Sentinel Node Localisation of Melanoma

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1. Introduction

A melanoma is mostly a malignancy of the skin. The sentinel lymph node (SLN) concept of sequential progression of metastases is validated for the malignant melanoma of the skin. Each part of the skin has its own first draining lymph node (sentinel node). The SLN is a lymph node upon which a lymph vessel, originating in the tumour, drains directly. A tumour may drain directly to more than one lymph node or lymph node basin. One lymph node may receive the tracer before the others, but all involved nodes are at risk of receiving tumour cells. The SLNs may be located in different lymph node regions especially when the primary melanoma is located in body sites with variable lymphatic drainage. The rationale for the SLN biopsy is based on 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 lymph nodes.

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 / contraindications

In the Dutch national guidelines on melanoma of the skin (2012) the SLN procedure is advised for those who want patient specific information about the prognosis. The SLN biopsy is indicated if an elective lymph node dissection is being considered. The European consensus based interdisciplinary guideline - Update 2012 - advises the SLN dissection routinely as a staging procedure in patients with tumours over 1 mm in thickness, although there is as yet no clear survival benefit for this approach.
However, early removal of a tumour positive lymph node has the potential to preserve the tumour negative status of the patient for a longer period, but a survival benefit has not been shown. The SLN procedure is not advised in patients with a malignant melanoma stage 1A. It is advised in patients with a malignant melanoma stage 1B or higher.

4. Information on request form

Details of previously performed excision of skin melanomas.
Localisation and Breslow tumour thickness of the primary melanoma.

5. Relation to other diagnostic procedures

Perioperatively, it is possible to identify the SLN guided only by dye; however, this technique has disadvantages (most importantly the lower detection rate). SPECT/CT offers increased spatial resolution and excellent anatomical localisation. SPECT/CT is of additional value especially when there is drainage to lymph nodes near the injection site and/or the SLNs contain very small amounts of radioactivity.

Other imaging techniques for lymph node staging (echo, CT, PET(-CT)): in stage I patients micro metastases may occur, which cannot be detected by other imaging techniques. The size of lymph nodes can be determined in many ways, but appears to be an unreliable indicator presence of metastases. An enlarged lymph node may occur as a response to the primary excision of the melanoma and is not always malignant.

6. Radiopharmaceutical

Tracer:	^{99m}Tc-nanocolloid
Nuclide:	Technetium-99m
Activity:	4 x 10-20 MBq (0,15 ml per injection) colloidal albumin (nanocolloid) in a small volume (<1 ml). Remaining activity of about 5-10 MBq at the time of surgery is enough for successful detection when using sensitive gamma probes. For two-day investigations the activity should be adjusted to the expected number of half-lives between the administration and the planned operation
Administration:	intradermal (needle: 27Gx1/2" = 0,4x12 mm)

7. Radiation safety

Approximately 4 h 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. In contrast with the EANM/SNMMI practice guideline for lymphoscintigraphy 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-penmarker)
- Waterproof ink (e.g. Fuchsin-silver nitrate) or surgical skin marker
- Gammaprobe, ^{99m}Tc-window 140 keV, 15% window
- ^{57}Co flood source for body contour detection

Procedure

There are several protocols in use. The following is just one of many variations that all have advantages and disadvantages. The investigation can take place during one day or over two days, depending on the scheduling of the operation. (When scheduling over 2 days, adjust the dose of the radiopharmaceutical to the number of expected half-lives between the administration and the planned operation). The procedure should be completed within 24 h, on the one hand to avoid dissociation of the nanocolloid and the radiotracer and on the other hand to avoid tracer wash out of the SLN, whereby decreasing the intra operative detection rate.

The injections are given intradermally on either side of the scar or around the remaining melanoma. For longer scars at least 2 injections are required on either side. Ideally this procedure occurs before or simultaneously with the primary excision or at re-excision

of the scar.
The gamma camera is positioned so the injection site and all likely first lymph node basins are within the image. If this is not possible the only the lymph gland basin should be in the FOV. If the tumour is localised on the trunk, the injection site must be central within the image so as allow for observation of potential bilateral drainage or drainage to both axillae and groin. Dynamic images are obtained for 20-30 min immediately after administration. After the dynamic images, a static image is taken in the same direction and at an angle of 90°. This is especially important in the axilla and the head-neck area to detect potentially superemposed nodes. An estimate of the depth of the gland can also be made in this way.
Preoperatively (at least 2 h after injection), the static imaging is repeated. Immediately following image aquisition the location of the SLN is marked on the skin with waterproof ink. This is done with the help of a cobalt source and/or a gamma probe. If localisation is on the trunk, all possible drainage basins are once again depicted.
Perioperatively the probe is used to detect the radioactive node. After removal of the SLNs the wound bed is checked with the probe for residual activity. Given the highly selective retention of this tracer in the lymph nodes, background activity is, as a rule, negligible. If the remaining activity is >10% of the activity in the excised node, further active nodes should be sought and removed.
Administration of patent blue in the same locations as the ^{99m}Tc-nanocolloid can, given the visualisation of the lymphatic tract and the SLN, accelerate the search for the SLN. Intradermal administration of patent blue should take place just prior to the excision. Patent blue is transported more quickly through the lymphatic system than colloid. Therefore, administration just prior to the excision reduces the chance of staining of the overflow nodes.
The intervention can cause morbidity, namely allergic reactions to the blue dye (0,4%), (mild/transient) lymphoedema (12%), or lymphatic fistula (1,2%). These adverse effects are not negligible, given the high frequency of tumour-negative preparations in these patients with stage-I, clinically non-disseminated disease (80% negative lymph node status). Besides this morbidity, follow-up of malignant melanoma patients who had undergone a SLN procedure, showed more interval metastases. Interval metastases are notoriously difficult to manage. They are usually multiple and have a high relapse rate. When an elective lymph node dissection is being considered, the benefits of the investigation are greatest in patients with stage I melanoma and where the Breslow thickness is 0,75-4 mm (tumour thickness >4 mm is often accompanied by simultaneous lymphogenic and haematogenous metastasis (55%), while tumour thickness <0,9 mm, is associated with a very small chance a positive lymph nodes).

9. Acquisition and processing

Gamma Camera

Energy:	^{99m}Tc setting, 140 keV
Window:	15-20%
Collimator:	LEAP or LEHR
Acquisition time:	Dynamic 20x60 sec, Static 120-240 sec/exposure, minimum 600.000 counts
Computer:	Matrix 64x64 or 128x128

Gamma probe

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

10. Interpretation and pitfalls

The SLN is the first permanently visible lymph gland. Through the branching of the lymph tracts or the existence of several separate lymph tracts, it is possible for multiple first echelon SLNs to be visualised. This shows the importance of the early, dynamic acquisition. Lymph vessels and sentinel nodes almost always (96%) become visible during the dynamic investigation, if not, then the dynamic acquisition should be extended. It must be assumed that each lymph vessel has its own SLN (occasionally, however, fusion of vessels is seen with a single SLN). Late images, often show multiple (though generally less active) nodes due to overflow of the tracer to second echelon nodes. When multiple nodes are visible on the scintigram, and it is not possible to designate one node as first echelon SLN, it is advisable to remove all visible nodes. Tangentially running vessels may give the impression of being lymph glands, especially early on in the dynamic acquisition. These hot spots often disappear during the dynamic investigation or on late images. The late images also serve for recognition of interval glands (glands located between the injection site and regional basin). Lymph vessels empty after 2 h, whilst the interval glands remain visible and must also be considered as SNs.
Therefore, the entire tract between the injection site and the regional basin must be depicted. The blue dye is useful in distinguishing lymph nodes (often only 0,5 cm in diameter) from fatty tissue. Patent blue can "overflow" to more proximal nodes. Therefore, confirmation is required that the blue node is indeed the radioactive SLN. In more than 80% of patients, the radioactive gland is also blue. As yet there is no uniform explanation for this discrepancy.

11. Report

In the report, the injection site is indicated (the precise location relative to the melanoma or the surgical scar) and the visualisation of lymph vessels and SLNs, whereby interval nodes (nodes outside the normal anatomical lymph gland basins) are regarded as SLNs. The meaning of all skin markings must be indicated.

12. Literature

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