# Detection and Evaluation of Differentiated Thyroid Carcinoma by using Tc99m and Iodinei 131 Scanning

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**Abstract:** ***The aim of this study was to demonstrate the clinical usefulness of simultaneous co-registration of 99m Tc MDP bone scanning as an anatomical landmark with 1311 scanning in the evaluation of metastatic DTC. A total of Twenty-five patients [16 females and 9 males, mean age + SD = 52 + 13 years] with metastatic DTC, [17 papillary, 8 follicular], were included. Who had undergone surgical thyroidectomy for DTC was evaluated prospectively. All patients had undergone technetium and iodine scintigraphy [IS]. Occasionally, additional simultaneous co-registration of localized detailed images was also performed. The two planar images were fused with optional fusion of SPECT images. TS had uptake values total number of metastases was 48 lesions, was in the lungs, bones or both, with a frequency of 10 [21%], 8 [16%] and 22[46%], respectively. Nodal 8 cases [16%]. Metastatic lesions were [56%] from papillary DTC and [44%] from follicular DTC Regional anatomical distribution of metastatic lesions showed that (42%) thoracic region, and head region [4%]. Variable anatomical distribution was seen in the neck .I-131 WBS There were 56 areas of focal. All metastatic lesions showed positive focal uptake However, an additional eight false positive focal areas were seen reducing the specificity to 86%. Findings in 131I-WBS were divided into two groups. Group A: Positive 1311 metastatic lesions that are well localized anatomically, which included 32 lesions [67%]. Group B: are the 1311 metastatic lesions that are anatomically indeterminate, which included 16/48 lesions [33%] and included 10 lesions in the thorax and 6 in the pelvis-abdominal region. Accordingly, these were considered false positive findings by 1311 WBS. The remaining 48 lesions were considered true positives, and, therefore, the specificity of the fusion scan was 100%. In group A, fusion scintigraphy confirmed the 1311 findings with concordant agreement between both 1311 and fusion scan of 100%. In group B, out of 16 anatomically indeterminate lesions, planner fusion scans localized 14 lesions accurately [87%]. The other two lesions were clearly identified by SPECT of fused 1311 and MDP scintigraphy and were in the thorax and pelvi-abdominal regions. Table 5 shows the effect of fused planner 1311/99mTc-MDP scans in the identification of indeterminate lesions by standard 1311 WBS. The results of this study demonstrate that the concordance of IS and TS depends on the IU level after suspension of replacement therapy. Measurements of IU and TS are of considerable value in evaluating patient response to therapy and will substantially reduce the need for repetitive radioiodine scans and unnecessary treatment doses in patients with undetectable Tgvalues. Fusion image were considered to improve image interpretation in comparison with standard 1311 scanning when they provided better localization of lesion.***

**Keywords:** Thyroid. Scintigraphy, Uptake [99mTc] pertechnetate, I-131 whole body scintigraphy (WBS)

## 1. Introduction

Blood Tg level determination and WBS are frequently used for patients with DTC as surveillance for cancer recurrence. After complete surgical and/or radioiodine ablation of the thyroid, serum Tg should be undetectable (generally <2 ng/ml) and I-131 uptake would be essentially background.[1] Although increased serum Tg and positive radioiodine scan are indicators of the presence of thyroid cancer, we have been struck by the number of patients with undetectable serum Tg levels despite the presence of persistent I-131 uptake in the thyroid bed.

Although identification of iodine avid tissue allows for more aggressive follow-up and/or therapy, the clinical significance of persistent radioiodine uptake in the thyroid bed in patients with undetectable serum Tg levels is not clear. Szilagyi et al. found that more than 50% of patients with total thyroidectomy have evidence of functioning thyroid tissue on I-131 scintigrapy.[2] It is important to know the size and amount of uptake in the thyroid tissue, which may or may not lead to administration of I- 131. A ‘tumor specific’ scintigraphic evaluation would improve the diagnostic assessment; however, available radiopharmaceuticals are far from being ideal [3].

The early detection of recurrence and/or metastases is essential for further management in DTC. Following thyroidectomy and post-surgical ablation, periodic follow up with 131I WBS remains a reliable test for the management of DTC patients. The presence of pathological foci of 131I accumulation in the neck, chest or skeletal system is strong evidence for recurrence or metastases.[5, 7-9]

However, several inherent limitations remain challenging and influence the reliability of this technique. One notable limitation is the physiological secretion and excretion of 131I from the salivary glands, stomach, bowel and urinary system, which are considered the most common causes of false-positive results. Moreover, accumulation of 131I in some inflammatory conditions, especially in bowel and lungs with variable rate of turnover, is not uncommon. This may provide a potential source of error when misinterpreted as positive for DTC. The limited anatomical information from this functional technique has a major impact in this misinterpretation and in many instances provides indeterminate results.[10,11] Recently the effectiveness of simultaneous dual isotope coregistration using a combination of99mTc-MDP diphosphonate and 131I scanning for localization of metastases of DTC has been reported. 99mTc-MDP scans can provide an internal anatomical landmark that, when fused with 1311 scanning, can help in the localization of iodine-avid foci. However, these reports did not show the technical details of the fusion process.[12,6] The aim of this technique is to fuse two simultaneously coregistered images with two different intensity scales yielding a single scale intensity image that preserves the data of the two scales with a high T/B ratio. There are several factors that should be considered with this technique, including: using single energy line isotopes, adequate energy gap between the two energy windows to limit cross talking, proper selection of collimator (use a higher energy collimator to reduce penetration of collimator septa), use of high-speed detector electronics (i.e. fast response time to enhance count efficiency) and finally consider the quantity of used radio-activity for each isotope to create a balance in the count collected for each study, based on the above-mentioned considerations.

The aim of this study was to demonstrate the clinical usefulness of simultaneous co-registration of 99m Tc MDP bone scanning as an anatomical landmark with 1311 scanning in the evaluation of metastatic DTC.

### 1.1 Material and Methods

The study was approved by the Committee Board of Radiotherapy and Nuclear Medicine Department at the King Fahad Medical City, Riyadh. Informed consent was obtained from all patients and/or their relatives, with a complete description of the procedures.

### 1.2 Scintigraphic procedures

Patients TSI-I levels were assayed 4-6 weeks after thyroidectomy during which thyroid hormone replacement was withheld. The patients were considered legible for 1311 diagnostic WBS when TSH was > 30lu/ml. then given a dose of 5 mCi 1311 orally and imaged 48-72 hours later.

The initial acquisition of 131I WBS was performed using a large field of view gamma camera (E-cam Dual head-Siemens) fitted with a high- energy parallel-hole collimator. The photo-peak was 364 keV with symmetrical 20% window. The whole-body scan was done with a table speed of 6 cm/min. The next step on the imaging day was to intravenously inject the patient with 5 mCi of 99mTc-MDP and image after 2-3 hours.

### 1.3 Fused 99mTc-MDP / 1311- WBS scanning

The fusion scan acquisition started 2-3 hours post 99mTc-MDP injection using the same camera equipped with high-energy parallel-hole collimators. This acquisition was simultaneous using two different windows (15% window centered on 364 keV for 131I and 15% window centered on 140 keV for 99mTc-MDP). The matrix resolution used in this fusion scan was 256X1024 and the table speed was 8 cm/min. In some patients, additional spot views in fusion mode (matrix256 X 256), were acquired for more anatomical delineation. Optionally, SPECT images were obtained with dual-energy windows, 32 projections for each detector and a matrix resolution of 64 X 64.

### 1.4 Data processing and image fusion

The planar data provide two simultaneously co-registered separate images with two different count intensity scales. Processing entails successful fusion of these tow images with preservation of the data from the two scale producing single scale image that maintain high target to background (T/B) ratio. This is obtained by tuning the intensity of 131I images using variable multiplication factor (K) for 131I matrix to approximate the count intensity of the 99mTc-MDP image. This count-intensity tuned image will be summated to the bone-scan image providing a single-scale image with satisfactory T/B ratio.

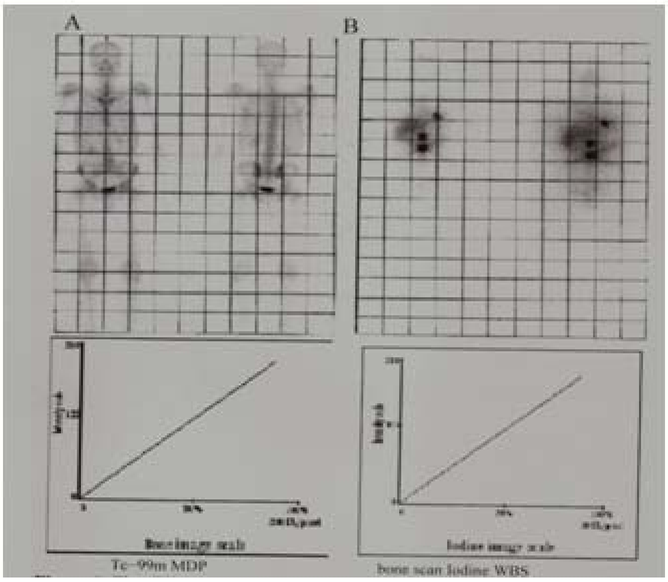


**Figure 1:** The difference in intensity scales and count per pixel for 99mTc-MDP and 1322 scans. A. Figure shows the difference in count intensity between bone for iodine and bone scale. Image manipulation entails the use of variable multiplication factor (K) for 1-131 image followed by summation of iodine and bone scan images producing fused image with single intensity scale AB.

### 1.5 Images analysis and interpretation

Two experienced nuclear medicine physicians were responsible for visual interpretation of the images on a lesion-by-lesion basis for detection of metastases in lymph nodes, lungs, bones and other regions. The findings were defined as positive or negative based on consensus. The 131I WBS and fusion scintigraphy were interpreted independently of each other, then all the images were re-evaluated based on the fusion images including knowledge of the results of the 131I -WBS scintigraphy.

The usefulness of fusion scintigraphy was assessed based on whether:

- Fusion scintigraphy provided additional anatomical information that solves the problem of indeterminate lesions on 131I -WBS
- Fusion scintigraphy provided additional anatomical information that changed the previous staging of the patient, based on the 131I -WBS alone.
- Fusion SPECT scintigraphy provided more detailed information than the planar fusion scintigraphy.

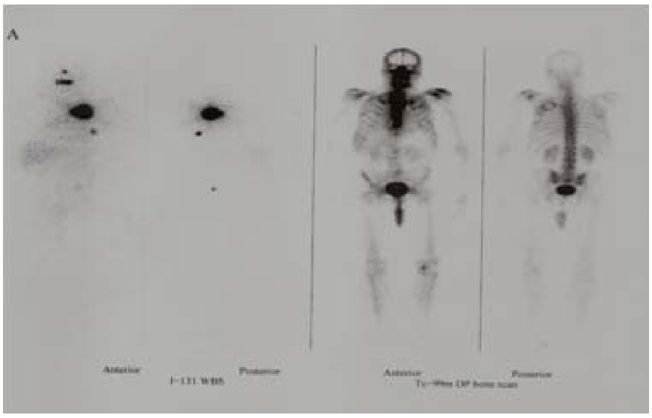

**Figure 2:** WBS and bone performed for 48-year-old male patient with metastatic disease before fusion FCT. Out of the three who demonstrated hot foci in 1311, two were indeterminately localized, one was located in the thoracic region and the other was located in the pelvic region.

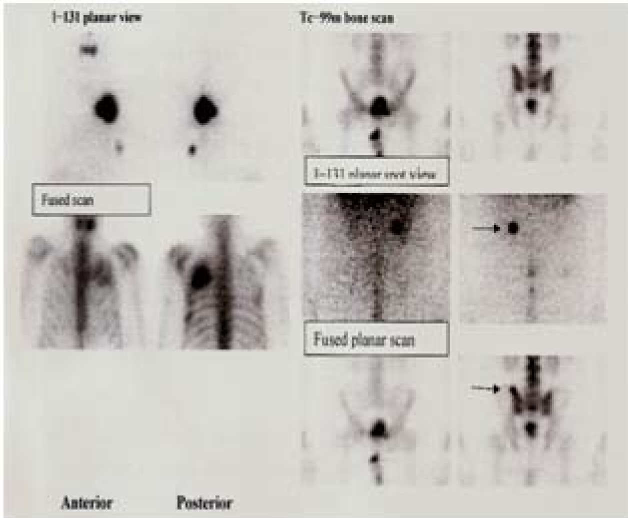


**Figure 3:** shows multi-spot anterior and posterior planar views before and after fusion. The used planar images clearly identify the location of hot foci in left ribs posteriorly as well as left ala close to tip of sacro-iliac region.

## 2. Results

### 2.1 Technetium scintigraphy [IS]

The work involved twenty-five patients with metastatic DTC (16 females and 9 males), average age 52 ± 13 years. Histologically, there were 17 patients with papillary DTC and 8 patients with follicular DTC. All patients had thyroidectomy (near-total in 10 and total thyroidectomy in 15). Detailed patient characteristics are presented in Table 1. All cases had metastatic disease and the metastases were defined based on the appearances on neck ultrasound, CT, MRI and 131I WBS. In addition, increased Thyroglobulin (Tg) levels, histological findings and evolution of the disease during subsequent follow up for at least 12 months were considered to confirm the presence of metastases.

**Table 1:** shows the Patients' disease characteristics and frequency

| | *PTC* | *FTC* |
|---|---|---|
| Number (n) | 17 | 8 |
| Age: Years (mean ± SD) | 48.8 ±12 | 55 ±15 |
| Female: male | 1.9 : 1 | 1.6 : 1 |
| Thyroidectomy | 17/17 | 8/8 |

The total number of definite metastases was 48 lesions. The highest distribution of metastatic lesions was in the lungs, bones or both, with a frequency of 10 (21%), 8 (16%) and 22 (46%), respectively. Nodal metastases were found in 8 cases (16%). Metastatic lesions were 27/48 (56%) from papillary DTC and 21//48 (44%) from follicular DTC. The details of the distribution and frequency of these metastatic lesions are shown in Figure 4.

PTC: papillary thyroid carcinoma; FTC: follicular' thyroid carcinoma

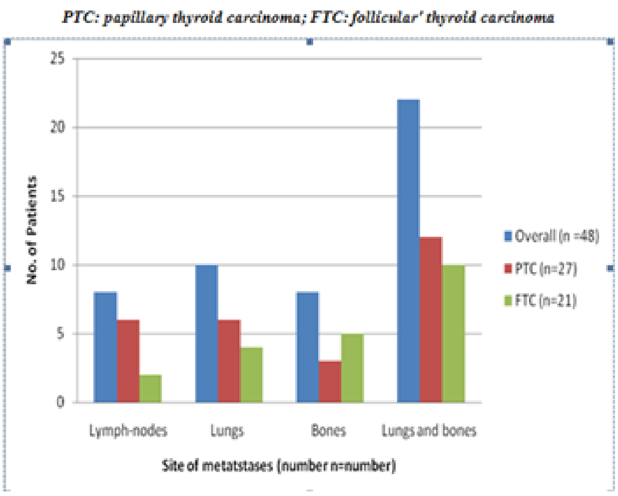


**Figure 4:** shows the sites of metastases from DTC

Regional anatomical distribution of metastatic lesions showed that the highest number 20/48 (42%) was present in the thoracic region, and the lowest was in the head region 2/48 (4%). Variable anatomical distribution was seen in the neck, extremities and pelvic-abdominal areas, as shown in Fig .5.

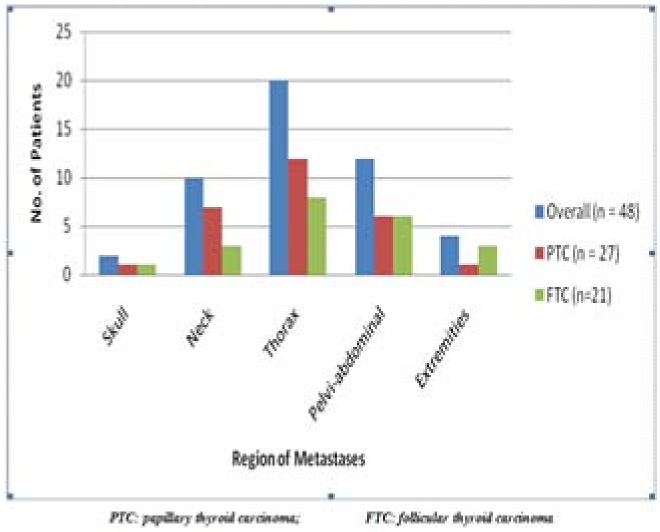


**Figure 5:** Distribution of metastases by region

### 2.2 1311 whole body scintigraphy (131I-WBS)

There were 56 areas of focal uptake on 1311 WBS. All metastatic lesions showed positive focal uptake on the 1311 Whole Body Scan (WBS) with a sensitivity of 100%. However, an additional eight false positive focal areas were seen reducing the specificity to 86%. Findings in 131I-WBS were divided into two groups. Group A: Positive 1311 metastatic lesions that are well localized anatomically, which included 32 lesions (67%). Group B: are the 1311 metastatic lesions that are anatomically indeterminate, which included 16/48 lesions (33%) and included 10 lesions in the thorax and 6 in the pelvis-abdominal region.

### 2.3131I-WBS and 99mTc-MDP bone scan fusion scintigraphy

The addition of bone scintigraphy and the resultant fusion (1311 and MDP) scintigraphy correctly identified 48 metastatic lesions out of the 56 1311 positive lesions. The remaining eight 1311 focal areas that were seen in 131I-WBS but not anatomically defined by 99mTc-MDP bone scan were located in the scalp, large bowel and pelvic regions. Accordingly, these were considered false positive findings by 1311 WBS. The remaining 48 lesions were considered true positives, and, therefore, the specificity of the fusion scan was 100%. In group A, fusion scintigraphy confirmed the 1311 findings with concordant agreement between both 1311 and fusion scan of 100%. In group B, out of 16 anatomically indeterminate lesions, planner fusion scans localized 14 lesions accurately (87%). The other two lesions were clearly identified by SPECT of fused 1311 and MDP scintigraphy and were in the thorax and pelvi-abdominal regions. Table 5 shows the effect of fused planner 1311/99mTc-MDP scans in the identification of indeterminate lesions by standard 1311 WBS.

*TP: true positive, FP: false positive, n: number of patients*

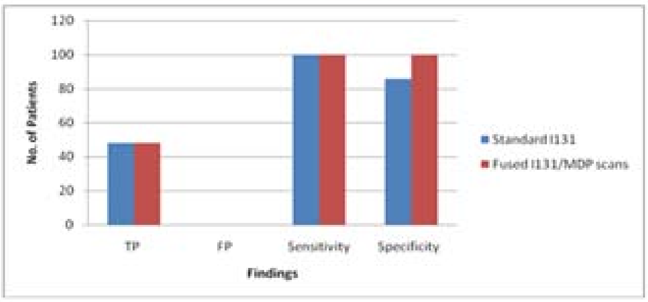


**Figure 6:** Findings of standard 1-131 / MDP bone scan

### 2.4 Change in management

Change in management of patients occurred in 3/8 patients who had false-positive findings by 131I-WBS alone. Of those three patients, one had false positive scalp lesion, and the other 2 patients had false-positive colonic activity. Those three patients were down-staged from distant metastases to local metastases, as they already had involved cervical lymph node metastases.

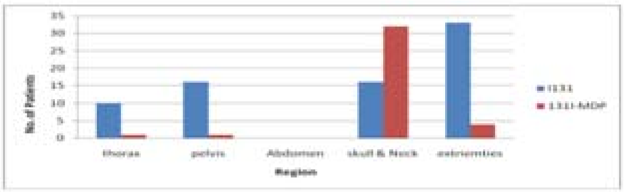


**Figure 7:** Effect fused planner 1-131 / MDP scans in identification of indeterminate lesions

## 3. Discussion

In this study, we tried to demonstrate the clinical usefulness of simultaneous co-registration of 99m Tc MDP bone scanning as an anatomical landmark with 1311 scanning in the evaluation of metastatic DTC. We used a high-energy collimator and limited the injected dose of 99Tc-MDP to 185-370 MBq, as the bone scanning was considered only as an anatomical landmark. This may yield a sub-optimal bone scan quality but avoids acquiring too much count from the scale of bone display, which may obscure the iodine-avid lesions and facilitates the process of fusion with a satisfactory T/B ratio. Therefore, the sensitivity of99mTc-MDP bone scan in the detection of DTC was relatively underestimated (40%) compared to other reports (60%) [13, 12]

Tuning between the two images with different count intensity scales was done through the use of variable multiplication factor (K) for 13 II image matrix before matrix summation, which yields a satisfactory fused image with a single intensity scale and provides a reasonable T/B ratio (Figure 1). This process of matrix multiplication and image summation is not applicable for fused SPECT images because separation between the acquired SPECT data in two different scales, one for each isotope, is not possible. However, the relatively limited injected dose of99mTc-MDP and collection of data through 360 degree around the object create a reasonable balance between T/B ratios after reconstruction (Figures 2, 3).

DTC has been reported to be 2-4 times more frequent in females than in males although the rate is lower for patients with distant metastases [14].

In our study, where all patients had metastases of DTC, the female: male ratio was 1.9:1 for PTC and 1.6:1 for FTC, further supporting the higher relative risk of distant metastases among males.[15] Similar to other results,[16, 17]in the present study FTC was more frequent in males and had a higher rate of metastatic potential compared to PTC (21 metastatic Iesions/8 FTC patients compared to 27 metastatic lesions for 17 PTC patients). The distribution by sites for distant metastases corresponded to the results of other studies.[3,4] In practice, indeterminate localization of iodine-avid foci in 1311 WBS requires complementary morphological imaging modalities (U/S, CT and/or MRI) for clarification. While these techniques provide excellent anatomical information compared to functional nuclear medicine imaging, they have some diagnostic limitations.

These limitation include the inability to detect disease in lymph nodes (LNs) that are not or are only slightly enlarged (sub centimeter nodes), differentiation of scar tissue or fibrosis from local recurrence, and the limited ability in monitoring the response to therapy. Moreover, the difference in the mechanisms of assessing malignancy with functional vs. anatomical imaging creates some discrepancy in their results. Another limiting factor is the use of CT with contrast, which limits further radioiodine administration.[6,11,18,19] The clinical usefulness of using a combination of99mTc-MDP and 1311 scanning for localization of metastases from DTC has been previously described by Johann Schoenberger and colleagues.[14] They gained additional information in 16 of 21 patients because the presence of osseous structures from bone scintigraphy facilitates the correct diagnosis of the lymph node involved; the identification of distant metastases and delineation of residual thyroid tissue from lymph node metastases after thyroidectomy. In the present study, simultaneous co-registered fused 131I/99m Tc-MDP scanning was able to depict eight false positive iodineavid foci in standard 1311 WBS. Most of these foci were linked to persistent focal colonic activity located in the pelvic-abdominal region. Therefore, the specificity of the simultaneous co-registered combined 131I /99mTc-MDP was 100% compared to 86% for standard 131I. This resulted in disease down-staging in three patients and a change in the strategy of therapy. The present study shows concordant agreement between both standard 131I and fusion planar scans in 32 out of 48 (67%) lesions concordant results were higher in the skull, neck and extremities compared to the thoracic and pelvic-abdominal regions.

On the other hand, the planar fused scans provided additional anatomical information in 87% of indeterminate lesions by outlining bones.

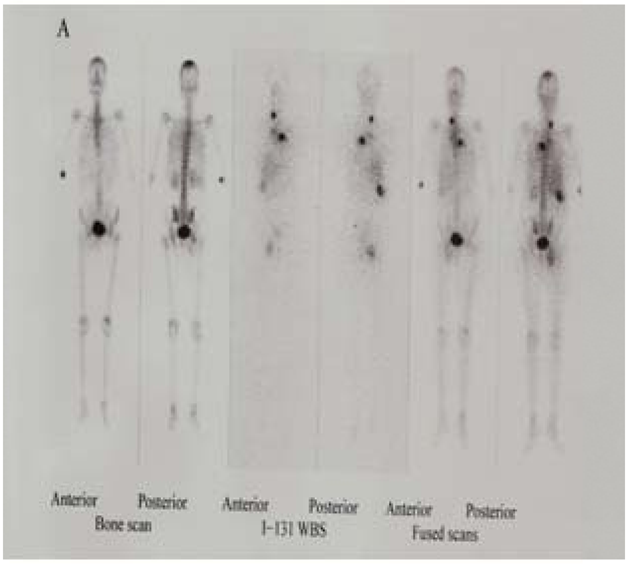


**Figure 8:** 99mTc-MDP bone scan (left column), standard 1311 WBS (middle column) and fused scans (right column) in a female patient with multiple. Metastatic hot foci. The planar used image cannot clarify totally the indicated intra-thoracic lesion because of overlapping structures.

Fused SPECT images improved the detectability of two indeterminate lesions in fused planar images by providing more anatomical information with better contrast enhancement and solved the problem of overlapping structures.

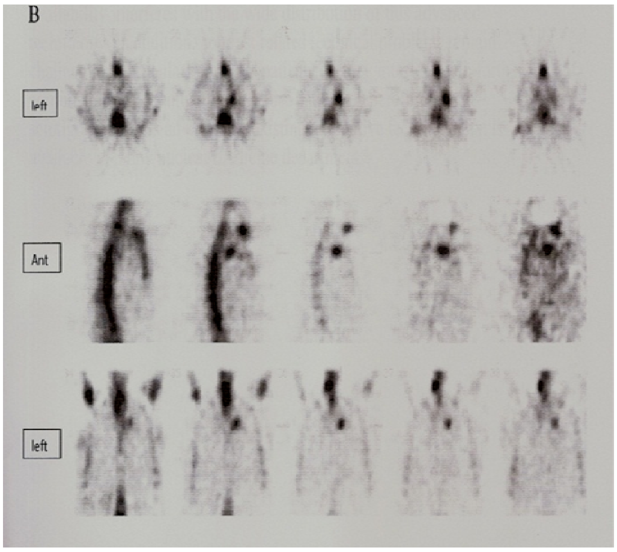


**Figure 9:** Reconstructured transverse, sagittal and coronal slices for thoracic region for the same patient showing the hot foci to be nodal mediational lesion.

It shows that , in selected cases, fusion scientigraphjy using the mentioned simultaneous co-registration of 131I /99mTcMDP method is helpful in the localization of pathological tracer accumulation through delineation of intra-and extra-osseous foci.

Moreover, simultaneous acquisition of both nuclides excludes patient motion artifact and facilitates fusion processing and manipulation. Recently, newly developed machines that combined CT and a gamma camera (SPECT/CT) were introduced and showed great potential. The combination of functional imaging with the anatomical details of multi-slice CT represents the best solution in cases involving metastatic DTC. However, the high cost of this machine and limited availability interferes with the wide distribution of this advanced technology. In addition, contrast related technical problems remain challenging, particularly in DTC patients, as they interfere with further administration of radioiodine in those patients. Therefore, fused scintigraphy offers an effective existing alternative technique that is available in many nuclear medicine departments.

## 4. Conclusion

Fusion imaging using simultaneous co-registration of 1311 And Tc99mMDP scanning is a simple and feasible technique that improves the anatomically limited interpretation of scintigraphy using 1131 alone/ in patients with metastatic DTC, Simultaneous exploration of osseous structures and areas of high 1131 uptake in fused scintigraphy allow clear delineation of osseous and extra osseous foci. Moreover/ they added, Anatomical information from fused scans significantly reduces false positive and indeterminate results. The diagnostic advantage of this technique seems to be more apparent in the thoracic and pelvi-abdominal regions than in the neck and extremities.

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