8. PET in Colorectal Carcinoma

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Colorectal cancer is the third most common malignancy in the United States, excluding skin carcinoma, and is the second leading cause of cancer-related death. The American Cancer Society estimated that approximately 145,000 new cases of colorectal cancer would be diagnosed in 2005 and approximately 56,000 people would die of the disease [1]. Colorectal cancer death rates have been steadily declining over the past 15 years due to increased public awareness, emphasis on early detection, and improvements in therapy.

Risk factors for developing colorectal cancer include age greater than 50, a positive family history, known genetic factors such as familial adenomatous polyposis and hereditary non-polyposis colorectal cancer, a history of colon polyps or inflammatory bowel disease, smoking, diabetes, and a diet which is high in fat, especially animal fat.

The obligatory precursor of colorectal cancer is the adenomatous polyp. While some patients may have occult bleeding and present with weakness related to anemia, the majority of patients with neoplastic colon polyps are asymptomatic and have hematologic indices that are within normal limits. If left undiagnosed, potentially curable disease can progress to an advanced stage. This is why colorectal cancer screening is so important. See Table 8.1 for the current American Cancer Society colorectal cancer screening guidelines [2]. Screening with stool guaiac testing, air contrast barium enema examination, and conventional optical colonoscopy have enabled physicians to detect the disease at an earlier and more successfully treatable stage. Computed tomography virtual colonoscopy is a relatively new and accurate screening technique which compares favorably with conventional colonoscopy. Its precise role in screening for colorectal neoplasm is continuing to grow and evolve. The 5-year survival rate for those with colorectal cancer detected early, before metastasis, can be better than 90%. See Table 8.2 for a breakdown of 5-year survival based on cancer stage [3].

Once cancer is detected, surgical options are available, and neoadjuvant and adjuvant chemoradiation therapy may be used to improve prognosis [4]. When metastasis occurs, surgical treatment may include local tumor resection, hepatic resection or pulmonary wedge resection. For liver or pulmonary metastasis radiofrequency ablation is used in selected patients. Despite advances, colon carcinoma remains a major cause of cancer-related deaths. Colon carcinoma recurrence is typically distant from the original tumor site, whereas locoregional recurrence is more common in rectal carcinoma. Colorectal cancer recurs in 37–45% of patients within 2 years of curative resection with early recurrence typically occurring at an average of 14 months after resection [5]. When cancer recurs locally, radical resection is the treatment of choice; however, few

Table 8.1. American Cancer Society colorectal cancer screening guidelines*

1. Fecal occult blood test (FOBT)† or fecal immunochemical test (FIT) every year, or
2. flexible sigmoidoscopy every 5 years, or
3. an FOBT† or FIT every year plus flexible sigmoidoscopy every 5 years (of these first three options, the combination of FOBT or FIT every year plus flexible sigmoidoscopy every 5 years is preferable), or
4. double-contrast barium enema every 5 years, or
5. colonoscopy every 10 years.

* Beginning at age 50, men and women who are at average risk for developing colorectal cancer should have one of the five screening options listed. Those at increased risk for colorectal cancer should undergo screening earlier and at more frequent intervals.
† For FOBT or FIT, the take-home multiple sample method should be used.
Source: From, "Can colorectal polyps and cancer be found early?" American Cancer Society (www.cancer.org); 2005 Accessed August 2005.

candidates are suitable for surgery. Surgery for palliation may include relief of obstruction by enteroenterostomy or stoma, adhesion lysis or removal of tumor causing hemorrhage. Research has shown the importance of good surgical technique, particularly in removing rectal cancers. Modifications of the surgical technique aimed at reducing local recurrence include wide and anatomic resection of the primary lesion with high vascular ligation and total mesorectal excision. The rectal stump is also subsequently washed with cytotoxic agents.

The locoregional recurrence rate of colorectal carcinoma has previously been described as high as 50% [6]. However, with modern surgical techniques recurrence rates are likely to be lower, typically in the range of 5–15% [7]. Only 4% of patients with locoregional recurrence who do not have re-resection are alive at 5 years [6]. Retroperitoneal recurrence is seen in 18% of patients, with 33%

Table 8.2. Five-year colorectal cancer survival rates by American Joint Committee on Cancer Stage

Stage	Five-year survival
I	93%
IIA	85%
IIB	72%
IIIA	83%
IIIB	64%
IIIC	44%
IV	8%

Source: From O'Connell, Maggard, Ko [3], by permission of the *Journal of the National Cancer Institute*.

of recurrence occurring in the liver; 25% of these patients with recurrence in the liver are suitable for curative resection. The 5-year survival post partial liver resection is 25–44% [8]. Liver resection itself has an operative mortality of 2–7% [9]. Lung metastasis occurs in 22% of patients for which resection potentially offers a cure. Pulmonary wedge resection, video-assisted pulmonary nodule resection or lobectomy have low perioperative mortality [10]. In patients with prior resection of hepatic metastasis, pulmonary metastasectomy also offers survival benefit [10].

The major role of ^{18}F fluorodeoxyglucose (FDG) PET imaging in colorectal carcinoma is in restaging and in the determination of the extent of metastatic disease prior to liver resection or pulmonary resection. For initial staging, CT, and in the case of rectal carcinoma, MRI, combined with operative lymph node resection of mesenteric lymph nodes remain the gold standard.

Technical Considerations

Oral contrast improves image interpretation on the CT scan, and, in many centers, is used routinely. Assessment of bowel wall lesions is improved by distension of the small or large bowel, which helps to eliminate the possibility of an erroneous CT correlate for focal physiologic bowel activity on the PET scan. Oral contrast was reported in early studies to cause artifacts on PET imaging in the bowel within areas of dense barium concentration because it causes overestimation of tissue FDG concentration. This appearance is readily recognizable on direct comparison with co-registered CT images. With the use of less dense oral contrast agents and improved reconstruction algorithms, oral contrast does not cause artifacts in the PET imaging from a PET/CT scanner. Many centers recommend the routine use of endorectal contrast in CT staging of rectal cancer, but this use has not gained acceptance in PET/CT. Intravenous contrast is used in CT to assess liver lesions and to distinguish retroperitoneal lesions from adjacent vascular structures. In PET/CT, intravenous contrast is used to improve accuracy of interpretation. The importance of using intravenous contrast with PET/CT is under evaluation.

Mucinous Adenocarcinoma

Mucinous colorectal carcinoma has been reported as demonstrating less uptake than non-mucinous carcinoma on FDG-PET imaging. The reduced uptake may reflect reduced cells per unit volume (tumor cells are surrounded by secreted mucin) or alterations in the intracellular metabolism of FDG. Sensitivity of PET for detection of primary and recurrent mucinous carcinomas has been reported to be as low as 58% [11]. Co-registered CT as part of PET/CT imaging is likely to increase sensitivity for mucinous tumor detection, especially if intravenous contrast is used.

Diagnosis

PET imaging is rarely used for colon cancer diagnosis, but may be used in the identification of a primary lesion in the colon in a patient presenting with metastatic carcinoma of unknown primary. Incidental gastrointestinal tract lesions are detected in 3% of all patients undergoing FDG-PET imaging for a variety of indications [2]. Of these lesions, 60% turn out to be cancers or precancerous lesions [12]. In colorectal carcinoma, the primary lesion is detected in 95% of patients (Figure 8.1); however, specificity is limited to 43%. Lesions of 11–14 mm may be detected [13]. However, the relatively low specificity makes screening with PET imaging impractical. The low specificity also reflects detection of colonic adenomas that, despite being associated with a risk of progression to colon carcinoma, are regarded as false positives. The degree of uptake in adenomas does not correlate with the degree of dysplasia. Low-grade radiotracer uptake can rarely be seen in hyperplastic polyps or thrombosed hemorrhoids. However, hyperplastic polyps typically demonstrate no FDG uptake. One study demonstrated adenomas having lower FDG uptake (SUV 3.56 ± 0.68) than colonic carcinomas (SUV 5.74 ± 2.26); however, this difference is not likely to be a useful discriminator [14]. The sensitivity for detecting adenomas is low for small lesions, with 24% of polyps measuring 5 mm or smaller identified [12], which is close to the lower limit of PET image resolution. Ninety percent of lesions measuring greater than 13 mm are identified. PET demonstrates a higher sensitivity for detecting adenomas in the cecum, ascending colon, and descending colon [13], which may relate to the relative lack of movement with respiration of these regions of the colon that are predominantly retroperitoneal. The lifetime risk of an adenoma progressing to cancer is up to 10%, and endoscopic or surgical resection is indicated [15].

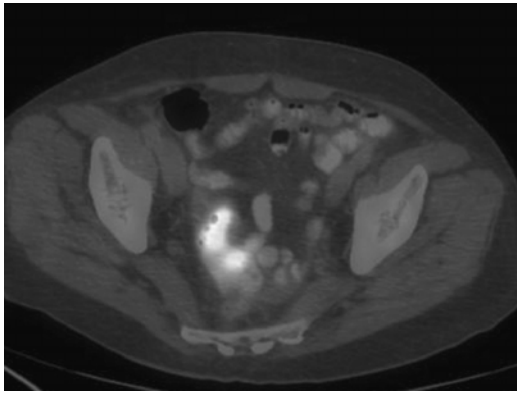

Figure 8.1. Axial fusion PET/CT image demonstrates intense focal radiotracer uptake in a primary sigmoid colon mass.

Initial Staging

PET imaging is reimbursed by the Centers for Medicare and Medicaid Services (CMS) for primary staging of colorectal carcinoma, but in many centers it is not used for this purpose, with operative staging of lymph node involvement by the TNM (Table 8.3) or Dukes' staging system being used instead. PET/CT is superior to CT in the detection of lymph node metastasis at initial staging, with the gold standard being surgical resection. When PET imaging is used in initial staging, it influences management mainly in the identification of liver or distal metastasis. Despite the presence of metastasis, surgery may still be performed to prevent colonic obstruction. In the presence of metastasis, con-

Table 8.3. TNM staging of colorectal carcinoma

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria*
T1	Tumor invades submucosa
T2	Tumor invades through muscularis propria
T3	Tumor invades through muscularis propria into subserosa or into non-peritonealized pericolic or perirectal tissues
T4	Tumor directly invades other organs or structures, and/or perforates visceral peritoneum (direct invasion in T4 includes invasion of other sections of the colon or rectum through the serosa)†,‡
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis in 1 to 3 lymph nodes
N2	Regional lymph node metastasis in 4 or more lymph nodes
Distant metastasis (M)	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

* Includes cancers confined within the glandular basement membrane (intraepithelial) or lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

† Direct invasion in T4 includes invasion of other segments of the colorectum by way of the serosa; for example, invasion of the sigmoid colon by a carcinoma of the cecum.

‡ Tumor that is adherent to other organs or structures, macroscopically, is classified T4. However, if no tumor is present in the adhesion, microscopically, the classification should be pT3. The V and L substaging should be used to identify the presence or absence of vascular or lymphatic invasion.

Source: Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Manual*, Sixth Edition (2002), published by Springer-Verlag, New York, www.springeronline.com.

servative treatment options are available and include metallic colonic stent placement. Because metastatic disease only occurs if the submucosa is involved, PET is not likely to be useful in initial staging of carcinoma in situ or post polypectomy with no evidence of residual tumor, and therefore PET imaging as part of initial staging is not recommended in most patients presenting with colorectal cancer [16].

PET imaging cannot exclude microscopic metastatic disease, and lymph node excision at initial surgery remains the gold standard for N staging. CT for colonic tumors and MRI for rectal tumors are used for nodal staging prior to surgery. MRI performed with an endorectal coil has an accuracy of 80% in local nodal staging [17], with similar results for external array MRI coils. In addition, local extension of rectal tumors into the mesorectal fascia can be identified. CT is used primarily to assess for retroperitoneal, hepatic, and pulmonary metastasis. PET may be used in selected patients where distal metastases are suspected at diagnosis. For CT and MRI, size criteria are used in the evaluation of perirectal nodes and 5 mm is used as the upper limit of normal lymph node size, rather than 6–10 mm as at other sites in the retroperitoneum or mediastinum [17]. In addition, the architecture of local lymph nodes on T2-weighted MRI is also useful. In locoregional lymph node staging, similar to PET imaging in esophageal cancer, peri-tumoral hypermetabolic lymph nodes can be missed because of "blooming" of intense radiotracer activity in an adjacent colonic primary lesion.

Restaging

The major role of PET in colorectal carcinoma is in restaging. Indications for restaging of colorectal carcinoma are potential curative surgery for isolated metastatic disease, differentiation of scar from recurrent tumor, particularly in the pre-sacral space, and evaluation of increased carcinoembryonic antigen level (CEA). Although restaging PET was initially used only in patients with abnormal CEA levels, currently PET is indicated in restaging colorectal carcinoma in patients with normal or elevated CEA levels. Colon carcinoma and rectal carcinoma behave differently in terms of recurrence site, with colon carcinoma typically recurring distant from the original site, either within the abdomen, retroperitoneum or the liver, whereas locoregional recurrence is more common in rectal carcinoma, typically in the pre-sacral region.

Neoadjuvant chemotherapy is used in colorectal carcinoma; however, the role of restaging in this context has had very limited evaluation. PET was superior to CT and MRI in detecting treatment response in rectal carcinoma in one study that demonstrated PET as having positive and negative predictive values of 77% and 100%, respectively. In comparison CT had positive and negative predictive values of 78% and 57%, respectively, with MRI at 83% and 50%, respectively [18]. Local radiotherapy has the potential to give false-positive findings relating to inflammation or inflammation with fibrosis. Restaging should be performed 6 months after radiation treatment to reduce false-positive results. This interval is often not practical, with earlier follow-up more frequently employed. Rarely, post-radiation changes may persist after 6 months.

PET, in common with imaging modalities including CT and MRI, may not detect very low-volume disease and microscopic disease cannot be excluded. In addition, PET has been reported as having lower sensitivity for detection of peritoneal carcinomatosis, likely related to the relatively small volume of peritoneal deposits. The lesion resolution of most standard PET imaging systems is 8–10 mm and small peritoneal deposits may be below this range in size. However, PET/CT helps to overcome this limitation, where the superior spatial resolution of CT avoids a misdiagnosis (Figure 8.2).

In evaluation of local or pelvic recurrence and distant metastasis, PET has higher sensitivity and accuracy than CT, with sensitivity of 79–100%, specificity of 58–100%, and accuracy of 83–100% [4] (Figure 8.3). CT has a reported sensitivity of 47–86%, specificity of 36–100%, and accuracy of 56–83% [4].

In rectal carcinoma PET is commonly used to differentiate post-surgical changes on CT from recurrent tumor in the pre-sacral space. Using CT alone, the only option for evaluation of soft tissue at this site is short interval follow-up CT at 2–3 months or image-guided biopsy. These approaches lead to a delay in the diagnosis of recurrence and unnecessary biopsy procedures. Increased FDG uptake may be identified in postoperative soft tissue in the pre-sacral space for up to 4 months after surgery [19]. When evaluation is made for recurrence at the anastomosis site, false-positive results have been described to result from postoperative inflammation or healing. PET is useful in the evaluation of small lymph nodes in the retroperitoneum or mesentery that may be considered within normal limits for size or indeterminate by CT criteria. In unusual cases where suspicious lymph nodes identified at CT are negative at PET, biopsy should nonetheless be performed. False-positive results on PET are rarely seen in reactive lymphadenopathy. PET/CT can be useful to identify small focal areas of pericolic tumor that may otherwise be difficult to identify on CT. Oral contrast is likely to improve sensitivity in this context.

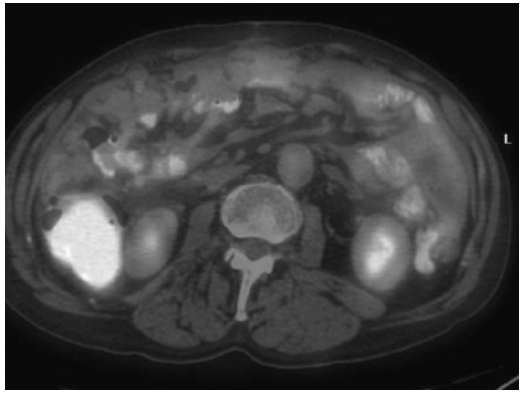

Figure 8.2. Intense hypermetabolic activity in a cecal carcinoma primary lesion with multiple adjacent foci of uptake identified consistent with diffuse peritoneal metastasis.

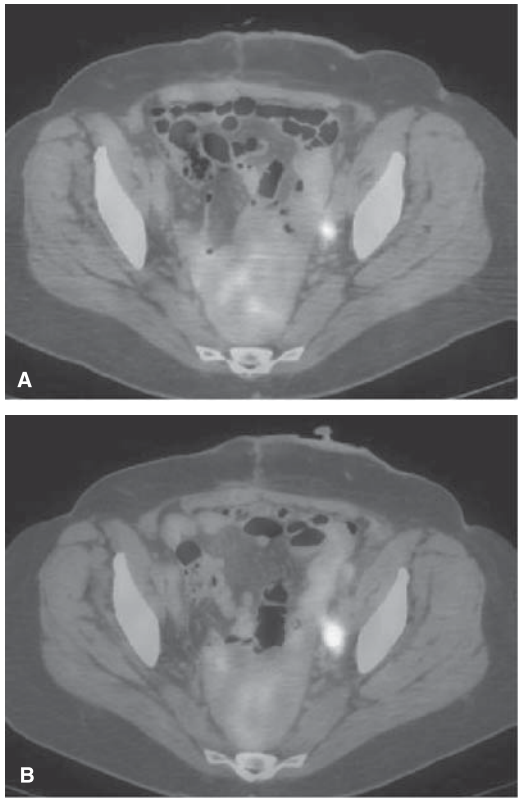

Figure 8.3. **(A)** Focal intense radiotracer uptake in a subcentimeter left pelvic side wall lymph node is consistent with metastasis. **(B)** Axial fusion PET/CT image in the same patient 3 months later demonstrates enlargement of the same pelvic side wall lymph node.

Partial hepatic resection is associated with a high rate of recurrence in patients with colorectal carcinoma, which suggests that current pre-surgical evaluation is suboptimal. PET may be used to reduce morbidity and mortality associated with inappropriate liver resection surgery. Five-year survival increases from 30% to 58% when PET imaging is negative for *extra hepatic disease* prior to resection [20]. In evaluation of recurrent liver metastasis, PET has higher specificity and accuracy than CT. In a lesion-by-lesion analysis, PET demonstrates 70% of liver masses identified histologically at liver resection, but with small lesions less apparent, where contrast MRI is superior in the detection of sub centimeter metastases [21]. The main added benefit of PET, however, is in the improved detection of extrahepatic metastatic disease. Other imaging modalities such as MRI and CT arterial-portography are limited in the detection of

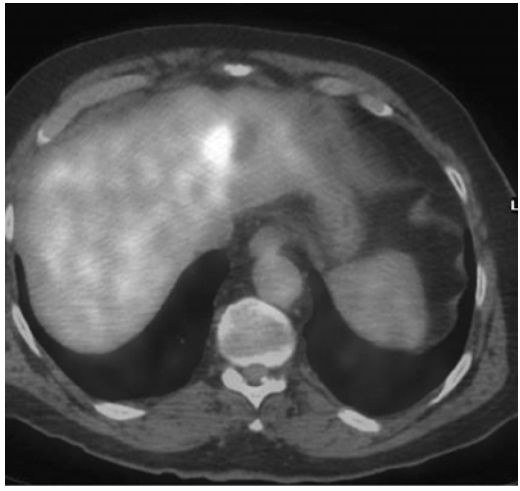

Figure 8.4. Axial fusion PET/CT demonstrates intense focal radiotracer uptake on the lateral margin of a radiofrequency ablation site in the liver. Recurrent disease was not apparent on conventional imaging.

extrahepatic disease. In potential partial resection candidates, PET changes management in 18–29% of patients [22]. In liver metastases, uptake in lesion margins with central photopenia (low uptake) indicates central necrosis, and confirmatory biopsy should be from the lesion margin. PET has been demonstrated to improve sensitivity in restaging liver metastasis following radiofrequency ablation (Figure 8.4). This improved sensitivity is likely to have an impact in the earlier detection of recurrence at the margin of the ablation site, in one study detecting tumor 3 months earlier by PET than on CT [23].

Interpretation Considerations

Bowel accumulation of FDG is identified in the colonic mucosa and is rarely in the bowel lumen. Bowel wall activity can be distinguished from recurrent tumor by lack of a CT soft tissue mass correlate or by demonstration of a typical pattern of bowel uptake. A "string of beads" appearance is used to describe the appearance of physiologic radiotracer uptake in bowel on PET imaging. Diffuse, intermediate level uptake is commonly identified in colon and small bowel. Although several methods of decreasing bowel accumulation of FDG have been tried, no technique has been demonstrated to consistently decrease bowel uptake of radiotracer. More focal uptake may be seen in diverticulitis, focal colitis, or following polypectomy. Focal physiologic activity may occasionally be very intense and close correlation is needed with associated CT images to assess for

focal wall thickening to rule out an associated lesion. Crohn's disease is a cause of potential false-positive colonic uptake that may be distinguished from tumor by the presence of diffuse bowel wall thickening, multifocal involvement, associated mesenteric changes, and characteristic or prior history. More diffuse colitis is clearly identified corresponding to longer segments of colonic involvement and is not likely to be mistaken for tumor. PET has the potential to identify synchronous bowel lesions, but colonoscopy, or in the case of narrow strictures, virtual colonoscopy, is more commonly used for this purpose.

PET/CT reduces false-positive results and leads to more definitive reports, improving accuracy from 78% to 89% in patients with colorectal cancer [24]. Accumulation of FDG may be seen in radiation proctitis, postoperative granulomas, peristomal colon, and laparoscopy ports. To reduce false-positive results, correlation with the patient's clinical history is needed. A patient questionnaire can confirm dates of surgery, radiotherapy, and current symptoms. On PET images focal accumulation of radiotracer in the ureter may have very intense activity similar to renal or bladder activity and should not be mistaken for metastasis. PET/CT allows direct correlation of this activity with a normal retroperitoneal ureter.

Pulmonary nodules less than 5–10 mm in size may have false-negative uptake because of relative motion in the lungs during normal respiration and the limited resolution of PET. Evaluation of non-attenuation-corrected PET images is recommended routinely in the assessment of radiotracer activity in small pulmonary nodules, especially in patients with significant misregistration of PET and CT images resulting from motion. Pulmonary nodules only partially consist of tumor, and the CT or radiographic opacity reflects tumor surrounded by inflammation, hemorrhage, necrosis or atelectasis within the adjacent lung, which results in relatively lower or a smaller focus of uptake on PET. In addition, respiratory motion artifactually lowers apparent radiotracer uptake particularly in lower lobe pulmonary lesions. This motion can be overcome by respiratory gating at the cost of extra scanning time, with the PET image acquisition time for the thorax typically being increased by a factor of 4. Respiratory gating is currently not widely available or utilized. If small pulmonary nodules are not identified on PET imaging, they may be identified on the CT portion of PET/CT imaging. So-called "cold" nodules require standard CT follow-up at 3 and 6 month intervals for stability, whereas wedge resection or chemotherapy may be indicated for "hot" or hypermetabolic lesions. The CT portion of PET/CT is commonly performed in either the end-tidal volume phase or during quiet respiration, which provide the closest match to PET for image co-registration. However, these phases of respiration lower CT sensitivity for detection of very small pulmonary nodules. Alternatively, a separate dedicated inspiratory CT may be performed as part of the imaging protocol solely for pulmonary nodule evaluation.

The accuracy and effectiveness of PET imaging in colorectal cancer has been well studied. In the assessment of data in the literature from the previous 10 years studying PET sensitivity for nodal involvement and distal metastatic disease, there are multiple confounding factors including the use of PET versus PET/CT, the use of emission only versus attenuation-corrected PET images, and the use of single versus multidetector CT scanning (MDCT). In addition, surgical gold standard staging varies in terms of number of lymph nodes resected,

Table 8.4. Limitations of PET in colorectal cancer

(a) False positives:
Physiologic colonic radiotracer uptake
Colonic adenoma (premalignant lesion)
Thrombosed hemorrhoid
Acute diverticulitis
Colonic fistula
Liver abscess
Post-radiation colitis/proctitis
Postoperative uptake – scar, stoma, laparoscopy ports, pre-sacral soft tissue (for up to 4 months postoperatively)
Crohn's disease
(b) False negatives:
Mucinous colorectal carcinoma (uncommon)
Peritoneal carcinomatosis (PET/CT may help to overcome this limitation)
Low volume nodal or metastatic disease (in common with all current imaging modalities)
Pulmonary nodules <1 cm on PET (PET/CT will identify small pulmonary nodules)
Liver metastases less than 1 cm in size detected by contrast MRI, but may be detected by contrast enhanced PET/CT

limited sampling of local lymph nodes, and whether total mesocolon resection is routinely performed. Histologic techniques also vary, with conventional histology demonstrating less nodal involvement in comparison to molecular biology techniques. Only limited data on the accuracy of PET/CT in terms of long-term follow-up or prognosis are available as yet. The ability of the radiologist or nuclear medicine physician to interpret both modalities of PET/CT is likely to increase the added benefit of the combination modality, with a recent study demonstrating 18% increased accuracy when dedicated reporting of the CT portion of a PET/CT examination was performed [25].

Postneoadjuvant chemotherapy, liver lesions with residual abnormality detected by CT, or MRI may no longer demonstrate increased FDG uptake at PET/CT consistent with treatment response by PET criteria. As a result these lesions are no longer identified on the PET component of the PET/CT study but are identified on the contrast CT component of PET/CT. Microscopic residual disease should be considered in such lesions prior to liver resection.

Conclusion

The limitations of PET in colorectal cancer are presented in Table 8.4. The strongest indications for PET or PET/CT imaging in colorectal carcinoma are in the diagnosis of recurrent disease, exclusion of extrahepatic metastasis prior

to liver resection, exclusion of extrapulmonary metastasis prior to lung resection, or in the evaluation of a rising CEA level. Optimal imaging assessment prior to liver resection is with a combination of PET/CT and contrast MRI. Despite the relatively increased cost of FDG-PET imaging in comparison to other modalities, it is cost-effective because of increased diagnostic accuracy in comparison to CT. The information provided by PET/CT is likely to combine the best imaging features of both modalities and become the gold standard for staging in colorectal carcinoma.

References

1. What are the key statistics for colorectal cancer? American Cancer Society (www.cancer.org); 2005 Accessed August 2005.
2. Can colorectal polyps and cancer be found early? American Cancer Society (www.cancer.org); 2005 Accessed August 2005.
3. O'Connell JB, Maggard MA, Ko CY. Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. J Natl Cancer Inst 2004;96(19):1420–1425.
4. Kitapci MT, Coleman RE. Colorectal cancer. In: Oehr P, Biersack HJ, Coleman E, editors. PET and PET/CT in Oncology. Berlin: Springer; 2003;20:213–226.
5. American Cancer Society 2003. Facts and figures. Atlanta, GA: ACS.
6. Nyam DC, Ho YH, Leong AF, Seow-Choen F. Palliative surgery for locally recurrent colorectal cancer. Singapore Med J 1999;40:333–335.
7. Heald RJ, Karanjia ND. Results of radical surgery for rectal cancer. World J Surg 1992;16:848–857.
8. Fuhrman GM, Curley SA, Hohn DC, Roh MS. Improved survival after resection of colorectal liver metastasis. Ann Surg Oncol 1995;2:537–541.
9. Holm A, Bradley E, Aldrete JS. Hepatic resection of metastasis for colorectal carcinoma: mortality, morbidity and pattern of recurrence. Ann Surg 1989;209:428–434.
10. Labow DM, Buell JE, Yoshida A, Rosen S, Posner MC. Isolated pulmonary recurrence after resection of colorectal hepatic metastasis – is resection indicated? Cancer J 2002;8:342–347.
11. Whiteford MH, Whiteford HM, Yee LF, et al. Usefulness of FDG PET scan in the assessment of suspected metastatic or recurrent adenocarcinoma of the colon and rectum. Dis Colon Rectum 2000;34:759–770.
12. Kamel EM, Thumshirn M, Truninger K, et al. Significance of incidental FDG accumulation in the gastrointestinal tract on PET/CT. Correlation with endoscopic and histologic results. J Nucl Med 2004;45:1804–1810.
13. Yasuda S, Hirofumi F, Nakahara T, et al. 18F-FDG PET in detection of colonic adenomas. J Nucl Med 2001;42:989–992.
14. Chen YK, Kao CH, Liao AC, Shenn YY, Su CT. Colorectal cancer screening in asymptomatic adults. The role of FDG PET scan. Anticancer Res 2003;23:4357–4361.
15. McArdle CS, Kerr DJ, Boyle P, editors. Colorectal Cancer. Oxford: Isis Medical Media; 2000.

16. Iyer RB, Silverman PM, DuBrow RA, Charnsangavej C. Imaging in the diagnosis, staging and follow-up of colorectal cancer. AJR Am J Roentgenol 2002;179:3–13.
17. Detry RJ, Kartheusen AH, Lagneaux G, Rahier J. Preoperative lymph node staging in rectal cancer: a difficult challenge. Int J Colorectal Dis 1996;11:217–221.
18. Denecke T, Rau B, Hoffmann KT, et al. Comparison of CT, MRI and FDG-PET in response predication of patients with locally advanced rectal cancer after multimodal preoperative therapy. Eur Radiol 2005;15:1658–1666.
19. Gordon BA, Flanagan FL, Dehdashti F. Wholebody PET: Normal variations, pitfalls and technical considerations. AJR Am J Roentgenol 1997;169:1675–1680.
20. Fernandez FG, Drebin JA, Linehan DC, et al. Five year survival after resection of hepatic metastasis from colorectal cancer in patients screened by PET with F18-FDG. Ann Surg 2004;240:438–447.
21. Fong Y, Saldinger PF, Akhurst T, et al. Utility of 18F-FDG PET scanning in selection of patients for resection of hepatic colorectal metastases. Am J Surg 1999; 178:282–287.
22. Flamen P, Strobaarts S, Van Cutsem E, et al. Additional value of wholebody PET with F18 FDG in recurrent colorectal cancer. J Clin Oncol 1999;17:894–901.
23. Blokhuis TJ, van der Schaaf MC, van den Tol MP, Comans EF, Manoliu RA, van der Sijp JR. Results of radiofrequency ablation of primary and secondary liver tumours: long term follow-up with CT and F18 PET scanning. Scand J Gastroenterol Suppl 2004;241:93–97.
24. Cohade C, Osman M, Leal J, Wahl RL. Direct comparison of 18F-FDG PET and PET/CT in patients with colorectal carcinoma. J Nucl Med 2003;44:1804–1805.
25. Kamel IR, Cohade C, Neyman E, Fishman EK, Wahl RL. Incremental value of CT in PET/CT of patients with colorectal carcinoma. Abdom Imaging 2004;29:663–668.