High Risk Multimodal Screening
Ulrich Bick, Charité Berlin
High-risk surveillance

- Goal is to prevent breast-cancer mortality as much as possible
- Prophylactic surgery as effective alternative
- Not comparable with population-based screening
- May be a temporary solution to delay prophylactic surgery from age 25 to after completion of family planning
Breast Cancer Screening

Population-based Screening
- mortality reduction in the entire population
- minimization of negative side effects (false-positives, overdiagnosis)
- cost considerations of high importance due to the large number of participants

High-risk Surveillance
- minimization of the individual mortality
- high sensitivity of the screening modalities
- high motivation of the participants
- individual optimization
Selecting women for high-risk screening

- lifetime risk for breast cancer as high as 60% in BRCA1 and 55% in BRCA2

- several additional moderate risk genes have recently been discovered (ATM, CDH1, CHEK2, PALPB2, PTEN, RAD51C/D, TP53), many of which are also associated with other malignancies

- risk prediction in women with strong family history but no known mutation difficult (all current risk models relatively unreliable)

- lifestyle factors may play a larger role than family history in postmenopausal women
How to screen high-risk women

- annual MRI starting at age 25 (30) cornerstone of any high-risk screening program

- more than 90% of the cancers detected at high-risk screening are visible on MRI and around 30% of cancers will be detected by MRI alone

- additional tailored mammography (from age 40) and second-look ultrasound in full knowledge of the MRI results will mainly increase specificity

- 6-month interval ultrasound or alternating MRI and mammography every 6 months in BRCA1/2
Limitations of Screening in BRCA1-Carriers

- Fast-growing triple-negative breast cancers (TNBC) very common (around 50%) in BRCA1-carriers
- Symptomatic interval cancers may occur despite screening every 6 months
- Correlation between tumor size at time of detection and likelihood of metastasis less stringent for TNBC, chemotherapy usually required even if detected small
- High likelihood of contralateral or even ipsilateral second cancers after breast-conserving therapy
My Medical Choice

By ANGELINA JOLIE
Published May 14, 2013    1543 Comments

LOS ANGELES

MY MOTHER fought cancer for almost a decade and died at 56. She held out long enough to meet the first of her grandchildren and to hold them in her arms. But my other children will never have the chance to know her and experience how loving and gracious she was.

We often speak of “Mommy’s mommy,” and I find myself trying to explain the illness that took her away from us. They have asked if the same could happen to me. I have always told them not to worry, but the truth is I carry a “faulty” gene, BRCA1, which sharply increases my risk of developing breast cancer and ovarian cancer.
<table>
<thead>
<tr>
<th>Family Constellation</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 3 BC, 2 of them before the age of 51</td>
<td>30.7%</td>
</tr>
<tr>
<td>≥ 3 BC at any age</td>
<td>22.4%</td>
</tr>
<tr>
<td>2 BC, both before the age of 51</td>
<td>19.3%</td>
</tr>
<tr>
<td>2 BC, 1 of them before the age of 51</td>
<td>9.2%</td>
</tr>
<tr>
<td>2 BC, 1 of them before the age of 51</td>
<td>48.4%</td>
</tr>
<tr>
<td>≥ 2 OC at any age</td>
<td>45.0%</td>
</tr>
<tr>
<td>1 bilateral BC, the 1st before the age of 51</td>
<td>10.1%</td>
</tr>
<tr>
<td>≥ 2 OC at any age</td>
<td>24.8%</td>
</tr>
<tr>
<td>≥ 1 male BC &amp; ≥ 1 female BC or OC</td>
<td>42.1%</td>
</tr>
</tbody>
</table>
MG NORMAL - US NORMAL

15-mm invasive lobular carcinoma
pT1c pN0(sn) G2

57-year-old asymptomatic female
with positive family history for
breast cancer
(ther at age 45)

7-mm invasive ductal carcinoma
pT1b pN0(sn) G1
# Annual high-risk screening with MRI

Influence of cancer incidence on screening performance

<table>
<thead>
<tr>
<th>annual incidence</th>
<th>cancers per 1000</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>ppv</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5% (BRCA1/2)</td>
<td>25</td>
<td>90%</td>
<td>90%</td>
<td>18.8%</td>
</tr>
<tr>
<td>1% (high risk)</td>
<td>10</td>
<td>90%</td>
<td>90%</td>
<td>8.3%</td>
</tr>
<tr>
<td>0.25% (average)</td>
<td>2.5</td>
<td>90%</td>
<td>90%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>
Breast Cancer Screening

Lead-time Bias

without screening

with screening

Birth 10 20 30 40 50 60 70 80 Age (years)
BI-RADS® 3 Lesions in High-Risk Patients

Probability of Malignancy

Normal Risk
Incidence 1:400*
< 2%

*annual breast cancer incidence in women > 50 years

Hereditary Breast Cancer
Incidence up to 10x higher
> 20%
BRCA 1, HIGH GRADE DCIS RIGHT, LOW GRADE DCIS LEFT
6 YEARS LATER: INVASSIVE DUCTAL CARCINOMA (RIGHT LOWER THORACIC WALL)
• There is no way around MRI!

• MRI first, mammography and sonography second

• optimized MRI-technic and resolution

• forget BI-RADS III in BRCA1/2-patients - if something is new, it has to be biopsied

• BRCA1/2 can develop cancer in any reminding tissue, even after radical mastectomy
Thank you very much for your attention!