7th Edition AJCC Staging Criteria: 

What's New for Breast Cancer?

Joseph Rabban MD MPH

Associate Professor

UCSF

University of California

San Francisco

PART VII

Summary of Changes

Cancer Staging Manual Summary of Changes From the Sixth Edition to the Seventh Edition

Breast (continued)
Breast Chapter

Longest of all organs

29 pages (up from 17 pages)

6 pages of F.A.Q.

Details buried in text

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Outline of Talk

- Current AJCC criteria for
  - pT
  - pN
  - pM
  - ypTNM discussed in separate lecture

- Highlight vague / controversial criteria

- Offer recommendations to consider

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Protocol for the Examination of Specimens From Patients With Invasive Carcinoma of the Breast

Arch Pathol Lab Med 2009; 133: 1515
Why does AJCC still matter in 2010?

Other prognostic / predictive data not used in AJCC:
- ER/PR/HER2
- Multi-gene expression signatures
- Molecular profiling for recurrence/response to therapy

AJCC Stage still essential for:
- Adjuvant therapy decision making
- Entry into clinical trials

pT Criteria
- Defining tumor size
- Multiple cancers
- Microinvasive cancer
- Inflammatory carcinoma

Defining Tumor Size
- Use microscopic size if invasive cancer fits in one block
- Use gross size if too big to fit in one block.

Problems:
- Gross may over-estimate pT if there is extensive DCIS
- Gross may under-estimate pT if there is extensive microscopic tumor, especially for invasive lobular carcinoma

Recommendation:
- Determine pT by careful correlation of gross & slides
Defining Tumor Size

Size should be reported at 0.1 cm increments

Tumor size from National SEER database

Abner et al. Cancer 1998; 83: 2502
- 14% cancers had > 0.5 cm difference between gross & microscopic pT
- 31% gross under-estimated pT
- 47% gross over-estimated pT
- Microscopic pT better at predicting 10 year recurrence than gross pT

Microscopic tumor size (cm)

Macroscopic tumor size (cm)
Method of Gross & Slide Correlation for pT

Gross description: 3 cm mass in slices 3,4,5

Cassettes:
- A1: normal, slice 1
- A2: normal, slice 2
- A3: mass, slice 3
- A4: mass, slice 4
- A5: mass, slice 5
- A6: normal, slice 6
Gross pT (3 cm) correlates with Slide pT (3 cm)

3 slices with tumor
Slices 1 cm each
pT = 3 x 1 cm
pT = 3 cm

Gross pT (3 cm) underestimates Slide pT (4 cm)

4 slices with tumor
Slices 1 cm each
pT = 4 x 1 cm
pT = 4 cm

pT Depends on Slice Thickness

Margin of error is up to twice the thickness of the slices!

example: a 1.6 cm tumor could be mis-calculated to be over 3 cm if the slices are 1 cm each

Tumor in 3 slices
3 x 1 cm = 3 cm
Stage pT2

Tumor in 3 slices
3 x 0.5 cm = 1.5 cm
Stage pT1
**How to salvage “too thick” slices**

- >1 cm thick slice
- Split flanking slices thinner

**Gross Description Template**

**SIZE OF SPECIMEN:**
- Medial to lateral: 7.5 cm
- Superior to inferior: 6 cm
- Anterior to posterior: 6 cm

**Total # of slices:** 15
- First Slice (slice #1): Medial Margin
- Last Slice (slice #15): Lateral Margin

**Gross Description:**
A 2.5 cm firm white stellate mass is present in the upper outer part of the specimen in slices #8 to #12.

**Cassettes:**
- A1: mass, slice 8, closest approach to deep margin
- A2: mass, slice 9
- A3: mass, slice 10
- A4: mass, slice 11
- A5: mass, slice 12, closest approach to lateral margin
- A6: normal tissue, slice 7
- A7: normal tissue, slice 13
- A8: normal tissue, medial margin, slice 1
- A9: normal tissue, lateral margin, slice 15

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**Defining pT... more details**

- Do not add size of tumor from different specimens
- Don’t add size in core to size in excision
- Use whichever size is largest

**? Tumor in multiple separately submitted parts**

- **Recommendation:**
  Stage the largest single cancer
  Report size in each separate part.
Does lymphovascular involvement count in pT?

- LVI

Invasive

Defining pT... more details

- Mucinous carcinoma

- Recommendation
  Include mucin, not just tumor cell, in pT
  Mucin at a margin is positive
  Mucin in a lymph node is presumed “positive”

Does lymphovascular involvement count in pT?

- LVI

Invasive

No.
Do not count LVI, in situ, or Paget disease in pT.
Do not count LVI at margins.

pT Criteria

- Defining tumor size
- Multiple cancers
- Microinvasive cancer
- Inflammatory carcinoma
Multiple Synchronous Cancers and pT

**Definition:** Tumors are > 0.5 cm apart.

**Assign pT to the single largest cancer**

Do not add cancers together

**Prognostic markers**

- If similar morphology/grade: perform on larger tumors
- Perform on any with distinct morphology/grade

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**Recommendation:**
Verify intervening benign tissue before calling multiple synchronous cancers

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**pT Criteria**

- Defining tumor size
- Multiple cancers
- Microinvasive cancer
- Inflammatory carcinoma
Microinvasive Carcinoma and pT

**Definition:** Invasive focus < 0.1 cm.

If multiple micro-foci:

Measure each individually. Do not add together.
If any one single focus is >0.1 cm, it is NOT micro-invasion

**Recommendation:**

- Exclude over-calling “tangential artifact” in DCIS as invasion
- Restrict diagnosis to clear cut extralobular invasion
- Use myoepithelial immunostains when uncertain

Conversely: heavily sample “mass-forming” DCIS to exclude micro-invasion

Inflammatory Carcinoma and pT4d

**Definition of pT4d**

1. Invasive carcinoma
2. Diffuse erythema/edema of >1/3 breast

This requires specific clinical information.
*Diagnosis cannot be made on pathology alone.*

Dermal lymphovascular invasion:
*Neither necessary nor sufficient*

Paget disease of nipple is not inflammatory carcinoma

Inflamatory Carcinoma and pT4d

**pT Criteria**

- Defining tumor size
- Multiple cancers
- Microinvasive cancer
- Inflammatory carcinoma

**Subcategories of pT4**

- Diffuse erythema/edema of >1/3 breast: pT4d
- Diffuse erythema/edema < 1/3 breast: pT4b
- Skin ulceration by tumor: pT4b
- Chest wall extension by tumor: pT4a
- Both pT4a and pT4b criteria: pT4c
“True” inflammatory carcinoma has worst outcome

| T4a | 47% |
| T4b | 40% |
| T4d | 34% |

5 year survival

p<0.0001

National Cancer Database
N= 9,865 cases

Suspected Inflammatory Carcinoma and pT

Recommended Diagnosis in Absence of Clinical Data:

Invasive carcinoma with dermal LVI.

Comment:
• If appropriate clinical features are present,
• this could represent inflammatory carcinoma.
• Stage based on tumor size.
• Do not stage as pT4.

Lymph Nodes and pN

• Processing nodes
• Staging micrometastases
• Definition of isolated tumor cells

Processing Lymph Nodes

Non-sentinel nodes:
• Entirely submit all nodal tissue if grossly negative
• Slices should be <0.2 cm thick
• One H&E per block

Sentinel nodes:
• No specific difference from non-sentinel nodes

Unresolved whether levels/immunostains should be standard.
**Processing Sentinel Lymph Nodes**

**Recommendation:**
- 3 H&E level sections
- reserve 2 unstained sections in case keratin needed
- no automatic keratins
- consider keratin if:
  - Atypical cells
  - Lobular type carcinoma
  - Post-treatment node with suspicious cells

**Micrometastasis and staging**

**Definition**
- Size 0.2 mm to 2 mm
  - or
- More than 200 tumor cells in a single slide

**Micromets are now stage IB not stage II**

**Micromets behave differently than Macromets**

10 year survival
- pN0: 76%
- pN1mic: 71%
- pN1a: 65%

SEER National Cancer Database
>209,000 patients

**Micomet Definition: A Moving Target**

<table>
<thead>
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<th>Edition</th>
<th>Definition</th>
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<tbody>
<tr>
<td>5th</td>
<td>No larger than 2 mm</td>
</tr>
<tr>
<td>6th</td>
<td>0.2 mm to 2 mm</td>
</tr>
<tr>
<td>7th</td>
<td>0.2 mm to 2 mm or &gt;200 tumor cells / slide</td>
</tr>
</tbody>
</table>
Micromets behave differently than Macromets

Should they be staged differently?

<table>
<thead>
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<th>Edition</th>
<th>Staging</th>
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<tbody>
<tr>
<td>6th AJCC</td>
<td>No</td>
</tr>
<tr>
<td>7th AJCC</td>
<td>Yes</td>
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</table>

Micromet Definition: A Moving Target

0.2 mm sphere of cells contains about 1000 cells

One section contains about 200 cells
Micromet Definition: A Moving Target

If >200 cells present in any pattern in single slide even if <0.2 mm:

Don’t diagnose ITC
Diagnose pN1mic

Role of the 200 cell threshold

Helps manage unusual scenarios of likely true mets <0.2 mm:

- Small volume/scattered lobular cancer metastases
- Multifocal scattered tiny clusters of metastases

Micromet Definition: A Moving Target

If a fibrous (desmoplastic) stromal reaction is present, the combined contiguous dimension of tumor cells and fibrosis = size of metastasis.

<0.2 mm each, <200 cells total = ? pN0i+ (ITC)

Stromal Reaction

Micromet Definition: A Moving Target

If a fibrous (desmoplastic) stromal reaction is present, the combined contiguous dimension of tumor cells and fibrosis = size of metastasis.
If a fibrous (desmoplastic) stromal reaction is present, the combined contiguous dimension of tumor cells and fibrosis = size of metastasis.

Before dismissing a node as ITC:
- Consider size
- Consider total cell number
- Consider if desmoplastic stromal reaction is present

Each cluster is <0.2 mm

and

Less than 200 cells in entire slide

and

No fibrous reaction between clusters

“Not all cases easily fit the rules

“The pathologist should use judgment “
Single Cluster

- < 0.2 millimeter
- < 200 cells
- No stromal reaction

ITC, pN0i+

Multiple Clusters

Each cluster < 0.2mm and < 200 cells each
No stromal reaction

Total sum of clusters > 200 cells
Positive node
Total sum of clusters > 200 cells
Positive node

Controversial:
- Size of metastasis?
- pN1mic

Dispersed single cells

< 200 cells → “ITC” = pN0i+
> 200 cells → not “ITC”

- True “positive” node
- pN1mic
- Not clear how to report size

Use judgment
Be descriptive

Fibrous stromal reaction and multiple clusters

Arch Pathol Lab Med 2009; 133: 1515
Keratin positive cells in fibrotic stromal reaction

Controversial

Metastases and pM

“Disseminated Tumor Cells” = DTC = pM0i+

Clinically / radiologically occult
<0.2 mm distant metastasis
Applies to bone marrow, distant nodes, distant organs

Rational:
True M1 is incurable; triggers palliative care
pM0i+ not necessarily worse outcome (limited data)

Occult metastatic breast cancer in ovary, <0.2 mm

pM0i+

Outline of Talk

- Current AJCC criteria for pT pN pM ypTNM discussed in separate lecture
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