

# Performance of integrated FDG PET/contrast-enhanced CT in the diagnosis of recurrent colorectal cancer: Comparison with integrated FDG PET/non-contrast-enhanced CT and enhanced CT

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## Abstract

**Purpose** The aim of our study was to evaluate the accuracy of integrated positron emission tomography and computed tomography (PET/CT) using  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) with IV contrast for depiction of suspected recurrent colorectal cancer and to assess the impact of PET/contrast-enhanced CT findings on clinical management

compared with PET/non-contrast-enhanced CT and CT component.

**Methods** One hundred seventy patients previously treated for colorectal cancer underwent PET/CT consisting of non-enhanced and contrast-enhanced CT for suspected recurrence. PET/contrast-enhanced CT, PET/non-contrast-enhanced CT and enhanced CT were interpreted by two experienced radiologists by consensus for each investigation. Lesion status was determined on the basis of histopathology, radiological imaging and clinical follow-up for longer than 6 months.

**Results** Patient-based analysis showed that the sensitivity, specificity and accuracy of PET/contrast-enhanced CT were 93.2 (69/74), 95.8 (92/96) and 94.7% (161/170), respectively, whereas those of PET/non-contrast-enhanced CT were 89.2 (66/74), 94.8 (91/96) and 92.4% (157/170), respectively, and those of enhanced CT were 79.7 (59/74), 93.8 (90/96) and 87.6% (149/170), respectively. Sensitivity and accuracy differed significantly among the three modalities (Cochran's Q test:  $p=0.0004$  and  $p=0.0001$ , respectively). The findings of PET/contrast-enhanced CT resulted in a change of management for 64 of the 170 patients (38%) and had an effect on patient management in 12 patients (7%) diagnosed by enhanced CT alone and 4 patients (2%) diagnosed by PET/non-contrast-enhanced CT. **Conclusion** Integrated PET/contrast-enhanced CT is an accurate modality for assessing colorectal cancer recurrence and led to changes in the subsequent appropriate therapy.

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## Introduction

Colorectal cancer is one of the most common cancer entities worldwide [1]. Radical resection and postoperative chemotherapy remain the major management options for colorectal cancer, but recurrence and/or metastasis occur in 30–50% of the patients after surgery [2–4]. An early diagnosis and accurate postoperative staging are crucial for prescribing an optimal individualized chemotherapy regimen and thus elevating the survival rate. Contrast-enhanced CT is currently the most established and important tool for restaging in patients with suspicion of colorectal cancer recurrence [5]. Recent advances in CT technology with the availability of multidetector row scanners and multiplanar images have the potential to improve the visualization of small lesions on curved surfaces throughout the whole body on patients with rectal cancer [6]. MRI is often used for detecting pelvic recurrence of colorectal cancer due to its excellent soft tissue resolution [7, 8]. However, when used alone, these conventional imaging modalities are poor at visualizing small intra-abdominal disseminated lesions and lymph node metastases and for differentiating tumour recurrence from postoperative or post-therapy changes.

In the late 1990s, positron emission tomography (PET) with  $^{18}\text{F}$ -fluorodeoxyglucose (FDG), which exploits the increased utilization of glucose by malignant cells, has opened a new field in clinical imaging and is widely used for staging, re-staging, therapeutic response monitoring and prognostication in patients with various cancers. It is possible to diagnose cancer recurrence and distant metastasis by PET in the preclinical stage before it becomes evident by conventional imaging modalities. Recently, integrated PET/CT, in which a full-ring detector clinical PET scanner and multidetector row helical CT (MDCT) scanner are combined, has made it possible to acquire both metabolic and anatomical imaging data using a single device in a single diagnostic session and provides precise anatomical localization of suspicious areas of increased FDG uptake and rules out false-positive PET findings [9, 10]. Several studies have described the usefulness of integrated PET/CT [10–16] for the diagnosis of recurrent colorectal cancer. These reports of PET/CT have included relatively small numbers of patients ( $n=45$ –90) and the quality of the CT component did not fully reach a sufficient diagnostic level in many studies. To our knowledge, only one group has used intravenous contrast material for the CT component of the PET/CT scan [16]. The purpose of the present study was to assess the diagnostic patient- and lesion site-based accuracies of PET/contrast-enhanced CT for the follow-up of large series of patients previously treated for colorectal cancer and the impact of PET/contrast-enhanced CT findings on patient management as compared with PET/non-contrast-enhanced CT and enhanced CT.

## Materials and methods

### Patients

One hundred seventy patients (age range: 35–81 years, mean: 56 years) with suspected recurrence and/or metastasis of colorectal cancer underwent PET/CT examinations consisting of non-enhanced and contrast-enhanced CT at our institution between April 2005 and May 2008, with the approval of the Institutional Review Board. Informed consent was obtained from each patient after the nature of the procedures had been fully explained. Primary cancer originated from the caecum ( $n=3$ ), ascending colon ( $n=13$ ), transverse colon ( $n=15$ ), descending colon ( $n=18$ ), sigmoid colon ( $n=40$ ), or rectum ( $n=81$ ). PET/CT examinations were performed at the time of follow-up at least 6 months (range: 6–70 months, mean: 19 months) after the surgery. Fifty-nine patients had undergone chemotherapy at PET/CT examinations. Recurrence was suspected on the basis of elevated levels of carcinoembryonic antigen (CEA) ( $n=86$ ), both elevated CEA levels and abnormal CT and/or MR imaging findings ( $n=39$ ), abnormal CT and/or MR imaging findings ( $n=28$ ) and physical examination ( $n=17$ ).

### FDG PET/CT study

Whole body imaging was performed using a combined PET/CT scanner (Biograph, Sensation 16 PET/CT system, Siemens AG, Erlangen, Germany). MDCT covered a region ranging from the meatus of the ear to the mid-thigh. The technical parameters of the 16-detector row helical CT scanner were a gantry rotation speed of 0.5 s and a table speed of 24 mm per gantry rotation. The PET component of the combined imaging system had an axial view of 16.2 cm (per bed position) with an interslice spacing of 3.75 mm in one bed position and provided an image from the meatus of the ear to the mid-thigh with six to seven bed positions. The transaxial field of view and pixel size of the PET images reconstructed for fusion were 58.5 cm and 4.57 mm, respectively, with a matrix size of  $128 \times 128$ . To avoid artefacts caused by the urinary tract, patients were asked to drink 1,000 ml of water 1–2 h prior to image acquisition and to void just before the start of acquisition. No urinary bladder catheterization was used. After at least 4 h of fasting, patients received an intravenous injection of 4.0 MBq/kg body weight of FDG. The blood glucose levels were checked in all patients before FDG injection and no patients showed a blood glucose level of more than 160 mg/dl.

About 50 min later, initially unenhanced low-dose CT was performed at 140 kV and 40 mA for attenuation correction of the PET image. A whole body emission PET scan was performed immediately after the low-dose CT,

with a 3-min acquisition per bed position using a three-dimensional acquisition mode. Attenuation-corrected PET images were reconstructed with an ordered subset expectation maximization iterative reconstruction algorithm (eight subsets, three iterations). Finally, diagnostic contrast-enhanced full-dose MDCT was performed for the same axial coverage at 140 kV and 230 mA, with a 2-mm slice thickness. Intravenous administration of a total volume of 150 ml (maximum) or 2 ml/kg of iodinated contrast material (iomeprole 300, Eisai, Tokyo, Japan) containing 300 mg of iodine/ml via power injection at a rate of 2.5 ml/s was performed, and the scan of neck~thorax, upper~middle abdomen and lower abdomen~pelvis was started at 45 s, 75 s and 90 s, respectively, after injection. No oral contrast agent was administered. PET, CT and fused PET/CT images were generated for review on a computer workstation (Azemoto Virtual Place Version 3.0035).

### Image analysis

Contrast-enhanced CT images were retrospectively evaluated in consensus by two experienced radiologists (reader A and reader B with 9 and 21 years of experience in CT, respectively) who had knowledge of neither the other imaging results nor the clinical data. CT images were viewed in coronal, axial and sagittal sections and inspected and appropriate windowing was applied. Peritoneal implantation was diagnosed when nodular, plaque-like or infiltrative soft tissue lesions with abnormal enhancement were seen in the peritoneal fat or on the peritoneal surface. Lymph nodes (LNs) with a short-axis diameter greater than 1 cm were defined as malignant. Furthermore, the presence of a central unenhancing area suggesting central necrosis was considered a sign of malignancy, and the presence of peripheral low attenuation suggesting a fatty hilum within an LN was considered a benign sign, regardless of node size [17–19].

PET/contrast-enhanced CT images were prospectively interpreted in consensus by two experienced radiologists (reader C and reader D with 4 and 6 years of experience in PET/CT, respectively) who had knowledge of neither the other imaging results nor the clinical data. PET/non-contrast-enhanced CT images were retrospectively interpreted in consensus by two experienced radiologists (reader E and reader F with 3 and 5 years of experience in PET/CT, respectively) who had knowledge of neither the other imaging results nor the clinical data. Attenuation-corrected PET images, contrast-enhanced CT or non-contrast-enhanced CT images and co-registered fused images were displayed together on the monitor. Recurrent or metastatic lesions were diagnosed when abnormal focal FDG uptake observed on PET images corresponded to an abnormal

mass on CT. LNs with increased glucose uptake were deemed positive for metastatic spread even if they were smaller than 1 cm in short-axis diameter. Conversely, LNs with no detectable tracer uptake were deemed negative for metastatic spread, even if they were larger than 1 cm in short-axis diameter. Semiquantitative analysis was not done in this study. This method of PET/CT image analysis was based on previous studies [17–19].

Diagnostic ability was determined on a patient basis and on a nine lesion site basis (neck LN, chest LN containing axillary LN, mediastinal LN, hilar LN, abdominal LN, pelvic LN, lung, liver, peritoneal carcinomatosis of various sites, pelvic local recurrence and bone).

The final diagnosis was obtained from the results of histopathological examination after surgery or biopsy ( $n=64$ ), or clinical follow-up of at least 6 months (range: 6–26 months, mean: 18 months) on the basis of CEA levels and contrast-enhanced CT findings ( $n=60$ ), and CEA levels and enhanced full-dose PET/CT findings ( $n=46$ ). We classified as recurrence and/or metastasis the cases if, for example, (1) the present study revealed highly suspected recurrence without pathological evidence and the patient underwent chemotherapy resulting in a decrease or disappearance in size and/or FDG uptake in the follow-up study and (2) the follow-up study revealed tumour recurrence with CT and/or PET/CT in a place where a tiny lesion without FDG uptake was imaged at the time of the initial (present) study.

### Statistical analysis

We performed patient-based and lesion site-based analyses of PET/contrast-enhanced CT results based on the consensus verdict in general compared with PET/non-contrast-enhanced CT and enhanced CT. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated using standard statistical formulae, and the 95% confidence interval (95% CI) was determined for each parameter. Differences among the three imaging modalities were tested with Cochran's Q test, followed by multiple comparisons using the McNemar test with Bonferroni adjustment;  $p$  values of less than 0.05 were considered to indicate statistical significance.

## Results

### Patient-based analysis

In 74 (44%) of the 170 patients, recurrence and/or distant metastasis was confirmed by pathological examination ( $n=60$ ) and clinical follow-up study of CEA and imaging

modality ( $n=14$ ). In the other 96 patients, no recurrence was confirmed by pathological examination ( $n=4$ ) and clinical follow-up study ( $n=92$ ). On patient-based analysis, interpretation by PET/contrast-enhanced CT was true positive in 69 of the 74 patients with recurrence and true negative in 92 of the 96 patients without recurrence, whereas interpretation by PET/non-contrast-enhanced CT was true positive in 66 of the 74 patients with recurrence and true negative in 91 of the 96 patients without recurrence and interpretation by enhanced CT was true positive in 59 of the 74 patients with recurrence and true negative in 90 of the 96 patients without recurrence (Table 1). Sensitivity and accuracy differed significantly among the three modalities (Cochran's Q test:  $p=0.0004$  and  $p=0.0001$ , respectively) and there was no significant difference in specificity ( $p=0.157$ ). Although there were significant differences in sensitivity between enhanced CT and PET/non-contrast-enhanced CT and between enhanced CT and PET/contrast-enhanced CT (McNemar test:  $p=0.025$  and  $p=0.0048$ , respectively), there was no significant difference in sensitivity between PET/non-contrast-enhanced CT and PET/contrast-enhanced CT (McNemar test:  $p=0.25$ ). Although there were significant differences in accuracy between enhanced CT and PET/non-contrast-enhanced CT and between enhanced CT and PET/contrast-enhanced CT (McNemar test:  $p=0.014$  and  $p=0.0015$ , respectively), there was no significant difference in accuracy between PET/non-contrast-enhanced CT and PET/contrast-enhanced CT (McNemar test:  $p=0.14$ ).

Lesion site-based analysis

Nine lesion sites, including neck LN, chest LN, abdominal LN, pelvic LN, lung, liver, peritoneum, local recurrence and bone, were evaluated for each patient (Table 2). There

were 140 sites of lesion recurrence: 2 in neck LNs, 3 in chest LNs, 18 in abdominal LNs, 14 in pelvic LNs, 25 in the lung, 30 in the liver, 15 in the peritoneum, 30 local recurrences and 3 in the bone.

PET/contrast-enhanced CT and PET/non-contrast CT detected more recurrence and/or metastasis than enhanced CT in seven lesion sites except for lung and liver. The sensitivity of lung and liver metastasis by PET/non-contrast-enhanced CT was a little inferior than that of enhanced CT. The sensitivity of seven lesion sites (abdominal LN, pelvic LN, lung, liver, peritoneum, local recurrence and bone) by PET/contrast-enhanced CT was a little superior than that of PET/non-contrast CT.

Three nonmetastatic LN (one neck LN, one chest LN, one abdominal LN) were overdiagnosed as LN metastasis due to tracer uptake by PET/CT with and without IV contrast. Three cases (one pulmonary *Cryptococcus* infection, one Wegener's granulomatosis and one pulmonary inflammatory change) were overdiagnosed as lung metastasis by PET/CT with and without IV contrast. Two cases (one hepatic abscess and one biliary infection) were overdiagnosed as liver metastasis by PET/contrast-enhanced CT. One case of physiological FDG uptake by the bowel was overdiagnosed as peritoneal dissemination by PET/CT with and without IV contrast. One case of post-therapeutic change was overdiagnosed as local recurrence by PET/CT with and without IV contrast. One vertebral degenerative change was overdiagnosed as bone metastasis by PET/non-contrast CT. One nonmetastatic chest LN 11 mm in short diameter was overdiagnosed and misinterpreted as LN metastasis by enhanced CT. Two cases (one pulmonary *Cryptococcus* infection and one pulmonary inflammatory change) were overdiagnosed as lung metastasis by enhanced CT. Two cases (one hepatic abscess and one biliary infection) were overdiagnosed as liver metastasis by enhanced CT. Enhanced CT overdiagnosed post-

**Table 1** Patient-based diagnostic result of interpretations by enhanced CT, PET/non-contrast-enhanced CT and PET/contrast-enhanced CT

				Sensitivity	Specificity	PPV	NPV	Accuracy	
	TP	FN	TN	FP	95% CI	95% CI	95% CI	95% CI	95% CI
CT	59	15	90	6	79.7 70.5~88.9	93.8 89.0~98.6	90.8 83.8~97.8	85.7 78.7~92.7	87.6 82.7~92.6
PET/CT <sup>a</sup>	66	8	91	5	89.2 82.1~96.3	94.8 90.4~99.2	93.0 87.1~98.9	91.9 86.5~97.3	92.4 88.4~96.4
PET/CT <sup>b</sup>	69	5	92	4	93.2 87.5~98.9	95.8 91.8~99.8	94.5 89.3~99.7	94.8 90.4~99.2	94.7 91.3~98.1

TP true positive, TN true negative, FP false positive, FN false negative, PPV positive predictive value, NPV negative predictive value

<sup>a</sup> PET/non-contrast-enhanced CT

<sup>b</sup> PET/contrast-enhanced CT

**Table 2** Lesion site-based diagnostic result of interpretations by CT, PET/non-contrast-enhanced CT and PET/contrast-enhanced CT

	Enhanced CT		PET/CT <sup>a</sup>		PET/CT <sup>b</sup>	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Neck LN	0% (0/2)	100% (168/168)	100% (2/2)	99.4% (167/168)	100% (2/2)	99.4% (167/168)
Chest LN	66.7% (2/3)	99.4% (166/167)	100% (3/3)	99.4% (166/167)	100% (3/3)	99.4% (166/167)
Abdominal LN	66.7% (12/18)	100% (152/152)	88.9% (16/18)	99.3% (151/152)	94.4% (17/18)	99.3% (151/152)
Pelvic LN	64.3% (9/14)	100% (156/156)	85.7% (12/14)	100% (156/156)	92.9% (13/14)	100% (156/156)
Lung	96.0% (24/25)	98.6% (143/145)	92.0% (23/25)	97.9% (142/145)	96.0% (24/25)	97.9% (142/145)
Liver	93.3% (28/30)	98.6% (138/140)	83.3% (25/30)	97.9% (137/140)	93.3% (28/30)	98.6% (138/140)
Peritoneum	66.7% (10/15)	98.7% (153/155)	80.0% (12/15)	99.3% (154/155)	93.3% (14/15)	99.3% (154/155)
Local recurrence	80.0% (24/30)	97.1% (136/140)	90.0% (27/30)	98.8% (138/140)	96.7% (29/30)	99.3% (139/140)
Bone	33.3% (1/3)	100% (167/167)	66.7% (2/3)	99.4% (166/167)	100% (3/3)	100% (167/167)

<sup>a</sup> PET/non-contrast-enhanced CT

<sup>b</sup> PET/contrast-enhanced CT

therapeutic change as peritoneal dissemination ( $n=2$ ) and as local recurrence ( $n=4$ ).

#### Effect of PET/CT on patient management

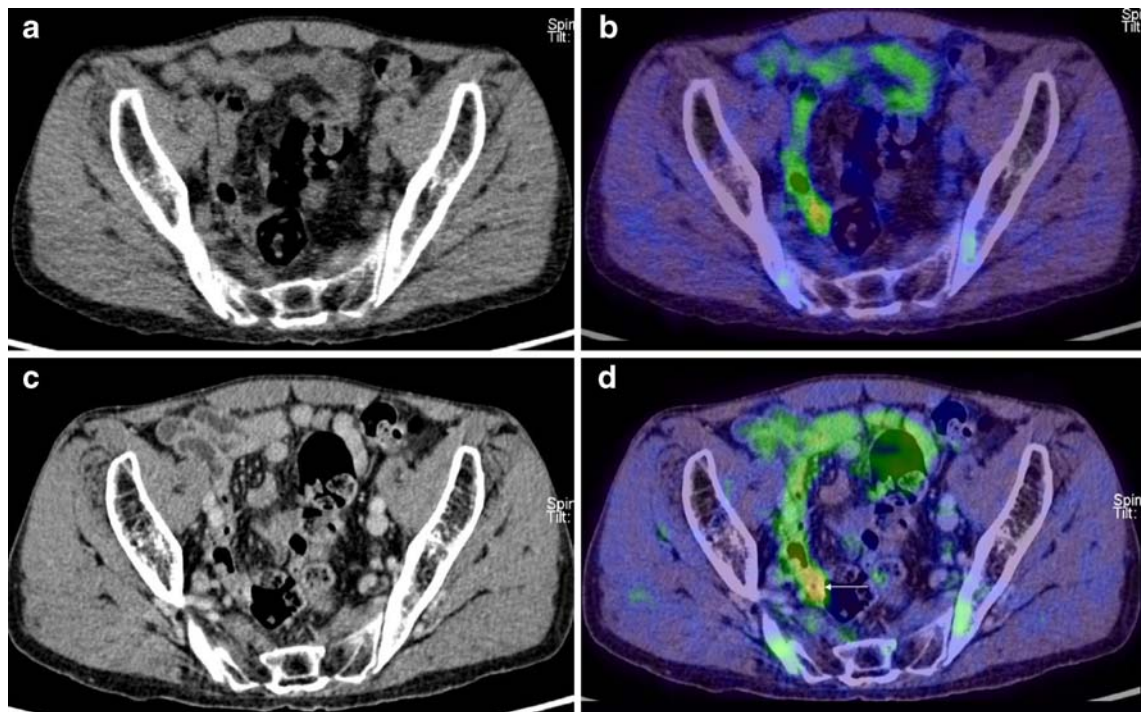
The findings of PET/contrast-enhanced CT resulted in a change of management for 64 of the 170 patients (38%) by initiating an unplanned treatment strategy ( $n=41$ ), by changing the treatment plan ( $n=14$ ) or by obviating the need for planned treatment ( $n=9$ ). Surgery and chemotherapy were undertaken in 27 patients, surgery in 8 and chemoradiotherapy in 6. Surgery plus radiotherapy was changed to chemoradiotherapy in seven patients, and surgery was changed to chemoradiotherapy in seven. Surgery was cancelled in five patients, and chemotherapy was cancelled in four. Improved diagnostic accuracy with PET/contrast-enhanced CT had an effect on patient management in 12 patients (7%) diagnosed by enhanced CT alone and 4 patients (2%) diagnosed by PET/non-contrast-enhanced CT. However, one patient underwent unnecessary surgery and three patients received unnecessary biopsy. Five patients (one patient with abdominal and pelvic LN metastasis, two patients with liver metastasis, one patient with lung metastasis and one patient with peritoneal dissemination and local recurrence missed by PET/contrast-enhanced CT) had lost proper therapy.

Among 170 patients, PET/contrast-enhanced CT could incidentally detect 8 patients having other cancers (lung cancer in 2 patients, thyroid cancer in 2, pancreas cancer in 1, biliary cancer in 1, tongue cancer in 1 and breast cancer in 1). PET/non-contrast CT could incidentally detect seven except for biliary cancer, and enhanced CT could incidentally detect six of these eight patients.

#### Discussion

Several authors have investigated the usefulness of PET/CT for post-therapy surveillance of patients with colorectal cancer and found that the sensitivity, specificity and accuracy were 86–98, 67–98 and 83–96%, respectively [10–16]. Only one group used intravenous contrast material for the CT component of the PET/CT scan [16]. These studies revealed that false-negative PET/CT cases included tiny LN metastasis, tiny liver metastasis, tiny peritoneal dissemination and tiny local recurrence, whereas false-positive PET/CT cases were due to liver inflammatory lesion, adrenal benign disease, physiological FDG uptake by the bowel and bone, postradiation change and postoperative change. Soyka et al. demonstrated that PET/non-contrast CT delivered correct additional information to the enhanced CT findings in 27 of 54 patients (50%) and PET/contrast-enhanced CT revealed additional information in 39 of 54 patients (72%), with therapeutic relevance in 23 patients compared with PET/non-contrast-enhanced CT [16].

PET/CT is a very accurate imaging modality to detect peritoneal dissemination, metastatic LNs and local recurrence. In our series, PET/CT with and without IV contrast could detect more metastatic LNs, peritoneal dissemination and local recurrence than enhanced CT. In our series, the sensitivity of detecting peritoneal dissemination by PET/contrast-enhanced CT was relatively high compared with enhanced CT (93.3 vs 66.7%) (Fig. 1). In our series, the overall node-based sensitivity, specificity and accuracy of PET/contrast-enhanced CT for detection of metastasis at all LN sites (neck LN, chest LN, abdominal LN and pelvic LN) were 94.6 (35/37), 99.5 (640/643) and 99.3% (675/680), respectively, whereas those of enhanced CT were 62.1



**Fig. 1** A 67-year-old male postoperative rectal cancer patient with peritoneal dissemination. **a** Unenhanced low-dose CT shows no abnormal findings. **b** PET/non-contrast-enhanced CT shows no abnormal findings. **c** Enhanced full-dose CT shows no abnormal findings. **d**

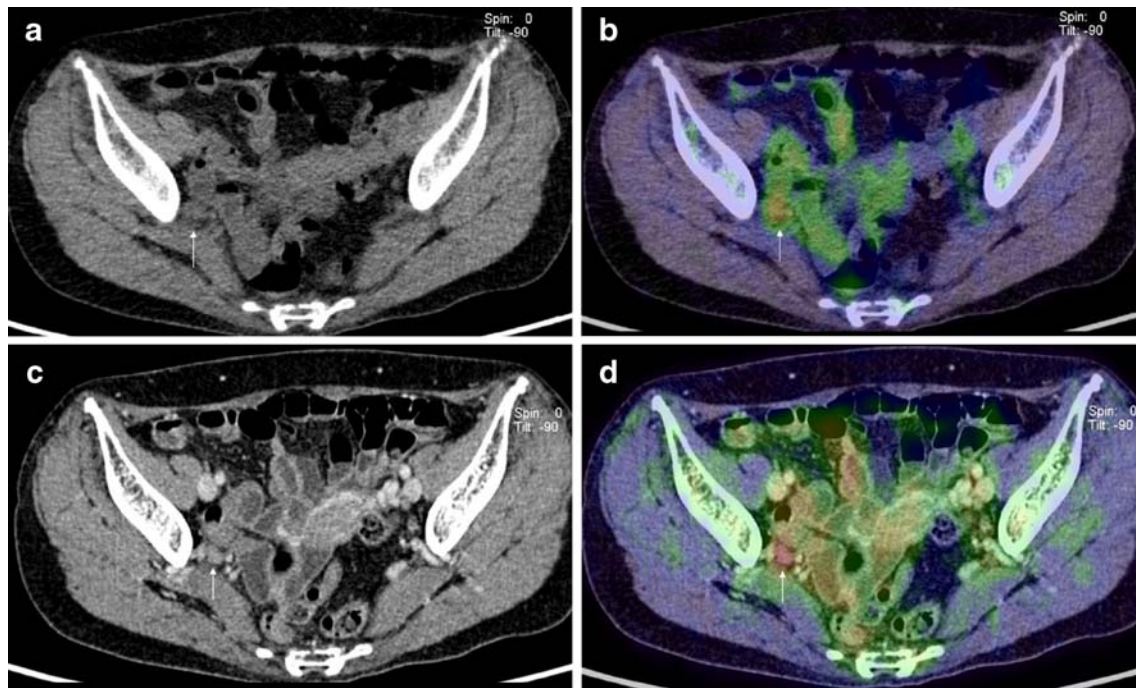
PET/contrast-enhanced CT shows strong FDG uptake corresponding to an enhanced soft tissue mass in the mesentery (*arrow*). Peritoneal dissemination was diagnosed. Histopathological examination of the surgical specimen revealed peritoneal dissemination

(23/37), 99.8 (642/643) and 97.8% (665/680), respectively (Fig. 2). PET/contrast-enhanced CT showed better sensitivity and accuracy for detection of metastatic LN than enhanced CT alone. Because the identification of metastatic LNs by morphological imaging modalities such as CT and MR is based on measurement of node size, a short-axis diameter exceeding 10 mm or 8 mm being the most accepted criterion for diagnosis of nodal involvement, the sensitivity of CT and MR imaging for diagnosis of metastatic LN is relatively low. However, FDG PET is a functional method based on the increased glucose metabolism of cancer cells, regardless of node size, and it seems that PET and PET/CT could enable the detection and localization of metastatic LNs that are not enlarged (i.e. smaller than 1 cm). Although PET and PET/CT can sometimes detect metastatic LNs smaller than 1 cm, the sensitivity of these modalities is insufficient because of their low spatial resolution [20, 21]. In our series, the sensitivity of detecting local recurrence by PET/contrast-enhanced CT was relatively high compared with enhanced CT (96.7 vs 80.0%). Sapir et al. demonstrated that the sensitivity of detecting pelvic recurrence of rectal cancer by PET/CT was very high (43 of 44 lesions in 23 of 24 patients) [13].

However, even PET/contrast-enhanced CT was unable to detect a total of seven tiny lesions (one in abdominal LN,

one in pelvic LN, one in the lung, two in the liver, one in the peritoneum and one local recurrence). The minimum size of lesions detected by PET/CT was 4 mm, and the maximum size of lesions undetected by PET/CT was 6 mm. PET or PET/CT can only detect lesions with a certain volume of malignant cells sufficient to change the observed glucose metabolism, and neither of these imaging modalities can detect micrometastasis [20–22]. Pannu et al. [22] demonstrated that for peritoneal lesions larger than 1 cm ( $n=8$ ), 50% were detectable by PET/CT, and that for peritoneal lesions no larger than 1 cm ( $n=23$ ), only 13% were detectable by PET/CT. The spatial resolution of PET scans is insufficient for detection of microscopic lesions. With a spatial resolution of 4–6 mm for currently available PET and PET/CT systems, the detection of microscopic lesions remains challenging. Improving the spatial resolution and sensitivity of PET and PET/CT scanners and developing new, more specific radioactive tracers may help to overcome this limitation in the future.

Although enhanced CT alone showed poor ability to differentiate tumour recurrence from postoperative or postradiation changes, viable tumour tissue can be differentiated from post-therapeutic change with PET/CT, which evaluates tumour metabolism. In our series, enhanced CT overdiagnosed post-therapeutic change as peritoneal dis-



**Fig. 2** A 65-year-old female postoperative sigmoid colon cancer patient with pelvic LN metastasis. **a** Unenhanced low-dose CT shows a small soft tissue mass in the right pelvic region (*arrow*). **b** PET/non-contrast-enhanced CT shows faint FDG uptake corresponding to a small soft tissue mass (*arrow*). Owing to the absence of precise anatomical landmarks, the accumulation of tracer depicted cannot be unequivocally attributed to lymph node metastasis. **c** Enhanced full-

dose CT shows a right internal iliac LN measuring 5×9 mm (*arrow*), which does not rule out LN metastasis on the basis of the size criterion for CT. **d** PET/contrast-enhanced CT shows strong FDG uptake corresponding to a small pelvic LN (*arrow*), suggesting the presence of nodal cancer spread. Histopathological findings confirmed extensive LN cancer involvement

semination ( $n=2$ ) and local recurrence ( $n=4$ ), and PET/contrast-enhanced CT overdiagnosed post-therapeutic change as local recurrence ( $n=1$ ).

The liver represents one of the main targets of metastatic spread of colorectal cancer and PET or PET/CT are useful modalities to detect liver metastasis with a certain volume [23]. Recently contrast-enhanced MRI has become widely accepted by radiologists and surgeons to be the most sensitive method for the identification of small liver metastases and regarded as an essential element of preoperative assessment [24]. Squillaci et al. demonstrated that the Gd-enhanced MRI had a better sensitivity to detect tiny liver metastasis than PET/contrast-enhanced CT [25]. Moreover, to date, a new contrast medium of MRI, gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA), could replace ultrasound or enhanced CT and become the preferred contrast agent for detecting liver metastases [26].

According to the literature reports, the use of CT contrast agents in PET/CT is still controversial [27]. Some argue that CT image data should be used only for attenuation correction of PET, reduction of acquisition time and localization of hypermetabolic lesions with a low radiation dose (“low-dose CT”) [28–30], whereas others advocate the

need to perform contrast-enhanced, full-dose and high-resolution CT (“diagnostic CT”) in various types of cancer [16, 19, 30–34]. Although even PET/non-contrast-enhanced CT is a fairly accurate diagnostic tool, PET/contrast-enhanced CT is a real “one-stop shop” examination. A recent report has demonstrated that there is an increase in standard uptake volume (SUV) in normal and pathological regions of high concentration when IV contrast-enhanced CT is used for attenuation; this increase is clinically insignificant in the evaluation of patients with cancer and contrast-enhanced CT could be used for attenuation correction [32]. In our series, PET/contrast-enhanced CT showed more superior patient-based and lesion-based results and an improved effect on patient management in four patients (2%) compared to PET/non-contrast-enhanced CT. But there was no statistical significance between the two imaging modalities, and PET/non-contrast-enhanced CT is a fairly accurate diagnostic tool. Moreover, PET/contrast-enhanced CT has disadvantages of additional radiation exposure and side effects due to contrast material over PET/non-contrast-enhanced CT. Further study in a larger patient population is needed to elucidate the efficacy and cost-effectiveness of PET/contrast-enhanced CT.

This study had certain limitations. First, the ideal gold standard for any analysis is histological confirmation of the findings. However, clinical follow-up is a valid way to evaluate diagnostic accuracy and response to therapy, and it would have been unethical to investigate all PET/CT-detected lesions using invasive procedures. Positive findings are easy to confirm, but negative findings only mean that it is not possible to acquire positive findings during the follow-up period, making it uncertain whether the findings are truly negative. Second, no oral contrast materials were used in this study. Adding an oral contrast agent would likely help to better delineate normal bowel activity and demonstrate pathological intra-abdominal activity (peritoneal implantation). Third, the enhanced CT images in our series were acquired as part of a PET/CT study, and we did not directly compare the diagnostic performance of PET/CT with separate CT.

In conclusion, integrated PET/contrast-enhanced CT is an accurate imaging modality for assessing colorectal cancer recurrence and led to changes in the subsequent clinical management of 38% of the patients in the present series. Improved diagnostic accuracy with PET/contrast-enhanced CT had an effect on patient management in 12 patients (7%) diagnosed by enhanced CT alone and 4 patients (2%) diagnosed by PET/non-contrast-enhanced CT.

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## References

- Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007;57:43–66.
- Arriola E, Navarro M, Pares D, Munoz M, Pareja L, Figueras J, et al. Imaging techniques contribute to increased surgical rescue of relapse in the follow-up of colorectal cancer. *Dis Colon Rectum* 2006;49:478–84. doi:10.1007/s10350-005-0280-9.
- Abir F, Alva S, Longo WE, Audiso R, Virgo KS, Johnson FE, et al. The postoperative surveillance of patients with colon cancer and rectal cancer. *Am J Surg* 2006;192:100–8. doi:10.1016/j.amjsurg.2006.01.053.
- Fernandes LC, Kim SB, Saad SS, Matos D. Value of carcinoembryonic antigen and cytokeratins for the detection of recurrent disease following curative resection of colorectal cancer. *World J Gastroenterol* 2006;12:3891–4.
- Engstrom PF. NCCN clinical practice guidelines in oncology: colon cancer. National Comprehensive Cancer Network; 2007:2. Available at <http://www.nccn.org>. Accessed 28 Jan 2008.
- Stueckle CA, Adams S, Stueckle KF, Szpakowski M, Schneider O, Friedrich C, et al. Multi-detector CT in the evaluation of patients with recurrence of rectal cancer. *Technol Cancer Res Treat* 2006;5:285–9.
- Titu LV, Nicholson AA, Hartley JE, Breen DJ, Monson JR. Routine follow-up by magnetic resonance imaging does not improve detection of resectable local recurrences from colorectal cancer. *Ann Surg* 2006;243:348–52. doi:10.1097/01.sla.0000201454.20253.07.
- Torricelli P, Pecchi A, Luppi G, Romagnoli R. Gadolinium-enhanced MRI with dynamic evaluation in diagnosing the local recurrence of rectal cancer. *Abdom Imaging* 2003;28:19–27. doi:10.1007/s00261-001-0127-3.
- Bar-Shalom R, Yefremov N, Guralnik L, Gaitini D, Frenkel A, Kuten A, et al. Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. *J Nucl Med* 2003;44:1200–9.
- Cohade C, Osman M, Leal J, Wahl RL. Direct comparison of <sup>18</sup>F-FDG PET and PET/CT in patients with colorectal carcinoma. *J Nucl Med* 2003;44:1797–803.
- Kim JH, Cremin J, Allen-Auerbach MS, Halpern BS, Fueger BJ, Hecht JR, et al. Comparison between <sup>18</sup>F-FDG PET, in-line PET/CT, and software fusion for restaging of recurrent colorectal cancer. *J Nucl Med* 2005;46:587–95.
- Kamel IR, Cohade C, Neyman E, Fishman EK, Wahl RL. Incremental value of CT in PET/CT of patients with colorectal carcinoma. *Abdom Imaging* 2004;29:663–8. doi:10.1007/s00261-003-0163-2.
- Even-Sapir E, Parag Y, Lerman H, Gutman M, Levine C, Rabau M, et al. Detection of recurrence in patients with rectal cancer: PET/CT after abdominoperineal or anterior resection. *Radiology* 2004;232:815–22. doi:10.1148/radiol.2323031065.
- Votrubova J, Belohlavek O, Jaruskova M, Oliverius M, Lohynska R, Trskova K, et al. The role of FDG-PET/CT in the detection of recurrent colorectal cancer. *Eur J Nucl Med Mol Imaging* 2006;33:779–84. doi:10.1007/s00259-006-0072-z.
- Chen LB, Tong JL, Song HZ, Zhu H, Wang YC. <sup>18</sup>F-FDG PET/CT in detection of recurrence and metastasis of colorectal cancer. *World J Gastroenterol* 2007;13:5025–9.
- Soyka JD, Veit-Haibach P, Strobel K, Breitenstein S, Tschopp A, Mende KA, et al. Staging pathways in recurrent colorectal carcinoma: is contrast-enhanced <sup>18</sup>F-FDG PET/CT the diagnostic tool of choice. *J Nucl Med* 2008;49:354–61. doi:10.2967/jnumed.107.048249.
- Antoch G, Statta J, Nemat AT, Marnitz S, Beyer T, Kuehl H, et al. Non-small cell lung cancer: dual-modality PET/CT in preoperative staging. *Radiology* 2003;229:526–33. doi:10.1148/radiol.2292021598.
- Antoch G, Saoudi N, Kuehl H, Dahmen G, Muller SP, Beyer T, et al. Accuracy of whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) for tumor staging in solid tumors: comparison with CT and PET. *J Clin Oncol* 2004;22:4357–68. doi:10.1200/JCO.2004.08.120.
- Kitajima K, Murakami K, Yamasaki E, Domeki Y, Kaji Y, Fukasawa I, et al. Performance of integrated FDG-PET/contrast-enhanced CT in the diagnosis of recurrent ovarian cancer: comparison with integrated FDG-PET/non-contrast-enhanced CT and enhanced CT. *Eur J Nucl Med Mol Imaging* 2008;35:1439–48. doi:10.1007/s00259-008-0776-3.
- Bristow RE, Giuntoli RL 2nd, Pannu HK, Schulick RD, Fishman EK, Wahl RL. Combined PET/CT for detecting recurrent ovarian cancer limited to retroperitoneal lymph nodes. *Gynecol Oncol* 2005;99:294–300. doi:10.1016/j.ygyno.2005.06.019.
- Kitajima K, Murakami K, Yamasaki E, Fukasawa I, Inaba N, Kaji Y, et al. Accuracy of FDG PET/CT in detecting pelvic and paraaortic lymph node metastasis in patients with endometrial cancer. *AJR Am J Roentgenol* 2008;190:1652–8. doi:10.2214/AJR.07.3372.
- Pannu HK, Cohade C, Bristow RE, Fishman EK, Wahl RL. PET-CT detection of abdominal recurrence of ovarian cancer: radiologic-surgical correlation. *Abdom Imaging* 2004;39:398–403.
- Bipat S, van Leeuwen MS, Comans EFI, Piji ME, Bossuyt PM, Zwinderman AH, et al. Colorectal liver metastases: CT, MR



- imaging, and PET for diagnosis—meta-analysis. *Radiology* 2005;237:123–31.
24. Ward J. New MR techniques for the detection of liver metastases. *Cancer Imaging* 2006;6:33–42. doi:10.1102/1470-7330.2006.0007.
  25. Squillaci E, Manenti G, Mancino S, Ciccio C, Calabria F, Donieli R, et al. Staging of colon cancer: whole-body MRI vs. whole body PET/CT—initial clinical experience. *Abdom Imaging* 2008;33:676–88. doi:10.1007/s00261-007-9347-5.
  26. Hammerstingl R, Huppertz A, Breuer J, Balzer T, Blakeborough A, Carter R, et al. Diagnostic efficacy of gadoxetic acid (primovist)-enhanced MRI and spiral CT for a therapeutic strategy: comparison with intraoperative and histopathologic findings in focal liver lesions. *Eur Radiol* 2008;18:457–67. doi:10.1007/s00330-007-0716-9.
  27. Coleman ER, Delbeke D, Guiberteau MJ, Conti PS, Royal HD, Weinreb JC, et al. Concurrent PET/CT with an integrated imaging system: intersociety dialogue from the joint working group of the American College of Radiology, the Society of Nuclear Medicine, and the Society of Computed Body Tomography and Magnetic Resonance. *J Nucl Med* 2005;46:1225–39.
  28. Cohade C, Wahl RL. Applications of positron emission tomography/computed tomography image fusion in clinical positron emission tomography—clinical use, interpretation methods, diagnostic improvements. *Semin Nucl Med* 2003;33:228–37. doi:10.1053/snuc.2003.127312.
  29. Schaefer NG, Hany TF, Taverna C, Taverna C, Seifert B, Stumpe KD, et al. Non-Hodgkin lymphoma and Hodgkin disease: coregistered FDG PET and CT at staging and restaging—do we need contrast-enhanced CT? *Radiology* 2004;232:823–9. doi:10.1148/radiol.2323030985.
  30. Rodríguez-Vigil B, Gómez-León N, Pinilla I, Hernández-Maraver D, Coya J, Martín-Curto L, et al. PET/CT in lymphoma: prospective study of enhanced full-dose PET/CT versus unenhanced low-dose PET/CT. *J Nucl Med* 2006;47:1643–8.
  31. Antoch G, Freudenberg LS, Beyer T, Bockisch A, Debatin JF. To enhance or not to enhance? <sup>18</sup>F-FDG and CT contrast agents in dual-modality <sup>18</sup>F-FDG PET/CT. *J Nucl Med* 2004;45:56–65.
  32. Mawlawi O, Erasmus JJ, Munden RF, Pan T, Knight A, Macapinlac HA, et al. Quantifying the effect of IV contrast media on integrated PET/CT: clinical evaluation. *AJR Am J Roentgenol* 2006;186:308–19. doi:10.2214/AJR.04.1740.
  33. Pfannenbergl AC, Aschoff P, Brechtel K, Müller M, Bares R, Paulsen F, et al. Low dose non-enhanced CT versus standard dose contrast-enhanced CT in combined PET/CT protocols for staging and therapy planning in non-small cell lung cancer. *Eur J Nucl Med Mol Imaging* 2007;34:36–44. doi:10.1007/s00259-006-0186-3.
  34. Pfannenbergl AC, Aschoff P, Brechtel K, Müller M, Klein M, Bares R, et al. Value of contrast-enhanced multiphase CT in combined PET/CT protocols for oncological imaging. *Br J Radiol* 2007;80:437–45. doi:10.1259/bjr/34082277.