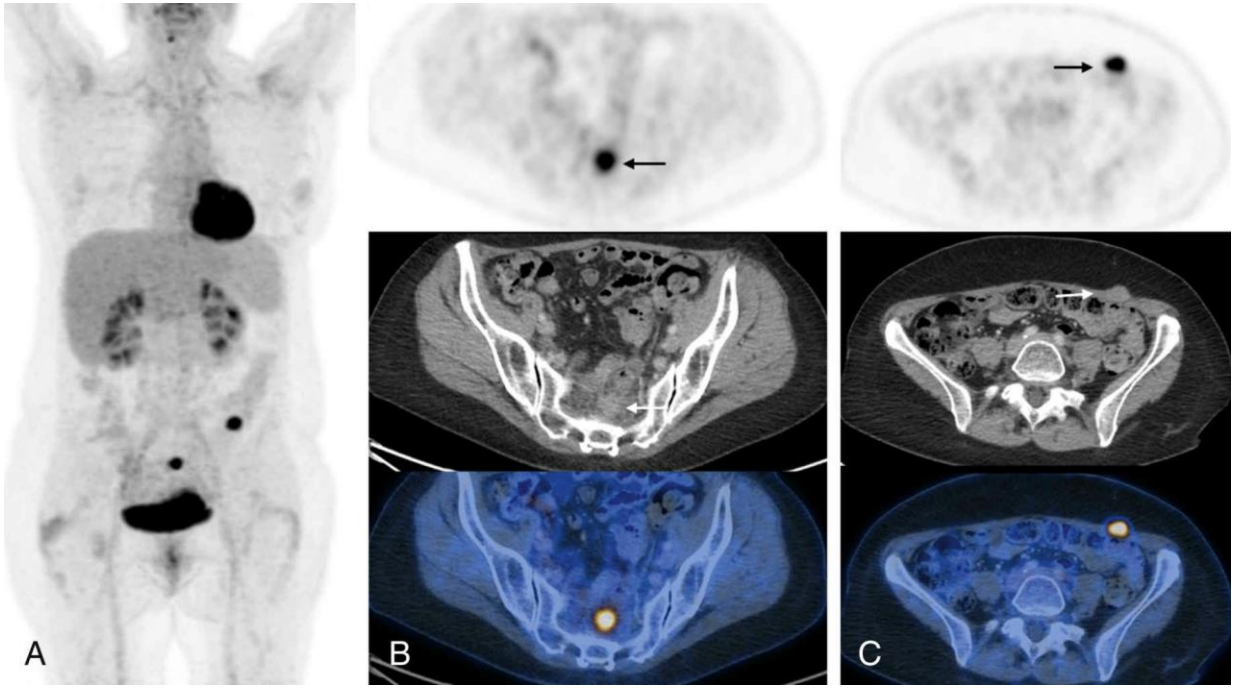
Recurrent rectal cancer. Coronal PET/CT demonstrates a large presacral recurrence of rectal cancer. A small local nodal metastasis (arrow) is present

Rectal Cancer Recurrence



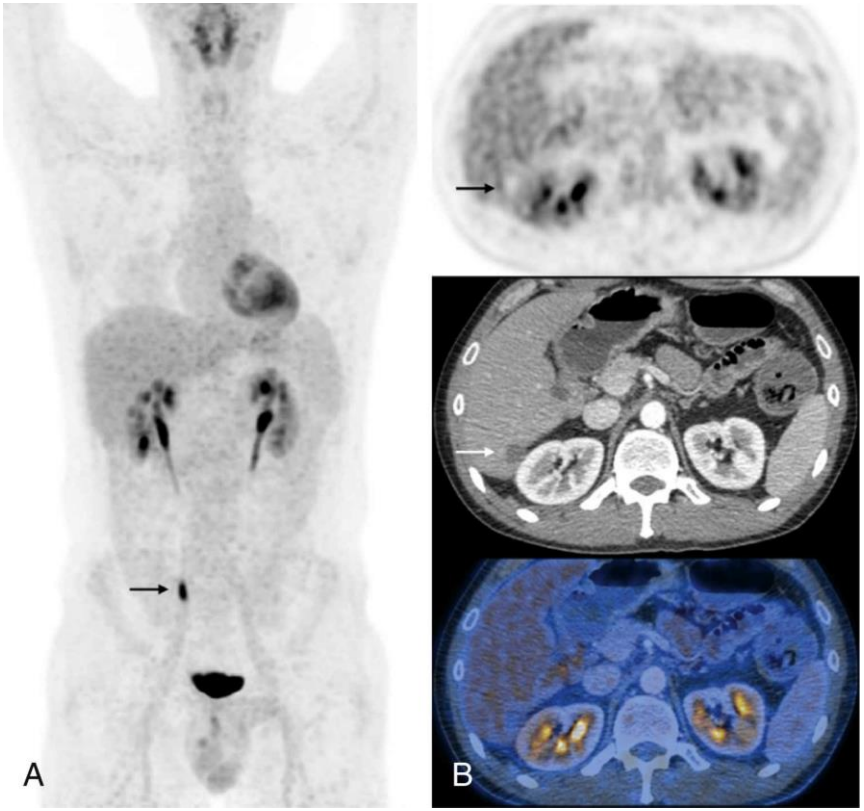
FDG PET/CT showing an increased tracer uptake of the anastomosis site (B, *arrow*). There is also a pathologic FDG-avid right supraclavicular lymph node (C, *arrow*), which is proved as metastasis on histopathologic examination

Sigmoid Cancer—Biochemical



FDG PET/CT showing a tracer-avid presacral soft tissue lesion (B, *arrow*), which was pathologically confirmed as recurrent sigmoid colon cancer. There is also an FDG-avid metastasis to the left abdominal wall (C, *arrow*). A, FDG PET MIP image

Follow-Up, Equivocal Morphologic Findings on CT



A 35-year-old male with history of colon cancer. Hypodense equivocal liver lesions on CT (B,*arrow*) without any pathologic FDG uptake. A, FDG PET MIP image

Liver Metastasis

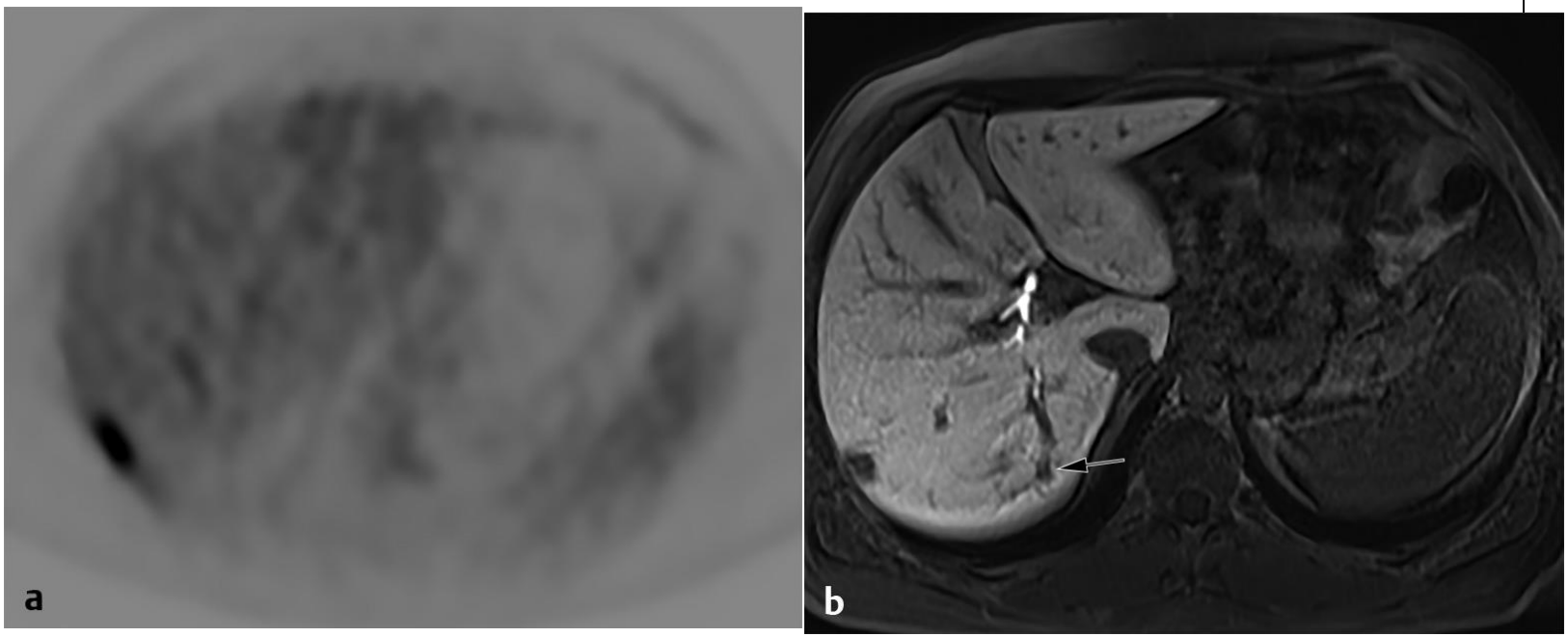


Fig. 25.8 Liver metastases. (a) Axial PET scan in a patient with rectal adenocarcinoma demonstrates a liver metastasis. (b) Axial hepatobiliary phase MRI performed with the hepatocellular contrast agent Eovist (gadolinium-EOB-DTPA, Schering AG), demonstrates the same metastasis in the peripheral right liver seen on PET, as well as an additional metastasis (arrow) not identified on PET