Advantages of Hybrid SPECT/CT *vs* SPECT Alone

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Abstract: We present our initial two year clinical experience with SPECT/CT, compare the interpretation to SPECT alone, provide illustrative cases, and review the published literature. Hybrid SPECT/CT has added clinical value over SPECT imaging alone primarily due to more precise anatomical lesion localization. After reading this report, the reader will appreciate the advantages of SPECT/CT imaging for clinical practice. We have reviewed SPECT/CT studies of 144 adult patients referred for various clinical indications in a busy nuclear medicine practice. The SPECT and fused SPECT/CT images were reviewed and interpreted separately to determine if addition of the fused CT images added incremental information, e.g., more definitive anatomic localization, more definitive diagnostic certainty, or changed final image interpretation compared to the SPECT images alone. Our analysis showed that SPECT/CT provided additional information for image interpretation in 54% (78/144) of cases. In most of these (68/78), the CT data improved localization of abnormal and physiologic findings. Diagnostic certainty was improved in 34/144 cases (24%) and image interpretation was beneficially altered in 18/144 cases (13%). The fusion of anatomical and functional information by hybrid SPECT/CT positively impacts image interpretation and adds diagnostic value over SPECT alone.

INTRODUCTION

Single photon emission computed tomography (SPECT) is cross-sectional nuclear imaging using single-photon emitting radiopharmaceuticals, e.g., technecium-99m (^{99m}Tc) diphosphonate bone scans, ^{99m}Tc-sestamibi cardiac perfusion imaging, gallium-67 for infection and tumor imaging, iodine-123 (^{123}I) or iodine-131(^{131}I) thyroid imaging, etc. SPECT has been shown to improve lesion detection compared to two-dimensional planar imaging by removing out-of-plane information and thus increasing image contrast [1]. However, functional images often lack the anatomic detail necessary for accurate lesion localization, which can decrease reader confidence in image interpretation and lead to uncertain or erroneous interpretations.

Image fusion software has been successfully used to merge nuclear medicine functional images and anatomic images, e.g., CT or MRI, acquired as separate studies [2-6]. However, differences in patient positioning, interval changes in organ position (i.e., bowel gas, bladder) between studies and respiratory or motion artifacts can make accurate alignment of images challenging and not always successful.

Positron emission tomography/computed tomography (PET/CT) has demonstrated the clinical diagnostic value of combining anatomical and functional imaging using a hybrid instrument [7-10]. Since its introduction in 2001, hybrid PET/CT has had rapid growth and become so successful that almost all PET cameras sold commercially today are PET/CT cameras [11, 12]. Commercial hybrid SPECT/CT was introduced slightly earlier but in the same general time period [13]. Published studies to date have confirmed a similar advantage, as was seen for PET/CT *vs* PET, for SPECT/CT over SPECT alone [14-18]. However, the growth of SPECT/CT has been slower than PET/CT. One reason is that the published literature demonstrating its clinical value is considerably less for SPECT/CT. In this paper, we will present our initial two year clinical experience with SPECT/CT and seek to determine if there is added diagnostic value to SPECT/CT over SPECT alone in a busy general nuclear medicine clinic. We will review pertinent published literature and show illustrative cases. After reading this report, the reader will appreciate the growing and important role of SPECT/CT imaging for routine clinical practice.

METHODS

Patient Population

One-hundred and forty-four adult patients (80 males, 64 females; mean age 53.2 ± 15.0 years, range 17-84) underwent SPECT/CT imaging between November 2002 and October 2004. All clinical studies were included, except for ^{99m}Tc-sestamibi parathyroid and myocardial perfusion studies, which will be reported separately. The radiopharmaceuticals used and indications for the studies are listed in Table **1**. Retrospective data review and image analysis were approved by our Institutional Review Board.

Image Acquisition and Reconstruction

Patient preparation, the radiopharmaceutical, its administered activity, and the SPECT acquisition parameters were determined for the specific study being performed based on the clinical indication and following our usual protocols. SPECT/CT studies were acquired routinely for the ^{111}In-

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Table 1. Radiopharmaceuticals and Study Indications

Study Type	Indication	Patient No.
^{111}In-Pentetreotide	Diagnosis-neuroendocrine tumor	18
	History of neuroendocrine tumor - evaluate for metastatic disease	24
	Pre-Somatostatin therapy evaluation	5
	Therapy response evaluation	2
	Zollinger-Ellison Syndrome – evaluate for recurrent tumor	2
	Total	**51**
^{111}In-Capromab Pendetide	Rising PSA	21
	Evaluate extent of local disease and for metastases	3
	Total	**24**
^{111}In-oxine leukocytes	Localize site of infection	6
	Evaluate for osteomyelitis of the maxillary sinus bone	4
	Total	**10**
^{67}Galliumcitrate	Sarcoidosis - diagnosis	7
	History of sarcoidosis - evaluate for active disease	3
	Infection/osteomyelitis	2
	Re-staging Hodgkin's disease	1
	Diagnosis - anterior mediastinal mass	1
	Total	**14**
^{131}I-MIBG	Adrenal mass - evaluate for pheochromocytoma	3
	History of paraganglioma - evaluate extent of disease	1
	Total	**4**
^{99m}Tc-MDP	Bone pain evaluation	10
	Evaluate – reflex sympathetic dystrophy	1
	Evaluate for osteomyelitis	3
	Abnormal MRI	1
	History of cancer – metastatic survey	8
	Total	**23**
^{99m}Tc-sulfur colloid	Evaluate for ectopic spleen	3
	Evaluate for extramedullary hematopoiesis	1
	Evaluate liver/spleen function	2
	Total	**6**
^{99m}Tc-DMSA	Cortical function	3
^{99m}Tc-RBC	Evaluate for hemangioma in liver	2
^{131}I-sodium iodide	Post-treatment metastatic survey	6
^{123}I-sodium iodide	Metastatic survey	1
	Total	**144**

Pentetreotide (Octreoscan®, Mallinckrodt Inc, St. Louis, MO), ^{111}In-Capromab Pendetide (ProstaScint®, Cytogen, Princeton, NJ), ^{99m}Tc-dimercaptosuccinic acid (DMSA), and ^{99m}Tc-red blood cells (RBC) imaging studies, but for the other studies, SPECT/CT was ordered at the discretion of the nuclear medicine physician based on the clinical indication and findings on planar images.

SPECT/CT studies were acquired and processed on either the Millennium VG or Infinia and Hawkeye hybrid SPECT/CT cameras and Xeleris workstations (GE Healthcare, Milwaukee, WI). SPECT acquisition was step and shoot, and the following parameters were used: angular range - 180 degrees, 128 x 128 matrix, 120 total steps (60 per head). The time per step (range: 25-60 seconds), energy window, and zoom varied depending on the administered radiopharmaceutical. The transmission map was generated based on data obtained from the concurrent CT scan. Reconstruction was performed using both iterative and filtered backprojection methods. CT attenuation correction was applied to the SPECT data. Single-slice CT scans were acquired with the following parameters: 140 kVp, 2.5 mA, 13.8 s/gantry rotation, 256 x 256 matrix, 10 mm slice thickness, and 8-10 minute total acquisition time.

SPECT and CT images were assessed for technical adequacy and patient motion by the covering nuclear medicine physician prior to patient discharge from the department. If excessive motion was present, a repeat scan was obtained.

Data Analysis

Images were retrospectively reviewed on a Xeleris workstation (GE Healthcare, Milwaukee, WI) independently by 2 experienced nuclear medicine physicians. The nuclear medicine SPECT studies were interpreted first. In a separate reading session, the hybrid SPECT/CT fusion images were interpreted. All SPECT images reviewed were CT attenuation corrected. SPECT and CT registration was visually assessed for proper alignment. Since no specific instructions were given to the patients regarding breathing during either the SPECT or CT acquisition, misregistration in the z-axis due to respiration was considered during the final image interpretation. Readers were not provided with clinical history at the time of the reading sessions. If results were discordant between the two readers, a third reader reviewed the images and a consensus reading was reached.

The nuclear medicine images were reviewed for findings, defined as a focal area of increased radiotracer uptake over-background which could potentially be considered to be abnormal. These findings were scored based on a 5-point scale for diagnostic certainty and a 3-point scale for finding localization. The diagnostic certainty scoring scale was as follows: 0 = definitely normal; 1 = probably normal; 2 = equivocal; 3 = probably abnormal; and 4 = definitely abnormal. The probably normal (1), equivocal (2), and probably abnormal (3) findings were grouped as "uncertain findings" for analysis, and the definitely normal (0) and definitely abnormal (4) findings were grouped as "certain findings" for analysis. The localization certainty scoring scale follows: 0 = unknown localization; 1 = probable localization; and 2 = definite localization.

The CT was considered to provide added value to the SPECT interpretation if it improved localization of the finding (i.e., an unknown localization became probable or definite or a probable localization became definite), improved diagnostic certainty (i.e., an "uncertain finding" became a "certain finding"), or changed the interpretation of the study. Added value of SPECT/CT *vs* SPECT alone was analyzed on a per patient and per finding basis.

Follow-up information was reviewed for all patients and included clinic notes, other anatomic or functional imaging studies, and histopathology when available. Mean follow-up time post-scan was 7.9 ± 5.6 months. Pathologic follow-up was available in 18 of 144 patients.

RESULTS, ILLUSTRATIVE CASES, AND LITERATURE REVIEW

Overall Results

SPECT/CT improved anatomic localization of findings in 68 of 144 patient studies (47%) and improved diagnostic certainty of findings in 34/144 studies (24%). SPECT/CT added diagnostic value over SPECT alone in 78 (54%) of the 144 patient studies (Table **2**). A primary benefit of accurate localization was differentiation of pathologic from physiologic findings. SPECT/CT changed overall image interpretation in 18 patients, altering management in 2 patients (Fig. **1**).

Both SPECT and SPECT/CT revealed abnormal findings in 102 of 144 patients. In the 102 patients, 238 positive findings were identified on both the SPECT and the SPECT/CT

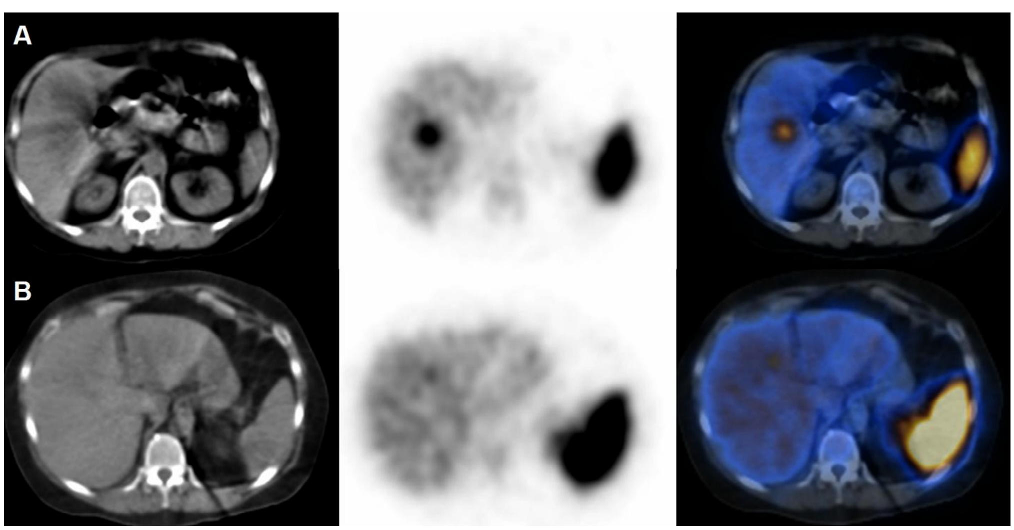

Fig. (1). A 54-year-old female with lung cancer and liver metastases was referred for an ^{111}In-leukocyte study to evaluate for possible abscess after presenting with bacteremia and fever of unknown origin. A diagnostic CT scan demonstrated numerous hypodense liver lesions consistent with liver metastases. SPECT/CT (**A**) precisely characterized and localized the abscess (**A**), distinguishing it from liver metastases (**B**). Physiologic radiotracer activity is visualized in the spleen in the left abdomen. Ultrasound-guided drainage yielded 4 milliliters of purulent material. The SPECT/CT served as a "road-map" in this case for the ultrasound-guided biopsy.

scans. Fourteen findings were seen on SPECT alone and 14 additional findings were identified only on SPECT/CT. The addition of CT to SPECT decreased the number of uncertain diagnostic findings by 48% (Table **3A**). SPECT/CT improved localization for 74% of findings (Table **3B**). In the cases in which CT did not add additional information, either the low resolution CT scan did not allow for accurate localization, or the SPECT findings were clearly localized to an organ, such as the liver (Fig. **2**).

Table 2. Added Value of SPECT/CT by Study Type

Study Type	CT Added Value to SPECT	Total Cases	Percentage
^{111}In-Pentetreotide	27	51	53%
^{111}In-Capromab Pendetide	15	24	63%
^{99m}Tc-MDP	11	23	48%
^{67}Gallium citrate	9	14	64%
^{111}In-oxine leukocytes	6	10	60%
^{99m}Tc-sulfur colloid	1	6	17%
^{131}I-MIBG	2	4	50%
^{99m}Tc-DMSA	1	3	33%
^{99m}Tc-RBC	0	2	0%
^{131}I-sodium iodide	5	6	83%
^{123}I-sodium iodide	1	1	100%
Total	78	144	54%

Neuroendocrine and Endocrine Scintigraphy

Fifty-one ^{111}In-Pentetreotide scans were performed in patients with known or suspected neuroendocrine tumors. SPECT/CT had added value over SPECT alone in 27 of 51 cases (53%). SPECT/CT improved diagnostic certainty and/or finding localization in 9 and 26 of the 51 cases, respectively (Fig. **3**). Five abnormal findings on SPECT alone were determined to be due to physiologic activity on SPECT/CT because they fused to normal anatomic structures (Fig. **4**).

Thirteen ^{111}In-Pentetreotide scans were negative on both SPECT and SPECT/CT. For the other 11 studies with abnormal findings on SPECT, CT did not add additional information either because it was difficult to precisely localize the radiotracer activity in the abdomen due to the low resolution and slow scan speed of the CT scan obtained or the findings clearly localized to the liver parenchyma on both SPECT and SPECT/CT.

Four ^{131}I-MIBG studies were performed for localization of suspected pheochromocytoma. SPECT/CT added additional information in 2. In both cases, CT enabled precise localization of abnormal ^{131}I-MIBG uptake (Fig. **5**).

Six ^{131}I-sodium iodide SPECT/CT cases were performed in patients with thyroid carcinoma. SPECT/CT scans were performed to better localize abnormal findings seen on whole-body planar metastatic surveys. Thirteen abnormal findings were identified. SPECT/CT improved diagnostic certainty for one finding and improved lesion localization in 9 findings (Figs. **6** and **7**). In the only ^{123}I-sodium iodide metastatic survey, SPECT/CT precisely localized increased iodine accumulation in abnormal soft tissue in the superior mediastinum. This mass was resected and pathology revealed metastatic papillary thyroid carcinoma (Fig. **8**).

A majority of the SPECT/CT literature has focused on its advantages in the evaluation of neuroendocrine and endocrine tumors [14-18]. In the largest study of 72 patients undergoing ^{111}In-Pentetreotide imaging, SPECT/CT improved lesion localization in 23 of 44 positive studies and altered management plans in 14% of patients by changing the surgical approach, sparing futile surgery, or changing medical management [15]. Our experience is similar with SPECT/CT providing added value in 56% of our neuroendocrine and endocrine cases.

The value of SPECT/CT for neuroendocrine and endocrine scintigraphy is most likely because the SPECT and CT images provide complimentary functional and anatomic information. The addition of the CT to the SPECT allows for precise lesion localization and identification and confirmation of lesions visualized on CT scan that do not have radiotracer uptake, and helps distinguish physiologic bowel activity from abnormal activity. Meanwhile, the addition of the SPECT to the CT provides a “road-map” for retrospec-

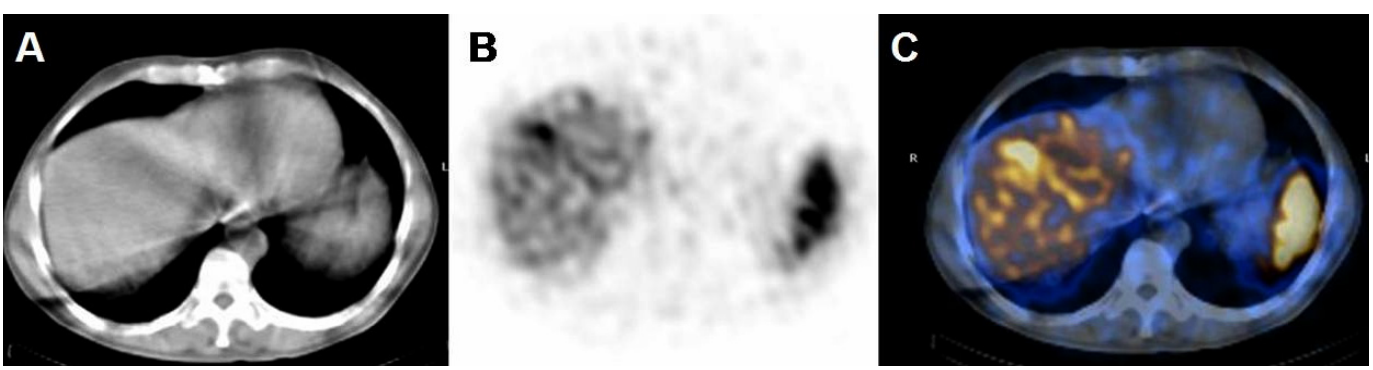

Fig. (2). 53-year-old male with a malignant pancreatic neuroendocrine tumor presented for ^{111}In-Pentetreotide imaging to evaluate for metastatic disease. A diagnostic CT scan of the liver suggested liver metastases. The ^{111}In-Pentetreotide scan revealed a focus of intense radiotracer activity near the dome of the liver (**B**). The focus could be localized to the liver on SPECT alone given the normal uptake in the surrounding hepatic parenchyma. No definite abnormality was visualized on the low resolution CT images (**A**). The fused SPECT/CT scan (**C**) did not add additional information in this case (**A**: CT; **B**: SPECT; **C**: Fused SPECT/CT).

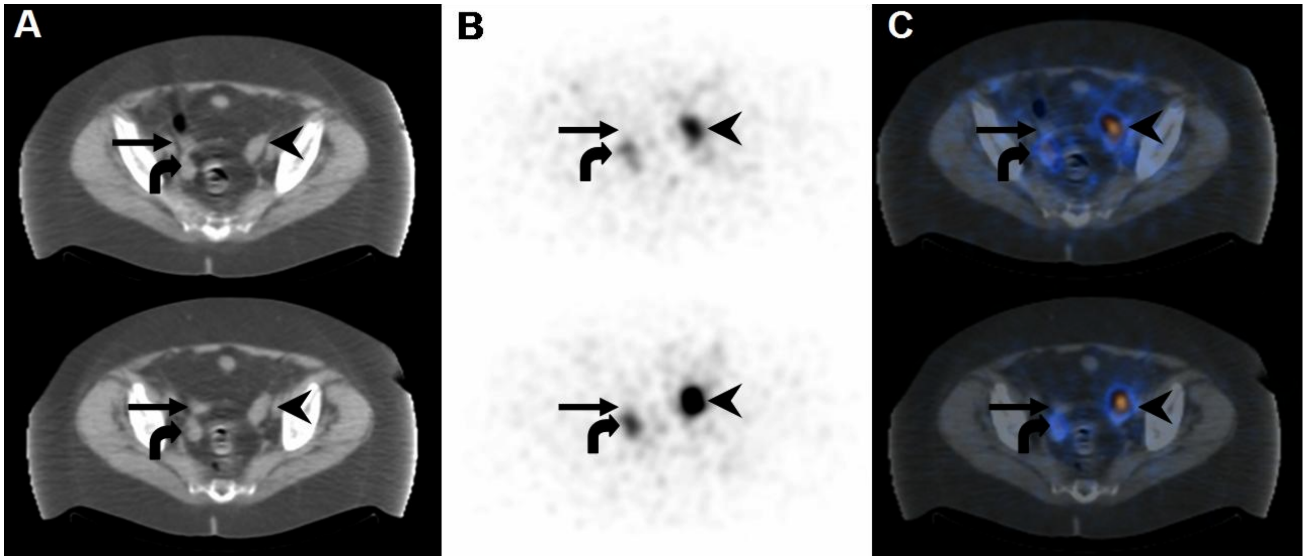

Fig. (3). A 72-year-old female with a history of an ileocecal carcinoid tumor status post resection presented for surveillance ^{111}In-Pentetreotide imaging following a negative MRI of the pelvis. The CT scan (**A**) on two contiguous transaxial slices demonstrated a loop of bowel (black arrow), a right adnexal mass (curved arrow), and a left adnexal mass (arrow head). SPECT imaging (**B**) demonstrated 2 foci of abnormal ^{111}In-Pentetreotide accumulation in the pelvis. The fused SPECT/CT images (C) demonstrated that the activity in the left pelvis fused to the left adnexal mass (arrow head) and that the right sided focus of activity (curved arrow) fused to the right adnexal mass and not the loop of bowel which was just anterior to it. The patient subsequently had a total abdominal hysterectomy and bilateral salpingo-oophorectomies. Histopathology revealed metastatic neuroendocrine tumors (**A**: CT; **B**: SPECT; **C**: Fused SPECT/CT).

tive lesion detection on CT (Fig. **9**), helps to identify bone involvement and abnormal activity in normal sized lymph nodes by CT criteria. True lesion extent is most accurately assessed by the fused images.

Table 3. Finding Analysis

A Score	Diagnostic Certainty	Number of Findings	
		SPECT	SPECT/CT
0	Definitely normal	10	23
1, 2, or 3	Probably or Equivocal	79	41
4	Definitely abnormal	149	174
	Total	238	238
B Score	**Localization Certainty**	**Number of Findings**	
		SPECT	**SPECT/CT**
0	Unknown	56	12
1	Probable	85	24
2	Definite	97	202
	Total	238	238

^{111}In-Capromab Pendetide (Prostascint®)

^{111}In-Capromab Pendetide imaging is requested by referring physicians to localize soft tissue metastases of recurrent metastatic prostate cancer. Images acquired of this radiolabeled monoclonal antibody often are of poor quality due to poor target to background ratios, lack of anatomic information, and the low count rate. This is a particular problem in the pelvis where the lack of anatomic detail makes interpretation challenging [19, 20]. Blood pool images with ^{99m}Tc-RBCs are often used in conjunction to provide some anatomic information. CT and MR alone have quite poor sensitivity due to the small size of the metastatic lymph nodes.

In this study, we found that the addition of CT aided interpretation by identifying anatomic landmarks in the pelvis. We were able to precisely localize all scintigraphic findings for our 24 patients undergoing ^{111}In-Capromab Pendetide scintigraphy. Three findings thought to represent normal blood pool activity on SPECT alone, when compared to the ^{99m}Tc-RBC scan, were determined to be abnormal foci in the prostate bed by SPECT/CT. One finding equivocal for blood pool activity on SPECT in conjunction with the ^{99m}Tc-RBC scan was determined to be precisely located in the aorta and physiologic on SPECT/CT without comparison to the ^{99m}Tc-RBC scan (Fig **10**). In another case, findings equivocal for abnormal lymphadenopathy on SPECT alone were determined to be physiologic bowel activity on SPECT/CT.

Our findings are in concordance with the limited number of other studies evaluating SPECT/CT for ^{111}In-Capromab Pendetide imaging [21-23]. Wong *et al.* found that SPECT image quality was improved when applying CT-based attenuation correction and that SPECT/CT facilitated image interpretation due to easier identification of the prostate gland and pelvic organs [23]. Another group has eliminated the simultaneous ^{99m}Tc-RBC blood pool imaging frequently performed in conjunction with ^{111}In-Capromab Pendetide scanning because of the superior anatomic information provided by the CT scan [22]. Our clinical experience supports this approach. We have also found SPECT/CT particularly useful for improving initial characterization of abnormal radiotracer activity in locations which would be atypical for metastatic disease from the primary tumor being evaluated (Fig. **11**).

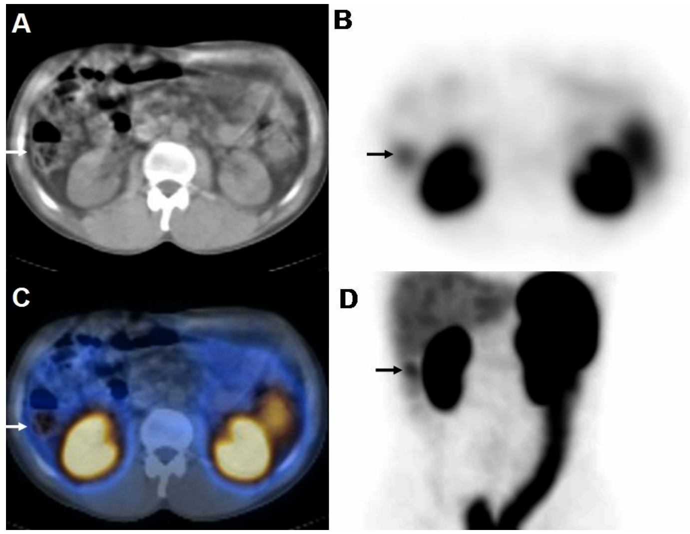

Fig. (4). A 32-year-old male with a history of pancreatic islet cell tumor status post resection. ^{111}In-Pentetreotide scan was performed to evaluate for metastatic disease. A focus of intense radiotracer activity was seen in the right upper quadrant (arrows) and was interpreted as a probable liver metastasis on SPECT alone (B, D). SPECT/CT (**A-C**) demonstrated that the focus of activity fused to a loop of bowel and was, therefore, determined to be physiologic (**A**: CT; **B**: SPECT; **C**: Fused SPECT/CT; **D**: Static maximum intensity projection image).

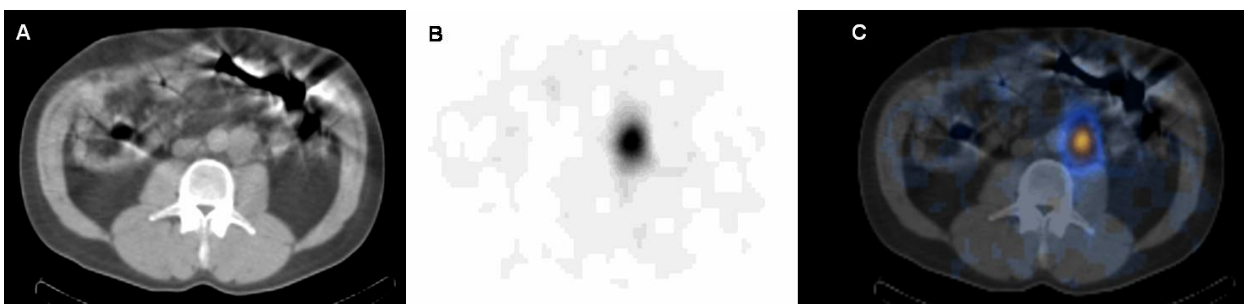

Fig. (5). A 39-year-old male with a history of extra-adrenal paraganglioma. Abdominal CT scan suggested liver metastases, and he was referred for a ^{131}I-MIBG scan to evaluate for extent of disease. Three foci of definitely abnormal findings were identified on both SPECT and SPECT/CT, two in the liver (not shown). The high target-to-background ratio, but poor anatomical information of the ^{131}I scan made localization of the 3rd abdominal focus difficult. The SPECT/CT accurately localized the focus to a left peri-aortic mass. All three lesions were resected and pathology revealed metastatic paraganglioma. The accurate localization of the third lesion by SPECT/CT aided in the planning of the patient's surgery (**A**: CT; **B**: SPECT; **C**: Fused SPECT/CT).

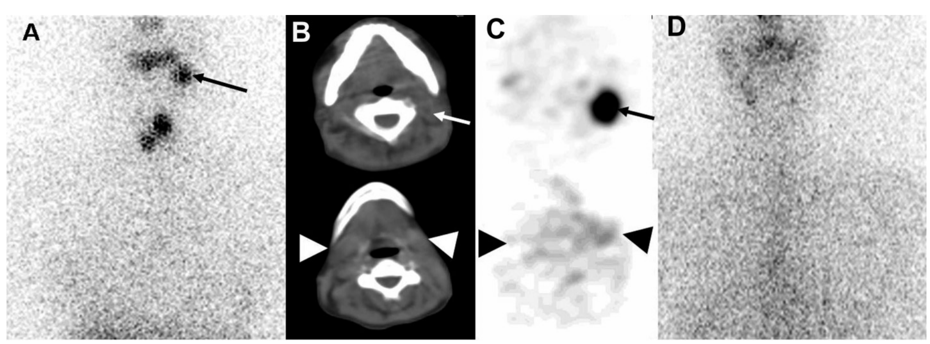

Fig. (6). A 39-year-old female with a recurrent papillary thyroid carcinoma presented for a 7 day post-therapy ^{131}I metastatic survey. On the planar image (**A**), abnormal foci of increased ^{131}I accumulation were seen in the midline neck which were most consistent with biopsy proven thyroid carcinoma. The intense focus of activity in the left cervical region (arrow) could have been due to asymmetric uptake in the left submandibular gland or in a left neck lymph node. SPECT/CT images (**B**,**C**) demonstrated that the focus of activity (B,C - arrows, top row) fused to asymmetric soft tissue in the left neck superior to the submandibular glands (**B**,**C** - arrowheads, bottom row). The activity was interpreted as consistent with recurrent thyroid carcinoma. On a follow-up metastatic survey 6 months later (**D**), the asymmetric focus of activity in the left neck region, as well as the midline neck foci, resolved confirming the interpretation (**A**: planar; **B**: CT; **C**: SPECT; **D**: planar).

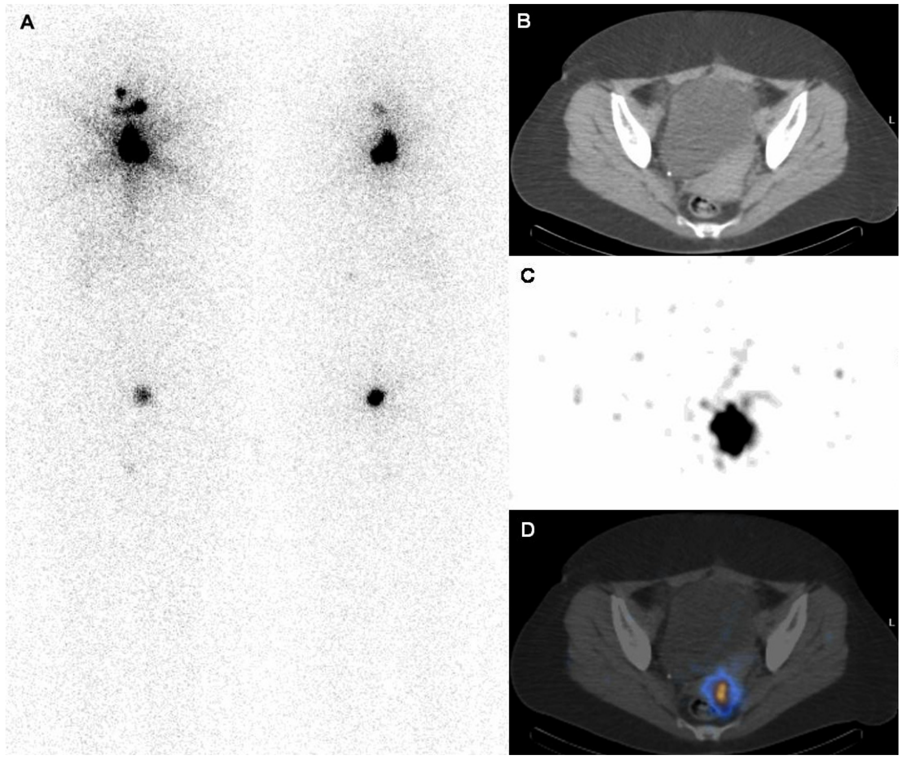

Fig. (7). A 55-year-old female with a history of papillary thyroid cancer status post total thyroidectomy underwent a whole body metastatic survey 7 days post-remnant thyroid ablation with 100 mCi ^{131}I. The planar images (**A**) demonstrated increased radiotracer activity in the midline pelvis which was initially interpreted as physiologic bladder activity. However, due to the more intense appearance of the activity on the posterior projections, a sacral bone focus was suspected and a SPECT/CT scan performed (**B-D**). SPECT/CT demonstrated that the activity fused to the uterus, and thus excluded a bone metastasis. Although an unusual finding, the activity was believed to be physiologic, possibly due to presence of sodium iodide symporters in endometrial glands [42] or increased blood flow. At her last follow-up 9 months after the scan, she was without clinical evidence of thyroid carcinoma (**A**: planar; **B**: CT; **C**: SPECT; **D**: fused SPECT/CT).

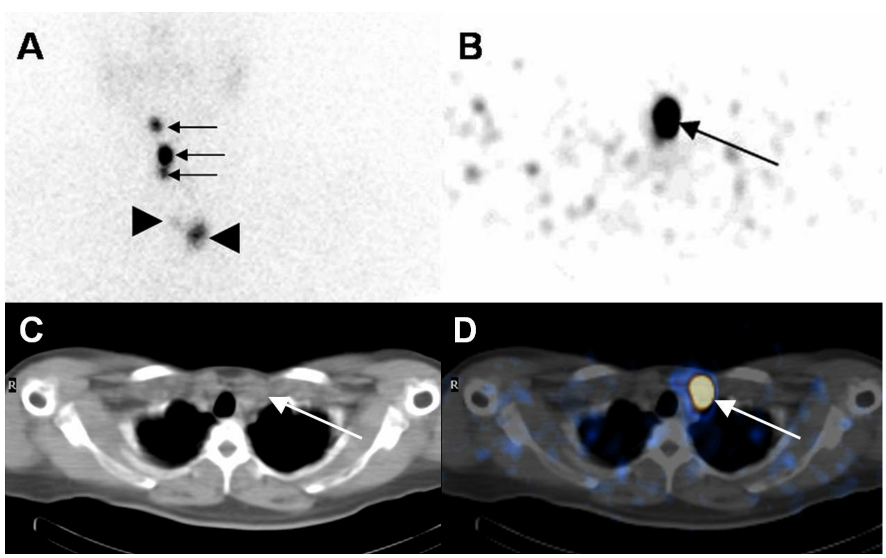

Fig. (8). A 42-year-old female with a history of a 1.7 cm papillary thyroid cancer status post thyroidectomy presented for her first ^{123}I metastatic survey prior to remnant thyroid ablation. Metastatic disease was found in left neck and level VI lymph nodes at surgery. The planar images (**A**) of the neck and upper thorax demonstrated 3 foci of abnormal activity in the neck (arrows). A fourth, and possibly a fifth, focus was visualized in the upper chest region (arrowheads). SPECT (**B**) shows high a target-to background but little anatomic information. Fused SPECT/CT (**D**) precisely localized the lesion to abnormal soft tissue at the left thoracic inlet (arrows), which was too low to be remnant thyroid tissue. She received a dose of radioactive ^{131}I to treat her metastatic disease (152 mCi). Follow-up IV contrast CT scan was obtained to better visualize the anatomy and it confirmed a soft tissue mass at the thoracic inlet. The mass was subsequently removed from the left paratracheal groove and pathology revealed metastatic papillary thyroid cancer (**A**: planar; **B**: SPECT; **C**: CT; **D**: fused SPECT/CT).

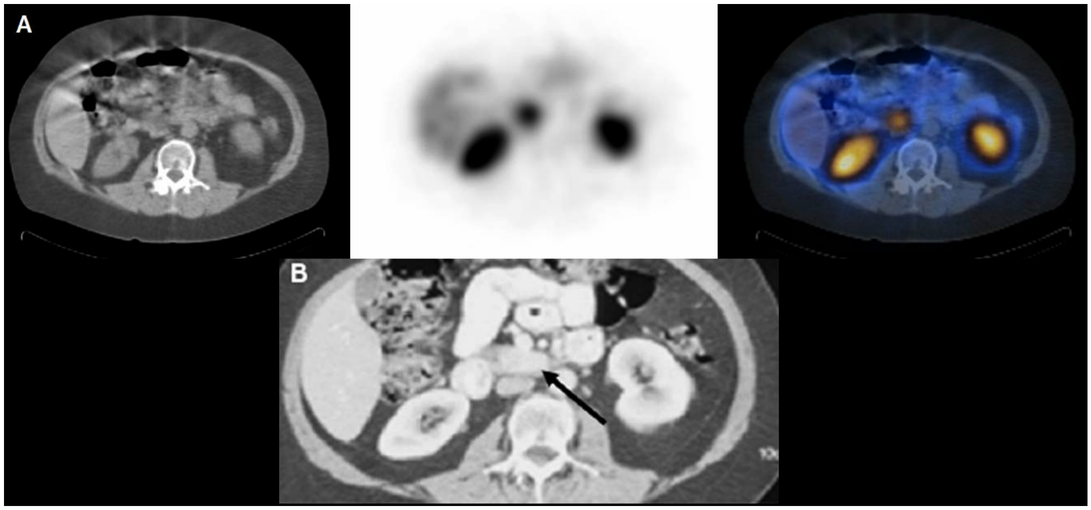

Fig. (9). A 52-year-old female with biochemically established Cushing's syndrome was referred for an ^{111}In-Pentetreotide study. The scan demonstrated a focus of intense ^{111}In-Pentetreotide accumulation in the region of the 2nd portion of the duodenum (**A**). Follow-up IV contrast CT scan was initially interpreted as normal, however, on retrospective review with correlation to the SPECT/CT images, a mass at the root of the mesentery (arrow) was identified (**B**). Resection was performed and histopathology revealed an islet cell tumor.

Bone Scintigraphy

SPECT/CT added diagnostic value to the interpretation of 11 of 23 ^{99m}Tc-MDP bone scans in our study. In 2 of these cases, diagnostic certainty was increased and in 10 lesions localization was improved. Equivocal findings for metastatic bone disease *vs* degenerative disease were most often precisely localized to osteophytes or facet joint degenerative changes and interpreted as benign on SPECT/CT. Determination of extent of local disease was also improved on bone scanning with SPECT/CT (Fig. **12**).

The results of our study and others suggest that SPECT/CT decreases equivocal findings, improves lesion localization and specificity *vs* SPECT alone for patients undergoing bone scintigraphy for evaluation of metastatic bone disease and osteomyelitis [24-28]. SPECT/CT of bone is not usually obtained as part of the routine protocol, but rather ordered at the discretion of interpreting physicians when equivocal findings are seen on planar or SPECT imaging. In one study, 45 of 76 patients (59%) were spared additional imaging/diagnostic workup for further evaluation of non-specific SPECT bone scan findings because readers were able to make a final diagnosis based on combined SPECT/CT images [24].

Leukocyte Scintigraphy

SPECT/CT for leukocyte imaging is usually obtained in patients with equivocal prior anatomic imaging or equivocal planar or SPECT imaging findings. SPECT/CT has been reported to add additional information compared to combined planar and SPECT images in 36-63% of cases [29, 30]. In the 6 of 10 ^{111}In-leukocyte studies in which SPECT/CT added diagnostic value, finding localization improved in 5 studies, 4 with abnormal findings (Fig. **13**) and one with physiologic findings. The addition of SPECT/CT altered interpretation and patient management in 2 cases (Fig. **1**). For evaluating bone and joint infections, hybrid SPECT/CT seems to be particularly useful for distinguishing cellulitis from osteomyelitis and defining extent of involvement [30].

Gallium Scintigraphy

Our experience expands the limited published data [17, 29, 31] evaluating hybrid SPECT/CT for ^{67}Gallium citrate

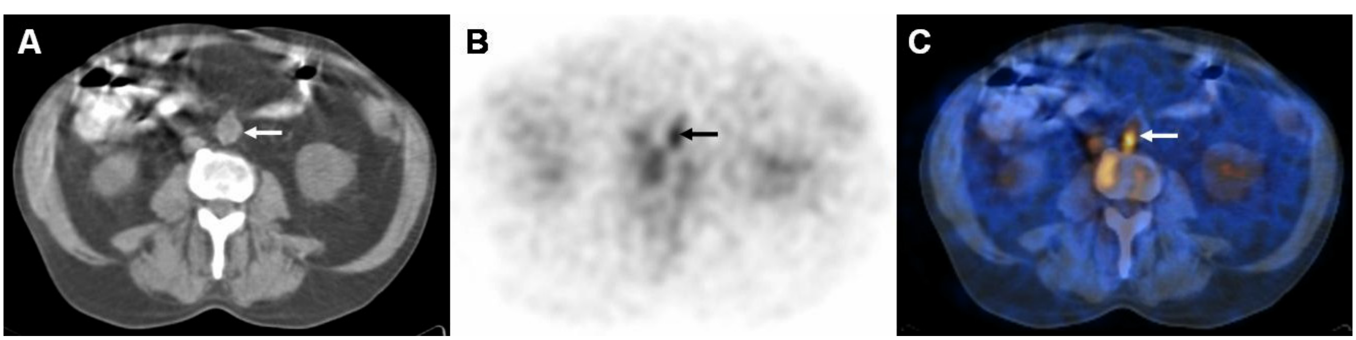

Fig. (10). A 73-year-old male with history of prostate cancer presented with a slowly rising PSA. A single focus of moderately increased ^{111}In-Capromab Pendetide (Prostascint$^{®}$) was seen in the left para-aortic region on SPECT alone (**B**). This activity fused to the aorta on the CT and SPECT/CT fused images (**A**,**C**) and was interpreted as physiologic radiotracer distribution without the need for comparison to a blood pool sudy. No abnormal lymph nodes were identified in this region on the CT scan (**A**: CT; **B**: SPECT; **C**: fused SPECT/CT).

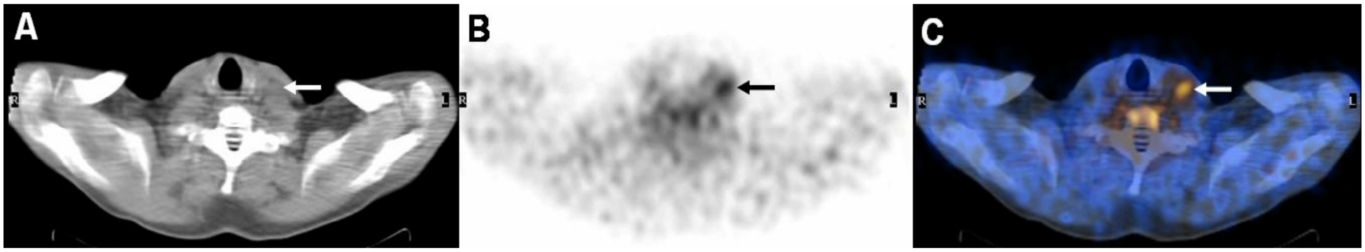

Fig. (11). A 72-year-old male with a history of prostate carcinoma status post prostatectomy presented with a rising PSA. The ^{111}In-Capromab Pendetide SPECT scan (**B**) demonstrated moderately increased radiotracer accumulation in the left cervical region. It was difficult to definitively localize the structure, lymph node *vs* vessel, on the CT (**A**) and fused SPECT/CT images (**C**). A follow-up diagnostic neck CT demonstrated a soft tissue mass between the scalene and sternocleidomastoid muscles. This was resected and found to be a schwannoma. The exact reason for accumulation of the radiotracer in a schwannoma is not certain; however, ^{111}In-Capromab Pendetide is a monoclonal antibody to prostate specific membrane antigen (PSMA) and PSMA has been reported to be expressed on the neovasculature of several tumor types [43, 44]. Schwannomas can be vascular and it is possible that the finding was due to binding of ^{111}In-Capromab Pendetide to PSMA on the endothelial cells of the schwannoma. Non-specific accumulation due to tumor hyperemia is also a possible etiology (**A**: CT; **B**: SPECT; **C**: fused SPECT/CT).

scintigraphy and suggests that SPECT/CT aids in improving localization and diagnostic certainty in patients' studies for a variety of indications.

We found that SPECT/CT added diagnostic value in 9 of 14 ^{67}Gallium scans. Localization improved in 7 of the 9 cases in which the SPECT/CT added diagnostic value. Diagnostic certainty improved in 6 cases. One patient had mild radiotracer uptake in a pulmonary infiltrate and one patient had mild radiotracer accumulation in right maxillary sinus mucosal thickening which were only appreciated after abnormalities were visualized on the concurrent CT scan. They probably represented mild inflammatory changes, however, we do not have definitive follow-up for these specific findings.

Hybrid SPECT/CT ^{67}Gallium imaging provided additional data in 54.2% of patients with lymphoma which led to alteration of patient management in 33.2% [31]. For infection imaging, SPECT/CT is reported to be less helpful for ^{67}Gallium scintigraphy than radiolabeled leukocyte imaging, but it is still contributory for a large percentage of patients [29].

Other Study Types

SPECT/CT was less helpful for the interpretation of the limited number of ^{99m}Tc-sulfur colloid, ^{99m}Tc-RBC, and ^{99m}Tc-DMSA studies, however, did provide additional information in 2 of these 10 cases. For one ^{99m}Tc-DMSA scan, the CT scan provided additional information in a patient with an uncertain finding of a cortical defect on SPECT alone by precisely identifying a right upper pole mass corresponding to the area of decreased radiotracer activity, increasing our diagnostic certainty. The patient underwent nephrectomy and histopathology revealed renal cell carcinoma. Abnormal ^{99m}Tc-sulfur colloid uptake was precisely localized to the bone marrow of the skull confirming extramedullary hematopoiesis in the second case. Schillaci *et al.* reported on the use of SPECT/CT in 12 patients for ^{99m}Tc-RBC imaging of hemangioma [32] and found that SPECT/CT was helpful for distinguishing hepatic hemangiomas from adjacent vascular structures in 4 patients (33%). Diagnostic accuracy of ^{99m}Tc-RBC imaging for hemangioma was improved from 71% with SPECT alone to 88% with SPECT/CT [32].

We did not specifically evaluate the usefulness of SPECT/CT for parathyroid imaging in our study. However, SPECT/CT allows precise localization of the adenoma, particularly in the post-surgical neck and mediastinum and facilitates surgical planning [33-35]. In addition, a recent comparison of the various methodologies for parathyroid scintigraphy, planar *vs* SPECT *vs* SPECT/CT and dual *vs* single-phase, demonstrated that the combination of early SPECT/CT with any delayed imaging was most accurate for localization of parathyroid adenomas in patients with primary hyperparathyroidism and a single adenoma [36].

SPECT/CT lymphoscintigraphy is reported to guide the surgical approach in head and neck squamous cell cancer, melanoma and bladder cancer. SPECT/CT finds more sentinel nodes close to the injection site, in adjacent but additional lymph node basins, and in-transit nodes [37-39].

SPECT/CT Cameras

The first hybrid SPECT/CT cameras combined a two-headed gamma camera with a single-slice low resolution CT system which does not produce high quality diagnostic CT images [13]. Our data and the data of others that we have reviewed have shown the diagnostic advantage of SPECT/CT in spite of the low resolution CT system. However, at times, the low resolution CT cannot reveal the exact anatomic site of abnormal radiotracer accumulation. We found this particularly true in interpreting abdominal findings on ^{111}In-Pentetreotide scans. SPECT lesions had high tumor-to-background ratios and were easily identified as abnormal; however, the CT did not add any diagnostic advantage. Another limitation is that the single-slice scanners acquire tomographic images over a 10-15 minute time period. This long CT acquisition time can result in increased patient motion and degradation of image quality.

Newer hybrid SPECT/CT cameras with multi-slice CT scanners are currently available from several vendors. These faster multi-slice CT scanners will lessen the problems of low resolution and long acquisition time. Similar to PET/CT, the nuclear medicine component of the scan is still limited by lesion size, target-to-background ratio, and the resolution of the gamma cameras.

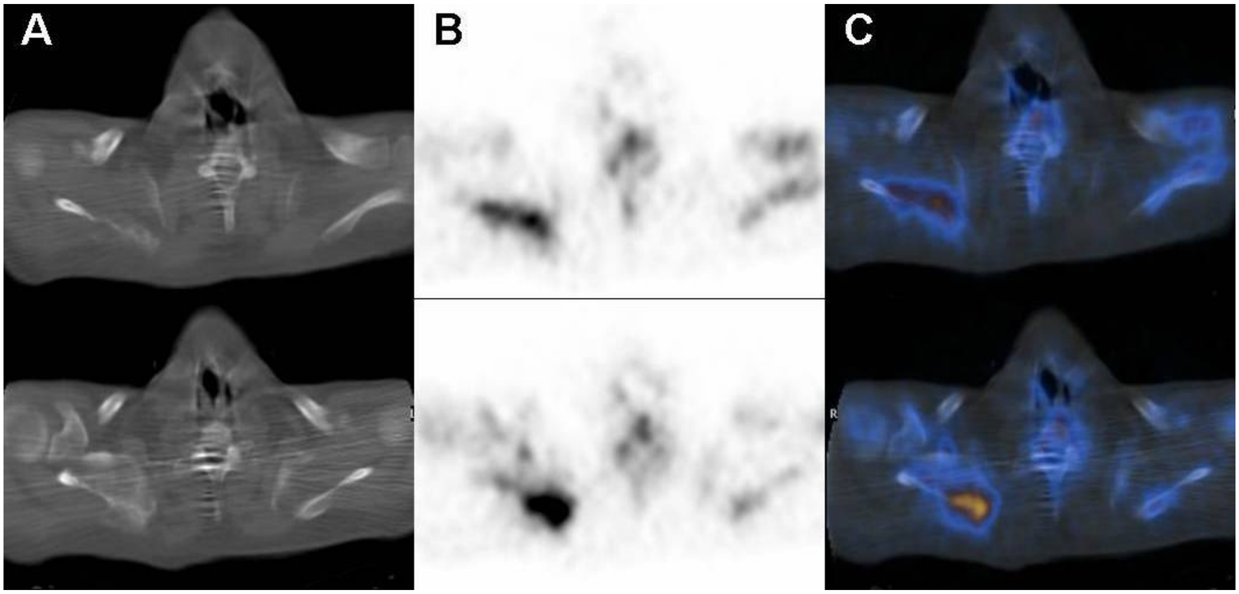

Fig. (12). A 50-year-old male with non-small cell lung carcinoma presented for evaluation for metastatic disease. A bone scan (not shown) detected a right scapular lesion on planar and SPECT images (**B**). Correlation with the fused SPECT/CT (**C**) images revealed that the lesion was more extensive and beginning to extend into the soft tissue posterior to the scapula (Top and Bottom Rows: **A**: CT; **B**: SPECT; **C**: fused SPECT/CT).

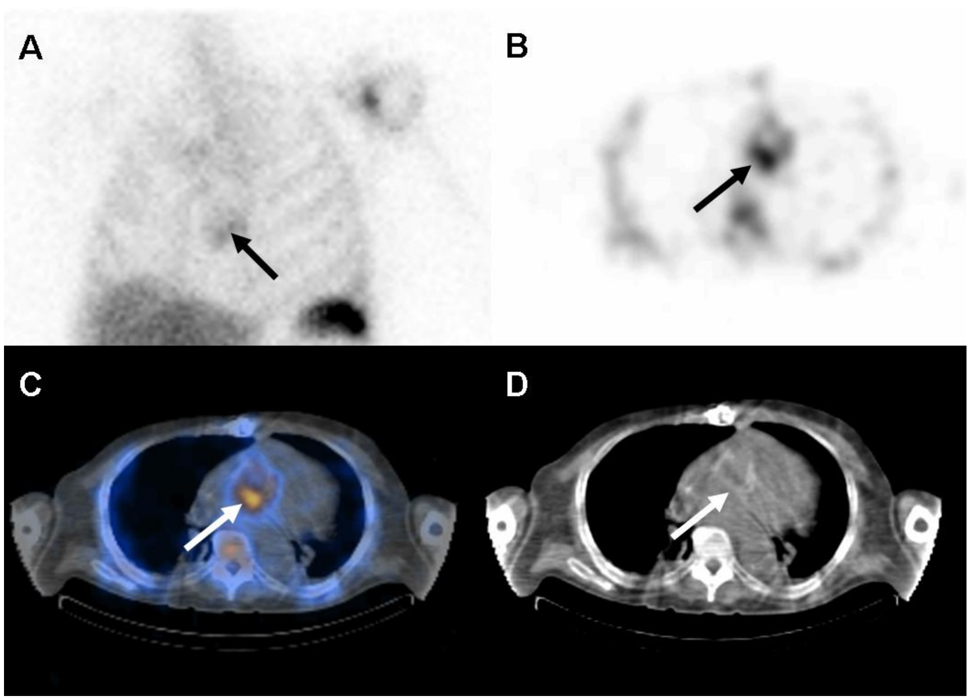

Fig. (13). A 69-year-old male with a history of cardiomyopathy status post two aortic valve replacements presented with high fevers and multiple septic joints. A transesophageal echocardiogram was unable to be performed for technical reasons. He was referred for an ^{111}In-leukocyte study to evaluate for endocarditis. A left anterior oblique planar image of the thorax (**A**) demonstrated focal white blood cell accumulation in the mid thorax behind the sternum. Combined SPECT/CT images (**B**: SPECT, **C**: Fused SPECT/CT, **D**: Diagnostic CT) allowed precise localization of the abnormal activity to the aortic value prosthesis. The length of the patient's antibiotic course was extended (**A**; planar; **B**: SPECT; **C**: fused SPECT/CT; **D**: CT).

There is little published data regarding SPECT/CT with multi-slice CT scanners [24]. Our early experience suggests that the high expectations for these new higher resolution systems are true (Figs. **14-16**). However, further data is needed. A study comparing hybrid SPECT/low dose CT, side-by-side SPECT and diagnostic CT, and side-by-side hybrid SPECT/low dose CT and diagnostic CT found that the combination of hybrid SPECT/low dose CT and diagnostic CT has the highest sensitivity, specificity, and accuracy for neuroendocrine tumor detection, supporting this hypothesis [16].

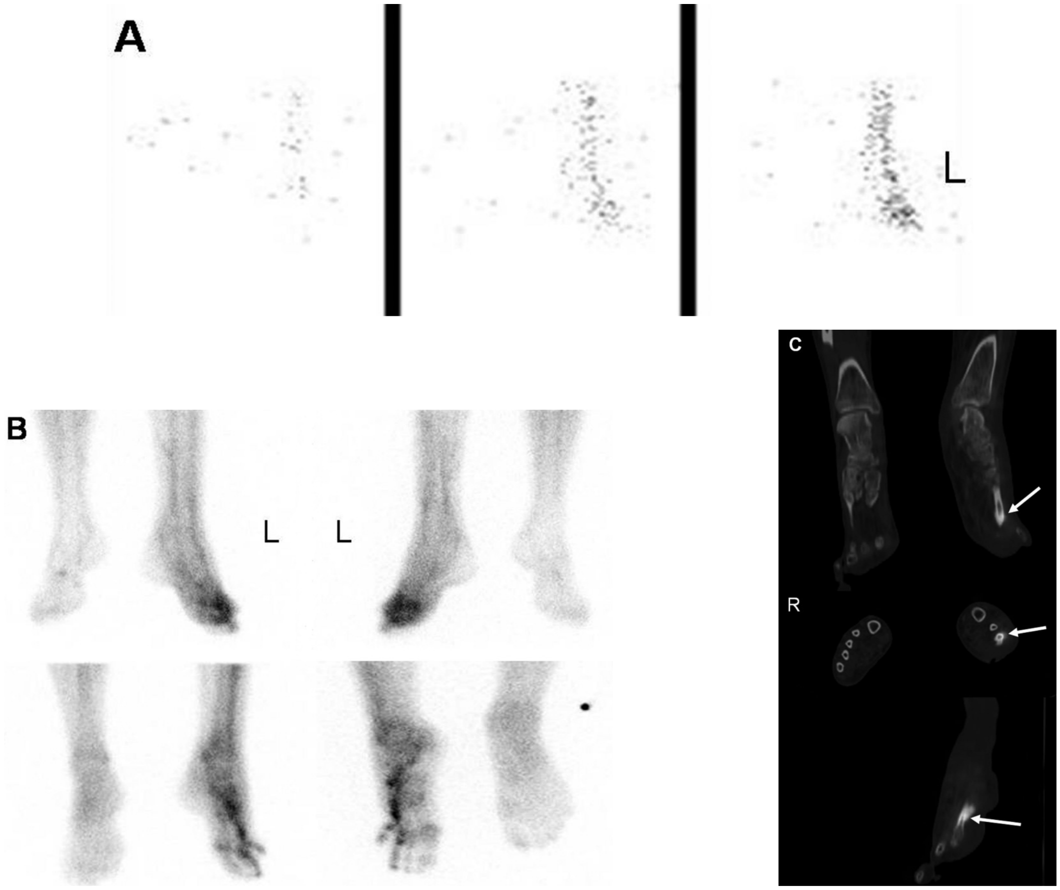

Fig. (14). A 65-year-old male with a history of IV drug abuse and methicillin resistant staphylococcus aureus infection presented with left foot edema, erythema, pain and chills for a three phase bone scan with ^{99m}Tc-MDP to evaluate for osteomyelitis. Flow images of the feet demonstrated increased blood flow to the left foot *vs* the right (**A**). Blood pool images (**B**: top row) demonstrated diffusely increased radiotracer uptake in the distal foot. There was more focal tracer accumulation in a linear pattern on the delayed bone images (**B**: bottom row) but it was difficult to definitely distinguish overlying soft tissue uptake from bone uptake. Fused SPECT/CT images (**C**) precisely localized the abnormally increased activity to left 3rd metatarsal. SPECT/CT confirmed that the diagnosis was osteomyelitis of the 3rd metatarsal and not cellulitis.

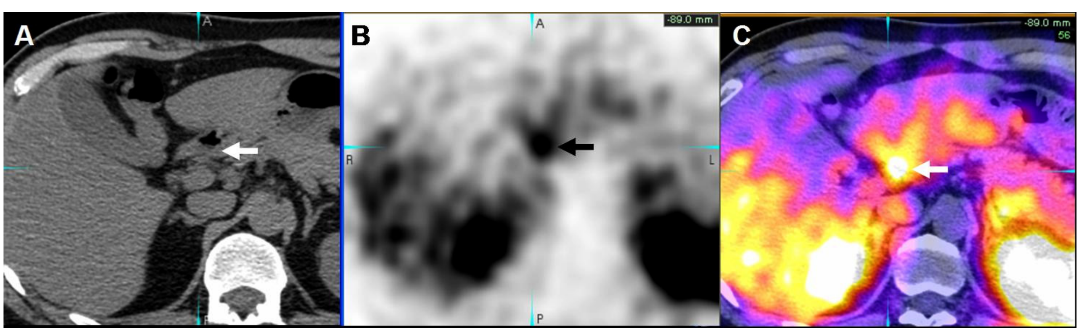

Fig. (15). A 52-year-old female presented with a profuse diarrhea and vomiting. Work-up revealed a duodenal carcinoid on endoscopic biopsy. Her symptoms resolved post-biopsy, and she was referred for ^{111}In-Pentetreotide imaging to evaluate for residual carcinoid tumor. SPECT images (**B**) demonstrated a focus of intense activity in the mid to right upper abdomen (black arrow). This activity fused to the duodenum on the concurrent CT scan obtained as part of the SPECT/CT study (**A**) and fused images (**C**, white arrows). Follow-up 3-D CT scan of the abdomen with IV contrast revealed a 9 mm hypervascular mass at the junction of the 1st and 2nd parts of the duodenum. Duodenectomy was performed and pathology confirmed the diagnosis of carcinoid tumor (**A**: CT; **B**: SPECT; **C**: fused SPECT/CT).

Like PET/CT, the CT data obtained from the combined scan is used to generate a transmission map for attenuation correction. Attenuation algorithms for SPECT/CT have been evaluated for ^{111}In-Capromab Pendetide scintigraphy [40, 41] and have been shown to improve SPECT image quality and result in improved reader confidence [21]. However, also like PET/CT, attenuation artifacts from metal or misregistration can be propagated into the SPECT images. Misregistration between the SPECT and CT scans can occur due to patient, bowel or respiratory motion and readers should quality control images while interpreting SPECT/CT images.

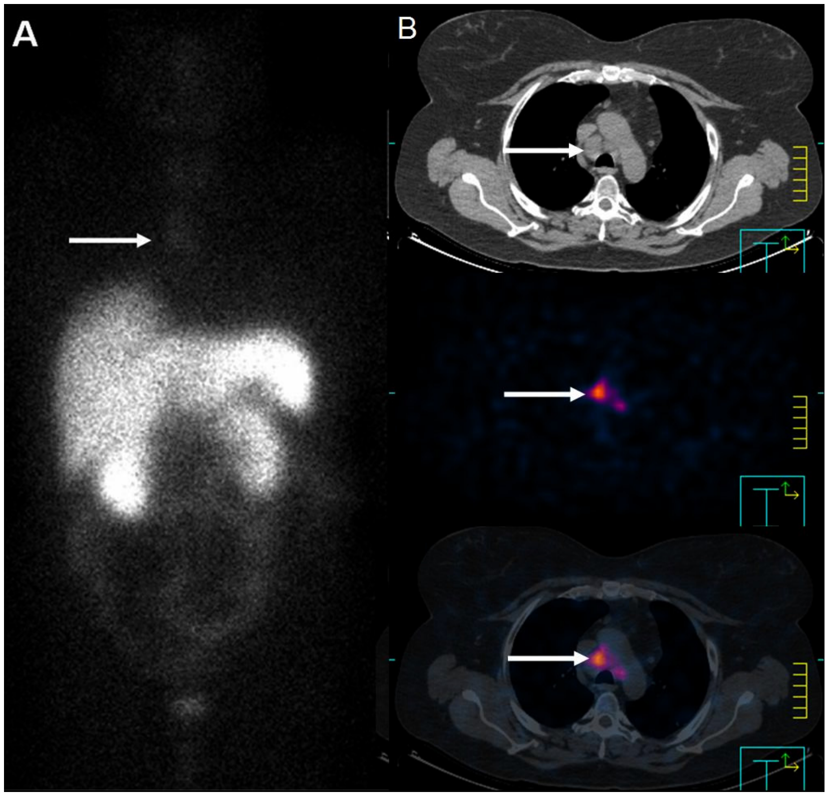

Fig. (16). A 44-year-old female with a history of metastatic adrenal cortical carcinoma to the liver was found to have mediastinal lymphadenopathy and referred for further evaluation with ^{111}In-Pentetreotide. Planar images at 24 hours demonstrated faint radiotracer activity in the mediastinal region (**A**, arrow). SPECT/CT images (**B**) demonstrated focal localization of ^{111}In-Pentetreotide to enlarged right paratracheal lymph nodes (arrows) most consistent with somatostatin receptor positive tumor. The precise localization of the questionable activity in the mediastinum to abnormal lymph nodes allowed us to make a definitive diagnosis. The plan was to treat the patient's metastatic disease with systemic therapy on a clinical trial.

The growth of SPECT/CT has been considerably slower than that of PET/CT. One reason is that less data has been published showing the advantage of SPECT/CT over SPECT alone. However, the data are growing, and we feel that our results further confirm the general clinical utility of SPECT/CT.

The CT portion of SPECT/CT results in additional radiation to the patient. Based on phantom studies, the typical radiation dose from the CT with hybrid SPECT/low dose CT scan ranged from 1.3 mGy at the center of the phantom to 5 mGy at the surface compared to the 20 mGy for a typical diagnostic quality CT scan [13]. The CT acquisition parameters in the phantom studies were the same that we used. Thus, the radiation dose to the patient is quite low, and our data and others suggest that the benefits of anatomic localization outweigh the low risk of additional radiation. With the new SPECT/multi-slice CT scanners the radiation dose will be higher. This issue is being discussed increasingly with multi-slice CT in general. Although the benefit *vs* risk ratio is often high, minimization of radiation dose to the patient is important. In the future, it would not be surprising if only a single diagnostic study will be ordered, i.e., a hybrid SPECT/diagnostic CT scan with or without contrast.

SUMMARY

Hybrid SPECT/CT imaging is clinically useful compared to SPECT alone because of improved anatomic localization and diagnostic certainty for wide a variety of clinical study types. Hybrid SPECT/low dose CT can also provide a "road-map" for identification of previously undetected, perhaps subtle findings on anatomic imaging. SPECT/CT has been particularly helpful for further evaluation of uncertain findings on planar or SPECT images alone. The added value of SPECT/CT ultimately impacts patient care and management decisions. The CT component of the hybrid SPECT/CT cameras is being upgraded from low-resolution, single-slice CT scanners to multi-slice scanners. In the future, patients may be able to undergo a fully diagnostic procedure at a single time point.

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