Sentinel Node Localisation of Breast Cancer

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1. Introduction

The sentinel lymph node (SLN) is defined as the lymph node (LN) that receives drainage from the tumour. The rationale behind the SLN biopsy is the premise that metastases does not progress randomly, but occurs in a stepwise fashion. Thus, if the SLN is not invaded then there should be no metastases in more distant LNs. This concept of stepwise progression of metastases in the lymphatic system has been validated for breast cancer. A negative SLN indicates an N0 status.

Patients who undergo a SNL procedure have fewer and less severe adverse effects compared to those who undergo axillary lymph node dissection. The former experience lower grade arm oedema, arm pain or both, less shoulder motion restrictions, and less arm numbness.

The lymph drainage and therefore the SLN can be visualised with ^{99m}Tc-nanocolloid, which can also be detected by a hand-held gammaprobe.

Labelled colloid particles have a dimension of 10-100 nm. This particle size is optimal for quick lymph transport and will be kept in the lymph node after arrival. The sentinel node procedure with radiopharmaceutical can be complemented by the use of patent blue during the operation for visualization of the sentinel node. Visualisation of a sentinel node with the radiopharmaceutical, occurs in nearly 100% of cases. However, in 20% of cases where patent blue alone is used there is no visualisation. Also, a portion of the injected blue dye is retained at the injection site and results in blue discoloration of the skin for a prolonged time.

2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indications

Patients with T1-2 breast cancer, without clinical suspicion of axillary metastases.

The SLN procedure should take place prior to neoadjuvant chemotherapy in order to allow for decision making with regards to axillary lymph node dissection and adjuvant treatment based on the node status prior to chemotherapy. The false negative rate for SLN procedure after neoadjuvant chemotherapy isgreater than 10%.

To be considered in DCIS, where ablation is considered and whereby riskfactors for invasive breast cancer exist (age < 55years, solid component on mammography, moderate or poorly differentiated DCIS in biopsy specimen, DCIS tumour 5 mm or larger, extensive DCIS, multifocality, microinvasion and high-grade charactersitics).

Proven axillary lymph node metastases is an absolute contraindication.Relative contraindications include prior (recent) surgery of the axilla, and ≥ T3 tumours. The recommendations are the same for male and female breast cancer patients. The SLN

procedure and ^{125}I-sead placement for non-palpable tumours be performed within the same session.

4. Information required

Size and localisation of tumour. Whether or not it is a palpable lesion. Biopsy result. Past surgical history regarding breast and axilla.

5. Radiopharmaceutical

Tracer:	^{99m}Tc-nanocolloid
Nuclide:	Technetium-99m
Activity:	40-80 MBq colloidal albumine (nanocolloid) in a small volume (0,5-1,0 ml for peritumoral and subcutaneous injections, and 0,1 ml when periareolar injections are given). 5-10 MBq at the time of surgery is enough for succesfull detection when using sensitive gamma probes. For two-day protocols higher doses of the radiopharmaceutical are given, adjusted to the expected number of half-lives between the administration and the planned operation.
Administration:	Attempts at standardisation to one or even a few injection techniques have not succeeded. The most widely used injection thechniques are peritumoral, subcutaneous and periareolar. Peritumoral injections are administerd at 2-4 sites around the tumour into the interstitial tissue of the breast. Subcutaneous injections are administered under the dermis above the tumour. Peri-areolar injections are advised in the peri-areolar region within the same quadrant as the tumour.

6. Relation to other diagnostic procedures

SPECT/CT offers increased spatial resolution and excellent anatomical localisation.
SPECT/CT is particularly valueable when there is drainage to extra-axillary lymph nodes and or when SLNs contain very small amouunts of radioactivity.
The sensitivity of preoperative diagnostic techniques (ultra-sound, CT, MRI, PET), for the detection of lymph node metastases, is very low.
However, preoperative axillary ultrasound-guided biopsy is a useful step in the process of axillary staging. Approximately 50% of women with axillary involvement can be identified preoperatively. Nevertheless, one in four women with a negative ultra sound-guided biopsy has a positive SLN. Therefore, the SLN procedure is still recommended after negative ultrasound of the axilla.

7. Radiation safety

Approximately 4 hours after administration of 80 MBq, the radiation dose for operating room personnel varies from about 16-1 µSv/h measured at a distance of between 25 to 75 cm from the injection site.
Effective dose for a patient (one breast) is 0,005 mSv/MBq. Based on the given reference in which an humanoid phantom and thermoluminescent detectors were used.
In contrast with the EANM/SNMMI practice guideline for lymphoscintigraphy and sentinel node localization in breast cancer, the ICRP-106 states that, despite tracer transfer into breastmilk, there is no need for interruption of breastfeeding

8. Patient preparation/essentials for procedure

Patient preparation

None

Essentials for procedure

- Marker source (^{57}Co pen)
- Waterproof ink (e.g. Fuchsin-silver nitrate) or surgical skin marker
- Gammaprobe
- ^{57}Co flood source for body contour detection

Procedure

a. The amount of radiopharmaceutical required for the procedure depends on the expected delay between injection and operation. A minimum delay of 3 h is advised between start of the sentinel node procedure and planned operation time. The procedure should be completed within 24 h. This in order to avoid dissociation of the nanocolloid and the radiotracer and also to avoid wash out of the tracer out of the SLN. Both cases lead to reduced SLN detection rates.
b. If the procedure is to occur after (a previous) tumour resection or surgical biopsy, the radiopharmaceutical should be injected on either side of the scar.
c. Echo led administration of the radiopharmaceutical may be done if a tumour is non-palpable or to avoid injection into a biopsy cavity or haematoma.
d. Dynamic acquisition under the gammacamera has the advantage of visualising the lymph vessels. This allows differentiation between first and second echelon SLNs.
e. Static acquisition several hours post injection and shortly prior to the operation gives additional information about second echelon SLNs and the expected activity of the first echelon SLN. A recording with an additional cobalt flood source behind the patient can give extra information.
f. Anterior, anterolateral oblique and lateral aquisitions may be performed. Note that for anterior aquisations the breast may need to be moved/held medially in order to avoid overprojection of the depot onto the axilla. The arm should be placed in 90° abduction, especially when marking the skin.
g. Outlining the body contour using a ^{57}Co flood source placed in between the patient and the camera can provide extra information about the localisation of the SLN.
h. During the operation the SLN is traced using the gammaprobe. The woundbed should be checqued after removal of the SLN. If over 10% of the activity removed persists, active lymph nodes are still present in the wound bed.
i. Additionally, blue dye, injected shortly before starting the operation, can be used to visualise lymph vessels. Patent blue is injected intra-/ subcutaneously, around the tumourbed or around the excision scar. The transport of blue dye is much faster than that of colloid and has to be performed shortly before the incision to avoid overflow to higher echelon SLNs. A disadvantage of patent blue is the discolouration of overlying skin for a prolonged period.

9. Acquisition and processing

Gamma Camera

Energy: ^{99m}Tc setting, 140 keV

Window:	15-20%
Collimator:	LEAP or LEHR
Counting time static acquisition:	2-4 sec per view or a minimum of 600.000 counts
Computer:	Matrix 64x64 or 128x128

Gamma probe

Energy:	^{99m}Tc setting, 140 keV
Window:	20%
Rate meter:	Scale range (x1, etc.) depending on the depth of the lymph node and the time between administration and surgery.

10. Interpretation and pitfalls

- Non-visualization of the SLN can be caused by too low a dose of nanocolloid, obstruction of the lymph vessels by tumour deposits (embolisation of the lymph vessels by tumour cells), or a haematoma in the breast. A high tumour burden in the SLN may also prevent penetration of the tracer into the SLN and may contribute to non-visualization of the SLN.
- Lymph transport can be diminished or absent after (prior) tumour resection due to damage of lymph vessels.
- If the SLN nearest to the tumour is not the most active SLN, foresee bypassing of the first echelon SLN because of obstruction of the node by tumour cells. Another explanation could be the existence of multiple lymph vessels with the most dominant one transporting the tracer to a more distant node than the non-dominant vessel. In this case, both LN's must be removed.
- Para-sternal SLN should be marked on the skin if the surgeon intends to remove them. There is no consensus on whether or not parasternal SLNs should be removed. If only parasternal SLNs are visualised, the current recommendation is to explore the axilla with patent blue.

11. Report

The report should include the injection sites in relation to the position of the tumour and the amount of radiopharmaceutical injected. The number and degree of activity of first and second echelon SLNs in the axilla. SLNs located outside the axilla, such as parasternal, intramammary or periclavicular nodes. Skin markings should be explained in the report. Localisation of the SLN with reference to the injection site should be mentioned especially when the SLN is located close to the injection site.

12. Literature

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