Clinical Usefulness of Fusion of $^{131}$I SPECT and CT Images in Patients with Differentiated Thyroid Carcinoma

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Precise localization of the foci of $^{131}$I uptake for management of patients with differentiated thyroid carcinoma can be difficult because of a lack of anatomic landmarks. The objective of the present study was to demonstrate the clinical usefulness of $^{131}$I SPECT/CT fusion images in patients with differentiated thyroid carcinoma. Methods: CT and SPECT were performed 7 d after administration of a therapeutic dose of $^{131}$I to 17 patients with differentiated thyroid carcinoma. External markers were placed at 3 locations on the skin of the patient to adjust the sections of CT and SPECT in the same geometric plane. Fusion images were constructed by combining the digital CT and SPECT images on a computer workstation. The data from both planar and SPECT $^{131}$I images and CT images were first separately assessed by 2 nuclear medicine physicians. $^{131}$I SPECT/CT fusion images were then interpreted. Fusion images were considered to improve image interpretation in comparison with CT and scintigraphy separately when they provided better localization of sites of increased radiopharmaceutical uptake. Results: Both CT and $^{131}$I SPECT showed the pathologic sites in 5 of 17 patients (29%). Fusion images were considered to be of benefit in 15 of 17 patients (88%). In 4 patients, CT showed normalized lymph nodes, whereas $^{131}$I SPECT showed abnormal findings. In 3 patients with bone metastasis, fusion images confirmed the precision of the localization of abnormal $^{131}$I uptake. Five bone metastases and 1 muscle metastasis were occult and were not seen on the CT images. Finally, $^{131}$I scintigraphy findings were abnormal for 2 patients for whom the CT findings were initially considered normal. Fusion images confirmed the precision of the localization of physiologic $^{131}$I uptake. Conclusion: For registration of anatomic and functional images in fusion imaging, the method using external markers was simple and practical. $^{131}$I SPECT/CT fusion images using this technique may improve anatomically limited interpretation of $^{131}$I scintigraphy alone in patients with differentiated thyroid carcinoma. Key Words: $^{131}$I; CT; fusion image; thyroid carcinoma

Nuclear medicine imaging provides excellent information on functional biology. However, the anatomic information obtained from this technique is generally quite limited. In contrast, CT and MRI are excellent anatomic imaging modalities. Combination of the functional information from nuclear medicine imaging and the anatomic information from CT and MRI can improve diagnostic capability and facilitate image interpretation (1,2).

$^{131}$I scanning is indispensable for the management of patients with differentiated thyroid carcinoma (3). However, precise localization of the foci of $^{131}$I uptake can be difficult because of a lack of anatomic landmarks. In addition, there are many other potential sites of physiologic uptake, such as the salivary glands, urinary bladder, gastrointestinal tract, and liver (4). Precise tumor localization for correct diagnosis and assessment of disease extent and metastatic spread is important for determining outcome in patients with thyroid carcinoma. SPECT should be performed to improve the sensitivity of $^{131}$I imaging and to allow better localization of the tumor site. However, precise localization of tumor foci can still remain difficult despite optimal technical conditions and careful correlation with morphologic imaging. These difficulties may be related to various factors including lack of anatomic landmarks and physiologic distribution of the tracer.

Multimodality image coregistration can be achieved by several techniques using external markers or internal landmarks. Recently, CT combined with SPECT or PET has been developed (5–7). However, because of high cost, these systems are available in few centers and are limited to the combination of the above 3 modalities. The purpose of the present study was to demonstrate the clinical usefulness of $^{131}$I SPECT/CT fusion images using external markers in patients with differentiated thyroid carcinoma.

MATERIALS AND METHODS

The study had 2 parts: a preclinical phantom study to validate the image fusion technique using CT and SPECT imaging systems, and a clinical feasibility study with 17 patients to assess the value of CT and $^{131}$I SPECT image fusion.
Preclinical Phantom Study

A cylindric phantom was prepared to check the accuracy and reproducibility of the methodology for registering CT and SPECT images. The phantom consisted of 5 ellipsoidal-shaped sources (5 cm long and 2 cm in maximum diameter) as internal landmarks filled with normal water and a 131I solution with an activity of 25 kBq/mL for the CT and SPECT studies, respectively. The rest of the phantom was filled with normal water and a 131I solution with an activity of 5 kBq/mL for the CT and SPECT studies, respectively. Three external markers (multimodality radiographic marker MM3003; IZI Medical Products) suitable for CT and SPECT scans were defined on the surface of the phantom. The MM3003 marker is disk shaped, with a sealant covering the top and forming a well in the center. For SPECT, 99mTc-pertechnetate (approximately 185 Bq per marker) was placed in the well of the external markers.

SPECT images were obtained using a dual-head γ-camera (Picker Prism 2000; Marconi Medical Systems) equipped with high-energy parallel-hole collimators. Acquisitions were performed with dual-energy windows: a 20% energy window centered at 364 keV for the 131I images and a 20% window centered at 141 keV for the markers (99mTc). The data acquisition included a 360° rotation with 72 projections and a matrix of 64 × 64. CT images were obtained using multislice spiral CT scanning (Aquilion; Toshiba).

Clinical Feasibility Study

Patients. 131I SPECT/CT fusion images after an oral therapeutic dose of 131I (3.7–7.4 GBq) were obtained for 17 consecutive patients whose 131I planar images showed an abnormality. The patients (8 male, 9 female; age range, 15–79 y; mean age, 49.5 y) had differentiated thyroid carcinoma (13 with papillary carcinoma, 7 with follicular carcinoma) and had undergone total thyroidec- tomy. Each patient gave informed consent for participation in the study.

CT. CT was performed 7 d after administration of a therapeutic dose of 131I. Before CT acquisition, 3 external markers were placed at 3 locations: on the glabella and left and right axillary areas for head; on the manubrium and left and right axillary areas for thoracic SPECT; around the umbilicus and the iliac crests for abdominal/pelvis SPECT; and on the pubic bone and left and right thighs for leg SPECT. While the patient was breathing naturally, multislice spiral CT scanning (Aquilion; Toshiba) was performed. The mean deviation expressed as rms in millimeters was 2.65 ± 0.74 (±SD). This deviation was less than the intrinsic resolution of the SPECT image (7 mm).

RESULTS

Preclinical Phantom Study

Using the 3 external markers, the mean deviation expressed as rms in millimeters for CT/SPECT fusions was 2.65 ± 0.74 (±SD). This deviation was less than the intrinsic resolution of the SPECT image (7 mm).

Clinical Feasibility Study

All lesions in the present study could not be confirmed by surgery and were validated by radiologic and clinical follow-up of at least 6 mo.
determine the precise location of the foci from SPECT images alone in 3 patients. In 2 patients, both imaging modalities showed abnormality in the mediastinal lymph node. In the remaining 12 patients, CT showed normal findings, whereas 131I scintigraphy showed abnormal findings.

131I SPECT/CT Fusion Data. Additional information for image interpretation was provided by 131I SPECT/CT fusion images in comparison with CT and 131I scintigraphy separately in 15 of 17 patients (88%). The details of imaging data are listed in Table 1. In 4 patients, CT showed normal-sized lymph nodes, smaller than 1 cm in diameter, whereas 131I scintigraphy showed abnormal findings. In 3 patients with bone metastasis, fusion images confirmed the precision of the localization of abnormal 131I uptake. Five bone metastases (Fig. 1) and 1 muscle metastasis (Fig. 2) were occult metastases and were not seen on the CT images. Finally, 131I scintigraphy showed abnormal findings for 2 patients for whom the CT findings were initially considered normal. Fusion images confirmed the precision of the localization of physiologic 131I uptake.

In 2 patients—patients 6 and 8 in Table 1—in whom bone metastasis with suspected nonosseous metastasis was detected separately on CT and SPECT, fusion images did not change the decision regarding the use of 131I treatment but did influence the therapeutic dose of 131I. In patients 14 and 15, on the other hand, fusion images excluded the tumor as the cause of uptake by showing the suspected focus to be in physiologic sites. These 2 patients were spared unnecessary treatment.

DISCUSSION

Using external markers, we have demonstrated the clinical usefulness of 131I SPECT/CT fusion images in patients with differentiated thyroid carcinoma. Different imaging modalities provide different but complementary information. Both CT and MRI are used primarily for imaging anatomic changes associated with an underlying pathology, whereas the molecular imaging techniques of PET and SPECT capture functional or metabolic changes associated with the pathology. The use of anatomic and functional image fusion is increasing in nuclear medicine, and especially in oncology (1,2,5–15). Anatomic and functional information are combined to aid diagnosis, allow accurate tumor localization, and improve the outcome of treatment planning (12).

### Table 1

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Histologic type</th>
<th>131I scintigraphy</th>
<th>CT/131I SPECT</th>
<th>Additional information from CT/131I SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>73</td>
<td>Papillary</td>
<td>Increased focal uptake in left neck</td>
<td>Uptake in left neck, normal-sized lymph node</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>76</td>
<td>Papillary</td>
<td>Increased focal uptake in upper mediastinum</td>
<td>Uptake in upper mediastinum, normal-sized lymph node</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>46</td>
<td>Papillary</td>
<td>Increased focal uptake in upper mediastinum</td>
<td>Uptake in upper mediastinum, normal-sized lymph node</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>24</td>
<td>Papillary</td>
<td>Increased focal uptake in upper mediastinum</td>
<td>Uptake in upper mediastinum, normal-sized lymph node</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>47</td>
<td>Papillary</td>
<td>Increased focal uptake in thoracic vertebra</td>
<td>Uptake in posterior portion of ninth rib</td>
<td>Detection of occult bone involvement</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>39</td>
<td>Papillary</td>
<td>Increased focal uptake in posterior midabdomen</td>
<td>Uptake in second lumbar spine</td>
<td>Detection of occult bone involvement</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>15</td>
<td>Papillary</td>
<td>Increased focal uptake in right pelvis</td>
<td>Uptake in right iliac wing</td>
<td>Detection of occult bone involvement</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>37</td>
<td>Papillary</td>
<td>Increased focal uptake in left upper mediastinum</td>
<td>Uptake in sternum</td>
<td>Detection of occult bone involvement</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>23</td>
<td>Papillary</td>
<td>Increased focal uptake in left thorax</td>
<td>Uptake in lateral portion of seventh rib</td>
<td>Detection of occult bone involvement</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>61</td>
<td>Follicular</td>
<td>Increased focal uptake in right pelvic bone</td>
<td>Uptake in right iliac wing</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>73</td>
<td>Follicular</td>
<td>Increased focal uptake in posterior midabdomen</td>
<td>Uptake in third lumbar spine</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>79</td>
<td>Follicular</td>
<td>Increased focal uptake in thoracic spine</td>
<td>Uptake in tenth thoracic spine</td>
<td>Localization of lesion</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>72</td>
<td>Papillary</td>
<td>Increased uptake in posterior part of right thigh</td>
<td>Uptake in biceps of right thigh</td>
<td>Detection of occult muscle involvement</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>39</td>
<td>Papillary</td>
<td>Increased uptake in lower abdomen</td>
<td>Uptake in urinary bladder (physiologic)</td>
<td>Localization of physiologic uptake</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>51</td>
<td>Papillary</td>
<td>Increased uptake in anterior lower neck</td>
<td>Uptake in site of tracheostomy (physiologic)</td>
<td>Localization of physiologic uptake</td>
</tr>
</tbody>
</table>
Whole-body imaging after an oral dose of $^{131}$I is commonly performed to identify residual or metastatic tumor during the treatment of differentiated thyroid carcinoma. Scintigraphic procedures after administration of $^{131}$I have a higher sensitivity for the detection of metastases from thyroid carcinoma than do anatomic imaging modalities. However, interpretation of $^{131}$I images is difficult because of the absence of readily identifiable anatomic structures. Therefore, precise lesion localization is often not possible. In addition, knowledge about $^{131}$I physiologic uptake is essential to avoid false-positive results in the interpretation of $^{131}$I SPECT. It is also important for assessing additional $^{131}$I treatment and monitoring the response to therapy. Correlation of anatomic and metabolic images is usually done visually by separate readings of CT/MRI and SPECT images. Misinterpretations can result, especially for small lesions. In the present study, $^{131}$I SPECT/CT fusion imaging allowed precise localization of $^{131}$I uptake in patients with differentiated thyroid carcinoma and, in comparison with separate analysis of CT and scintigraphy, improved the diagnosis in 15 of 17 patients (88%). In the abdominal and pelvic areas, $^{131}$I SPECT/CT fusion imaging helped in differentiating physiologic urinary bladder elimination of $^{131}$I from its abnormal uptake. The therapeutic dose of $^{131}$I was changed in 2 patients because of the findings of fusion imaging. Two other patients were spared unnecessary treat-

![Figure 1](image1.png)

**FIGURE 1.** A 47-y-old woman (patient 5) with differentiated papillary thyroid carcinoma underwent total thyroidectomy. (A) $^{131}$I whole-body images (left, anterior view; right, posterior view). (B) CT images (first row), $^{131}$I transaxial SPECT images (second row), and $^{131}$I SPECT/CT fusion images (third row). $^{131}$I planar and SPECT images show intense focal uptake in posteromedial region, but slightly on left side of chest, suggesting thoracic spine involvement. Uptake in neck is thyroid bed. Bone appears normal on diagnostic CT scan. $^{131}$I SPECT/CT fusion images show that intense tracer uptake is in posterior portion of 9th rib and not in thoracic vertebra. In this patient, final diagnosis was made on basis of follow-up; follow-up period was 12 mo, and clinically, fusion images confirmed precision of localization of abnormal $^{131}$I uptake.

![Figure 2](image2.png)

**FIGURE 2.** A 72-y-old woman (patient 13) with differentiated papillary thyroid carcinoma underwent total thyroidectomy. (A) $^{131}$I whole-body images (left, anterior view; right, posterior view). (B) CT images (first row), $^{131}$I transaxial SPECT images (second row), and $^{131}$I SPECT/CT fusion images (third row). $^{131}$I planar and SPECT images show focal uptake in posterior part of right thigh, suggestive of right femoral bone or muscle involvement. Intense uptake in neck is thyroid bed. Bone appears normal on diagnostic CT scan. $^{131}$I SPECT/CT fusion images show that intense tracer uptake is located in biceps of right thigh and not in femoral bone. In this patient, final diagnosis was made on basis of follow-up; follow-up period was 9 mo, and clinically, fusion images confirmed precision of localization of abnormal $^{131}$I uptake.
ment because of the fusion findings. For these 4 patients, the information provided by the image registration technique had an impact on management.

Peraut et al. assessed the feasibility of registration with CT in 13 patients with endocrine carcinoma evaluated with 131I, 131I-MIBG, and 111In-pentetreotide (14). The investigators obtained simultaneous dual-isotope acquisitions using these agents and 99mTc-methylene diphosphonate to get information on skeletal structures that could subsequently be correlated with anatomic data provided by CT. In their study, fused images allowed the detection and correct localization of 6 unsuspected sites of disease. At 2 sites, fusion led to better localization of known lesions; at 2 other sites, disease uptake was related to inflammatory changes seen on CT scans. The clinical value of combined transmission and emission tomography imaging was assessed using 131I, 123I-MIBG, 75Se-cholesterol, 111In-pentetreotide, and 99mTc-MIBI in 27 patients with endocrine tumors (15). For 41% of the patients, fused images improved the accuracy of nuclear medicine studies by providing better localization of SPECT-detected lesions. For one third of the patients, image fusion had a clinical impact on management.

Multimodality image coregistration can be achieved by several techniques using external markers or internal landmarks. Most fusion algorithms have been developed for brain imaging. The brain, being a rigid body, allows accurate registration (16). Internal landmarks relating to well-known sites of physiologic uptake have not been used with 131I SPECT, probably because of the lack of reliable potential internal markers. In the present study, the method used external markers placed at specific positions on the patient’s body. This method requires that CT and SPECT be performed on the same day, that the patient be imaged in the same position for both CT and SPECT, and that external markers be carefully matched. Respiration might affect that relationship, thus affecting the reliability and usefulness of the registration process. In our study, CT and SPECT were both performed while the patients were breathing freely. This was possible even in moderately cooperative patients, because of the short scanning time of helical CT. In point matching, the transformation parameters were determined by establishing a correspondence between a set of landmarks visible in both imaging modalities and minimizing the mismatch between these points. The rms error of 2.65 mm obtained in this study appears to be sufficient in view of the SPECT resolution. The accuracy obtained with the markers described here should be sufficient for image fusion of CT and SPECT. One partial solution to positioning problems is provided by integrated SPECT/CT or PET/CT systems that acquire both anatomic and functional information in the same examination (5–7). These systems allow the patient to be imaged in exactly the same position, reducing the artifacts that occur because of unavoidable minimal differences in positioning when CT and SPECT are performed successively. However, combination of the 2 modalities in the clinical setting is associated with many practical problems, such as high cost and lack of availability.

Realignment is fast when external markers are used, and a technologist trained to work with the realignment software can perform the entire procedure in less than 10 min. For clinically oriented settings, establishing such a method may be a cost-effective alternative to investment in a combined SPECT/CT device. However, it is difficult to overlap images on the correct plane because SPECT images are not sharp. In addition, because the marker definition was done manually, a small intra- and interobserver variability was possible. In the future, automated landmark selection will replace most of the manual landmark selection used in this study and should decrease the time required for fusion. Overall, the present study had some limitations. First, no lesions could be validated by histologic examination. All were validated by radiologic and clinical follow-up. This limitation was due to a selection bias toward patients presenting with occult metastasis not shown on conventional imaging or advanced disease without the need for lesion biopsy or surgery. Second, choosing the CT-scanning area on the basis of 131I planar images and not on SPECT images might have led to missed lesions. Third, only 3 external markers were used. Further studies on the clinical usefulness of fusion images are needed, using more than 3 external markers and with precise coordination between anatomic and functional images.

CONCLUSION

For registration of anatomic and functional images in fusion imaging, the external-marker method of the present study was simple and practical. 131I SPECT/CT fusion images obtained with this technique may improve the anatomically limited interpretation of 131I scintigraphy alone for patients with differentiated thyroid carcinoma.

REFERENCES


