OPTIMISING TREATMENT
IN OLDER BREAST CANCER PATIENTS
Challenges in Screening: the management of DCIS

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Disclosures

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  – Pfizer
  – Novartis
A. Asymptomatic  
*(detected by screening mammography)*
  
a. Microcalcifications (~80%)
b. Distortion, mass etc. ± microcalcifications  
  - Core biopsy

B. Symptomatic
  
a. Lump
b. Nipple discharge  
  - Core biopsy  
  - Open biopsy
Life expectancy: 10~15 yrs

Diagnosis

Comorbidities

Stable
Progress without invasion
Progress to Invasive disease

Death from other causes

Metastasis
QoL

20-30%

10~15 yrs
Management of Screen detected DCIS in Old pts

Questions

1. **Risk assessment**
   - what is the chance that this DCIS will progress to or recur with DCIS or Invasive Carcinoma

2. **Patient evaluation - CGA**
   - Life expectancy
   - Co-morbidities
   - Current QoL

3. **Risk and Benefits of additional treatment**
   - benefit of Surgery, RxT, HT or Multimodality treatment
   - risk in relation to co-morbidities & current QoL
“Currently, most women with DCIS undergo surgical resection ± radiotherapy ± endocrine therapy”

Q.: Cases of over-treatment? YES!

• DCIS is not a single disease process
  (clinically, radiologically, histopathologically, biologically, genetically)

• Low- and High-grade DCIS are not equivalent
  (different likelihood of progression to invasive disease)

• Medical intervention might not be always necessary
  (some DCIS may never progress even without any treatment)
Age factor

- **The risk of recurrence** of DCIS **decreases with Age**, independent of other clinical and pathological factors.
- **The risk of invasive recurrence** is also low.*

**Prediction of recurrence** with DCIS or invasive BC is currently based on pathological factors:
  - Grade
  - ER and PR status
  - HER2 status

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«Low risk» DCIS

Low-grade DCIS

Intermediate grade DCIS

«High risk» DCIS

Low-Intermediate Grade, ER/PR positive, HER2 negative

High-grade DCIS with central necrosis

«High risk» DCIS

High-grade, ER/PR negative and/or HER2 positive
Facts: Risk of Recurrence

- **High-grade** DCIS is more likely to develop invasive disease than Low-grade DCIS\(^1\)
- **ER-negative** DCIS has a higher rate of recurrence (12.2%) than ER-positive DCIS (3.7%) at 5 years\(^2\)
- **HER2-positive** DCIS has an increased risk of recurrence\(^3,4\)

Active Surveillance vs Surgery

Surveillance only

- Low grade
- ER / PR positive
- HER2 negative

Life expectancy
Co-morbidities

* only 6-7% of screen detected Low grade DCIS cases might have an invasive component
Active Surveillance Prospective Trials

• **LORD** trial - EORTC
• **LORIS** trial - UK
• **COMET** trial - USA
• **LARRIKIN** trial - AU

- Asymptomatic DCIS, detected by population-based or opportunistic screening mammography*
- Pure low- or non-high grade DCIS based on vacuum assisted core biopsies

Randomization (1:1)

- **Standard treatment** according to local policy
  - \( WLE \pm RxT \) or MRM, \( \pm \) Tamoxifen
- **Active surveillance**

- **Monitoring**: annual digital mammography for 10 years

* Women \( \geq 40, \geq 45 \) and \( \geq 55 \) years old
Radiotherapy following WLE could aim to:

- decrease IBCR with DCIS or Invasive disease
- increase Overall Survival
Reduced IBCR at 10 years\textsuperscript{1-4}:

- overall by more than half (28.1% to 12.9%)
- with invasive disease from 11.0% to 5.0%

More recent studies\textsuperscript{5,6} for low-risk DCIS:

- lower benefit, but still a small effect
- Non high grade: 6.7% vs 0.9% with RxT at 10yrs

However, radiotherapy:

- does not affect BC-specific survival\textsuperscript{7}
- carries risks: lung, esophagus, cardiovascular\textsuperscript{1}

\textsuperscript{1}EBCTCG. J Natl Cancer Inst Monogr. 2010;2010(41):162–77.
\textsuperscript{7}Narod SA, et al. JAMA Oncol. 2015;1(7):888–96.
# Van Nuys Prognostic Index

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Nuys Classification</td>
<td>Group 1</td>
<td>Group 2</td>
<td>Group 3</td>
</tr>
<tr>
<td></td>
<td>Non high nuclear grade without necrosis</td>
<td>Non-high nuclear grade with necrosis</td>
<td>High nuclear grade with or without necrosis</td>
</tr>
<tr>
<td>Margins</td>
<td>≥10 mm</td>
<td>1–9 mm</td>
<td>&lt;1 mm</td>
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<tr>
<td>Size</td>
<td>&lt;15 mm</td>
<td>16–40 mm</td>
<td>&gt;40 mm</td>
</tr>
<tr>
<td>Age</td>
<td>&gt;60</td>
<td>40–60</td>
<td>&lt;40</td>
</tr>
</tbody>
</table>

**Prognosis**

- **Low risk**: 4 – 5 – 6
- **Intermediate risk**: 7 – 8 – 9
- **High risk**: 10 – 11 – 12

Modified from Silverstein; Ductal Carcinoma in situ of the breast 2nd ed. 2002.
### Prognosis by Treatment Modality

**Surgery +/- Radiotherapy**

<table>
<thead>
<tr>
<th>USC/VNPI Score, Margin Width</th>
<th>Patients (N = 1673)</th>
<th>Treatment Needed</th>
<th>12-Year Recurrence</th>
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</thead>
<tbody>
<tr>
<td>All 4, 5, or 6</td>
<td>420</td>
<td>Excision alone</td>
<td>≤7%</td>
</tr>
<tr>
<td>7, margins ≥3 mm</td>
<td>196</td>
<td>Excision alone</td>
<td>16%</td>
</tr>
<tr>
<td>7, margins &lt; 3 mm</td>
<td>117</td>
<td>Excision plus radiation</td>
<td>14%</td>
</tr>
<tr>
<td>8, margins ≥3 mm</td>
<td>128</td>
<td>Excision plus radiation</td>
<td>14%</td>
</tr>
<tr>
<td>8, margins &lt; 3 mm</td>
<td>183</td>
<td>Mastectomy</td>
<td>0%</td>
</tr>
<tr>
<td>9, margins ≥5 mm</td>
<td>43</td>
<td>Excision plus radiation</td>
<td>17%</td>
</tr>
<tr>
<td>9, margins &lt; 5 mm</td>
<td>197</td>
<td>Mastectomy</td>
<td>0%</td>
</tr>
<tr>
<td>All 10, 11, 12</td>
<td>389</td>
<td>Mastectomy</td>
<td>7%</td>
</tr>
</tbody>
</table>

- 1673 patients with DCIS with 86 months of follow-up
- M. Silverstein, 2014 Miami Breast Cancer Conference
Radiotherapy following WLE could be omitted in

- Low-risk DCIS
- Low to Intermediate VNPI score
  - Life expectancy
  - Co-morbidities
A Genomic Risk Stratification Tool - Includes 12 genes
Provides individualized risk based on underlying tumor biology

- **Validation**: ECOG E5194\(^1\) & Ontario Cohort\(^2\)
- **DCIS** treated by WLE ± RxT ± Tam, any ER

- Independent **predictor** of LR at 10 years of
  - any DCIS or invasive LR
  - an invasive LR

- **DCIS Score** (0-100) risk groups:
  - Low < 39  Intermediate 39 – 54  High ≥ 55

- **Clinical implication**: information to **omit** RxT in Low-risk DCIS

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Hormonal Therapy

**NSABP B-24**  pre- & postM with DCIS, WLE + Radiotherapy

**Tamoxifen**
- reduces the risk of IBCR by 30% and CBC by 50%
- absolute overall risk: 13% placebo vs. 8% Tamoxifen
- **Survival**: no effect\(^1\)

**UK/ANZ DCIS trial**  postM, WLE of DCIS ± Radiotherapy

**Tamoxifen vs no adjuvant therapy**
- no effect in preventing invasive IBCR
- **Survival**: not improved by Tamoxifen or RxT\(^2\)

**IBIS II trial**  postM, WLE of DCIS ± Radiotherapy

**AI vs Tamoxifen/Placebo**
- no improvement (HR 0.89, \(p = 0.49\))

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Could Tamoxifen replace Radiotherapy or add more benefit?

<table>
<thead>
<tr>
<th>Study</th>
<th>DCIS</th>
<th>Locoregional recurrence following BCS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No radiotherapy</td>
</tr>
<tr>
<td>Correa</td>
<td>28.1%</td>
<td>12.9%</td>
</tr>
<tr>
<td>Stuart</td>
<td>24.7%</td>
<td>With Tamoxifen</td>
</tr>
<tr>
<td>Stuart</td>
<td>9.7%</td>
<td>With Tamoxifen</td>
</tr>
</tbody>
</table>

Benefit

- reduction in contralateral disease
- potential reduction of local recurrence

Common Side Effects

- Tamoxifen: hot flashes, DVT, endometrial cancer
- Aromatase Inhibitors: hot flashes, arthralgia

Real world concerns

- Adherence: only 70% of pts in the IBIS II trial at 5 years\(^1\)
- Canadian cohort study: only 26% of pts take Tam for DCIS\(^2\)
- for 1 pt to benefit, 15 need to be treated with HT\(^3\)

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Facts: DCIS and Survival

• **Death from breast cancer** after a diagnosis of DCIS is rare\(^1\)
  - 1.1% at 10 years and 3.3% at 20 years
  - Increased risk in: ER-negative, high grade, comedo type

• **Surgery**
  - Improves survival for intermediate and high-grade DCIS, *but* not for low-grade DCIS\(^2\)
  - *Not significant difference* with Mastectomy vs BCS\(^1\)

• **Radiotherapy**
  - *Is not* associated with a survival advantage\(^1\)

• **Tamoxifen**
  - *Is not* associated with a survival advantage\(^3\)

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IN OLDER BREAST CANCER PATIENTS
Challenges in Screening: the management of DCIS

Conclusion
Management of Screen detected DCIS

Diagnosis

- Low risk: Gr1, ER/PR+, HER2–
- Intermediate risk: Gr2, ER/PR±, HER2±
- High risk: Gr3, ER/PR–, HER2+

Recurrence

- Very old & Frail
- Frail
- Fit

- >90
- Life expectancy
- >75

- Surveillance
- WLE
- WLE ± RxT
- WLE + RxT ± HT
Multidisciplinary team approach is most important!
Assess patient’s risk based on disease parameters
Assess patient’s life expectancy, fitness, current QoL
Be aware of the risks & benefits of therapy
Find the balance between over- and under-treatment
Treatment should be oncologically optimum but, safe

DO NOT FORGET
Older women value most: QoL & independence
Engage them in the decision-making process
Thank you!

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