

## Usefulness of thallium-201 SPECT imaging for the evaluation of local recurrence of colorectal cancer

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**Purpose:** To clarify the accumulation of thallium-201 in recurrent tumors in patients who had undergone resection of colorectal cancer and to evaluate the usefulness of thallium-201 single photon emission computed tomography (SPECT) images for distinguishing recurrent tumors from postoperative changes.

**Materials and Methods:** Thallium-201 SPECT images and CT images of 22 consecutive patients suspected to have local recurrence of colorectal cancer based on clinical symptoms and signs were reviewed. CT was performed on all patients.

**Results:** In nine of the 11 patients who had local recurrence, SPECT images showed positive thallium uptake, but in 10 of the 11 patients confirmed to have no recurrence, SPECT images showed negative thallium uptake. Sensitivity was 81.8% (9/11) specificity was 90.9% (10/11), and accuracy was 86.4% (19/22). There were five patients in whom CT results were inconclusive. All of them had rectal cancer and had undergone Miles' operation, and all were correctly diagnosed by thallium-201 SPECT.

**Conclusion:** Thallium-201 exhibited intense uptake in recurrent colorectal cancer. Thallium-201 SPECT is considered to be a useful diagnostic tool for the detection of recurrence of colorectal cancer, particularly in patients with inconclusive CT results.

**Key words:** local recurrence of colorectal cancer, thallium-201 SPECT, CT

### INTRODUCTION

COLORECTAL CANCER is the major cause of cancer-related death throughout developed countries, and local recurrence is one of the most important factors in predicting the prognosis.<sup>1</sup> Never the less, postoperative changes such as fibrosis, adhesion and distortion of normal architecture, can lead to difficulties in diagnosing recurrent tumors with various imaging methods such as computed tomography (CT) and magnetic resonance imaging (MRI).<sup>2-4</sup> Accurate diagnosis of local recurrence is clinically im-

portant in determining appropriate treatment during the postoperative course of colorectal cancer.

Thallium-201 has been used for myocardial imaging and evaluation of myocardial viability.<sup>5</sup> While performing myocardial imaging, Tonami et al. incidentally found increased uptake of thallium-201 in lung cancer.<sup>8</sup> Subsequently, thallium-201 has been used in imaging a variety of malignant diseases including tumors of the thyroid, lung, brain, bone and breast.<sup>7-12</sup> We have also noted accumulation of thallium-201 in colorectal cancer on scanning resected specimens.<sup>13</sup>

Accumulation of thallium-201 has been observed in viable tumor tissue, reflecting the proliferative potential of tumor cells on the basis of Na-K-ATPase activity.<sup>14,15</sup>

Early diagnosis of recurrent tumor may be elusive in patients without definite clinical, endoscopic or CT findings. To our knowledge, there have been few reports that describe the usefulness of thallium-201 single photon emission computed tomography (SPECT) imaging for the detection of local recurrence of colorectal cancer.

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The purposes of this study were first, to clarify the accumulation of thallium-201 in recurrent tumor of patient who had undergone resection of colorectal cancer, and second, to evaluate the usefulness of thallium-201 SPECT images in distinguishing recurrent tumors from postoperative changes in patients with inconclusive CT results.

## MATERIALS AND METHODS

### Patients

Twenty-two consecutive patients (11 men and 11 women, aged 41 to 71 years mean age 57.1) with suspected local recurrence of colorectal cancer based on clinical symptoms and signs participated in thallium-201 SPECT and CT studies at our institution from June 1990 to November, 1994.

The primary colorectal cancer was located in the rectum in 20 patients and the ascending colon in two. Miles' operation had been undergone in 11 patients, low anterior resection in 9 patients and right hemicolectomy in two. The histopathological diagnosis of the primary lesion was adenocarcinoma in all 22 patients, and was well differentiated in 17, moderately differentiated in two poorly differentiated in one and unknown in two.

The diagnosis of recurrence was confirmed by pathological examination (n = 10) and/or clinical and radiological follow up (n = 12). The follow up interval was 5 months to 72 months (mean 27.9 months).

### Thallium-201 SPECT

A dose of 111 MBq (3 mCi) <sup>201</sup>Tl-chloride was injected intravenously, and thallium-201 imaging was begun ten minutes later.

SPECT was performed with a single-headed rotating gamma camera (GCA-90A super jumbo camera, Toshiba,

Japan) equipped with a low-energy, high-resolution collimator, which collected 60 projection images over 20 seconds, and 360 and with an acquisition matrix of 128 × 128. The energy peak and window level were set at 80 keV 20%. Total acquisition time was approximately 25 minutes. Spatial resolution at the center of the field was 20 mm (FWHM) and the slice thickness was 5.8 mm. A series of transverse slices were reconstructed by filtered back-projection with Butterworth and Ramp filters. No attenuation correction was performed.

Except for fasting, no special preparation such as an injection of an anticholinergic agent was done.

### Image Interpretation and Analysis

The SPECT images were interpreted retrospectively by three observers with knowledge of the patient's history of colorectal cancer and surgery but without knowledge of CT finding or the clinical findings that suggested possible recurrence.

Interpretive criteria for recurrent pelvic colorectal cancer depicted on thallium-201 scans included any increased foci of activity in the pelvis that were believed not to be due to physiological excretion or vascular activity.

CT scans were interpreted retrospectively by the same three observers without knowledge of the SPECT findings or clinical information.

Interpretive criteria for recurrent pelvic colorectal cancer depicted on CT scans included suspect masses, enlarging masses if prior postoperative CT scans were available for comparisons, bowel wall thickening, serosal masses or ascites, which suggested the presence of peritoneal tumor implants.

A consensus decision as to the positive, negative or inconclusive nature of the CT results and positive or negative thallium-201 uptake in each case was reached.

## RESULTS

### Accumulation of Thallium-201

The results of the thallium-201 SPECT imaging are summarized in Table 1.

Eleven of the 22 patients had recurrent tumors but the remaining 11 had no recurrence as confirmed by pathological examination in 10 and by a combination of clinical, tumor marker and/or radiological follow-up studies in 12.

**Table 1** Visual analysis of thallium-201 SPECT findings

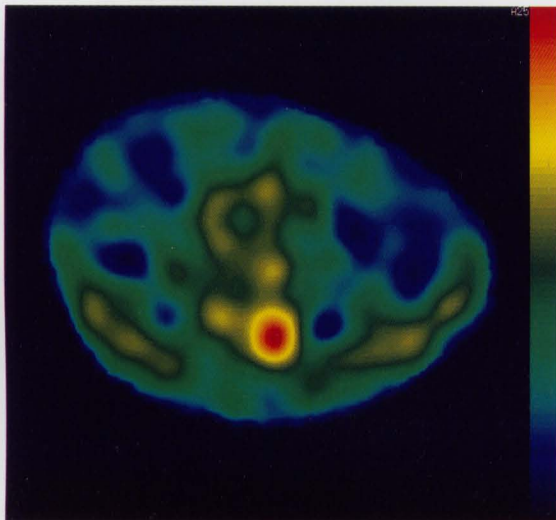
		Thallium-201 SPECT	
		Positive	Negative
Recurrence	11	9	2
No recurrence	11	1	10
Sensitivity :		81.8%	(9/11)
Specificity :		90.9%	(10/11)
Accuracy :		86.4%	(19/22)

**Table 2** Information of inconclusive cases

No.	Age	Sex	Primary site	Operation	Mass size	Tl-201	Recurrence
1.	70	man	rectum	Miles'	35 mm	positive	recurrence
2.	59	man	rectum	Miles'	30 mm	negative	no recurrence
3.	71	woman	rectum	Miles'	35 mm	negative	no recurrence
4.	53	man	rectum	Miles'	30 mm	negative	no recurrence
5.	61	woman	rectum	Miles'	30 mm	negative	no recurrence



a



b

**Fig. 1** Inconclusive CT and positive thallium-201 SPECT. Patient 1 was a 70-year-old man who had undergone Miles' operation six months previously. (a) An irregularly shaped mass lesion was demonstrated on follow-up CT scans. (b) Thallium-201 SPECT showed increased uptake at the tumor site.

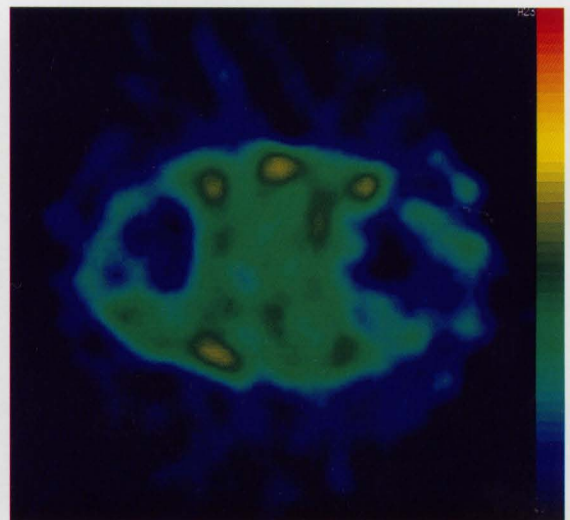
In nine of the eleven patients who had local recurrence, SPECT images showed positive thallium uptake but in ten of the eleven patients confirmed to have no recurrence, SPECT images showed negative thallium uptake. Sensitivity was 81.8% (9/11), specificity was 90.9% (10/11) and accuracy was 86.4% (19/22).

#### *Clinical Usefulness*

There were five patients in whom CT results were inconclusive. Table 2 shows the clinical features of these inconclusive cases. All of them had rectal cancer and had



a



b

**Fig. 2** Inconclusive CT and negative thallium-201 SPECT. Patient 4 was a 53-year-old man who had undergone Miles' operation five months previously. (a) An irregularly enhanced mass lesion was demonstrated on follow-up CT scans. (b) No abnormal accumulation was seen in the SPECT images. The absence of recurrence has been confirmed by clinical and radiological examinations over the last 42 months.

undergone Miles' operation.

All of them were correctly diagnosed by thallium-201 SPECT. One patient had a recurrent tumor (Fig. 1) and the other four patients had no recurrent tumors (Fig. 2).

#### **DISCUSSION**

Thallium-201 uptake is considered to reflect the regional perfusion and viability of tumor cells.<sup>14,15</sup> It has been

reported that Na-K-ATPase is involved in the mechanism of thallium-201 uptake by tumors.<sup>14,15</sup> This technique has been shown to be useful for detecting various malignant tumors in the lung, brain, thyroid gland, bone and breast.<sup>7-12</sup>

In a previous study of colorectal cancer, we obtained preliminary results indicating the value of thallium-201 SPECT for delineation of tumors, which appear as hot spots upon scanning of resected specimens.<sup>13</sup> In this study, there was no difference between accumulation in the early and delayed images. Therefore only early scans were used in the present study.

In one of the patients in the present series, accumulation of thallium-201 in a recurrent colorectal cancer was also confirmed by scanning of the resected specimen, in accordance with our preliminary data.

The present study showed that thallium-201 SPECT had a sensitivity of 81.8% (9/11), a specificity of 90.9% (10/11), and an accuracy of 86.4% (19/22) for detection of recurrent tumors. It was therefore confirmed that local recurrence of colorectal cancer can be visualized as an increase in tracer accumulation on thallium-201 SPECT image.

In the present study, five patients showed inconclusive CT results. All of them had rectal cancer and had undergone Miles' operation. Postoperative fibrosis was the factor creating most difficulty in distinguishing recurrent tumors. Although we cannot reach firm conclusions about the ability of thallium-201 SPECT to distinguish recurrent tumors from postoperative fibrosis because of the limited number of inconclusive cases in this study, all of the cases were correctly diagnosed by this technique. Thallium-201 SPECT is therefore expected to become a useful diagnostic tool for distinguishing recurrent tumors from postoperative changes in patients whose CT results are inconclusive.

Nevertheless, in blind evaluations without CT and/or MRI, the signal-to-noise ratio of thallium-201 SPECT is sometimes too low to allow abnormal uptake by the tumor to be distinguished from significantly higher tracer uptake in the intestine. This is one limitation of the use of thallium-201 as an abdominal tumor-seeking agent. In the one false-positive case and one of the two false-negative cases in the present study, the primary tumors were located in the ascending colon. Physiological excretion of thallium-201 into the small intestine was thought to have been responsible for these misdiagnoses. There are a few possible methods for overcoming this disadvantage. First, premedication such as injection of an anticholinergic agent might decrease the excretion of thallium-201 chloride into the intestine, and thus improve the image quality. Second, it is expected that a newer multi-headed SPECT camera with a special fan-beam collimator would enable FWHM to be 10 mm and provide superior SPECT images to those obtained with our system, thus allowing smaller lesions to be detected.

On the other hand, certain limitations of CT and MRI diagnosis for detecting recurrent tumors in patients after surgery have been described previously.<sup>2-4</sup> Recurrent tumor deposits less than 10 mm in diameter, which do not enlarge normal anatomic structures such as the bowel wall or lymph nodes, cannot be detected on CT images. In addition, postoperative fibrosis may be indistinguishable from viable tumors. We speculate that thallium-201 SPECT also cannot improve the detectability of small lesions, but thallium-201 SPECT may distinguish recurrent tumor from postoperative fibrosis. Complementary use of CT and/or MRI is therefore considered necessary to achieve an accurate and complete diagnosis.

In conclusion, thallium-201 SPECT is expected to be a useful diagnostic tool for the detection of recurrent colorectal cancers in patients with inconclusive CT results but, further study is recommended to determine the effectiveness of thallium-201 SPECT in differentiating recurrent tumors from postoperative changes.

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