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 11

Evaluation of lymphatic drainage patterns to the groin and implications for the extent of groin dissection in melanoma patients

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Abstract

Introduction: Early conventional lymphoscintigrams can distinguish sentinel nodes from second-tier nodes and the new SPECT/CT technology shows their precise anatomical location. The purpose of the study was to analyze lymphatic drainage patterns to the groin using these techniques and to determine the implications for a potential groin dissection.

Methods: Fifty-five groins in 50 patients were analyzed using lymphoscintigrams and SPECT/CT. The superficial groin was divided in five Daseler-zones, and the pelvic region in three zones.

Results: A total of 106 sentinel nodes were depicted, 10% in the superior lateral, 13% superior medial, 42% inferior medial, 26% central and 8% in the external iliac zone. The second-tier nodes were mostly visualized in the external iliac zone (54%). No drainage at all was seen to the inferior lateral zone. In lower trunk melanoma, 81% of the sentinel nodes were in the superior and central zones, and no second-tier nodes were observed in the inferior zones. Twelve sentinel nodes were involved: ten in the inferior medial and two in the central zone.

Conclusion: Most (involved) sentinel nodes were found in the inferior medial and central zones. The high frequency of pelvic second-tier nodes indicates the need for a deep completion groin dissection in the majority of sentinel node-positive patients. In none of the patients, lymphatic drainage was seen to the inferior lateral zone, which suggests that this area need not be included in a completion dissection. In patients with lower trunk melanoma, the inferior medial zone may not need to be removed either.
Introduction

Conventional lymphoscintigraphy visualizes lymphatic drainage patterns in melanoma patients. The images provide information with regard to the number and location of sentinel nodes and early dynamic images can distinguish sentinel nodes from nodes higher up the lymphatic chain. Based on the hypothesis that malignant disease disseminates through the lymphatic system in a step-wise fashion, the second-tier node is likely the next lymph node to be involved when the sentinel node contains metastasis. Increased knowledge of the anatomical location of the sentinel node and subsequent nodes may guide the extent of a completion lymph node dissection in sentinel node-positive patients. For the groin, this may imply that not all superficial and deep lymph node regions need to be included in a completion dissection if a sentinel node or if second-tier nodes are found only in certain areas.

The recently introduced hybrid single-photon emission computed tomography combined with CT (SPECT/CT) visualizes the exact anatomical location of sentinel nodes and second-tier nodes. The purpose of this study was to analyze lymphatic drainage patterns in the groin using both conventional lymphoscintigrams and two- and three-dimensional SPECT/CT images in patients with a melanoma on the leg or the lower trunk. The possible implications for the extent of a completion groin dissection in sentinel node-positive patients were evaluated based on the location of the second-tier nodes.

Patients and methods

The population consisted of 50 patients; 32 women and eighteen men. The mean age was 53 years. Forty-one patients had a melanoma on the leg and nine on the lower trunk. The day before surgery, lymphoscintigraphy was performed after intracutaneous injection of a dosage of 80 MBq technetium-99-nanocolloid (Nanocoll®, GE-Healthcare, Eindhoven, the Netherlands), divided in four equal deposits around the primary tumour or biopsy site. Conventional static imaging was performed at fifteen minutes and two hours after injection of the radiopharmaceutical and was preceded by a dynamic study of ten minutes. 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 views if needed. A cobalt-57 flood source was placed behind the patient to outline the body contour.

Hybrid SPECT/CT was introduced in 2006 as an additional tool to improve lymphoscintigraphic imaging and is performed in specified situations only. SPECT/CT images were made immediately after the two-hour conventional images. No additional dose of the radiopharmaceutical was given. The SPECT/CT system (Symbia...
Daseler divided the superficial groin into five zones with the saphenofemoral junction as intersection. SL: superior lateral zone; SM: superior medial zone; IL: inferior lateral zone; IM: inferior medial zone; C: central zone.
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. A second-tier node was defined as a lymph node that lies on a direct lymphatic pathway from the sentinel node. Sentinel nodes were pursued in all regions indicated by the lymphoscintigraphic and SPECT/CT imaging. All harvested sentinel 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).

A completion dissection was carried out only in patients with a metastasis with an invasion depth of 1.0 mm or deeper according to the Starz-classification as part of a prospective trial at our institute. All lymph nodes harvested from the dissection specimen were examined in 4 mm sections stained by haematoxylin and eosin. All patients were followed at our own institute. A nuclear medicine physician and a research physician determined the number and exact location of the sentinel nodes and second-tier nodes in the groin based on the conventional lymphoscintigrams and on the two- and three-dimensional SPECT/CT images. Following the description by Daseler, the superficial groin was divided into four anatomical zones by drawing a vertical and horizontal line over the saphenofemoral junction and a fifth zone was directly overlying this junction (figures 1 and 2).

![Figure 2. Daseler zones projected in SPECT/CT image of the groin.](image-url)
The pelvic region was divided into three zones: the external iliac, the common iliac and the obturator zone.

**Results**

At least one sentinel node was depicted in each of the 50 patients, on average 2.1, with a maximum of five. A total of 106 sentinel nodes were depicted in the 55 groins: eleven (10%) in the superior lateral zone, fourteen (13%) superior medial, 45 (42%) inferior medial, 28 (26%) in the central zone and eight (8%) in the external iliac zone (table). Sentinel nodes were never found in the inferior lateral zone, in the common iliac zone or in the obturator zone.

At least one second-tier node was depicted in each patient, on average 2.0, with a maximum of three. A total of 104 second-tier nodes were identified: twelve (12%) in the superior lateral zone, nine (9%) superior medial, five (5%) inferior medial, fourteen (13%) in the central zone, 56 (54%) in the external iliac zone, two (2%) in the common iliac zone and six (6%) in the obturator fossa. Second-tier nodes were absent in the inferior lateral zone.

The 41 patients with a melanoma on the leg had 84 sentinel nodes. All these patients had at least one superficially located sentinel node and six patients also had a deep sentinel node (figures 3 and 4). A total of 90 second-tier nodes were detected in the 41 patients with a melanoma on the leg. Twenty-three patients had second-tier nodes in a superficial zone and all patients had at least one second-tier node in the deep compartment of the groin.

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<th>Superficial groin</th>
<th>Deep groin</th>
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<td>N</td>
<td>SL N (%)</td>
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<td>Melanoma on the leg: 41 patients</td>
<td>Sentinel nodes</td>
<td>84</td>
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<td>Melanoma on the trunk: 9 patients</td>
<td>Sentinel nodes</td>
<td>22</td>
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<td>Second-tier nodes</td>
<td>90</td>
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**Table.** Division sentinel- and second-tier nodes in 50 patients with drainage to the groin. N: number of nodes, SL: superior lateral zone, SM: superior medial zone, IM: inferior medial zone, IL: inferior lateral zone, C: central, EI: external iliac zone, CI: common iliac zone, O: obturator fossa.
The nine patients with a melanoma on the lower trunk had 22 sentinel nodes depicted in fourteen groins (figure 5). All these patients had at least one superficially located sentinel node and two also had a deep sentinel node. The second-tier nodes were situated in a superficial zone in seven patients and in a deep zone in five. Patients with a melanoma on the trunk never had second-tier nodes in the inferior medial zone, in the central zone or in the common iliac zone.

Twelve sentinel nodes were tumour-positive in nine patients, all with a melanoma on the leg. Ten of these nodes were located in the inferior medial zone (83%) and two were found in the central zone (17%). Six of these patients did not receive a completion dissection because of a small tumour load in the sentinel node. Three of these patients had second-tier nodes confined to the superficial groin and the other three had a deep second-tier node. The three remaining sentinel node-positive patients had second-tier nodes in the deep compartment of the groin on their pre-operative lymphoscintigrams and received a superficial and deep completion dissection. One of these three patients was found to have a positive node in the obturator zone, where a second-tier node had been displayed on the lymphoscintigram.
Figure 4. A patient with a melanoma on the leg. An anterior three-dimensional SPECT/CT image (A) depicts three nodes in the groin. The most cranial node (horizontal arrow) is presumable located in the deep compartment, the middle node in the central zone and the caudal node in the inferior medial zone of the superficial groin. An anterior three-dimensional SPECT/CT view (B) with a caudal rotation shows both superficial nodes and indeed visualizes the cranial node (horizontal arrow) in the external iliac zone of the deep lymph node region. A blue lymphatic vessel was intraoperatively detected running to each of the nodes that were therefore considered to be sentinel nodes.

Figure 5. A patient with a melanoma on the lower back. An anterior three-dimensional SPECT/CT image (A) and a three-dimensional SPECT/CT view with a caudal rotation (B) depict two sentinel nodes and a second-tier node (descending arrow) in the groin. The most lateral sentinel node is detected in the superior lateral zone lateral from the spina iliaca anterior, a rare spot for such a node. The medially visualized sentinel node is located in the superior medial zone of the inguinal groin.
Discussion

The majority of the 50 studied patients with lymphatic drainage to the groin had sentinel nodes in the inferior medial (42%) and central (26%) zone of the superficial groin. The tumour-positive sentinel nodes were confined to these areas as well. No sentinel nodes were found in the inferior lateral zone. Deep sentinel nodes were seen in the external iliac zone in 8% of the patients but not beyond.

In 199 comparable patients who have previously been studied at our institute, more sentinel nodes were found in the inferior medial zone (63% versus 42% in the present study) and less in the central zone (1% versus 5%). This disparity could be due to the difference in imaging technique. The conventional lymphoscintigraphy used in the earlier study is less precise in locating lymph nodes, especially around the central zone. The two- and three-dimensional SPECT/CT that was used in the present study shows the anatomy in detail and is considerably more accurate for the purpose. Presumably, some of the sentinel nodes depicted in the medial inferior zone in the previous study were actually located in the central zone.

No lymph nodes at all were seen in the inferior lateral zone, which suggests that this zone could be excluded from any completion dissection in sentinel node-positive patients. In 92% of all patients, including all patients with a melanoma on the leg, second-tier nodes were located in the deep zones of the groin, which suggests the need for a combined superficial and deep dissection in case of a tumour-positive superficial sentinel node.

This policy to base the need for a deep groin dissection in sentinel node-positive patients on the location of the second-tier nodes was tested in an earlier study at our institute. In that study, seventeen patients in whom the presence of sentinel nodes and second-tier nodes was restricted to the superficial groin received a superficial dissection only. Twenty-four patients with deep second-tier nodes underwent a superficial and deep dissection and in two (8%) of them additional positive lymph nodes were detected in the deep dissection specimen. In the present study this percentage was eleven, with one of the nine patients with involved superficial sentinel nodes having additional deep nodal metastasis. In published studies of elective groin dissection, the incidence of deep nodal metastases was similar. In our former series, no lymph node recurrences were detected during a median follow-up time of 61 months. None of the presently studied patients recurred either. These findings appear to justify our approach to spare sentinel node-positive patients with superficially located second-tier nodes a deep groin dissection. If there is an indication for further surgery after sentinel node biopsy, it is our opinion that a superficial and deep groin dissection should be performed in case of a positive pelvic sentinel node or in case of a pelvic second-tier node. This strategy may prevent troublesome pelvic recurrences and reduces the number of needless surgical procedures.

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with a deep dissection if the initial superficial dissection reveals more metastatic disease.

The majority of sentinel nodes (81%) of the patients with melanoma of the lower trunk were detected in the superior and central zones, which is in accordance with former suggestions that lymph vessels coming from the abdominal skin and genital area run towards nodes cranially from the saphenofemoral junction. These results are also in agreement with the outcome of a study at our institute in penile carcinoma patients in whom no lymphatic drainage towards the inferior inguinal zones was found. It has been suggested that these inferior zones need not be removed in sentinel node-positive penile carcinoma patients undergoing groin dissection. Such a selective superficial groin dissection may also be considered in patients with lower trunk melanoma and positive sentinel nodes in the superior and central zones, as in our series no second-tier nodes were detected in the zones caudally from the saphenofemoral junction. Selective groin dissection seems justifiable because sentinel node-positive patients have an early stage of lymphatic dissemination without extra nodal disease, which renders the risk of tumour spill negligible.

One might even consider routine pursuit of second-tier nodes to determine more precisely the need for a completion dissection. The finding of a tumour-positive second-tier node would indicate the need for some form of node dissection, whereas a tumour-free second-tier node would obviate the need for further lymph node removal. Although it implies redundant node removal in the majority of patients, in some cases such a policy would prevent an unnecessary groin dissection and it would thus result in further tailoring of regional lymph node surgery to the needs of the individual patient.

We conclude that the combination of early conventional lymphoscintigraphy and SPECT/CT enables precise localization of sentinel nodes and second-tier nodes. The present study suggests that a selective completion dissection based on the location of the second-tier nodes may be appropriate in sentinel node-positive melanoma patients. The majority of sentinel node-positive patients require deep completion groin dissection due to the presence of pelvic second-tier nodes. The inferior lateral zone can possibly be excluded from any dissection, since in none of the patients lymphatic drainage was seen to this region. In patients with a melanoma on the lower trunk, the inferior medial zone might be left in situ as well. Further study in more patients is necessary, especially in those with a trunk melanoma, to confirm the current findings and to draw more definitive conclusions on the extent of a completion groin dissection.
References


