FDG-PET and PET/CT in Colorectal Cancer

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KEYWORDS

• PET-CT • FDG • Colorectal cancer • Recurrence • Staging

Colorectal cancer (CRC) is the second most common cause of cancer-related deaths in Western countries. Treatment relies on curative surgery. For rectal cancer, combined approaches with adjuvant radio-chemotherapy plus surgery have proven effective. However, even after a well-conducted curative-intent treatment, 30% to 50% of patients experience tumor relapse.

Accurate initial staging of CRC is mandatory for optimal therapeutic planning. As a whole-body imaging technique, fluorodeoxyglucose (FDG) positron emission tomography (PET) and PET-CT have the unique capability of providing staging for the tumor (T) stage, nodal (N) stage, and metastatic (M) stage in a single imaging session. This article covers the use of FDG PET and PET-CT scanning for the initial staging, and for the detection and staging of tumor relapse. The particular aspect of treatment monitoring is covered in a separate contribution elsewhere in this issue.

PRACTICAL CONSIDERATIONS

Several specific considerations apply when using FDG PET-CT for colorectal cancer imaging. First, physiologic bowel uptake is observed in many patients. Usually this uptake is faint, homogeneous, and predominant in the right colon. However, in some cases, it can be very intense and spotty, mimicking pathologic uptake. Bowel uptake is mainly related to motility, but can also result from lymphoid tissue activation, especially in younger patients. Moreover, numerous benign diseases, such as enterocolitis, inflammatory bowel diseases, and diverticulitis, can lead to increased and spotty bowel uptake. Careful evaluation of the uptake pattern is mandatory to avoid false-positive interpretations. The CT signs (in case of PET-CT examination) can also be helpful.[1] Full bowel preparation (ie, cleansing using an iso-osmotic solution given the day before the procedure) has been shown to significantly decrease the physiologic bowel uptake.[2] However, such an approach has not been widely implemented in clinical centers.

Second, a quick look at the histology of the primary tumor is useful because mucinous adenocarcinomas are poorly avid for FDG. Indeed, given a low cellularity and high fatty component, their overall FDG uptake is low and yields to a very limited sensitivity. When interpreting a PET scan, one should be aware of the histopathological subtype and, if mucoid, then one should clearly state on the report that there is a high probability of false-negative findings.[3]

Third, the liver is the main metastatic organ in colon cancer and the normal liver parenchyma can display a rather high uptake of FDG, impeding the visualization of small liver metastases. Normal liver cells can further metabolize FDG after the initial phosphorylation step. In time, the tracer is dephosphorylated and leaves the hepatocyte, while remaining inside the tumor cell. Thus, a longer delay between injection of the tracer and the image acquisition can be helpful. This allows for a higher tumor-to-liver ratio (ie, a higher tumor uptake together with a decreased normal liver uptake). Indeed, recent research has shown that FDG PET scans 120 minutes after injection found hepatic lesions that were missed in 17% of images obtained 90 minutes after injection.[4] This is an interesting finding, especially when one considers

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PET Clin 3 (2008) 147–153
doi:10.1016/j.cpet.2008.08.004
1556-8598/08/$ – see front matter © 2008 Elsevier Inc. All rights reserved.

that the clinical standard in many centers is to image patients as soon as 60 minutes after injection.

Finally, forced diuresis by intravenous hydration with or without diuretics should be considered for rectal cancer imaging. Again, delayed imaging would allow for a complete bladder voiding and dilution of the excreted activity, thereby increasing the signal-to-noise ratio in the pelvic area.

INCIDENTAL COLORECTAL HOT SPOTS

Incidental FDG hot spots have been reported in up to 3% of the patients having an FDG PET-CT procedure. In up to 78% of the cases, hot spots correspond to an actual lesion, either benign (hyperplasic polyps, ulcers, adenomas, hemorrhoids) or malignant (adenocarcinomas, villous tumors).[5–8] FDG uptake is more intense with increasing grade of colonic adenomas.[9] Therefore, incidental hot spots seen on FDG PET scans must be taken seriously and further exploration (ie, colonoscopy) is mandatory.

INITIAL DIAGNOSIS AND PRETHERAPEUTIC STAGING OF COLORECTAL CANCER

The current guidelines do not recommend FDG PET-CT for the initial preoperative staging of CRC. Despite a high sensitivity for the primary tumor as well as for distant metastases detection, FDG PET was initially shown to have a marginal impact on patient management, compared with preoperative abdominopelvic CT. The sensitivity for detection of locoregional lymph node metastases is low because lymph nodes are usually close to the primary tumor and cannot be differentiated from the primary tumor.[10–12] CT might help in the detection of small lymph nodes adjacent to the primary but it is still difficult to classify a small lymph node as metastatic if its uptake cannot be clearly separated from the primary, which is often bulky.[13] Interestingly, Inoue and colleagues[14] recently reported that they were able to increase the detection rate of lymph nodes on FDG PET by applying an iterative algorithm for image interpretation. After three iterations, the sensitivity increased from 51.3% (visual analysis) to 79.4%. This kind of approach is interesting but relies on quite complex image processing and has to be implemented in a clinical environment.

As a pretherapeutic staging modality, FDG PET mainly alters patient management by detecting distant metastases in cases where conventional imaging methods were either inconclusive or false negative. Compared with CT, PET-CT provides similar diagnostic performance for hepatic metastases detection. However, PET is more accurate for the detection of extrahepatic sites, such as periportal lymph nodes, para-aortic lymph nodes, and peritoneal carcinomatosis.[15,16] PET is also able to detect synchronous colonic lesions when it is impossible to pass through the primary lesion with the endoscope.[12] In terms of patient management, some studies indicate that FDG PET does modify the patient management,[12–15] but other studies report that PET is no better than multidetector CT.[17] Differences observed might be partly due to differences in study population. Indeed, in the (positive for PET) study of Park and colleagues, patients were included on the basis of either elevated carcinoembryonic antigen (CEA) (equal to or above 10 ng/mL) or equivocal CT. Thus, compared with patients from a general unselected population, patients with equivocal CT were more likely to obtain an accurate restaging with PET.

Recent studies using combined PET-CT colonography (ie, with dedicated colon preparation and image-acquisition protocols) have reported that, in staging colon cancer, combined PET-CT colonography delivers accuracies superior to CT alone and to CT plus PET performed separately.[18,19] A combined PET-CT colonography procedure requires adequate colon cleansing and takes a little bit longer than conventional PET-CT, but has the advantage of providing a full staging report in a single procedure. Veit-Haibach and colleagues[18] reported an 80% sensitivity for N stage and a 100% sensitivity for M detection in a pilot study of 47 patients. They also reported that PET-CT colonography affected the therapy decisions in 4 patients (9%). This technique has also shown good results to assess the colon proximal to an obstructive CRC.

Should PET be a part of the standard initial staging of CRC? Somehow conflicting results on the impact of FDG PET-CT in the initial preoperative staging of CRC coexist in the literature. In the United States, PET is reimbursed if "staging is uncertain following conventional imaging, and if the clinical management of the patient may differ according to the stage."[20] PET-CT is not presently part of the international guidelines for CRC initial staging.[21,22] However, it is recommended when CT is inconclusive or equivocal in advanced CRC.[23] This looks like a fair assumption and should be considered as the current guideline. New technical approaches, such as PET-CT colonography, still need more investigations, especially in terms of cost-efficacy.

Some studies have focused specifically on rectal cancer, and have shown a significant percentage (around 30%) of tumor stage change with FDG PET. Recently, Davey and colleagues[24] conducted a prospective study to assess the impact of FDG

PET on patient management and reported that the management was altered in 10 of 83 (12%) patients. The TNM stage was changed in 31% of patients, with upstage and downstage occurring in almost equal proportions. Change in management seems more frequent (27%) in low rectal cancers, as reported by Gearhart and colleagues,[25] in particular by detecting positive inguinal lymph nodes that are a characteristic metastatic site of low rectal tumors. Rectal cancer staging raises the specific questions of both tumor volume delineation (for radiotherapy treatment planning) and of monitoring of tumor response to preoperative chemoradiation, which is the standard of care for locally advanced tumors. Metabolic imaging using PET-CT can identify tumor subvolumes that are more aggressive and should receive higher doses of radiation. A high FDG uptake before therapy is indeed related to reduced overall survival.[26] Modern radiotherapy techniques, such as intensity-modulated radiation therapy, allow for precise dose sculpting and the concept of "biological target volume" has recently emerged, based on the use of PET for tumor volume delineation. Also, FDG PET accurately measures the response to chemoradiation, while both CT and MR imaging have consistently failed to discriminate responders from nonresponders. Late (4 to 5 weeks after the end of chemoradiation) or even very early (as soon as 12 days after the start of chemoradiation) FDG PET correlates with the histopathological tumor regression grade.[27,28] It is therefore likely that FDG PET-CT will soon become a standard for the staging of locally advanced rectal tumors, both because it can change the TNM stage, and because it can be used for tumor volume delineation and for (early) assessment of response. Such a case is illustrated in **Fig. 1**.

DETECTION OF TUMOR RECURRENCE

There is a general agreement that systematic postoperative surveillance of CRC patients is useful because it has been demonstrated that early treatment of tumor relapse improves patients' prognoses.[29] A recent prospective trial showed that an intensive follow-up scheme, adding abdominal/chest imaging and colonoscopy to CEA monitoring, yielded a higher rate of resectable recurrences, and improved survival in patients with stage II or rectal tumors.[30]

Follow-up based on sequential CEA dosage raises the question of identifying the site of relapse once the marker level is found abnormal. FDG PET-CT is a very sensitive imaging technique in that setting. In a study of 50 patients, Flamen and colleagues[31] indeed showed that PET detected tumor relapse in 79% of cases and led to curative-intent surgery in 14 of 50 patients (28%). More recently, a randomized controlled trial has shed light on the potential use of FDG PET as a surveillance imaging technique in CRC patients. One hundred and thirty patients operated on with curative intent were randomly assigned to either conventional follow-up or to conventional-plus-PET follow-up. Recurrence was diagnosed in 44 of 130 patients, 23 in the PET group and 21 in the conventional group. The time interval from baseline to recurrence detection was significantly reduced in the PET group compared with the conventional group (12.1 months vs 15.4 months, $P = .01$). Not only did PET allow for an earlier diagnosis of relapse, but the rate of successful curative intent surgery (R0) was significantly higher in the PET group: Ten out of 23 patients could be treated with curative intent, versus 2 out of 21 in the conventional group ($P<.01$) (**Fig. 2**).[32] Also, CEA is not a good indicator of tumor activity in all patients, and clinical and follow-up imaging workup can be the first sign of possible recurrence. Even in patients with a normal CEA level but with a clinical suspicion of recurrence, the positive predictive value of FDG PET is very high (85%).[33] There is also evidence supporting the use of FDG PET-CT for the detection of loco-regional relapse, especially at the pelvic level where fibrotic or scar tissue is difficult to discriminate from recurrence on CT or MR image.[34] These data clearly suggest that FDG PET should be used very early in the evaluation of patients with treated CRC, and even maybe as a systematic surveillance technique in high-risk patients, especially during the first 2 years after initial treatment because 80% of recurrences occur during that period.

STAGING OF RECURRENCE AND ASSESSMENT OF RESECTABILITY

The most common clinical application of FDG PET-CT is in the assessment of resectability of a known tumor recurrence, diagnosed by so-called "first-line" imaging techniques (liver ultrasound, follow-up CT). Given the limited availability of FDG PET-CT even nowadays, recurrence is often diagnosed by other means and PET is ordered for staging purposes. Strong evidence in the literature supports the use of FDG PET or PET-CT in that setting. The liver is the main site of CRC recurrence. Metastasectomy (either alone or combined with chemotherapy, chemoembolization, and radiofrequency ablation) is indicated provided the disease is limited to the liver. FDG PET has consistently outperformed CT in detecting extrahepatic disease, yielding a more accurate patient selection for liver surgery, an improved resectability rate, and prolonged survival in

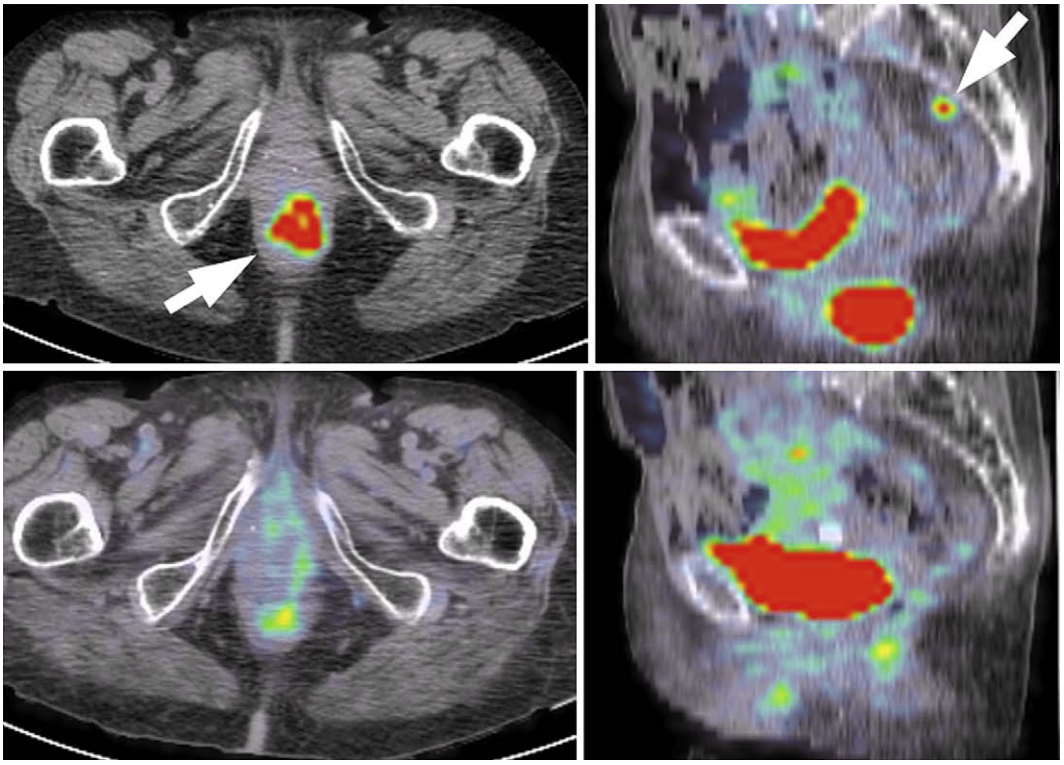

Fig. 1. Pre- and posttherapeutic FDG PET-CT of a 90-year-old woman with anorectal cancer. (*Top*) Baseline PET-CT showing a high uptake in the primary tumor (primary tumor standardized uptake value 12), and a positive lymph node in the presacral basin (*arrows*). (*Bottom*) FDG PET-CT obtained 11 weeks after completion of radiotherapy (60 Gy) delivered on the primary tumor and PET-positive lymph nodes. There is a good metabolic response at the primary tumor level (primary tumor standardized uptake value drops to 3.1). The large reduction in the primary tumor standardized uptake value at the primary level (−75%) together with the complete disappearance of the presacral hot spots classify the patient as responder.

patients with limited disease on PET.[35–40] Two meta-analyses reported that FDG PET had a higher sensitivity/specificity for detecting extrahepatic disease (91.5% to 95.4% vs 60.9% to 91.1%) compared with CT[41] or to MR imaging (sensitivity of 94.6% vs 75.8%, respectively).[42] In a recent publication, Wiering and colleagues[43] reported on 203 patients with liver metastases from CRC accrued between 1995 and 2003, and compared those staged without (n = 100) and with FDG-PET (n = 103). The number of patients with futile surgery (ie, in whom at laparotomy the extent of disease was too large for a curative-intent resection) was 28% in the group without PET, compared with 19.4% in the group with PET used for staging. Interestingly, 10 patients (10%) from the group without PET showed unsuspected extrahepatic abdominal disease at laparotomy, versus only 2 patients from the group with PET, illustrating the higher sensitivity of FDG PET to depict extrahepatic tumor seeding.

Overall, FDG PET significantly alters the management of patients with recurrent CRC in approximately 30% of cases.[44] With the introduction of combined PET-CT, the overall diagnostic performance has even been increased. The number of equivocal findings on PET (due to physiologic bowel uptake, urinary tract interference, or poor spatial localization of hot spots) has been reduced by 50%, and the staging accuracy improves from 78% to 89%.[45] Moreover, PET-CT with contrast-enhanced CT (ie, full diagnostic CT) further adds pertinent diagnostic information to classical PET-CT (without CT contrast injection). In a series of 54 patients included for restaging CRC, PET-CT added correct diagnostic findings in 27 patients (50%) compared with contrast-enhanced CT alone. However, PET with contrast-enhanced CT (ie, the CT part of PET-CT being full diagnostic with contrast injection) added diagnostic information in 39 patients compared with PET-CT (72%), and altered the therapeutic

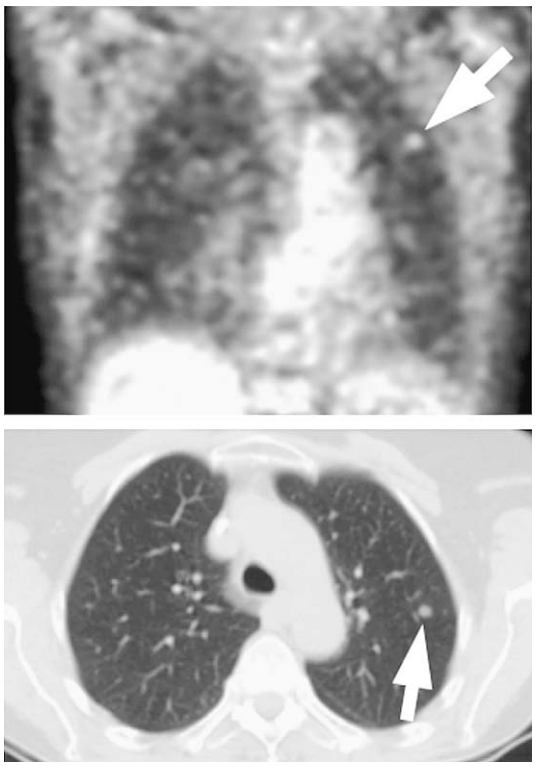

Fig. 2. A 69-year-old woman operated on 16 months before for a T3N2 sigmoid adenocarcinoma, presenting with an increasing CEA level (12 ng/mL). Whole-body FDG PET-CT shows a hot spot in the upper part of the left lung (*top, arrow, coronal view*), corresponding to a 6-mm nodule on the low-dose CT (*bottom, arrow*). This turned out to be a lung metastasis.

management in 23 patients. The incremental value of contrast enhanced PET-CT was mainly a correct segmental localization of liver metastases, which is important information as far as treatment planning is concerned.[46]

A new whole-body procedure, whole-body MR imaging, has been recently developed and is presented as a potential challenger to whole-body FDG PET-CT for staging of cancer. The initial clinical experience comparing whole-body MR imaging and PET-CT in CRC patients has been recently published. Whole-body MR imaging detected more hepatic metastases than PET-CT (27 vs 23 lesions), but each technique classified the same number of patients[15] as having liver metastases. PET-CT depicted more lung metastases (25 vs 19 lesions) in more patients (7 vs 5). Performances of both techniques were equivalent for detecting bone and peritoneal metastases.[47]

RISK STRATIFICATION

Beyond its huge potential as a cancer-detecting tool, PET-CT imaging further allows for the in vivo characterization of tumor biology. High FDG uptake measured by PET correlates with poorer outcome (reduced survival, reduced disease-free survival) of solid tumors, such as breast cancers.[48] Such a prognostic value of FDG uptake by recurrent CRC has been evaluated by de Geus-Oei and colleagues[49] In a series of 152 patients with metastatic CRC (67 operated, 85 treated with chemotherapy), they were able to show that the FDG uptake (as measured by standardized uptake values [SUV]) was a significant and independent predictor of the overall survival. The median survival was 32 months in the group with low FDG-uptake tumors (SUV < 4.26) and 19 months in the group with highly metabolic tumors (SUV > 4.26). Accordingly, the 2-year and 3-year survival rates were reduced in the high-uptake group: 37% and 28% versus 59% and 45% in the low-uptake group. Riedl and colleagues[50] measured the FDG uptake in liver metastases before surgical resection in a group of 90 patients. They showed that for highly metabolic tumors, the median survival after surgery was reduced. These preliminary results pave the way for a more subtle patient selection for adjuvant treatment after surgery (ie, combining chemotherapeutic and biological agents in patients with highly metabolic tumors).

SUMMARY

Strong scientific evidence supports the use of whole-body FDG PET-CT in the assessment of suspected recurrence of CRC or in the pretherapeutic staging before liver (or lung) metastasectomy. FDG PET-CT should be considered a standard of care in these clinical situations. Recent results emphasize the use of PET as a first-line imaging procedure for the follow-up of high-risk patients (typically, stage III-IV CRC), even as a systematic surveillance procedure.

New potential indications are the baseline pretherapeutic staging of rectal cancers, especially in the framework of modern multimodal therapies (neoadjuvant chemoradiation).

REFERENCES

1. Prabhakar HB, Sahani DV, Fischman AJ, et al. Bowel hot spots at PET-CT. Radiographics 2007;27:145–59.
2. Miraldi F, Vesselle H, Faulhaber PF, et al. Elimination of artifactual accumulation of FDG in PET imaging of colorectal cancer. Clin Nucl Med 1998;23:3–7.
3. Berger KL, Nicholson SA, Dehdashti F, et al. FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. AJR Am J Roentgenol 2000;174:1005–8.

4. Kuker RA, Mesoloras G, Gulec SA. Optimization of FDG-PET/CT imaging protocol for evaluation of patients with primary and metastatic liver disease. Int Semin Surg Oncol 2007;4:17.
5. Agress HJ, Cooper BZ. Detection of clinically unexpected malignant and premalignant tumors with whole-body FDG PET: histopathologic comparison. Radiology 2004;230:417–22.
6. Drenth JP, Nagengast FM, Oyen WJ. Evaluation of (pre-)malignant colonic abnormalities: endoscopic validation of FDG-PET findings. Eur J Nucl Med 2001;28:1766–9.
7. Israel O, Yefremov N, Bar-Shalom R, et al. PET/CT detection of unexpected gastrointestinal foci of 18F-FDG uptake: incidence, localization patterns, and clinical significance. J Nucl Med 2005;46: 758–62.
8. Kamel EM, Thumshirn M, Truninger K, et al. Significance of incidental 18F-FDG accumulations in the gastrointestinal tract in PET/CT: correlation with endoscopic and histopathologic results. J Nucl Med 2004;45:1804–10.
9. van Kouwen MC, Nagengast FM, Jansen JB, et al. 2-(18F)-fluoro-2-deoxy-D-glucose positron emission tomography detects clinical relevant adenomas of the colon: a prospective study. J Clin Oncol 2005; 23:3713–7.
10. Abdel-Nabi H, Doerr RJ, Lamonica DM, et al. Staging of primary colorectal carcinomas with fluorine-18 fluorodeoxyglucose whole-body PET: correlation with histopathologic and CT findings. Radiology 1998;206:755–60.
11. Kantorova I, Lipska L, Belohlavek O, et al. Routine (18)F-FDG PET preoperative staging of colorectal cancer: comparison with conventional staging and its impact on treatment decision making. J Nucl Med 2003;44:1784–8.
12. Llamas-Elvira JM, Rodriguez-Fernandez A, Gutierrez-Sainz J, et al. Fluorine-18 fluorodeoxyglucose PET in the preoperative staging of colorectal cancer. Eur J Nucl Med Mol Imaging 2007;34:859–67.
13. Shin SS, Jeong YY, Min JJ, et al. Preoperative staging of colorectal cancer: CT vs. integrated FDG PET/CT. Abdom Imaging 2008;33:270–7.
14. Inoue K, Sato T, Kitamura H, et al. Diagnosis supporting algorithm for lymph node metastases from colorectal carcinoma on 18F-FDG PET/CT. Ann Nucl Med 2008;22:41–8.
15. Park IJ, Kim HC, Yu CS, et al. Efficacy of PET/CT in the accurate evaluation of primary colorectal carcinoma. Eur J Surg Oncol 2006;32:941–7.
16. Selzner M, Hany TF, Wildbrett P, et al. Does the novel PET/CT imaging modality impact on the treatment of patients with metastatic colorectal cancer of the liver? Ann Surg 2004;240:1027–34 [discussion: 1035–6].
17. Furukawa H, Ikuma H, Seki A, et al. Positron emission tomography scanning is not superior to whole body multidetector helical computed tomography in the preoperative staging of colorectal cancer. Gut 2006;55:1007–11.
18. Veit-Haibach P, Kuehle CA, Beyer T, et al. Diagnostic accuracy of colorectal cancer staging with whole-body PET/CT colonography. JAMA 2006;296: 2590–600.
19. Nagata K, Ota Y, Okawa T, et al. PET/CT colonography for the preoperative evaluation of the colon proximal to the obstructive colorectal cancer. Dis Colon Rectum 2008;51:882–90.
20. Herbertson RA, Lee ST, Tebbutt N, et al. The expanding role of PET technology in the management of patients with colorectal cancer. Ann Oncol 2007;18:1774–81.
21. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of 18F-FDG PET in oncology. J Nucl Med 2008;49:480–508.
22. Van Cutsem EJ, Oliveira J. Colon cancer: ESMO clinical recommendations for diagnosis, adjuvant treatment and follow-up. Ann Oncol 2008;19(Suppl 2): ii29–30.
23. Van Cutsem EJ, Oliveira J. Advanced colorectal cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. Ann Oncol 2008; 19(Suppl 2):ii33–4.
24. Davey K, Heriot AG, Mackay J, et al. The impact of 18-fluorodeoxyglucose positron emission tomography–computed tomography on the staging and management of primary rectal cancer. Dis Colon Rectum 2008;51:997–1003.
25. Gearhart SL, Frassica D, Rosen R, et al. Improved staging with pretreatment positron emission tomography/computed tomography in low rectal cancer. Ann Surg Oncol 2006;13:397–404.
26. Calvo FA, Domper M, Matute R, et al. 18F-FDG positron emission tomography staging and restaging in rectal cancer treated with preoperative chemoradiation. Int J Radiat Oncol Biol Phys 2004;58:528–35.
27. Capirci C, Rampin L, Erba PA, et al. Sequential FDG-PET/CT reliably predicts response of locally advanced rectal cancer to neo-adjuvant chemo-radiation therapy. Eur J Nucl Med Mol Imaging 2007;34:1583–93.
28. Cascini GL, Avallone A, Delrio P, et al. 18F-FDG PET is an early predictor of pathologic tumor response to preoperative radiochemotherapy in locally advanced rectal cancer. J Nucl Med 2006;47:1241–8.
29. Renehan AG, Egger M, Saunders MP, et al. Impact on survival of intensive follow up after curative resection for colorectal cancer: systematic review and meta-analysis of randomised trials. BMJ 2002;324:813.
30. Rodriguez-Moranta F, Salo J, Arcusa A, et al. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection:

a prospective, multicenter, randomized, controlled trial. J Clin Oncol 2006;24:386–93.
31. Flamen P, Hoekstra OS, Homans F, et al. Unexplained rising carcinoembryonic antigen (CEA) in the postoperative surveillance of colorectal cancer: the utility of positron emission tomography (PET). Eur J Cancer 2001;37:862–9.
32. Sobhani I, Tiret E, Lebtahi R, et al. Early detection of recurrence by 18FDG-PET in the follow-up of patients with colorectal cancer. Br J Cancer 2008; 98:875–80.
33. Sarikaya I, Bloomston M, Povoski SP, et al. FDG-PET scan in patients with clinically and/or radiologically suspicious colorectal cancer recurrence but normal CEA. World J Surg Oncol 2007;5:64.
34. Strauss LG, Clorius JH, Schlag P, et al. Recurrence of colorectal tumors: PET evaluation. Radiology 1989;170:329–32.
35. Arulampalam T, Costa D, Visvikis D, et al. The impact of FDG-PET on the management algorithm for recurrent colorectal cancer. Eur J Nucl Med 2001; 28:1758–65.
36. Kalff V, Hicks RJ, Ware RE, et al. The clinical impact of (18)F-FDG PET in patients with suspected or confirmed recurrence of colorectal cancer: a prospective study. J Nucl Med 2002;43:492–9.
37. Kong G, Jackson C, Koh DM, et al. The use of (18)F-FDG PET/CT in colorectal liver metastases—comparison with CT and liver MRI. Eur J Nucl Med Mol Imaging 2008;35:1323–9.
38. Lonneux M, Reffad AM, Detry R, et al. FDG-PET improves the staging and selection of patients with recurrent colorectal cancer. Eur J Nucl Med Mol Imaging 2002;29:915–21.
39. Ruers TJ, Langenhoff BS, Neeleman N, et al. Value of positron emission tomography with [F-18]fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study. J Clin Oncol 2002;20: 388–95.
40. Strasberg SM, Dehdashti F, Siegel BA, et al. Survival of patients evaluated by FDG-PET before hepatic resection for metastatic colorectal carcinoma: a prospective database study. Ann Surg 2001;233: 293–9.
41. Wiering B, Krabbe PF, Jager GJ, et al. The impact of fluor-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases. Cancer 2005;104:2658–70.
42. Bipat S, van Leeuwen MS, Comans EF, et al. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis–meta-analysis. Radiology 2005;237: 123–31.
43. Wiering B, Krabbe PF, Dekker HM, et al. The role of FDG-PET in the selection of patients with colorectal liver metastases. Ann Surg Oncol 2007;14:771–9.
44. Huebner RH, Park KC, Shepherd JE, et al. A meta-analysis of the literature for whole-body FDG PET detection of recurrent colorectal cancer. J Nucl Med 2000;41:1177–89.
45. Cohade C, Osman M, Leal J, et al. Direct comparison of (18)F-FDG PET and PET/CT in patients with colorectal carcinoma. J Nucl Med 2003;44: 1797–803.
46. Soyka JD, Veit-Haibach P, Strobel K, et al. Staging pathways in recurrent colorectal carcinoma: Is contrast-enhanced 18F-FDG PET/CT the diagnostic tool of choice? J Nucl Med 2008;49:354–61.
47. Squillaci E, Manenti G, Mancino S, et al. Staging of colon cancer: whole-body MRI vs. whole-body PET-CT—initial clinical experience. Abdom Imaging 2008.
48. Emmering J, Krak NC, Van der Hoeven JJ, et al. Preoperative [18F] FDG-PET after chemotherapy in locally advanced breast cancer: prognostic value as compared with histopathology. Ann Oncol 2008; 19:1573–7.
49. de Geus-Oei LF, Wiering B, Krabbe PF, et al. FDG-PET for prediction of survival of patients with metastatic colorectal carcinoma. Ann Oncol 2006;17:1650–5.
50. Riedl CC, Akhurst T, Larson S, et al. 18F-FDG PET scanning correlates with tissue markers of poor prognosis and predicts mortality for patients after liver resection for colorectal metastases. J Nucl Med 2007;48:771–5.