
The New Technology of Combined Transmission and Emission Tomography in Evaluation of Endocrine Neoplasms

Einat Even-Sapir, Zohar Keidar, Jonathan Sachs, Ahuva Engel, Lise Bettman, Diana Gaitini, Luda Guralnik, Nahum Werbin, Galina Iosilevsky, and Ora Israel

Departments of Nuclear Medicine and Diagnostic Radiology, Rambam Medical Center, Haifa; The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa; and Departments of Nuclear Medicine and Surgery A, Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

The clinical value of a novel technology of combined transmission and emission tomography (TET) was assessed in patients with endocrine tumors. **Methods:** TET technology, which combines simultaneous acquisition of SPECT and CT images, using the same imaging device, allows correct fusion of images of both modalities. TET was performed on 27 patients with known or suspected endocrine tumors. The radiopharmaceuticals used for the emission part of the study were chosen according to the tumor type: ^{111}In -octreotide for patients with neuroendocrine tumors ($n = 10$), $^{99\text{m}}\text{Tc}$ -sestamibi for patients with primary hyperparathyroidism ($n = 8$), ^{131}I for patients with thyroid cancer ($n = 4$), and ^{123}I -metaiodobenzylguanidine and ^{75}Se -cholesterol for patients with adrenal masses ($n = 3$ and $n = 2$, respectively). The additional information provided by TET compared with scintigraphy was assessed for both image interpretation and clinical utility. **Results:** TET did not provide any additional data in 16 patients (59%), including 5 patients with normal scintigraphy. In 11 patients (41%) with abnormal SPECT findings, TET improved image interpretation by providing a better anatomic localization of SPECT-detected lesions. It showed unsuspected bone involvement in 4 patients, it identified the organs involved and the relationship of the lesions to neighboring structures in 5 patients, and it differentiated physiologic uptake from tumor uptake in 2 patients. TET provided additional information of clinical value in 9 patients (33%). It assisted in better planning of surgery in 2 patients with neuroendocrine tumors and in 2 patients with ectopic parathyroid adenomas. It changed the treatment approach in 2 patients with neuroendocrine tumors and 1 patient with thyroid carcinoma, and it altered prognosis in 2 patients with thyroid malignancy. **Conclusion:** TET enhances the already unique role of nuclear medicine procedures in the assessment and management of patients with endocrine neoplasms.

Key Words: endocrine neoplasms; combined imaging; fusion

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Nuclear medicine plays an important role in the management of patients with endocrine and neuroendocrine tumors. It provides information on functional status, tissue viability, metabolism, and receptor expression. Scintigraphic procedures have a higher sensitivity for the detection of endocrine tumors than anatomic imaging modalities. Nuclear medicine contributes to clinical decision making, such as establishing resectability, planning the surgical approach, and choosing the optimal treatment strategy for advanced disease. For example, recent studies indicate that somatostatin receptor scintigraphy (SRS) is more sensitive than anatomic imaging modalities, including sonography, CT, MRI, and angiography, for identifying tumors such as gastrinoma or carcinoid and their metastases (1-3). A recent study on 160 patients with gastroenteropancreatic tumors reported that SRS led to a change in classification of 24% and a change in the surgical strategy in 25% of the study population (4). However, nuclear medicine procedures are limited by their lack of ability to define the precise anatomic localization of suspected lesions and, therefore, often require correlation with anatomic imaging techniques such as CT or MRI.

Structural and functional imaging modalities have a complementary role in the evaluation of endocrine and neuroendocrine neoplasms. However, their correct alignment can be difficult. Previous attempts to integrate nuclear medicine and CT or MRI studies of the torso have used either external or internal landmarks or a combination of both (5,6). Errors in realignment of functional and anatomic data obtained separately on different devices, on different days, may occur as a result of variations in positioning, in bowel gas or urine content, or may be associated with respiration and motion. Minimizing registration errors is a challenging task and depends on recognition of correct corresponding target landmarks.

A novel imaging device combining a dual-head, variable-

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For correspondence or reprints contact: Ora Israel, MD, Department of Nuclear Medicine, Rambam Medical Center, Haifa, Israel.

angle gamma camera with coincidence acquisition capabilities with a low-dose x-ray tube has been introduced recently (7–9). Transmission and emission tomography (TET) is performed in the same setting, without changing the patient's position, thereby allowing correct fusion of images of both modalities. The purpose of this study was to assess whether fused images of SPECT and low-dose CT have an impact on image interpretation of both, nuclear medicine and conventional CT studies, and whether TET provides information of added clinical value in patients with endocrine tumors.

MATERIALS AND METHODS

Patient Population

TET was performed on 27 consecutive patients (15 male, 12 female; mean age, 52 y; age range, 5–81 y) with known or suspected endocrine or neuroendocrine tumors. The study was approved by the institutional ethics committee. Table 1 summarizes the clinical data of the study population.

Selection of the appropriate radiopharmaceutical for the emission (nuclear medicine) part of the procedure was based on the type of tumor. Ten patients with known or suspected neuroendocrine tumors were imaged 4 and 24 h after intravenous injection of

TABLE 1
Clinical Data on 27 Patients with Endocrine Neoplasms Evaluated by TET

Patient no.	Sex	Age (y)	Diagnosis	Radiopharmaceutical	Reason for test
1	M	44	Gastrinoma	¹¹¹ In-octreotide	Suspected recurrence, elevated gastrin levels, normal CT
2	M	41	Recurrent nonsecreting NE tumor	¹¹¹ In-octreotide	Retroperitoneal mass on CT, resectability assessment
3	F	58	Nonsecreting NE tumor	¹¹¹ In-octreotide	Pancreatic mass on CT, resectability assessment
4	F	57	Metastatic carcinoid	¹¹¹ In-octreotide	Known liver metastases, extent of disease, treatment planning
5	M	47	Metastatic carcinoid	¹¹¹ In-octreotide	Known liver metastases, extent of disease, treatment planning
6	M	60	Metastatic carcinoid	¹¹¹ In-octreotide	Known liver metastases, suspected lesion R lower lung on CT, extent of disease, treatment planning
7	M	40	Medullary thyroid carcinoma	¹¹¹ In-octreotide	Mediastinal mass on CT, treatment planning
8	M	36	Medullary thyroid carcinoma	¹¹¹ In-octreotide	Suspected recurrence, elevated calcitonin levels, normal CT
9	F	53	Suspected gastrinoma (excluded)	¹¹¹ In-octreotide	Elevated gastrin levels, normal CT
10	M	31	Suspected insulinoma (excluded)	¹¹¹ In-octreotide	Hypoglycemia, suspected pancreatic mass on CT
11	M	70	Parathyroid adenoma	^{99m} Tc-sestamibi	Diagnosis and localization
12	M	28	Parathyroid adenoma	^{99m} Tc-sestamibi	Diagnosis and localization
13	F	48	Parathyroid adenoma	^{99m} Tc-sestamibi	Diagnosis and localization
14	F	81	Parathyroid (ectopic) adenoma	^{99m} Tc-sestamibi	Localization of adenoma before surgery
15	F	70	Parathyroid (ectopic) adenoma	^{99m} Tc-sestamibi	Localization of adenoma before surgery
16	F	54	Suspected parathyroid adenoma (excluded)	^{99m} Tc-sestamibi	Diagnosis
17	F	65	Suspected parathyroid adenoma (excluded)	^{99m} Tc-sestamibi	Diagnosis
18	M	48	Suspected parathyroid adenoma (excluded)	^{99m} Tc-sestamibi	Diagnosis
19	M	46	Papillary thyroid carcinoma	¹³¹ I	Known lung metastases, extent of disease, treatment planning
20	M	77	Papillary thyroid carcinoma	¹³¹ I	Known lung metastases, extent of disease, treatment planning
21	F	68	Papillary thyroid carcinoma	¹³¹ I	Lung metastases, state after radioiodine treatment, evaluation of residual disease
22	M	68	Follicular thyroid carcinoma	¹³¹ I	Lung and bone metastases, extent of disease
23	F	68	Suspected pheochromocytoma (excluded)	¹²³ I-MIBG	Hypertension (suspected secondary), normal CT
24	F	48	Suspected pheochromocytoma	¹²³ I-MIBG	Elevated catecholamines, suspected R adrenal mass on CT
25	M	5	Neuroblastoma	¹²³ I-MIBG	Residual mass on CT, monitoring response to treatment
26	M	59	Suspected aldosteronoma	⁷⁵ Se-cholesterol	Bilateral mild adrenal enlargement on CT
27	F	40	Suspected aldosteronoma (excluded)	⁷⁵ Se-cholesterol	Adrenal mass on CT

CT = high-resolution, contrast-enhanced conventional CT; NE = neuroendocrine.

148 MBq (4 mCi) ^{111}In -octreotide (SRS-TET; $n = 10$), 8 patients with suspected primary hyperparathyroidism were imaged 1 h after intravenous injection of 888 MBq (24 mCi) $^{99\text{m}}\text{Tc}$ -sestamibi (sestamibi-TET; $n = 8$), 4 patients with well-differentiated thyroid carcinoma were imaged 48 h after administration of 185 MBq (5 mCi) ^{131}I (^{131}I -TET; $n = 4$), 3 patients with known or suspected adrenal tumors were imaged 4 h after intravenous injection of 148 MBq (4 mCi) ^{123}I -metaiodobenzylguanidine (MIBG-TET; $n = 3$), and 2 patients with suspected adrenocortical tumors were imaged 48 h after intravenous injection of 9.25 MBq (0.25 mCi) ^{75}Se -cholesterol (cholesterol-TET; $n = 2$).

TET Technology

TET was performed using a dual-head, variable-angle, gamma camera equipped with a low-power x-ray system (Millennium VG & Hawkeye; General Electric Medical Systems, Milwaukee, WI). The imaging system is composed of an x-ray tube and a set of detectors fixed on opposite sides of the gamma-camera gantry. This system rotates around the patient along with the γ -detectors. Transmission and emission acquisition can follow an interchangeable sequence. For transmission data, "half-scan" acquisition is performed over 220° in 16 s for each transaxial slice. Multiple slices are obtained by moving the table by a slice step before acquiring the next slice. The full field of view consisting of 40 slices is completed in 10 min. Transmission data of the patient are corrected and reconstructed using filtered backprojection to produce cross-sectional attenuation images in which each pixel represents the attenuation of the imaged tissue. Resolution of radiographic scans is 1 mm, but localization images are produced on a 4-mm pixel size, similar to the nuclear medicine images. The radiographic images are reconstructed into a 256×256 matrix. Radiation doses for a transmission scan, calculated on the basis of phantom studies, range from 1.3 mGy at the center to 5 mGy at the surface (7,8).

Planar and SPECT acquisition protocols depend on the administered radiopharmaceutical and were similar to those used routinely in nuclear medicine procedures. For $^{99\text{m}}\text{Tc}$ - and ^{123}I -labeled radiopharmaceuticals, high-resolution, low-energy collimators were used and 360° SPECT images were acquired in a matrix size of 128×128 , a zoom of 1.28, a 3° angle step, and a time of 20 s per frame. For ^{111}In - or ^{75}Se -labeled radiopharmaceuticals and ^{131}I , medium-energy collimators were used, with a 6° angle step and a time of 30 s per frame. The collected data were reconstructed using the filtered backprojection technique.

X-ray images were reconstructed using the nuclear medicine workstation (eNTEGRA; General Electric Medical Systems), and transmission data were integrated into the nuclear medicine database. Matching pairs of x-ray and nuclear medicine images were fused using the eNTEGRA software, and images overlying the transmission (CT) and emission (SPECT) data were generated.

Interpretation and Analysis of TET Images

The nuclear medicine and high-resolution conventional CT studies were initially interpreted independently, without prior knowledge of findings on other imaging modalities. Data from both planar and SPECT images were used for scintigraphic assessment. Thereafter, a team of specialists of both modalities interpreted the fused TET images. Scintigraphy was compared with TET-fused images. Transmission data acquired during TET, being inferior in quality to conventional contrast-enhanced CT images, were used for anatomic localization of scintigraphic findings and guided retrospective evaluation of high-resolution CT.

TET was considered to improve image interpretation when it provided a better definition of sites of increased radiopharmaceutical uptake such as determination of the involved organs, the accurate relationship between lesions and neighboring structures, or the exclusion of disease in sites of physiologic radiopharmaceutical uptake, or when it allowed for retrospective detection of lesions missed previously on conventional CT. TET findings were compared with the results of surgery and with clinical and radiologic follow-up. TET was considered to provide additional information of clinical value when the improved accuracy of image interpretation led to a change in prognosis or in treatment approach.

RESULTS

Of the 27 patients who were evaluated in this study, 5 patients had scintigraphic studies with normal findings and 22 patients had abnormal findings. In 16 patients (59%), including the 5 patients with normal scans and 11 patients with abnormal scans, TET did not add any significant information to image interpretation and clinical decision making.

Ten patients with suspected or known neuroendocrine tumors were evaluated by SRS-TET. Eight of these patients had abnormal SPECT findings. In 5 of 8 patients with abnormal SRS, SRS-TET improved lesion localization. In 1 patient with suspected recurrent gastrinoma, a focus of abnormal uptake seen in the abdomen was localized by TET in a normal-sized retroperitoneal lymph node. This patient had a history of adhesions and multiple episodes of small bowel obstruction, and correct localization allowed for minimizing the surgical field, thus avoiding unnecessary adhesiolysis. In a second patient with a recurrent nonsecreting tumor, TET showed that the soft-tissue tumor seen on scintigraphy had penetrated to the adjacent vertebra (Fig. 1). Therefore, the planned curative surgical procedure was canceled. In a third patient with a known pancreatic tumor, SPECT detected a second uptake site localized by TET to the pancreas. This lesion had been missed previously on CT and was detected only retrospectively. The surgical approach was changed to allow removal of both tumor sites. A fourth patient with a carcinoid and extensive liver involvement diagnosed by CT showed multiple abdominal sites of uptake on SPECT. TET excluded extrahepatic disease, and the patient was referred for chemoembolization. In a fifth patient with medullary thyroid carcinoma, TET showed an extension of a known mediastinal tumor to the clavicle, leading to a change in the patient's prognosis.

Sestamibi-TET was performed on 8 patients with suspected primary hyperparathyroidism. Five of these patients had an abnormal study. TET added no information in 3 patients with adenoma in the neck that had been detected on scintigraphy. In 2 patients with ectopic thoracic adenoma, TET was the only imaging procedure to provide precise anatomic localization of the lesion for planning of the surgical approach (Fig. 2).

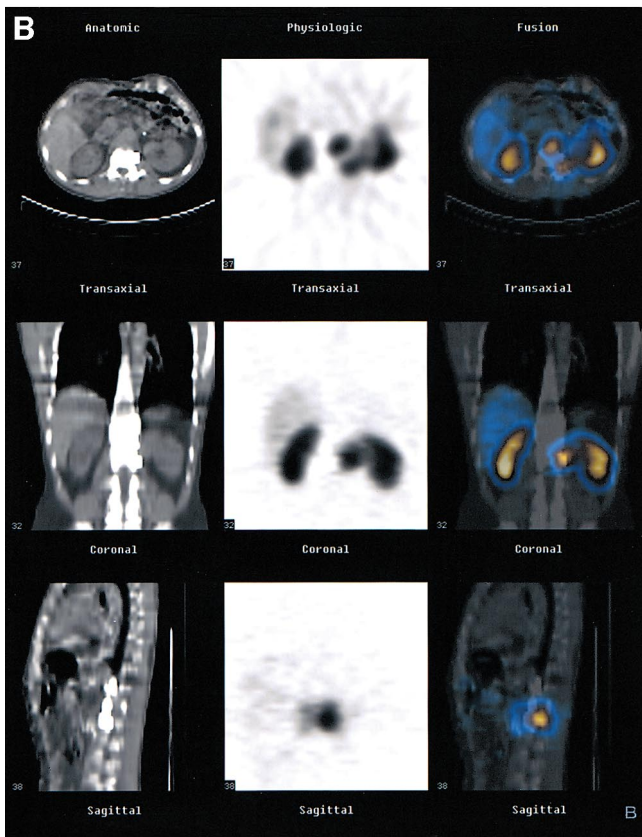
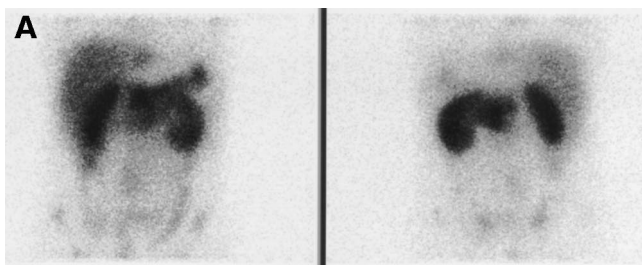


FIGURE 1. SRS-TET in patient with neuroendocrine tumor. (A) Scintigrams show 2 foci of increased ^{111}In -octreotide uptake in midabdomen. (B) TET images (CT, left column; SPECT, center column; fusion, right column) show precise localization of 2 sites of uptake in retroperitoneal, paravertebral region and show involvement of T12 and L1 vertebrae. MRI confirmed findings, and surgery for resection was canceled.

^{131}I -TET was performed on 4 patients with thyroid carcinoma. All had abnormal sites of ^{131}I uptake. TET detected the presence of unsuspected bone involvement in 2 patients. One of these lesions was refractory to high-dose ^{131}I treatment. The patient was referred for surgery.

Five patients were evaluated for suspected adrenal tumors, 3 with MIBG-TET and 2 with cholesterol-TET. Four of these patients had abnormal SPECT studies. In 2 patients, TET excluded a tumor as the cause of uptake by localizing the suspected focus in physiologic sites of increased activity, the bowel in 1 patient and the ureter in the second patient. The same final reading could also have been reached by rescheduling the patients for repeated delayed

scans. Therefore, these findings improved image interpretation but were not considered to be of clinical value in further analysis of the results.

TET improved image interpretation in 11 of the 27 patients (41%). In 5 patients, it allowed precise localization of disease sites and determination of their relationship with neighboring organs and structures. Anatomic localization provided by TET was confirmed by surgery in all 5 patients. In 4 patients, TET detected previously unsuspected bone involvement. In 2 of these patients, bone involvement was confirmed by MRI after scintigraphy. One patient, in whom

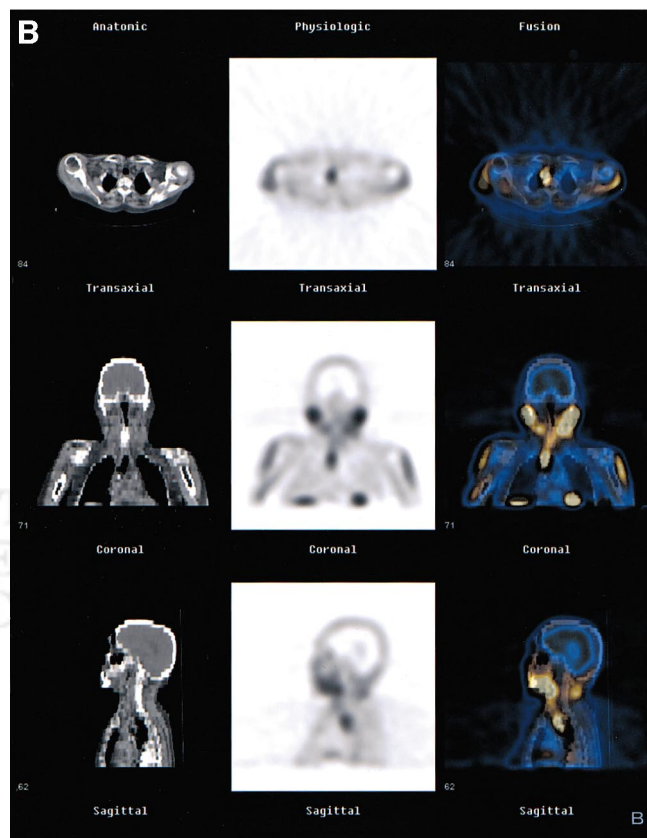
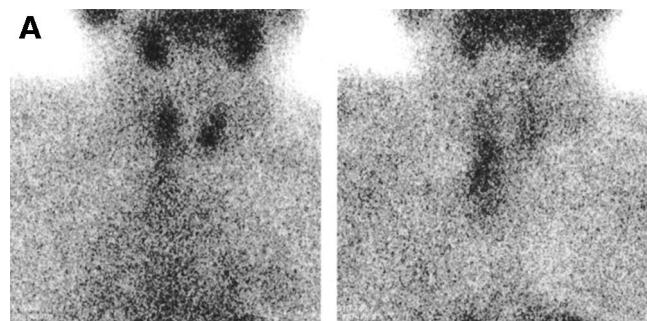


FIGURE 2. Sestamibi-TET in patient with ectopic parathyroid adenoma. (A) $^{99\text{m}}\text{Tc}$ -sestamibi scintigrams (early phase, left; late phase, right) show parathyroid adenoma located inferior to right lobe of thyroid, extending into right thorax. (B) TET images (CT, left column; SPECT, center column; fusion, right column) show precise posterior localization of adenoma in right paratracheal region. Surgical approach was planned according to these findings, and adenoma was removed.

MIBG-TET excluded the presence of an adrenal tumor, had a disease-free follow-up at 14 mo. In 1 patient with a carcinoid, clinical and CT follow-up at 8 mo confirmed the absence of extrahepatic involvement. In 1 patient, repeated evaluation of high-resolution, contrast-enhanced CT studies after TET allowed the retrospective detection of a second pancreatic tumor confirmed by surgery. Conventional CT did not detect the scintigraphic findings of bone lesions in 3 patients, 2 ectopic parathyroid adenomas, and 1 metastatic normal-sized retroperitoneal lymph node with gastrinoma. In these 6 patients, TET provided the only imaging evidence of disease before surgery.

TET provided information of additional clinical value in 9 of the 27 patients (33%). It altered the prognosis in 2 patients with thyroid malignancy. It changed the therapeutic approach in 3 patients; on the basis of TET results, 1 patient was referred for surgery, 1 patient was spared unnecessary surgery, and in 1 patient chemoembolization was chosen as the appropriate mode of treatment. TET also assisted in surgery planning in 4 patients, 2 with neuroendocrine tumors and 2 with ectopic parathyroid adenoma (Table 2).

DISCUSSION

Nuclear medicine procedures are sensitive and independent delineators of the functional characteristics of tumors and are used routinely for diagnosis and follow-up of endocrine tumors. However, scintigraphy is limited in its ability to determine the precise anatomic localization of detected foci of increased uptake and often requires correlation with high-resolution imaging modalities for better topographic definition (4,10). Precise tumor localization, correct determination of disease extent, and diagnosis of metastatic spread are important factors affecting outcome in patients with endocrine tumors.

A novel technology of combined SPECT and low-dose CT acquisition using the same imaging device has been introduced recently (7-9). Acquisition of transmission (CT) and emission (SPECT) data is performed during the same session without a change in patient positioning, thereby allowing correct registration of both imaging modalities.

In our study, TET improved image interpretation compared with scintigraphy alone in 11 of the 27 study patients (41%). It provided better definition of the organs involved and determined the precise relationship of the detected lesions with neighboring structures. False-positive results have been described with different radiopharmaceuticals because of their physiologic excretion in the urinary and gastrointestinal tracts (11). TET allowed for exclusion of disease in sites of physiologic radiopharmaceutical uptake, thus improving the specificity of scintigraphy, as was the case in 2 of our patients. Rescheduling for delayed images on different days was unnecessary. After TET, retrospective interpretation of conventional CT detected a pancreatic tumor that was missed on independent reading. TET results

indicated the need for a further assessment of unsuspected bone lesions on MRI. In 6 patients, fused TET images provided important topographic data before surgery in the precise definition of lesions detected only on scintigraphy. The low-dose CT used for fused TET imaging is not optimized because of its low resolution and the absence of contrast use. Therefore, it is not meant to replace high-resolution, contrast-enhanced, conventional CT, which maintains its complementary role to nuclear medicine in the evaluation of patients with endocrine tumors.

TET provided additional information of clinical value in 9 of the 27 study patients (33%). Similar results on the clinical contribution of combined imaging have been reported recently (9,12). Using the same imaging device with ^{18}F -fluorodeoxyglucose, Delbeke et al. (9) found that the fused images were clinically relevant in 31% of 35 cancer patients. Charron et al. (12) used a combined dedicated PET-CT device and found fused images to be more precise than PET alone for tumor localization in 24% of cases.

The results of TET imaging in this study allowed a change or optimization of the therapeutic approach and determination of the correct prognosis. Surgery remains the optimal treatment modality for patients with localized neuroendocrine tumors (13). Correct preoperative detection of all tumor sites minimizes the chances for overlooking lesions during surgery. TET assisted in the surgical planning of 2 patients with neuroendocrine tumors. Fused images targeted the surgical field in 1 patient with a recurrent gastrinoma and multiple abdominal adhesions and enabled the planning of the appropriate surgical strategy in a second patient with 2 sites of nonsecreting pancreatic tumor. Accurate localization is particularly important but is difficult to achieve in ectopic parathyroid adenomas. In the absence of correct preoperative localization, the reported rate of surgical failure varies between 33% and 40% and the complication rate is as high as 21% (14,15). In both patients with ectopic parathyroid adenoma evaluated in the current study, TET was the only imaging modality that provided relevant functional and topographic data for surgery planning.

The incidence of multiple organ involvement in patients with neuroendocrine tumors is high. Knowledge of the precise extent of disease plays a major role in determining the appropriate treatment option and choice of treatment procedures such as chemotherapy, cytoreductive surgery, embolization, or liver transplantation (16-20). In 1 patient, TET showed that the metastatic involvement of a carcinoid was limited to the liver, suggesting the use of a local rather than a systemic mode of treatment.

TET identified the presence of unsuspected bone involvement in 4 patients. Diagnosis of bone metastases is of prognostic significance, indicating short survival. In addition, in the presence of bone metastases, patients may be spared unnecessary surgery, insofar as operative removal of a primary tumor is not a curative option (21-26).

TABLE 2
Added Value of TET for Image Interpretation and Clinical Management of 11 Patients with Endocrine Neoplasms

Patient no.	Sex	Age (y)	Tumor type	Radiopharmaceutical	NM results	TET results	Added value of TET for image interpretation	Clinical value of TET
1	M	44	Gastrinoma	¹¹¹ In-octreotide	Increased focal uptake in upper abdomen	Uptake in retroperitoneal, normal-sized lymph node, at level of renal vein	Localization of lesion	Better planning of surgical approach
2	M	41	Recurrent NE tumor	¹¹¹ In-octreotide	Two foci of increased uptake in midabdomen	Uptake in retroperitoneum, paravertebral; involvement of bone	Localization of lesions, detection of bone involvement	Change in therapeutic approach (surgery canceled)
3	F	58	NE tumor	¹¹¹ In-octreotide	Two foci of increased uptake in midabdomen	Two foci of uptake in L1 vertebrae	Localization of both lesions to pancreas, retrospective detection of second lesion on CT	Better planning of surgical approach
5	M	47	Carcinoid tumor	¹¹¹ In-octreotide	Multiple abdominal lesions	Multiple hepatic lesions, no extrahepatic sites of uptake	Localization of lesions, exclusion of extrahepatic disease	Choice of therapeutic approach (chemoembolization)
7	M	40	Medullary thyroid carcinoma	¹¹¹ In-octreotide	Increased uptake in lower neck and upper mediastinum	Uptake in upper L mediastinum and R clavicle	Localization of lesion, detection of bone involvement	Change in prognosis
14	F	81	Suspected parathyroid adenoma	^{99m} Tc-sestamibi	Increased uptake in R upper mediastinum	Uptake in R paratracheal region extending posteriorly	Localization of ectopic adenoma	Better planning of surgical approach
15	F	70	Suspected parathyroid adenoma	^{99m} Tc-sestamibi	Increased uptake in R upper mediastinum	Uptake in R upper anterior mediastinum	Localization of ectopic adenoma	Better planning of surgical approach
19	M	46	Papillary thyroid carcinoma	¹³¹ I	Increased uptake in lungs and L upper thorax	Foci of uptake in both lungs and L coracoid	Localization of lesion, detection of bone involvement	Change in prognosis
21	F	68	Papillary thyroid carcinoma	¹³¹ I	Increased uptake in upper mediastinum	Focal uptake in sternum only	Localization of lesion, detection of bone involvement	Change in therapeutic approach (referral for surgery)
23	F	68	Suspected pheochromocytoma	¹²³ I-MIBG	Increased uptake in R posterior midabdomen	Focal uptake in R ureter	Localization of physiologic uptake	Exclusion of disease
26	M	59	Suspected aldosteronoma	⁷⁵ Se-cholesterol	Increased uptake in L abdomen, suspected additional uptake in R abdomen	Focal uptake in L adrenal (tumor), focal uptake in R colon (physiologic)	Localization of lesion to L adrenal only, localization of physiologic uptake	Exclusion of disease

NM = nuclear medicine; NE = neuroendocrine; CT = high-resolution, contrast-enhanced conventional CT.

CONCLUSION

The results of this study indicate that TET improves image interpretation and provides correct anatomic localization of scintigraphic findings in patients with endocrine neoplasms. TET enhances the already unique role of nuclear medicine procedures in the assessment of these tumors. This accurate, simply achieved method of registration of functional and anatomic data is of importance particularly when lesions are detected only on scintigraphy. It allows a more precise staging and determination of prognosis and leads to better therapeutic management.

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REFERENCES

1. Krenning EP, Kwekkeboom DJ, Bakker WH, et al. Somatostatin receptor scintigraphy with [¹¹¹In-DTPA-D-Phe1]- and [¹²³I-Tyr3]-octreotide: the Rotterdam experience with more than 1000 patients. *Eur J Nucl Med.* 1993;20:716–731.
2. Gibril F, Reynolds JC, Doppman JL, et al. Somatostatin receptor scintigraphy: its sensitivity compared with that of other imaging methods in detecting primary and metastatic gastrinomas. *Ann Intern Med.* 1996;125:26–34.
3. Termanini B, Gibril F, Reynolds JC, et al. Value of somatostatin receptor scintigraphy: a prospective study in gastrinoma of its effect on clinical management. *Gastroenterology.* 1997;112:335–347.
4. Lebtahi R, Cadiot G, Sarda L, et al. Clinical impact of somatostatin receptor scintigraphy in the management of patients with neuroendocrine gastroenteropancreatic tumors. *J Nucl Med.* 1997;38:853–858.
5. Weber DA, Ivanovic M. Correlative image registration. *Semin Nucl Med.* 1994;24:311–323.
6. Perault C, Schwartz C, Wampach H, Liehn JC, Delisle MJ. Thoracic and abdominal SPECT-CT image fusion without external markers in endocrine carcinomas. *J Nucl Med.* 1997;38:1234–1242.
7. Bocher M, Balan A, Krausz Y, et al. Gamma camera-mounted anatomical x-ray tomography: technology, system characteristics and first images. *Eur J Nucl Med.* 2000;27:619–627.
8. 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.
9. Delbeke D, Martin WH, Patton JA, Sandler MP. Value of iterative reconstruction, attenuation correction and image fusion of FDG PET images with an integrated dual-head coincidence camera and x-ray based attenuation maps. *Radiology.* 2001;218:163–171.
10. Caplin ME, Buscombe JR, Hilson AJ, Jones AL, Watkinson AF, Burroughs AK. Carcinoid tumour. *Lancet.* 1998;352:799–805.
11. Bonnin F, Lumbroso J, Tenenbaum F, Hartman O, Parmentier C. Refining interpretation of MIBG scans in children. *J Nucl Med.* 1994;35:803–810.
12. Charron M, Beyer T, Bohnen NN, et al. Image analysis in patients with cancer studies with a combined PET and CT scanner. *Clin Nucl Med.* 2000;25:905–910.
13. Norton JA, Doppman JL, Jensen RT. Curative resection in Zollinger-Ellison syndrome. *Ann Surg.* 1992;215:8–18.
14. Peeler BB, Martin WH, Sandler MP, Goldstein RE. Sestamibi parathyroid scanning and preoperative localization studies for patients with recurrent/persistent hyperparathyroidism or significant comorbid conditions: development of an optimal localization strategy. *Am Surg.* 1997;63:37–46.
15. Medrano C, Hazelrigg SR, Landreneau RJ, Boley TM, Shawgo T, Grusch A. Thoracoscopic resection of ectopic parathyroid glands. *Ann Thorac Surg.* 2000;69:221–223.
16. Weber HC, Venzon DJ, Lin JT, et al. Determinants of metastatic rate and survival in patients with Zollinger-Ellison syndrome: a prospective long-term study. *Gastroenterology.* 1995;108:1637–1649.
17. Orloff SL, Debas T. Advances in the management of patients with Zollinger-Ellison syndrome. *Surg Clin North Am.* 1995;75:511–524.
18. Alexander HR, Fraker DL, Norton JA, et al. Prospective study of somatostatin receptor scintigraphy and its effect on operative outcome in patients with Zollinger-Ellison syndrome. *Ann Surg.* 1998;228:228–238.
19. Girelli ME, Nacamulli D, Pellizzo MR, et al. Medullary thyroid carcinoma: clinical features and long term follow-up of seventy-eight patients treated between 1969 and 1986. *Thyroid.* 1998;8:517–523.
20. Kebebew E, Ituarte PH, Siperstein AE, Duh QY, Clark OH. Medullary thyroid carcinoma: clinical characteristics, treatment, prognostic factors, and a comparison of staging systems. *Cancer.* 2000;88:1139–1148.
21. Gibril F, Doppman JL, Reynolds JC, et al. Bone metastases in patients with gastrinomas: a prospective study of bone scanning, somatostatin receptor scanning, and magnetic resonance image in their detection, frequency, location and their effect of their detection on management. *J Clin Oncol.* 1998;16:1040–1053.
22. Lebtahi R, Cadiot G, Delahaye N, et al. Detection of bone metastases in patients with endocrine gastroenteropancreatic tumors: bone scintigraphy compared with somatostatin receptor scintigraphy. *J Nucl Med.* 1999;40:1602–1608.
23. Mazzaferri EL. Treating differentiated thyroid carcinoma: where do we draw the line? *Mayo Clin Proc.* 1991;66:105–111.
24. DeGroot LJ, Kaplan EL, McCormick M, Straus FH. Natural history, treatment and course of papillary thyroid carcinoma. *J Clin Endocrinol Metab.* 1990;71:414–424.
25. Pittas AG, Adler M, Fazzari M, et al. Bone metastases from thyroid carcinoma: clinical characteristics and prognostic variables in one hundred forty-six patients. *Thyroid.* 2000;10:261–268.
26. Van Tol KM, Hew JM, Jager PL, Vermey A, Dulaart RP, Links TP. Embolization in combination with radioiodine therapy for bone metastases from differentiated thyroid carcinoma. *Clin Endocrinol (Oxf).* 2000;52:653–659.