Sentinel nodes in complex areas: innovating radioguided surgery

Vermeeren, L.

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Chapter 4

SPECT/CT for sentinel lymph node mapping in head&neck melanoma

L. Vermeeren
R.A. Valdés Olmos
W.M.C. Klop
I.M.C. van der Ploeg
O.E. Nieweg
A.J.M. Balm
M.W.M. van den Brekel

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ABSTRACT

Background: The additional value of single photon emission computed tomography with computed tomography (SPECT/CT) for detection and localization of sentinel nodes in patients with a melanoma of the head and neck was determined.

Methods: Thirty-eight patients received conventional lymphoscintigraphy followed by hybrid SPECT/CT. The number of sentinel nodes visualised and anatomic information provided were analysed. Changes in surgical approach due to additional information from the SPECT/CT were evaluated in twenty patients.

Results: SPECT/CT visualised a mean of 2.6 sentinel nodes per patient (range 1-6). SPECT/CT depicted an additional sentinel node in 16% of the patients and clearly showed the anatomic location of the hot nodes in all patients. The surgical approach was adjusted on the basis of SPECT/CT images in eleven patients (55%).

Conclusions: SPECT/CT visualises more sentinel nodes than conventional images and shows their anatomic location. SPECT/CT is recommended in patients with a melanoma in the head or neck.

INTRODUCTION

The tumour status of the sentinel node constitutes relevant prognostic information for melanoma patients, and preliminary information suggests that there is a survival benefit if a node dissection is carried out early on the basis of a positive sentinel node biopsy.[1] Melanoma patients are offered a sentinel node biopsy in many centres, although the therapeutic consequences that should follow the finding of a positive sentinel node are a subject of discussion.[2,3] Sentinel node biopsy in the head and neck is often more difficult than in other nodal basins, due to the complex anatomy and the variable drainage patterns in this region.[4-7] Elsewhere in the body, patent blue is used in addition to a radiotracer to visualise the lymphatic channel that leads to the sentinel nodes. In the head and neck, a blue channel is more difficult to find because of the inconsistent drainage pathways. Sentinel nodes in this region are less often stained blue.[8] This makes the use of the radiotracer even more important. The conventional method for preoperative sentinel node detection consists of dynamic and successive static planar lymphoscintigraphy. Dynamic images can visualise the lymph duct from the primary tumour and allows a sentinel node to be distinguished from nodes further downstream. Sequential static images provide an overview of the injection area and the radioactive nodes. Anatomic referencing on these images is limited to orientation in relation to the body contour, which can be visualised using a flood-field source. The site of a sentinel node can be marked on the skin with aid of an external radioactive marker (cobalt-source pen), but its exact location and its relation to surrounding anatomical structures cannot be determined. A better imaging technique is thus desired, especially for patients with disease in an area as complex as the head and neck.

Hybrid imaging using single photon emission computed tomography and computed radiographic tomography (SPECT/CT) is a new multimodal imaging technique that fuses the radioactivity distribution detected by SPECT with the anatomic information gathered by CT. SPECT/CT has two advantages over conventional lymphoscintigraphy. The tomographic nature of the technique and the CT correction for tissue attenuation and scatter of the gamma ray signals imply a better sentinel node visualisation. The visualisation of the node in relation to anatomic structures facilitates interpretation and optimally prepares the surgeon for the operation.

In breast cancer, SPECT/CT detects more sentinel nodes than conventional images, and often shows a node when conventional images do not depict a hot spot.[9] Several investigators have reported the additional value of the exact anatomic localization of the sentinel nodes

and advise to use SPECT/CT in difficult situations like unexpected drainage patterns, non-visualisation or in obese patients.[10,11] Studies on the additional value of SPECT/CT in patients with melanoma are scarce. The authors of the few recent publications conclude that detection rates as well as anatomic localization appear to be considerably better than with conventional imaging.[12,13] The purpose of the current study was to evaluate the value of SPECT/CT for detection and localization of sentinel nodes in head and neck melanoma and to define whether SPECT/CT is indicated in all these patients.

PATIENTS AND METHODS

Patients

Thirty-eight patients with a melanoma of the head or neck with a Breslow-thickness of at least 1mm or Clark level IV were prospectively enrolled, after a diagnostic excision with 2mm margin had been performed. For these patients, lymphatic mapping is a routine procedure at our institute and informed consent was obtained in all. Ultrasound of the neck and parotid region was routinely carried out and was combined with fine-needle-aspiration-cytology in case of a suspicious node. Patient characteristics are outlined in table 1. Fourteen patients have also been included in a previous study regarding the value of SPECT/CT for lymphatic mapping of melanoma patients in general.[12]

Table 1 | patient and tumour characteristic

Age (years)	Gender No. of patients (%)	Melanoma location No. of patients (%)	Breslow thickness (mm)
Mean: 53 Range: 24-86	Male: 30 (79%) Female: 8 (21%)	Face: 18 (47%) Scalp: 11 (29%) Ear: 4 (11%) Neck: 5 (13%)	Median 2.2 (mean 2.9) Range 0.8-7.8

Imaging

A mean dose of 71 megabequerel (1.9 millicurie) of 99mTechnetium-nanocolloid (GE Healthcare, Eindhoven, the Netherlands), was injected intracutaneously in four deposits of 0.1ml around the scar of the primary excision. Conventional dynamic planar lymphoscintigraphy was performed immediately after injection followed by static imaging after ten minutes and two hours. Directly after the last conventional images, two hours after injection of the

radiopharmaceutical, SPECT and CT data were acquired, using a hybrid camera (SymbiaT, Siemens, Erlangen, Germany). The SPECT (128 x 128 matrix, 60 frames, 25 seconds/frame) was performed using 6° angular steps in a 20-second time frame. For CT (130 kilovolt, 40 milliampere, B30s kernel), 5mm slices were obtained. After correction for attenuation and scatter, corresponding SPECT and CT axial 5mm slices were generated using an Esoft 2000 application package (Siemens). Images were fused using an Osirix Dicom viewer in a Unix-based operating system (MAC OS X, MacPro; Apple Inc., Cupertino, U.S.A.).

The images were analysed by two-dimensional orthogonal re-slicing in axial, sagittal and coronal directions. A three-dimensional presentation was generated with volume rendering in order to localize sentinel nodes in relation to anatomic structures. All images were available on a separate SPECT/CT screen in the operation room.

Nodes on a direct drainage pathway from the primary tumour site were regarded as sentinel nodes.[14] For interpretation of the images this meant that the nodes with an afferent lymphatic vessel from the primary lesion site and nodes appearing first in each nodal basin were considered to be the sentinel nodes. Nodes appearing later in the same regions were considered to be higher-echelon nodes. Additional hot spots that were depicted later and that were closer to the injection area were also considered to be sentinel nodes. The location of the sentinel nodes was marked on the skin with indelible ink.

Surgical and pathological procedures

Patients were operated under general anaesthesia. Re-excision of the scar of the diagnostic excision was performed first. Skin marks, conventional images, SPECT/CT images and counting with the gamma ray detection probe (Neoprobe; Johnson & Johnson Medical, Hamburg, Germany) were used to determine the site for the incision and guided the search. Second-echelon nodes were left in situ.

Sentinel nodes were sectioned into 2-4mm slices after formalin-fixation. Following embedding in paraffin, experienced pathologists examined the nodes using haematoxylin-eosin staining and immunohistochemistry with S-100 and HMB-45 at a minimum of six levels (50-150 µm intervals).

Analysis

SPECT/CT images were compared to the conventional preoperative lymphoscintigraphy that is currently used at our institute. Primary outcome characteristics were preoperative detection

of sentinel nodes and anatomic localization of these nodes by SPECT/CT. We evaluated whether SPECT/CT detected more sentinel nodes than conventional imaging and whether better localization information was provided.

Changes in the surgical approach due to additional information from the SPECT/CT were analysed in the first twenty patients. In these patients, the surgeons were asked to score the clinical value of the SPECT/CT images with regards to the impact on their surgical approach of the sentinel nodes. Immediately after the operation, the surgeons determined whether the location of the sentinel nodes was visualised better with SPECT/CT and whether the location of sentinel nodes was other than suggested on the conventional images. Changes in the surgical approach based on SPECT/CT were also recorded.

RESULTS

Both conventional lymphoscintigraphy and SPECT/CT visualised at least one sentinel node in all patients. The conventional technique visualised a total of 94 sentinel nodes, whereas SPECT/CT showed an additional sentinel node in six patients. Two additional sentinel nodes were depicted due to the better sensitivity of the SPECT/CT; two nodes had been hidden by the large amount of radioactivity at the nearby injection area and one by the radioactivity of another sentinel node. One node was classified as sentinel node because of its location on a direct drainage pathway, which had not been clear on conventional images. Figure 1 shows an example of both techniques. SPECT/CT revealed that a presumed sentinel node was actually caused by tracer leakage or skin contamination (figure 2) in three patients (8%).

Ninety-two of the 97 visualised nodes on SPECT/CT (95%) were harvested during surgery. In four patients, the search for a sentinel node deep inside the parotid gland was abandoned because the risk of damaging the facial nerve did not outweigh the benefit of more accurate staging. In one patient with faint radioactivity uptake, the surgeon decided not to pursue the node (figure 3). Four of the six additional sentinel nodes visualised by SPECT/CT were harvested and tumour-free, one was harvested (in combination with a sentinel node which was visualised on conventional images) and was tumour-positive and one was not identified intra-operatively (figure 3).

In contrast to conventional imaging, SPECT/CT depicted the sentinel nodes in relation to anatomic structures in all patients, as exemplified by the three figures. According to the operating surgeons, sentinel nodes were more accurately localized by SPECT/CT in all cases and sentinel nodes were correctly placed at another site with this modality in six patients

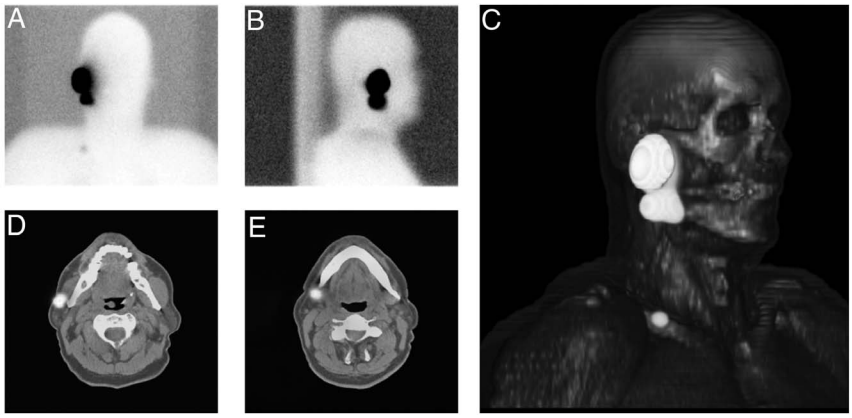

Figure 1 | A 62-year old man with a pre-auricular melanoma. Conventional images (A, B) show a sentinel node caudal from the injection area and a second-echelon node near the clavicle. The three-dimensional reconstruction of the single photon emission computed tomography with computed tomography (SPECT/CT; C) shows a cluster of two radioactive nodes in relation to the injection area and the mandible. Two-dimensional SPECT/CT fusion images (D, E), clearly show one sentinel node at the mandibular angle and another one located more ventrally, just caudal from the mandible. This latter node was tumour-positive.

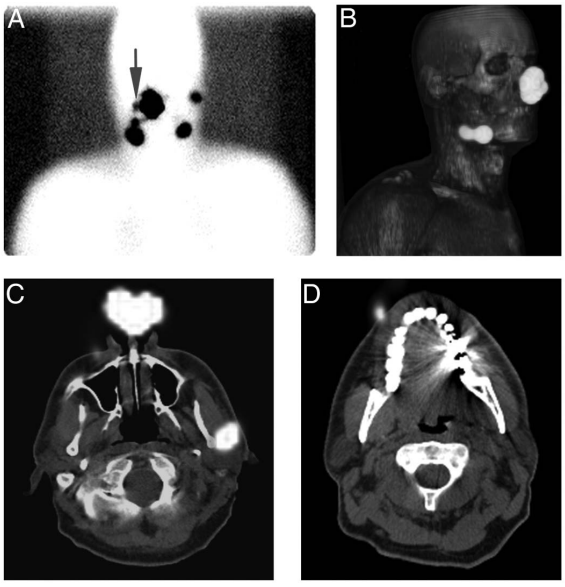

Figure 2 | A 46-year old man with a melanoma on the tip of the nose. Conventional images after two hours (A) show bilateral drainage. Two hot spots in the left neck were regarded as sentinel node, and three hot spots in the right neck were classified as sentinel node (blue arrow and two caudal hot spots). This three-dimensional reconstruction of the single photon emission computed tomography with computed tomography (SPECT/CT; B) shows an overview of the radioactivity on the right side only. Two-dimensional SPECT/CT fusion images (C, D) show that the cranial hot spots on the right side are caused by skin contamination. The caudal and most intense hot spot on anterior conventional images (A) appears to be based on two submandibular sentinel nodes (B).

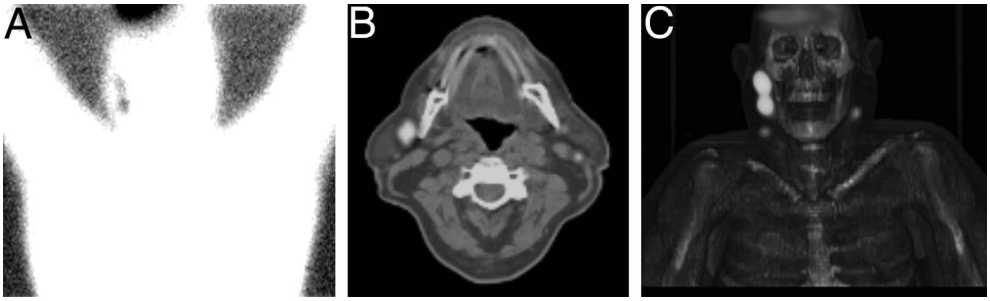

Figure 3 | A 73-year old man with a melanoma on the scalp. One hour after reinjection of the tracer because of initial non-visualisation, the conventional images show two sentinel nodes in the right neck (A). Two-dimensional fusion images (B) place these sentinel nodes deep in the medial part of the parotid gland and also a (weak) sentinel node in the left neck medial from the parotid gland is visualised. Three-dimensional reconstruction (C) shows an overview of the two sentinel nodes and a second-echelon node in the right neck as well as the sentinel node on the left side.

(30%, figure 3). The surgical approach was planned on the basis of the SPECT/CT images and in eleven of twenty patients (58%) the operating surgeons indicated that the approach would have been different with just conventional images. In these cases the incision was placed differently or the intra-operative search was facilitated.

A sentinel node was tumour positive in seven patients (18%); one of them had two involved sentinel nodes. None of the node-negative patients developed a recurrence in the regional nodal basin during the median follow-up of twelve months (range 2–31 months).

DISCUSSION

SPECT/CT can optimize sentinel node visualisation and localization in the head and neck region. We demonstrated that an additional sentinel node can be depicted with SPECT/CT in 16% of the patients, while skin contamination, resembling a sentinel node on conventional images, can also be identified as such. We also showed that an additionally found sentinel node on SPECT/CT may be the only tumour-positive node. We do however not know, whether the one tumour-positive node that we detected only on SPECT/CT, would have been found without the SPECT/CT images by intra-operative searching with the gamma probe, after excision of the other sentinel node.

Knowing the accurate location of a node is important for both nuclear medicine physicians and surgeons. SPECT/CT demonstrates more accurately at which level a sentinel node in the neck is situated and visualises the relation of the radioactive node with anatomical structures such as the mandible, parotid gland, jugular vein and sternocleidomastoid muscle. The three-dimensional reconstruction images appear to be helpful in this respect giving an overview of the location of all the hot spots. SPECT/CT also shows whether the nodes are superficial underneath the skin or buried below other structures. Based on this information, the surgical approach was adjusted in 58% of the patients. Although the use of evaluation forms can be subjective and we only analysed this in a subgroup, SPECT/CT appears to facilitate the intra-operative search for sentinel nodes.

Our findings are in line with previous study results. SPECT/CT led to a change in surgical approach in one third of a large group of melanoma patients with unusual drainage, difficult to interpret conventional images or non-visualisation on conventional images.[12] Even Sapir et al. found that SPECT/CT depicted additional sentinel nodes in 43% of patients with a melanoma of the head and neck or trunk or with an oral cavity carcinoma.[15] Covarelli et al. compared conventional imaging to only SPECT/CT and found that the latter reduced the mean biopsy time from 31 to 21 minutes (p=0.006).[16] Their interpretation of the SPECT/CT images could have been even better when they would have been combined with dynamic and sequential conventional imaging to visualise the drainage pathways. Depiction of lymph vessels enables the distinction of sentinel nodes from secondary nodes.

To our knowledge, no other cohort studies specifically addressing the value of SPECT/CT in head and neck melanoma have been published so far. Several publications on this technique in patients with oral cavity carcinoma showed that SPECT/CT visualised additional sentinel nodes, especially the ones adjacent to the injection area and improved their localization.[15,17-22] Some investigators showed that presumed sentinel nodes could sometimes be identified as the injection site or tracer leakage from the injection site.[15,22]

The identification rate of sentinel nodes in the head and neck is around 85%, which is less than the almost 100% in other locations.[23] The 95% of sentinel nodes that could be harvested in our population after preoperative SPECT/CT is fairly good. The head and neck as site of a primary melanoma has been found to be a predictive factor for a false-negative sentinel node biopsy and the reported number of false-negative sentinel node biopsies in this region varies between 12% and 44%.[5,7,8] This relatively high number might be reduced by optimal preoperative localization with SPECT/CT. Although we did not encounter a recurrence, our

patient group is too small and follow-up is relatively short to draw a definitive conclusion about the false-negative rate.

CONCLUSION

SPECT/CT provides useful anatomic information about the location of sentinel nodes. Especially nodes near the injection site are more clearly depicted with SPECT/CT. SPECT/CT detects more sentinel nodes than conventional images and can also distinguish nodal uptake from skin contamination. Conventional images remain useful to visualise the dynamic process of lymph drainage. The routine use of SPECT/CT for lymphatic mapping of head and neck melanomas is recommended to optimize detection and localization of tumour-draining lymph nodes in this area.

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