Ductal Carcinoma In-Situ

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Case Presentation

• 53-year-old female underwent routine bilateral screening mammogram
  – Findings: architectural distortion and coarse, clumped calcifications in the retroareolar left breast. Right breast normal.

• PMH
  – Otherwise healthy
Case Presentation

• OB/Gyn History
  – G0P0
  – Age at menarche: 13
  – Menopause at 46
  – No history of oral contraceptives
  – No history of hormone replacement therapy

• Family History
  – Mother with ovarian cancer at 79
  – No family history of breast cancer

• Social History
  – Non-smoker
  – 2-3 alcoholic drinks/week
Physical Exam

- General: Well appearing Caucasian female in no acute distress
- HEENT: PERRLA, EOMI. Sclerae anicteric. No thyromegaly
- Lymphatic: No palpable cervical, supraclavicular, infraclavicular or axillary lymphadenopathy
- CV: Regular rate and rhythm. No murmurs, rubs or gallops
- Lungs: Clear to auscultation. No wheezes, rhonchi or rales
- Abdomen: Soft, non-tender and non-distended
- Breast: Inspection and palpation of the bilateral breasts demonstrates no erythema, edema, peau d’orange, nipple inversion, nipple discharge, or palpable masses. No axillary or supraclavicular lymphadenopathy.
- Extremities: No clubbing, edema or cyanosis
Workup

• Diagnostic bilateral mammogram
  – Magnification views of left breast show clustered pleomorphic calcification in the retroareolar region

• Bilateral breast ultrasound
  – 1.9 x 1.8 x 1.8 cm irregular, hypoechoic mass in the left retroareolar region at the 1:00 position
Left Breast Mammogram

Magnification views show clustered pleomorphic calcification in the retroareolar region.
1.9 x 1.8 x 1.8 cm irregular, hypoechoic mass in the left retroareolar region at the 1:00 position
Workup

• Core needle biopsy
  – Ductal carcinoma in situ, solid type
  – ER- 95% positive; PR- 85% positive; HER-2 not obtained
  – Intermediate nuclear grade
Overview of DCIS

• Noninvasive malignant epithelial cell proliferation limited to the ductal system
  – No basement membrane invasion
  – May be limited to few or several duct tubules
• With the introduction of routine screening mammography it now constitutes 15-20% of all breast cancers
  – Represented only 1-5% of breast cancers in the pre-mammography era (Parker et al)
• 30% of DCIS cases may be multicentric (Fonseca et al)
• Classification according to:
  – Architecture: solid, comedo, cribriform, papillary, and micropapillary
  – Grade: high, intermediate, and low (grades 1-3)
  – Comedo Necrosis: Yes or No
Treatment Options

DCIS (Tis N0 M0)

Lumpectomy

+/- Radiotherapy *

* Lumpectomy + RT = Breast Conserving Therapy (BCT)

RT reduces risk of local recurrence. Older patients with small, low-grade tumors excised with widely negative margins benefit less from radiation. (Silverstein et al)

Total Mastectomy +/- SLN biopsy

Consider for diffuse malignant microcalcifications, multicentric disease, persistently positive margins or patient preference

(Silverstein et al)
Role of Radiotherapy after BCS

• No randomized trials compare BCT to mastectomy for DCIS, but comparisons of BCT to historic mastectomy controls suggest no OS difference

• 4 published randomized trials demonstrate benefit in local control with addition of whole breast RT compared to lumpectomy alone in DCIS:
  – NSABP B-17
  – EORTC 10853
  – UK/Australia/New Zealand cooperative trial (UK/ANZ)
  – Swedish Trial
Role of Radiotherapy after BCS

• Adjuvant RT after lumpectomy reduces the risk of ipsilateral breast tumor recurrence at 15 years by 52% versus lumpectomy alone (Wapnir et al)
  – Lumpectomy alone: 19.4%
  – Lumpectomy + RT: 8.9% (B-17)
  – Lumpectomy + RT: 10.0% (B-24)
  – Lumpectomy + RT + Tamoxifen: 8.5% (B-24)

• Approximately half of recurrences are invasive breast cancer and half are DCIS
Role of Tamoxifen after Lumpectomy

- **NSABP B-24**: The addition of tamoxifen to RT reduces overall cancer events at 5 years (Fisher et al. Lancet 1999)
  - Decreased breast cancer events from 13.4% to 8.2%
  - Ipsilateral 9.5% vs. 6.0%
  - Contralateral 3.4 vs. 2.0%
  - No difference in regional or distant mets

- In ER positive as opposed to ER negative tumors, the benefit of Tamoxifen is greater (Allred et al)
  - ER positive ⇒ 59% reduction of all breast cancer events
  - ER-negative⇒ no significant benefit was observed
Margin Status in DCIS

• The definition of a negative margin is controversial
• Margins of 10 mm are accepted as negative
• Margins <1 mm are considered inadequate and re-excision should be performed
• Close margins (<1 mm) at the chest wall or skin do not mandate surgical re-excision, but may warrant higher doses of radiation (i.e. a boost)

NCCN version 3.2014
Case Treatment

• Lumpectomy
  – Pathology showed a 2.0 cm focus of DCIS, solid type, nuclear grade 2
  – All margins were negative with the closest margin being 2.2 mm superiorly.
  – ER (95%), PR (85%)
• Post-lumpectomy mammogram showed no residual calcifications
• Whole breast radiation therapy was delivered in the supine position (typically delivered 4-8 weeks after surgery)
  – Prescribed dose was 5000 cGy in 25 fractions to the whole breast using IMRT and 6 MV photons
  – Tumor bed received an additional 1000 cGy in 5 fractions using mini-tangents and 6 MV photons
• Systemic therapy
  – Aromatase inhibitor was started after completion of radiation
Boost for DCIS

- No prospective randomized trials examining a boost for DCIS
  - Institutional preference
  - Retrospective, institutional experiences demonstrate varied outcomes
- EORTC 22881/10882 demonstrated reduction in local recurrence in patients with invasive breast cancer receiving a 16 Gy tumor cavity boost after BCS
  - Greatest benefit in women < 50 years old, however all patients benefitted
  - Data often extrapolated to DCIS
- DCIS Collaborative Group Study
  - One of the largest, landmark trials showing a reduction in local recurrence with radiation for DCIS
  - 72% of patients on this trial received a boost
Treatment Planning

• 2D Treatment Planning
  – Uses plain x-rays for generating the plan
  – Assessment of treatment plan done by evaluating dose distribution at midplane of breast
  – Wedges used to compensate for differences in tissue thickness
  – Significant dose heterogeneity on off axis regions (IM fold, axilla)

• 3D/IMRT Treatment Planning
  – Uses CT scan for generating the plan
    • allows for better evaluation of target coverage, hot spots and dose to normal tissues
  – IMRT improves dose homogeneity
    • decreases acute and chronic skin toxicity
    • Improves dose conformality
      – better sparing of heart for left-sided cancers and lung
  – Many different techniques utilized
    • field in field AKA fluence planning AKA forward planned IMRT
    • inverse planning AKA traditional IMRT
3D/IMRT

• Field in Field (Forward Planned)
  – Open medial and lateral tangents + segmental fields added manually to attenuate beam in higher dose areas
  – MLCs used to improve homogeneity and to shield critical structures

• IMRT (Inverse Planned)
  – Computerized algorithm used to reduce hot spots
  – Multiple weighted segments and beam angles can be used to achieve optimal conformality
  – May result in more low dose spread
    • Minimized by restricting beam angles to normal tangential arrangement
Treatment Planning

• CT Simulation
  – Supine with arms up on a 15-20 degree breast board
    • Goal is to bring sternum parallel to the table
  – Wire palpable breast tissue, clinical breast borders and lumpectomy incision
    • Medial border → mid sternum
    • Lateral border → 2 cm lateral to palpable breast tissue (mid axillary line)
    • Inferior border → 2 cm below the inframammary fold
    • Superior border → head of the clavicle or 2\textsuperscript{nd} intercostal space
GTV
Surgical cavity; includes seroma and surgical clips when present.
CTV:
*Posteriorly* - Excludes pec major/minor
*Anterior* - Skin
*Cranial/Caudal* - Per clinical breast borders
*Medial* - Sternal/rib junction
*Lateral* - Mid axilla per clinical reference

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Surgical cavity; includes seroma and surgical clips when present.
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Cranial/Caudal - Per clinical breast borders
Medial - Sternal/rib junction
Lateral - Mid axilla per clinical reference

PTV
Breast CTV + 7 mm expansion (excluding heart and not crossing midline)

GTV
Surgical cavity; includes seroma and surgical clips when present.
**PTV**
Breast CTV + 7 mm expansion (excluding heart and not crossing midline)

**PTV-EVAL**
Excludes chest wall & pectoralis muscles; Extends to 5 mm from skin

**CTV:**
*Posteriorly -* Excludes pec major/minor; *Anterior – Skin; Cranial/Caudal -* Per clinical breast borders; *Medial - Sternal/rib junction; Lateral - Mid axilla per clinical reference*

**GTV**
Surgical cavity; includes seroma and surgical clips when present.
Isodose Distribution
Isodose Distribution
Isodose Distribution
Dose Volume Histogram

- Total Volume: 1027.21 cc
- Inclusion: 100%
- Minimum Dose: 3808.0 cGy
- Maximum Dose: 5385.0 cGy
- Mean Dose: 5079.0 cGy
- Cursor Volume: 85.13%
- Plan ID: LTBREAST1
- Line Type: Solid
- Thickness (pixels): 2
# Dose-Volume Constraints
(Per RTOG 1005)

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<th>Structure</th>
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<tr>
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<td></td>
<td>1.86 Gy</td>
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<tr>
<td>Thyroid</td>
<td>Max point dose does not exceed 2% of prescribed dose</td>
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Surveillance and Follow-up

- History and physical exam every 6-12 months for 5 years, then annually
- Mammogram every year
  - 6-12 months post-radiation therapy if breast conserved
Teaching Points

• Multidisciplinary management is critical in the treatment of patients with DCIS

• The use of radiotherapy after lumpectomy in patients with DCIS decreases the risk of ipsilateral breast tumor recurrence in all patients but does not improve overall survival
  – This risk reduction becomes increasingly small in patients with favorable features such as age > 60, small, unifocal low grade tumors excised with widely negative margins (> 1 cm).
  – Thus, lumpectomy alone or lumpectomy followed by Tamoxifen can be considered in these patients

• The use of Tamoxifen in patients with ER+ DCIS reduces ipsilateral and contralateral breast tumor recurrence

• Patients undergoing mastectomy generally do not require adjuvant radiation
References

• NCCN version 3.2014