

Lymphoscintigraphy and Radiopharmaceutical Safety

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Outline

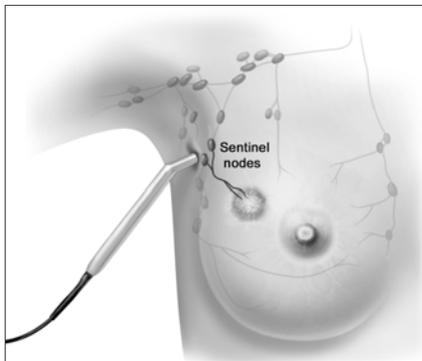
- Review Sentinel node concept
- Procedure
 - Nuclear medicine perspective
 - Radiopharmaceuticals
 - Probes
 - Injection techniques/locations
 - Lymphoscintigraphy
- Melanoma/Breast cancer examples
- Radiation Safety
- Area for further clarification

Sentinel Lymph Node Mapping

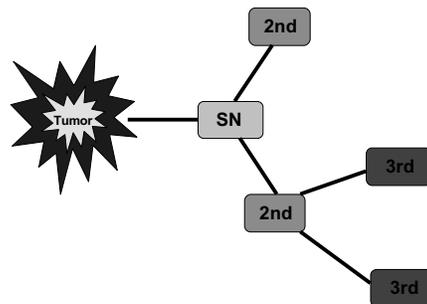
- Late 1980's Morton (surgeon) & Cochran (pathologist) proposed concept of lymph node mapping with sentinel lymph node biopsy.

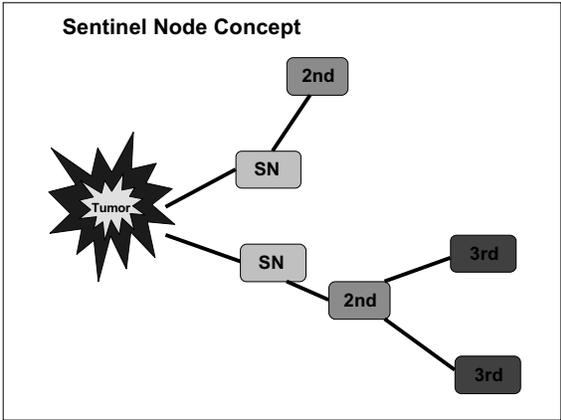
Definitions

- Sentinel lymph node: The first lymph node(s) in a lymph node basin to receive lymphatic drainage from a tumor
 - Often there is direct drainage from the tumor to more than 1 lymph node within a regional lymph node basin.
- Lymphoscintigraphy: Imaging pathways of lymphatic flow and lymph nodes after injection of a radiopharmaceutical that is absorbed by the lymphatics

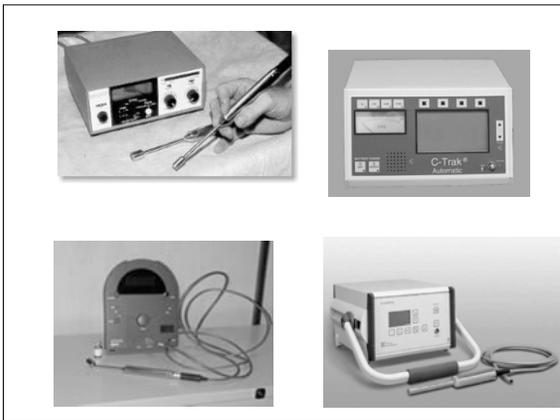
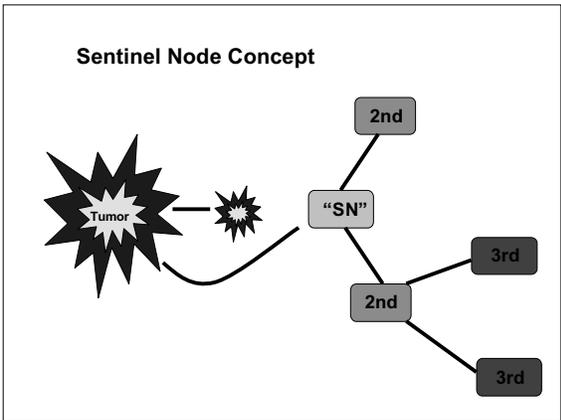
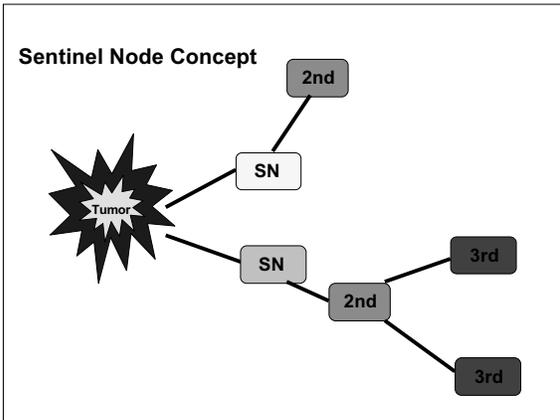
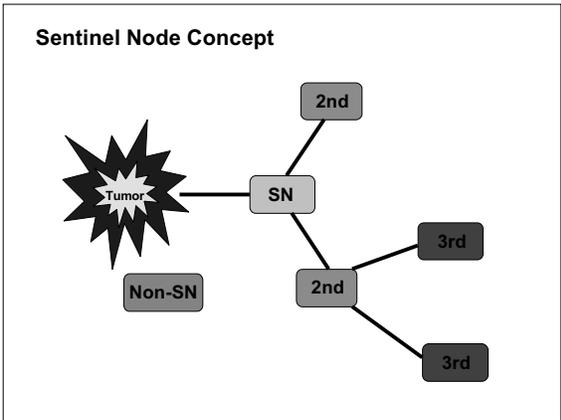


Sentinel Node Concept





- Other definitions of Sentinel Node**
- Closest node to the primary lesion
 - First node detected on lymphoscintigraphy
 - Node with highest count rate
 - Node with count rate 3-5X higher than background
 - Blue Node



Discover Node Seeker™!

Auto Peak Alert

Indicates that the user has identified a "hot" spot and displays peak counts.

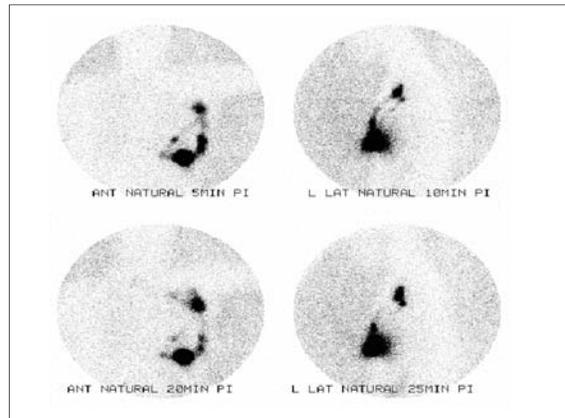
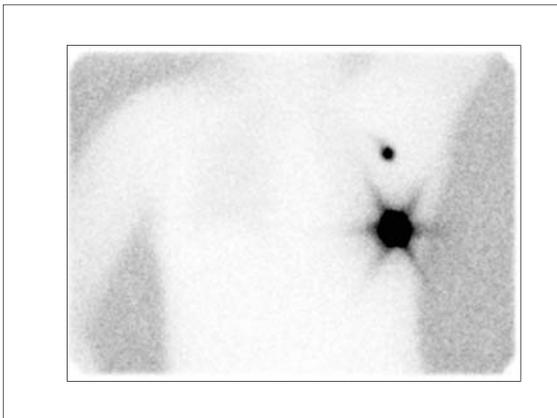


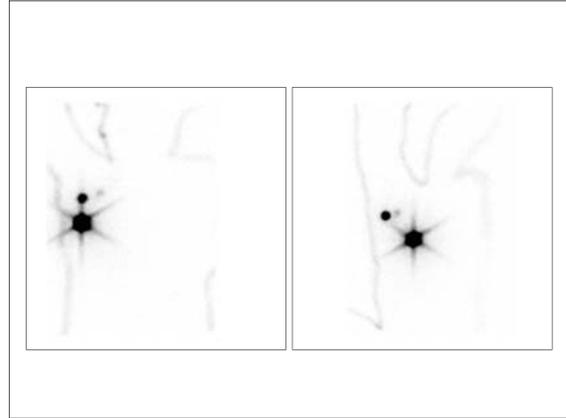
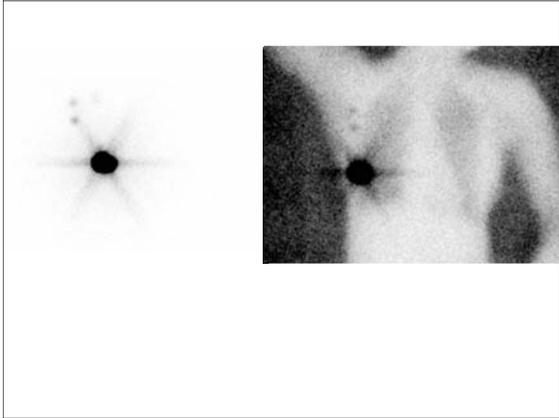
Node Seeker™
For the Advanced Surgical Detection of Tumors and Lymph Nodes



Lymphoscintigraphy

- Imaging pathways of lymphatic flow and lymph nodes after injection of a radiopharmaceutical
- Performed with standard gamma camera



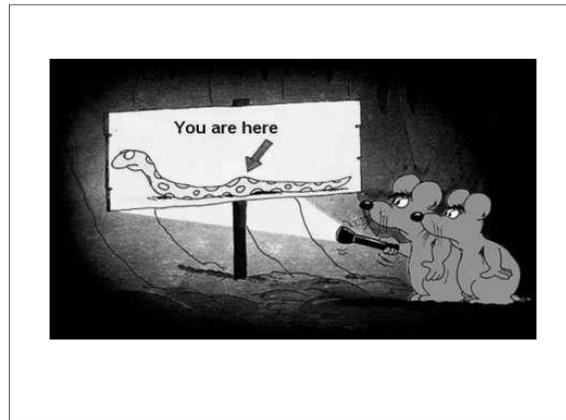
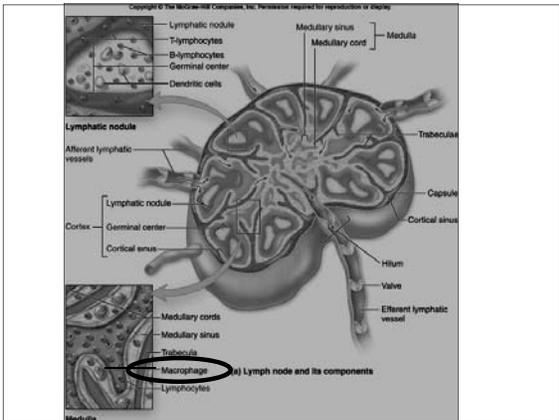


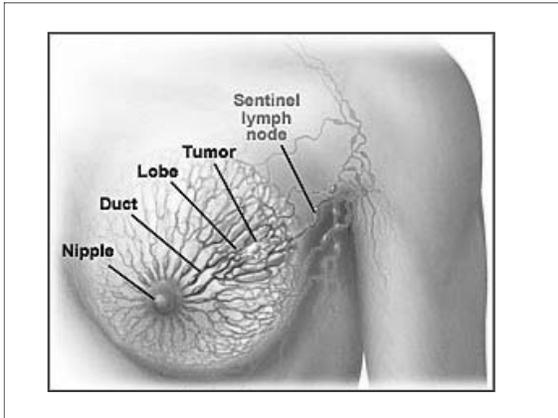
Lymphoscintigraphy

- Ideal Radiopharmaceutical
 - 100% migration from injection site
 - 100% retention within sentinel node

Lymphoscintigraphy

- Radiopharmaceuticals
 - Tc-99m Sulfur colloid 10-1000 nm
 - Filtered Tc-99m Sulfur colloid 10-50 nm
 - Tc-99m Antimony colloid 5-20 nm
 - Tc-99m Human serum albumin 2-3 nm





Lymphoscintigraphy -Breast Cancer

- There are no dietary or medication restrictions for the procedure. Patients should follow preoperative restrictions if the procedure is performed on the same day as scheduled surgery.
- 1-2 mCi of Tc-99m Filter sulfur colloid

Surgeons Disagree on Value of preoperative lymphoscintigraphy to identify Axillary SLNs

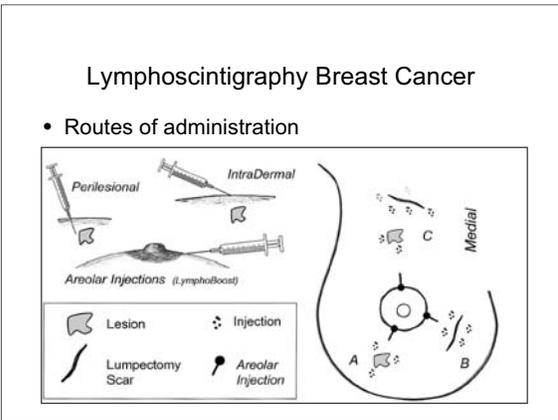
- Preoperative Lymphoscintigraphy for Breast Cancer does not improve Ability to identify SLNs.
McMasters KM et al: Ann of Surg;231:724-31.
- "If IM nodes light up and an axillary node is positive, IM node radiation Rx is indicated"... "Concordance between vis of SLN and finding it at operation is virtually 100%"...
Copeland,EM: AnnSurg
- "In my experience, this is a very reliable test...Knowing exactly where it is-...I can cut down directly on it, and it saves a tremendous amount of OR time."
Morris, DM Ann of Surg;231:724-31.

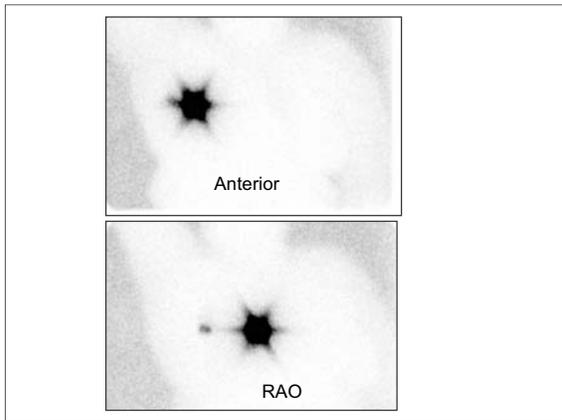
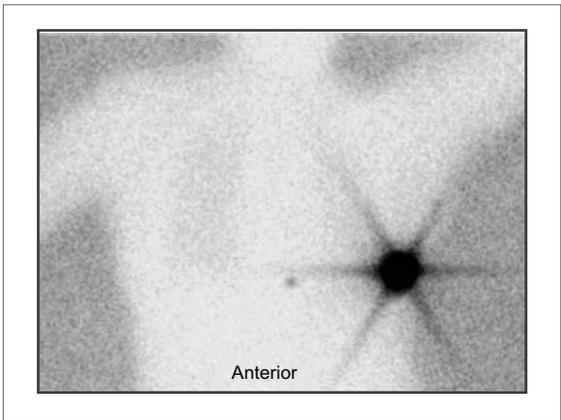
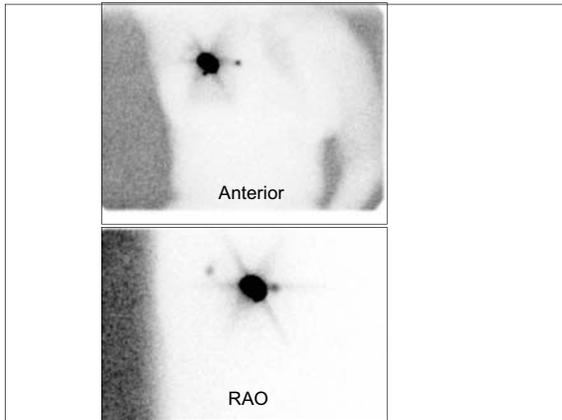
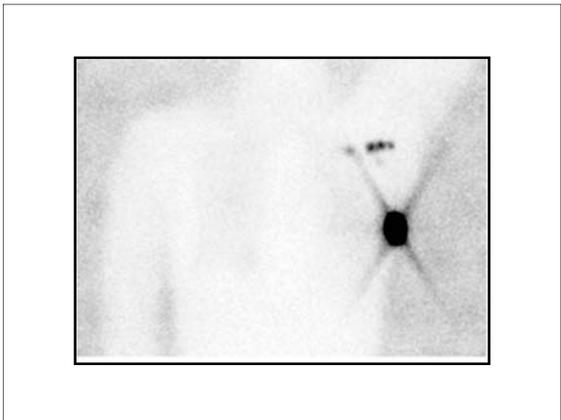
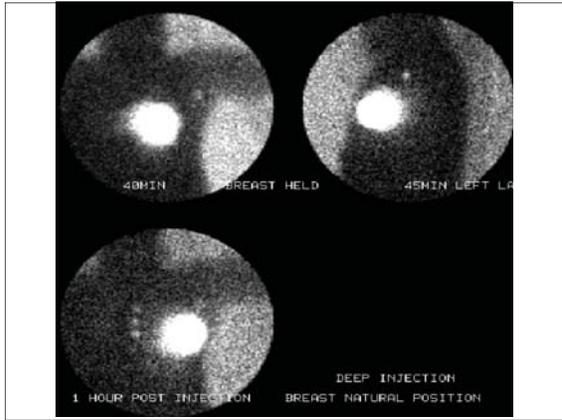
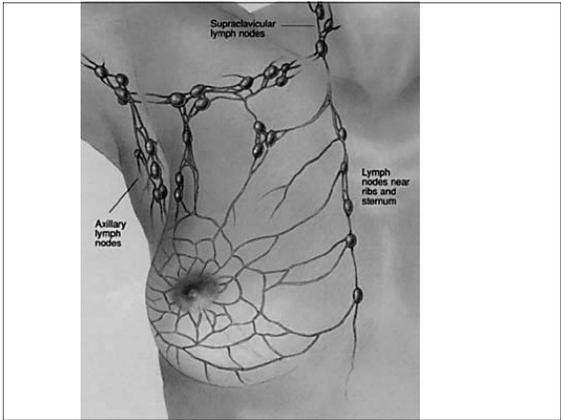
Lymphoscintigraphy- Breast cancer Why bother ?

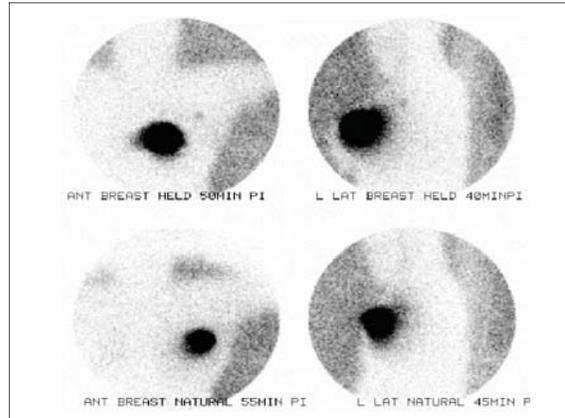
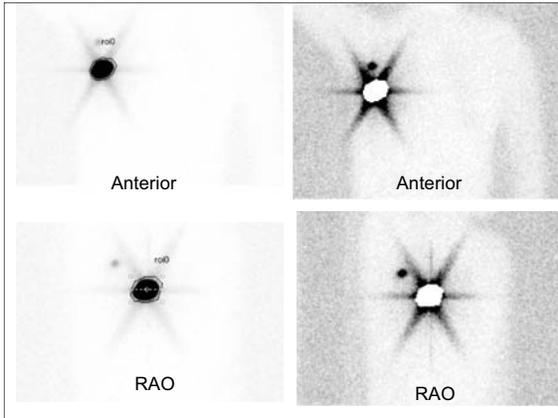
- Lymphatic drainage for the breast is not clinically predictable
- Imaging is needed to confidently identify the location and number of SLN(s)
- Smaller incision, faster procedure

Variability of Breast Lymphatic drainage

- 92% of medial quadrant lesion drain into the axillia
- 25 % of outer quadrant lesions drain into internal mammary nodes
- 45% of patients demonstrate breast lymphatic drainage across the midline







Sentinel Node Biopsy: Standard or Investigational?

- Use of SNB increased from 8% (1997) to 58% (late 2000)
- There are several extensive, randomized NCI trials comparing SNB and Axillary Node Dissection, 1999-2007.
- There is debate on whether surgeons should wait for those trial results before using SNB routinely.

Surgeons "Vote With Their Feet" for Sentinel Node Biopsy for Breast Cancer Staging

From Hamilton, PhD

Several extensive studies comparing the accuracy of sentinel and axillary node dissection, is now routinely performed despite the fact that clinical trials on test to validity, are still years from completion, according to a new study in the *Journal of the National Cancer Institute* (J Natl Cancer Inst. 2003;95:1314-1321).

The study, which involved 3003 women with stage 1 or stage 2 breast cancer who were treated at five comprehensive cancer centers between 1997 and 2003, reports that the use of SNB increased from 8% in 1997 to 58% in the last half of 2003.

Surgeons estimate that SNB is even more prevalent today, and its appeal is obvious. Axillary node dissection, which is removal of all the axillary lymph nodes to examine them for the presence of metastatic cancer cells, can leave women with arm pain and swelling for months to years—effects that are significantly reduced with the less invasive SNB. In the latter procedure, sur-

geons, if cancer is not found, the presumption is that the other nodes are also negative, and the patient is able to avoid axillary node dissection.

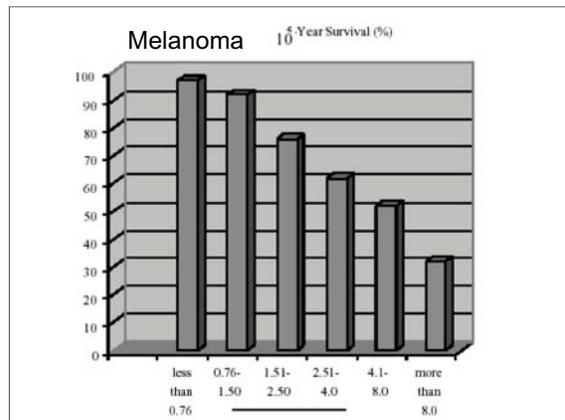
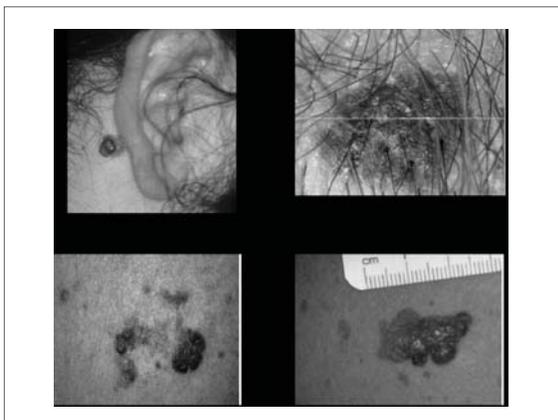
Several extensive studies comparing the accuracy of sentinel and axillary node dissection were initiated by the National Cancer Institute in 1996, and they will not be complete until 2007. But in the meantime, breast cancer surgeons were encouraged by studies of SNB followed by axillary node dissection at various hospitals that indicated that SNB accurately predicts the status of the remaining axillary nodes over 90% of the time (*Breast Cancer Res Treat*. 2003;1:104-108; *Cancers* [Goncalves]. 2003;1:215-235-337), and widespread adoption of investigational SNB over the standard axillary procedure as the initial staging procedure followed.

But the *Journal of the National Cancer Institute* study raises the question: should surgeons wait for randomized clinical trials to end before performing SNB on a regular basis?

Sentinel Lymph Node Biopsy

Axillary Lymph Node Dissection

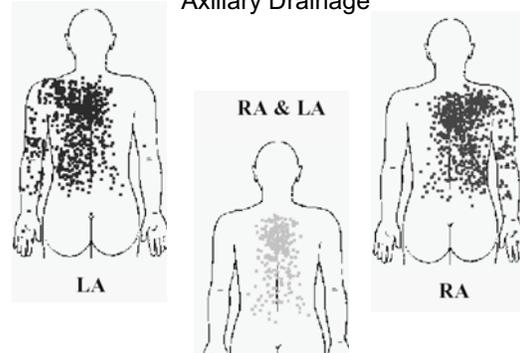
JAMA Dec 17, 2003 vol 290, No 23



Melanoma

- Elective lymph node dissection (ELND) of the lymphatic bed believed most likely to drain the primary tumor site (based on Sappey's classic anatomic description of cutaneous lymphatic flow) was used as part of the staging procedure for melanoma

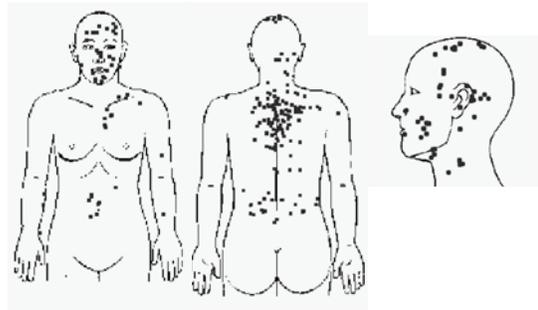
Axillary Drainage



Melanoma

- The sentinel lymph node excisional biopsy is simple procedure and not associated with significant morbidity.
- Provides accurate information about lymphatic drainage patterns.

Drainage to > 2 Nodal groups



Common Indications

- Sentinel node localization and excision using radionuclide methods are performed in patients with:
 - Intermediate stage primary melanoma (Breslow 0.76 mm–4.0 mm).
 - No clinical evidence of nodal involvement
 - No clinical evidence of distant tumor spread
- Exclusions may include patients with:
 - Extensive previous surgery in the region of the primary tumor site or targeted lymph node bed.
 - Patients with known metastases.

Procedure

- **Society of Nuclear Medicine Procedure Guideline for Lymphoscintigraphy and the Use of Intraoperative Gamma Probe for Sentinel Lymph Node Localization in Melanoma of Intermediate Thickness**

Procedure - Melanoma

- If surgery is to be performed using the intraoperative gamma probe to assist in finding the sentinel node, the tracer must be injected approximately 0.5–3 hr before surgery.
- 0.2-0.4 mL containing at least 17 MBq Tc-99m sulfur colloid, filtered (0.22 μ millipore filter), is administered
- 2- 4 peritumoral intradermal injections
 - within 1 cm from the melanoma or the excisional biopsy site at which the melanoma was located.

Procedure- Melanoma

- Injections should surround the lesion or biopsy site to best sample lymphatic drainage in all directions. (Exception- primary cutaneous melanoma in the head or neck)
- Gentle finger massage should be considered at each injection site to promote uptake of the tracer into lymphatic channels and lymphatic flow.
- The injection site should be covered with a bandaid to prevent leakage of activity through the needle puncture site.

Image Acquisition

- Sequential or continuous imaging begins immediately after completion of injections and continues for 30–60 minutes.
- For trunk lesions, images of both axillary and inguinal regions should be obtained.
- Lateral or oblique views are often helpful

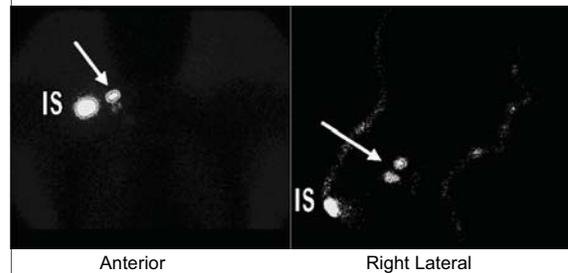


Image Acquisition

- For extremity lesions, the knee or elbow regions should be included in the field of view on dynamic and static images to detect “in-transit” or intercalated lymph nodes, which are sentinel lymph nodes.

In-transit Node

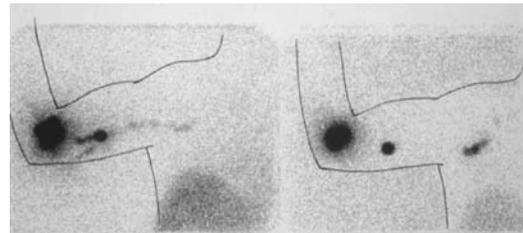
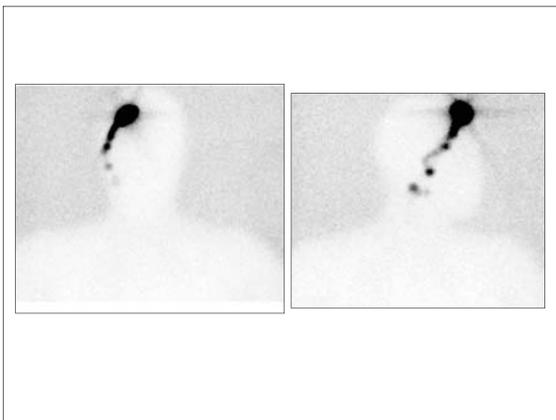
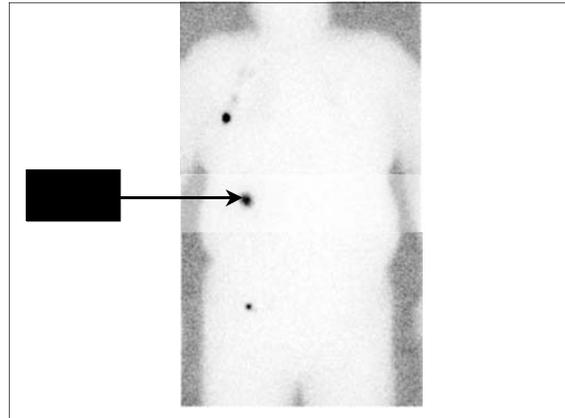


Image Interpretation

- Sentinel lymph node is the first to receive drainage from the tumor site.
- When drainage to more than 1 anatomic region is seen (e.g., axilla and inguinal), each of those regions must have at least 1 sentinel lymph node.
- Intraoperative probe criteria- A sentinel lymph node usually has at least 10 times the background counts



Radiation safety

- Exposures from these procedures are sufficiently low that badging is not essential
- Radiation dose to the hands of the surgeon has been estimated to be 5–94 μSv per patient
- At an altitude of 30,000 feet, the dose rate was about 4 μSv per hour at the latitudes of North America and Western Europe

Radiation safety

- Radiation doses to pathology personnel who handle the radioactive sentinel node and primary tumor specimen for a limited period would be no greater than that received by the surgeon.
- Therefore, the histological specimen can be processed without delay, and patient care is not compromised.

Radiation Safety - Patient

- Deterministic effects (e.g., local skin necrosis) are not a concern for Tc-99m-labeled radiopharmaceuticals.
- Effective doses:
 - Lymphoscintigraphy 0.05-0.1 mSv
 - CT Head 2.0 mSv
 - CT Chest 8.0 mSv
 - CT Abdomen 10.0 mSv
 - Angioplasty 7.5 - 55.0 mSv

The Sentinel Node Concept

- Success story
 - The SLN Concept originated with surgeons
 - Popularized by surgeons
 - Radionuclide Imaging and Intraoperative Probe detection for SLN introduced by a surgeon
 - Validated by surgeons

Problems

- Standardization of injection technique (breast carcinoma)
- False Negative rate or skip rate
- More extensive histological evaluation
 - IHC stains, RT-PCR