BNMS Procedure Guidelines for Radionuclide Lymphoscintigraphy for Sentinel Node Localisation in Breast Carcinoma

Report September 2009
**Purpose**

The purpose of this guideline is to assist practitioners in recommending, performing, interpreting and reporting sentinel node imaging for identifying sentinel nodes for excisional biopsy in patients with breast carcinoma. This guideline stipulates minimum requirements for good practice; individual centres may wish to expand these recommendations.

**Background**

Sentinel lymph node biopsy (SLNB) is becoming established as an accurate method of staging axillary lymph node involvement in breast cancer and relies on the assumption that if the sentinel node is clear of metastases, the remainder of nodes in the axilla are too. The major advantages of staging with SLNB compared with staging by axillary lymph node dissection are significantly reduced patient morbidity, avoidance of extensive surgery in the majority of patients without nodal metastases, detection of nodal metastases at an earlier stage because the few sentinel nodes from each patient can be subjected to more detailed histological analysis than the larger numbers of nodes from an axillary clearance and significant cost savings because only a minority of patients (approx 20 – 30%) will have axillary metastases and need to go on to conventional axillary clearance. However, it is not yet known whether SLN improves long-term survival compared with conventional axillary clearance.

**Definition**

A Sentinel lymph node (SLN) is any lymph node which receives lymphatic drainage directly from a tumour (Morton, 1992). SLNs may not be the hottest nodes at the time of imaging, they may not be the ones closest to the tumour and there may be more than one SLN.

**ARSAC Enquiries**

ARSAC licenses for breast SLNB will normally be held by radionuclide radiology/nuclear medicine specialists. The prospective license holder needs to provide proof, when applying for an ARSAC license, that any surgeons performing the technique have undergone appropriate theoretical and supervised practical training. Suitable training programmes are being organised by the Royal College of Surgeons (ref final document when it’s out of draft format). To obtain an ARSAC license so that the supervised training can take place on site, applicants need to provide written evidence from the Royal College of Surgeons that surgeons involved in the technique have both undergone a 3 day training course and committed to supervised in-house training (draft ARSAC Notes for Guidance, Appendix IVc).
Aims of Lymphoscintigraphy

1. To demonstrate which lymphatic drainage basin(s) are potential sites of metastatic disease
2. To determine the number and location of SLNs within those drainage basins
3. To demonstrate SLNs with aberrant drainage, ie which are outside normal lymphatic drainage basins
4. To mark the location of any SLNs for subsequent surgical dissection
5. To try to distinguish SLNs from second-tier lymph nodes

Indications

SLNB is recommended in patients

1. with T1 and T2 stage invasive breast carcinoma
2. with N0 and M0 invasive breast carcinoma
3. with high risk and microinvasive ductal carcinomas in situ
4. with good prognostic group tumours (tubular, medullary, mucinous, papillary)
5. following primary chemotherapy

Patients with larger tumours eg T3 tumours may also undergo SLNB to help determine prognosis provided there is no evidence of regional nodal disease or metastases.(N0M0)

Contraindications

1. Patients with regional or distant metastases
2. Previous extensive surgery or radiotherapy to tumour site or ipsilateral axilla
3. Known allergy to patent blue dye or to albumin colloid (Patent blue dye may be omitted of the patient has allergy to this agent)
4. Patients who are unwilling to undergo subsequent axillary therapy should their SLN contain metastases.

Procedure

1. Patient preparation

Patients should be counselled about the current status of SLNB in the management of breast carcinoma and alternative methods of staging disease and should understand that by agreeing to SLNB, they may also need to undergo axillary therapy should their SLN contain metastases. There is no special preparation for the procedure, other than
preoperative restrictions if sentinel node imaging is being performed on
the same day as surgery.
Patient should undress from the waist upwards and wear a front-opening
patient gown. As per routine practice, the patients bra and all relevant
metallic items (coins, jewellery etc.) should be removed.

2. **Radiopharmaceutical/administered activity**

2.1 $^{99m}$Tc Human Serum Albumin nanocolloids has an optimal
particle size (4-100nm, with >95% particles < 80nm) for passage
through the lymphatic system and is the favoured
radiopharmaceutical in the UK and Europe.

2.2 $^{99m}$Tc-Tilmanocept which is a specific mannose receptor agent
and does not work by filtration but targets macrophages in the
lymph node

2.3 High specific activity in injectate (Valdes Olmos Nuc Med Comm

2.4 Administered activity according to when surgery is planned,
aiming for at least 10 MBq activity in the patient at the time of
imaging (Koizumi, Nuc Med Comm 2003; Morton BJR 2003),
calculated according to radioactive decay, illustrated in table 1.

Table 1.

<table>
<thead>
<tr>
<th>Delay between injection and surgery (h)</th>
<th>Activity to inject (MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>18</td>
<td>40</td>
</tr>
<tr>
<td>24*</td>
<td>75*</td>
</tr>
</tbody>
</table>

*Approved only for $^{99m}$Tc-Tilmanocept

2.5 Small volume of injection, ie 0.2 – 1ml. With air behind fluid
volume to ensure that all of the small volume is delivered.

3. **Injection Technique**

Table 2.

<table>
<thead>
<tr>
<th>Palpable</th>
<th>Impalpable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior excision biopsy</td>
<td>15 – 20 MBq* in 0.2ml Nanocoll injected intradermally on either side of excision scar</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>No prior excision biopsy</td>
<td>15 – 20 MBq* in 0.2ml Nanocoll injected intradermally overlying tumour</td>
</tr>
</tbody>
</table>

3.1 *Applies to imaging the same day as surgery. If imaging the day before surgery, the administered activity should be increased appropriately (table 1)

3.2 Must be performed by a trained, competent operator (as specified by IRMER)

3.3 Should take place within nuclear medicine department unless absolutely impracticable to do so

3.4 Should observe all radiation protection precautions outlined in section 9

3.5 Patients surrounding skin covered to avoid splash contamination
3.6 25 G needle or finer

3.7 Where tumours are still in situ, injections should be placed intradermally in the skin overlying palpable tumours and in the index quadrant of the subareolar region if tumours are impalpable. If patients have already undergone previous excision biopsy, injections should be placed intradermally on either side of the excision scar (see Table 1)

3.8 cover injection site with gauze/cotton wool ball whilst withdrawing the needle to avoid skin contamination and seal with a small waterproof plaster immediately the needle is removed

3.9 patient to massage injection site for 2 mins to promote uptake of tracer into lymphatic channels

4. Image acquisition

4.1 Gamma camera detector size of at least 20cm; LEHR collimator. Note a dedicated small field of view digital gamma camera may also be used

4.2 Pixel matrix size of at least 128 X 128, ideally 256 x 256

4.3 For intradermal / subareolar injections, patient may be injected on camera couch and imaging commenced immediately after injection (re-positioning of patient into pre-determined optimal position under camera can be performed while patient is massaging injection site).

4.4 Patient should be supine, with arm on affected side completely abducted to allow head of gamma camera to come as close as possible to the axilla. Use an injection stand or other equivalent support for the arm. This position should mirror that of the patient at surgery – consult with surgical team to ensure this.
4.5 Tape breasts away from axilla if necessary

4.6 Early static or dynamic images (within 15-20 minutes of injection) may demonstrate lymphatic tracks and help distinguish between SLNs and second-echelon nodes (Lee, 2002; Mariani, 2001).

4.7 The majority of SLN should be visible by 2.5 hours of radiocolloid injection (Birdwell, Radiology 2001)

4.8 Minimum dataset is to acquire the views listed below at/by 3 hours post injection of radiocolloid

4.8.1 Anterior oblique 5 min (400,000 – 500,000 counts), 30 degree reference angulation.

4.8.2 Lateral 5 min - patient positioned for lateral image with arm abducted and camera positioned vertically in contact with region from neck to diaphragm, including both anterior and posterior surfaces of patient

4.8.3 Anterior (if internal mammary nodes visualised)

4.8.4 SPECT-CT may be helpful in localizing internal mammary nodes

4.8.5 If a dedicated small field of view digital gamma camera is used then these views maybe modified

4.9 Transmission images (Co-57 flood source); anterior oblique, lateral and anterior (if anterior emission image acquired) should each be acquired immediately after their emission image equivalent to ensure that patient is in same position under the camera. The transmission image is acquired using a $^{57}$Co flood source positioned on the opposite side of the patient to the detector, and parallel to the camera face, to generate a ‘shadow’ of the patient’s outline. An injection stand may be used to support the flood source for the lateral image. The transmission
image should be of sufficient duration that the lungs can be
delineated within the patient’s outline as an additional landmark.

4.9.1 This allows the emission and transmission data to be
added to give a combined image containing the
information from both datasets.

4.9.2 If all images are negative for SLN, then further imaging at
a later timepoint may be performed, either 6 hrs post
injection (Birdwell Radiology 2001) or next morning, if
time permits prior to surgery.

Skin marking

a) Skin marking is recommended. However, the final
decision as to whether to mark the skin overlying any
SLNs may be made locally following discussion with
the surgical team.

b) If skin marking is performed, the site of the shortest
skin-to-node distance should be marked, ie axillary
SLNs are best marked using anterior-oblique views
and internal mammary nodes using anterior views

c) SLN may be located using a radioactive marker
source moved over the patient’s skin during an image
acquisition until its position coincides with the surface
projection of the SLN, or by using a gamma probe.

d) The skin overlying the SLN should be marked with an
indellible marker pen

5. Image Processing

Each pair of emission and transmission datasets should be added together
to generate a combined image containing the information from both
datasets. These combined images should be displayed alongside their
corresponding emission datasets and annotated. Hardcopy or PACS
softcopy images of these should then be created for reporting and transfer
to the surgeon for reference at the time of surgery.
6. **Image Interpretation**
Images should be reviewed on the computer console with appropriate windowing of low-count areas.

7. **Reporting**

7.1 PACS softcopy output and if appropriate hard copy images of the emission and combined (emission+transmission) image data and a written report of the imaging findings should be available to the surgeon at the time of sentinel node excision biopsy; this is best achieved by written entry in the patient’s hospital clinical record.

7.2 A system of tabulating SLNs should be agreed locally with the surgeons and histopathologists, for ease of identifying which drainage basins any positive SLNs originate from.

8. **Reporting terminology**
Morton’s anatomical definition of the SLN does not always translate easily into imaging findings. Suggested terminology is

8.1 Highly probably SLN – ie if there is a single SLN, more than one SLN, but in different nodal basins, aberrant nodes, a second node appearing in between the first SLN and the injection site.
All need surgical sampling

8.2 Probable/possible SLN – A node which contains > 25% activity of the highest activity node as estimated from ROI analysis on the gamma camera images. Needs assessment with the gamma probe at surgery to determine if the activity is above 25 % of the activity in the hottest node. The surgical assessment is needed since the 25 % threshold assessment with imaging is affected by attenuation affects.

8.3 Probably not a SLN – this would include nodes where it is not clear from imaging whether they are SLN or second-tier, persistent unexplained foci of activity in lymphatic tracks (if early imaging performed) etc. Need correlation with surgery – if intraoperative gamma probe indicates that activity is below 25 % of hottest node, then don’t need sampling.
8.4 Definitely not an SLN – a clear second tier node, or activity below 25% of the hottest node.

9. **Sources of error**

9.1 Skin contamination

9.2 Operative position significantly different from patient position when overlying skin is marked

9.3 Differentiation of SLN from sites of lymphatic hold-up eg confluences

9.4 Differentiation of SLN from second-tier nodes

9.5 Failure to locate SLN accurately if relying on images in one plane only

9.6 Failure to locate low-count SLNs

9.7 Incorrect or failure of communication of report to surgical team

9.8 Apparent non-drainage: associated with higher chance of aberrant SLN and of metastases to SLN

---

**Intraoperative Probe/imaging**

See guidance from the UK Gamma Working group: purchase specification, user examination.

Training in the use of the gamma probe is encompassed by the Royal College of Surgeons training courses in breast SLNB.

If trained intra-operative imaging with hand held gamma cameras may be used.

---

**Outcome Analysis**

1. SLNB is a multi-disciplinary staging procedure and the success of the technique depends on the strengths of the individual components (surgery, imaging, histopathology) and how well they communicate. All patients should be reviewed in a multi-disciplinary team meeting.

2. Patient outcomes should be audited regularly against published standards, for example those determined by the Royal College of Surgeons

3. The accuracy of the technique can be assessed by the proportion of patients whose SLNs contain metastases, which should match that of
axillary clearance and the % of patients with clear SLNs' who develop recurrent disease early (false negatives)

4. Suggested standards are
   - SLN’s should be located in > 95% patients
   - 20 – 30% SLN’s should contain metastases, depending on patient population/tumour size
   - The false negative rate should be < 5% (Clarke, 2004)

Radiation Protection

Careful attention to the established principles of good radiation protection practice when administering a radionuclide by injections is essential when performing the injection of radiocolloid to prevent the possibility of spillage or spread of injectate as surface contamination. Any injectate inadvertently transferred to the skin surrounding the injection site, clothing or the camera couch will confound interpretation of the image data obtained, and is generally difficult to remove without difficulty. The following points should be observed:

1. Perform all necessary examination and preparation of the injection site before preparing the injectate syringe for administration.

2. Ensure that the injection(s) are delivered through a small port cut into an inco-pad draped over the area surrounding the chosen injection site. Ensure that the remainder of the patients thorax and axilla are covered by the front-opening gown. This will prevent inadvertent contamination of the adjacent skin by a droplet of spilt injectate.

3. Immediately following injection of the radiopharmaceutical, the injection site(s) should be sealed with a small plaster and massaged for two minutes by the patient with a cotton wool ball to encourage lymphatic drainage. This will prevent any transfer of any small volume of injectate which may subsequently leak from the puncture to the surrounding skin.

Controversies

1. Route of injection. The intradermal route is favoured because it is the most practicable; lymphatic drainage from the dermis is faster than from deep injections. However, internal mammary nodes will not be identified with this injection route.
2. Use of dynamic/continuous sequential imaging – can be useful in aiding image interpretation especially when a site first starts SLN imaging.

3. Timing of imaging – whilst the majority of SLN may be visible early post injection, a small proportion require later imaging. Imaging at/by 3 hours should demonstrate SLN(s) in the majority of patients – but what proportion of patients require later imaging – and how much later?

4. Is imaging needed in every patient? Imaging reveals the number and location of each sentinel node. This informs the surgeon where to investigate prior to the biopsy procedure, and informs the surgeon of the total number of sentinel nodes to investigate. Yes, until surgeons have proven that patient outcomes aren’t compromised by not using it. However, if the standards referred to in section 9 can be attained with probe-only studies, imaging may still have a role in either patients where no SLN can be found or in revalidation of surgeons.

5. SLNB results seem consistent on a population basis, but very little known about within-patient reproducibility (ie would you find the same SLN each time if you did SLNB more than once in each patient?)

6. Long-term patient outcomes

7. Is it important to demonstrate drainage to internal mammary nodes?

8. How should patients with drainage to internal mammary nodes be managed?

References


Gommans, G.M.M; van der Zant,F.M; van der Schors,T.M; van Dongen, A; Teule,G.J.J; Clarijs, W.W.J; Langenhorst,B.L.A.M; de Ward,J.W.D. Effect of

Lee, A.C; Keshtgar, M.R.S; Waddington, W.A; Ell, P.J. The role of dynamic imaging in sentinel lymph node biopsy in breast cancer. European J of Cancer 2002;38:784-787

Mariani, G; Moresco, L; Viale, G; Villa, G; Bagnasco, M; Canavese, G; Buscombe, J; Strauss, H.W; Paganelli, G. Radioguided Sentinel Lymph Node Biopsy in Breast Cancer Surgery. J. Nuc Med 2001;42:1198-1215


Koizumi, M; Nomura, E; Yamad, Y; Takiguchi, T; Tanaka, K; Yoshimoto, M; Makita, M; Sakamoto, G; Kasumi, F; Ogata, E. Sentinel node detection using 99mTc-rhenium sulphide colloid in breast cancer patients: evaluation of 1 day and 2 day protocols and a dose-finding study. Nuc Med Comm 2003:24;663-670

Lee, A.C; Keshtgar,M.R; Waddington,M.A; Ell,P.J. The role of dynamic imaging in sentinel lymph node biopsy in breast cancer. Eur.J Cancer.2002:38(6);784-7

Valdes Olmos,R.A; Tanis,P.J; Hoefnagel,C.A; Nieweg, O.E; Muller, S.H; Rutgers,E.J.Th; K Kooi,M.L.K; Kroon, B.B.R. Improved sentinel node visualization in breast cancer by optimizing the colloid particle concentration and tracer dosage, Nuc Med Comm 2001, 22, 579-586


Preliminary draft pack - RCS
Revised activity entered in line with EANM guidance 31/07/09

<table>
<thead>
<tr>
<th>Comment</th>
<th>Date</th>
<th>Version</th>
<th>Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>First draft</td>
<td>Aug 2011</td>
<td>1</td>
<td>Vidhiya Vinayakamoorthy, Charlotte Fowler and Mike Peters</td>
</tr>
<tr>
<td>Final version</td>
<td>Sep 2018</td>
<td>2</td>
<td>John Buscombe</td>
</tr>
<tr>
<td>Next review</td>
<td>Sep 2023</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>