Review Article

Hybrid single-photon emission computed tomography-computed tomography: A review of literature

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Abstract

The use of hybrid imaging consisting of single-photon emission computed tomography (SPECT) and X-ray transmission computed tomography (CT) scan has the advantage of providing functional and morphologic information for a given lesion or pathology in a single session. Internet search of PubMed and Google Scholar databases was undertaken. Key phrases searched were SPECT-CT and lesion categorization or characterization. Studies considered for review include a comparison of SPECT-CT versus SPECT scintigraphy, SPECT-CT versus SPECT versus planar scintigraphy, and SPECT-CT in patients with indeterminate lesions on conventional scintigraphy either for benign or malignant conditions. Fusion of functional information obtained from radionuclide imaging with morphologic information obtained from X-ray CT has improved lesion localization, characterization, and observer confidence. It has been shown to change patient management.

Keywords: Computed tomography, hybrid imaging, lesion localization and categorization, planar imaging, single-photon emission computed tomography-computed tomography

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INTRODUCTION

The use of hybrid imaging consisting of single-photon emission computed tomography (SPECT) and X-ray transmission computed tomography (CT) scan is increasing globally. Radionuclide imaging with SPECT is currently an important component of the evaluation of various diseases with a high degree of sensitivity due to its ability to provide functional information early in the disease even before morphological changes become visible on other imaging modalities.[1,2] However, the limited spatial resolution of SPECT necessitated the introduction of X-ray-based CT which has superior spatial resolution and provides morphologic information that helps in better localization of lesions seen on functional and metabolic imaging. This form of hybrid imaging has improved the staging of disease as well as the prognostic and treatment monitoring potentials of the functional and metabolic information provided by conventional nuclear medicine examinations.[3,4]

The aim of this literature review is to appraise the available reports on the use of SPECT-CT on lesion categorization as well as review the impact of SPECT-CT on lesion categorization when compared to conventional planar scintigraphy and SPECT imaging.

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METHODS

Internet search of PubMed and Google Scholar databases was undertaken. Key phrases searched were SPECT/CT AND lesion categorization OR characterization. Studies considered for review include a comparison of SPECT-CT versus SPECT scintigraphy, SPECT-CT versus SPECT versus planar scintigraphy, and SPECT-CT in patients with indeterminate lesions on conventional scintigraphy either for benign or malignant conditions.

DISCUSSION

Over the years, the main advantages of hybrid SPECT-CT imaging included accurate localization and characterization of endocrine and neuroendocrine tumors (NETs), solitary pulmonary nodules, lung cancers, brain tumors, lymphoma, prostate cancer, malignant and benign bone lesions, sentinel lymph node localization as well as precise definition of the diagnostic and prognostic profile of cardiovascular patients.[4] Adaptation of the CT field of view to foci of increased bone metabolism in a technique referred to as SPECT-guided CT has been shown to accurately classify previously indeterminate lesions on planar and SPECT imaging in the axial skeleton with certainties of 92%–100%.[5-7]

In a report of initial 2-year clinical experience with SPECT-CT by Jacene *et al*., 54% of the cases studied had additional information for image interpretation derived from the fusion of the SPECT with the CT images mostly as a result of improved localization of abnormal and physiologic SPECT findings by the CT data.[3] This study reported improved diagnostic certainty in 24% of the cases and beneficial alteration of image interpretation in 13% of the cases. However, some of the limitations included the low-resolution single-slice CT used which did not reveal the exact anatomical sites of abnormal radiotracer accumulation and prolonged CT acquisition time of 10–15 min by the single-slice scanners which resulted in increased patient motion with consequent degradation of image quality. Prolonged acquisition time has been addressed by the recent introduction of multi-slice CTs in newer versions of the SPECT-CT systems.[4] Therefore, the increasing availability of new hybrid SPECT-CT imaging equipment with advanced technology offers the opportunity to shorten image acquisition time and to provide accurate attenuation correction and image coregistration.

BONE SCINTIGRAPHY

In a retrospective study of 57 SPECT-guided CTs done by Römer *et al*.[6] among cancer patients referred for bone scintigraphy who showed foci of increased metabolism, 52 foci (91%) were classified as indeterminate lesions on SPECT alone. Of these indeterminate SPECT findings, 63% were correlated with benign findings following the application of CT. The majority of these benign findings included osteochondrosis, spondylosis, and spondylarthrosis of the spine. With the application of CT in this study, 29% of the lesions were categorized as osteolysis or sclerotic metastasis.[6] Nevertheless, 8% of the lesions remained indeterminate despite application of CT. These lesions were mainly in the ribs and the scapula. This study was able to clarify more than 90% of the SPECT findings otherwise classified as indeterminate [Figures 1-4].

Strobe *et al*.,[7] in a prospective study assessed the performance of planar bone scintigraphy compared with SPECT and SPECT fused with CT in the characterization of focal bone lesions in the axial skeleton. This study evaluated the visibility of lesions, diagnostic performance, certainty in diagnosis and performance for specific diagnoses using histologic, magnetic resonance imaging and clinical follow-up findings as reference standards. The study revealed that sensitivity and specificity for differentiation of benign from malignant bone lesions were respectively 82% and 94% for planar scintigraphy, 91% and 94% for SPECT, and 100% and 100% for SPECT fused with CT. The study also showed that SPECT fused with CT significantly ($P = 0.004$) increased certainty in diagnosis when compared with planar scintigraphy or SPECT, and as such SPECT-CT was considered the best tool for making a specific diagnosis.[7]

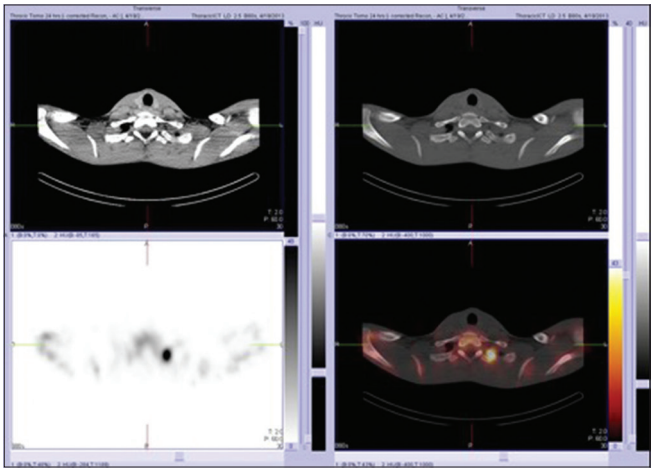

Figure 1: Bone scintigraphy with ^{99m}Tc-methylene diphosphonate. Single-photon emission computed tomography image revealed a solitary focal area of intense increased uptake of methylene diphosphonate on the left side of T1 vertebra (lower left image). The fused single-photon emission computed tomography-computed tomography image (lower right image) localized the focal area of uptake to a lytic lesion in the vertebral end of the left first rib

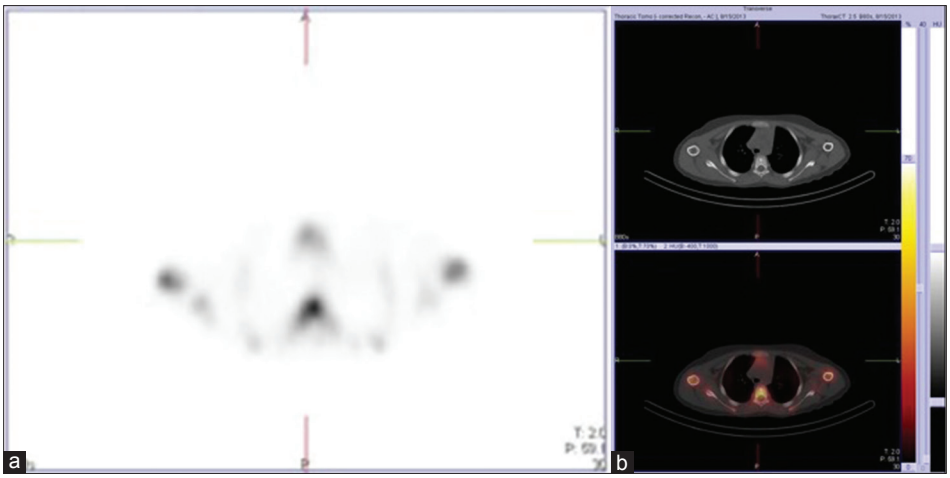

Figure 2: Bone scintigraphy with ^{99m}Tc-methylene diphosphonate. Single-photon emission computed tomography image revealed a focal area of moderate increased uptake of methylene diphosphonate on the left side of T4 vertebra (a). This finding is nonspecific. The fused single-photon emission computed tomography-computed tomography image (b) localized this area of uptake to a mixed lytic-sclerotic lesion in the vertebral body

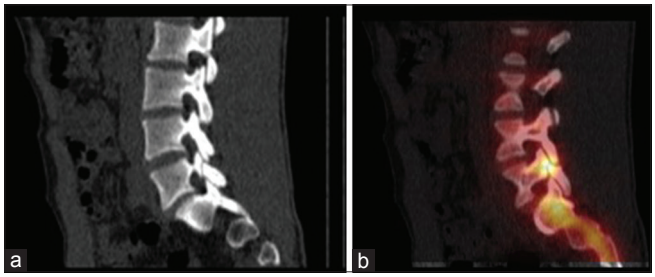

Figure 3: Sagittal low-dose computed tomography (a) and fused sagittal single-photon emission computed tomography-computed tomography (b) images showing moderate to intense ^{99m}Tc-methylene diphosphonate uptake localized to an oblique lucency traversing the pars interarticularis of L5, in keeping with a fracture in a young athlete[12]

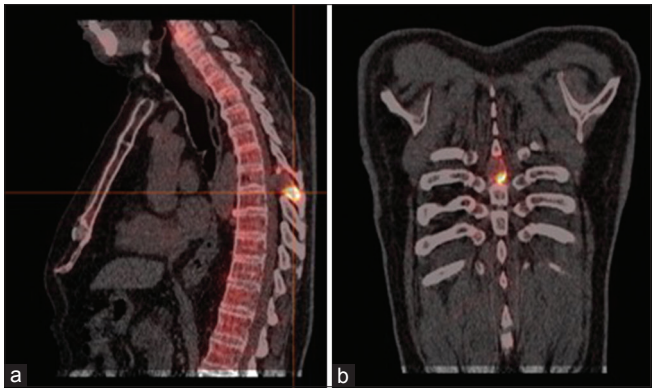

Figure 4: Sagittal (a) and coronal (b) fused single-photon emission computed tomography-computed tomography images showing an area of intense ^{99m}Tc-methylene diphosphonate uptake adjacent to an expansile lytic lesion localized to the spinous process and lamina of T6[12]

In a review by Mohan *et al.* on the assessment of the additional value of SPECT-CT amongst patients referred from the orthopedic clinics, it was observed that SPECT-CT provided additional information in 81% of the patients when compared with planar imaging.[8] SPECT-CT provided specific diagnosis in 46% of the patients in this series, and more accurate localization of degenerative or postsurgical changes in the remaining 54% of the patients. This is similar to findings by Langroudi *et al.* and Mohan *et al.*, when they compared SPECT-CT with planar imaging in the evaluation of foot and ankle pathology.[9,10]

Ndlovu *et al.* reported an SPECT-CT accuracy of 52% in a study of cancer patients with equivocal lesions on planar bone imaging for skeletal metastases.[11] This study showed a significant reduction in the proportion of lesions and patients with equivocal findings on planar scintigraphy following the utilization of SPECT-CT. In a similar study on the assessment of the impact of the application of SPECT-CT on lesion categorization, Yunusa and Brink[12] reported re-categorization of 83.3% of the lesions previously categorized as indeterminate on planar scintigraphy. In addition, this study reported that SPECT-CT improved observer confidence by demonstrating lesion detection, localization, and categorization certainties of 100%, 99.1%, and 94.7% respectively.

Recently, in a prospective study by Palmedo *et al.*[13] designed to assess the additional value of SPECT-CT of the trunk used in conjunction with conventional nuclear medicine imaging and its effects on patient management in a large patient series, it was observed that the sensitivities, specificities, and negative and positive predictive values on a per-patient basis were 93%, 78%, 95%, and 59% for planar imaging; 94%, 71%, 97%, and 53% for SPECT, and 97%, 94%, 97%, and 88% for SPECT-CT, respectively. SPECT-CT improved diagnostic accuracy for defining the extent of multifocal metastatic disease in 34.6% of the patients in this study. Therefore, it was concluded that

SPECT-CT had a significant effect on clinical management because of correct down staging and upstaging better definition of the extent of metastases and a reduction in further diagnostic procedures.

SENTINEL LYMPH NODE IMAGING

Kizu *et al*.[14] reported an accuracy of 87.1% after using SPECT fused multidetector CT images for the localization of pelvic sentinel nodes (SNs) in 11 patients with prostatic carcinoma. Similarly, Zhang *et al*. reported SPECT-CT to be superior to planar imaging in the detection of SNs in 27 patients with early stage cervical cancer scheduled for a radical hysterectomy and total pelvic lymphadenectomy.[15] This was attributed to the exact anatomical localization of the SN provided by the CT component of the SPECT-CT.

Report of comparison of planar imaging with SPECT/16-slice CT among pediatric patients by Andersen *et al*. showed that additional structural information was gained in 93% of the cases and additional functional information was gained in 80% of the cases, while specific information for biopsy guidance was gained in 40% of the cases studied.[16]

Lerman *et al*.[17] assessed whether SPECT-CT improves SN identification in overweight patients. In this study, SPECT-CT accurately identified SNs in 75% of patients for whom the identification of SNs by the intraoperative blue dye technique failed. Even-Sapir *et al*.[18] and Lerman *et al*.[19] reported that SPECT-CT data allowed the detection of "hot" nodes missed by planar imaging, excluded sites of false-positive nonnodal uptake, and accurately localized axillary and extra-axillary hot nodes. These studies are also in agreement with the findings by Husarik and Steinert[20] who evaluated the clinical use of integrated SPECT-CT in the identification of SNs in patients with operable breast cancer. This study showed that localization and identification of SNs was more accurate by integrated SPECT-CT imaging compared with planar or SPECT images, respectively. SPECT-CT showed more accurate information in 82% of the patients by demonstrating the exact anatomical information needed to assign the SN levels according to the American Joint Committee on Cancer. SNs close to the injection sites that were not visible on planar images due to scatter radiation were detected with SPECT-CT in 14% of the patients.

Kretschmer *et al*. found SPECT-CT to be an excellent tool to anatomically localize the SN in malignant melanoma-draining to the pelvic region.[21] In a prospective study, Garcia-Burillo *et al*.[22] assessed the impact of SPECT-CT sentinel lymph node identification in papillary thyroid carcinoma (PTC) with respect to lymphatic staging and surgical management improvement. This study showed that lymphoscintigraphy revealed at least one SN in 19 of 24 patients (79%) on planar and SPECT-CT images. SPECT-CT detected laterocervical drainage in a significant percentage of patients, thereby allowing the detection of occult lymph node metastases and improving the surgical management in patients with (PTC). In a similar study Wagner *et al*. evaluated SPECT-CT topographic mapping of SNs before gamma-probe-guided biopsy in thirty patients with head and neck squamous cell carcinoma and found that SPECT-CT enhanced anatomical localization, improved diagnostic sensitivity, and detected more SNs than planar lymphoscintigraphy.[23]

INFECTION AND INFLAMMATION IMAGING

In a study by Filippi and Schillaci[24] carried out to assess the usefulness of hybrid SPECT-CT in ^{99m}Tc-HMPAO labeled leukocytes scintigraphy for bone and joint infections, SPECT-CT provided accurate anatomic localization of all positive foci and also provided significant additional contribution with regards to the final diagnosis in 10 of the 28 patients (35.7%) studied. SPECT-CT differentiated soft tissue from bone involvement in patients with osteomyelitis and in patients with orthopedic implants. It allowed correct diagnosis of osteomyelitis in patients with structural alterations after trauma and identified synovial infection without prosthesis involvement in patients with knee implant. In a similar study using $^{99\ m}$Tc-labeled antigranulocyte antibodies Horger *et al*.[25] reported that SPECT-CT improves the accuracy of immunoscintigraphy for the diagnosis of chronic osteomyelitis, especially in discriminating soft tissue from bone involvement.

ENDOCRINE IMAGING

Differentiated thyroid carcinoma

In the assessment of the incremental value of SPECT-CT versus planar imaging using Iodine-131 (^{131}I) SPECT-CT in the follow-up of differentiated thyroid carcinoma Spanu *et al*.[26] observed that SPECT-CT correctly characterized 48 foci that were hitherto unclear on planar imaging, and precisely defined their location and extent. SPECT-CT was a sole determinant in classifying as neoplastic those foci for which planar imaging seemed to exclude malignancy. SPECT-CT also discriminated between residual primary disease and lymph node metastases in the neck, some of which were adjacent to the salivary glands and had been missed on planar scintigraphy. This study showed that SPECT-CT had an incremental value over planar imaging

in 67.8% of patients, modified therapeutic management in 35.6% of positive cases, and avoided unnecessary treatment in 20.3% of patients with a single benign lesion or physiologic uptake.

Tharp *et al*.[27] also demonstrated that SPECT-CT had an incremental diagnostic value in 58% of the patients studied. SPECT-CT improved the characterization of indeterminate findings as definitely benign in 13% of patients and the precise localization of metastases to the skeleton in 17% of patients, and to the lungs versus the mediastinum in 7% of patients. SPECT-CT further optimized the localization of radioiodine uptake to nodal metastases versus remnant thyroid tissue [Figure 5]. Overall, additional findings at SPECT-CT had an effect on the management in 41% of patients by influencing the referral for ^{131}I treatment, tailoring of the administered radioiodine dose, and/or the addition of surgery or external radiation therapy when indicated. The findings are similar to that of Ruf *et al*.[28] in which SPECT-CT correctly classified most radioiodine-avid foci as benign or malignant, provided a superior anatomical localization for 44% of lesions, and modified the therapeutic procedure in 25% of patients.

Parathyroid adenoma

Krausz *et al*. reported that ^{99m}Tc-MIBI SPECT-CT of the parathyroid glands contributed to the localization of parathyroid adenomas in patients with primary hyperparathyroidism, and to planning the surgical exploration in 39% of patients with predominantly ectopic parathyroid adenomas or those with distorted neck anatomy from previous surgeries.[29] This is in agreement with the findings by Serra *et al*.[30] who examined the role of SPECT-CT in the preoperative assessment of hyperparathyroid patients and reported that SPECT-CT provided additional data in 39% of lesions and modified the surgical approach in 19% of patients with retrotracheal parathyroid glands.

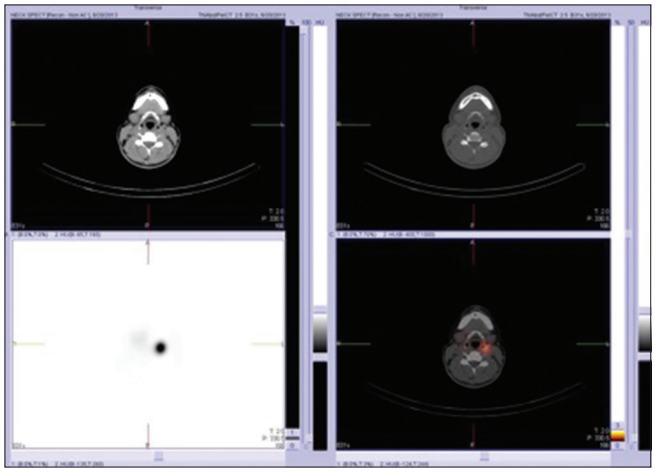

Figure 5: Diagnostic Iodine-131 whole body scan in a patient previously treated for papillary carcinoma of the thyroid. Single-photon emission computed tomography image showed focal area of intense increased uptake of Iodine-131 in the left side of the neck (lower left image). Single-photon emission computed tomography-computed tomography localized the focus of Iodine-131 uptake to a subcentimeter left submandibular lymph node (lower right image)

Neuroendocrine tumors

Hillel *et al*. in a study of 29 patients most of whom had a diagnosis of carcinoid and were referred for ^{111}In-pentetreotide somatostatin receptor imaging (SRI) with SPECT-CT, 64% of the abnormal foci were established to a previously unknown location while SPECT-CT changed the location of at least one lesion in 36% of the cases.[31] This study concluded that the application of SPECT-CT improves the reporting accuracy for SPECT SRI with a significant impact on patient management. In a similar study by Castaldi *et al*.[32] involving 54 patients with known or suspected NET, SPECT-CT improved image interpretation in 23 (43%) cases, provided precise anatomical localization of increased tracer uptake in 20 (37%) cases and disease exclusion in sites of physiological uptake in 5 (9%) cases. SPECT-CT also allowed the definition of the functional significance of lesions detected by diagnostic CT in 10 (19%) patients. In addition, SPECT-CT led to modification of clinical management in 14 (26%) cases by changing the diagnostic approach in 8 (15%) and the therapeutic modality in six (11%). Krausz *et al*. reported that SPECT-CT affected the diagnostic interpretation in 32% of patients with known or suspected NETs and resulted in a change in management in 14% by altering the surgical approach, sparing unnecessary surgery, and/or modifying the therapeutic modality.[33] Pfannenberg *et al*.[34] reported that, therapy was modified in 28% of patients owing to the results of image fusion: in 5 patients, tumor could be excluded, in three patients, the individuals were spared from undergoing unnecessary surgery due to detection of additional lesions indicating systemic tumor spread, in four patients the surgical approach was modified owing to precise tumor localization and minimization of the surgical field, and in two patients medical and radiopeptide therapy was modified.

In the evaluation of the added value of MIBG SPECT-CT in patients with neuroblastoma and pheochromocytoma, Rozovsky *et al*.[35] reported that SPECT-CT provided the additional clinical information in 53% of the cases. SPECT-CT differentiated between bilateral symmetric upper thoracic activity related to physiological muscular or brown fat uptake, and malignant lesions, such as skeletal metastases in the scapula, ribs, or malignant supraclavicular lymphadenopathy.

^{99M}TC-LABELED RED BLOOD CELL SCAN

Schillaci *et al.* evaluated the usefulness of ^{99m}Tc-red blood cell (RBC) SPECT and SPECT-CT performed simultaneously with a hybrid imaging system for correct characterization of hepatic lesions in patients with suspected hemangioma, and assessed the additional value of fused SPECT-CT images compared with SPECT alone. SPECT-CT had a significant impact on results in 33.3% of the patients with four lesions defined as indeterminate on SPECT images, accurately characterizing the hot spot foci located near vascular structures.[36] SPECT-CT has also been used to localize foci of ^{99m}Tc-RBC uptake attributable to residual splenic tissue following splenectomy [Figure 6].

The applicability of SPECT-CT in patients with acute lower gastrointestinal bleeding undergoing scintigraphy with ^{99m}Tc-RBC and assessment of the additional clinical value of fused images when compared to the standard radionuclide scan were evaluated by Schillaci *et al.*[37] In this study, SPECT-CT had a significant impact on the scintigraphic results in 7 of 19 patients (36.8%), it precisely localized the bleeding foci whose location could not be identified on standard scans in 6 patients, and in one it excluded the presence of an active gastrointestinal hemorrhage.

RADIOIMMUNOSCINTIGRAPHY

In a review of the synergistic value of SPECT-CT in radioimmunoscintigraphic imaging of prostate cancer, Sodee *et al.*[38] opined that ^{111}In-Capromab Pentetide (ProstaScint), SPECT-CT imaging can be used not only to identify primary, metastatic and prostate cancer recurrence but also to guide external beam radiation therapy, intensity modulated radiation therapy, and brachytherapy as well as to monitor treatment of the disease. This corroborated the earlier observations by Jana and Blaufox[39] that SPECT-CT increases the accuracy of ProstaScint scan.

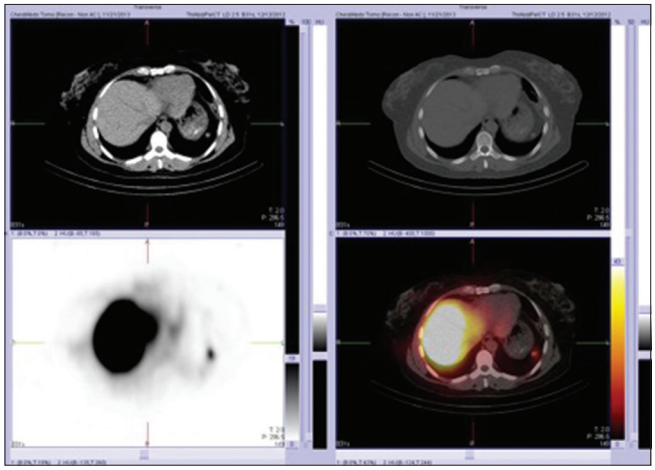

Figure 6: Spleen scan using heat damaged red blood cell labeled with ^{99m}Tc in patient known with autoimmune hemolytic anemia (Evan's syndrome). The patient had splenectomy. Single-photon emission computed tomography image (lower left) showed a focal area of ^{99m}Tc-red blood cell uptake which was localized by the fused single-photon emission computed tomography-computed tomography to a residual splenic tissue in the splenic bed posterolateral to the splenic flexure of the colon consistent with splenunculi

CONCLUSION

The fusion of functional information obtained from radionuclide imaging with morphologic information obtained from X-ray CT has improved lesion localization, characterization, and observer confidence. These advantages have changed patient management and in some instances prevented further unnecessary imaging.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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