ADDITIONAL VALUE OF POST-THERAPY ¹³¹I SPECT/CT IN PATIENTS WITH DIFFERENTIATED THYROID CANCER

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BACKGROUND
Generally, it is seen that SPECT/CT images are more useful than the planar images. We compared post-therapy ¹³¹I imaging findings on planar and SPECT/CT scans to assess the clinical utility of SPECT/CT in management of patients with differentiated thyroid cancer.

MATERIALS AND METHODS
Post-therapy imaging was performed at 4-7 (when 5mR/hrs. exposure rate were observed by the survey meter) days after ¹³¹I administration and all patients underwent whole-body scintigraphy and SPECT/CT scanning on the same day. A generalised McNemar² was used to determine to establish the agreement between planar whole-body imaging and SPECT/CT for the assignment of benign, equivocal and malignant findings.

RESULTS
In 44 patients, 32 of the 44 patients underwent postsurgical ¹³¹I ablation of residual thyroid tissue and 12 of 44 patients, 2 patients were treated twice. Hence, a total of 46 scans were analysed. SPECT/CT helped to localise focal iodine uptake and characterise it as either normal or abnormal thereby reducing the need for additional imaging studies. In post-thyroidectomy patients, SPECT/CT findings affected the ATA risk classification with implications for management by changing the interval for clinical followup and the need for additional imaging and laboratory tests. Our study found an 11% change in nodal status in the postsurgical group. Change in patient management was observed in 18%.

CONCLUSION
SPECT/CT enabled more accurate characterisation of focal iodine accumulation in patients.

KEYWORDS
Differentiated Thyroid Cancer, ¹³¹I, Post-Therapy Scan, SPECT/CT.


BACKGROUND
Thyroid carcinoma has reported incidence of 2.58% of patients presenting with thyroid disease.² Differentiated thyroid cancer, which includes papillary and follicular histologies carries a favourable prognosis compared to other cancers. However, optimal outcomes are achieved only with accurate detection of tumour in the body.³ The recent increase in the incidence of thyroid cancer has been proposed to be partially due to enhanced detection.⁴ Dinneen et al⁵ reported that the 10year overall and cause-specific survival rates decreased to 24% and 27%, respectively, in patients with distant metastasis. In well-differentiated thyroid carcinoma patients with metastasis, the presence or absence of iodine-131 (¹³¹I) uptake in the metastatic foci during radioiodine therapy also has a major effect on outcome. Durante and co-workers⁶ showed that the 10-year survival rate in well-differentiated thyroid carcinoma with ¹³¹I uptake in metastases after radioiodine therapy was 56% versus a mere 10% in patients without any ¹³¹I uptake.

The anatomic position and nature of foci of radioactivity are often difficult to ascertain on planar scintigraphy with ¹³¹I images. One difficulty has been distinguishing carcinoma from normal structures that can concentrate ¹³¹I such as residual thyroid tissue. Three-dimensional imaging via SPECT offers an opportunity to more fully assess radioactive foci that appear ambiguous, but its impact has been modest. Reports have shown promise for this technology in patients with DTC.⁷,⁸ SPECT/CT instruments allow contemporaneous SPECT and CT scanning for anatomic localisation, better prognosis and plan of therapy, which increases the certainty of information available from...
the post-therapy images. This study was planned to assess the impact of SPECT/CT in the additional identification of foci of malignancies from normal structures that can concentrate $^{131}$I in patients with differentiated thyroid cancer in intermediate and high-risk patients.

**MATERIALS AND METHODS**

This study included 44 consecutive patients treated with $^{131}$I at tertiary cases center between April 2014 and December 2015. All patients were treated according to the standard of care in our practice. Patients with microscopic invasion into perithyroidal tissue, cervical lymph node metastases, aggressive histology or vascular invasion are classified as being at intermediate risk and patients with macroscopic invasion, gross extrathyroidal extension, incomplete tumour resection or distant metastases are classified as being at high risk of recurrence. These two category patients were considered for treatment with $^{131}$I. These patients were referred either for initial postsurgical $^{131}$I ablation or for $^{131}$I therapy of recurrent or metastatic disease. The study protocol was approved by our Institutional Ethical Committee.

A total of 44 patients (37 females and 7 male patients) were included in our study. The patients’ ages ranged from 25 to 69 years and the mean age was 50.85±13.89 years as shown in Table 1. For female patients, the age range was 23-73 years and the mean age was 50.62 years±14.2. For male patients, the age range was 25-68 years and the mean age was 51.13 years±14 (P=21). Thirty two of the 44 patients underwent postsurgical $^{131}$I ablation or for $^{131}$I therapy of recurrent or metastatic disease. The study protocol was approved by our Institutional Ethical Committee.

For male patients, the age range was 25 to 69 years and the mean age was 50.85±13.89 years. Two patients with metastatic disease were administered $^{131}$I ablation and all patients were given a low-dose of $^{131}$I for diagnostic purposes. For each patient, a total of 46 studies were analysed. All patients underwent complete thyroid hormone withdrawal 4 weeks before radioiodine therapy for the purpose of Thyroid-Stimulating Hormone (TSH) stimulation and all patients were given a low-dose of $^{131}$I for 2 weeks in preparation for $^{131}$I administration (25-68 years and the mean age was 51.13 years±14 (P=21)). Thirty two of the 44 patients underwent postsurgical $^{131}$I ablation or for $^{131}$I therapy of recurrent or metastatic disease. Two patients with metastatic disease were administered radiiodine twice and hence a total of 46 studies were analysed. All patients underwent complete thyroid hormone withdrawal 4 weeks before radioiodine therapy for the purpose of Thyroid-Stimulating Hormone (TSH) stimulation and all patients were given a low-dose of $^{131}$I for 2 weeks in preparation for $^{131}$I administration (25-68 years and the mean age was 51.13 years±14 (P=21)).

Data were recorded including lymph node size, lytic or sclerotic bone lesions and the like. For each patient, focal $^{131}$I uptake on planar or SPECT/CT images was analysed for the thyroid bed, lymph nodes in the neck and distant sites in the chest, liver and bones.

**RESULTS**

In this study, we compared post therapy $^{131}$I imaging findings on planar and SPECT/CT scans, assessed the clinical utility of SPECT/CT in identification of the patients with differentiated thyroid in intermediate- and high-risk patients. We observed that planar whole body images showed uptake in neck in 44/46 scans. Of these 41 was interpreted as remnant uptake and 11 images showed additional foci of uptake interpreted as lymph node uptake. SPECT CT was in agreement in 41 scans but in 3 scans the foci seen on whole body images was localised to lymph nodes. 3 patients showed focal uptake in lymph nodes that was not visible in whole body images. Of 11 scans where uptake was interpreted as lymph nodal, 9 were confirmed on SPECT CT and 2 was localised to physiological uptake in esophagus (McNemar Test, p< 0.05). Similarly, in 5 cases planar Whole Body scan showedequivocal uptake of iodine in distant lesions. These were proven to be localised to distant metastatic sites by SPECT/CT (McNemar Test, p< 0.05).
### Table 1. Demographic Data of Studied Patients

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Gender</th>
<th>Mean±SD*</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>Males</td>
<td>50.85±13.99</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>50.62±14.2 years</td>
</tr>
<tr>
<td>Gender ratio (Male:Female)</td>
<td>7:9</td>
<td></td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>Males</td>
<td>118.42±27.30</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>117.06±35.00</td>
</tr>
<tr>
<td>Thyroglobulin</td>
<td>Males</td>
<td>3098.21±1554.7</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>337.42±1934.9</td>
</tr>
<tr>
<td>Radioiso (mCi)</td>
<td>Males</td>
<td>83.09±25.48</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>83.60±24.27</td>
</tr>
</tbody>
</table>

* = Standard Deviation

### Table 2. Diagnosis of Histology (N=44)

<table>
<thead>
<tr>
<th>History</th>
<th>No of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary</td>
<td>22 (50.0%)</td>
</tr>
<tr>
<td>Follicular</td>
<td>17 (38.6%)</td>
</tr>
<tr>
<td>Hurthle Cell Ca, Ca thy with occultal bone mets.</td>
<td>2 (4.34%)</td>
</tr>
<tr>
<td>Insular [poorly differentiated ca thy]</td>
<td>2 (4.34%)</td>
</tr>
</tbody>
</table>

#= Histological history.

### DISCUSSION

We analysed the impact of addition of SPECT/CT in the characterisation of lesions resulting in the detection of more sites of radiodine-avid disease compared with the planar whole body images alone. Other authors also evaluated SPECT/CT in this setting, but in some studies SPECT/CT was obtained only in light of equivocal planar scans. Some prior studies investigated the role of combined SPECT/CT in patients after thyroidectomy, but before treatment with $^{131}$I.1,11 Therapy with $^{131}$I is effective for thyroid cancer patients who are at an intermediate to high risk for recurrence or intermediate to high risk of dying from their disease.12 Patients with microscopic invasion into

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**Figure 1(a).** 50-Year-Old Male Underwent Total Thyroidectomy, Histopathological Examination Confirmed Follicular Carcinoma of Thyroid with Lymphovascular and Capsular Invasion. Pathological Staging was pT1bMxNx. Post Therapy Whole Body Iodine-131 Images show Focal Uptake in Neck, Thorax and Upper Abdomen

**Figure 1(b).** SPECT/CT Localised the Uptake in Thorax to an Expansile Lesion in left 2nd rib

**Figure 1(c).** The Lesion in Abdomen was Localised to a Large Hypodense Lesion in Left Lobe of Liver (Figure 1B)
perithyroidal tissue, cervical lymph node metastases, aggressive histology or vascular invasion are classified as being at intermediate risk and patients with macroscopic gross extrathyroidal extension, incomplete tumour resection or distant metastases are classified as being at high risk of recurrence. SPECT/CT instruments allow contemporaneous SPECT and CT scanning for anatomic localisation. In this study, we compared post-therapy $^{131}$I imaging findings on planar and SPECT/CT scans assessed the clinical utility of SPECT/CT in clarifying equivocal findings and in detecting additional sites of metastasis not visualised on planar images.

The utility of SPECT/CT has been previously studied in patients with thyroid carcinoma. Tharp K et al\textsuperscript{9} reported that Integrated $^{131}$I-SPECT/CT was found to have an additional value over planar imaging in patients with thyroid cancer for correct characterisation of equivocal tracer uptake seen on planar imaging as well as for precise localisation of malignant lesions in the neck, chest and skeleton. SPECT/CT optimised the localisation of $^{131}$I uptake to lymph node metastases versus remnant thyroid tissue to lung versus mediastinal metastases and to the skeleton. Wong KK et al\textsuperscript{11} has reported that iodine-131 SPECT/CT is useful for accurate evaluation of regional and distant activity in characterisation of foci as residual thyroid tissue or nodal, pulmonary or osseous metastasis. Suspected physiologic mimics of disease can be confirmed with increased reader confidence. Schmidt D et al\textsuperscript{14} found that SPECT/CT determines lymph node involvement at radio ablation performed for thyroid cancer more accurately than does planar imaging. SPECT/CT may alter management in roughly one quarter of patients with thyroid carcinoma by upstaging or down staging their disease. Spanu A et al\textsuperscript{12} has reported that SPECT/CT improved planar data interpretation showing a higher number of DTC lesions, more precisely localising and characterising DTC foci and more correctly differentiating between physiologic uptake and metastases, thus permitting the most appropriate therapeutic approach to be chosen. A wider use of this method is suggested complementary to planar imaging in selected DTC patients. The above-mentioned studies have shown that SPECT/CT has an incremental diagnostic value over planar imaging and that it may change management in 25%-50% of patients.\textsuperscript{6,8,11} The study by Grewal et al\textsuperscript{10} confirms some of these data, but it differs in several important aspects.

We found that SPECT/CT helped to localise focal iodine uptake and characterise it as either normal or abnormal, thereby reducing the need for additional imaging studies. In post-thyroidectomy patients, SPECT/CT findings affected the ATA risk classification with implications for management by changing the interval for clinical follow-up and the need for additional imaging and laboratory tests. Other authors also evaluated SPECT/CT in all cases, but in some studies SPECT/CT was obtained only in light of equivocal planar scans. In the present study, SPECT/CT demonstrated iodine uptake in neck lymph nodes in 3 of 27(11%) patients with suspected recurrence in whom the planar scan failed to localise the iodine uptake, which is14\% in study by Gerawal et al. Our study found an 11% change in nodal status in the post-surgical group. This change is similar to that found by Schmidt et al\textsuperscript{14} who noted a change in nodal status with SPECT/CT in 8 of 57 patients (14%). Our study also showed an 18% change in patient management based on the elimination of additional imaging studies. This number is again similar to the numbers reported in prior studies. Some prior studies investigated the role of combined SPECT/CT in patients after thyroidectomy, but before treatment with $^{131}$I. In one of these studies, SPECT/CT findings changed the therapeutic management in 21 of 108 patients by better selection of surgery or $^{131}$I therapy.

In patients with differentiated thyroid carcinoma post-ablation,$^{131}$I scintigraphy aims to detect residual neck disease and distant metastases usually found in lungs and bones. In our study, SPECT/CT changed the risk classification for 13 of the 46 patients, thereby altering the overall to confirm or to rule out residual disease in most cases where WBS remains indeterminate. In a more recently published large study by Menges et al\textsuperscript{13} of 123 patients, author has reported that SPECT/CT has significant incremental diagnostic value is higher in lesions outside the neck than in those in the neck and absent in patients without iodine-positive foci on planar imaging.

The identification of nodal disease on post-therapy scans will alter risk classification especially with small nodal volume. In the present study, only one physician made all the decisions regarding appropriate patient management based on either planar scan findings or SPECT/CT findings. This may introduce bias because physician preference and clinical practice patterns may vary (e.g., work-up of findings on post-therapy scan); however, this bias is mitigated by the fact that the same bias was applied uniformly to all patients. Our results chiefly apply to patients in the intermediate- and high-risk groups. Most low-risk patients are not treated with $^{131}$I; the utility of SPECT/CT in this setting remains uncertain. The small size and the single centricity of the study was also an important limiting factor in the study.

Finally, although it is conceivable that our approach may save costs by eliminating dedicated additional imaging studies, the issue of cost-effectiveness should be addressed in future work.

CONCLUSION
SPECT/CT significantly reduced the number of equivocal findings on post-therapy planar $^{131}$I scans and enabled more accurate characterisation of focal iodine accumulation in patients. This improved accuracy helped avoid additional imaging studies.

REFERENCES


