Role of ^{18}F-FDG Dual-Head Gamma-Camera Coincidence Imaging in Recurrent or Metastatic Colorectal Carcinoma

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^{18}F-FDG PET has been shown to be of high diagnostic accuracy for the evaluation of recurrent colorectal cancer. However, the limited availability of PET scanners precludes ^{18}F-FDG assessment of many patients for whom the study is indicated. An alternative is the SPECT system in coincidence mode. The aim of this study was to determine the role of dual-head camera ^{18}F-FDG coincidence imaging (DHC ^{18}F-FDG) in patients with recurrent colorectal cancer. **Methods:** Sixty-seven DHC ^{18}F-FDG studies were performed on 62 patients with suspected recurrent colorectal cancer. Reports of contemporary CT were available for the purpose of correlation for 61 of the studies. The final diagnosis of the imaging findings was based on histology or clinical and imaging follow-up of at least 6 mo. **Results:** In lesion-based analysis, 103 tumor sites were suspected on DHC ^{18}F-FDG, CT, or colonoscopy. Ninty-three of them were found to be true tumor sites. For DHC ^{18}F-FDG, the sensitivity was 88%, specificity was 80%, positive predictive value (PPV) was 98%, negative predictive value (NPV) was 42%, and accuracy was 87%. For CT, the sensitivity was 63%, specificity was 10%, PPV was 85%, NPV was 3%, and accuracy was 57%. In patient-based analysis, DHC ^{18}F-FDG differentiated patients with recurrent cancer from disease-free patients with a sensitivity of 91%, specificity of 73%, PPV of 94%, NPV of 62%, and accuracy of 88%. DHC ^{18}F-FDG detected tumor sites in 12 (67%) of 18 patients with elevated carcinoembryonic antigen and negative CT findings. **Conclusion:** DHC ^{18}F-FDG is an adequate readily available technique for assessment of recurrent colorectal cancer and has a diagnostic accuracy better than that of CT.

Key Words: colorectal cancer; cancer recurrence; coincidence; ^{18}F-FDG

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Colorectal cancer (CRC) is the second most common cause of cancer-related death in the United States. Although metastatic disease is detected at the time of diagnosis in approximately 20% of patients, up to 40% of patients will suffer from recurrence or metastatic spread even after curative resection of the primary tumors. Unlike some other malignancies of the gastrointestinal tract, patients with limited metastatic spread from CRC will benefit from surgical resection, with cure rates of up to 25%, provided that extirpation of all disease is accomplished. The outcome of patients with recurrent or metastatic colorectal cancer depends on early diagnosis and appropriate selection of patients for either surgery or nonsurgical modes of treatment. The cornerstone for selection is preoperative imaging (*1–6*).

CT has been the conventional imaging modality for identifying and localizing metastatic disease. Its sensitivity in this clinical setting, however, varies between 29% and 100% (average, 71%) according to different studies, with hepatic and lymph node metastases being the most frequently missed tumor sites (*7–10*).

Functional imaging is rapidly developing as a whole-body method to detect metastases. The most widely cited is ^{18}F-FDG PET, the sensitivity of which ranges between 82% and 100% for the detection of extraluminal CRC (*6,9,11–16*). The number of available dedicated PET scanners, however, is still limited, and PET is therefore inaccessible to a large number of patients. Multihead conventional gamma cameras that are used in the routine practice of nuclear medicine have been modified recently to use in the coincidence mode for the detection of positron emitters, enhancing the potential for imaging a greater number of patients with FDG (*17,18*). Several studies have been reported on the use of coincidence imaging of FDG for the detection of various malignancies, including lymphoma, head and neck tumors, breast cancer, pulmonary lesions, renal malignancies, and others (*19–21*).

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In this study, we report our experience with dual-head camera ^{18}F-FDG coincidence imaging (DHC ^{18}F-FDG) in the evaluation of patients with suspected recurrent or metastatic CRC.

MATERIALS AND METHODS

Patient Population

The study was retrospective. Between June 1999 and February 2001, 73 DHC ^{18}F-FDG studies were performed for the assessment of suspected recurrent or metastatic disease in 67 patients with CRC. ^{18}F-FDG studies were performed twice on 4 patients and 3 times on 1 patient during the study period. All patients had undergone surgery for the removal of the primary colorectal tumor.

Indications for DHC ^{18}F-FDG were as follows: (a) elevated carcinoembryonic antigen (CEA) levels and negative CT or colonoscopy findings ($n = 18$ studies); (b) the need to evaluate the extent of disease before surgical removal of a local recurrence ($n = 17$ studies) or of metastases ($n = 35$ studies); and (c) the need to differentiate between residual tumor and fibrosis in pelvic masses remaining after treatment ($n = 3$ studies).

We reviewed the medical records of all study patients, which included the clinical data, laboratory results, and reports of CT and colonoscopy performed within 8 wk of the ^{18}F-FDG study. CT result reports (not films) were available for correlation for 61 of the 67 ^{18}F-FDG studies. Outpatients brought CT films for correlation at the time of the ^{18}F-FDG study. The CT report was kept in the patient's records, as were changes made in the original CT report when read concomitantly with the ^{18}F-FDG.

Six studies on 5 patients were excluded from the analysis of results because of a follow-up of <6 mo for 3 normal studies and because the final diagnosis could not be assessed for 3 additional studies. The final study data were thus retrieved from 67 studies on 62 patients (28 women, 34 men; age range, 32–85 y; mean age, 62 ± 13 y).

Surgery was performed within 1 mo after the ^{18}F-FDG study on 37 patients: 11 patients referred because of elevated CEA levels (indication a), 24 patients referred for evaluation of the extent of the disease (indication b), and 2 patients referred for differential diagnosis between viable tumor and fibrosis (indication c).

^{18}F-FDG Imaging

The patients fasted for at least 4 h before administration of ^{18}F-FDG. Bladder catheterization was performed to minimize interference from urinary bladder activity. In the last 23 patients to be assessed, 20 mg furosemide (Lasix; Hoechst-Roussel Pharmaceuticals, Somerville, NJ) were administered intravenously to eliminate uptake in the renal collecting system.

On the basis of the patient's weight, 370–592 MBq (10–16 mCi) ^{18}F-FDG were injected intravenously. Imaging started 60–150 min after injection. The timing of imaging was determined by measurements of the ratio between detected and processed photons. The chest, abdomen, and pelvis were imaged in 2 or 3 steps. If bowel activity and tumor sites needed to be differentiated, acquisition was repeated after changing the patient's positioning.

Dual-Head Coincidence Technique. DHC ^{18}F-FDG studies were performed using a dual-head gamma camera with coincidence imaging capacity (Millenium VG; General Electric Medical Systems, Milwaukee, WI). The system is equipped with two 1.6-cm-thick, large-area (54 × 40 cm) NaI(Tl) detectors. For coincidence detection of 511-keV photons, the system has a coincidence-timing circuitry for the coincidence detection of 2 events that hit the respective opposed detectors within less than a 6.5-ns timing window. Slit collimators containing thin layers of lead, tin, and copper (graded absorber) were used to prevent activity from outside the field of view. The only type of scatter that cannot be reduced by the graded absorbers is that in the crystal itself. These scatter events, termed Comptons, are 511-keV photons that collide in the crystal but lose only part of their energy, while the remaining energy leaves the crystal in the form of another photon. The energy that is measured for Compton events is <340 keV. Compton events may result in degradation in resolution but they improve sensitivity. The system offers 3 modes of operation: a high-resolution mode that uses only photopeak–photopeak (P–P) coincidence pairs, a normal mode that uses photopeak–Compton (P–C) coincidence pairs in addition to the P–P pairs, and a high-sensitivity mode that also uses Compton–Compton (C–C) coincidence pairs. We used 2 combinations of energy windows: 511 keV ± 10% for P–P events and 132–321 keV for P–C events in cases of poorer sensitivity.

Not all single photons that pass the septa collimators are accepted and processed. The manufacturer's suggested optimal imaging timing after injection for the system is when the ratio between the processed photons and the detected single photons is in the range of 85%–92%. This ratio was achieved in our patients between 60 to 150 min after injection.

Data acquisition lasted 30 min, corresponding to 10 rotations of the gantry. The matrix size was 128 × 128. The data were stored in a list mode (CLIST) in a 30- to 40-MB file. Reconstruction was done either on Xpert or on eNTERGA workstations. The proprietary algorithm, COSEM (coincidence list ordered set expectation maximization), which is a 3-dimensional algorithm that directly processes the CLIST, was used for the reconstruction of the CLIST (*17*,*22*).

Image Interpretation and Analysis of Results. DHC ^{18}F-FDG images were interpreted by 2 nuclear medicine experts who were unaware of the clinical data and the results of other imaging modalities. Abdominal lesions were called if they were detected outside the region of bowel activity, renal collecting systems, or residual urinary bladder activity. A pathologic lesion in the gastrointestinal tract was noted only if a site of increased uptake persisted on repeated acquisitions.

The final diagnosis of the imaging findings, either scintigraphic or CT, was based on histopathologic results obtained at surgery or by biopsy, on a correlation between ^{18}F-FDG and contemporary CT and colonoscopy findings, and on clinical and CT follow-up of at least 6 mo.

Lesion-Based Analysis. In the analysis of results of detected tumor sites, ^{18}F-FDG or CT findings were categorized as true-positive for tumor (TP), true-negative (TN), false-positive (FP), and false-negative (FN) using similar criteria for both modalities. A scintigraphic lesion was considered TP if (a) the lesion was confirmed by biopsy; (b) CT or colonoscopy performed at the same time as the ^{18}F-FDG study or at a later follow-up detected a pathologic lesion at the same location as ^{18}F-FDG; or (c), in patients with elevated CEA levels and negative CT who had not undergone surgery, an ^{18}F-FDG uptake suggestive of metastatic disease in normal-sized lymph nodes or the peritoneal seeding was considered to reflect true tumor sites if a rapid deterioration occurred clinically.

Scintigraphy was considered TN for lesions detected on CT or colonoscopy if the lesion was negative on histology or if the lesion

disappeared or remained unchanged on CT for at least 6 mo without treatment.

Scintigraphy was considered FN in sites of a positive biopsy obtained within 1 mo of the ^{18}F-FDG study or if a suspected tumor that had been revealed on CT, but not on ^{18}F-FDG, showed progression on follow-up.

An ^{18}F-FDG site of uptake interpreted as tumor was considered FP if it was negative for tumor histology or if there was no evidence of tumor on clinical and CT follow-up for at least 6 mo without treatment.

Patient-Based Analysis. To assess the role of ^{18}F-FDG in the differentiation of disease-free patients and those with recurrent or metastatic disease, a positive ^{18}F-FDG study was considered TP if it detected tumor sites in patients with active disease and was considered TN if it was negative in disease-free patients.

Statistical Analysis

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and 95% confidence intervals were calculated for DHC ^{18}F-FDG and for CT (*23*).

RESULTS

Lesion-Based Analysis

One hundred three tumor sites were suspected on the ^{18}F-FDG study, CT, or colonoscopy. They included lesions in the liver (n = 33), pelvis (n = 17), abdominal lymph nodes (n = 15), extraabdominal lymph nodes (n = 5), lungs (n = 10), colon or at the previous site of surgery (n = 10), bone (n = 2), ovary (n = 2), pancreas (n = 2), peritoneal seeding (n = 2), adrenal (n = 1), abdominal wall (n = 1), kidney (n = 1), breast (n = 1), and thyroid (n = 1). The final diagnosis was based on histopathologic results obtained at surgery or by biopsy, by correlation between ^{18}F-FDG findings and contemporary CT or colonoscopy, and by clinical and CT follow-up of at least 6 mo. Ninety-three the 103 suspected lesions were true tumor sites, of which 15 (16%) were extraabdominal (Fig. 1).

On ^{18}F-FDG imaging, 82 of the 103 suspected lesions were TP, 8 were TN, 11 were FN, and 2 were FP, resulting in a sensitivity of 88%, specificity of 80%, PPV of 98%, NPV of 42%, and accuracy of 87%.

Correlation with CT reports was available for 93 of the 103 suspected lesions: 52 were TP, 1 was TN, 9 were FP, and 31 were FN, resulting in a sensitivity of 63%, specificity of 10%, PPV of 85%, NPV of 3%, and accuracy of 57%. Table 1 summarizes the statistical results of lesion detection by DHC ^{18}F-FDG and CT according to regions.

Patient-Based Analysis

Fifty-six studies were done on patients with disease and 11 were done on disease-free patients. Fifty-one ^{18}F-FDG studies were TP, 8 were TN, 3 were FP, and 5 were FN. DHC ^{18}F-FDG differentiated patients with tumor from disease-free patients with a sensitivity of 91%, specificity of 73%, PPV of 94%, NPV of 62%, and accuracy of 88%.

In the 18 patients referred for an ^{18}F-FDG study because of elevated CEA levels and negative CT and colonoscopy, 12 DHC ^{18}F-FDG studies were positive for tumor (67%), detecting abdominal lymph node involvement (n = 5), lung metastases (n = 3), peritoneal seeding (n = 2), liver metastases (n = 1), and a pelvic mass (n = 1). Figures 2 and 3 illustrate 2 of the latter patients. DHC ^{18}F-FDG studies were negative in the other 6 patients: 3 of them continued to have no evidence of disease on follow-up, whereas the tumor sites became detectable later on follow-up CT or further DHC ^{18}F-FDG study in the other 3 patients (2 had

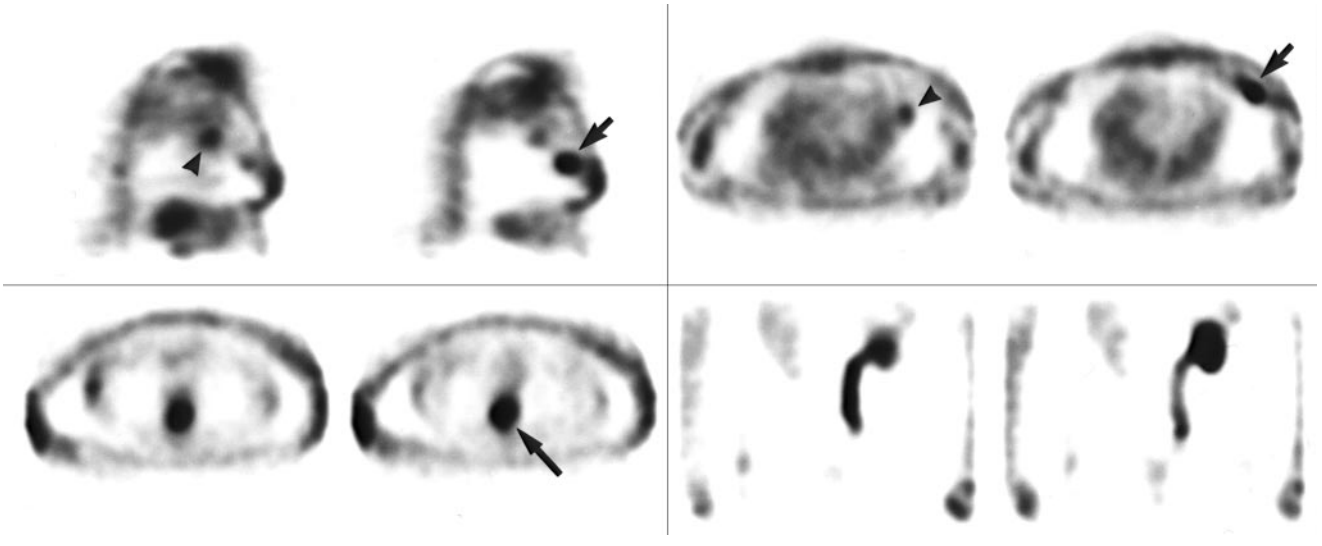

FIGURE 1. Unexpected extraabdominal disease in 64-y-old woman with known perirectal recurrent adenocarcinoma. DHC ^{18}F-FDG study was assessed for staging before surgery. In addition to recurrent tumor (long arrow), sites of increased uptake were also detected in left breast (short arrow) and left axilla (arrowhead), suggesting second metastatic primary cancer. Left hydronephrosis and hydroureter were also detected. Removal of perirectal tumor and mastectomy with axillary dissection were performed during surgery.

TABLE 1
Statistical Analysis of Lesion Detection by DHC ^{18}F-FDG and CT According to Regions

Region	Modality	*n**	Sensitivity† (%)	Specificity† (%)	PPV† (%)	NPV† (%)	Accuracy† (%)
All	DHC ^{18}F-FDG	103	88 (80–94)	80 (44–97)	98 (92–100)	42 (20–66)	87 (79–93)
	CT	93	62 (51–73)	10 (0.2–44)	85 (74–93)	3.1 (0–16)	57 (46–67)
Liver	DHC ^{18}F-FDG	33	77 (58–90)	100 (29–100)	100 (85–100)	30 (7–65)	79 (61–91)
	CT	33	77 (58–90)	0 (0–70)	88 (70–97)	0 (0–41)	70 (51–84)
Lymph nodes	DHC ^{18}F-FDG	21	100 (83–100)	0 (0–97)	95 (76–100)	0 (0–97)	95 (76–100)
	CT	18	29 (10–56)	100 (2.5–100)	100 (48–100)	8 (0.2–36)	33 (13–59)
Pelvis	DHC ^{18}F-FDG	17	100 (79–100)	100 (2.5–100)	100 (79–100)	100 (2.5–100)	100 (80–100)
	CT	14	77 (46–95)	0 (0–97)	91 (59–100)	0 (0–71)	71 (42–92)
Lung	DHC ^{18}F-FDG	10	100 (66–100)	100 (2.5–100)	100 (66–100)	100 (2.5–100)	100 (69–100)
	CT	8	28 (4–71)	0 (0–97)	67 (9–99)	0 (0–52)	25 (3–65)
Bowel and primary tumor bed	DHC ^{18}F-FDG	10	75 (35–97)	50 (1–99)	86 (42–99)	33 (0–90)	70 (35–93)
	CT	9	86 (42–100)	0 (0–84)	75 (35–97)	0 (0–97)	67 (30–92)
Other‡	DHC ^{18}F-FDG	13	82 (48–98)	100 (16–100)	100 (66–100)	50 (7–93)	85 (55–98)
	CT	11	67 (30–93)	0 (0–84)	75 (35–97)	0 (0–71)	55 (23–83)

* *n* = number of lesions.
† 95% confidence intervals are in parentheses.
‡ Other: bone, *n* = 2; ovary, *n* = 2; peritoneal seeding, *n* = 2; pancreas, *n* = 2; breast, *n* = 1; thyroid, *n* = 1; adrenal, *n* = 1; abdominal wall, *n* = 1; kidney, *n* = 1.

liver metastases, 1 had presacral lymph nodes). In this group the sensitivity was 80%, specificity was 100%, PPV was 100%, NPV was 50%, and accuracy was 83%. Seven patients were referred for surgery after the DHC ^{18}F-FDG studies that were positive for tumor.

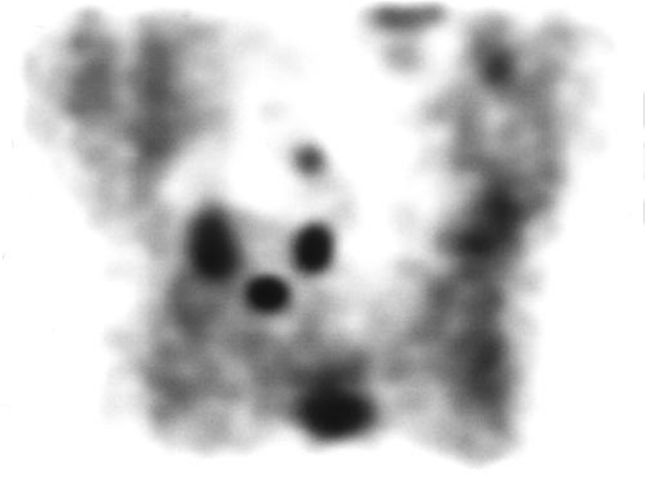

FIGURE 2. A 74-y-old man with elevated CEA levels and negative CT. DHC ^{18}F-FDG study detected several sites of increased uptake, suggesting diffuse abdominal metastatic spread. Patient was referred for chemotherapy; however, rapid clinical deterioration followed and he died 4 mo after scan was obtained.

DISCUSSION

^{18}F-FDG is avidly concentrated in CRC. Its clinical applications in patients with recurrent or metastatic CRC include screening (mainly in the case of elevated CEA levels and negative or equivocal CT), staging of recurrent disease and determination of extent and operability, and differentiation of recurrent tumor from scar tissue after therapy (*5*,*6*,*13*,*24*,*25*). Several studies have shown that ^{18}F-FDG PET has a higher sensitivity, specificity, and predictive accuracy than CT for the detection of recurrent CRC (*6*,*8*,*9*,*12*,*13*,*24*–*26*). PET has an additional diagnostic value compared with conventional diagnostic modalities in 20% of the patients with presumed resectable localized disease (*27*). Whole-body FDG findings of several studies have been reported to result in alteration of staging and patient management in 30%–50% of the patients (*8*,*12*,*14*,*26*, *28*,*29*). On the basis of these results, in some institutions the first step in the algorithm for the evaluation of patients presenting with recurrent CRC is the performance of ^{18}F-FDG PET (*30*). These data, however, reflect the use of dedicated PET devices that, at least at present, are still limited in number and therefore inaccessible for the assessment of many patients with this common disease.

Conventional gamma cameras that are used in the routine practice of nuclear medicine for the detection of single photon emitters have been modified recently to also be applicable for the detection of positron emitters, raising the potential of imaging a greater number of patients with FDG. Attempts to improve the resolution and sensitivity of these

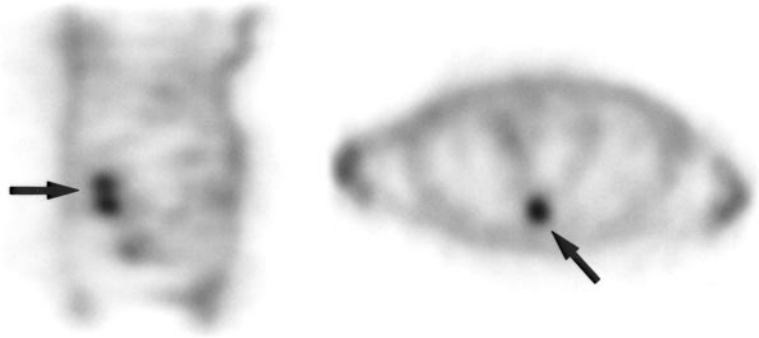

FIGURE 3. A 54-y-old woman with elevated CEA levels and negative CT and colonoscopy. DHC ^{18}F-FDG study detected increased sites of uptake in presacral region (arrow). Presence of tumor tissue at this location was confirmed on histologic examination.

cameras for FDG imaging include adding dual-head coincidence electronics, increasing the thickness of the NaI(Tl) crystals, and using iterative algorithms for reconstruction (*17*,*18*,*30*,*31*). The technique has been shown to have a high spatial resolution and sensitivity, but it is degraded by the proportion of scatter and random coincidence events. The limited sensitivity is a major problem that affects the quality of the images and may result in a failure to detect small lesions. Comparison of the performance of a dual-head SPECT camera operated in a coincidence mode with that of a PET scanner revealed that the coincidence technique can depict many of the lesions depicted with PET, particularly in the lungs, but has a lower sensitivity for lesion detection in the abdomen (*15*).

The purpose of this study was to assess the role of DHC ^{18}F-FDG in patients with suspected recurrent CRC, a tumor known to commonly recur in the abdomen and pelvis. The results indicate an improved overall tumor detection for DHC ^{18}F-FDG compared with CT. Although the high-resolution CT technique has a basic anatomic resolution better than that of DHC ^{18}F-FDG, the latter was more accurate for tumor detection, particularly in the case of normal-sized metastatic lymph nodes and peritoneal spread (Figs. 2–4), as well as for differentiating tumor from fibrosis or changes caused by prior surgery. Abdominal and pelvic sites of physiologic ^{18}F-FDG uptake were a potential cause for difficulties in image interpretation because the longer acquisition time of a whole-body coincidence study, compared with that of PET, is associated with filling of the bladder and the renal collecting system. These physiologic sites of ^{18}F-FDG uptake increase the proportion of scatter events. For this reason, our patient preparation protocol

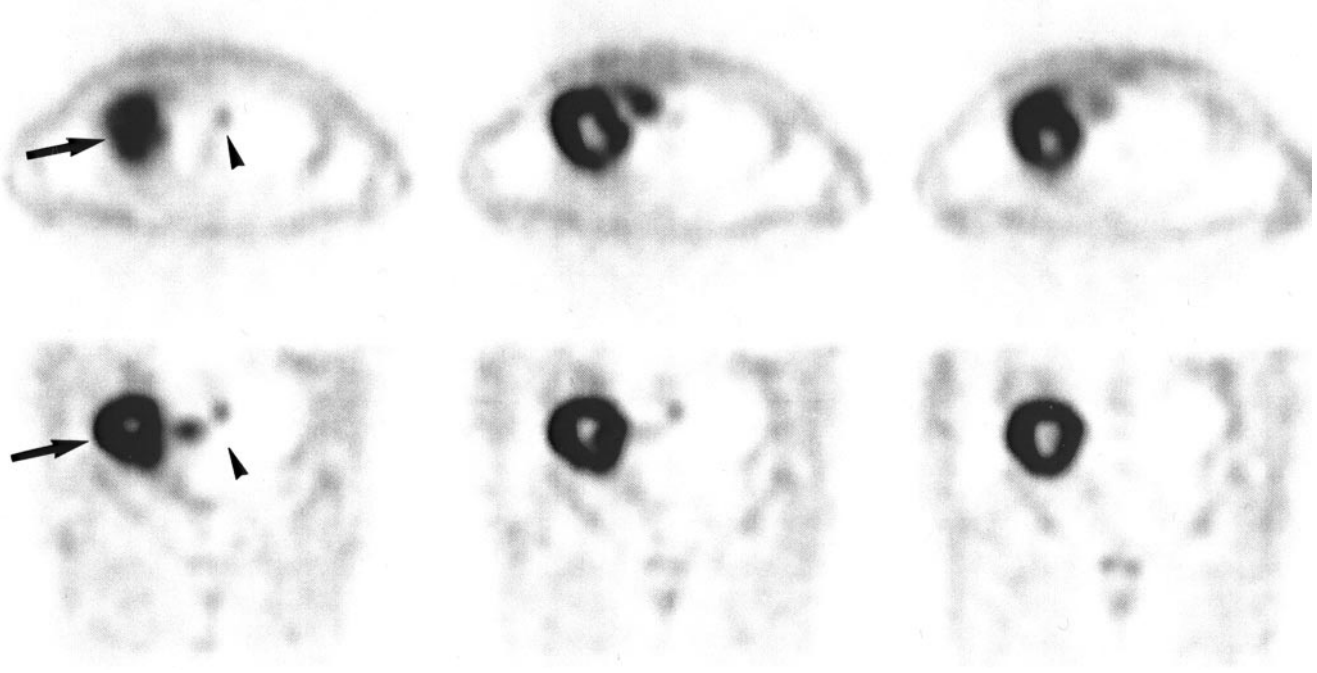

FIGURE 4. Unsuspected metastatic disease in 61-y-old woman with known recurrent colon carcinoma and negative CT for metastases. DHC ^{18}F-FDG study was performed for staging before surgery. In addition to local recurrence in right abdomen (arrow), 2 other sites of uptake were detected, suggesting lymph node metastases (arrowhead). Latter diagnosis was confirmed on histologic examination.

included bladder catheterization and, recently, the administration of diuretics as well. In most cases, bowel activity was identifiable by its characteristic linear pattern or on 3-dimensional cine. The presence of tumor in the bowel itself was not commonly interpreted and was interpreted only if a focus of uptake was detected as being unchanged on repeated acquisitions (Fig. 4). Chest CT is not always a routine practice in the follow-up of patients with colorectal disease. The benefit of the whole-body imaging protocol of DHC ^{18}F-FDG was reflected in the 16% rate of tumor lesions found outside the abdomen and pelvis.

CEA monitoring is only 59% sensitive and 84% specific for the detection of colorectal recurrence (*32*). Valk et al. (*9*) performed whole-body PET on 33 patients with elevated CEA levels and negative CT. PET was TP in 67% of the patients, with a PPV of 95% and an NPV of 85% (*9*). Flanagan et al. (*33*) assessed the role of FDG PET in 22 patients with unexplained elevation of CEA levels and found a PPV of 89% and an NPV of 100%. In this study, the DHC ^{18}F-FDG detected sites of tumor in 67% of the 18 patients with elevated CEA levels and normal CT or colonoscopy results. The PPV determined was 100%; however, the NPV was 50%, which probably reflects a higher FN rate of the coincidence mode compared with dedicated PET studies.

Our study had several limitations. This was a retrospective investigation. The enrolled patients were preselected by the referring physician to undergo a DHC ^{18}F-FDG study. The lower accuracy of the CT technique compared with that of DHC ^{18}F-FDG is caused, in part, by a bias in patient selection because approximately one third of the study cohort was referred for scintigraphy to assess the cause of elevated CEA levels in the presence of negative CT. Reports (not films) of the CT studies were available for correlation. In addition, an accurate diagnosis of suspected tumor sites was not always possible, as often occurs in studies assessing tumor detection. Some of our patients had unresectable disease (e.g., peritoneal tumor seeding), and rapid clinical deterioration was the only indication that the scintigraphic findings might represent true tumor sites. It should be borne in mind that, when one is assessing tumor detection by a new imaging modality, some suspected tumor sites cannot be characterized histologically and, when one is comparing the results of different imaging modalities, the more sensitive technique will provide its own standard of criteria (*9*).

CONCLUSION

When a PET scanner is not available, DHC ^{18}F-FDG imaging is an alternative technique that can be used in a complementary manner to conventional imaging modalities for the assessment of recurrent CRC. Coincidence imaging with upgraded SPECT cameras allows wider accessibility of ^{18}F-FDG imaging to patients with recurrent metastatic disease.

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REFERENCES

1. Boyle P, Leon ME. Recent developments in the epidemiology of colorectal cancer. In: Bleiberg H, Kemeny N, Rougier P, Wilke H, eds. *Colorectal Cancer: A Clinical Guide to Therapy.* London, U.K.: Martin Dunitz; 2001:11–29.
2. August DA, Ottow RT, Sugarbaker PH. Clinical perspective on human colorectal cancer metastases. *Cancer Metastasis Rev.* 1984;3:303–324.
3. Steele G, Bleday R, Mayer RJ, Lindblad A, Petrelli N, Weaver D. A prospective evaluation of hepatic resection for colorectal carcinoma metastases to the liver: gastrointestinal tumor study group protocol 6584. *J Clin Oncol.* 1991;9:1105–1112.
4. Bruinvels DJ, Stiggelbout AM, Kievit J, van Houwelingen HC, Habbema JD, van de Velde CJ. Follow-up of patients with colorectal cancer: a meta-analysis. *Ann Surg.* 1994;219:174–182.
5. Fong Y, Saldinger PF, Akhurst T, et al. Tomography scanning on selection of patients for resection of hepatic colorectal metastases. *Am J Surg.* 1999;178:282–287.
6. 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;43:759–770.
7. Abdel-Nabi H, Doerr RJ, Lamonica DM, et al. Staging of primary colorectal carcinoma with fluorine-18 fluorodeoxyglucose whole body PET: correlation with histopathologic and CT findings. *Radiology.* 1998;206:755–760.
8. Vitola JV, Delbeke D, Sandler MP, et al. Positron emission tomography to stage suspected metastatic colorectal carcinoma in the liver. *Am J Surg.* 1996;171:21–26.
9. Valk PE, Abella-Columna E, Hasemann MK, et al. Whole-body PET imaging with F-18 fluorodeoxyglucose in management of recurrent colorectal cancer. *Arch Surg.* 1999;134:503–513.
10. Sugarbaker PH, Grianola FJ, Dwyer S, et al. A simplified plan for follow up of patients with colon and rectal cancer supported by prospective studies of laboratory and radiologic test results. *Surgery.* 1987;102:79–87.
11. Strauss LG, Conti PS. The application of PET in clinical oncology. *J Nucl Med.* 1991;32:623–648.
12. Pounds TR, Valk PE, Haseman MK, et al. Whole body PET-FDG imaging in the diagnosis of recurrent colorectal cancer [abstract]. *J Nucl Med.* 1995;36(suppl):57P.
13. Gupta N, Bradfield H. Role of positron emission tomography scanning in evaluating gastrointestinal neoplasms. *Semin Nucl Med.* 1996;26:65–73.
14. Delbeke D, Vitola JV, Martin MP, et al. Staging recurrent metastatic colorectal carcinoma with PET. *J Nucl Med.* 1997;38:1196–1201.
15. Shreve PD, Steventon RS, Deters EC, Kison PV, Gross MD, Wahl RL. Oncologic diagnosis with 2-[fluorine-18]fluoro-2-deoxy-D-glucose imaging: dual-head coincidence gamma camera versus positron emission tomographic scanner. *Radiology.* 1998;207:431–437.
16. Gambhir SS, Czernin J, Schwimmer J, Silverman DH, Coleman RE, Phelps ME. A tabulated summary of the FDG PET literature. *J Nucl Med.* 2001;42(suppl):1S–93S.
17. Patton JA, Delbeke D, Sandler MP. Image fusion using an integrated, dual-head coincidence camera with x-ray tube-based attenuation maps. *J Nucl Med.* 2000;41:1364–1368.
18. Kunz WD, Baehre M, Richter E. PET with a dual-head coincidence camera: spatial resolution, scatter fraction, and sensitivity. *J Nucl Med.* 2000;41:1067–1074.
19. Yutani K, Tatsumi M, Shiba E, Kusuka H, Nishimura T. Comparison of dual-head coincidence gamma camera FDG imaging with FDG PET in detection of breast cancer and axillary lymph node metastasis. *J Nucl Med.* 1999;40:1003–1008.
20. Bousson V, Moretti JL, Weinmann P, et al. Assessment of malignancy in pulmonary lesion: FDG dual-head coincidence gamma camera imaging in association with serum tumor marker measurement. *J Nucl Med.* 2000;41:1801–1807.
21. Montravers F, Grahek D, Kerrou K, et al. Evaluation of FDG uptake by renal malignancies (primary tumor or metastases) using a coincidence detection gamma camera. *J Nucl Med.* 2000;41:78–84.
22. Levkovitz R, Falikman D, Wilk M. The design and implementation of COSEM,

an iterative algorithm for a fully 3D list mode data. In: Proceedings of the 1999 International Meeting on Fully Three Dimensional Image Reconstruction in Radiology and Nuclear Medicine; June 23–26, 1999; Egmond aan Zee, The Netherlands.
23. Royal HD, McNeil BJ. The evaluation and impact of diagnostic tests. In: Gottschalk A, Hoffer PB, Potchen EJ, eds. *Diagnostic Nuclear Medicine: Golden's Diagnostic Radiology*. Baltimore, MD: Williams and Wilkins; 1996: 183–198.
24. Strauss LG, Clorius BM, Schlag P, et al. Recurrence of colorectal tumors: PET evaluation. *Radiology.* 1989;170:329–332.
25. Gupta N, Frank A, Mailord J, et al. Accurate detection of liver metastases in patients (PTS) with primary malignancies using PET-FDG imaging [abstract]. *J Nucl Med.* 1993;34(suppl):6P.
26. Lai DT, Fulhman M, Stephen MS, et al. The role of whole-body positron emission tomography with [^{18}F] fluorodeoxyglucose in identifying operable colorectal cancer metastases in the liver. *Ann Surg.* 1996;131:703–707.
27. Flamen P, Stroobants S, Cutsen EV, et al. Additional value of whole-body positron emission tomography with fluorine-2-fluoro-2-deoxy-D-glucose in recurrent colorectal cancer. *J Clin Oncol.* 1999;17:894–901.
28. Meta J, Selzer M, Schiepers C, et al. Impact of ^{18}F-FDG PET on managing patients with colorectal cancer: the referring physician's perspective. *J Nucl Med.* 2001;42:586–590.
29. Tucker R, Coel M, Morris P, Druger G, McGuigan P. Impact of fluorine-18 fluorodeoxyglucose positron emission tomography on patient management: first year's experience in a clinical center. *J Clin Oncol.* 2001;19:2504–2508.
30. Delbeke D, Martin WH, Patton JA, Sandler MP. Value of iterative reconstruction, attenuation correction, and image fusion in the interpretation of FDG PET images with an integrated dual-head coincidence camera and x-ray-based attenuation maps. *Radiology.* 2001;218:163–171.
31. Boren EL Jr, Delbeke D, Patton JA, Sandler MP. Comparison of FDG PET and positron coincidence imaging using a dual-head gamma camera with 5/8-inch NaI(Tl) crystals in patients with suspected body malignancies. *Eur J Nucl Med.* 1999;26:379–387.
32. Moertel CG, Fleming TR, MacDonald JS, et al. An evaluation of the carcinoembryonic antigen (CEA) test for monitoring patients with resected colon cancer. *JAMA.* 1993;270:943–947.
33. Flanagan FL, Dehdashti F, Ogunbiyi OA, Konder IJ, Siegel BA. Utility of FDG-PET for investigating unexplained plasma CEA elevation in patients with colorectal cancer. *Ann Surg.* 1998;3:319–323.