Sentinel lymph node biopsy in breast cancer: the node to recovery

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Abstract

The widespread adoption of sentinel lymph node biopsy to stage the axilla has led to decrease in arm and shoulder morbidity. Sentinel lymph node biopsy is suitable for patients with clinically/radiologically node negative invasive breast cancer and selected patients with DCIS (those with clinical/radiological mass or extensive lesions requiring mastectomy). The combined isotope-blue dye injection technique gives the best results. We inject the isotope intra-dermally preoperatively and blue dye subdermally after anesthetic induction into the tumour quadrant peri-areolar tissue. Lymphoscintiscan is not necessary but is useful during the learning phase. Sentinel node biopsy can be performed through a small transverse or vertical axillary incision (~3 cm) appropriately placed to allow axillary lymph node clearance if needed.

Keywords Breast cancer · Blue dye · Sentinel lymph node biopsy · Radioisotope

Introduction

Over the past decade, sentinel lymph node (SLN) biopsy has become well established as a new standard for axillary node staging in early stage invasive breast cancer. Since the initial reports of SLN mapping by Krag in 1993 (using radioisotope),¹ by Giuliano in 1994 (using blue dye),² and by Albertini in 1995 (using a combination of isotope and dye),³ 6 randomized trials^{4–9} and numerous observational studies of SLN biopsy validated by a completion axillary lymph node dissection have established that SLN biopsy is feasible, accurate and safe.

Patient selection

SLN biopsy is suitable for *virtually all* patients with clinically node-negative invasive breast cancer (T1–3, N0) and for selected patients with DCIS (primarily those with masses or extensive lesions requiring mastectomy).¹⁰ Many putative ‘contraindications’ (including prior surgi-

cal biopsy, large tumour size and multicentricity) have been disproved, but the role of SLN biopsy following neoadjuvant chemotherapy remains a subject of debate. Finally, SLN biopsy may be suitable for selected patients with clinically-positive axillae, 25% of whom may be node-negative on final histology.¹¹ In this setting we perform ultrasound (US)-guided fine-needle aspiration (FNA); patients with a positive FNA can proceed directly to axillary lymph node dissection (ALND) and those who are negative undergo SLN biopsy.

Methodology – SLN biopsy

Our own data combined with that of many others show that a combined technique maximizes both the success and accuracy of SLN biopsy.^{12–14} Data from MSKCC also show that isotope identifies the SLN more often than blue dye, and that with increasing experience the ‘marginal benefit’ of blue dye (the proportion of procedures in which the SLN is identified *by dye alone*) is quite small, ~2–3%.¹⁵

Choice of radioisotope

All lymphatic mapping protocols rely on ^{99m}Tc technetium (^{99m}Tc) complexed to a carrier molecule, and radiocolloid uptake in lymph nodes represents active phagocytosis of the particulate material by macrophages. Radiocolloid preparations with a large particle size tend to remain at the injection site with little or no migration to regional nodes; conversely, those with a small particle size rapidly migrate to SLN and beyond, causing diffuse nodal uptake and requiring the removal of excessive additional nodes. The goal is to use an isotope preparation with an optimal and consistent particle size which will identify 1–3 SLNs in most patients.

Three preparations are in widespread use and all appear to work well. ^{99m}Tc -sulfur colloid, used in the United States and Canada, is characterized by a wide variation in particle size (50–2,000 nm, median 300 nm) and therefore some day-to-day variation in performance; filtering of the radiocolloid to remove those particles >200 nm (0.2 μ) allows more rapid visualization of the afferent lymphatic vessels and of the SLN. ^{99m}Tc -albumin nanocolloid, used by us in the UK and in most European centres, appears to have a more consistent particle size (50–200 nm, median 40 nm) and less day-to-day variation in performance. ^{99m}Tc -antimony trisulfide is widely used for SLN procedures in Australia and may have the most consistent particle size of all (3–30 nm, median 20).

Dose of radioisotope

The literature reports good results for SLN biopsy with radioisotope doses ranging from 0.1 to 10.0 mCi (3.7–370 MBq). A typical dose for most centers is ~1.0 mCi and there are few comparative data to suggest that any one dosage is optimal. Our standard radioisotope dosage for SLN biopsy is 0.3–0.5 mCi. Licensure for the acquisition and use of radioactive material varies by country, as do the protocols for handling and disposal. It is worth noting that the dose of radioisotope used in SLN biopsy is trivially small by comparison, a conventional bone scan requires about 25 mCi (925 MBq) and therefore does not require any special precautions.

Site and volume of injection

In the early reports of SLN biopsy for breast cancer, isotope was given as a deep peritumoural injection into the breast parenchyma at four sites, requiring a total volume of 4–8 cc. Since then, many investigators have reported equally good results with the intradermal, subdermal or subareolar routes of injection, and a comparably low rate of false-negative procedures.^{16,17} It appears from these studies that most of the breast tissue *and its overlying*

skin drains to the same few axillary SLNs regardless of injection site. Intradermal and subdermal injections are given as a single dose into the breast skin directly over the tumour or just cephalad to a previous biopsy scar. Subareolar injections are given into the subareolar lymphatic plexus independently of the tumour site. Superficial injection techniques require a much lower-volume of injection than the peritumoural method, and leave a much smaller ‘hot spot’ in the breast. This facilitates the identification of SLN, especially for patients with tumours high in the axillary tail of the breast.^{18,19}

Our standard method is to inject the isotope intradermally at a single periareolar site in the tumour quadrant (or cephalad to the previous biopsy scar), in a volume of 0.05 cc of normal saline (Fig. 1). Blue dye injection is always given in the operating room just prior to surgery. We inject subdermally at a single periareolar site in the tumour quadrant.

Timing of injection

Radioisotope may be injected the morning of, or the day before, surgery (as noted above, blue dye is always injected in the operating room). Same-day injection and day-before mapping have equivalent results.²⁰ Since ^{99m}Tc has a half-life of 6 h, we allow for decay by giving a larger isotope dose for day-before than for same-day mapping (0.5 mCi vs 0.3 mCi), and with this protocol have observed comparable isotope counts and number of SLNs for each method. Day-before injection has the advantage of allowing patients to proceed directly to surgery on the following day, thereby minimizing operating room delays.

Lymphoscintigraphy

Postinjection lymphoscintigraphy (LSG) with a large field-of-view gamma camera is a routine part of SLN

Fig. 1 Intradermal injection of radioisotope

Fig. 2 Lymphoscintiscan (anterior view) showing multiple 'hot' sentinel lymph nodes

Fig. 3 Blue stained lymphatic leading to a blue sentinel lymph node

mapping at many centres. The advantages of LSG are: (1) the identification of non-axillary SLN; and (2) estimating the number of axillary SLNs (the surgeon should identify *at least that many* SLNs at operation) (Fig. 2). The disadvantages are: (1) added cost; and (2) added time. Since most patients with a negative LSG will still have 'hot' SLN identified intra-operatively by the hand-held gamma probe (a much more sensitive instrument than the gamma camera)²¹, many centres have abandoned routine LSG.

Operative technique

We inject 2 cc of patent blue V dye subdermally at start of the procedure. We always perform SLN biopsy prior to the breast operation, using the hand-held gamma probe to identify the hot spot in the axilla, marking the site on the skin, and making a small transverse axillary skin line incision appropriately placed to allow an ALND if needed.

The incision is deepened through the clavipectoral fascia, maintaining 2- to 3-point countertraction with retractors, and taking care to preserve any blue-stained lymphatics and the intercostal sensory nerves (T2–4). Using direct inspection and the hand-held gamma probe, all blue and/or 'hot' sentinel nodes are carefully identified and removed (Fig. 3). In ~80% of cases the SLNs are found predictably in the mid-portion of level I; the remaining 20% are found variably in the axillary tail of the breast, high up along the axillary vein, in levels II–III, or in the interpectoral (Rotter's) space. The goal is to remove a median of 1–2 SLNs per patient.

While a blue node is defined as any node which is visibly blue (or contiguous with a blue lymphatic vessel), there is no universal definition of a 'hot' SLN. The most popular are the '10% rule' (which defines a SLN as any node with isotope counts at least 10% those of the hottest SLN) and those which employ various threshold ratios of SLN counts to axillary background counts (4–1, 5–1, 10–1). None are perfect but all work well. Some patients will have isotope uptake by many nodes presenting as a 'diffusely hot' axilla. In these cases, it is particularly important to remove the *hottest SLN* (this node is positive in 80% of node-positive patients),²² but it is rarely necessary to remove >4 SLN (we have shown that 98.5% of positive SLNs are identified within the first 3, and 99.6% within the first 4 SLNs removed).²³

The final step in SLN biopsy (after removal of all blue and/or hot SLN) is careful palpation of the axilla, and the removal of any *palpably suspicious* nodes. Axillary palpation reduces the false-negative rate for SLN biopsy. This concept makes sense intuitively; nodes replaced by tumour may be dysfunctional and cannot be expected to take up dye or isotope normally.

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