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PET/CT Scan in Colorectal Cancer

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Colorectal Cancer: Role of PET/CT Scan

General

- FDG focal uptake frequently may indicate a malignant or premalignant colonic lesion is present in the GI tract.
- TNM staging by PET/CT: Results can change management in up to third of patients,
- Advantage of whole body assessment
- Limited value for T and N results
- PET/CT should be considered in any potentially resectable metastatic disease, with dedicated contrast enhanced CT or MRI
- FDG PET/CT has an impact on the accurate planning of external beam radiation therapy
- PET/CT should be considered for localizing site(s) of disease recurrence in patients who have a rising serum CEA level and non-diagnostic conventional imaging.

Staging

- Significant allergy to iodinated CT contrast and gadollinum contraindication due to chronic renal failure without dialysis
- Equivocal finding on a contrast-enhanced CT scan
- Potentially surgically curable metastatic (M1) synchronous disease

Therapy monitoring

- Documented resectable metastasis on CT scan

Surveiilance

- Serial CEA elevation with negative chest, abdominopelvic Contrast enhanced CT scan
- Currently, PET/CT is not indicated for post-treatment surveillance.

Pronostication

- FDG PET/CT is superior to conventional imaging for prognostication

Staging:

Primary Tumor (T)

TX: Primary tumor cannot be assessed
T0: No evidence of primary tumor
Tis: Carcinoma in situ: Intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosa)
T1: Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2: Tumor invades the muscularis propria
T3: Tumor invades through the muscularis propria into the pericolorectal tissues
T4: Tumor invades the visceral peritoneum or invades or adheres to adjacent organ or structures
T4a: Tumor invades through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b: Tumor directly invades or adheres to adjacent organs or structures

Regional lymph nodes (N):

NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0·2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a: One regional lymph node is positive
N1b: Two or three regional lymph nodes are positive
N1c: No regional lymph nodes are positive, but there are tumor deposits in the subserosa, mesentery or non-peritonealized pericolic, or perirectal/mesorectal tissues
N2: Four or more regional lymph nodes are positive
N2a: Four to six regional lymph nodes are positive
N2b: Seven or more regional lymph nodes are positive

Distant metastasis (M):

• M0: No distant metastasis by imaging, etc; no evidence of tumor in distant sites or organs
• M1: Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
• M1a: Metastasis to one site or organ is identified without peritoneal metastasis
• M1b: Metastasis to two or more sites or organs is identified without peritoneal metastasis
• M1c: Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

Stage 0	Tis	N0	M0
Stage I	T1-T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage IIIA	T1-T2	N1/N1c	M0
	T1	N2a	M0
Stage IIIB	T3-T4a	N1/N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
Stage IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N1-N2	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b
Stage IVC	Any T	Any N	M1c

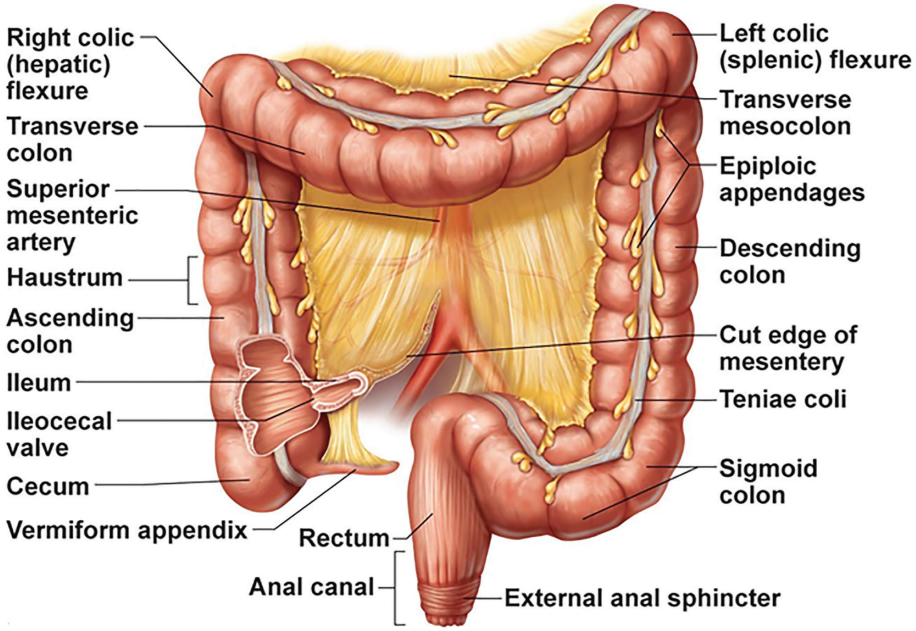


Fig : Anatomy of large intestine

FDG PET/CT

Development of positron emission tomography (PET) with 2-[18F] fluoro-2-deoxy-D-glucose (FDG), which exploits increased utilization and high uptake of glucose by malignant cells, in the late 1990s opened a new field in clinical oncologic imaging. More recently, integrated positron emission tomography/computed tomography (PET/CT), which combines a full-ring-detector clinical PET scanner with a multi-detector-row helical CT scanner, has made it possible to acquire both metabolic and anatomic imaging data with a single device in one diagnostic session, and has been demonstrated to show precise anatomic localization of suspicious areas of increased FDG uptake.

FDG-PET/CT use in clinical settings results in significant improvement in diagnostic accuracy, with considerable impact on patient management, including diagnosis, initial staging, treatment optimization, restaging, monitoring of response to therapy, and prognostication of various malignant tumors. We present here a review of the current and future roles of FDG-PET/CT for management of patients with colorectal cancer (CRC), as well as its usefulness and limitations.

Key Points

- **FDG focal uptake frequently indicates that a malignant or premalignant colonic lesion is present, but physiological FDG uptake is observed in the GI tract and may complicate CRC detection**
- **TNM staging by PET/CT: results can change management in up to third of patients, advantage of whole body assessment but limited value for T and N results**
- **PET/CT should be considered in any potentially resectable, either primary or secondary metastatic disease, with dedicated contrast enhanced CT or MRI**
- **FDG PET/CT has an impact in the accurate planning of external beam radiation therapy**
- **Currently, PET/CT is not indicated for post-treatment surveillance.**
- **PET/CT should be considered for localizing site(s) of disease recurrence in patients who have a rising serum CEA level and non-diagnostic conventional imaging.**
- **PET/CT is superior to conventional imaging for prognostication**

Introduction:

Colorectal cancer is the fourth most frequently diagnosed cancer and the second leading cause of cancer death.

Although there is increasing improvements in incidence and mortality of CRC as a result of cancer prevention and earlier diagnosis through screening and better treatment modalities, a retrospective study of the SEER registry found that the incidence of CRC in patients younger than 50 years has been increasing.

Risk Factors:

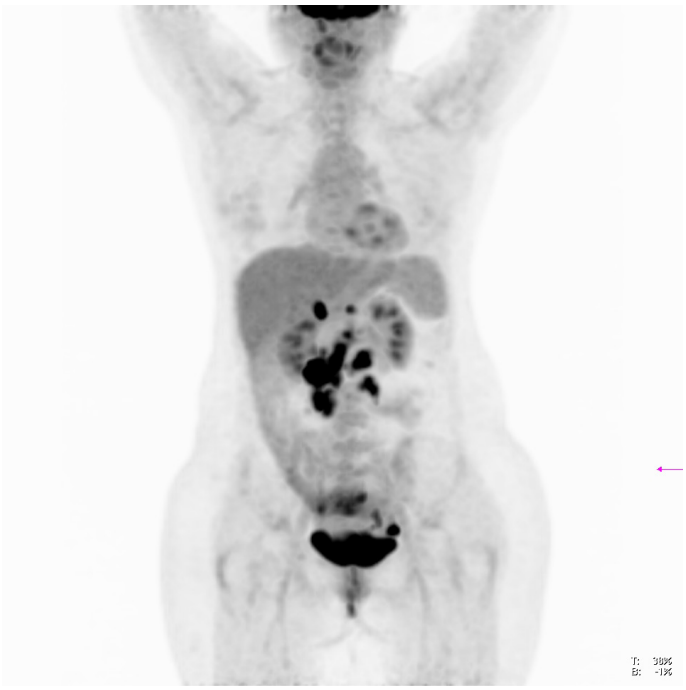
Approximately 20% of cases of colon cancer are associated with familial clustering and 1st degree relatives of patients with CRC are at increased risk for colorectal cancer. However, a family history of CRC improves the prognosis.

Genetic susceptibility to CRC includes syndromes such as Lynch syndrome and FAP. Other risk factors for colon cancer include IBD, smoking, the consumption of red and processed meats, alcohol consumption, diabetes mellitus, low level of physical activity, metabolic syndrome and obesity. Some data suggest that consumption of dairy, fish and legumes may lower risk for development of colorectal cancer. Furthermore, the use of aspirin or NSAIDS may also decrease the risk for CRC.

The most important treatment strategy for CRC in the early stage is potentially curative surgery. However, for locally advanced rectal cancer (pT3–4 N0 M0 or any T N1 M0), a multimodality strategy has been shown to be the best option to improve local control. Multimodality treatment includes preoperative concomitant chemotherapy and radiotherapy, followed by surgery. Particularly, neoadjuvant CRT helps to decrease tumor volume and stage, thus increasing the chance for potential resectability and sphincter conservation.

Diagnosis:

PET/CT Scan can aid in CRC detection, but frequent physiological FDG uptake is observed in the gastrointestinal tract and may complicate CRC detection. Also, diffuse uptake can be considered to be a normal variant, it can also occur secondary to inflammation or administration of certain drugs such as ***metformin*** that significantly increase FDG uptake in the colon and, to a lesser extent, the small intestine. In contrast, a finding of focal uptake frequently indicates that a malignant or premalignant colonic lesion is present. While the measurement of SUV does not allow the differentiation of benign from malignant processes of the colon, the presence of focal colonic FDG uptake as an incidental finding on PET/CT justifies a colon screening examination and PET/CT fusion can be particularly helpful for localization of lesions.



MIP image of an 18F-FDG PET/CT in a patient with colon cancer

Staging:

Staging	Therapy monitoring	Surveiilance	Pronostification
Significant allergy to iodinated CT contrast and gadollinum contraindication due to chronic renal failure without dialysis	***Documented resectable metastasis in CT scan***	***Serial CEA elevation; and negative chest, abdominopelvic CT scan with contrast***	***FDG PET/CT superior to conventional imaging for prognostication***
Equivocal finding on a contrast-enhanced CT scan			
Potentially surgically curable metastatic (M1) synchronous disease			

TNM staging of CRC is typically assessed by CT and/or MRI with the addition of endorectal ultrasonography with considering an MRI to assist with the diagnosis of rectal cancer, which includes tumors below a virtual line from the sacral promontory to the upper edge of the symphysis.

PET can be useful for pre-operative staging of colorectal cancer. ***The greatest value of PET lies in the fact that total body coverage allows detection of distant sites of disease.***

PET and PET/CT are clearly limited for T staging of the primary tumor due to limited spatial resolution and inability to distinguish the layers of the colonic wall. Trans-rectal ultrasound (US) and magnetic resonance imaging (MRI) provide much better anatomic resolution and are of greater value for T staging.

Nodal staging can be difficult with cross sectional imaging techniques such as US, CT and MRI. *On cross-sectional imaging, size (greater than 1 cm) remains the primary criterion for predicting nodal metastasis,* although it is well known that size is not an ideal indicator of disease. ***The advantage of PET lies in the ability to use metabolic activity to help distinguish benign from malignant adenopathy at sites away from the immediate vicinity of the primary tumor. Nodes in the immediate vicinity of the primary tumor are very difficult to detect with PET due to FDG activity of the primary*** which may obscure small lymph nodes. Small nodes are also not easily detected with PET. ***The overall sensitivity for nodal staging is therefore reported to be quite low.***

Accurate staging also requires the detection of distant sites of metastatic disease. This is important because limited disease spread such as liver involvement may be curable by surgery. Therefore, pre-operative knowledge of tumor extent is very important to determine if curative resection is feasible. It has been suggested that FDG-PET is more sensitive than CT in the detection of hepatic and pulmonary metastases and in identifying other sites of intra-abdominal disease. FDG-PET showed greatest accuracy

in the detection of liver metastases with reported accuracy up to 99%, sensitivity up to 100% and specificity up to 98% . It is important to keep in mind that lesion size is an important criterion for detection and small hepatic lesions are still not easily detected due to relatively high background liver activity. Also the limited spatial resolution of PET/CT alone makes surgical planning difficult. PET may also identify sites of disease that may preclude surgery or change the surgical approach. ***Several studies have shown that findings on PET and PET/CT results in change in stage and thereby alters management in up to 1/3 of patients.***

1 Colon cancer appropriate for resection (non-metastatic) :

When a non-metastatic colon cancer is suspected, the patient should be totally evaluated by chest, abdomen and pelvic CT with intravenous iodinated contrast and oral contrast material unless contraindicated. Routine use of PET/CT is not indicated in this setting.

When iodinated contrast material is contraindicated, MR examination of the abdomen and pelvis with IV-gadolinium-based contrast agent (GBCA) can be obtained instead.

If iodinated contrast and gadolinium are both contraindicated due to significant allergy or chronic renal failure without dialysis, then MR without IV contrast or PET/CT imaging should be considered. *In cases of equivocal finding on a contrast-enhanced CT scan, PET/CT should be considered .*

2 Suspected or proven metastatic synchronous adenocarcinoma (Any T, any N, M1):

When a metachronous, potentially resectable, metastatic disease with dedicated contrast enhanced CT or MRI is documented, characterization of the disease extent should be considered using PET/CT, if a surgical cure of M1 disease is feasible. PET/CT is used at this juncture to promptly characterize the extent of metastatic disease and to identify possible sites of extrahepatic disease that preclude surgery.

Therapy Monitoring:

Again, if metachronous metastasis is documented by CT, MRI and/or biopsy, and the patient is considered resectable, then an FDG PET/CT is considered.

FDG PET/CT has an impact in the accurate planning of external beam radiation therapy. It helps to protect normal tissue, especially in rectal cancer, in which radiation therapy is an essential part of the treatment. Furthermore, it allows for the evaluation of response to therapy.

Post-treatment surveillance:

After curative surgery and adjuvant chemotherapy, post-treatment surveillance of patients with colorectal cancer is performed to evaluate for feasible therapeutic complications, discover a recurrence that is potentially resectable for cure and identify new, metachronous neoplasms. *In this setting, PET/CT is not indicated.*

American Society of Clinical Oncology (ASCO) recommends that assay by carcinoembryonic antigen (CEA) be performed every 3 months for the first 3 years, CT scan of the chest, abdomen and pelvis be performed every year for the first 3 years and an endoscopy at 3 years in patients with stage 2 and stage 3 colorectal carcinoma.

Recurrence:

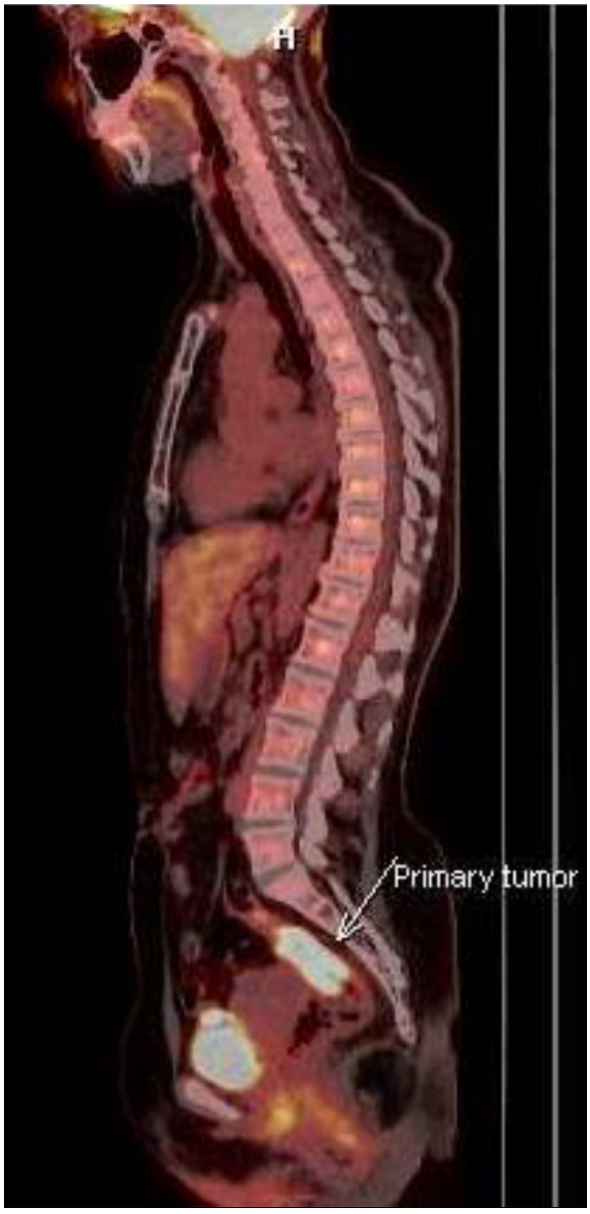
PET/CT should be considered for localizing site(s) of disease recurrence in patients who have a rising serum CEA level and non-diagnostic conventional imaging evaluation following primary treatment. In this setting, PET/CT scanning can potentially localize occult disease, permitting the selection of patients who may benefit from exploratory laparotomy.

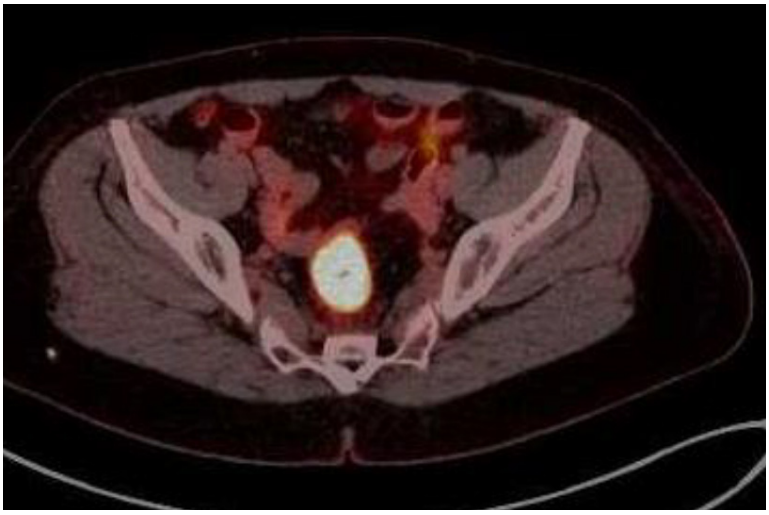
Prognostication:

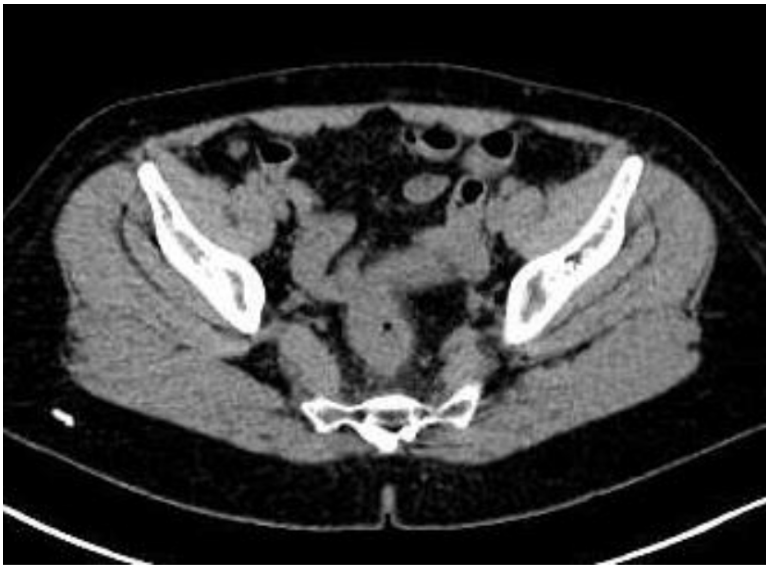
FDG PET/CT has also a prognostic role in CRC. It is superior to conventional imaging for prognostication.

Case Presentations

Case 1: PET image shows a primary FDG avid tumor in the rectosigmoid (arrow) in a patient with newly diagnosed colorectal cancer.

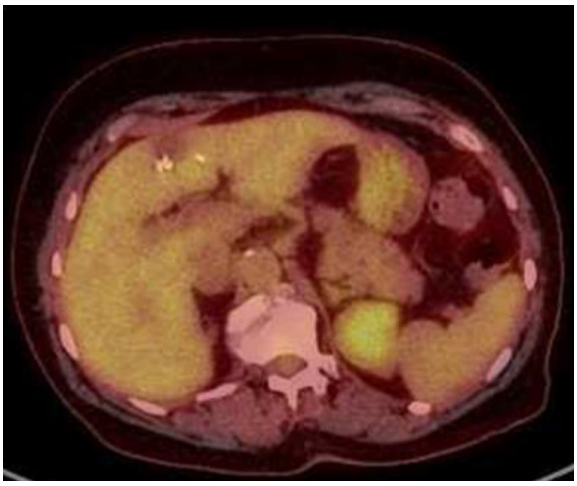


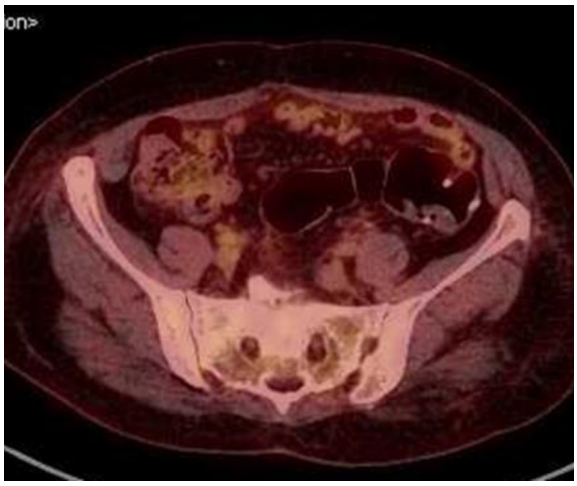




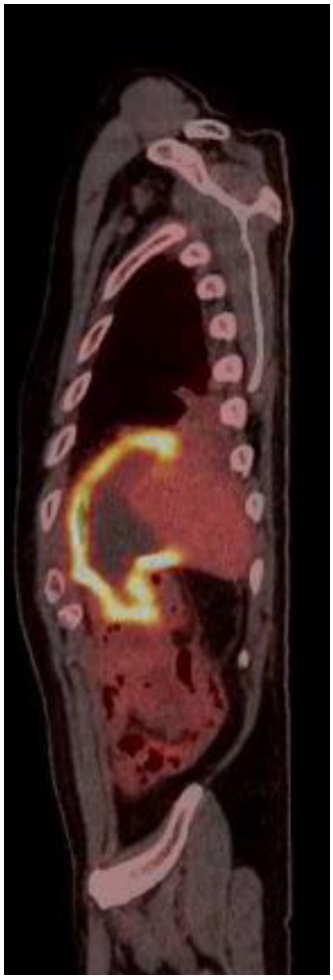
update in version 1·2018 of the NCCN guideline

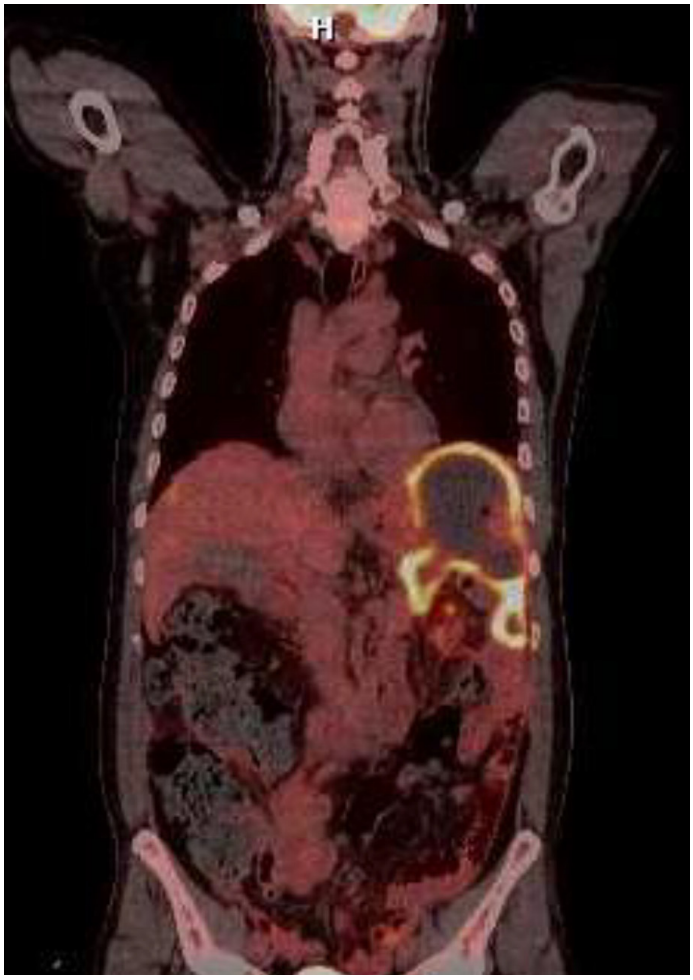
Case 2: The patient is referred for restaging of sigmoid adenocarcinoma one year after tumor resection and 6 months after hepatic metastatectomy with no evidence of malignancy recurrence in either surgical beds.



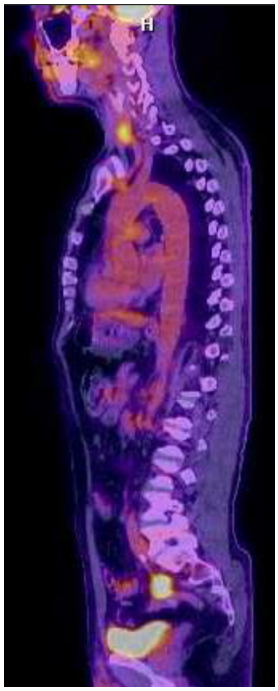


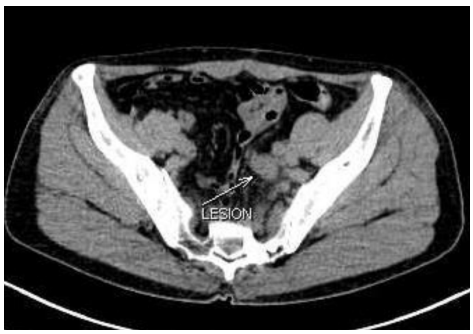
Case 3: Incidental finding: Foci of fluid filled, peripherally FDG avid pockets in a patient with high grade colon adenocarcinoma; status post left hemi colectomy, compatible with abscess formation.

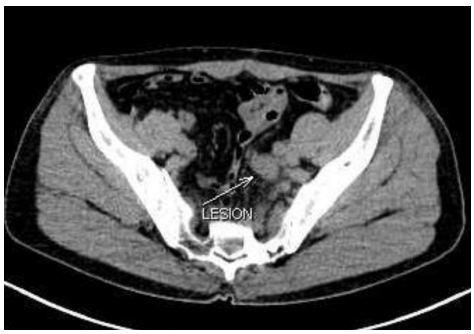


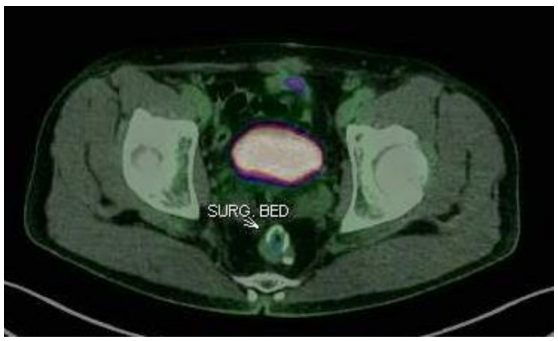


Case 4: An intensely FDG avid pelvic peritoneal soft tissue lesion; at the level of external iliac artery with no evidence of local malignancy recurrence in a patient with elevated CEA 2 years after rectosigmoid tumor resection

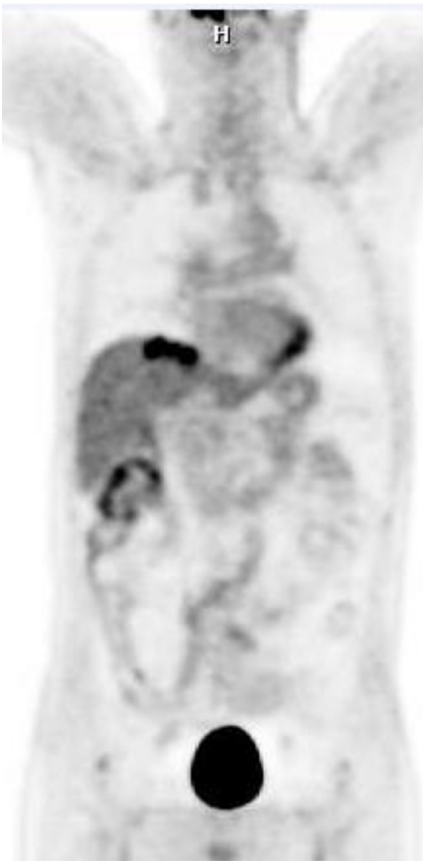


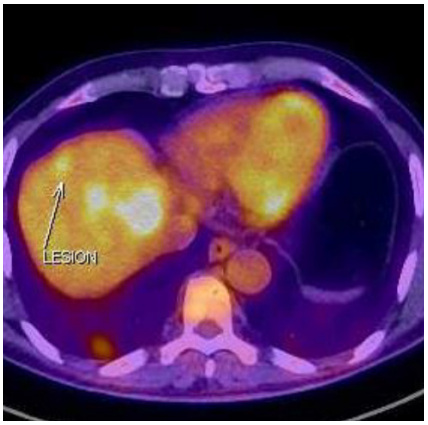


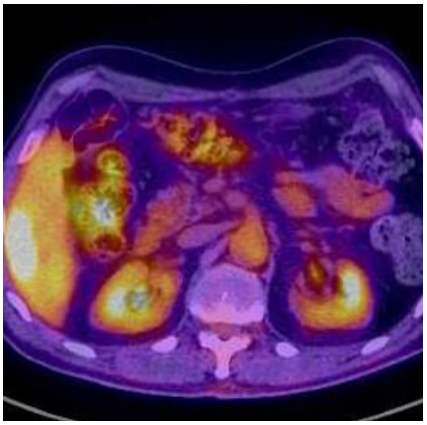


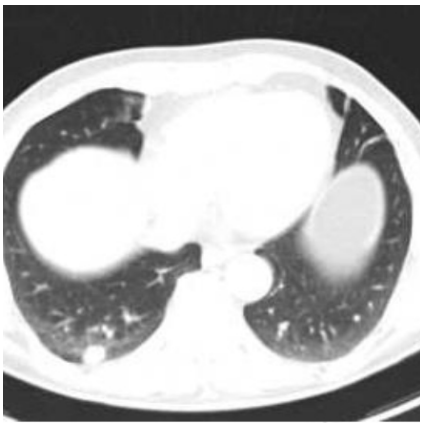


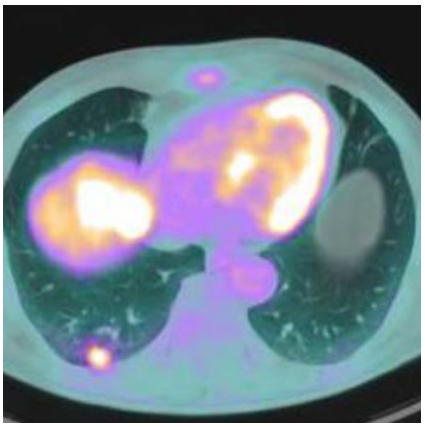
Case 5: Unexpected lung metastasis is a patient with known hepatic metastasis from resected sigmoid cancer; referred for staging











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