

# Staging Recurrent Metastatic Colorectal Carcinoma with PET

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Accurate detection of recurrent colorectal carcinoma remains a diagnostic challenge. The purposes of this study were to assess the accuracy of  $^{18}\text{F}$ -FDG-PET in patients with recurrent colorectal carcinoma in detecting liver metastases compared with computed tomography (CT) and CT portography, detecting extrahepatic metastases compared with CT and evaluating the impact on patient management. **Methods:** Fifty-two patients previously treated for colorectal carcinoma presented on 61 occasions with suspected recurrence and underwent  $^{18}\text{F}$ -FDG-PET of the entire body. PET, CT and CT portography images were analyzed visually. The final diagnosis was obtained by pathology ( $n = 44$ ) or clinical and radiological follow-up ( $n = 17$ ). The impact on management was reviewed retrospectively. **Results:** A total of 166 suspicious lesions were identified. Of the 127 intrahepatic lesions, 104 were malignant, and of the 39 extrahepatic lesions, 34 were malignant. Fluorine-18-fluorodeoxyglucose imaging was more accurate (92%) than CT and CT portography (78% and 80%, respectively) in detecting liver metastases and more accurate than CT for extrahepatic metastases (92% and 71%, respectively). Fluorine-18-fluorodeoxyglucose detected unsuspected metastases in 17 patients and altered surgical management in 28% of patients. **Conclusion:** These data identify that  $^{18}\text{F}$ -FDG-PET is the most accurate noninvasive method for staging patients with recurrent metastatic colorectal carcinoma and plays an important role in management decisions in this setting.

**Key Words:** neoplasms; computed tomography; fluorine-18-FDG; portography

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In 1996, there were approximately 133,500 new cases of colorectal carcinoma diagnosed in the United States, and 54,900 patients died of their neoplasm that same year (1). About 14,000 patients per year present with isolated liver metastases at their first recurrence (2), and about 20% of these patients die with metastases exclusively to the liver. Hepatic resection is the only curative therapy in these patients, but it is associated with a mortality of 2%–7% (3) and has the potential for significant morbidity. Early detection and prompt treatment of recurrences may lead to a cure in up to 25% of the patients (4). However, the size and number of hepatic metastases and the presence of extrahepatic disease all affect the prognosis. The poor prognosis of extrahepatic metastases is believed to be a contraindication to hepatic resection (5). Therefore, accurate noninvasive detection of inoperable disease with imaging modalities plays a pivotal role in selecting patients who would benefit from surgery.

The measurement of serum levels of carcinoembryonic antigen (CEA) may be used to monitor the detection of recurrences with a sensitivity of 59% and specificity of 84% but does not localize recurrent lesions (6). Computerized tomography (CT)

has been the conventional imaging modality used to localize recurrence, but it fails to demonstrate hepatic metastases in up to 7% of patients and underestimates the number of lobes involved in up to 33% of patients (7). In addition, metastases to the peritoneum, mesentery and lymph nodes are commonly missed on CT (8–11), and the differentiation of postsurgical changes from tumor recurrence is often equivocal (11). CT portography (superior mesenteric arterial portography) is more sensitive (80%–90%) than CT (70%–80%) for detection of hepatic metastases (11–15) but has a considerable rate of false-positive findings, lowering the positive predictive value (16,17).

Functional imaging is a rapidly developing field for detecting metastatic disease. The glucose analog  $^{18}\text{F}$ -fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) is a positron emitter allowing direct evaluation of glucose metabolism with PET. Malignant cells, in general, and colorectal carcinoma, in particular, demonstrate increased glucose utilization (12,18,19), probably due to an increased number of glucose transporter proteins and increased enzyme levels of hexokinase and phosphofructokinase promoting glycolysis (20,21). A strong potential role for  $^{18}\text{F}$ -FDG-PET as an imaging modality for detecting primary colorectal carcinoma and its recurrences has been demonstrated by several studies (12,18,19,22–31).

The purpose of this study was to assess the accuracy of  $^{18}\text{F}$ -FDG-PET for detecting liver metastases compared with CT and CT portography, detecting extrahepatic metastases compared with CT and evaluating the impact on management of patients with recurrent colorectal carcinoma.

## MATERIALS AND METHODS

### Patient Population

Fifty-two consecutive patients presented on 61 occasions for evaluation of suspected recurrent colorectal carcinoma. There were 31 men and 21 women, with a mean age of  $63 \pm 11$  yr. All patients had prior surgical excision of the primary tumor, and, in 14 patients, patients had a history of previous surgical resection of metastases. Fluorine-18-fluorodeoxyglucose imaging was performed at least 2 mo after the last surgical treatment. Recurrence was suspected based on elevation of CEA levels or abnormal findings on CT. PET, CT and CT portography were performed within a 2-mo interval of each other.

### CT Scan and CT Portography

All patients with suspected liver lesions either underwent a CT scan of the abdomen ( $n = 48$ ), a CT portography ( $n = 40$ ) or both ( $n = 29$ ) within 2 mo of the PET scan. The patients who did not undergo CT portography had known extrahepatic disease and were not surgical candidates. Patients with abnormal findings on PET in extraabdominal areas had an additional CT scan of that region.

CT images were obtained through the liver with contiguous 8-mm slices after oral contrast and before and after the injection of

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contrast. The CT portography was begun 20 sec after initiation of infusion of contrast medium by means of a superior mesenteric arterial catheter at a rate of 4 ml/sec, for a total of 70 ml. The CT scan was performed using a spiral technique with 8-mm collimation and a table speed of 8 mm/sec (pitch = 1). The images were then reconstructed at a thickness of 5 mm.

## PET

Fluorine-18-fluorodeoxyglucose was performed with a tomograph (Siemens ECAT 933/08/16), which has 8 ring detectors that simultaneously collect images in 15 planes, each of 8-mm thickness. The axial field of view of this system is 12.8 cm, with an intrinsic resolution at the center of the field of 4.8 mm and with a reconstructed resolution of  $6.5 \times 6.5 \times 8.0$  mm (full width at half maximum).

Patients were required to fast for at least 4 hr before the PET scan. They were scanned in as many sequential images as necessary to include the entire thorax, abdomen and pelvis. Transmission images were obtained for 10 min per bed position to correct for photon attenuation using a germanium-68 ring source. After intravenous administration of 370 Mbq (10 mCi) of  $^{18}\text{F}$ FDG, emission images were acquired for 15 min per bed position. The uptake period between  $^{18}\text{F}$ FDG injection and the beginning of the emission scan was  $70 \pm 25$  min (range 34–137). Accurate positioning of the patient between transmission and emission scans was performed using laser marks.

Both attenuated and nonattenuated images were interpreted visually, and attenuated images were analyzed semiquantitatively using the standard uptake ratio (SUR) in all but one patient, because of motion artifact. Regions of interest measuring  $1.0 \pm 0.5$  cm<sup>2</sup> were drawn over areas of maximum activity within each lesion. The SUR was calculated as follows:  $\text{SUR} = (\text{activity in regions of interest in } \mu\text{Ci/ml}) / (\text{injected dose in mCi/weight in kg})$ .

## Data Analysis

The CT and CT portography scans were interpreted by two independent radiologists expert in the field of body imaging. The PET scans were interpreted by two nuclear medicine physicians expert in PET. At the time of the interpretation, the observers were blinded to the findings of the other imaging modalities. The findings of the imaging modalities were then correlated with the final diagnosis.

The final diagnosis of suspicious lesions was obtained pathologically in 44 patients, including 107 hepatic lesions and 24 extrahepatic lesions.

The pathological proof of the nature of the lesions was obtained during laparotomy in all patients, except for two lesions that were examined after percutaneous fine needle aspiration. Pathological examination was possible only for the resected specimen. For the lesions that were not resected, surgical examination was used as a standard of reference, as well as intraoperative ultrasound, to examine the liver. Intraoperative ultrasound previously has been found to have a sensitivity of 96% for the detection of liver metastases (15).

In 17 patients, including 20 hepatic lesions and 15 extrahepatic lesions, the presence or absence of malignancy was established with clinical and radiological follow-up. In 13 of 17 patients, disease was unresectable, and in 4 patients there was minimally elevated CEA but no other evidence of disease. A lesion was considered malignant if it increased in volume (estimated by bidimensional measurement) by more than 20% of its original size on follow-up radiographic studies. A lesion was considered benign if, without treatment, the size had not changed on CT and the patient had not developed clinical signs and symptoms suggesting recurrence during a follow-up of more than 1 yr after the initial evaluation.

**TABLE 1**  
Comparison of PET, CT and CT Portography to Detect Liver Metastases from Colorectal Carcinoma

Modality	TP	FN	TN	FP	SEN (%)	PPV (%)	AAC (%)
CT	66	15	9	6	81	92	78
CT portography	78	2	1	18	97	81	80
PET	95	9	22	1	91	99	92

Lesions of all sizes were included. TP = true-positive; FN = false-negative; TN = true-negative; FP = false-positive; SEN = sensitivity; PPV = positive predictive value; AAC = accuracy.

## Statistical Analysis

Results were expressed as mean  $\pm$  s.d., and comparison was performed using the Student's t-test for unpaired data. A p value < 0.05 was considered to be statistically significant.

## RESULTS

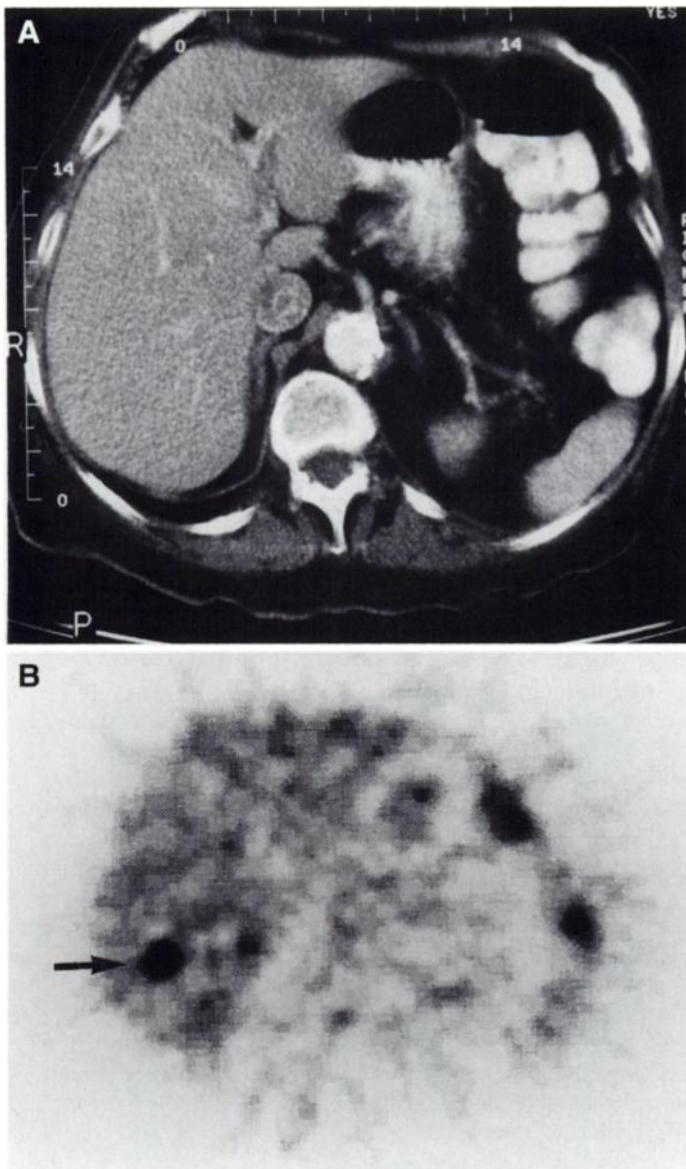
### Analysis of Lesions (n = 166)

A lesion was defined as a site of recurrence found pathologically or a site of suspected recurrence identified by one or more of the imaging modalities: CT, CT portography or PET. There were a total of 166 lesions: 127 intrahepatic and 39 extrahepatic (11 in the lungs, 28 in the abdomen or pelvis). Of the 127 intrahepatic lesions, 104 were malignant and 23 were benign, and of the 39 extrahepatic lesions, 34 were malignant and 5 were benign.

All malignant lesions were metastases from adenocarcinoma consistent with colon primary, except one malignant lesion, a lymphoma, in a mesenteric lymph node, which was the second malignancy for this patient. The 23 benign lesions in the liver were normal liver (n = 7), benign postsurgical sites (n = 8), focal fibrosis (n = 2), resolving abscess (n = 1), benign hepatic cysts (n = 4) and hematoma (n = 1). The five benign extrahepatic lesions were two lung nodules and three pseudolesions in the abdomen or pelvis where no pathology was found at surgical exploration.

**Intrahepatic Lesions.** We analyzed the sensitivity and positive predictive value of CT, CT portography and PET to detect hepatic recurrences (Table 1). The intrahepatic lesions ranged from 0.3–6 cm in size. The accuracy of PET was 92%, compared with 78% for CT and 80% for CT portography. If only the lesions with pathologically proven disease are included in the analysis, the sensitivity, positive predictive value and accuracy of the three imaging modalities stayed within 1% of the values shown in Table 1. Figure 1 shows an example of a solitary liver metastasis detected only by PET. There was one false-positive PET lesion in the liver that was also a false-positive on CT portography. Histological examination of the surgical specimen demonstrated a resolving abscess at a postoperative site. Among the nine false-negative lesions on PET, eight were less than 1 cm and one was in a patient undergoing chemotherapy. There were 23 lesions measuring less than 1 cm; 18 of these small lesions were malignant, and 10 of them were seen with PET. When lesions measuring less than 1 cm were excluded, the sensitivity and accuracy of CT portography did not change; the sensitivity of CT increased from 81% to 87% and the accuracy from 78% to 83%; the sensitivity of PET increased from 91% to 99% and the accuracy from 90% to 98%.

**Evaluation of Intrahepatic Postsurgical Sites.** PET was accurate in differentiating postsurgical changes from malignant recurrence in 12 of 14 sites with an accuracy of 86% (one false-positive and one false-negative). CT and CT portography



**FIGURE 1.** Axial CT (A) and PET (B) images of a patient status postresection of a colorectal carcinoma and recent elevation of the CEA level. The abdominal CT was interpreted as normal. PET revealed a focus of increased uptake of  $^{18}\text{F}$ FDG in the liver (arrow, SUR = 4.2) that led to surgical resection, and the lesion was proved malignant.

were only available for 11 sites. CT was misleading in 4 of 11 sites with an accuracy of 64% (1 false-positive and 3 false-negatives), and CT portography was misleading in 6 of 11 sites with an accuracy of 45% (5 false-positives and 1 false-negative).

**Extrahepatic Lesions.** Thirty-nine extrahepatic lesions were found in 30 patients. Thirty-four of the 39 extrahepatic lesions were malignant, and 5 were benign. Twenty-eight of these lesions were located in the abdomen or pelvis and 11 in the chest. The accuracy of PET in detecting extrahepatic malignancy was 92%, with three false-positives in the pelvis and no false-negatives. The accuracy of CT was 71%, with two false-positive lung lesions and eight false-negative lesions (seven in the pelvis and one in the lung) (Table 2).

In the chest, PET showed  $^{18}\text{F}$ FDG uptake in unsuspected lung lesions from three patients, leading to further evaluation by CT and confirmation of metastases. In one patient who had undergone resection of a single pulmonary metastasis in the past and presented with new elevation of CEA level, the postsurgical site

**TABLE 2**

Comparison of PET and CT in Detecting Extrahepatic Metastases from Colorectal Carcinoma

Modality	TP	FN	TN	FP	SEN (%)	ACC (%)
CT	23	8	2	2	74	71
PET	34	0	2	3	100	92

Lesions of all sizes were included. The specificity is not reported because of the small number of true-negative lesions. TP = true-positive; FN = false-negative; TN = true-negative; FP = false-positive; SEN = sensitivity; ACC = accuracy.

was interpreted as benign on CT but had  $^{18}\text{F}$ FDG uptake on PET, and a biopsy proved malignant recurrence. Seven lung lesions were indeterminate nodules on CT (considered positive for malignancy for the purpose of this study); PET showed  $^{18}\text{F}$ FDG uptake in five nodules proved to be malignant, and no  $^{18}\text{F}$ FDG uptake in two nodules from a single patient proved to be benign by biopsy.

Twenty-eight foci of abnormal  $^{18}\text{F}$ FDG uptake were identified by PET in the abdomen or pelvis. For three of these foci (two in the same patient presenting on two occasions), no pathological findings were found at surgical exploration when these patients underwent resection of liver metastases (three false-positive PET lesions). CT showed no corresponding lesion for one patient and was equivocal for the other patient. There were eight false-negative CT lesions. Four of the malignant pelvic lesions with  $^{18}\text{F}$ FDG uptake were considered to represent benign postsurgical change on the CT scan. In three patients, PET identified sites of tumor involvement that were not seen on CT or interpreted retrospectively as equivocal, as illustrated in Figure 2. In one patient, PET was the only test that identified an abnormal area of increased uptake in the mesentery, and biopsy revealed that the patient had lymphoma as a second malignancy.

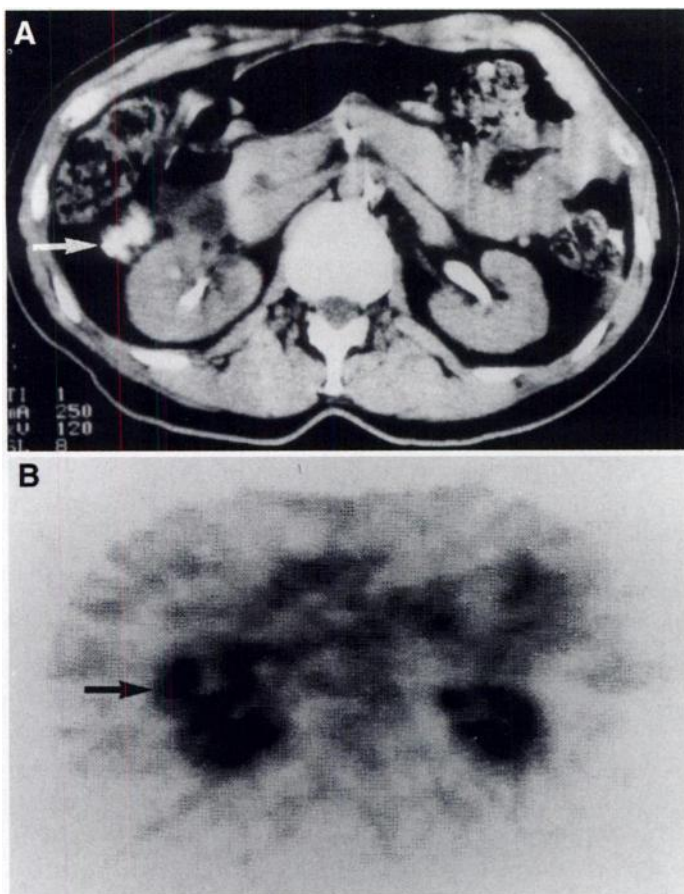
**Differences in  $^{18}\text{F}$ FDG Uptake between Malignant and Benign Hepatic Lesions.** One hundred and one hepatic lesions were included in this analysis, 83 malignant and 18 benign. Lesions measuring less than 1 cm ( $n = 23$ ) were excluded, as well as the three lesions in the patient who moved during the PET scan. The calculated SUR for malignant lesions was  $8.1 \pm 4.1$ , which was significantly higher than the SUR obtained for benign lesions,  $2.0 \pm 1$  ( $p < 0.0001$ ). All but one malignant lesion greater than 1 cm had an SUR higher than 3.5, and all but one benign lesion had an SUR below 3.5 (Fig. 3). We found that the SUR was useful in differentiating malignant from benign lesions in the liver when the size was known to be greater than 1 cm. For extrahepatic lesions, the SUR did not help in differentiating bowel uptake from metastases. The pattern of uptake, location and corresponding findings on CT were more helpful.

#### Analysis of Patients ( $n = 61$ )

Fifty-five of the 61 patients were found to have recurrent disease, and six were found to be disease-free. Of the 55 patients with recurrence, 45 had hepatic metastases (16 of which had concomitant extrahepatic disease), and 10 had extrahepatic disease only.

PET identified all patients with recurrent carcinoma with the exception (one false-negative) of a patient having a single hepatic metastasis measuring less than 1 cm, which was identified with CT portography. There was one false-positive patient identified with PET demonstrating focal  $^{18}\text{F}$ FDG uptake both in the pelvis and at a postsurgical site in the liver (also





**FIGURE 2.** Axial CT (A) and PET (B) images of a patient previously treated with sigmoidectomy for colon carcinoma and presenting with elevated CEA and a small liver lesion on CT portography (not shown). PET revealed an additional focus of increased  $^{18}\text{F}$ FDG uptake in the right abdomen (arrow). Retrospectively, an equivocal lesion was identified on the CT (arrow). Both lesions were resected surgically and proved malignant.

identified on CT portography and proved to be a resolving abscess by biopsy) of a patient free of recurrence. The liver was evaluated by CT in 48 patients, and there were three false-positive and three false-negative CT scans for detection of

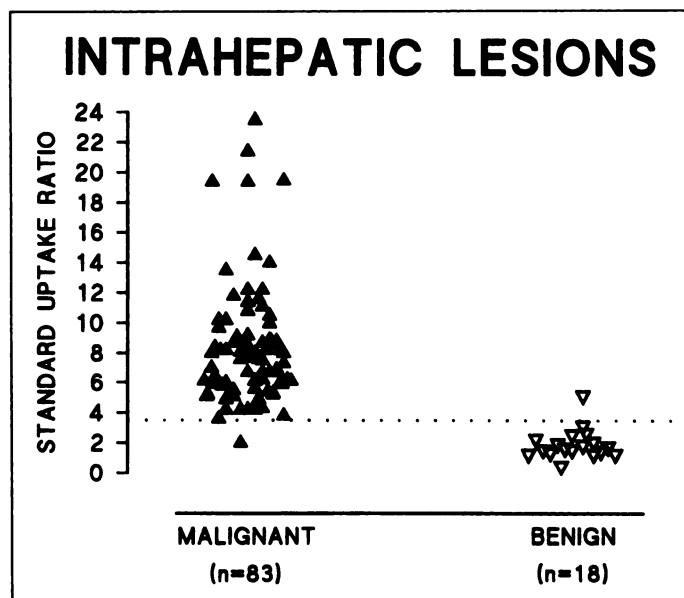
patients with liver metastases. Evaluation of the liver by CT portography in 40 patients resulted in 4 false-positives results.

### Effect of PET on Management

The effect of PET imaging on surgical management was retrospectively reviewed with the surgeons. PET helped clarify the final diagnosis misinterpreted on CT and/or CT portography in 28% of the patients ( $n = 17$ ), leading to a change in surgical management. PET helped to plan surgery in 6 patients by identifying a resectable site of recurrence and helped to avoid unnecessary surgery in 11 patients by identifying unresectable disease.

*PET Helped to Plan Surgery ( $n = 6$ ).* In two patients with elevated CEA, PET was the only modality that identified a single liver metastasis, leading to surgical resection (Fig. 1). In one patient, there was no  $^{18}\text{F}$ FDG uptake at a postsurgical site in liver interpreted as suspicious on CT, and PET identified a metastasis in the chest leading to a different surgical procedure than the one originally planned. In one patient, there was no  $^{18}\text{F}$ FDG uptake in two lung nodules from the same patient interpreted as probable metastases on CT, leading to the curative resection of the single liver metastasis seen on both CT and PET. In two patients with resectable liver metastases, PET identified, in addition to the liver metastases, one single focus of uptake in the abdomen when CT was negative, leading to the intraoperative biopsy and resection of both the liver metastases and mesenteric malignant lesions.

*PET Helped to Avoid Unnecessary Surgery ( $n = 11$ ).* A negative PET avoided laparotomy in two patients who had an equivocal CT. In nine patients, PET demonstrated unsuspected extrahepatic metastases, leading to a change in surgical management: for example, a partial hepatectomy initially planned was not performed. In two of these patients, PET identified multiple lung metastases confirmed late by a chest CT, which was not planned in the preoperative work-up. In three patients, PET confirmed the malignancy of an indeterminate lung nodule on CT. In four patients, PET identified recurrence in the abdomen or pelvis, either local recurrence at postoperative sites where CT was interpreted as probably benign ( $n = 2$ ) or metastases in mesenteric lymph nodes when CT was negative ( $n = 2$ ).

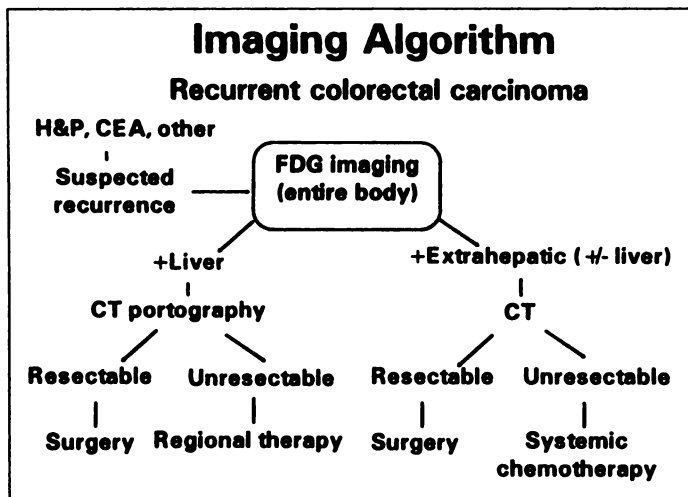


**FIGURE 3.** Distribution of SUR for malignant and benign hepatic lesions measuring more than 1 cm. The horizontal lines represent the optimal cutoff level, which differentiates malignant from benign lesions ( $p < 0.0001$ ).

### DISCUSSION

The noninvasive differentiation between malignant and benign lesions in suspected recurrent colorectal carcinoma remains a diagnostic challenge. The liver is the most common site of recurrent colorectal carcinoma, followed by abdominal lymph nodes. In rectal carcinoma, pulmonary metastases can occur before liver metastases because hemorrhoidal veins drain into the vena cava. The conventional imaging modality for evaluating these patients is CT, which is relatively sensitive in detecting liver metastases but less sensitive in detecting lymph node metastases and poorly specific in differentiating local recurrence from fibrosis and scar formation (11). CT portography is the most sensitive modality for detecting liver metastases but is invasive (12-15).

Our study demonstrates that a metabolic-based imaging technique such as PET using  $^{18}\text{F}$ FDG is extremely useful for detecting both hepatic and extrahepatic metastases from colorectal carcinoma. We found that the sensitivity and accuracy of  $^{18}\text{F}$ FDG-PET in detecting metastatic colorectal carcinoma are in the same range as reported by others (22-31) but also showed the effect on patient management. Fluorine-18-fluorodeoxyglucose had a higher accuracy (92%) than CT (78%) and CT portography (80%) in detecting liver metastases, and although



**FIGURE 4.** Imaging algorithm used to evaluate patients with suspected recurrent colorectal carcinoma.

the sensitivity of  $^{18}\text{F}$ FDG-PET (91%) was lower than CT portography (97%), the accuracy was much higher, particularly at postsurgical sites. In addition, PET imaging allows evaluation of the entire body without additional radiation to the patient and can identify metastatic disease to the chest, abdomen or pelvis that can guide follow-up CT of these regions to evaluate the exact anatomic location and potential resectability of these lesions. Outside the liver,  $^{18}\text{F}$ FDG-PET was especially helpful in detecting nodal involvement, differentiating local recurrence from postsurgical changes and evaluating the malignancy of indeterminate pulmonary nodules—indications for which CT has known limitations. As reported in a preliminary study (27), PET changed the surgical management in 28% of patients, either by identifying a resectable metastasis or by demonstrating unresectable extrahepatic metastases that were unsuspected clinically, not seen or were equivocal on CT. An impact of  $^{18}\text{F}$ FDG-PET on surgical management of the same magnitude has been recently demonstrated in preliminary studies by other groups of investigators (29,30).

Based on these data, patients who present with suspected recurrent colorectal carcinoma at our institution are now evaluated according to the algorithm shown in Figure 4. An  $^{18}\text{F}$ FDG-PET scan is performed first; if only a few liver metastases are seen, CT portography is performed to evaluate their resectability and the possible presence of additional small metastases. If the PET scan identifies the presence of extrahepatic metastases with or without liver metastases, a CT of the corresponding region of the body is performed to confirm the presence of a lesion, even equivocal (versus normal bowel, for example). In our experience using this approach, among the 28% of patients for which PET changed the management, surgery was planned in one-third of the patients and avoided in two-thirds of the patients. A cost-effectiveness analysis per se was not performed because of the assumptions involved regarding the performance, cost and reimbursement of various procedures. However, the data generated from this study suggest that the high accuracy of  $^{18}\text{F}$ FDG-PET will prove this modality to be cost effective, in addition to more accurately selecting patients who will benefit from surgery and, more importantly, patients who will not benefit from laparotomy and liver resection because of unsuspected or unrecognized extrahepatic recurrence.

Currently, manufacturers are developing conventional nuclear medicine cameras to image positron emitters using the coincident mode for both brain and oncology imaging. In the

future, the availability of  $^{18}\text{F}$ FDG coincidence imaging on dual-head SPECT cameras may make  $^{18}\text{F}$ FDG imaging in patients with oncological diseases more widely available.

#### Limitations of PET as a Diagnostic Tool

False-negative lesions can be due to partial volume averaging (32), leading to underestimation of the uptake in small lesions (<1 cm) or in necrotic lesions with a thin viable rim, classifying these lesions as benign instead of malignant. In our study, the nine false-negative liver lesions on PET were in seven patients, but four of these patients had other lesions larger than 1 cm that were easily detected by PET, and two of these patients had unsuspected extrahepatic metastases detected with PET.

Some inflammatory lesions, mainly granulomatous, can have  $^{18}\text{F}$ FDG uptake presumably due to activated macrophages and can be mistaken for malignancies (33). Fluorine-18-fluorodeoxyglucose uptake normally present in the gastrointestinal tract can sometimes be difficult to differentiate from a malignant lesion. In our study, there were four false-positive PET lesions in three occurrences. Three of these lesions were in the abdomen or pelvis and were probably due to bowel uptake, and one lesion was a resolving abscess in the liver.

#### Limitations of the Study

A limitation of the study is that some patients were not explored surgically because of the presence of unresectable disease. Some of these patients had a follow-up time of less than 1 yr because chemotherapy was started or they died. These patients may have had metastases undetected by any of the imaging modalities in the study, which may overestimate the sensitivity of these modalities. This is especially true for extrahepatic metastases, since only 24 of 39 of these lesions were in patients explored surgically.

#### CONCLUSION

Fluorine-18-fluorodeoxyglucose is more accurate than CT in detecting metastases from colorectal carcinoma, both in the liver and outside the liver, and more accurate than CT portography in the liver. The limitations of PET include the lack of detection of some small metastases and possible false-positive findings due to normal gastrointestinal tract uptake and in lesions containing activated macrophages. However,  $^{18}\text{F}$ FDG-PET is an invaluable imaging modality for detecting lymph node involvement and recurrence at postsurgical sites, for which the limitations of CT are well known. In this study, PET led to a change in surgical management in 28% of the patients.

Fluorine-18-fluorodeoxyglucose should be considered as a screening method for the entire body in detecting suspected recurrent colorectal carcinoma and staging patients considered for resection of metastases. The findings on PET should guide the performance, increase the specificity of CT and CT portography, and help to identify patients with resectable disease. The high accuracy of  $^{18}\text{F}$ FDG-PET may prove this imaging procedure to be cost-effective for the work-up of patients with suspected recurrent colorectal carcinoma.

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## Arteriovenous Shunts in Patients with Hepatic Tumors

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The study aimed to investigate the influence of tumor type, tumor size, tumor vascularity and treatment on arteriovenous shunts between the liver and lungs in patients with hepatic cancer. **Methods:** Our previous assessment of the degrees of lung shunting using intra-arterial <sup>99m</sup>Tc-macroaggregated albumin in 125 patients with hepatocellular carcinoma (HCC) was extended to include 377 patients with HCC and 25 patients with colorectal liver metastases. Patients were given 111 MBq (3 mCi) of <sup>99m</sup>Tc-macroaggregated albumin during hepatic angiography. The lungs and the liver were localized as regions of interest on the digitized gamma scintigraphic image. The total counts taken over the lungs divided by the total counts taken over both the lungs and the liver gave the percentage of lung shunting. Tumor size was measured by computerized tomography or ultrasound scan. Tumor vascularity was assessed based on the degree of neovascularization. Linear regression and Wilcoxon rank test were used for statistical analysis. **Results:** Patients with HCC had a higher median (7.6%) and a wider range (<1-75.4%) of percentages of lung shunting when compared with those with colorectal liver metastases (median, 4.7%; range, <1-23.9%). The lung shunting correlated with the tumor size in the 377 patients with HCC ( $r = 0.359$ ;  $p < 0.0001$ ). Excluding one outlier, we found a similar correlation in 24 patients with colorectal metastases ( $r = 0.686$ ;  $p < 0.0001$ ). In HCC, the mean lung shunting increased with increasing tumor size, up to 15 cm, and then remained almost unchanged, up to a size of >20 cm. The mean lung shunting also increased with increasing vascularity grades, as assessed by hepatic angiography. The difference between any two vascularity grades was statistically significant ( $p = 0.0001-0.0148$ ). Similar

analysis by subgroups in colorectal liver metastases was impossible because of the small number of patients. Lung shunting decreased in HCC patients after the tumors were treated, but it might increase or decrease when the disease recurs. **Conclusion:** The lung shunting was influenced by the type, size and vascularity of the hepatic tumor. The change in lung shunting with the status of the tumor after treatment further suggests a neoplastic nature of the blood vessels involved in the arteriovenous shunt.

**Key Words:** lung shunting; factors; hepatic cancer

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**R**egional targeted treatments for hepatic cancer aim at exposing the tumor to a high local concentration of cytotoxic agents, such as chemotherapeutic drugs or radioactive substances, including <sup>131</sup>I-Lipiodol or <sup>90</sup>Y microspheres. Ideally, the agent should be concentrated in the tumor or at least be confined to within the liver. Shunting of part of the agent to neighboring organs, such as the lungs and the gastroduodenum, reduces the efficacy of the treatment and may cause damage to these organs when a radioactive substance is used.

Technetium-99m-macroaggregated albumin (<sup>99m</sup>Tc-MAA), which has an average particular size close to that of <sup>90</sup>Y microspheres, has been widely used to assess the degree of shunting into the pulmonary circulation in metastatic liver tumors before treatment with <sup>90</sup>Y microspheres (1-5). Patients who have a high percentage of lung shunting and, thus, an increased risk of radiation pneumonitis (6) should be excluded from <sup>90</sup>Y microsphere therapy.

Lung shunting, as assessed by <sup>99m</sup>Tc-MAA, in 125 patients with hepatocellular carcinoma (HCC) has been analyzed and

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