Sentinel Node Biopsy in Breast Cancer

The “Optimal Technique”
Systems not individual

Greg McKinnon MD FRCSC

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. Guiliano JCO 18, 2000
Definition of SN

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 ≥ 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 mCi = 37 MBq
- Half-life of Tc is 6 hours
- Range of mrem dose/procedure = .9-3.2
- Labelling unnecessary for specimens < 37 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 directionalit 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

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

<table>
<thead>
<tr>
<th>SLN, sentinel lymph node; SNB, sentinel node biopsy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Positive SNBs</td>
</tr>
<tr>
<td>Highest uptake node positive</td>
</tr>
<tr>
<td>Highest uptake node negative, another SLN positive</td>
</tr>
</tbody>
</table>

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

SNB: Not necessarily the hottest node
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

<table>
<thead>
<tr>
<th>Sentinel Nodes Removed</th>
<th>False Neg.</th>
<th>True Neg.</th>
<th>False Pos.</th>
<th>True Pos.</th>
<th>False Negative Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>25</td>
<td>13</td>
<td>7</td>
<td>22</td>
<td>4%</td>
</tr>
<tr>
<td>Two or more</td>
<td>80</td>
<td>225</td>
<td>10</td>
<td>47</td>
<td>4%</td>
</tr>
</tbody>
</table>

* * p = 0.0004, chi-square

• What about internal mammary nodes?

Lymph drainage to Internal Mammary Nodes

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

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 < 2mm
- 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

<table>
<thead>
<tr>
<th>Immunohistochemistry</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>45 (6%)</td>
</tr>
<tr>
<td>Negative</td>
<td>103 (14%)</td>
</tr>
</tbody>
</table>

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

Figure 1. The learning curve effect of increasing surgeon experience on the sentinel lymph node identification rate and false-negative rate.

Learning rate in ALMANAC Trial

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

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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

<table>
<thead>
<tr>
<th>No of nodes retrieved</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

### Calgary SNB

<table>
<thead>
<tr>
<th>SNB</th>
<th>AND Pos</th>
<th>AND Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Negative</td>
<td>19</td>
<td>0</td>
</tr>
</tbody>
</table>
• Are any breast cancers too large or too small for SNB?

Node positivity by primary tumor size

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?

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>
<thead>
<tr>
<th>Series</th>
<th>Number of patients with positive sentinel lymph nodes</th>
<th>Percentage of these patients with additional axillary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner [38]</td>
<td>194</td>
<td>45%</td>
</tr>
<tr>
<td>Reynolds [37]</td>
<td>60</td>
<td>47%</td>
</tr>
<tr>
<td>Krag [7]</td>
<td>101</td>
<td>40%</td>
</tr>
<tr>
<td>Hwang [36]</td>
<td>131</td>
<td>41%</td>
</tr>
</tbody>
</table>

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

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)