

BREAST LYMPHOSCINTIGRAPHY AND LYMPHATIC MAPPING

C. BERMAN, H. Lee Moffitt Cancer Center,
University of South Florida, Tampa, Florida, USA

Axillary lymph node dissection (ALND) is a standard staging procedure in patients with invasive carcinoma of the breast. The presence of axillary nodal metastasis establishes the presence of stage II disease and identifies a group of patients at high risk for eventual widespread relapse. The importance of ALND stems from the increased cure rate obtained when patients with axillary nodal metastases are identified and given systemic adjuvant treatment. Unfortunately, ALND entails significant morbidity and expense. The morbidity is well known and includes chronic lymphedema, which may be severe, and chronic paresthesias in addition to the acute surgical morbidity of seroma and possible infection. Given the extent of surgical dissection, hospitalization is requisite and the management of complications, in particular the problems associated with chronic severe lymphedema, may entail substantial ongoing professional and economic commitments. For these reasons, a selective lymph node sampling approach has been advocated based on physiologic methods for identifying the sentinel lymph node (SLN), the first lymph node draining the lesion. In both melanoma and more recently carcinoma of the breast, techniques based on SLN identification have been shown to accurately predict the pathologic status of the draining lymph node basin.(1)

A significant advantage of SLN sampling, not often enough stressed, is the opportunity provided the pathologist to perform more meticulous sectioning and diverse staining of the high risk nodal material. Indeed, in the early melanoma experience from John Wayne Cancer Institute, nearly half of the 21% of patients found to have metastatic sentinel node adenopathy were identified solely by immunohistochemical staining which would not be practical to apply to the volume of tissue yielded by an anatomic nodal basin dissection.(2)

Two methodologies have been applied successfully for identification of the SLN. Morton's group at the John Wayne Cancer Institute in Santa Monica have reported on a group of patients in whom the SLN was identified using isosulfan blue vital dye, injected into the breast lesion and its periphery at the time of surgery. In their group of 174 patients, the SLN was successfully identified in 114 (65.5%). Among these patients the pathologic status of the SLN accurately predicted the pathologic status of the whole axilla obtained by standard axillary dissection with an accuracy of 95.6%. The authors noted a distinct learning curve with all their false negative studies falling within the first half of their series.(3) At the University of Vermont, 99m-technetium sulfur colloid lymphatic mapping has yielded a 71% success for SLN identification.(4)

At the H. Lee Moffitt Cancer Center and Research Institute we have combined the two approaches of vital dye and radiocolloid mapping. Technetium 99m-sulfur colloid is passed through a 0.2 micron filter to obtain a radiocolloid particle size small enough to avoid phagocytosis. Four hundred fifty microcuries in 6cc of diluent is injected circumferentially around the tumor or seroma cavity in six equal aliquots. Care is made not to inject into the tumor or seroma cavity as this diminishes lymphatic flow. For nonpalpable lesions the radiopharmaceutical is not administered through the localization needle but circumferentially, surrounding the tip of the needle, at the desired depth. Sonography is frequently employed for guidance. We have found 3-5 minutes of breast massage focused to the area of injection to improve lymph node uptake. The patient is then positioned supine beneath the gamma camera. A large field of view scintillation camera with a high resolution collimator is used. Cine images can be helpful. The arm is extended above the head and the hand placed under the head to optimize axillary exposure. The breast can be shielded with lead and can be taped or positioned away from the area of interest. The persistence scope is used to identify accumulations of the radiopharmaceutical corresponding to lymph nodes. Internal mammary and supraclavicular lymph nodes can be tattooed or marked in the anterior projection, while the axillary lymph nodes are tattooed or marked with the patient in the lateral position with the arm above the head. The hand held gamma probe can be used to assure accuracy of lymph node marking while the patient is in the same position as when they will be operated on. Images are acquired over 8-10 minutes per view to assure high count density. Images are obtained in the anterior, lateral and oblique positions. The patient can be imaged on a cobalt flood source to define the body contour. Alternatively, the body contour and landmarks can be demonstrated using a technetium-99m marker. Imaging is performed immediately after injection and subsequently, following a 2-4 hour delay.

In the operative suite the surgeon will first scan the axilla as well as the tattooed or marked sites to identify areas of high activity. The primary tumor site is injected with blue isovital dye using 5-10 cc with a technique similar to the radiopharmaceutical injection. Incisions are then made over the suspect SLN sites and dissection follows the blue stained afferent lymphatics to the sentinel lymph node. Particular care is taken to avoid spillage of blood or lymphatic fluid. A hand held gamma probe augments this examination. Sentinel lymph nodes are defined as any blue node or any node with greater than or equal to three times in vivo background counts per minute (ex vivo, ten times the counts per minute of a nonsentinel node). After initial excision, the gamma probe is returned to the axillary bed. Dissection is continued if the lymph node bed has more than 150% of background counts.

Among our initial 62 phase I patients, in whom both sentinel node biopsy and axillary node dissection were performed, we achieved a 92% rate of SLN identification. All patients in whom a SLN was not identified had medial lesions and may in fact not have had axillary nodal drainage of their tumors. Thirty two percent of our patients, all of whom had benign

axillary physical examinations, were found on pathology to have axillary metastases, in keeping with the known and expected incidence for this clinical group. Importantly, all patients with axillary metastasis had metastatic disease within the SLN. In two thirds of patients with axillary metastasis, the SLN was the only site of metastatic disease. (5)

Historically, the axillary lymph node drainage has been defined anatomically as levels I, II and III with nodes medial to the pectoralis minor muscle constituting level III, those deep to the muscle level II and those lateral to the muscle level I. In our series, 12% of SLN were in level II only. This reflects one of the great advantages of our technique in that it tracks the physiologic pathway(s) for the given lesion, allowing a focused dissection based on the particular in vivo physiology rather than arbitrary anatomic designations. We have now completed phase I studies on 115 patients, and have embarked on phase II studies in which patients have not undergone 'control' axillary dissections. Pathologic material is available on 418 patients among whom diagnosis at the primary site was obtained with roughly equal frequency by excisional biopsy versus stereotactic or fine needle aspiration biopsy. The success rate for identifying the SNL was 95.2% and 92.2%, respectively. Metastatic disease was identified in 23.8% of patients. There was one false negative study. Twenty seven and six tenths percent of SLN's were both hot and blue; 40.2% were only hot; 32.2% were only blue. Of particular interest, positive SLN's were found in 4.6% of patients with DCIS, 16% of patients with T1a and T1b disease, 32.8% of patients with T1c disease, 40.8% of patients with T2 disease and 75% of patients with T3 disease.(6)

We feel, as do others, that immediate ("dynamic") scanning is an essential component of any SLN identification procedure.(7) Although the identification of afferent lymphatics during breast lymphoscintigraphy is far less common than in melanoma cases, noting the accumulation of uptake within the lymph nodes and which lymph nodes appear to accumulate the radiopharmaceutical first assures identification of SLN. Conventional wisdom suggests that most breast carcinomas arise within the upper outer quadrant of the breast, so nodal drainage will be to the axilla and only the most medial tumors will drain to the internal mammary chain. Uren studied 32 patients with antimony sulfur colloid lymphoscintigraphy and found that there was ipsilateral axillary node drainage in 85% of the cases. However, the multiplicity and variability of drainage patterns was unexpected. Twenty eight percent of patients with outer quadrant tumors showed unexpected drainage to internal mammary nodes while 33% of inner quadrant tumors showed axillary drainage. Thus one third of patients with lateralized tumors had drainage which crossed the midline of the breast. Twenty percent of patients with upper quadrant tumors showed direct drainage to supraclavicular or infraclavicular nodes. In one patient an in-transit intramammary node, lying in the breast parenchyma between the primary lesion and the axilla, was discovered. This in-transit lymph node was in fact the SLN and contained metastatic disease. Standard axillary dissection would not have identified this node and, by implication, the patient's need for systemic adjuvant therapy.(8)

Preoperative breast lymphoscintigraphy offers the opportunity for identification of the unique pattern of nodal drainage for each malignant lesion. Directing the surgeon to the site of the SLN minimizes the operative time and the extent of dissection and likelihood of late morbidity. Identification of in-transit lymph nodes opens up a subset of patients inadequately examined by standard axillary dissection techniques. Identification of internal mammary SLN allows for rational radiotherapeutic planning in patients who might not otherwise be recognized to be at high risk. The combined technique of vital dye and radiocolloid lymphatic mapping appears to be a practical technique for identifying SLN, allowing for selective lymphadenectomy in patients with carcinoma of the breast. It is cost effective. It reduces morbidity and it improves the diagnostic yield.

References

1. Alazraki N. Lymphoscintigraphy and the intraoperative gamma probe. *J Nucl Med*, 1995;36:1780-1783.
2. Morton DL, Wen DR, Cochran AJ. Management of early-stage melanoma by intraoperative lymphatic mapping and selective lymphadenectomy: an alternative to routine lymphadenectomy or "watch and wait". *Surg Oncol Clin North Am*, 1992;1:247-259.
3. Guiliano AE, Kirgan DM, Guenther JM, et al. Lymphatic mapping and sentinel lymphadenopathy for breast cancer. *Ann Surg*, 1994;220:391-401.
4. Krag DN, Weaver DL, Alex JC, et al. Surgical resection and radiolocalization of the sentinel lymph node in breast cancer using a gamma probe. *Surg Oncol*, 1993;2:335-339.
5. Albertini JJ, Lyman GH, Cox C, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA*, 1996;276:1818-1822.
6. Cox C, Haddad F, Bass S, et al. Lymphatic mapping in the treatment of breast cancer. *Oncology*, 1998;12(9):1283-1298.
7. Taylor A, Murry D, Herda S, et al. Dynamic lymphoscintigraphy to identify the sentinel and satellite nodes. *Clin Nuc Med*, 1996;21:755-758.
8. Uren RF, Howman-Giles RB, Thompson JF, et al. Mammary lymphoscintigraphy in breast cancer. *J Nucl Med*, 1995;36:1775-1780.