Sentinel Lymph Nodes in Breast Cancer: Histology, reporting, and clinical implications

Sentinel Lymph Node
First node in regional nodal basin that drains a primary tumor and reflects the tumor status of the entire nodal basin
Surgical aspects per Dr. Morrow

Gold Standard, before sentinel methodology accepted
• Axillary lymph node dissection (although minimal cases missed)
• Histopathologic study of nodes
• report # of positive nodes/ # nodes present

Sentinel Lymph Node
• Gross examination
• Frozen section
• Touch prep
• Immunohistochemistry
• PCR [not indicated, high false +]

• Stage 0 – increase
• Stage 1 - increase
• Stage 2 node negative – stable
• Stage 3, 4 – stable
• Stage 2, node positive - increase of as much as 30%, most minimal involvement

Metastasis in SLN

<table>
<thead>
<tr>
<th></th>
<th>SLND</th>
<th>ALND</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. patients</td>
<td>162</td>
<td>134</td>
</tr>
<tr>
<td>% positive</td>
<td>42%</td>
<td>29%</td>
</tr>
<tr>
<td>% &lt;2mm)</td>
<td>38%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Giuliano, Ann Surg 1995
Outcome and Node Analysis
Early, 1999, espouse conservative

“IHC metastases do not appear to adversely affect prognosis”
“IHC should not be routinely performed” on SLN, “nor should treatment decisions be made” [recall that average size is T1c, and grades are mostly low.]


CO$T CON$IDERATION
Don Weaver, MD

• In order to detect single cells:
  – Section at 10 micron (0.01 mm) intervals
  – One paraffin block (2 mm) results in 200 slides
• $12 per slide = $4800 per case
• Newly diagnosed breast cancer in US = $900 million annually
• 77 million slides

Significance of isolated tumor cells and Cell Clusters (ITCs)

Patterns: missed & detected micrometastases

Pathologists’ charge
Minimal epithelial cells need to be examined and analyzed without the assumption that they represent relevant node involvement by cancer
Quantitatively and Qualitatively

Patterns of missed micrometastases for various strategies

Don Weaver
False Positive Nodal Involvement

CK staining of dendritic macrophages, and plasmablasts as well as degenerating cell debris
Benign inclusions
Viable fragments of papillomas
Benign transport: usually fragments of hyperplasia as seen in the displaced clusters in granulation tissue of biopsy site or papilloma(s)
Artifactual keratinocytes in plane above node

Benign Transport

- 15 cases from breast consult files
- Node dissection 15 days after biopsy
- 7 of 15 with DCIS
- Cluster (<100\(\mu\)m) of epithelial cells in subcapsular sinus accompanied by hemosiderin-laden macrophages, giant cells, and altered RBC’s

Nl. Glands at Bx. Site

CLUSTER OF 3 DEGENERATING CELLS IN SINUS WITH SURROUNDING MACROPHAGE REAXN.
**AJCC Cancer Staging 2002**
- Micromets distinguished from ITC
- Identifiers added to indicate SLN and IHC
- Major classification of lymph node status designated according to number of involved axillary nodes

**AJCC/UICC Cancer Staging 6th edition**
Isolated tumor cells (ITCs) defined as single tumor cells or small clusters not greater than 0.2 mm
- pN0 (it)
Modified by Singletary, et al., Cancer; 2003

**ITC = Isolated tumor cells and cell clusters**

**AJCC Cancer Staging 2003**
- Micrometastasis (greater than 0.2 mm, none greater than 2.0 mm)
- pN1mi

**ITC**
Dense small cell groups, probably significant = < 2mm.

Individual Tumor Cells and Clusters, = ITC
Some more “real” than others. Still small

Normal glandular inclusions in capsule

Benign Inclusion, in capsule substance

Nodal Inclusion, nl. polarized cells

ITC or Benign transport
Lymph Node Sinusoid, Nl. Gland & giant cell

Individual tumor cells and clusters

Sinusoid

CK, B9 transport & squamous metaplasia

Benign papilloma “inclusion” in node

Benign transport, subcapsular sinus
Anucleate squames in subcapsular sinus

Occult Cells in Lymph Nodes

Does the finding change the prognosis from that already indicated by other information?

Implication of minimal cells in other nodes not = survival prediction
But may indicate other nodes with tumor

Viale et al, Ann. Surg;2005

Further axillary involvement was significantly associated with the type and size of SLN metastases, the number of affected SLNs, and the occurrence of peritumoral vascular invasion. A predictive model was able to identify subgroups of patients at significantly different risk for further axillary involvement. CONCLUSIONS: Patients with the most favorable combination of predictive factors still have no less than 13% risk for nonsentinel lymph node metastases and should be offered completion ALND outside of clinical trials of SLN biopsy without back-up axillary dissection.

Pinder et al, Br.J.Cancer;2005

- Metastatic deposits were classified as macrometastasis (>2.0 mm), micrometastasis (0.2-2.0 mm) or isolated tumour cells (ITC, <0.2 mm). Of the 216 patients, 56 (26%) had metastasis as identified by H&E. IHC detected metastatic deposits in a further nine patients (4%), of whom four (2%) had micrometastasis and five (2%) had ITC only. Those with micrometastases were all, on review, visible on the H&E sections. IHC detects few SLNs, of which were either micrometastasis or ITC. Until the prognostic significance of these deposits has been determined, IHC may be of limited value in the histopathological examination of SLNs.

The Milan Studies involve complete analysis of each node

There are varieties of epithelial presence other than benign transport in lymph nodes
There are also instances of cytokeration staining of other than epithelial cells, particularly of dendritic macrophages
Micrometastasis ≤2 mm
Recorded: N1
Prognostically: N0
AJCC Staging Manual 5th edition

2. Chatur B, Maldonado LP, Saini AA, et al.: Clinical outcome of patients with lymph node-negative breast carcinoma who have occult lymph node micrometastases detected by immunohistochemistry. Cancer 2005, 103:1584-6

Cancer. Feb. 2006
AJCC reporting and CAP Guidelines: 
Pathology and practice 

2. Chatur B, Maldonado LP, Saini AA, et al.: Clinical outcome of patients with lymph node-negative breast carcinoma who have occult lymph node micrometastases detected by immunohistochemistry. Cancer 2005, 103:1584-6

Cancer. Feb. 2006
AJCC reporting and CAP Guidelines: 
Pathology and practice

2. Chatur B, Maldonado LP, Saini AA, et al.: Clinical outcome of patients with lymph node-negative breast carcinoma who have occult lymph node micrometastases detected by immunohistochemistry. Cancer 2005, 103:1584-6
Re-Examining Axillary Dissection

- Increased frequency of small mammographically detected tumors
- Systemic therapy of N+ and N0 Cancers
- Neoadjuvant Chemotherapy

Results of SN Biopsy: Single Institution Trials

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>% SN identified</th>
<th>% False negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giuliano</td>
<td>107</td>
<td>94</td>
<td>0</td>
</tr>
<tr>
<td>Borgstein</td>
<td>130</td>
<td>94</td>
<td>2</td>
</tr>
<tr>
<td>Veronesi</td>
<td>376</td>
<td>99</td>
<td>6.7</td>
</tr>
<tr>
<td>DeCicco</td>
<td>250</td>
<td>96</td>
<td>2.5</td>
</tr>
<tr>
<td>Zervos</td>
<td>149</td>
<td>89</td>
<td>4</td>
</tr>
<tr>
<td>Cox</td>
<td>186</td>
<td>93</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Is SN Biopsy the Standard of Care?

- Can the results of single institution studies be generalized?
- What is an acceptable false negative rate?
- Long-term outcomes
  - Local control
  - Morbidity

NSABP B32

ACOSOG Sentinel Node Study
Comparison of NSABP B32 and ACOSOG Z10

<table>
<thead>
<tr>
<th></th>
<th>ACOSOG Z10</th>
<th>NSABP B32</th>
</tr>
</thead>
<tbody>
<tr>
<td># Cases</td>
<td>5327</td>
<td>5210</td>
</tr>
<tr>
<td># Surgeons</td>
<td>198</td>
<td>233</td>
</tr>
<tr>
<td>Technique</td>
<td>Any</td>
<td>combined</td>
</tr>
<tr>
<td>Training</td>
<td>20-30 cases + ALND</td>
<td>Proctor, 5 cases + ALND</td>
</tr>
<tr>
<td>Patients</td>
<td>$T_1, T_2, N_0 + \text{BCT}$</td>
<td>$T_1, T_2, N_0$, any surgery</td>
</tr>
</tbody>
</table>

Factors Associated with SN Identification

- BMI $p \leq 0.0001$
- Age $p \leq 0.0001$
- Cases accrued $p \leq 0.0001$

- Not Significant
  - Nodal status
  - T size
  - Tumor location
  - Histology
  - Biopsy Type

Results of SN Biopsy: Collaborative Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Patients</th>
<th>Technique</th>
<th>(%) SN Identification</th>
<th>False - Rate(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krag</td>
<td>443</td>
<td>R</td>
<td>91</td>
<td>11</td>
</tr>
<tr>
<td>McMasters</td>
<td>806</td>
<td>Any</td>
<td>88</td>
<td>7.2</td>
</tr>
<tr>
<td>Shivers</td>
<td>560</td>
<td>B&amp;R</td>
<td>85</td>
<td>4.0</td>
</tr>
<tr>
<td>Tafra</td>
<td>535</td>
<td>B&amp;R</td>
<td>87</td>
<td>13</td>
</tr>
<tr>
<td>Bergkvist</td>
<td>498</td>
<td>B&amp;R</td>
<td>90</td>
<td>11</td>
</tr>
<tr>
<td>NSABP</td>
<td>5210</td>
<td>B&amp;R</td>
<td>97</td>
<td>9.7</td>
</tr>
</tbody>
</table>

R - radioactivity
B - blue dye

SN Biopsy Reliably Stages the Axilla

<table>
<thead>
<tr>
<th>% Nodal Metastases</th>
<th>SN Biopsy</th>
<th>Axillary Dissection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mansel</td>
<td>24.8%</td>
<td>23.8%</td>
</tr>
<tr>
<td>N = 1031</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veronesi</td>
<td>35.5%</td>
<td>32.3%</td>
</tr>
<tr>
<td>N = 516</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Local Control After SN Biopsy Alone

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Mean Follow-up (months)</th>
<th>no. Axillary Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roumen</td>
<td>100</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Shivers</td>
<td>309</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>Dessureault</td>
<td>890</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Chung</td>
<td>206</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>Hansen</td>
<td>238</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>Loza</td>
<td>168</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Badgwell</td>
<td>159</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>Veronesi</td>
<td>259</td>
<td>46*</td>
<td>0</td>
</tr>
<tr>
<td>Cody</td>
<td>2,222</td>
<td>31*</td>
<td>3</td>
</tr>
</tbody>
</table>

* median

Total 4,551 5 (0.001%)
Initial Results: ACOSOG Z10
n=5327
- 16 axillary LRs (0.3%) at a median of 31 mo follow-up
- 3/16 1+SN, no ALND
  1/16 3+ SN, ALND done
  12/16 SN negative, no ALND
- Median to recurrence 16 mo
  (4.2 – 40.1 mo)

Is SN Biopsy the standard of care?
- SN biopsy reliably identifies axillary nodal metastases with low morbidity.
- Long term local control rates after SN biopsy are excellent.
- SN biopsy is the procedure of choice for managing the clinically node negative axilla today.

Rationale for Axillary Surgery in DCIS
- Incomplete sampling
- Diagnosis by core bx
- DCIS has the ability to metastasize

How Common is Undiagnosed Invasive Cancer?
- Cause specific survival rates of 97% - 100% NOT compatible with high rates of invasive cancer
- Smaller mammographic DCIS seen today less likely to have undiagnosed invasion
- Pathologic sampling more extensive

DCIS Diagnosed by Core Biopsy: How Common is Sampling Error?

<table>
<thead>
<tr>
<th>Author</th>
<th># Patients</th>
<th>% Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kestin 2000</td>
<td>130</td>
<td>7.7</td>
</tr>
<tr>
<td>Rosenfeld Darling 2000</td>
<td>289</td>
<td>14</td>
</tr>
<tr>
<td>Cox 2001</td>
<td>240</td>
<td>12.5</td>
</tr>
<tr>
<td>Cox 2003</td>
<td>499</td>
<td>9.4</td>
</tr>
<tr>
<td>Morrow</td>
<td>238</td>
<td>13.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Pendas n=87</th>
<th>Klauber-DeMore n=76</th>
</tr>
</thead>
<tbody>
<tr>
<td>SN+</td>
<td>5 (6%)</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>IHC only</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Addl. + nodes</td>
<td>0</td>
<td>1/6</td>
</tr>
<tr>
<td>Invasion in primary</td>
<td>1</td>
<td>18 “suspicious”</td>
</tr>
</tbody>
</table>

Does DCIS Have The Capacity To Metastasize?
**What do IHC Positive Cells in DCIS Mean?**

- Retrospective review
  - 79 DCIS patients F/U > 10 years
  - Axillary Dissection performed
  - Nodes recut, IHC performed
  - 4 IHC positive patients (5.1%)

Outcome: 8/79 patients recurred, NONE with IHC+

*Cox, Moffit*

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**When Should Sentinel Node Biopsy Be Performed in DCIS**

- Microinvasive carcinoma
  - Metastases in 3% - 20% of cases
- DCIS treated by mastectomy
  - Opportunity lost if invasion found
- Done as a second procedure if invasion found after lumpectomy
  - Prior biopsy does not interfere with mapping

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**Contraindications to SN Biopsy**

- Locally advanced breast cancer
- Pregnancy and Lactation
- Prior axillary surgery

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**Is a Repeat SN Biopsy Feasible?**

Intra, et al n=18

100% SN identification

2/18 positive

No axillary recurrence at 12.7 mo median

*Ann Surg Oncol 2005*

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**Controversies**

- Multicentricity
- Internal Mammary Nodes
- Neoadjuvant Therapy

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**SN Biopsy for Multicentric Cancer**

- Original hypothesis: Unique drainage pathway for each cancer.
- Concordance studies indicate the majority of breast tumors drain via central collecting system.
- Reasonable to do a subareolar injection or separate peritumoral injections.
**SN Biopsy for Multicentric Cancer**

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Cases</th>
<th>% SLN identified</th>
<th>% Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kumar, et al</td>
<td>10</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Tousimis, et al</td>
<td>70</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>Kumar, et al</td>
<td>59</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td>Ozmen, et al</td>
<td>21</td>
<td>86</td>
<td>89</td>
</tr>
<tr>
<td>Fernandez, et al</td>
<td>53</td>
<td>98</td>
<td>100</td>
</tr>
<tr>
<td>Jin Kim, et al</td>
<td>5</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Schrenk, et al</td>
<td>19</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>237</strong></td>
<td><strong>95.4</strong></td>
<td><strong>96.9</strong></td>
</tr>
</tbody>
</table>

**Internal Mammary Node Metastases**

- 7070 Patients
- 22.4% I.M. node positive
- 4.9% I.M. node were only site of metastases

**How Common are Isolated IM Metastases?**

- Dupont, et al: 3/1273 = 0.2%
- Vander Ent, et al: 3/256 = 1.2%
- ALMANAC: 5/1139 = 0.4%

**Nodal Response to Neoadjuvant Therapy?**

**SN Biopsy After Neoadjuvant RX Studies Since 2002**

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>% SN Identified</th>
<th>% False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stearns 2002</td>
<td>34</td>
<td>85</td>
<td>14</td>
</tr>
<tr>
<td>Brady 2002</td>
<td>14</td>
<td>93</td>
<td>0</td>
</tr>
<tr>
<td>Miller 2002</td>
<td>35</td>
<td>86</td>
<td>0</td>
</tr>
<tr>
<td>Reitsamer 2003</td>
<td>30</td>
<td>87</td>
<td>7</td>
</tr>
<tr>
<td>Balch 2003</td>
<td>32</td>
<td>97</td>
<td>5</td>
</tr>
<tr>
<td>Vigario 2003</td>
<td>37</td>
<td>94</td>
<td>39</td>
</tr>
<tr>
<td>Piatro 2003</td>
<td>42</td>
<td>98</td>
<td>17</td>
</tr>
<tr>
<td>Schwartz 2003</td>
<td>21</td>
<td>100</td>
<td>9</td>
</tr>
<tr>
<td>Kang 2004</td>
<td>80</td>
<td>76</td>
<td>7</td>
</tr>
<tr>
<td>Patel 2004</td>
<td>42</td>
<td>95</td>
<td>0</td>
</tr>
<tr>
<td>Shimazu 2004</td>
<td>47</td>
<td>94</td>
<td>12</td>
</tr>
</tbody>
</table>
SN Biopsy After Neoadjuvant RX

HIGHLY VARIABLE RESULTS DUE TO:

- SMALL NUMBERS 2/17 STUDIES > 50 PTS
- DIVERSE POPULATIONS
  T1 – T4
  N0, N+
- ? CLASSIFICATION PALPABLE, ABNORMAL NODES

NSABP B27

T1C - T3, N0 or N1

Randomize

AC x 4
AC x 4
AC x 4

Surgery
Surgery
Docetaxol x 4

Surgery

Accuracy of SN Biopsy

<table>
<thead>
<tr>
<th>NEoadjuvant RX</th>
<th>Primary Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B27</td>
<td>Metaanalysis, 2002</td>
</tr>
<tr>
<td></td>
<td>69 Studies</td>
</tr>
<tr>
<td>n=428/2365</td>
<td>n=10,000</td>
</tr>
</tbody>
</table>

SN identified 85% 90%
False negative 11% 8.4%

Relationship Between SN False Negative Rate and Response

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>% FALSE NEGATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>8.7</td>
</tr>
<tr>
<td>Other</td>
<td>11.6</td>
</tr>
</tbody>
</table>

p=ns

Accuracy of SN Biopsy by Pathologic Response

<table>
<thead>
<tr>
<th>RESPONSE</th>
<th>% ACCURACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>98.4</td>
</tr>
<tr>
<td>CCR, Residual tumor</td>
<td>96.0</td>
</tr>
<tr>
<td>PR/Stable</td>
<td>94.9</td>
</tr>
</tbody>
</table>

p=ns

Unresolved Problems

- Is Completion Axillary Dissection Necessary After a Positive SN Biopsy?
- Significance of Micrometastases
Management of the Positive SN

Is Axillary Dissection Indicated?
- Small primary tumors
- Small metastatic deposits not seen intraop

Risk of Additional Metastases: T1b Cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chu</td>
<td>-</td>
<td>13</td>
</tr>
<tr>
<td>Wong</td>
<td>41</td>
<td>22</td>
</tr>
<tr>
<td>Nos</td>
<td>61</td>
<td>12</td>
</tr>
<tr>
<td>Viale*</td>
<td>200</td>
<td>34</td>
</tr>
<tr>
<td>Van Zee</td>
<td>171</td>
<td>26</td>
</tr>
</tbody>
</table>

*T1a+b

Risk of Additional Metastases by Size of Metastatic Deposit

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Size</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viale</td>
<td>116</td>
<td>&lt;0.2 mm</td>
<td>14.5</td>
</tr>
<tr>
<td></td>
<td>212</td>
<td>0.2 – 1 mm</td>
<td>16.9</td>
</tr>
<tr>
<td>Leidenius</td>
<td>39</td>
<td>&lt;0.2 mm</td>
<td>20.5</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>0.2 – 1 mm</td>
<td>34.3</td>
</tr>
</tbody>
</table>

Risk of Additional Metastases by Size/Detection Method: Micrometastases

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Method</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mignotte</td>
<td>44</td>
<td>IHC</td>
<td>15.9</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>H&amp;E</td>
<td>33.2</td>
</tr>
<tr>
<td>Kamath</td>
<td>26</td>
<td>IHC</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>H&amp;E</td>
<td>25.0</td>
</tr>
</tbody>
</table>

Multivariate Analyses of Factors Predictive of Involvement of Non-Sentinel Nodes

n=4017 Patients, 10 Studies

- Tumor Size: 5/10
- Tumor Grade: 0
- Metastases Size: 7/10 # SN involved: 6/9
- LVI: 4/10 # SN removed: 3/4

Axillary Dissection? Pros:
- Significant risk of additional nodal disease
- Small survival benefit for dissection cannot be excluded
- Information on the status of remaining nodes may help clarify decisions about adjuvant rx
Unresolved Questions

- Significance of micrometastases

Pathologic Analysis of Lymph Nodes

- Pre-SLND
  - Bivalve lymph nodes
  - Half of lymph node discarded
  - Section from 1/2 lymph node evaluated with H&E

- Post-SLND
  - Serial sections of sentinel node
  - Evaluation with H&E and IHC

Micrometastases

- Present in 7% - 32% H & E negative nodes
- Heterogeneous - ranging from missed tumors greater than 2mm to single cells in subcapsular sinus
- Prognostic significance uncertain
  - no benefit
  - important in postmenopausal women
  - DFS differences 2% - 14%

Significance of Micrometastases: Ludwig Trial

- Method: Retrospective analysis of a prospective trial
  - 736 of 921 patients included
  - Serial sections
  - Single section from first level of node stained for AE-1 and CAM5-2
  - Median follow-up 12 yrs

Detection of Micrometastases: Ludwig Trial

<table>
<thead>
<tr>
<th>Method</th>
<th>H&amp;E</th>
<th>IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serial Selection</td>
<td>7%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Cote, Lancet 1999
**Prognostic Significance of Micrometastases**

Time Since Randomization (years) vs. Disease Free Survival (%)

Cote, Lancet 1999

**John Wayne Prospective Study of Micrometastases**

- n = 683
- Stage I and II cancer 1/92 - 4/99
- SN Step Sectioned, H & E stained
  - If H & E → IHC
- Stratified by SN met size

**Results**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean Age</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neg</td>
<td>419</td>
<td>58</td>
<td>SN (-) H&amp;E &amp; IHC</td>
</tr>
<tr>
<td>IHC</td>
<td>56</td>
<td>58</td>
<td>SN (+) IHC</td>
</tr>
<tr>
<td>Micro</td>
<td>76</td>
<td>58</td>
<td>SN (+) H&amp;E&lt;br&gt;Mets ≤ 2 mm</td>
</tr>
<tr>
<td>Macro</td>
<td>132</td>
<td>56</td>
<td>SN (+) H&amp;E&lt;br&gt;Mets &gt; 2 mm</td>
</tr>
</tbody>
</table>

**Disease Free Survival**

- 5-yr DFS (%)
  - Neg: 98.01
  - IHC: 96.67
  - Micro: 97.09
  - Macro: 73.56
- Median F/U: 44 mos

**Conclusions**

- IHC Should NOT be used routinely
- Decisions regarding Stage and the need for adjuvant therapy should be made on the basis of H & E staining

**CAP Consensus**

Phila Concensus

- SN Biopsy is the procedure of choice for managing the clinically node negative axilla
- Axillary dissection remains standard management for the SN+ patient
- Routine use of IHC awaits results of prospective trials
Sentinel Node Biopsy and Clinical Decision Making

Monica Morrow, M.D.
USCAP, February 12, 2005

References

Ki M, Giuliano AE, Lyma GH. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma. Cancer 2005 [Epub ahead of print]


