An Update on the Biology, Pathology and Implications of Breast Cancer Risk Lesions

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“High Risk” Lesions

- Risk of subsequent development of carcinoma – same or contralateral breast

- Risk of there being more advanced lesion present associated with the process at the same time in adjacent tissue = “upgrade”
Plan of talk

- Identification of high risk lesions
- Core biopsy and upgrade rates
- Long term risk
- Low grade clonal epithelial proliferations
- Intraductal or intralobular
### Intraductal Epithelial Proliferations

<table>
<thead>
<tr>
<th>UEH</th>
<th>ADH</th>
<th>LG DCIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular, peripheral slits. Streaming</td>
<td>Features of UEH &amp; of low grade DCIS</td>
<td>Punched-out spaces, rigid bars, micropapillae</td>
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<tr>
<td>Uneven distribution &amp; overlapping of nuclei. Variation in appearance, including oval nuclei.</td>
<td>Cells similar to low grade DCIS. Microfocal; &lt;2 spaces with complete involvement (mixed with UEH or CCL)</td>
<td>Evenly-spaced. Small, regular cells. Round uniform nuclei.</td>
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Usual epithelial hyperplasia – mixed cytology, mosaic immunophenotype; not clonal; not high risk lesion
ADH – uniform cytology, homogeneous immunophenotype; clonal; high risk lesion
Low Risk DCIS Trial Schema

932 patients

**Patient diagnosed with low/intermediate grade DCIS**

- **Obtain informed consent for central pathology review**

**REGISTER**

- **Low/intermediate grade DCIS confirmed by central pathology review**
  - Yes
  - **RANDOMISE**
    - **STANDARD TREATMENT**
      - Proceed to Surgery
      - Follow-up as per Local Practice
    - **ACTIVE MONITORING**
      - Annual Mammograms for 10 years
  - No
  - End of participation

- **RANDOMISE**
  - Pre-specified new abnormality detected - triggers investigation algorithm
  - No invasion or grade migration
    - Invasive disease/grade migration. Treat as newly diagnosed with surgery +/- adjuvant therapy continue follow up

**All randomised patients to complete QoL Questionnaires until 5 years post-randomisation**

**All randomised patients to be followed-up for a minimum of 10 years**
# Atypical Intralobular Risk Lesions

<table>
<thead>
<tr>
<th>ALH</th>
<th>LCIS</th>
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<tr>
<td>Moderately sized, uniform, discohesive cells; round nuclei;</td>
<td>More than half of acini filled and distended with no central lumen;</td>
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<tr>
<td>often intracytoplasmic vacuoles</td>
<td>8 or more cells within cross-section of acinus</td>
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<tr>
<td>Less than half of acini; partial filling of acinus; lumen may still remain</td>
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</table>
Pleomorphic LCIS
Ca2+ dependent cell–cell adhesion protein

Chromosome 16q22.1

Mutations early - in ALH & LCIS

Depending on morphological stringency in diagnosis of lobular lesions, lack of E-cadherin protein expression in 55% to 100% of cases [Christgen M et al. Pathol Res Pract. 2016;212:583-97]

May be CDH1 mutations, which preserve epitopes recognized by anti-E-cadherin antibodies or inactivating mutation in another member of the cadherin-catenin complex