Screening for Breast Cancer
Screening

- Why is screening required? Does it make a difference?
- What is screening for?
- Morbidity from screening
- Who should be screened? When should it be done?
Why is screening required? Does it make a difference?

- **Effective screening saves lives**
  - Multiple studies show 30% decrease in breast cancer deaths with screening

<table>
<thead>
<tr>
<th>Study</th>
<th>Period</th>
<th>Decrease in Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Insurance Plan of New York</td>
<td>1963 – 1966</td>
<td>25%</td>
</tr>
<tr>
<td>Malmö Mammographic Screening Trial</td>
<td>1988</td>
<td>36%</td>
</tr>
<tr>
<td>Gothenburg Breast Cancer Screening Trial</td>
<td>1997</td>
<td>45%</td>
</tr>
</tbody>
</table>
What is screening for?

• **Early detection of cancer**
  – Early detection usually translates to detecting smaller, and hence earlier cancer

• **Early cancer = better prognosis and survival**
  – Early cancer also associated with decreased rates of recurrence (cancer returning) and metastasis (cancer spread)
Could screening be bad for you?

• Can screening result in unnecessary biopsies?
  – Indeterminate (2%), Suspicious (30%), Malignant (>90%)

• Anxiety

• Overdiagnosis
  – Definition: finding a cancer that would not become relevant
    • For every 11 cancers detected, 2 lives saved, 1 would be overdiagnosed

• Can too much radiation cause cancer?
  – Average Mammogram – 7mGy, 20MMG = 140 mGy
    • Average treatment dose: 55 kGy
      – (1Gy = 1000mGy, 1000Gy = 1kGy)
    • No one has developed cancer because of screening
      – Bijwaard, H. Radiation Research, 2010 Jun (PMID 20726723)

Could screening be bad for you?

- **Radiation exposure**
  - Ave mammogram: 2 mGy per exposure.
  - 30% less for digital mammograms
- **For every 100,000 women undergoing MMG, 1 extra cancer can be expected from radiation exposure**
  - For every breast cancer caused by radiation, MMG detect 300 breast cancers
- **Radiation-induced breast cancer decreases with age**
  - 10-19 yrs: 2.95% / Gy
  - 20-29 yrs: 0.52% / Gy
  - 30-39 yrs: 0.43% / Gy
  - 40-49 yrs: 0.20% / Gy
  - 50-59 yrs: 0.06% / Gy
  - 60-69 yrs: 0.00% / Gy
Who should be screened? When should it be done?

- **Age 20-29**
  - Regular breast self examination (BSE) every month
  - Physician examination every 2-3 yrs

- **Age 30-39**
  - Monthly BSE, Annual examination by doctor
  - High risk of breast cancer – start mammograms

- **Age 40 and above**
  - 40 to 50: Annual Mammogram, and clinical examination with doctor
  - >50 – 65: Mammogram every 2 years, annual check with a doctor
At-risk populations to target

- Diabetes
- Obese
- Alcohol intake
- Nulliparous
- Late age at first pregnancy
- Patients on HRT, OCP

- Patients That Should be Followed by Breast Surgeon
  - Previous malignancy
  - Previous diagnosis of ADH, ALH, LCIS
  - Strong family history
Screening Modalities

- **Digital mammography**
  - Only technique with proven efficacy in detecting breast cancer
  - Complements physical examination
  - Mammographic detected lesions usually <1.5cm
Screening Modalities

- **Ultrasound scans**
  - Very good at distinguishing cystic from solid masses
  - ADJUNCT to mammograms &/or physical examination
  - Not recommended as a standalone screening method
  - Lower sensitivity than MMG for cancer detection
  
  - High risk FHx or personal risk for cancer
  - High mammographic density
    - Better in denser breasts cf fatty breasts
Screening Modalities

• MRI
  – More sensitive than MMG and US combined
  – But LESS specific
    • More false positives
  – Adv: MRI-only detected cancers usually small, node negative
  – When used together with MMG, no need for US
  – Recommended ONLY for screening of women at high risk of breast cancer
Screening Modalities

• **Elastography**
  – Assess the elasticity of the lump
    • Adjunct to regular tools
    • Not to be used as a stand-alone screening tool

• **Tomosynthesis**
  – Allows viewing of Mammogram in 3D, better detection of lumps
    • Not to be used as a stand-alone screening tool
Screening Modalities

- Tumour markers
- CA 15-3, 125, 19-9
- NOT a screening tool
- Only useful in diagnosed cases
Surgery for Breast Cancer
What’s in, What’s new

• Surgical treatment
• Different choices
• Consequences of surgery
• New techniques
Surgical Treatment

• **Aim of surgery**
  – Remove all cancer from breast and lymph nodes
    • Margins are crucial

• **Timing for surgery**
  – Usually the first line of treatment
    • In a small group of patients, there is greater benefit if surgery is performed after chemotherapy

• **Secondary aim**
  – Oncoplastic techniques
  – Improved aesthetic outcomes
  – Retain natural form
Surgical Choices

- **Complete removal of the breast**
  - Required if cancer is large
    - Reconstruction of the breast is always an option

- **Conservation of the breast**
  - Radiotherapy is necessary after conservation

- **Lymph node assessment**
  - Axillary dissection
    - Important for deciding on additional treatment
      - Runs a low risk of lymphedema
Oncoplastic Surgery

Resection of cancer according to oncological principles, and re-modelling of the remaining breast to maintain normal form and contour / shape

- Breast is usually smaller
- May require downsizing of the other side

Figure 5 Volume displacement. Round block approach to reconstruct peripheral defect.

Sentinel Lymph Node Biopsy

Suitable for some patients

- Allows patients to avoid axillary surgery and complications
Factors predictive for residual axillary disease

- **Size of LN met : ITC vs. micromet vs. macromet**
  - Micromets (0.2-2mm): risk of other positive nodes 13-24%
  - Macromets (>2mm): risk of other positive nodes 45-79%

- **Tumour size**

- **Presence of LVI**
Table 2. Frequency of Positive Sentinel Lymph Nodes (SLNs) and Nonsentinel Nodes (NSNs) by Tumor Stage

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>Patients, No.</th>
<th>Positive SLNs, No. (%)</th>
<th>Positive NSNs, No. (%)</th>
<th>≥4 Positive Axillary Nodes, No. (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a</td>
<td>89</td>
<td>7 (8)</td>
<td>1/7 (14)</td>
<td>1/7 (14)</td>
</tr>
<tr>
<td>T1b</td>
<td>268</td>
<td>41 (15)</td>
<td>9/41 (22)</td>
<td>3/41 (7)</td>
</tr>
<tr>
<td>T1c</td>
<td>537</td>
<td>147 (27)</td>
<td>44/147 (30)</td>
<td>26/147 (18)</td>
</tr>
<tr>
<td>T2</td>
<td>343</td>
<td>171 (50)</td>
<td>77/171 (45)</td>
<td>52/171 (30)</td>
</tr>
<tr>
<td>T3</td>
<td>31</td>
<td>23 (74)</td>
<td>13/23 (57)</td>
<td>10/23 (43)</td>
</tr>
<tr>
<td>Total</td>
<td>1268</td>
<td>389 (31)</td>
<td>144/389 (37)</td>
<td>92/389 (24)</td>
</tr>
</tbody>
</table>
Distribution of mets according to size of SLN mets

<table>
<thead>
<tr>
<th>Sentinel Lymph Node Metastases</th>
<th>Sentinel Lymph Node Metastasis Size</th>
<th>No. of Cases</th>
<th>Additional Axillary Node Status</th>
<th>Additional Axillary Node Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>All metastases</td>
<td>Any size</td>
<td>1228</td>
<td>744</td>
<td>484</td>
</tr>
<tr>
<td>ITC</td>
<td>&lt;0.2 mm</td>
<td>116</td>
<td>99</td>
<td>17</td>
</tr>
<tr>
<td>Micrometastases</td>
<td>≤2 mm</td>
<td>318</td>
<td>250</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>≤1 mm</td>
<td>212</td>
<td>176</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>&gt;1 mm</td>
<td>106</td>
<td>74</td>
<td>32</td>
</tr>
<tr>
<td>Macrometastases</td>
<td>&gt;2 mm</td>
<td>794</td>
<td>395</td>
<td>399</td>
</tr>
</tbody>
</table>

ITC indicates isolated tumor cells.

Annals of Surgery • Volume 241, Number 2, February 2005
Mets in Non SLN according to primary tumour size

<table>
<thead>
<tr>
<th>Author</th>
<th>T1a (≤.5 cm)</th>
<th>T1b (6–1.0 cm)</th>
<th>T1c (1.1–2.0 cm)</th>
<th>T2 (2.1–5.0 cm)</th>
<th>T3 (&gt;5.0 cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen⁹</td>
<td>0%</td>
<td>13%</td>
<td>29%</td>
<td>38%</td>
<td>71%</td>
</tr>
<tr>
<td>Reynolds²¹</td>
<td>[25% for T1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turner²²</td>
<td>17%</td>
<td>20%</td>
<td>46%</td>
<td>48%</td>
<td>73%</td>
</tr>
<tr>
<td>Kamath¹⁰</td>
<td>25%</td>
<td>30%</td>
<td>40%</td>
<td>46%</td>
<td>80%</td>
</tr>
<tr>
<td>Rahusen²⁴</td>
<td>50%</td>
<td>50%</td>
<td>49%</td>
<td>50%</td>
<td>—</td>
</tr>
<tr>
<td>Weiser²⁶</td>
<td>8%</td>
<td>21%</td>
<td>37%</td>
<td>48%</td>
<td>—</td>
</tr>
<tr>
<td>Wong²⁷</td>
<td>14%</td>
<td>22%</td>
<td>30%</td>
<td>45%</td>
<td>57%</td>
</tr>
<tr>
<td>Viale²⁸</td>
<td>100%</td>
<td>14%</td>
<td>25%</td>
<td>24%</td>
<td>—</td>
</tr>
<tr>
<td>Sachdev²⁹</td>
<td>[13% for T1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mignotte³⁰</td>
<td>[14%]</td>
<td></td>
<td></td>
<td>54%</td>
<td>52%</td>
</tr>
</tbody>
</table>

SLN, sentinel lymph node.

Incidence of non SLN mets after IHC detection of SLN mets

### TABLE 5. Studies reporting incidence of non-SLN metastases in patients with IHC-detected SLN metastases

<table>
<thead>
<tr>
<th>Author</th>
<th>Proportion</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teng(^{22})</td>
<td>3/26</td>
<td>12</td>
</tr>
<tr>
<td>Kamath(^{10})</td>
<td>2/26</td>
<td>8</td>
</tr>
<tr>
<td>Wong(^{27})</td>
<td>3/28</td>
<td>11</td>
</tr>
<tr>
<td>Mignotte(^{30})</td>
<td>7/44</td>
<td>16</td>
</tr>
<tr>
<td>Jakub(^{31})</td>
<td>9/62</td>
<td>15</td>
</tr>
</tbody>
</table>

SLN, sentinel lymph node; IHC, immunohistochemistry.

Incidence of non SLN mets in presence of LVI

### TABLE 3. Studies reporting incidence of non-SLN metastases in axillae with positive SLN(s), by presence of LVI in primary tumor

<table>
<thead>
<tr>
<th>Author</th>
<th>No LVI</th>
<th>LVI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds\textsuperscript{21}</td>
<td>43%</td>
<td>62%</td>
</tr>
<tr>
<td>Turner\textsuperscript{25}</td>
<td>37%</td>
<td>65%</td>
</tr>
<tr>
<td>Abdessalem\textsuperscript{23}</td>
<td>31%</td>
<td>62%</td>
</tr>
<tr>
<td>Rahusen\textsuperscript{24}</td>
<td>42%</td>
<td>30%</td>
</tr>
<tr>
<td>Weiser\textsuperscript{26}</td>
<td>26%</td>
<td>41%</td>
</tr>
<tr>
<td>Viale\textsuperscript{28}</td>
<td>21%</td>
<td>26%</td>
</tr>
<tr>
<td>Sachdev\textsuperscript{29}</td>
<td>12%</td>
<td>32%</td>
</tr>
</tbody>
</table>

LVI, lymphovascular invasion; SLN, sentinel lymph node.
Recurrence rates

- 20,000 patients observed after excision of positive LN
  - Micromets: RR 0.4%
  - Macromets: RR 1.0%

- J Clin Oncol
ASCOG Z0011

• No age restrictions (25-92)
• T1, T2 (median 1.7cm/1.6cm)
• Wide local excision only
  • Clear margins – no tumour at inked surface
• SNB positive
  • Identified using FS / touch print / H&E (IHC detected mets were excluded)
  • Fewer than 3 positive nodes / matted nodes / ENE
• Randomized to observation or ALND
  • ALND = level I & II, 10 LN
• All receive WBRT
• Systemic therapy according to MTC
Results

FU: 6.3 yrs median (5.2-7.7)
94 deaths (SLND: 42, ALND: 52)
5YSR SLND: 92.5%, ALND: 91.8%
5YDFS SLND: 83.9%, ALND 82.2%
SLND group had significantly less morbidity (25% vs 70%)
Axillary nodal recurrence rate
- SLND – 2.5% at 5 yrs
- ALND – 3.6% at 5 yrs
Aims of ALND

- Locoregional control
- Prognostic staging
  - Need for adjuvant therapy
- NO survival benefit
SNB

• **Not indicated for**
  – T3, T4 disease (LABC)
  – Inflammatory breast cancer
  – DCIS in BCS
    • Except in large DCIS, >5cm
    • Palpable DCIS
    • microinvasion
  – Pregnancy
  – Previous extensive breast / axillary surgery
  – Presence of suspicious clinical LN
Neoadjuvant Chemotherapy for Breast Cancer
Chemotherapy

• Standard regime:
  • 5FU, Anthracycline (Doxorubicin), Cyclophosphamide

• Now more are using:
  • ACT: Anthracycline, Cyclophosphamide, Taxane
  • Or AT
  • With or without Herceptin
Neoadjuvant chemotherapy

• **Rationale:**
  – Downsize locally advanced breast cancers where margins are doubtful
  – Discovered that a proportion were able to have breast conserving surgery
  – Indications now include patients with cancers that are borderline conservable, to facilitate ease of conservation
NSABP-18

- Compared survival benefits of neoadjuvant chemotherapy vs adjuvant chemotherapy
- Patient population: T 1-3, N0-1, M0
- Randomized to 4 #s of neoadjuvant or adjuvant doxorubicin + cyclophosphamide
- At 16 yrs FU, no treatment difference in OS, DFS or Event Free Survival (EFS)
- But in neoadjuvant group
  - More patients had pathologically negative LN (58% vs 42%, p<0.0001)
  - Patients had higher conservation rates (68% vs 60%)
  - Women with pathological complete response, RFS 85.7%;
    - Residual pathologic invasive disease RFS 76.9%
    - Clinical partial response RFS 68.1%
    - Clinically no response RFS 63.9%
Neoadjuvant chemotherapy

- **Response rates**
  - 90% of patients will respond to chemotherapy
  - 5-10% will have complete pathological response
    - If patients are ER negative, grade 3, Her 2 positive (most chemosensitive gp), pCR rates could be 25-30%
    - Triple negative cancers have highest pCR rates (up to 40%)
  - 20-30% will have sufficiently good enough response to allow breast conservation
  - 30-40% will have a partial response, but not enough for conservation
  - 10% will have progressive disease
Neoadjuvant chemotherapy

- **Advantages**
  - Enables direct observation of chemotherapy response
  - Opportunity for breast conservation
  - Good model in which to test new chemotherapeutic agents
  - Patients with pCR response have better prognosis.

  - Emerging group of patients that may benefit from neoadjuvant chemo are those with high nodal burden of disease.
  - If have very good response with downstaging of axillary disease, have better survival.

Alternative avenues

• **Neoadjuvant endocrine therapy**

• **Targeted therapy**
  – Anti-angiogenic factors, Bevacizumab
  – Herceptin
Thank you for your attention