VIA MEDICA

Nuclear Medicine Review 2012, 15, 2: 101–107
10.5603/NMR.2012.0003

ISSN 1506–9680

Original

Localisation of sentinel lymph nodes in patients with melanomas by planar lymphoscintigraphic and hybrid SPECT/CT imaging

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[Received 5 I 2012; Accepted 20 I 2012]

Abstract

BACKGROUND: The aim of the study was to assess the role of planar lymphoscintigraphy and fusion imaging of SPECT/CT in sentinel lymph node (SLN) identification in patients with melanomas.
MATERIAL AND METHODS: Planar and hybrid SPECT/low-dose CT lymphoscintigraphy were performed in 113 consecutive patients with melanomas (59 men, 54 women, mean age 57.6 with range 11–87 years, BMI 29.4 ± 12.5). The radiopharmaceutical was injected around the tumour (Group A, 59 patients), or around the scar (Group B, 54 patients). Localisation of melanomas: head and neck 4, trunk 55, upper extremities 28, lower extremities 26. Planar and SPECT/CT images were interpreted separately by two nuclear medicine physicians. Abilities of these two techniques to image SLN were compared.
RESULTS: SLNs were detected on lymphoscintigraphy comprising planar and SPECT-CT images in 108 (95.6%) study patients; there was failure to detect SLNs in the remaining 5 (4.4%) patients. Planar images identified 253 SLNs in 100 (88.5%) pts, with a mean of 2.2 ± 1.7 (range 0–9 nodes) per patient. In the remaining 13 (11.5%) patients no SLNs were detected on planar images. On SPECT-CT images, 334 hot nodes were detected in 107 (94.7%) patients with a mean of 3.0 ± 2.1 (range 0–9) nodes per patient. In the remaining 6 (5.3%) patients, SPECT-CT was negative.
SPECT/CT visualised lymphatic drainage in 8 (7.1%) patients with non-visualisation on planar imaging.
CONCLUSIONS: In some patients with melanomas SPECT/CT improves detection of sentinel lymph nodes. It can image nodes not visible on planar scintigrams, exclude false positive uptake and exactly localize SLNs.
KEY words: sentinel node, malignant melanoma, lymphoscintigraphy, planar scintigraphy, SPECT/CT

Nuclear Med Rev 2012; 15, 2: 101–107

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Background

In patients with a histopathologic diagnosis of cutaneous melanoma, the tumour must be staged to determine prognosis and treatment. Tumour thickness is the single most important prognostic factor. Melanoma is staged with the TNM system. Preoperative lymphoscintigraphy can contribute to nodal staging by revealing lymphatic drainage patterns and the locations of single or multiple sentinel lymph nodes [1]. It helps the surgeon to minimise the size of the incision.

SLN biopsy is the most accurate and the only reliable method for nodal staging which can diagnose microscopic tumour spread to the regional lymph nodes. Lymphoscintigraphy visualises where lymph from the primary tumour site travels and is, therefore, an essential element of lymphatic mapping [2, 3].

An essential step in the procedure for SLN biopsy is to locate the first-echelon node of draining basin. In some patients,

Table 1. Location of SLNs

	GROUP A		GROUP B		OVERALL	
	SPECT/CT	Planar	SPECT/CT	Planar	SPECT/CT	Planar
Axilla	98	57	83	48	181	105
Inguina	49	22	50	37	99	59
Others	25	9	29	11	54	20
Equivocal	0	46	0	23	0	69

however, the lymphoscintigram shows a drainage pattern that is difficult to interpret and in a small minority no sentinel node is depicted at all [4].

In this study we compare hybrid SPECT/CT and planar lymphoscintigraphy in melanoma patients with exploration the value of SPECT/CT — mainly for detection of additional SLNs and the exact anatomical localization of SLNs.

Materials and methods

Patients population: Planar and hybrid SPECT/low-dose CT lymphoscintigraphy were performed in 113 consecutive patients (59 men, 54 women, mean age 57.6 with range 11–87 years, BMI 29.4 ± 12.5) with malignant melanoma, with no clinical evidence of lymph node metastases (N0) and no remote metastases (M0). 55 patients had melanoma on their trunk, 4 in the head and neck region, and 54 on an extremity (upper extremity 28, lower extremity 26). In all these 113 patients, SPECT/CT images were made immediately after the conventional images without a second injection of the radiopharmaceutical.

Lymphoscintigraphic method: On the day of surgery (one day protocol) an activity of 100 MBq ^{99m}Tc labelled colloid divided in four equal aliquots of 0.5 ml was injected by nuclear medicine physician in four intradermal injection around the tumour (59 pts, Group A) or around the scar (54 pts, Group B) after excision of the melanoma. We have used following ^{99m}Tc colloids: Nanocis (size of colloid particles 100 nm — 12 pts), Nanocoll (size of colloid particles to 80 nm — 75 pts), SentiScint (size of particles to 200 nm — 1 pt), NanoAlbumon (size of particles to 80 nm — 25 pts). Choice of radiopharmaceuticals (Rf) was totally random. Type of Rf was not important because we have compared planar scintigraphy and SPECT/CT performed by the same Rf. We estimated effectiveness of various Rf for the detection of SLNs in our previous papers [5–8] and that was not the aim of this study. Furthermore we did not compare the rate of successful preoperative and peroperative detections of SLNs, which was also described previously.

Planar static (parameters: matrix 128 × 128, 5 min per view) and dynamic scintigraphy (parameters: matrix 128 × 128, 30 frames, 20 s per frame) and SPECT/CT lymphoscintigraphy were performed using a hybrid system composed of a dual-head gamma camera with a low-dose CT installed in a gantry (Symbia T2 Siemens).

SPECT/CT images were acquired immediately after planar images. The SPECT/CT system (Symbia T2; Siemens, Erlangen, Germany) consisted of a dual-head variable-angle gamma camera equipped with low-energy high-resolution collimators and a two-slice spiral CT scanner optimized for rapid rotation. SPECT acquisition (matrix 128 × 128, 60 frames at 20 s per view) was performed using steps of 6°. For CT (130 kV, 17 mA, B60s kernel), 5 mm slices were created. The iterative reconstruction (OSEM 3D) was used for generating SPECT slices.

Both SPECT and CT slices were fused using an Esoft 2000 application package software (Siemens, Erlangen, Germany). Two nuclear medicine physicians evaluated the images. The SPECT/CT images were also viewed using two-dimensional orthogonal re-slicing in axial, sagittal and coronal orientation. Maximum intensity projections with a three-dimensional display were generated to localize sentinel nodes in relation to anatomic structures.

Image analysis was performed prospectively by two experienced nuclear medicine physicians in consensus reading. All images were analysed in two steps: 1. analysis of planar images; 2. analysis of coregistered SPECT/CT images. The location of SLNs was categorised as axillar, inguinal and in other lymphatic basins.

In the analysis of the results, fused SPECT/CT images data were concluded to be clinically relevant if they identified SLNs which were missed on planar images, if they excluded SLN suspected on planar images, or if they localized SLNs in additional or different basins than those suggested by planar images. The surgeon is notified of the findings on both planar and SPECT/CT images. Student's paired t-test was used for comparing numbers of found nodes by both techniques. Values were considered significant when $P < 0.05$.

Results

SLNs were detected on lymphoscintigraphy comprising planar and SPECT-CT images in 108 (95.6%) study patients; there was failure to detect SLNs in the remaining 5 (4.4%) patients.

SPECT/CT visualized lymphatic drainage in 9 (8,0%) patients with non-visualization on planar imaging. SPECT/CT showed the exact anatomical location of all visualized sentinel nodes.

Planar images identified 253 SLNs in 100 (88.5%) pts, with a mean of 2.5 ±1.6 (range 0–9 nodes) per patient. In the remaining 13 (11.5%) patients no SLNs were detected on planar images. On SPECT-CT images, 334 hot nodes were detected in 107 (94.7%) patients with a mean of 3.1 ± 2.1 (range 0–9) nodes per patient. In the remaining 6 (5.3%) patients, SPECT-CT was negative. Among the patients in whom SPECT-CT identified hot nodes, the location of these nodes was as follows (Table 1).

The overall hot SLN detection rate by planar and SPECT-CT lymphoscintigraphy in GROUP A was 98.3% (58 patients). In 1 patient (1.7%) both imaging techniques failed to detect hot SLNs. In 4 patients (6.8%), hot SLNs were detected only by SPECT-CT and there was no patient with a hot SLN detected only by planar images.

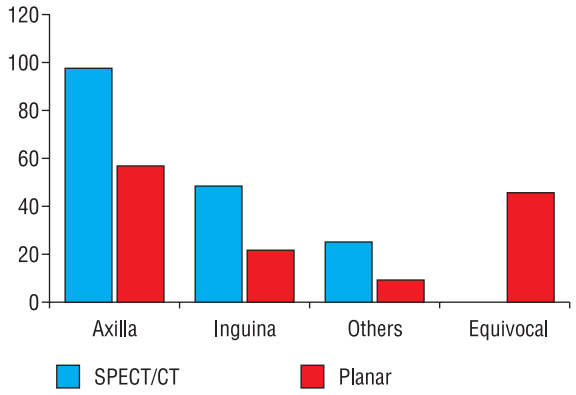

Figure 1. Numbers of found lymph nodes on SPECT/CT and planar imaging in GROUP A

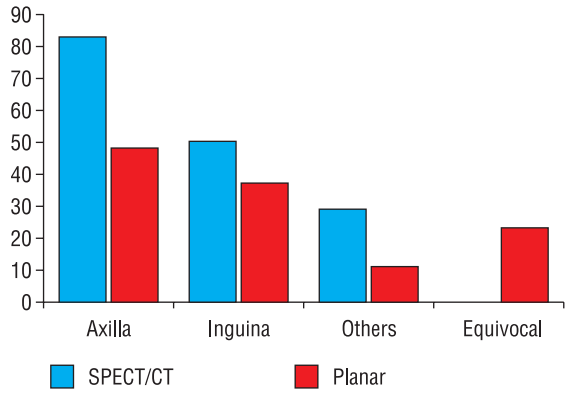

Figure 2. Numbers of found lymph nodes on SPECT/CT and planar imaging in GROUP B

The overall hot SLN detection rate on planar and SPECT-CT in GROUP B was 92.6% (50 patients). In 4 patients (7.4%) both planar and SPECT-CT imaging failed to detect hot SLNs and in 5 (9.3%) patients, hot SLNs were detected only on SPECT/CT images.

Discordant results between planar and SPECT-CT nodal identification (Figure 1, 2): SPECT-CT was positive in 9 patients with negative planar imaging, while conversely, positive planar imaging and negative SPECT-CT were found only in 1 patient.

SPECT/CT showed higher number of hot lymph nodes in 49 patients (43,4%, range 1–6 nodes), in the GROUP A it was in 23 patients (39,0%, range 1–5 nodes), and in the GROUP B it was in 26 patients (48,1%, range 1–6 nodes). The number of SLNs was exactly the same in 58 patients (51,3%), in the GROUP A in 33 (55,9%) patients, in the GROUP B in 25 (46,3%) patients.

In 26 patients (23,0%), the exact anatomical localization was equivocal on planar images, whereas SPECT/CT showed the exact anatomical information. In one patient in GROUP A SPECT/CT revealed superficial contamination.

In general, the SPECT/CT imaging brought statistically higher numbers of found hot lymph nodes, compared to planar scintigraphy, in both groups ($P < 0.001$ for both groups). Comparing both groups together, there are about 20% more cases in GROUP B, where hybrid scans visualized higher number of nodes than in GROUP A. Respectively, the situation, where sentinel lymph node was detected only on hybrid images, there was approximately 40% higher in GROUP B than in GROUP A.

Discussion

A sentinel node was defined as a lymph node upon which the primary tumour drains directly [9], i.e. the first lymph node that is at risk from metastatic cells [10].

The histopathologic findings in the excised SLNs may indicate the need for a further dissection of the nodal basin if metastatic spread or micrometastases are found. Alternatively, if the SLN is tumour free, the nodal basin can be regarded as free of disease and an unnecessary dissection can be avoided. Even in the era of emerging tumour imaging modalities, such as PET/CT, SLN biopsy is considered the only reliable method for identifying micrometastatic disease in regional lymphatic nodes [11]. SLN biopsy is considered the „gold standard" investigation tool for the detection of lymph node metastases [12].

In patients with cutaneous melanoma, in particular, the SLN status has been found to be strongly prognostic [13]. Because elective lymph node dissection has not been shown to improve the survival benefit in patients with melanoma [14], the accurate localization of SLN for tissue sampling has become increasingly important for clinical management. The survival of melanoma patients staged as node-negative with elective regional lymph node dissection was significantly less as compared to patients staged as node-negative following sentinel lymph node biopsy, regardless of their T stage [15]. Melanoma patients are staged more accurately following SLN assessment [16].

SLN biopsy in patients with clinically node-negative malignant melanoma is a valuable procedure for nodal staging and for prognostic stratification [17]. It allows the detection of clinically occult metastases by an exhaustive histopathological examination. Accurate visualization of the SLN is required for the best results. The variability of SLN drainage in melanoma in areas such as the trunk, the head and the neck makes lymphoscintigraphy very useful [18]. Lymphoscintigraphy has been found to accurately predict the number of nodes in only 81% of the basins, overlooking nodes that were superimposed and could not be separated from other nodes or from the injection site or lymphatic channels and nodes that were beyond the resolution of the planar images [19].

The better anatomic definition and improved resolution that characterise SPECT images may overcome the above limitations of planar images. Localization of hot lymph nodes on SPECT images without anatomic landmarks is not possible.

SPECT/CT was introduced in lymphatic mapping with the goal to show more sentinel nodes and to show them more clearly than is possible with conventional lymphoscintigraphy.

Hybrid SPECT/CT camera fuses tomographic lymphoscintigrams (physiological information) with anatomical data from CT [20, 21]. In comparison with traditional single-modality imaging approaches, the dual-modality systems offer unique capabilities in combining data from two imaging modalities in way that simplifies, yet facilitates, image correlation with the goal of revealing useful diagnostic information that is not easily extracted when the imaging studies are performed independently [22]. Hybrid SPECT/CT provides better contrast and resolution than planar imaging with possibility to correct an attenuation and scatter [23, 24]. SPECT/CT images provide the topographic landmarks that may further facilitate surgical exploration [21] with improvement

of surgical SLNs detection. If only used to correct the radionuclide image for photon attenuation, the CT data can be acquired with a considerably lower statistical quality and coarser spatial resolution than required for diagnostic-quality imaging and therefore can deliver a significantly lower radiation dose than that for a diagnostic CT study [22]. Hybrid system allows transmission (low-dose CT) and emission (SPECT) scans to be performed without changing the patient's position, thereby allowing for automatic and correct record of images obtained with two modalities. Fusion of two images into one image is easier [21, 25].

The introduction of hybrid SPECT/CT into daily practice is associated with additional costs and requires extra time [4]. The advantages of additional SPECT/CT may prevail when used in specific situation only [26]. In special instances, SPECT/CT imaging allows for improved detectability and interpretation of lymphatic drainage. Contamination, nodes close to the injection site, and overweight patients are three noted instances in which SLN identification and localization are better with SPECT than with standard planar methods [27, 28]. In malignant melanoma dynamic lymphoscintigraphy and fusion of SPECT and CT can detect aberrant pelvic SLNs [10].

Besides melanoma [17], the use of SPECT/CT has been described in SLN lymphadenectomy for breast cancer, head and neck cancer, prostate cancer, bladder cancer, vulvar, cervical and endometrial cancer - the value of SPECT/CT for SLN identification and localization has been described in several reports [12, 29–37].

Low radiation dose is added to the scintigraphic mapping by the low-dose CT, ranging from 1.3 mGy at the centre to 5 mGy at the surface of the body [21, 38].

SPECT/CT should be performed in selected patients, i.e. those with an unusual lymphatic drainage pattern, with planar images that are difficult to interpret or with no visualization on planar images. In these patients, SPECT/CT appears to have additional value. The use of SPECT as well as coregistered CT images in vaginal melanoma proves to be useful in detection and localization of SLN not seen on planar imaging alone for use in staging and treatment planning [39].

SPECT/CT provides an anatomical overview in two- and three-dimensional perspectives creating a surgical road-map that cannot be provided by planar images or intraoperative lymphatic mapping techniques. The present study confirms the additional value of SPECT/CT in the anatomical localization of (additional) SLNs. Other investigators have also concluded that additional SPECT/CT after planar lymphoscintigraphy resulted in an improved anatomical localization of SLNs. Especially SLNs outside the axilla and nodes close to the injection site were easier to identify using SPECT/CT [26]. SPECT/CT was able to accurately bring to light sites of skin contamination with the radiopharmaceutical, that were mistaken for sentinel nodes in 1 patient (0.88%) on planar images.

The problem is masking of the sentinel node by the injected tracer because of the close proximity of the tumour site to the draining node. Most often, the sentinel node is overlooked because of the smear of the tracer overlying the draining node [40], i.e. the "shine effect"[41].

Van der Ploeg et al. [26] limited the use of SPECT/CT to difficult and unusual cases because they believe planar lymphoscintigraphy is an excellent preoperative mapping technique for most patients. They added nonvisualization as a new indication, because SPECT/CT visualized drainage in patients whose planar images did not reveal a SLN. They believe that the added costs and extra time for SPECT/CT are more justified when the procedure is used for this new indication. SPECT/CT is useful for finding the exact anatomic location of sentinel nodes and in detecting additional sites of drainage. The use of routine SPECT/CT imaging is very suitable in vaginal melanoma for pelvic lymphoscintigraphic studies or as an adjunct tool for localizing SLN in cases that would not be demonstrated with planar imaging alone [39]. Preoperative SPECT/CT lymphoscintigraphy is ideal for mapping the unpredicted lymphatic drainage pathways within the complex pelvic anatomy in vulvovaginal melanoma [42]. These advantages facilitate surgical exploration and eventually lead to more accurate staging. SPECT/CT may also obviate preoperative skin marking and may replace delayed lateral planar imaging. Whether SPECT/CT should be used on all patients or only for specific indications needs to be studied further [26]. The better anatomic definition and improved resolution that characterise SPECT images may overcome limitations of planar images. Localisation of hot lymph nodes on SPECT images without anatomic landmarks is not possible. However, it is possible by fusing the SPECT image with the anatomic data obtained by performing low-dose CT at the same setting as with the SPECT acquisition [20]. Van Ploeg et al. in other paper [43] concluded that SPECT/CT detects additional drainage and shows the exact anatomical location of sentinel nodes in patients with inconclusive conventional lymphoscintigrams. SPECT/CT justifies the additional time and costs for patients in whom conventional lymphoscintigrams shows a lymphatic drainage pattern that is unusual or difficult to interpret, or when no sentinel node is shown. SPECT/CT better visualizes the sentinel nodes in more than half of the patients and changes the surgical approach in more than a third. In a fair number of patients, additional sentinel nodes are detected that would have not been found otherwise. SPECT/CT facilitates surgical exploration in difficult cases and may improve staging.

Even-Sapir et al. [20] concluded that the improved lesion detectability of tomographic images and the anatomic landmarks of CT would be the more likely explanation for the additional data provided by SPECT/CT but potential explanations for identification of additional nodes by SPECT/CT could have been the effect of time, inadequate planar technique, or improved tomographic imaging technology. 3-D SPECT/CT images may identify hidden nodes due to a good separation between counts related to the tracer injection and those of a closely located hot lymph node [25] (Figure 3, 4).

Conclusions

SPECT/CT shows the exact anatomical location of visualized sentinel nodes and detects additional drainage, compared with planar scintigraphy — in our study this was observed in 43.3% of patients examined. Furthermore, hybrid imaging brought additional value especially in the group of patients with scar after extirpation of melanoma, where SPECT/CT visualized higher number of SLNs in 20% more cases than in the group of patients prior the primary surgery. This should be also taken into

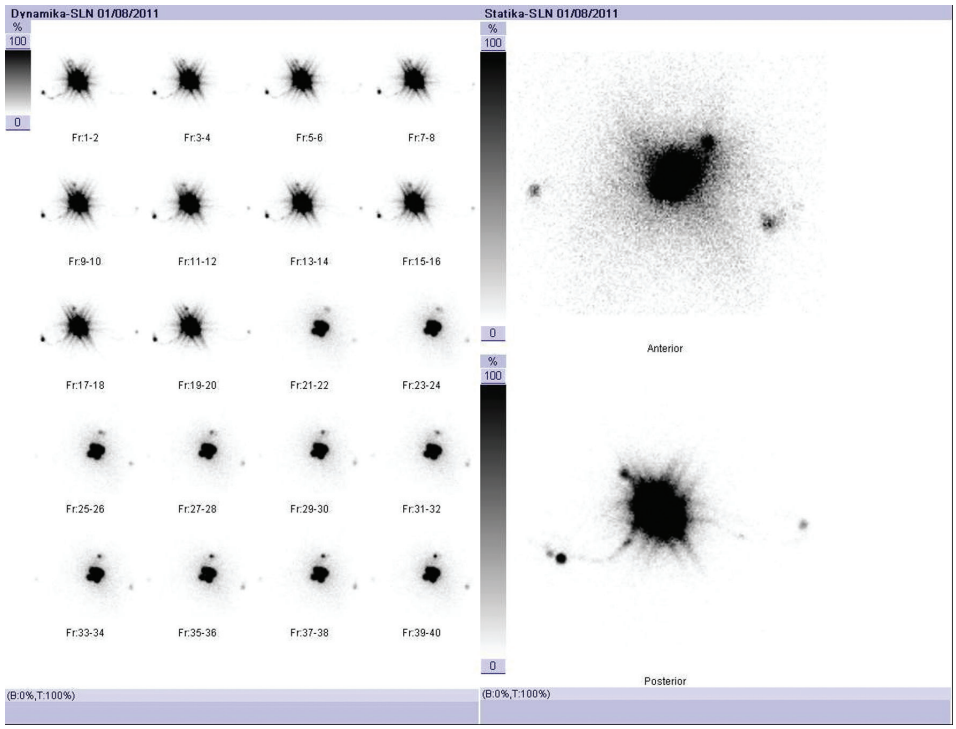

Figure 3. Dynamic and static lymphoscintigrams in 59 years old man with melanoma on the left side of the back with no possibility the exact localization of the SLNs

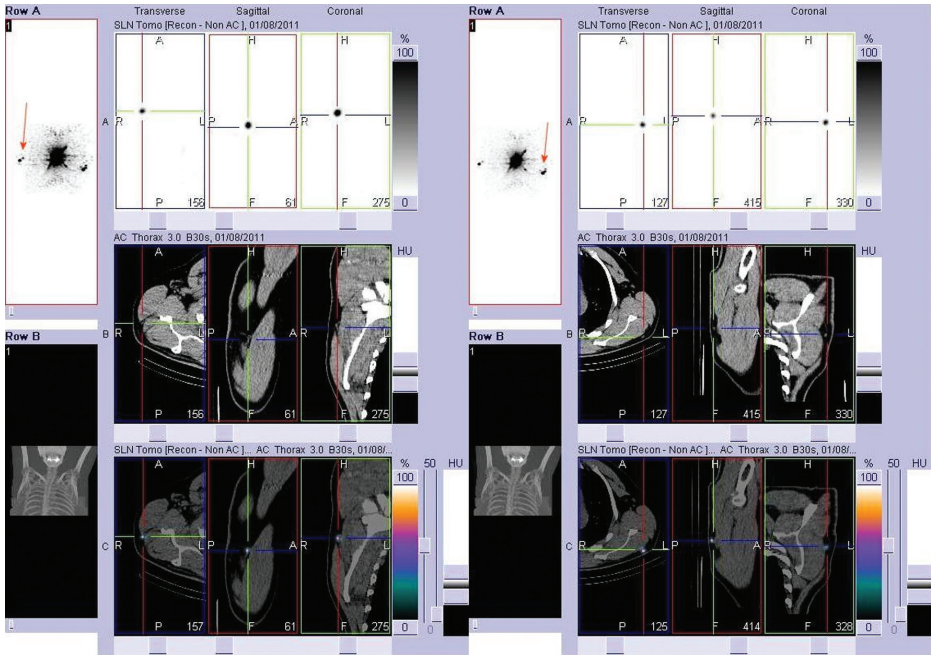

Figure 4. The same patient as in the figure 3. Fusion of SPECT and CT. Exact localization of two SLNs in the left axilla, and two SLNs in the right axilla

account, if there is need to narrow the patient selection for the examination on hybrid camera. The added radiation exposure from CT source should be considered. According to low-dose scanning protocol we evaluated the radiation exposure from spiral CT to about 1.5 millisieverts (mSv). The hybrid system allows the CT scanning following SPECT acquisition directly. There is not needed additional manipulation with patient, so the total acquisition time is not prolonged considerably.

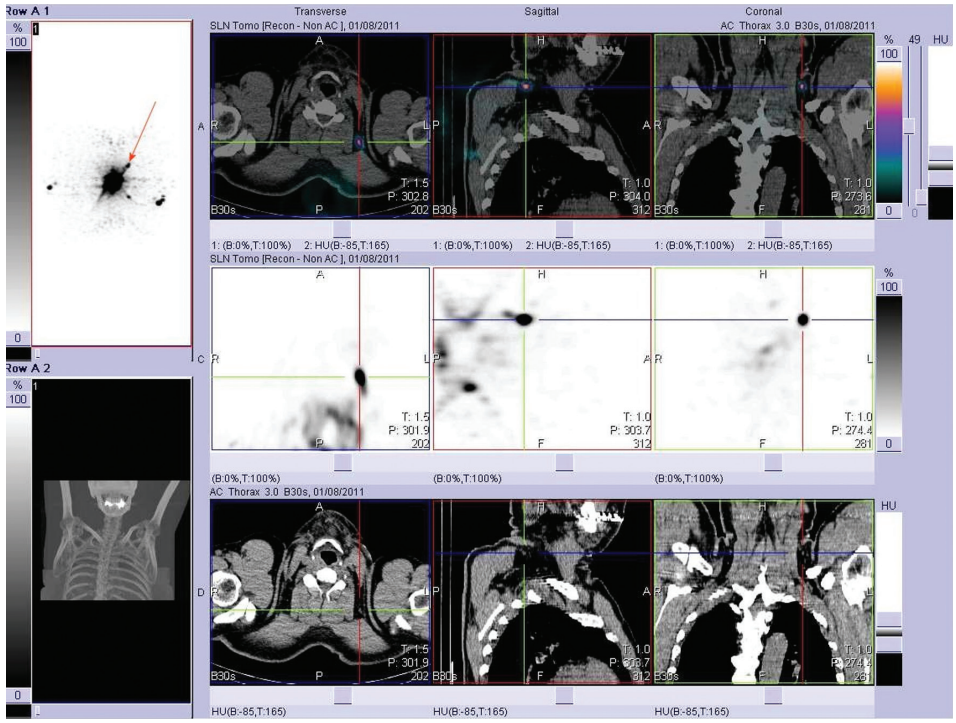

Figure 5. The same patient as in the figure 3 and 4. Fusion of SPECT and CT. Exact localization of SLN on the left side of the neck

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