

Sentinel Node Biopsy in Breast Cancer

The “Optimal Technique”
Systems not individual

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Objectives

- Definitions
- Lymphoscintigraphy
- Surgical technique
- Pathologic assessment of tissue
- Specific issues
- Implementation
- Patient selection

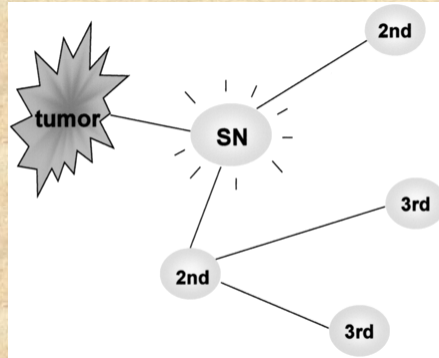
Sentinel node: definitions

- A node on the direct drainage pathway
- Closest to the primary lesion
- Node with the highest count rate
- First node depicted on dynamic lymphoscintigraphy
- Radioactive node
- Count ratio greater than 10
- A blue node

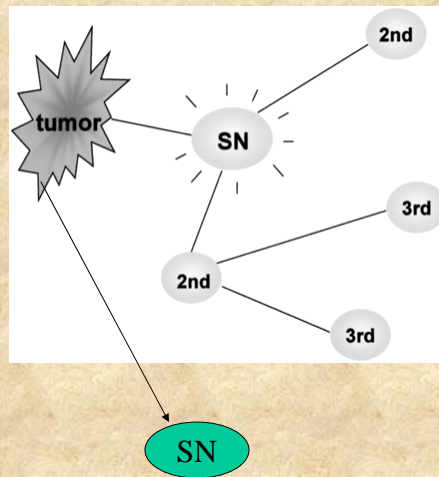
Sentinel Node: Definitions

- “The first LN to receive lymphatic drainage from the primary breast cancer and therefore the most likely to contain metastatic tumor cells.
- A. Giuliano JCO 18, 2000

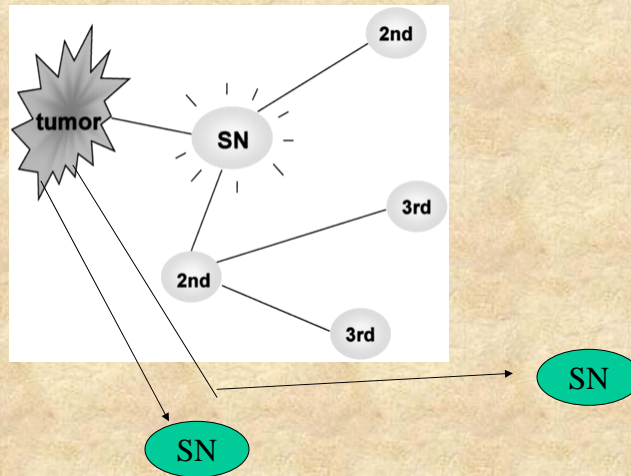
Definition of SN



Niewig OE, Estourgie HE. *Annals of Surgical Oncology* 2004;11(3):169S-173S



Niewig OE, Estourgie HE. *Annals of Surgical Oncology* 2004;11(3):169S-173S



Niewig OE, Estourgie HE. *Annals of Surgical Oncology* 2004;11(3):169S-173S

Sentinel Node: Definitions

- Any blue node or any node substantially radioactive above background.
- Any node containing radioactive counts \geq 10% of the hottest node

McMasters KM et al: *JCO* 18, 2000

Sentinel Node: Definitions

Blue, Hot or Blue and Hot?

“ The sentinel node is the one which contains metastatic tumor while the others do not.”

Nathanson: Ann Surg Oncol, 1999

- What is a sentinel node?
- What is an acute abdomen?

Radiopharmaceuticals

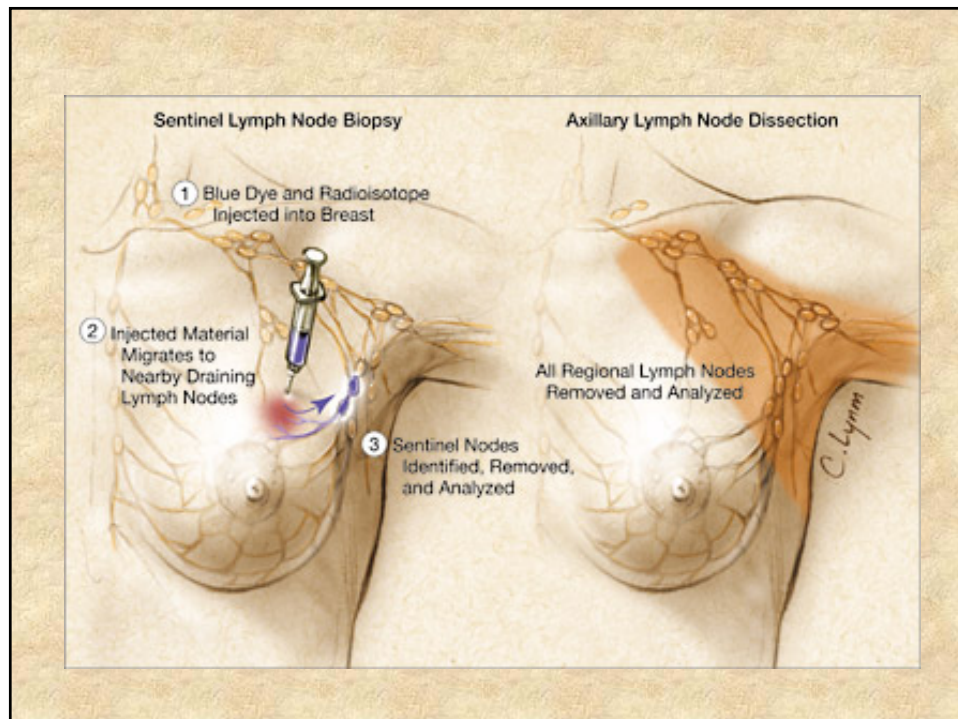
- Tc – labelled Sulfur Colloid 15-5000 nm
- Tc – nanocolloid HAS 4-100 nm
- Tc-Antimony 3-30 nm
- “Ideal” 100-200 nm
- Node retention is phagocytosis not mechanical

Radiation

- $1 \text{ mCi} = 37 \text{ MBq}$
- Half-life of Tc is 6 hours
- Range of mrem dose/procedure = .9-3.2
- Labelling unnecessary for specimens $< 37 \text{ MBq}$
- Sort this out before implementing protocol

Type of injection

- Intratumoral
- Peritumoral
- Intradermal
- Subareolar



Intramammary versus Intradermal

• N = 298		
•	IP(%)	ID(%)
• Identification	89	98
• Concordance	93	92
• FN rate	4	4
• IM nodes	9 (IM alone 1)	1

Martin R et al Surgery 130:2001

Technical pitfalls - 1

- Don't count on blue dye
- Use directionality of prob
- Avoid "shine through"
- Poor directionality usually means distance from node
- Minimize tissue disruption
- Avoid intercostalbrachial nerves

Technical pitfalls - 2

- Clip or tie afferent lymphatics
- Don't disrupt node capsule
- Afferent lymphatics a good "handle"
- "honest" node bed count
- Remove any suspicious nodes

SNB: Not necessarily the hottest node

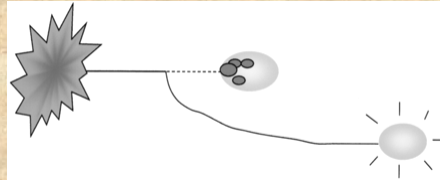
TABLE 2. Frequency, number, and positivity of multiple SLNs

No. Positive SNBs	54/141	38%
Highest uptake node positive	46/54	85%
Highest uptake node negative, another SLN positive	8/54	15%

SLN, sentinel lymph node; SNB, sentinel node biopsy.

Quan ML et al: *Annals of Surgical Oncology* Jun 1 2002: 467

FN causes: Tumor blockage?



Niewig OE, Estourgie HE. *Annals of Surgical Oncology* 2004;11(3):169S-173S

Impact of Number of Sentinel Nodes Removed on the False Negative Rate

SLN removed (n)	Patients with SLN identified (n)	Patients with true positive SLN (n)	Patients with false negative SLN (n)	False negative rate (%)
One	537	132	22	14.3
Two or more	750	223	10	4.3*

* $p = 0.0004$, chi-square

Wong S et al *J Am Coll Surg*, Volume 192, June 2001

- What about internal mammary nodes?

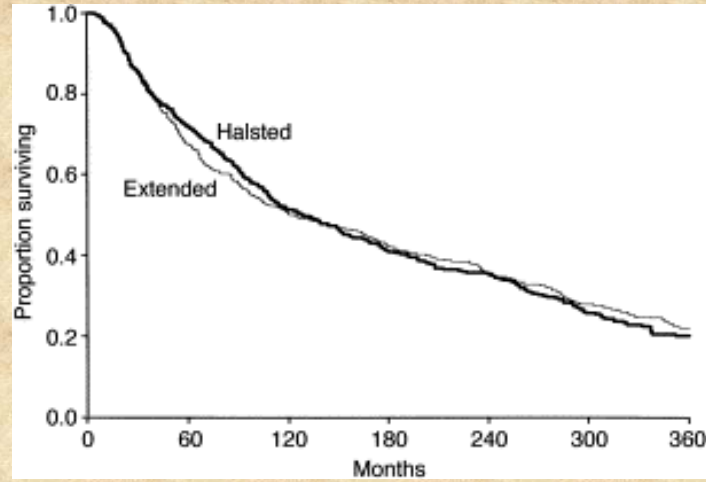
Lymph drainage to Internal Mammary Nodes

Table 4
Frequency of lymphoscintigraphy-demonstrated drainage to the internal mammary lymph nodes

Series	Number of cases	Tumor location	Percentage that drain to the IMC
Uren [47,48]	159	Overall	45%
	16	Inner quadrant/central	44%
Johnson [44]	80	Overall	12%
	32	Inner quadrant/central	12%
Byrd [42]	220	Overall	17%
	61	Inner quadrant/central	17%–29%
Haigh [43]	76	Overall	20%
Laronga [45]	331	Overall	22%
	105	Inner quadrant/central	24%
Smitt [46]	89	Overall	18%

Buchholtz et al: Surg Clin North Am. 2003 Aug;83(4):911-30

30-year RCT: Halsted versus Extended Dissection (Inc. internal Mammary nodes) n = 716



Veronesi et al: Eur J Cancer. 1999 Sep;35(9):1320

Pathologic Assessment

Nodal Metastases

- Isolated tumor cells = isolated cells or cluster < 0.2 mm
- Micrometastases = > 0.2 mm < 2 mm
- IHC v.s. serial sectioning
- Size criteria are arbitrary

Ludwig Breast Cancer Group

- N = 736 node negative patients on routine histology
- serial sections at multiple levels stained with H&E
- Single section stained with IHC
- 12 year median follow-up

Cote RJ et al: Lancet 1999

Micrometastases cont.

- Serial sectioning with H&E: 52/736 (7%)
- IHC 148/736 (20%)

Cote RJ et al: Lancet 1999

H&E v.s IHC

		<u>Immunohistochemistry</u>	
		Positive	Negative
H&E	Positive	45 (6%)	7 (1%)
	Negative	103 (14%)	581 (79%)

Cote RJ et al: Lancet 1999

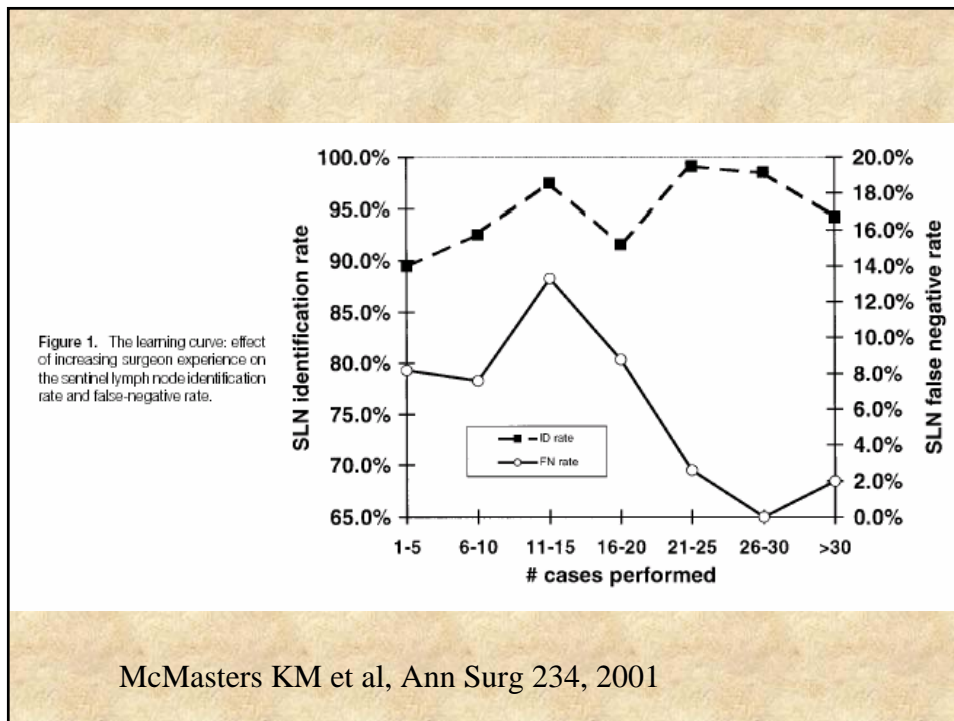
Significance

- IHC detects more micrometastases
- Clinical significance is questionable
- Accurate assessment as a prognostic variable awaits accurate quantification, i.e., it matters what you find, not how you find it.

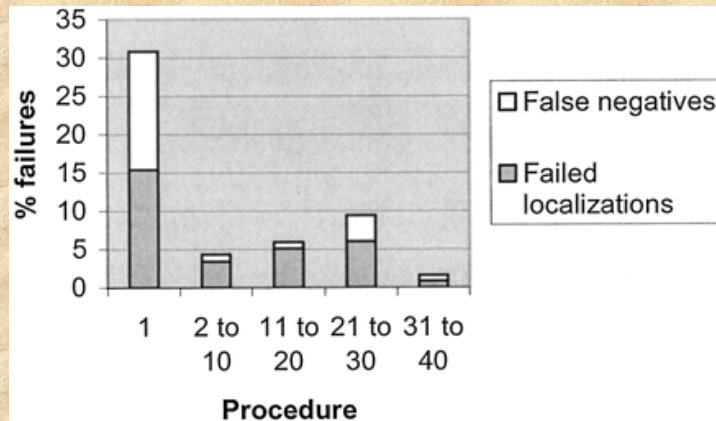
Calgary protocol

- LN fixed in 10% Formalin
- 18 sections 200 micron intervals
- Bivalved- H&E stain
- If negative 18 sections at 200 micron intervals
- 6 slides examined- rest for IHC if necessary
- Frozen section an option

Procedure Implementation



Learning rate in ALMANAC Trial



Clarke D. *Annals of Surgical Oncology* 11:211, 2004

SNB for Breast Cancer in Calgary

- Started in 1996
- 5 surgeons (3 replaced routine AND)
- 88 in 2003

- Why the difference between U.S and Canada?

Calgary Technique

- Isotope plus Lymphazurin
- Peri-areolar injection 2 X 2 MBq
- Lymphoscintigraphy
- 10 % rule for node removal
- Routine H&E

Quality Audit

- 30 patients 1997 – 1999
- 29 female 1 male
- 30 successful

Calgary SNB

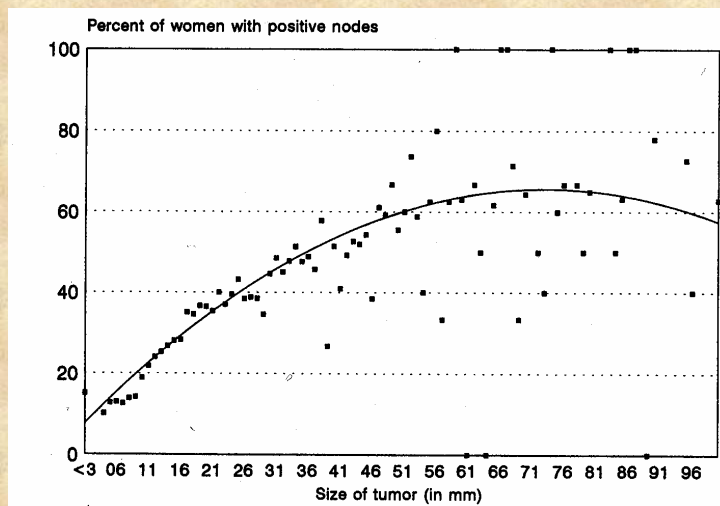
No of nodes retrieved	No. of Patients
1	16
2	9
3	4
5	1

Calgary SNB

SNB		AND Pos	AND Neg
Positive	11	5	6
Negative	19	0	16

- Are any breast cancers too large or too small for SNB?

Node positivity by primary tumor size



SEER data 1983-1987: Surg Oncol Clin NA 3:35, 1994

Occult Micrometastases in DCIS

- N = 102
- DCIS with AND before 1992
- F/U 10-28 years
- 13 had micromets with IHC (7 high grade comedo)
- 7 patients recurred (none with pos nodes)
- Conclusion: no significance

- Heisenberg effect?

Lara et al: Cancer:98, Nov 2003

SNB in patients with DCIS

- Clinical reasoning rather than trial data
- Not indicated for patients treated with segmental mastectomy and RT
- May be performed in patients undergoing TRAM reconstruction
- Stages axilla if occult invasion is found

- Is it ever wise to not do a completion dissection in the face of a positive SNB?

Table 3
Likelihood of additional axillary disease in patients with positive sentinel lymph nodes

Series	Number of patients with positive sentinel lymph nodes	Percentage of these patients with additional axillary disease
Turner [38]	194	45%
Reynolds [37]	60	47%
Krag [7]	101	40%
Veronesi [11]	168	58%
Hwang [36]	131	41%

Buchholtz et al: Surg Clin North Am. 2003 Aug;83(4):911-30

Breast Nomogram

Breast Nomogram Results

Patient Name: _____

Routine Frozen Section	No	Predicted probability of +LN	20%
Pathological size	1		
Nuclear grade	Ductal, I		
Number of positive SLN	1		
Method of detection	Routine		
Number of negative SLN	1		
Lymphovascular invasion	No		
Multifocal	No		
Estrogen receptor positive	Yes		

DISCLAIMER

The prediction tools, also known as prognostic nomograms, located on the MSKCC website are for general health information only. The prediction tools are not to be used as a substitute for medical advice, diagnosis or treatment of any health condition or problem.

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Completion AND after Positive SNB

- Should be done in all cases
- Except, perhaps, after detection of micrometastases by IHC

- Can SNB be done after neoadjuvant chemotherapy?

SNB After Neoadjuvant Treatment

- NSABP B-27 n = 2365
- 343 pts had SNB + AND after chemo
- Procedure accurate in 328/343 (96%)
- Sensitivity 89%
- 203/218 negative (Neg predictive value:93%)
- Conclusion: Useful even after neoadjuvant treatment

Mamounas: Surg Clin North America 2003

Summary

- SNB best approached from a systems point of view
- There is no magic number of learning procedures
- It is a good idea to document results (as with any operation)