In search of the sentinel node: validation and sophistication of lymphatic mapping and sentinel node biopsy in breast cancer and melanoma
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CHAPTER 17

Three-dimensional anatomical visualization of sentinel nodes in breast cancer and melanoma using volume-rendering of fused SPECT/CT images

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Submitted
Abstract

Introduction: The hybrid single photon-emission computed tomography camera with integrated CT (SPECT/CT) fuses tomographic lymphoscintigrams with anatomical data of CT. Volume-rendered SPECT/CT provides a three-dimensional insight in the location of sentinel nodes. The purpose of this feasibility study was to explore this new potential of SPECT/CT in patients with melanoma or breast cancer.

Methods: After correction of SPECT for attenuation and scatter, three-dimensional volume-rendering of fused SPECT/CT was performed to depict sentinel nodes and surrounding muscle and bone structures. This specific setting was evaluated in 23 melanoma patients and seven breast cancer patients.

Results: Conventional imaging depicted 81 sentinel nodes in the 30 patients (mean 2.7 nodes, range 1-6). Two-dimensional and volume-rendered three-dimensional SPECT/CT visualized four additional sentinel nodes in three patients. These were tumour-negative. The combination of both SPECT/CT techniques accomplished a more precise anatomical location of sentinel nodes in 23 of the 30 patients (77%). The location of sentinel nodes was different on SPECT/CT images in six patients (20%). The surgical approach was changed in fifteen patients (50%) based on the SPECT/CT images. The surgeon decided to make a shorter incision in three patients, a longer incision in two and to move the incision in six patients. An extra incision was made in one patient and an incision was omitted in three patients.

Conclusion: The present pilot study demonstrates the feasibility of volume-rendered three-dimensional SPECT/CT in patients with melanoma or breast cancer. The combination of two- and three-dimensional images provided relevant new information in the majority of patients.
Introduction

The hybrid single photon emission computed tomography camera with incorporated CT (SPECT/CT) integrates anatomical and functional information into one image. The combination of these two imaging modalities in one device makes additional computer software and external fusion landmarks unnecessary. The patient can stay in one position during imaging, and any scatter or attenuation of the SPECT and CT images is corrected.\(^1\)\(^-\)\(^4\) Two-dimensional SPECT/CT image display has been shown to improve the notion of the exact anatomic location of sentinel nodes in patients with conventional lymphoscintigrams that are difficult to interpret or show unusual drainage.\(^5\) SPECT/CT also shows additional sentinel nodes and detects sentinel nodes in patients in whom no node is visualized on the conventional images.\(^6\)\(^7\)

Recently, we introduced a new concept of SPECT/CT imaging at our institute. Three-dimensional volume rendering was applied to fused SPECT/CT slices with a special setting to display the surrounding skin, muscle and bone structures. The purpose of this pilot study was to explore the feasibility of making these volume-rendered three-dimensional SPECT/CT images and to investigate their additional value in sentinel node localization in patients with melanoma or breast cancer.

Patients and methods

Lymphoscintigraphy is an integral element of lymphatic mapping at The Netherlands Cancer Institute. Hybrid SPECT/CT was introduced in December 2006 to improve the lymphoscintigraphic imaging and is performed in specified situations only.\(^5\) Volume-rendered three-dimensional SPECT/CT imaging was added in April 2008. The first 30 patients who underwent both two-dimensional and three-dimensional SPECT/CT were enrolled in this feasibility study. Twenty-three patients had melanoma and seven had breast cancer. The mean age was 56 years.

A dosage of 80 MBq technetium-99-nanocolloid (Nanocoll®, GE-Healthcare, Eindhoven, the Netherlands) was injected intracutaneously in four equal deposits around the primary tumour or biopsy site in melanoma patients, and a dosage of 120 MBq technetium-99m-nanocolloid was injected into the breast tumour in a volume of 0.2 ml. Conventional static images were performed at fifteen minutes and two hours after injection of the radiopharmaceutical and were preceded by a dynamic study of ten minutes in the melanoma patients. In the breast cancer patients, conventional imaging was performed ten minutes, two hours and four hours after injection of the radiopharmaceutical. A dual-head gamma camera equipped with low-energy high-resolution collimators (Vertex®, Philips, Eindhoven, the Netherlands) was used. Both anterior and lateral images were routinely obtained and additional images if needed. In breast cancer patients, the lateral view was made with the hanging breast technique. A
cobalt-57 flood source was placed behind the patient to outline the body contour. SPECT/CT was only done in patients with problematic conventional images, the selection criteria for additional SPECT/CT have been described before: a drainage pattern that is difficult to interpret, an unusual pattern or no visualization of drainage. A drainage pattern that was difficult to interpret is for example when sentinel nodes are closely located to the injection site of the primary tumour or deeply located sentinel nodes, an unusual pattern for example is drainage not to the nearest or to more than one lymph node region. Conventional images of five melanoma patients showed an unusual lymphatic drainage pattern and the lymphatic drainage was difficult to interpret in eighteen. Three breast cancer patients had an unusual lymphatic drainage pattern and in four the lymphatic drainage was difficult to interpret.

SPECT/CT images were made immediately after the last conventional image. The SPECT/CT system (Symbia T, Siemens, Erlangen, Germany) consists of a dual-head variable-angle gamma camera equipped with low-energy high-resolution collimators and a multislice spiral CT optimized for rapid rotation. SPECT acquisition (matrix 128x128, 60 frames at 25 seconds per view) was performed using six-degree-angle steps. The CT settings were 130 KV, 17 mAs, B60s kernel. After reconstruction, the SPECT images were corrected for attenuation and scatter. Both SPECT and CT axial five millimetre slices were generated using an Esoft 2000 application package (Siemens, Erlangen, Germany). Fusion of images was performed using an Osirix Dicom viewer (Osirix Foundation, Geneva, Switzerland) and software (versions 3.1 and 3.2) running in a Mac Pro computer (MAC OS X, Power G5, Apple Inc., Cupertino, CA, U.S.A.). The fused SPECT/CT images were viewed using two-dimensional orthogonal reslicing in axial, sagittal and coronal orientation. Volume rendering of fused SPECT/CT images was performed using a three-dimensional preset (16-bit colour look-up table with defined opacity, basic smooth filter 5x5) for soft tissue, bone and skin. Based on this three-dimensional view, opacity was manually adjusted to visualize these structures and different colours were used to display each of them: red for muscle, ochre for bone, and blue for skin. The sentinel node was displayed in yellow.

The number and location of the sentinel nodes were determined and described after the conventional imaging as well as after SPECT/CT by a nuclear medicine physician. The location of a sentinel node was marked on the skin with indelible ink. The operating surgeons preoperatively filled out a questionnaire concerning the additional value of two- and three-dimensional SPECT/CT images, e.g. visualization of an extra sentinel node or a more accurate anatomical localization. The viewed SPECT/CT images were selected and provided by the nuclear medicine physicians. They indicated whether this combination of SPECT/CT techniques led to a larger or smaller incision, to an incision at a different location, an extra incision or the omission of an incision. The length of the incision was for example changed based on the different location or the change in depth of the sentinel nodes, an extra incision was necessary when a sentinel node was found in a different lymph node region than
conventional images suggested and an incision was omitted whenever the primary tumour and sentinel node could be removed by the same incision.

The next day, 1 ml patent blue dye (Laboratoire Guerbet, Aulnay-Sous-Bois, France) was injected at the tumour site, immediately before the operation. The dye and a gamma-ray detection probe (Neoprobe®, Johnson & Johnson Medical, Hamburg, Germany) were used to identify the sentinel node(s). A sentinel node was defined as a lymph node upon which the primary tumour drains directly. Sentinel nodes were pursued in all regions indicated by lymphoscintigraphy. Palpable, suspicious looking non-sentinel nodes were also routinely removed. All harvested nodes were fixed in formalin, bisected, embedded in paraffin, and cut at a minimum of six levels at 50 to 150 μm intervals. Pathological evaluation included multiple sections, haematoxylin-eosin and immunohistochemical staining (CAM 5.2; Becton Dickinson, San Jose, CA, USA).

<table>
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<th>Diagnosis</th>
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<th>Location SN more precise (N)</th>
<th>Location SN different (N)</th>
<th>Extra SN (N)</th>
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Table. Sentinel node localization by SPECT/CT imaging compared to conventional imaging. SN: sentinel node

Results

Conventional imaging depicted 81 sentinel nodes in the 30 patients (mean 2.7 nodes, range 1-6). The combination of two- and three-dimensional SPECT/CT imaging showed these same nodes and visualized three additional nodes in the axilla and one in the groin in three melanoma patients. All visualized sentinel nodes were intraoperatively identified. The four additionally depicted sentinel nodes were both radioactive and blue, and pathologic evaluation did not reveal metastatic disease. Eight sentinel nodes shown by both conventional and SPECT/CT images did harbour tumour cells in six patients. These metastases prompted an axillary completion dissection in five patients, and an inguinal node dissection in the remaining patient.

The questionnaires filled out by the surgeons revealed that two- and three-dimensional SPECT/CT imaging provided a detailed surgical roadmap in all patients (figures 1-3). The notion of the anatomical location of the sentinel nodes was improved in 23 of
the 30 patients (77%) (table). In six patients (20%), the two SPECT/CT techniques showed the sentinel nodes to be in another location than the conventional images had suggested. The surgical approach was changed in fifteen patients (50%) based on the combination of the two- and three-dimensional SPECT/CT images. The surgeons decided to make a shorter incision in three patients, a longer incision was made in two patients and the incision was made somewhere else in six patients. An extra incision was necessary in one patient and an incision was omitted in three patients.

**Figure 1.** A patient with a melanoma on the left lower leg. Conventional anterior (A) and lateral (B) images visualize four sentinel nodes in the groin, each with their own lymphatic vessel. The two-dimensional SPECT/CT image (C) shows these same nodes in more detail plus a second-tier node (arrow). The sagittal two-dimensional view (D) shows three of these sentinel nodes, the caudal two in the superficial node region and the cranial node seems to be located in the deep compartment. The three-dimensional SPECT/CT images (E, F) display all sentinel nodes in an even more detailed anatomical landscape of the surrounding muscle and bone structures and confirm the para-iliac location of the cranial node.

**Discussion**

In the present study, the combined use of two- and three-dimensional SPECT/CT images improved the anatomical sentinel node localization in 23 of the 30 patients (77%). A different location of the sentinel node was shown in six patients (20%), and the surgical approach was changed in fifteen patients (50%). The volume-rendered SPECT/CT fused images showed the anatomical location of the sentinel node in a three-dimensional view displaying the surrounding muscle and bone structures.
in detail. It was not possible to evaluate the contributions to changing the surgical approach of the two- and three-dimensional SPECT/CT images separately since both techniques can only be subsequently applied in the same lymphatic mapping protocol. The three-dimensional images were made based on and after construction of the two-dimensional images, which makes a separate analysis of these two quite impossible. The two SPECT/CT settings combined showed four additional sentinel nodes in three patients (10%). These nodes were all radioactive and blue and located in the nearest lymph node region that would have been explored anyway. Therefore, these additional nodes could possible have been detected intraoperatively with the help of the gamma ray detection probe and the patent blue.

Figure 2. A woman with right breast cancer. The conventional anterior (A) image shows an axillary sentinel node (descending arrow) and a sentinel node medially from the primary tumour site (horizontal arrow). These nodes are projected over each other on the lateral conventional image (B). An axial two-dimensional SPECT/CT image (C) depicts the axillary sentinel node and another axial view (D) shows the medial sentinel node to be an internal mammary chain node. The three-dimensional SPECT/CT images (E, F) project both sentinel nodes in their anatomical landscape of muscle and bone structures. The internal mammary chain sentinel node is in close proximity to the sternum in the second intercostal space.

The volume-rendered three-dimensional SPECT/CT technique has not been described previously. The additional value of two-dimensional SPECT/CT imaging in lymphatic mapping has been discussed in literature before. In a previous study, we demonstrated that two-dimensional SPECT/CT visualized the sentinel node in all patients, like in the current study, and that it showed additional sentinel nodes in
13% of the melanoma and breast cancer patients combined. These additional nodes were tumour-positive in 5% of the patients leading to upstaging and a better-tailored management. In the present study no patients were upstaged by SPECT/CT.

The studies on SPECT/CT in melanoma patients mostly concern patients with a lesion in the head and neck region. Lymphatic mapping is often problematic in such patients and they are therefore attractive candidates for additional SPECT/CT imaging. Dissection of the lymphatic vessels and identification of the small and sometimes deeply located sentinel nodes in the head and neck region is technically more demanding than sentinel node biopsy in the axilla or inguinal region. Volume-rendered three-dimensional images could facilitate finding sentinel nodes in the neck and help preserve the important and fragile anatomical structures.

We feel that we have improved the localization of sentinel nodes since the introduction of SPECT/CT. Our first attempt to visualize the sentinel node in a three-dimensional perspective was to use maximum intensity projections. The sentinel nodes were indeed depicted in an overall view of the anatomical surrounding, but not with enough detail to tell the surgeon at glance how the sentinel node should be approached. The volume-
rendered SPECT/CT images show the exact anatomical location of the sentinel node even more detailed than the two-dimensional SPECT/CT images alone. In addition, the location of a sentinel node is illustrated by the surrounding muscle and bone structures. The present pilot study demonstrates the feasibility of the volume-rendered three-dimensional SPECT/CT technique in patients with melanoma or breast cancer. It provides the surgeons with a detailed three-dimensional roadmap, which is a welcome addition to the anatomical insight provided by two-dimensional SPECT/CT. The combination of the two- and three-dimensional images provided relevant new information in 77% of the patients and changed the surgical approach in 50% of the patients in this selected population.

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References

