Sentinel nodes in complex areas: innovating radioguided surgery
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Chapter 10

Using a portable gamma camera for preoperative lymphatic mapping: a comparison with a conventional gamma camera

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ABSTRACT

Introduction: Planar lymphoscintigraphy is routinely used for pre-operative sentinel node visualisation, but large gamma cameras are not always available. We evaluated the reproducibility of lymphatic mapping with a smaller and portable gamma camera.

Methods: In two centres, 52 patients with breast cancer received pre-operative lymphoscintigraphy with a conventional gamma camera with a field of view of 40x40cm. Static anterior and lateral images were performed at fifteen minutes, two hours and four hours after injection of the radiotracer (99mTechnetium-nanocolloid). At two hours after injection, anterior and oblique images were also performed with a portable gamma camera (Seninella, Oncovision) positioned to obtain, a field of view of 20x20cm. Visualisation of lymphatic drainage on conventional images and images with the portable device were compared for number of nodes depicted, their intensity and localization of sentinel nodes.

Results: The images performed with the conventional gamma camera depicted sentinel nodes in 94% while the portable gamma camera showed drainage in 73%. There was however no significant difference in visualisation between the two devices when a lead shield was used to mask the injection area in 43 patients (95% vs 88%, p=0.25). Second-echelon were visualized in 62% of the patients with the conventional gamma camera and in 29% of the cases with the portable gamma camera.

Conclusion: Preoperative imaging with a portable gamma camera fitted with a pinhole collimator to obtain a field-of-view of 20x20cm is able to depict sentinel nodes in 88% of the cases, if a lead shield is used to mask the injection site. This device may be useful in centres without the possibility to perform a preoperative image.
INTRODUCTION

Sentinel node biopsy is routinely used for nodal staging of patients with breast cancer. After the injection of a radiopharmaceutical, planar lymphoscintigraphy is usually performed pre-operatively to visualise lymphatic drainage from the breast. Sequential planar images will show successive stages of drainage and thereby help to determine the number and location of sentinel nodes.1-3 Unfortunately, gamma cameras are not always used or available and therefore patients are sometimes operated without pre-operative images.4,5 Surgeons then rely on the gamma probe only to guide excision of radioactive sentinel nodes, and in many cases patent blue is used as an additional guide.5-7 In this way, extra-axillary sentinel nodes can not be harvested and surgeons are not informed about the number of sentinel nodes to be expected.

A portable gamma camera has recently been introduced for intra-operative visualization of radiotracer activity and can help to localise the tumour and the sentinel nodes during operation.8,9 The intra-operative use of this portable device might lead to excision of additional sentinel nodes.10 In theory, this camera can also be used to improve pre-operative sentinel node visualisation. Provided that image quality and field of view are sufficient, a portable gamma camera could be used when a conventional gamma camera is unavailable or occupied. The aim of this study was to evaluate whether preoperative lymphatic mapping in breast cancer is possible, using a portable gamma camera positioned to obtain a field of view of 20x20cm. Images from this portable device were compared to conventional gamma camera imaging.

PATIENTS AND METHODS

Retrospective proof of concept

Anterior and lateral planar images of ten breast cancer patients, who had previously undergone planar lymphoscintigraphy with the conventional gamma camera (SymbiaT, Siemens), were reviewed. The images were reduced to only show a 20x20cm field of view. In the majority of patients, this area covers a region from supraclavicular to inframammary areas and from parasternal to arm areas. This zone is where the normal breast lymphatic drainage shows the sentinel lymph node localization. These 20x20cm images were compared to the original 40x40cm images to evaluate if all hot spots could be detected within the smaller field of view.
Prospective study
Fifty-two patients who were scheduled for sentinel lymph node biopsy were prospectively included. All patients had negative axillary nodes on clinical examination and ultrasonography. Patients who had previously undergone treatment of the breast or axilla were excluded. Thirty-five patients were treated at the Hospital Clinic Barcelona and seventeen patients at the Netherlands Cancer Institute in Amsterdam. All patients gave informed consent.

The radiotracer, 99mTechnetium-nanocolloid (GE Healthcare), was injected intratumourally. The injected dose was 111–140 MBq in 0.2-0.5ml. Routine imaging was performed, consisting of planar static images with the conventional gamma camera (E-Cam or SymbiaT, Siemens or Infinia Hawkeye, General Electric) at fifteen minutes, two hours and four hours after injection. Static images consisted of an anterior (patient lying on the back or upright) and lateral (hanging breast or upright) image with an acquisition time of five minutes each. Directly after the conventional two hour static images, images with the portable gamma camera (Sentinella, Oncovision) were made. We compared images with the two devices at two hours because at this time point the yield of lymphatic mapping is higher than at thirty minutes. Furthermore, performing lymphoscintigraphy at four hours was not routinely made in one of the facilities, due to logistic limitations.

The portable gamma camera is equipped with a 4mm pinhole collimator and the field of view depends on the distance between the camera and the imaging plane. Based on the findings of the above mentioned retrospective study we used a field of view of 20x20cm, This was obtained by placing the detector at a distance of 18cm above the breast (figure 1). Technical details of this portable gamma camera are previously described by Sanchez et al.\(^\text{11}\) In every patient anterior and lateral oblique images (patient lying on the back, breast fixated medially if necessary) were performed with an acquisition time of three minutes each. In 43 patients lead shielding of the injection site was performed in order to achieve a better depiction of the sentinel nodes. Nine patients were studied without lead shielding, because at one of the facilities lead shielding was not routinely used at the beginning of the study.

Location of the sentinel nodes was marked on the skin after the delayed conventional static images. Intra-operative sentinel node excision followed within 24 hours after radiotracer injection and was assisted by the use of a gamma probe (Navigator\(^\text{®}\),Neoprobe\(^\text{®}\) or Europrobe\(^\text{®}\); RMD Instruments Corp, Neoprobe Corp, Eurorad, respectively) and patent blue.
Preoperative lymphatic mapping with a portable gamma camera

Analysis
Two hour conventional planar images and portable camera images were collected in a database and scored by a team of three nuclear medicine physicians. Items that were scored for each image were: number of sentinel nodes and higher echelon nodes visualized, the location of the nodes (axillary or extra-axillary) and intensity of nodal uptake (visualization score 1–3, where 1=weak intensity, 2=moderate and 3=intense). Visualisation rates with the conventional camera and portable device were compared with McNemar’s test (SPSS for Windows). Mean numbers of sentinel nodes depicted were compared for both devices with the paired sample t-test (SPSS for Windows). The main endpoint of the study was to assess the feasibility of lymphatic mapping in breast cancer with the portable gamma camera. Secondary endpoints were differences in the number of visualised nodes, location of visualised nodes and image quality between the conventional images and portable camera images.

RESULTS

Retrospective proof of concept
In the ten consecutive patients sixteen sentinel nodes were visualised on two hour planar images. All these nodes were confined within a 20x20cm field of view.

Lymphoscintigraphic results
The images performed with the conventional gamma cameras showed adequate sentinel node visualization, in 49 out of 52 patients (94%). The preoperative images performed with
the portable gamma camera demonstrated regional lymphatic drainage and sentinel node localization in 39 of 52 patients (75%). This visualisation difference is statistically significant (p=0.001).

When a lead shield was used to mask the injection activity, a sentinel lymph node was observed with the conventional gamma camera in 41 out of 43 patients (95%) and in 38 of 43 cases with the portable gamma camera (88%) (figure 2). This visualisation difference is not statistically significant (p=0.25).

In this particular group of patients without shielding, the portable gamma camera was able to visualize a sentinel node in seven patients (78%). Visualized sentinel nodes were mostly located in the axilla, but in the parasternal region in two patients.

![Figure 2](image)

**Figure 2** | Lead shielding yields a higher percentage of sentinel node visualisation when the portable gamma camera is used. Planar lymphoscintigraphy shows one axillary sentinel node (A) which is also seen with the portable gamma camera (B). When a lead shield is placed over the injection area, the axillary sentinel node is much more clearly depicted (C).

**Number of sentinel nodes and area of drainage**
Conventional images showed 74 sentinel nodes (1.4 per patient), while on the images with the portable gamma camera without lead shielding 47 sentinel nodes were depicted (0.9 per patient). Sixty-four percent of sentinel nodes depicted by conventional gamma camera were exactly reproduced with the portable gamma camera. The mean number of nodes depicted on the portable gamma camera was 0.5 less (p<0.001).

In 77.5% of the patients with visualisation, sentinel nodes were located in the axilla only (38 out of 49). In eight patients, sentinel nodes were visualized both in axilla and in the parasternal region and three patients presented with a solitary sentinel node in the inner mammary chain.
Twelve axillary nodes as well as four inner mammary chain nodes were not depicted. In the remaining cases (eleven hotspots), the portable gamma camera depicted one hotspot in the position where two separate ones were visualised on conventional images.

When a lead shield was placed over the injection site, conventional images showed 58 sentinel nodes (1.4 per patient), while on the images with the portable gamma camera 48 sentinel nodes were depicted (1.1 per patient). The mean number of nodes depicted on the portable gamma camera was 0.2 node per patient less than on conventional images ($p=0.01$). In this scenario, five axillary lymph nodes depicted by the conventional gamma camera were not visualized with the portable gamma camera. In five patients, one sentinel node was visualized with the portable gamma camera, while two nodes were depicted on the conventional gamma camera images. In one patient, the portable gamma camera depicted two nodes while one node was shown on the conventional image.

Second-echelon lymph nodes were visualized in 62% of all patients with the conventional gamma camera and in 29% with the portable gamma camera. When lead shield was used, the latter percentage rose to 37%.

In the group with lead shielding, all inner mammary chain nodes depicted with the conventional gamma camera were reproduced by the portable gamma camera. In the group without shielding, four sentinel nodes in the internal mammary chain nodes were not visualized on portable gamma camera images.

![Figure 3](image.png)

**Figure 3** | Axillary sentinel node visualised with conventional gamma camera but not with portable gamma camera. Planar images show an axillary sentinel node (A, B), which is not depicted on screen of the portable gamma camera (C, D).
Intensity of uptake

The intensity of uptake, as scored by a team of three nuclear medicine physicians, is outlined in table 1. With conventional images, a mean intensity value of 2.2 per sentinel node was found. This value was 1.8 per sentinel node on the images with the portable gamma camera.

When shielding with lead was performed, mean intensity value was 2.1 per sentinel node on conventional images, compared to 2.3 on portable gamma camera images.

Table 1 | Comparison of intensity uptake of sentinel nodes between conventional gamma camera and portable gamma camera (with and without shielding). Non-visualisation is mentioned as percentage of all patients, while the numbers per intensity score are mentioned as a percentage of the visualised nodes.

<table>
<thead>
<tr>
<th>Score</th>
<th>Without shielding</th>
<th>With shielding</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conventional 74 nodes</td>
<td>Portable Gamma Camera 47 nodes</td>
</tr>
<tr>
<td>0</td>
<td>3 patients (6%)</td>
<td>16 patients (31%)</td>
</tr>
<tr>
<td>1</td>
<td>18 nodes (24%)</td>
<td>15 nodes (32%)</td>
</tr>
<tr>
<td>2</td>
<td>21 nodes (28%)</td>
<td>27 nodes (47%)</td>
</tr>
<tr>
<td>3</td>
<td>35 nodes (47%)</td>
<td>5 nodes (11%)</td>
</tr>
</tbody>
</table>

0=no uptake; 1=weak; 2=moderate; 3=intense
DISCUSSION

Pre-operative lymphoscintigraphy is sometimes considered a time consuming approach without a real impact on intra-operative sentinel node harvesting. Therefore its utility in terms of cost-effectiveness is questioned in some countries. Dixon et al. reported a potentially more efficient and practical technique of immediate preoperative injection of blue dye and radiopharmaceutical by the surgeon. After injection of the radiopharmaceutical in the operation room sentinel node biopsy was performed and succeeded in 161 out of 163 women.5 This method does however not allow for late draining nodes to be detected, and, since no sequential images are available, second echelon will not be distinguished from the first draining node(s). In order to ensure optimal nodal harvesting, some countries have strict regulation with regards to injection and images, which must involve lymphoscintigraphy at the department of nuclear medicine.12,13 Furthermore, excision without images does imply that extra-axillary nodes will be missed.

The use of a portable gamma camera enables the nuclear medicine physician to perform lymphoscintigraphies in a separate room, without additional occupation of the conventional gamma camera. Several portable gamma cameras have been developed recently.14-17 The portable gamma camera tested has a continuous scintillation crystal and a position-sensitive photomultiplier tube. The intrinsic spatial resolution is approximately 2mm, and the energy resolution is 13% at 140 keV.11

Normally, the field-of-view of conventional gamma cameras is 40x40cm. In breast cancer we evaluated a set of different images coming from two tertiary hospitals and established that an area of 20x20cm included all sentinel nodes depicted in those studies. Based on this experience, we adjusted the distance of a pin-hole based portable gamma camera to the body surface of the patient to get the same 20x20cm area.

Our results indicate that such a portable gamma camera can detect sentinel nodes in 88% of the patients if adequate shielding is performed. Although statistical power is limited due to the small number of patients included, the visualisation rate on conventional images is slightly better (non significant in our statistical analysis) and the intensity of the visualised nodes is comparable. The current number of depicted sentinel nodes per patient on portable gamma camera images is however less then the yield with conventional images at two hours after injection. Per patient a mean of 0.2 sentinel nodes was visualised on conventional images, while missed on the images with the portable gamma camera. This means that in one out of five patients, a sentinel node was missed on the portable gamma camera images compared
to conventional images. Probably the most important explanation for this lower detection rate with the portable gamma camera, is the distance (18cm) used to position the camera in relation the patient. This hypothesis also explains the low second-echelon nodes depicted with the portable gamma camera. In intra-operative conditions the portable gamma camera is positioned closer to the patient (5cm), which increases the sensitivity. The replacement of the pinhole collimator by a flat diverging one might solve this problem. In the current situation a field of view of 20x20cm appears to be sufficient to visualise axillary as well as extra axillary nodes. In case of an obese patient two or three images might be performed in order to cover the whole axilla as well as intra-mammary, parasternal and peri-clavicular regions. In the future, new collimators might provide better resolution and sensitivity. Possibly, improvements could also be made to the imaging protocol. Lead shielding appears to be important in this respect, but acquisition time and distance to the body might also be varied in order to define optimal conditions. In the meantime, pre-operative lymphatic mapping with a portable gamma camera and adequate shielding of the injection site may be useful in situations where no conventional gamma camera is available. The portable gamma camera also allows for intra-operative lymphoscintigraphy in situations when intra-operative injection is desired. This especially is the case in sentinel node mapping for other tumours such as laryngeal and colon cancers.

**CONCLUSION**

A field of view of 20x20cm appears sufficient to detect axillary and extra-axillary sentinel nodes in most cases of breast cancer. The pre-operative yield of sentinel nodes with a portable gamma camera is however less than the yield on conventional gamma camera images. This difference in yield is not significant if adequate injection site shielding is used. Pre-operative sentinel node mapping with a portable gamma camera might be an alternative to guide intra-operative harvesting when no conventional gamma camera is available or when intra-operative tracer injection is required. In other situations, sequential lymphoscintigraphic imaging with a conventional gamma camera remains the modality of choice.
REFERENCES


