Treatment of DCIS in the USA

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Massachusetts General Hospital, Boston, MA
Background
Selection of Treatment for Patients with DCIS is Complex

• Heterogeneity in biology/extent
• Difficulties assessing size and margins
• Protracted natural history (especially for low grade lesions) requires long follow up
• Inability to predict clinical outcome can lead to over- or under-treatment
Margins Consensus Statement for DCIS Managed with Excision + RT

2 mm margin is enough

- Multidisciplinary panel
- Used meta-analyses of margin width and ipsilateral LR
- Included 20 studies, 7883 patients
- 2 mm margin minimized LR compared w/smaller margins
- Wider margins not significantly better than 2 mm

Morrow, J Clin Oncol 2016
Options:

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen or Arimidex
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and Partial Breast Irradiation
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
Options:

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>FU</th>
<th>E alone (%)</th>
<th>E + RT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B-17</td>
<td>814</td>
<td>17 y</td>
<td>35%</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>invasive: 20%</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DCIS: 15%</td>
<td>9%</td>
</tr>
<tr>
<td>EORTC</td>
<td>1010</td>
<td>15.8 y</td>
<td>30%</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>invasive: 15%</td>
<td>9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DCIS: 15%</td>
<td>8%</td>
</tr>
<tr>
<td>UK</td>
<td>1030</td>
<td>12.7 y</td>
<td>19%</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>invasive: 7%</td>
<td>4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DCIS: 12%</td>
<td>3%</td>
</tr>
<tr>
<td>Swedish</td>
<td>1067</td>
<td>8 y</td>
<td>27%</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>invasive: 12%</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DCIS: 15%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Absolute reduction IBTR: 15.2%

All 4 randomized trials of RT vs no RT
N = 3729
Regardless of age, extent of surgery, use of tamoxifen, margins, grade, size

Correa, JNCI Monogr 41:162-177, 2010
Excision + RT: Local Recurrence in Modern Retrospective Series

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Year</th>
<th>FU (mos)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDACC</td>
<td>977</td>
<td>1996-2007</td>
<td>62</td>
<td>2.4%</td>
</tr>
<tr>
<td>Harvard</td>
<td>246</td>
<td>2001-2007</td>
<td>58</td>
<td>0%</td>
</tr>
<tr>
<td>Norway</td>
<td>871</td>
<td>1993-2007</td>
<td>120</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Higher Local Recurrence with RT in Earlier Trials (7-20%)

Alvarado, Ann Surg Oncol 2012
Halasz, Int J Radiation Oncol Biol Phys 2012
Falk, Breast Cancer Res Treat 2011
RTOG 9804: RCT of lumpectomy vs lumpectomy/RT for low risk DCIS

Eligibility Criteria:
- Grade 1, 2 DCIS
- <2.5 cm
- 3mm margins or greater

N = 585, median FU 7 yrs
Tamoxifen in 62%

McCormick B et al, JCO 2015
Radiation Therapy for DCIS

• Consistently reduces local recurrence

• Reduces LR by >60% (both DCIS and invasive LR)

• Reduces LR across all subsets

• No demonstrated survival benefit…
Options:
1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen or Arimidex
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
# Long-Term Results from NSABP B-24

(Median FU = 13.6 yrs)

<table>
<thead>
<tr>
<th></th>
<th>RT</th>
<th>RT + Tam</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipsilateral Event</td>
<td>16.6%</td>
<td>13.2%</td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td>9.0%</td>
<td>6.6%</td>
<td>0.025</td>
</tr>
<tr>
<td>DCIS</td>
<td>7.6%</td>
<td>6.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Contralateral Event</td>
<td>8.1%</td>
<td>4.9%</td>
<td>0.023</td>
</tr>
</tbody>
</table>

Reduction = 32% for ipsilateral and contralateral events
Nonsignificant reduction in ipsilateral DCIS events
**Benefit only in ER+ DCIS**

Wapnir, JNCI 2011
# Adding Tamoxifen to Excision: UK/ANZ Trial

<table>
<thead>
<tr>
<th></th>
<th>No Tam</th>
<th>Tam</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBTR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No RT</td>
<td>17%</td>
<td>13%</td>
<td>0.04</td>
</tr>
<tr>
<td>RT</td>
<td>2.4%</td>
<td>2.6%</td>
<td>0.8</td>
</tr>
<tr>
<td>CBC</td>
<td>4%</td>
<td>2%</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Cuzick, Lancet Oncol 2011

2,566 pts
12 y FU
Tamoxifen vs Arimidex

**NSABP B-35**
- 3,104 post-menopauseal pts
- FU 10 years
- Improvement mostly in pts <60 yo

**IBIS II**
- 2,980 post-menopausal patients
- FU median 7.5 years
- No difference (AI non-inferior)

*Lancet 2016*
Tamoxifen or Arimidex in DCIS

- Modest benefit in ER+ DCIS
  - Reduces Contralateral Breast Cancer
- With RT, may further reduce LR
- Small benefit after excision alone
- No or little superiority in favor of AI
- Await data from NSABP B-43 (trastuzumab)
Options:

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
### BOOST : Séries RETROSPECTIVES

<table>
<thead>
<tr>
<th></th>
<th>Année Public</th>
<th>n</th>
<th>Age med</th>
<th>Follow-up (Year)</th>
<th>No bst/ boost</th>
<th>RL (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Curie (1)</td>
<td>2002</td>
<td>343</td>
<td></td>
<td></td>
<td>243 / 100*</td>
<td>13 / 6%</td>
<td>0.08</td>
</tr>
<tr>
<td>Rare Cancer Network (2)</td>
<td>2006</td>
<td>373</td>
<td>41</td>
<td>6</td>
<td>150 / 166</td>
<td>28 / 14%</td>
<td>0.02</td>
</tr>
<tr>
<td>NSABP B-24 (3)</td>
<td>2008</td>
<td>1569</td>
<td>53</td>
<td>14</td>
<td>877 / 692</td>
<td>14,3 / 13,8</td>
<td>0.69</td>
</tr>
<tr>
<td>Wai ES (4)</td>
<td>2011</td>
<td>957</td>
<td>56</td>
<td>9,3</td>
<td>-</td>
<td>6 / 9%</td>
<td>0.65</td>
</tr>
<tr>
<td>Mc Gill (5)</td>
<td>2012</td>
<td>220</td>
<td>58</td>
<td>3,8</td>
<td>121 / 79</td>
<td>4 / 0</td>
<td>Effet boost</td>
</tr>
<tr>
<td>Canada (6)</td>
<td>2013</td>
<td>1895</td>
<td>56</td>
<td>10</td>
<td>1344 / 561</td>
<td>12 / 13%</td>
<td>0.30</td>
</tr>
</tbody>
</table>

#### Conflicting results

**Biases:** High grade, close/positive margins, young patients

*Courtesy David Azria*

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(1) Fourquet A: in DCIS book Silverstein 2002
(2) Rare Cancer Network : Omlin A, Lancet Oncology 2006, 7 : 652-56
(3) Julian TB, JCO 2008; 28
(4) Wai ES , Cancer 2011, 117:54-62
(5) Wong P; IJROBP 2012, Vol 82 e153
(6) Rakovitch E - JROBP 2013 Jul 1, 86(3):491-7
Etude BONBIS: PHRC 2008

- Age
- HT
- Centre
- Grade
- Circonstances
- Marges

Whole breast RT

Whole breast RT + 16Gy boost

Courtesy David Azria
BOOST in DCIS

Role is not clear
Options:

1. Lumpectomy + standard whole breast RT

2. Role of Tamoxifen

3. Role of a boost

4. Lumpectomy with WBI using hypofractionation

5. Lumpectomy and PBI

6. Lumpectomy alone

7. Oncotype

8. Observation without excision (trial)
Randomisation A

- **Surgery**
  - Age (<50, 50+)
  - Endocrine Rx (yes, no)
  - Centre

Randomisation:

- Whole breast RT
  - Standard fractionation
  - Short fractionation

- Whole breast and boost RT
  - Standard fractionation
  - Short fractionation

Dosages:

- 50 Gy +/- 16 Gy boost
- 42.5 Gy +/- 16 Gy boost

Courtesy David Azria
HYPOFRACTIONATION in DCIS

Role is not clear
Options:

1. Lumpectomy + standard whole breast RT

2. Role of Tamoxifen

3. Role of a boost

4. Lumpectomy with hypofractionation WBI

5. Lumpectomy and PBI (Partial Breast Irradiation)

6. Lumpectomy alone

7. Oncotype

8. Observation without excision (trial)
### PBI: Retrospective studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts#</th>
<th>DCIS grade</th>
<th>Technique</th>
<th>FU</th>
<th>LF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al</td>
<td>53</td>
<td>I, II, III</td>
<td>Mammosite</td>
<td>3.6 y</td>
<td>2%</td>
</tr>
<tr>
<td>Jeruss et al</td>
<td>194</td>
<td>I, II, III</td>
<td>Mammosite</td>
<td>4.5 y</td>
<td>3.1%</td>
</tr>
<tr>
<td>Goyal et al</td>
<td>41</td>
<td>I, II</td>
<td>Mammosite</td>
<td>5 y</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>III</td>
<td>Mammosite</td>
<td>5 y</td>
<td>5.3%</td>
</tr>
<tr>
<td>Stull et al</td>
<td>106</td>
<td>I, II, III, unknown</td>
<td>Mammosite</td>
<td>3 y</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

- DCIS excluded from 11 of 13 ABPI studies with ≥ 4yrs F/U
NSABP B-39/RTOG 0413
Phase III APBI Trial

Eligible Patients with Lumpectomy

RANDOMIZED

Whole Breast Irradiation after Adjuvant Chemotherapy

50 Gy (2.0 Gy/fraction) or 50.4 Gy (1.8 Gy/fraction) to whole breast, followed by optional boost to ≥ 60 Gy

Partial Breast Irradiation prior to Adjuvant Chemotherapy

For a total of 10 treatments given on 5 days over 5 to 10 days:

- 34 Gy in 3.4 Gy fractions
- Interstitial Brachytherapy or Mammosite Balloon Catheter
- 38.5 Gy in 3.85 Gy fractions
- 3D Conformal External Beam

DCIS grade I, II, III
4,217 pts
2005-2013
ASTRO and GEC ESTRO guidelines

- Guidelines based on published trials released by ASTRO, ESTRO, etc.

<table>
<thead>
<tr>
<th>ASTRO-suitable</th>
<th>GEC-ESTRO-low-risk</th>
</tr>
</thead>
</table>

**Table 2. Patients “suitable” for APBI if all criteria are present**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient factors</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>≥60 y</td>
</tr>
<tr>
<td>BRCA1/2 mutation</td>
<td>Not present</td>
</tr>
<tr>
<td>Pathologic factors</td>
<td></td>
</tr>
<tr>
<td>Tumor size</td>
<td>≤2 cm*</td>
</tr>
<tr>
<td>T stage</td>
<td>T1</td>
</tr>
<tr>
<td>Margins</td>
<td>Negative by at least 2 mm</td>
</tr>
<tr>
<td>Grade</td>
<td>Any</td>
</tr>
<tr>
<td>LVSI</td>
<td>No</td>
</tr>
<tr>
<td>ER status</td>
<td>Positive</td>
</tr>
<tr>
<td>Multicentricity</td>
<td>Unicentric only</td>
</tr>
<tr>
<td>Multifocality</td>
<td>Clinically unifocal with total size ≤2.0 cm²</td>
</tr>
<tr>
<td>Histology</td>
<td>Invasive ductal or other favorable subtypes²</td>
</tr>
<tr>
<td>Pure DCIS</td>
<td>Not allowed</td>
</tr>
<tr>
<td>EIC</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Associated LCIS</td>
<td>Not allowed</td>
</tr>
<tr>
<td>Nodal factors</td>
<td></td>
</tr>
<tr>
<td>N stage</td>
<td>pN0 (i, i⁺)</td>
</tr>
<tr>
<td>Nodal surgery</td>
<td>SN Bx or ALNDⅡ</td>
</tr>
<tr>
<td>Treatment factors</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant therapy</td>
<td></td>
</tr>
</tbody>
</table>

**Characteristic**

| Patient age      | >50 years                                       |
| Histology        | IDC, mucinous, tubular, macrocystic, colloid cc.|
| ILC              | Allowed                                         |
| Associated LCIS  | Not allowed                                     |
| DCIS             | Any                                            |
| HG               | Not allowed                                     |
| Tumour size      | pT1–2 (≤30 mm)                                  |
| Surgical margins | Negative (≥2 mm)                                |
| Multicentricity  | Unicentric                                      |
| Multifocality    | Unifocal                                        |
| EIC              | Not allowed                                     |
| LVI              | Not allowed                                     |
| ER, PR status    | Any                                            |
| Nodal status     | pN0 (by SLNB or ALNDⅡ)                         |
| Neoadjuvant chemotherapy |                                               |

**ASTRO –suitable 2016 Guidelines Update**

- Age: >50 years
- Stage: Tis / T1
- DCIS: <2.5 cm grade I-II, 3 mm margins

Smith et al., 2009 IJROBP  Polgar et al., 2010 Radiother Onc
Table 3. “Cautionary” group: Any of these criteria should invoke caution and concern when considering APBI

<table>
<thead>
<tr>
<th>Factor</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient factors</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>50–59 y</td>
</tr>
<tr>
<td>Pathologic factors</td>
<td></td>
</tr>
<tr>
<td>Tumor size</td>
<td>2.1–3.0 cm*</td>
</tr>
<tr>
<td>T stage</td>
<td>T0 or T2</td>
</tr>
<tr>
<td>Margins</td>
<td>Close (&lt;2 mm)</td>
</tr>
<tr>
<td>LVSI</td>
<td>Limited/focal</td>
</tr>
<tr>
<td>ER status</td>
<td>Negative†</td>
</tr>
<tr>
<td>Multifocality</td>
<td>Clinically unifocal with total size 2.1–3.0 cm³</td>
</tr>
<tr>
<td>Histology</td>
<td>Invasive lobular</td>
</tr>
<tr>
<td>Pure DCIS</td>
<td>≤3 cm</td>
</tr>
<tr>
<td>EIC</td>
<td>≤3 cm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>B/Intermediate-risk group – possible candidates for APBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age</td>
<td>&gt;40–50 years</td>
</tr>
<tr>
<td>Histology</td>
<td>IDC, ILC, mucinous, tubular, medullary, and colloid cc</td>
</tr>
<tr>
<td>ILC</td>
<td>Allowed</td>
</tr>
<tr>
<td>Associated LCIS</td>
<td>Allowed</td>
</tr>
<tr>
<td>DCIS</td>
<td>Allowed</td>
</tr>
<tr>
<td>HG</td>
<td>Any</td>
</tr>
<tr>
<td>Tumour size</td>
<td>pT1–2 (≤30 mm)</td>
</tr>
<tr>
<td>Surgical margins</td>
<td>Negative, but close (&lt;2 mm)</td>
</tr>
<tr>
<td>Multicentricity</td>
<td>Unicentric</td>
</tr>
<tr>
<td>Multifocality</td>
<td>Multifocal (limited within 2 cm of the index lesion)</td>
</tr>
<tr>
<td>EIC</td>
<td>Not allowed</td>
</tr>
<tr>
<td>LVI</td>
<td>Not allowed</td>
</tr>
<tr>
<td>ER, PR status</td>
<td>Any</td>
</tr>
<tr>
<td>Nodal status</td>
<td>pN1mi, pN1a (by ALNDa)</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>Not allowed</td>
</tr>
</tbody>
</table>

ASTRO–cautionary 2016 Guidelines Update

Age: 40 – 49 years if all criteria of suitable 50 + if at least one path criteria

DCIS: <3 cm if criteria in suitable are not fully met
PBI in DCIS
Promising but not definitive data
USA
Options:

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
Prospective Trials of Excision Alone for Low or Intermediate Grade DCIS

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Median age (range)</th>
<th>Median FU (yrs)</th>
<th>Median size (range)</th>
<th>Margins</th>
<th>Tam</th>
<th>LR @ 10 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong (2014)</td>
<td>143</td>
<td>51 (35-81)</td>
<td>11</td>
<td>0.9 cm (0.1-2.5)</td>
<td>≥ 1 cm</td>
<td>No</td>
<td>15.6%</td>
</tr>
<tr>
<td>Hughes/Solin (2013)</td>
<td>273</td>
<td>60 (22-88)</td>
<td>8.8</td>
<td>0.6 cm (0.1-2.5)</td>
<td>≥ 0.3 cm (50% ≥ 1 cm)</td>
<td>31%</td>
<td>14.6%</td>
</tr>
</tbody>
</table>

RTOG 9804: RT vs. Observation

7-yr LR:
- RT: 0.9%
- No RT: 6.4% (p=0.0005)

Wong JS, J Clin Oncol 2006
Wong JS, Breast Cancer Res Treat 2014
Hughes LL, J Clin Oncol 2009
Solin LJ, J Natl Cancer Inst 2013

USA
Options:
1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
The 12-gene “DCIS Score” is a subset of the Recurrence Score

CANCER RELATED GENES

Hormone: ER, PR, Bcl2, SCUBE2
Proliferation: Ki-67, STK15, Survivin, Cyclin B1, MYBL2
HER2: GRB7, HER2
Invasion: Stromelysin 3, Cathepsin L2
Others: CD68, GSTM1, BAG1

REFERENCE GENES: Beta-actin, GAPDH, RPLPO, GUS, TFRC

3 risk groups:
- Low < 38
- Intermediate 39 – 53
- High > 54

Comparison of 10-year Risk of Local Recurrence by DCIS Score Group: Ontario Cohort and E5194

3 pre-specified risk groups defined, score associated with LR at 10 yrs:
- "low risk" = 10.6% (invasive: 3.7%)
- "intermediate risk" = 26.7% (invasive: 12.3%)
- "high risk" = 25.9% (invasive: 19.2%)

Solin L, JNCI 2013
Rakovitch E, BCRT 2015
Options:

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
What happens if you don’t “treat” DCIS?
SEER 1988-2011

- No surgery: 98.6%

Sagara et al, JAMA Surgery 2015
Active Surveillance Trials for DCIS

- Trials have been initiated
- Newly diagnosed clinically “low risk” DCIS
- Primary outcome: ipsilateral invasive cancer-free survival
- Randomization: usual care (surgery and/or RT) vs. active surveillance
- Regular surveillance with imaging
- Intervene if evidence of progression to invasive cancer

LORIS -> UK
LORD -> EORTC
COMET -> USA

USA
# NCCN Guidelines Version 2.2017

## Ductal Carcinoma in Situ (DCIS)

### NCCN Evidence Blocks™

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>WORKUP</th>
<th>PRIMARY TREATMENT</th>
</tr>
</thead>
</table>
| DCIS Stage 0 Tis, N0, M0 | - History and physical exam  
- Diagnostic bilateral mammogram  
- Pathology review  
- Determination of tumor estrogen receptor (ER) status  
- Genetic counseling if patient is high-risk for hereditary breast cancer  
- Breast MRI (optional) | Lumpectomy\(^e,f\) without lymph node surgery\(^g\) + whole breast radiation therapy\(^h,i,j,k,l\) (category 1)  
or  
Total mastectomy with or without sentinel node biopsy\(^g,j\) ± reconstruction\(^m\)  
or  
Lumpectomy\(^e,f\) without lymph node surgery\(^g\) without radiation therapy\(^h,i,j,k,l\) (category 2B) |
### NCCN Guidelines Version 2.2017

**Ductal Carcinoma in Situ (DCIS)**

### NCCN Evidence Blocks™

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>WORKUP</th>
<th>PRIMARY TREATMENT</th>
</tr>
</thead>
</table>
| DCIS Stage 0 Tis, N0, M0 | - History and physical exam  
- Diagnostic bilateral mammogram  
- Pathology review<sup>a</sup>  
- Determination of tumor estrogen receptor (ER) status  
- Genetic counseling if patient is high-risk for hereditary breast cancer<sup>b</sup>  
- Breast MRI<sup>c,d</sup> (optional) | - Lumpectomy<sup>e,f</sup> without lymph node surgery<sup>g</sup>  
+ whole breast radiation therapy<sup>h,i,j,k,l</sup> (category 4A)  
| or | Total mastectomy with or without sentinel node biopsy<sup>g,j</sup> ± reconstruction<sup>m</sup>  
| or | Lumpectomy<sup>e,f</sup> without lymph node surgery<sup>g</sup>  
| without radiation therapy<sup>h,i,j,k,l</sup> (category 2B) | |
NCCN guidelines 2017

NCCN Guidelines Version 2.2017
Ductal Carcinoma in Situ (DCIS)
NCCN Evidence Blocks™

DIAGNOSIS
DCIS Stage 0
Tis, N0, M0

WORKUP
• History and physical exam
• Diagnostic bilateral mammogram
• Pathology review
• Determination of tumor estrogen receptor (ER) status
• Genetic counseling if patient is high-risk for hereditary breast cancer
• Breast MRI (optional)

PRIMARY TREATMENT
Lumpectomy<sup>e,f</sup> without lymph node surgery<sup>g</sup> + whole breast radiation therapy<sup>h,i,j,k,l</sup> (category 1)

See Postsurgical Treatment (DCIS-2)

Total mastectomy with or without sentinel node biopsy<sup>g,j</sup> ± reconstruction<sup>m</sup>

or
Lumpectomy<sup>e,f</sup> without lymph node surgery<sup>g</sup> without radiation therapy<sup>h,i,j,k,l</sup> (category 2B)
# NCCN Guidelines Version 2.2017

## Ductal Carcinoma in Situ (DCIS)

### NCCN Evidence Blocks™

### Diagnosis

- History and physical exam
- Diagnostic bilateral mammogram
- Pathology review
- Determination of tumor estrogen receptor (ER) status
- Genetic counseling if patient is high-risk for hereditary breast cancer
- Breast MRI (optional)

### Workup

<table>
<thead>
<tr>
<th>DCIS Stage 0</th>
<th>Tis, N0, M0</th>
</tr>
</thead>
</table>

### Primary Treatment

- **Lumpectomy**\(^{e,f}\) without lymph node surgery\(^g\)
  - + whole breast radiation therapy\(^{h,i,j,k,l}\) (category 1)
  - or
  - Total mastectomy with or without sentinel node biopsy\(^g\) ± reconstruction\(^m\)

- **Lumpectomy**\(^{e,f}\) without lymph node surgery\(^g\)
  - without radiation therapy\(^{h,i,j,k,l}\) (category 2B)

See Postoperative Treatment (DCIS-2)
Merci pour votre Attention
Treatment of DCIS in USA

1. Lumpectomy + standard whole breast RT
2. Role of Tamoxifen or Arimidex
3. Role of a boost
4. Lumpectomy with hypofractionation WBI
5. Lumpectomy and PBI
6. Lumpectomy alone
7. Oncotype
8. Observation without excision (trial)
Active Surveillance Trials for DCIS (COMET)

• Age >40 at diagnosis; agree to randomization

• Pathologic confirmation of grade I/II DCIS without invasion by 2 local pathologists (microinvasion not allowed)

• ER ≥ 10%; HER2-negative (0, 1+, or 2+ if testing performed)
Long-Term Outcomes for Invasive IBTR for NSABP B-17, B-24

Wapnir, et al, JNCI 2011
### NSABP B-24

(N=732, median FU = 14.5 yrs)

<table>
<thead>
<tr>
<th></th>
<th>RT</th>
<th>RT + Tamoxifen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IBTR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER+</td>
<td>17%</td>
<td>14%</td>
</tr>
<tr>
<td>ER-</td>
<td>17%</td>
<td>21%</td>
</tr>
<tr>
<td><strong>CBC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER+</td>
<td>12%</td>
<td>6%</td>
</tr>
<tr>
<td>ER-</td>
<td>7%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Allred, J Clin Oncol 2012
Conclusions

- Role of APBI in DCIS remains unclear
- Clinical & pathological features of DCIS suggest significant portion are widely spread
- Few studies to date suggest possible role for APBI in small, localized DCIS
- No randomized trials to date
  - Few prospective studies
  - Small sample sizes
  - Await results of NSABP B-39
COMET Trial for low risk DCIS

Comparison of Operative to Monitoring and Endocrine Therapy for Low Risk DCIS:
The COMET Trial

E. Shelley Hwang
Ann Partridge
Alastair Thompson
Advocate Lead: Liz Frank

Sponsors: PCORI and Alliance Foundation Trials (AFT)
DCIS diagnosed on core biopsy or surgical biopsy with positive margins

Declines Trial

Accepts Trial

Informed consent, Registration, and Randomization

Guideline Concordant Care (n=600) +/- endocrine therapy

Accepts Allocation (n=450)

Declines Allocation (n=150)

Active Surveillance (n=600) +/- endocrine therapy

Accepts Allocation (n=450)

Declines Allocation (n=150)
Adding Tamoxifen to Excision: UK/ANZ Trial

- Randomized 2 x 2 trial of RT and tamoxifen
- Tamoxifen randomized: 1536
- RT randomized: 1030
- Median FU: 12.7 years
- Study design allowed for one or both randomizations
- Only randomized trial assessing role of tamoxifen after excision alone

Cuzick, Lancet Oncol 2011
Background
Selection of Treatment for Patients with DCIS is Complex

- Heterogeneity in biology/extent
- Difficulties assessing size and margins
- Protracted natural history (especially for low grade lesions) requires long follow up
- Inability to predict clinical outcome can lead to over- or under-treatment
Margins Consensus Statement for DCIS Managed with Excision + RT

2 mm margin is enough

• Multidisciplinary panel
• Used meta-analyses of margin width and ipsilateral LR
• Included 20 studies, 7883 patients
• 2 mm margin minimized LR compared w/smaller margins
• Wider margins not significantly better than 2 mm

Morrow, J Clin Oncol 2016
EBCTCG Meta-Analysis

• All 4 randomized trials of RT vs no RT
• N = 3729
• RT reduced absolute 10-yr risk of ipsilateral breast events by 15.2%
• Regardless of age, extent of surgery, use of tamoxifen, margins, grade, size
• Greater proportional reduction in older patients
• No effect on survival
• No excess mortality from RT

Correa, JNCI Monogr 41:162-177, 2010
Oncotype DX Recurrence Score for DCIS

- 327 patients (ECOG E5194)
- Median FU 8.8 yrs
- Recurrence score calculated using optimized gene expression algorithm
- 3 prespecified risk groups defined, score associated with LR at 10 yrs
  - “low risk” = 10.6% (invasive: 3.7%)
  - “intermediate risk” = 26.7% (invasive: 12.3%)
  - “high risk” = 25.9% (invasive: 19.2%)

Solin, et al., JNCI 2013
Higher Local Recurrence in Earlier Trials

- Older mammographic techniques, lack of magnification views, post-excision mammograms
- Patient selection
- Less meticulous pathologic evaluation and surgical techniques
- Less attention to margins