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The Role of Lymphoscintigraphy in Lymphatic Mapping for Melanoma and Breast Cancer

Breast cancer and melanoma are two cancers that strike tens of thousands of people every year, but which can be complicated to stage. Over the past 5 years, the care of melanoma patients has been altered dramatically with the development of new lymphatic mapping techniques. These procedures reduce the cost and morbidity of nodal staging and can be combined with more sensitive assays for occult melanoma metastases and effective adjuvant therapy (Interferon alfa-2b) to increase the survival of the patient with melanoma.

In breast cancer as well as melanoma, the most common site of metastases is the regional nodes, and regional nodal status is the most powerful predictor of recurrence and survival for both tumors. Most believe that axillary nodal staging is an important part of the primary breast cancer therapy in order to identify which patients are candidates for more aggressive chemotherapy protocols and to add to the regional control of disease. However, complete axillary node dissection has significant morbidity such as lymphedema; in fact, women undergoing breast cancer surgery list the physical complaints resulting from the dissection as their most troubling side effect from the surgery.

The theory behind lymphatic mapping is that the sentinel lymph node (SLN), defined as the first node in the chain that receives afferent lymphatic flow from the primary tumor, is the node that tumor cells will spread to first. If the SLN is negative for metastatic disease, then the remaining lymph nodes in the basin should also be negative. Clinicians aim to obtain full nodal staging with a more conservative lymph node biopsy procedure rather than with a more radical complete node dissection. With the more conservative surgery, the tumor can be more accurately staged because pathologists can perform a more detailed examination of the SLN, which may include more sections, immunohistochemical staining and molecular biology assays of occult metastases.

In order to perform effective lymphatic mapping, close collaboration between nuclear medicine physicians, surgeons and pathologists is necessary. We would like to explore the technical details of what takes place in nuclear medicine departments. Through our experience, we have found that nuclear imaging procedures have a direct bearing on how successful our surgeons will be in the operating room.

Purpose of Lymphoscintigraphy

Preoperative lymphoscintigraphy serves as a road map for the surgeon and has 4 distinct uses in planning the surgical procedure. These include:

1. To identify all nodal basins at risk for metastatic disease (Figure 1).
2. To identify any in transit nodes that can be tattooed by the nuclear medicine colleague for later harvesting. In transit metastases occur in 5% of the melanoma population and may, by definition, be considered the SLN (Figure 2).
3. To identify the location of the SLN in relation to the rest of the nodes in the basin (*4*). The location of the SLN may be variable in a basin and ideally the surgeon needs a mark of the position of the SLN in reference to other nodes in the basin, in order to perform the harvest under local anesthesia with a minimal incision. Preoperative lymphoscintigrams can do this quite well, according to data from our clinical trials. In one study, 29 patients with clin-

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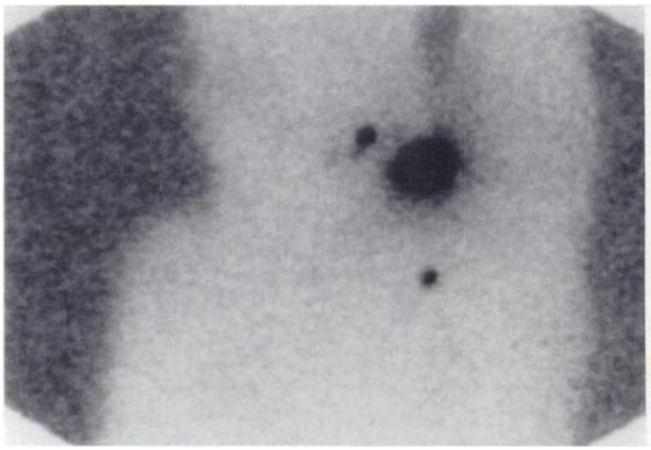

Figure 1. A left neck melanoma of intermediate thickness that drains into both the left neck and left axilla. Both basins are equally at risk for micro metastatic disease and both have to be harvested.

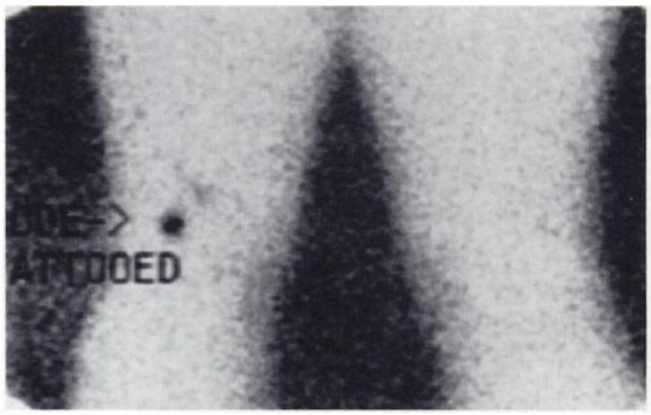

Figure 2. Pre-operative lymphoscintigraphy in a patient with a right foot melanoma. 450 μCi is injected into the dermis around the primary melanoma and scans of the patient 10 minutes after the injection of the radiocolloid show uptake in an in-transit SLN located in the right popliteal space. Since this is the first node in the chain from the primary site, by definition this is the SLN and needs to be harvested.

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scar of a previous excisional biopsy that was used to diagnose melanoma. This injection needs to be intra-dermal and outside the scar of the excisional biopsy. If the injection is into the subcutaneous tissue or into the scar, the mapping agents will not migrate.

The nuclear physician also must consider whether the patient has undergone previous surgery at the primary site which can disrupt the cutaneous or breast lymphatics. Studies have shown that if the mapping is attempted after a wide local excision (WLE) of a melanoma or after an excisional biopsy of a breast tumor, the mean number of SLNs that are removed increases, the number of patients that require dissection of two or more basins increases significantly and the accuracy of the procedures decreases. More technical failures can occur as can an increase in the number of "skip metastases" (where the SLN is negative SLN but nodes that are higher in the basin are positive). The highest success rates for sentinel node mapping in melanoma patients are in patients who have a conservative excisional biopsy (1–2 mm margin of excision). The amount of injected radioactivity is approximately 450 μCi, an amount 44 times less than the amount of radioactivity used for your typical bone scan. The volume of injection should be 0.25–1.0 cc/per direction of anticipated drainage.

Dynamic studies are important to locate tracer in second tier nodes.

Imaging Technique

Lymphoscintigraphy for lymphatic mapping involves dynamic imaging (flow imaging) and static (late) imaging. The dynamic part of the study is performed shortly after the injection of the radiocolloid (which is why the injection of the colloid should be performed on the table that has the gamma camera) and at times can visualize the afferent lymphatic leading to the regional basin and the SLN. Dynamic studies are important because when images are created over a period of 5–10 minutes, some of the tracer may be seen in second tier nodes. A gamma camera with a large field of view and a low energy, high resolution, parallel-hole collimator is recommended.

We also perform a dynamic study to obtain a number of serial images over a short duration. One approach patterned after the Sydney Melanoma Unit involves the dynamic acquisition of 60 frames of 20 seconds in a matrix of 128 × 128 × 16 begun immediately after the injection of the tracer. In this fashion, we obtain a stack of sequential images over a period of 20 minutes, 3 images per minute. Each image contains the information on the lymphatic flow for 20 seconds. The SLN can be visualized with the afferent lymphatics, and the process takes approximately 20 minutes.

Static images are obtained 2 hours after the injection of the radiocolloid to assure that there are no basins being identified with delayed drainage. If so, these need to be noted and the SLN marked, since these basins are equally at risk for metastatic disease. If a regional basin is identified 2 hours after the injection of the radiocolloid, then any intra-operative mapping with the blue dye or radiocolloid needs to be scheduled to take into account this delay in cutaneous lymphatic flow.

Application to Breast Cancer

For melanoma, lymphoscintigraphy, if performed correctly, should be able to identify the basin at risk for metastases greater than 99% of the time. Breast lymphoscintigraphy, when performed correctly, images an axillary SLN only 70%–90% of the time. In addition, the colloid takes longer to migrate and the initial views for breast cancer are obtained 30–45 minutes after the injection of the radiocollid. The mapping agent is injected into the breast parenchyma around the tumor or around the biopsy cavity. Breast parenchymal lymphatics are not as rich as cutaneous lymphatics and larger volumes are used in breast mapping in an attempt to get the mapping agents close to a lymphatic.

Lymphatic drainage is complex in the head and neck area and this may be the most difficult field for interpretation. Up to 84% of the time, cutaneous lymphatic flow from primary site in the head and neck are discordant from the clinical prediction, and no flow from the primary site can be noted in up to 10% of the cases. Multiple SLNs in the head and neck area are depicted in most patients with an average of 2.5/patient with 5–6 SLNs identified not uncommonly. Overall, lymphoscintigraphy studies are reproducible: Several studies found a concordance rate of 98% when different nuclear medicine physicians interpret the lymphoscintigraphy images of the same patient.

Training in Lymphoscinitgraphy and Radioguided Surgery

To train surgeons, nuclear physicians and pathologists in radioguided surgery and lymphatic mapping, a national training network has being established by Moffitt Cancer Center and four other cancer centers throughout the country (for information call 888-456-2840 or 813-972-8482). A team of physicians can meet with experts in the field and witness live nuclear medicine studies and surgery, while interacting with the surgeons during the procedure. The network also provides mechanisms for hands-on experience with animal laboratories and provides for a mentoring (certification) of the initial cases at a registrant's own institution.

For breast cancer, most experts agree that the

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learning curve for lymphatic mapping is about 30 cases in which the surgeon performs the SLN harvest followed by a complete axillary node dissection. Doing 30 cases ensures that the collaboration among nuclear medicine, pathology and surgery is in place to perform the technique successfully. Clinicians only learn how well the technique is being performed in those patients with micro metastatic disease. In these first 30 cases, perhaps 10 may have metastatic disease. The success rate for finding the axillary SLN should be 90% or greater and the skip metastases rate should be less than 1% to consider withholding the complete node dissection in the SLN negative patients. The final decision as to when an institution is ready to alter the course of lymph node removal based on the finding of a negative SLN should be made in conjunction with the medical and radiation oncologists at the institution, as well as the credentials committee.

The success rate for finding the axillary SLN should be 90% or greater

At Moffitt Cancer Center, we have recently examined the learning curves of various surgeons who used the gamma probe with lymphatic mapping in breast cancer patients. Learning curves were generated for each surgeon as a plot of the failure rate versus the number of cases performed. Following an initial low success rate (70%–80%) there was a rapid increase in the success rate for finding an axillary SLN node after the first 20 cases. A learning curve representing the mean of 5 surgeons' experience with over 700 cases indicates that after 23 cases, the success rate of finding an axillary SLN was 90% and that after 53 cases, the success rate rose to 95% (*7*).

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Call for Nominations, 1999
Society of Nuclear Medicine Elections

Members of the Society have an excellent opportunity this winter not only to assure SNM's future success, but also to plot the future course of the field of nuclear medicine by encouraging their fellow members to seek elected office. As the SNM strategic planning process continues to move toward completion of a plan by mid-1999, we need to encourage the best and the brightest to run for Society leadership positions.

The SNM Committee on Nominations, chaired by H. William Strauss, MD, and comprising all SNM chapter presidents, is currently assembling the slate of candidates for the 1999 elections. The committee is seeking nominations for the following senior leadership positions.

- Vice President-Elect, 1999-2000
- Historian, 1999-2002
- Four Delegates-at-Large to the House of Delegates, 1999-2003
- Three elected chapter Delegates to the House of Delegates, 1999-2003

Candidates must be Society members (full, associate, emeritus, or associate members) and should submit a current curriculum vitae (in a form provided by committee staff), a current photograph, and–in the case of candidates for the office of Vice President-elect– a platform statement.

To suggest a qualified candidate to the Committee on Nominations, please contact your chapter president, or H. William Strauss, MD (Fax: 650-498-5047; E-mail: billstra@leland.stanford.edu.