Breast Cancer in Young Women
Arrow Project
June 6th 2013

Aharona Gutman
Dr. Shani Paluch-Shimon
Overview - Breast Cancer in Young Women

- 10% of breast cancers are diagnosed in women under 40
- Breast cancer is the leading cause of death amongst women under 45 in the Western world and is a major cause of morbidity
- Only 30% of breast cancers in women under 40 are caused by known genetic mutations
- Unlike in older women, we don’t know what causes breast cancer in most young women
Breast cancer in young women – is a challenge!

- It is rare.

- Paucity of modifiable risk factors.

- Lack of screening.

- Fertility issues are unique to this group
Breast Cancer in Young Women

- Breast cancer in young women strikes them at the peak of:
  - Their careers
  - Their reproductive years
  - Their motherhood and most active years of family life
Age-Specific Probabilities of Developing Breast Cancer

By age 30 ... 1:1985
By age 40 ... 1:229
By age 50 ... 1:68
By age 60 ... 1:37
By age 70 ... 1:26
By age 80 ... 1:24
By lifetime... 1:8

(ACS Research, SEER 2005)
Ten leading causes of death in women aged 15-44 by country income group, 2004

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>Deaths (000s)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Road traffic accidents</td>
<td>14</td>
<td>10.2</td>
</tr>
<tr>
<td>2</td>
<td>Self-inflicted injuries</td>
<td>13</td>
<td>9.8</td>
</tr>
<tr>
<td>3</td>
<td>Breast cancer</td>
<td>11</td>
<td>7.9</td>
</tr>
<tr>
<td>4</td>
<td>Poisonings</td>
<td>5</td>
<td>3.8</td>
</tr>
<tr>
<td>5</td>
<td>Stroke</td>
<td>5</td>
<td>3.6</td>
</tr>
<tr>
<td>6</td>
<td>Ischaemic heart disease</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>7</td>
<td>Violence</td>
<td>4</td>
<td>2.9</td>
</tr>
<tr>
<td>8</td>
<td>HIV/AIDS</td>
<td>3</td>
<td>2.6</td>
</tr>
<tr>
<td>9</td>
<td>Trachea, bronchus and lung cancers</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>10</td>
<td>Cirrhosis of the liver</td>
<td>3</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Women & Health, WHO Report, 2009
Ten leading causes of death in women aged 20-59 by country income group, 2004

<table>
<thead>
<tr>
<th>Rank</th>
<th>Cause</th>
<th>Deaths (000s)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast cancer</td>
<td>49</td>
<td>11.5</td>
</tr>
<tr>
<td>2</td>
<td>Trachea, bronchus, lung cancers</td>
<td>28</td>
<td>6.7</td>
</tr>
<tr>
<td>3</td>
<td>Ischaemic heart disease</td>
<td>28</td>
<td>6.7</td>
</tr>
<tr>
<td>4</td>
<td>Suicide</td>
<td>22</td>
<td>5.1</td>
</tr>
<tr>
<td>5</td>
<td>Stroke</td>
<td>20</td>
<td>4.8</td>
</tr>
<tr>
<td>6</td>
<td>Colon and rectum cancers</td>
<td>16</td>
<td>3.8</td>
</tr>
<tr>
<td>7</td>
<td>Road traffic accidents</td>
<td>16</td>
<td>3.8</td>
</tr>
<tr>
<td>8</td>
<td>Cirrhosis of the liver</td>
<td>13</td>
<td>3.1</td>
</tr>
<tr>
<td>9</td>
<td>Ovarian cancer</td>
<td>12</td>
<td>2.8</td>
</tr>
<tr>
<td>10</td>
<td>Cervical cancer</td>
<td>10</td>
<td>2.4</td>
</tr>
</tbody>
</table>
The Decrease in Breast-Cancer Incidence in 2003 in the United States

Peter M. Ravdin, Ph.D., M.D., Kathleen A. Cronin, Ph.D., Nadia Howlader, M.S., Christine D. Berg, M.D., Rowan T. Chlebowski, M.D., Ph.D., Eric J. Feuer, Ph.D., Brenda K. Edwards, Ph.D., and Donald A. Berry, Ph.D.

Figure 1. Annual Incidence of Female Breast Cancer (1975–2004).
Data are from nine of the NCI's SEER registries. SEER sites include San Francisco, Connecticut, Detroit (metropolitan area), Hawaii, Iowa, New Mexico, Seattle–Puget Sound, Utah, and Atlanta (metropolitan area).
WHAT CAUSES BREAST CANCER IN YOUNG WOMEN?
Major Breast Cancer Risk Factors

GENDER

AGE

ATYPICAL HYPERPLASIA / LCIS

FAMILY HISTORY

Br Ca Dx'd 28y Ov Ca Dx'd 33y

Colon Ca Dx'd 50y Dx'd 45y

Unknown Ca Dx'd 70y

Dx'd 30y Dx'd 38y

Dx'd 39y Dx'd 53y
Family history is not enough
Proven Risk factors for Early Onset Breast Cancer

- Birth weight, growth rate in childhood, attained height – effects are small.
- High BMI is protective against breast cancer in premenopausal.
- Oral contraceptives – actual risk increase is small.
- Breastfeeding is protective - more modest effect in premenopausal.
- Increasing parity – the effect is less protective in young women.
- Exposure to ionizing radiation (depends on the age of exposure and the radiation dose.) – relative risk is higher for early onset BC <35.
- Genetic factors.
WHAT’S DIFFERENT ABOUT BREAST CANCER IN YOUNG WOMEN?
TNM STAGING

- Primary tumor (T)
- Regional lymph nodes (N) – clinical/pathologic
- Distant metastasis (M)
Pathological stage according to TNM (pTNM), tumor size and degree of axillary node involvement as a percentage of the respective age cohorts.

Expression of ERs, PgRs, presence of peritumoral VI, grading (G), expression of Ki-67, overexpression of HER2/neu, as percentage of the respective age cohorts.

Association between very young age and adverse characteristics of breast cancer at presentation amongst Israeli women

- Of 1448 newly diagnosed breast cancer patients, 61 very young (<35) and 94 less-young (40-50) patients were identified.
- Significantly more very young patients had metastatic disease at presentation (20% vs. 3%, respectively, $P = 0.0007$).
- The very young patients were more likely to have high grade, HR- tumors than the less young patients.
- After controlling for stage and tumor grade, very-young age was not shown to be an independent risk factor for reduced survival.
Survival by age

Fig. 1. Overall 10-year survival for age. Numbers in parentheses indicate total number and number at risk.

Jayasinghe ANZ J Surg. 2005
Disease Free Survival by Age

Only women over 80 do worse.
Other issues:

- Early onset menopause
- Fertility preservation
- Sexual dysfunction
- Pregnancy after breast cancer
- Psycho-social issues
Ongoing studies
Objective

- Little research performed specifically on breast cancer in young women
- Age as an independent risk factor
- Conclusions regarding screening, prognosis & treatment
Method - Clinical data base

- Data abstraction
- 200 young patients
- Descriptive analysis
Data abstraction is fun!
## Goals

Characterization of breast cancer in young women – before treatment

<table>
<thead>
<tr>
<th></th>
<th>40 &gt;</th>
<th>50 &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shown on mammography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shown on ultrasound</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shown on MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNM Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progesteron</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Her-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history (cancer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history (breast cancer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Goals

Characterization of breast cancer in young women - before treatment

<table>
<thead>
<tr>
<th></th>
<th>40 &gt;</th>
<th>50 &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mode of diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shown on mammography</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Shown on ultrasound</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shown on MRI</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>TNM Stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progesteron</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Her-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history (cancer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history (breast cancer)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Goals

- Assessing treatment effectiveness – example: Relumpectomy
- Age as an independent risk factor for bad prognosis (stage per stage)
- Long term outcome
Method – prospective study

- International study – Dana-Farber
- Epidemiological questioners
Goals

- Etiology - Risk factors
- Psychosocial effects
- Quality of life - Treatment side effects
- Clinical character
Method – prospective study

- Genetic epidemiological study
- New mutations in young women
- Genetic data base
Timeline:

Prospective international study

Data analysis – clinical database

Genetic database

May 2013
December 2013
June 2014
2015
2016
Thank you!