DCIS Standard Treatment & New Emerging Strategies of Care

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2017 NPSS
Asheville, NC
DCIS Treatment & New Emerging Strategies of Care

- I have no industry or other financial disclosures to report.
## Breast Cancer Incidence

**Table 91-1**  
Risk of Breast Cancer in U.S. Women  


<table>
<thead>
<tr>
<th>Age Range (years)</th>
<th>Breast Cancer Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–40</td>
<td>1 : 227</td>
</tr>
<tr>
<td>40–50</td>
<td>1 : 68</td>
</tr>
<tr>
<td>50–60</td>
<td>1 : 42</td>
</tr>
<tr>
<td>60–70</td>
<td>1 : 28</td>
</tr>
<tr>
<td>Lifetime (to age 110 years)</td>
<td>1:8</td>
</tr>
</tbody>
</table>
DCIS Stats

• 10 yr disease specific survival across all loco regional treatment subgroups exceeds 98%
• 20 yr study period decreasing unilateral mastectomy 44.9% to 19.3%
• Lump+XRT increased from 24.2 % to 46.8%
• Rate of bilat mast increased from 0% to 8.5%
• Axillary dissection replaced with sentinel node biopsy although 15/3% & 2.8% having AXLND in 2010

DCIS Pair and Share

Think Pair Share
DCIS Diagnosis

- Nipple discharge or asymptomatic
- Diagnostic mammogram
- IF abnormal calcifications biopsy by radiologist or surgeon
- DCIS diagnosis refer to surgeon breast specialty and radiation oncologist
Breast Cancer and DCIS image

- Invasive Lobular Carcinoma (ILC)
- Invasive Ductal Carcinoma (IDC)
- Ductal Carcinoma In Situ (DCIS)
DCIS Incidence

- Statistics – 50,000 in US in 2016
- 1 of 33 women (life time)
- 88 per 100,002
- Common 50-64 increase with age
- Improved imaging increase diagnosis

Hall, S. (2017)
DCIS – various terms?

- Stage 0 non-invasive carcinoma
- Intra ductal carcinoma
- Pre-invasive cancer cells
- Abnormal cells
Breast Cancer Staging

<table>
<thead>
<tr>
<th>Stage 0: Carcinoma <em>in situ</em> (DCIS or LCIS) — the tumor has not spread past the ducts or lobules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I: The tumor is small (less than 2 cm) and well-localized (has not spread to the lymph nodes)</td>
</tr>
<tr>
<td>Stage II: The tumor meets any of the following conditions:</td>
</tr>
<tr>
<td>• Small (less than 2 cm) and has spread to axillary lymph nodes</td>
</tr>
<tr>
<td>• 2 to 5 cm and has not spread to axillary lymph nodes</td>
</tr>
<tr>
<td>• 2 to 5 cm and has spread to axillary lymph nodes</td>
</tr>
<tr>
<td>• No tumor evident in the breast but has spread to axillary lymph nodes</td>
</tr>
<tr>
<td>• Larger than 5 cm and has not spread to axillary lymph nodes</td>
</tr>
<tr>
<td>Stage III: The tumor meets any of the following conditions:</td>
</tr>
<tr>
<td>• Smaller than 5 cm and has spread to connected axillary lymph nodes</td>
</tr>
<tr>
<td>• Larger than 5 cm and has spread to single or attached axillary lymph nodes</td>
</tr>
<tr>
<td>• Has spread to chest wall; diagnosed as inflammatory</td>
</tr>
<tr>
<td>• Has spread to lymph nodes under and above the collarbone and inside the breast and nodes, but not other parts of the body</td>
</tr>
<tr>
<td>Stage IV: The cancer has spread to other organs in your body, such as your bones, lungs, liver or brain</td>
</tr>
</tbody>
</table>
Mammogram features

90% **micro-calcifications** on mammogram
Pattern: fine granular calcifications grade 1-2.
Linear/branching or segmental types **pleomorphic micro-calcifications grade 3 DCIS**
DCIS Imaging

- Mammograms underestimate DCIS size.
- Get diagnostic/magnification views
- Determine morphology and extent of microcalcifications
- MRI is not better than mammo. Not routinely indicated.

DCIS Diagnosis Pathology

• Diagnosis size (mm or cm) --- Small < 4 cm

• Stage 0 non-invasive

• Grade 1-3: low, intermediate, high grade

• Features: comedo, necrosis (high grade)

• ER/PR rating
DCIS Grading

- **Grade 1 (well differentiated)** –
  - Cancer cells look slightly different. Slow growth well-organized patterns.

- **Grade 2 (moderately differentiated)** –
  - Don’t look like normal cells, moderate growth.

- **Grade 3 (poorly differentiated)** –
  - Look very different from normal cells. Quick growth in disorganized, irregular patterns.
DCIS histopathology

- Comedo/Necrosis type
- Higher risk, grade 3

- The duct round ring that is too thick with grey color cells. In the center is a round purple plug of more cells, some alive, some dead, mixed with debris. That plug is the “comedo”.

DCIS less aggressive type

- Non-comedo DCIS
- Low grade
- Multiple Patterns:
  - Cribriform, micro papillary, papillary, and solid

DCIS Treatment

• Breast conserving surgery Lumpectomy or Mastectomy (multifocal/multi centric)
• Two or more foci of cancer within the same breast quadrant = multifocal
• Two or more foci of cancer in different quadrants of the same breast = multi centric.

• Radiation External beam +/-
• Pre-op or 3 weeks- 6 weeks

• Adjuvant endocrine therapy: ER/PR (+) 5 yrs
DCIS Surgical Treatment

- Surgical margins:
- Vary by institution
- No tumor on ink or 1 mm

- Sentinel node when?
- Extensive DCIS and/or mastectomy
- Higher risk of microinvasion
Surgical Treatment DCIS

- Local excision DCIS + XRT
- Local recurrence risk 5-15%
- Mastectomy Local recurrence risk 2%
- Treatment with tamoxifan after surgery risk reduction by 50%

DCIS Genetic Testing?

- If high risk (>10% chance) for carrying a high risk mutation or genetic testing for personal interest

- Referral for genetic counseling, particularly for women with a family history of breast cancer

- Insurance covers if meets criteria for testing NCCN guidelines.

Surgery Side Effects

- Smaller breast
- Asymmetry contralateral breast
- Possible affect breast feeding future.
- Scar tissue
- Pain
- Swelling if lymph nodes removed
DCIS surgery images
Biomarkers for DCIS

Estrogen biomarkers for DCIS
Most 80% positive (+)

65% ER+/PR-
13% ER+/PR-

25% ER-/PR-
2% ER-/PR+
Hormone Receptor Ratings

• Test immunohistochemical staining assay (IHC)
• Percentage of cells staining 0-100%
• Allred score 0-8. Score of 8 very +. Percentage of cells test + and intensity of staining.
• Reported “positive” or “negative” – ask for more info.
Mechanism of action SERM

- ER +
- Tamoxifen – blocks estrogen receptors in breast cancer cells acts like anti-estrogen in breast cells
- Estrogen effects in uterus/bones
- Given to premenopausal women
- 5 years lower chance of DCIS coming back. Decrease risk of invasive breast cancer

Endocrine Therapy Side Effects

• SERM (tamoxifen)

• Hot flashes, fatigue, vaginal bleeding, vaginal discharge, mood changes, endometrial cancer, blood clots (DVT), stroke (rare), MI (may increase risk).
Aromatase Inhibitors

- Aromatase Inhibitors - Drugs that stop estrogen production. Small amount estrogen made in fat tissue by aromatase.
  - Block aromatase from making estrogen
  - (Exemestane, Anastrozole, Letrozole)
- Side effects:
  - Arthralgia, bone density thinning, muscle pain
  - Switch to different AI.

Radiation Use

• External beam individualized length of tx.
• Pre-op, 3 week or 6 week course given daily

• Shorter course smaller size/low/intermediate grade

• Individualized especially age 70 > may omit
• DCIS score – omission of radiation
DCIS score

- DCIS oncotype score
- Analyzes activity of 12 genes.

**Recurrence Score < 39:** The DCIS has a low risk of recurrence. The benefit of radiation therapy is likely to be small & will not outweigh the risks of side effects.

**Recurrence Score 39 - 54:** Intermediate risk of recurrence. Unclear whether benefits of radiation therapy outweigh risks of side effects.

**Recurrence Score > 54:** High risk of recurrence & benefits of radiation therapy are likely to be greater than risks of side effects.

Radiation Therapy Side Effects

- Smaller breast
- Hyperpigmentation of skin (poss permanent)
- Moist/Dry desquamation of skin temporary
- Swelling of breast
Radiation Side Effects

- Cardiac – atherosclerosis possible heart disease.

- Lung – pneumonitis, lung scarring, rib fragility,
Effects from radiation therapy
Partial Breast Irradiation

A. Symptomatic fat necrosis 1 month after Mammo Site brachytherapy.

B. Resolution fat necrosis 2 months later

Rabinovitch, Rachel, Early Diagnosis and Treatment of Cancer: Breast Cancer, 22, 327-342

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New Emerging Strategies

- Active Surveillance Research Protocols
- Appropriate patient selection
- Low grade, ER positive, small size $\leq 4$ cm
- Complete imaging & confirm no invasive cancer
- Q 6 -12 month imaging (unilateral)
- Take adjuvant endocrine therapy
Emerging strategies

- Endpoints
- If progress to invasive breast cancer- surgery
- Anxiety about surveillance option may choose surgery/standard of care
Surveillance Studies

What studies are available?

3 randomized controlled trials low risk DCIS

Study safety/efficacy, & trade off of active surveillance with usual care
Surveillance Studies

LORIS (multicenter UK)

LORD (EORTC study)

COMET (cooperative group US study) not enrolling yet (approved 1/2017)
EORTC Study

- RCT role XRT after excision of DCIS
- 10 yr Local recurrence (LR) free rate
- 74% surgery vs 85% with XRT

- Risk of DCIS and Invasive LR
- 42% in surgery only vs 48% in surg +XRT

- At 10.5 yrs follow up 47% reduction in recurrence.
EORTC Study

• Factors associated with increase risk of LR
• <= 40 years
• Symptomatic detection
• Grade 2-3
• Cribriform or solid growth pattern
• Doubtful surgical margins
• Treatment with surgery only
EORTC

• Both groups Surgery and Surgery + XRT
• Similar low risk of metastases and death!

• EORTC reported a **10-year** cancer-specific survival for **DCIS** of more than **97%**

  • Bijker et al., 2006
LORIS study

- 193 LORIS participants lumpectomy alone
- Only 6 invasive cancer at 10 years

COMET

• Hypothesis:

• The management of low risk DCIS using an active surveillance (AS) approach does not yield inferior cancer or quality of life outcomes compared to guideline concordant care (GCC)

• Clinicaltrials.gov/ct2/show/NCT02926911
• Comparison of Operative to Monitoring and Endocrine Therapy (COMET)
• Trial for Low Risk DCIS (COMET)
COMET Study

- Not yet open (1/2017)
- Randomized trial Standard care surgery, XRT+/-, endocrine therapy, q 12 mo. mammogram
- Active surveillance with endocrine therapy q 6 month mammogram
- Primary outcome at 2 yrs new dx invasive cancer in GCC vs AS at 2 yrs follow up

Clinicaltrials.gov/ct2/show/NCT02926911
Comparison of Operative to Monitoring and Endocrine Therapy (COMET)
Trial for Low Risk DCIS (COMET)
Surveillance Studies

• Endpoint of all studies evaluate invasive cancer progression and quality of life

• DCIS with radiation reduced recurrence following lumpectomy for DCIS at least by 50%, breast cancer mortality was not impacted!

Benefits of Surveillance Model

- DCIS response to treatment endocrine therapy
- No surgery continue surveillance
- Downsize and smaller surgery needed
- Long term data DCIS conversion to invasive cancer over time (what is it ?)
Risks/Benefits of Surveillance Model

- **RISKS:**
  - Anxiety during surveillance
  - Missed invasive cancer
  - May progress on surveillance to invasive cancer
  - May not tolerate endocrine therapy
DCIS RISK

- Risk of death is low at 1.99% at 10 years! after DCIS diagnosis

In women over 70 yrs. Discuss competing causes of mortality 40% CV death and only 5.4% due to breast cancer.

Worni, et al. (2015)
DCIS risk of death

- Higher for women dx <35 years
- 7.8 % vs 3.2 %
- Black ethnicity

DCIS Case 1

- E.B. 46 yo pre-menopausal, G3P0, OCP x 8 years. Fertility tx 2 years. Genetic testing neg. VUS NF1. Polish ancestry.
- FH Pancreatic cancer MGM.
- L breast 10 o’clock 4 mm calcifications
- DCIS, grade 3, micropapillary, cribriform, comedo ER 99% PR 98%
- Mammographic detected. Asymptomatic.
- 2nd site L breast 12 o’clock benign calcs.
DCIS Case 1

- Treatment recommendations
- ????
DCIS Case 2

- S.H. 44 yo, Premenopausal, G0P0, No, OCP/Fertility. Declined genetic testing. Iranian ancestry.
- LEFT breast 8.5 cm calcifications nipple to posterior breast; R br 4 mm calcs.
- Bilateral DCIS grade 2, ER100%; PR 90%
- Detected on mammogram asymptomatic
- Treatment options ???
DCIS case 2

- Treatment options:
- Active surveillance
- Surgery: lumpectomy, mastectomy, sentinel node biopsy?
- Radiation?
- Endocrine Therapy?


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