Problems and Pitfalls of Sentinel Node Biopsy

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Sentinel Node Biopsy - Breast Cancer

- SLNB is associated with a lesser morbidity than standard axillary node dissection in terms of lymphedema and sensory deficits
- Nodal status is the most powerful predictor of longterm survival and essential information for determining adjuvant therapies
- SLNB is an accurate staging of nodal status

Sentinel Lymph node Biopsy

- Axillary node dissection is the “gold” standard for axillary staging
- ALND has a false negative rate of up to 5%
- False negative rate of SLNB should be less than 5% to be considered accurate
- Routine level 1 and 2 node dissection can be eliminated for negative sentinel nodes

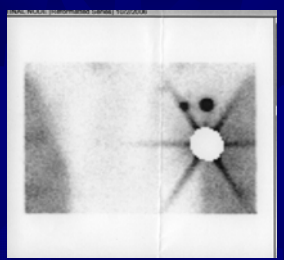
Indications for SLNB

- Clinically node negative
- Contraindications :
  - pregnant or breast feeding
  - severe allergies
  - DCIS
  - ? T3 tumors
  - ? Previous surgery-augmentation or reduction

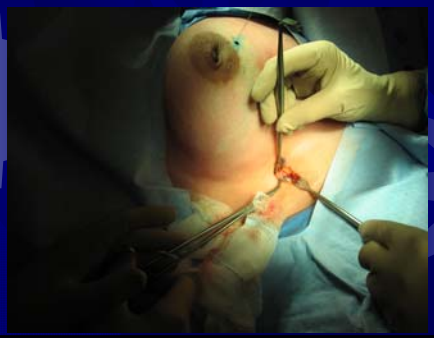
Technique

- Injection of radionucleotide (Te sulphur colloid)
- Scan at nuclear medicine dept
- Injection of blue dye –Lymphozurin (isosulfan blue) in operating room
- Scan with probe
- Remove blue and hot nodes

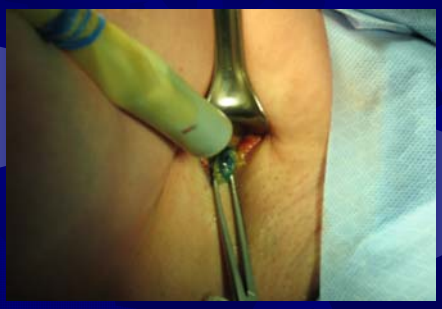
Nuclear Medicine Scan



Sentinel Node Biopsy



Sentinel Node Biopsy



Problems

- Training
- Institutional-nuclear medicine dept
  -pathology dept
- Logistical –timing, probe access, etc
  ?intraoperative pathology
- Team approach

Training

- Learning of technique
  residency
  post residency

Difficult to get time to mentor

Should competency be 20 cases or 5 cases with ALND ?

Guidelines in place

Institutional

- Need access to nuclear medicine
- Pathology department needs to be aware of the technique of processing the nodes

Logisitical

- Timing of injection
  day of surgery?
  day before surgery?
  intraoperative? Need to be able to work with radioactive isotopes
- Timing when associated with fine wire localization

Logistical

- Type of injection
  - peritumoral
  - subdermal
  - subareolar
- Radionucleotide only
- Blue dye
- Both

Type of Injection

Table 1. Peritumoral Injection: Validation Studies with More Than 100 Patients

First author	n	Technique	Identification rate (%)	False-negative rate (%)
Krag[7]	443	Tc	91	11
Borgstein[86]	130	Tc	94	1.7
Giuliano[87]	107	Dye	93	0
Giuliano[5]	174	Dye	65.5	11.9
McMasters[16]	1,074	Tc + Dye	90	8.3
Guenther[88]	145	Dye	71	9.7
Krag[33]	157	Tc	75.8	4.9
Tafra[89]	535	Tc + Dye	87	13
Fraile[90]	132	Tc	96	4
Noguchi[91]	674	Tc + Dye	94	10.2
Bass[24]	186	Tc + Dye	93	1.9
Kollias[41]	117	Tc + Dye	81	6.5

Dye, blue dye; Tc, technetium (radioactive colloid).

Type of injection

Table 3. Subareolar Injection: Validation Studies and Concordance Studies

Study	First author	n	Identification rate (%)	False-negative rate (%)	Concordance rate (%)
Validation*	McMasters[16]	85	99	5.9	–
	Kern[20]	40	98	0	–
	Smith[22]	19	100	0	–
Concordance†	Bauer[46]	245	96	–	90
	Klimberg[19]	68	94	–	100
	Tuttle[21]	159	100	–	98
	Borgstein[47]	130	96	–	95

Type of injection

Table 2. Dermal or Subdermal Injection: Validation Studies and Concordance Studies

Study	First author	n	Identification rate (%)	False-negative rate (%)	Concordance rate (%)
Validation*	McMasters[16]	511	98	6.5	–
	Veronesi[42]	163	98	4.7	–
	Boolbol[43]	100	99	9.0	–
	Casalegno[44]	102	86	5.4	–
Concordance†	Linehan[45]	100	100	–	95
	Borgstein[15]	33	100	–	100

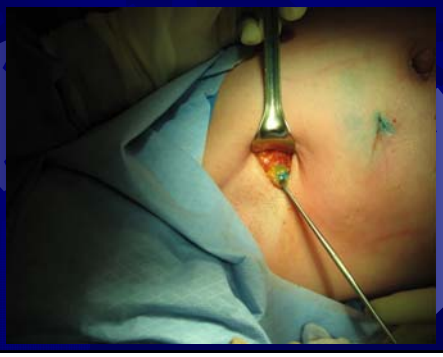
Specific problems

Related to the surgical procedure

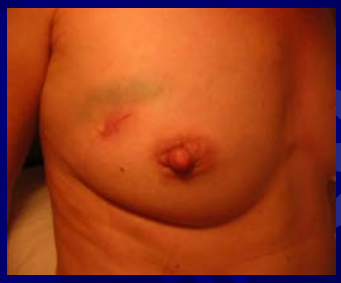
Blue Dye (Lymphozurin)

- Tattoo effect
- Blue breast (may last for months)
- O 2 sat's down in OR
- 80% accuracy if used alone
- Allergic reactions

Blue Dye



Blue Breast



Blue Dye- Methylene Blue

- Less expensive
- Can be associated with skin necrosis

Allergic Reactions

- Case 1

Ms J. 28 female with .8 cm tumor in upper outer right breast.

Taken to OR and injected with 5ml lymphozurin. Axillary incision made. Anesthesiologist outside door talking and rushes back to room as BP drops to 50. Patient has slight rash. No other changes. Given steroids, benedryl, etc and BP comes up. Surgery completed.ICU overnight with no adverse outcome.

Allergic reactions

- Case 2 Mrs G 78 yr old with 1.5 cm tumor left breast

Has had previous MI 5 years prior. Otherwise in good health.

OR procedure to be partial mastectomy and SLNB. Becomes hypotensive during case about 10 minutes after injection of lymphozurin. Difficult for anesthesiologist to determine cause and difficult to get pressure back up. Eventually case finished. Patient to ICU and had multiple problems with multiple organ failure. Eventually recovers after 10 days in ICU. Out of hospital in one month.

Allergic Reactions

Table 1. Selected Studies of Allergic Reactions to Blue Dye

First author, year	Blue dye type	No. of cases (type)	Incidence (%)	No. of second reactions
Lyew,[47] 2000	Isosulfan blue	1 (anaphylactic)	NR	0
Cimmino,[48] 2001	Isosulfan blue	5 (3 anaphylactic;* 2 blue urticaria)	2	0
Albo,[49] 2001	Isosulfan blue	7 (all anaphylactic)	1.1	2/7 (%)
Montgomery,[50] 2002	Isosulfan blue	39 (27 blue hives; 12 anaphylactic)	1.6	NR
Ebron,[51] 2002	Isosulfan blue	1 (anaphylactic)	NR	0
Laurie,[52] 2002	Isosulfan blue	2 (anaphylactic)	NR	0
Stefanutto,[53] 2002	Isosulfan blue	1 (anaphylactic)	NR	0
Crivellaro,[54] 2003	Patent blue	1 (anaphylactic)	NR	0
Sprung,[55] 2003	Isosulfan blue	1 (anaphylactic)	NR	Possibly; protracted hypotension noted

NR, not reported.
*Series includes two cases of lymphatic mapping performed for breast cancer.

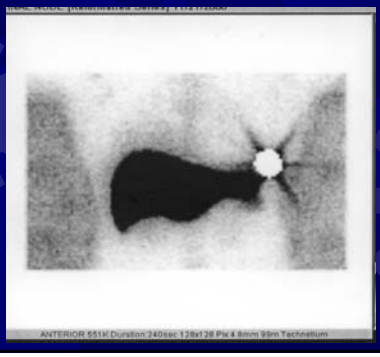
Blue Dye Summary

- There is a move away from using blue dye in experienced hands
- Still useful in ease of identification (especially in obesity)
- Useful for teaching
- Can pre-medicate with steroids and benedryl

Failure to image nodal drainage on scan

- Not usually a problem
- Positive nodes tend to be found at the time of operation
- Blue dye may be effective in localization
- If nothing at all found should do ALND

Unusual sentinel location



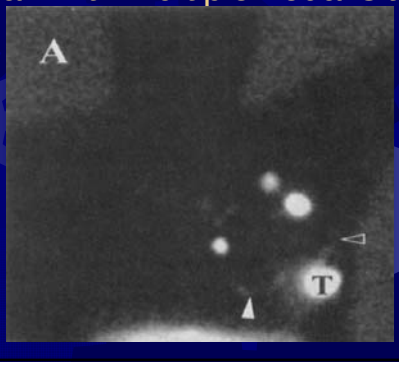
Technique failure

- Ms. L 54 yr old with susp calcifications on right mammogram. FNA done HK shows malignant cells.
- FWLB done showing DCIS multifocal, extensive and ER +ve so goes on to mastectomy with SLNB and immed recon. Hot and blue fat identified. No abnormal nodes so ALND not done (DCIS only)
- Final path 2.5mm HER 2 +ve invasive cancer and DCIS . All margins clear. Do you go back for ALND?

Failure of technique

- Nothing on scan from nuclear medicine
- Nothing to find with probe
- No blue dye uptake
- Happens about 3-5% of the time
- Do ALND

Scan with multiple nodal sites



Scan with multiple nodal sites

- Surgery should involve sentinel node biopsy of axillary nodes- go up to level 3 if needed
- Document rest of drainage pattern

Internal Mammary Lymph Node Biopsy

- Bleeding
- Pleural effusion
- Pneumothorax
- Costochondritis
- Unsightly scar

Internal Mammary Node Biopsy – Halsted Revisited

- IM nodes found to be positive in approx 23% of patients
- Almost all concomitant with axillary node metastases
- Metastases alone in IM chain occur in 2-11%
- Extended radical mastectomy abandoned in the 1970's because of low rate of IM metastases in the absence of axillary mets and removal of all the IM nodes (with no adjuvant treatment) did not improve prognosis

Internal Mammary drainage Position of Tumor

	Upper outer	Inner/central
Uren	28%	37.5%
Johnson	12.5%	12.5%
Byrd	15%	21%

Internal Mammary Nodes Change of Treatment

- 7 studies of biopsy of IM SLN performed found SLN metastases in 18% (15/83) who underwent biopsy
- Of these 15 only 2 were negative in the axillary nodes
- There was a change in treatment in 2.4% of patients
- If 1/3 were to get added benefit from adjuvant treatment there would be potential benefit in 0.8% of these patients

Only positive node drainage is Internal Mammary

- No clear guidance

If an IM node is positive, the vast majority of women will also have axillary node metastases. Therefore,it is advisable to do an ALND

Multiple Nodes

- When to stop?
- what is the ideal number of nodes to obtain
  - -one is probably not enough in most cases
  - -three seem ideal
  - -10 is too many

Optimal number of nodes

	1or 1st node	2nd node
Low (2006) 113 pts 33% positive	87.9% accuracy	97% accuracy
Wong (2001) 1436 pts Sloan Kettering	False negative 14%	False negative 4.3%

Optimal number of nodes

Table 1. Summary of Published Literature on Number of Sentinel Lymph Nodes Removed

Lead author, year	Technique	n	Mean	Range	Accuracy (%)
Krag, 1993[12]	Tc-SC	22	3.4	NA	100
Veronesi, 1997[23]	Tc-alb	163	1.4	1–3	98
Krag, 1998[26]	Tc-SC	443	2.6	1–4	97
Offodile, 1998[24]	Tc-dex	41	3.0	1–7	100
Borgstein, 1998[27]	Tc-alb	130	1.5	1–3	99
Winchester, 1999[28]	Tc-SC	180	3.1	NA	NA
Giuliano, 1994[29]	Blue dye	174	1.8	NA	96
Giuliano, 1997[30]	Blue dye	107	1.8	1–8	100
Flett, 1998[31]	Blue dye	68	1.2	NA	95
Barnwell, 1998[32]	Blue dye + Tc-alb	38	1*	1–3	100
Bass, 1999	Blue dye + Tc-SC	700	2.0	NA	99
Hill, 1999[9]	Blue dye + Tc-SC	500	2.1	1–8	NA

Optimal number or nodes

Table 4. Number and Percentage of Patients with Metastasis to Sentinel Lymph Nodes by Site Examined

Number of SLN sites examined	Number of patients with a positive SLN	Cumulative percentage with a positive SLN
1	338	75.3
1 or 2	417	92.9
1, 2 or 3	440	98.0
1, 2, 3, or 4	445	99.1
1, 2, 3, 4, or 5	447	99.6
1–8	449	100

SLN, sentinel lymph node.

Technical problems

- Obesity-difficult to find nodes
  - -mapping failure
- Get into bleeding
- Hot fat (not nodes)
- Blue everywhere
- Radioactivity everywhere
- Multiple nodes positive (when to stop?)
- No nodes identified (do ALND)

Factors Influencing Successful SLN Identification

- Should be able to obtain 95% identification rate
- There is failure of the technique in the best of hands
- Plan to do ALND if mapping fails
- Biopsy technique,tumor size, tumor location, cell type and surgeon experience not predictors of mapping failure

Predictors of technique failure

- Obesity
- Elderly
- Multiple nodes “full” of tumor so lymphatics “plugged” and do not allow passage of dye or radionuceotide
- Previous wide surgery of upper outer quadrant of breast

Advice for Accurate Staging

- Remove all nodes that are “hot”
- Remove all nodes that are blue
- Put in finger and remove all nodes that feel suspicious

Example of positive finger test

- Ms. C. 50 yr old Asian physiotherapist with 1 cm tumor detected by mammography. Core Biopsy grade 2 invasive cancer. Surgery booked as fine wire guided partial mastectomy and SLN biopsy. At surgery one hot and blue node easily identified. Finger in rest of axilla felt very abnormal. 10 hard nodes removed and ALND completed. The only node negative for metastases was the sentinel node.

Sentinel Node Biopsy in DCIS

- Generally not recommended
- However, if DCIS extensive and mastectomy done is a reasonable option as cannot do later if a small amount of invasion is found on the final pathology. Especially recommended if mastectomy is followed by immediate reconstruction.

Why do Sentinel Node Biopsy

- Less morbidity
- Avoid harvesting negative nodes
- Better staging-nodes can be in unusual places as level 3 or intra-mammary

Example of better staging

- Mrs. A 65 yr old with 2.5cm invasive ca right upper breast. Severe bronchiectasis and allergies. After discussion with radiation oncology decided to have partial mastectomy and ALND. Pathology showed 14 nodes negative but margins close. Decided for completion mastectomy. Had node in tail of breast positive for malignancy. Probably would have identified with SLN biopsy

Need for completion ALND

- Ms M (Japanese woman) presented at age 52 with very small, screen detected but difficult to find grade 1, less than 1cm tumor in outer upper quadrant left breast.
- SLN biopsy done as well as partial mastectomy. Three sentinel nodes harvested-one level 1 and two at different areas of level and 2 axilla. All nodes positive for metastatic cancer. Tumor in breast 1 cm low grade widely excised.

Need for completion ALND

- Who?
- When?
- Will intra-operative pathology help?
- What to do about micrometastases?
- Predictive modelling

Problems with repeat surgery

- Scarring-much more difficult sometimes
- Injury to nerves –sacrifice intercostobrachial nerve
- Potential injury to vessels and motor nerves because of dense scar tissue

Selection of appropriate patients for SLN biopsy

- Most early stage ,clinically node negative women are suitable for the procedure
- Predict problems pre-operatively
- Predict high chance of node positivity and do ALND