Recent and Future Developments in Breast Cancer Imaging

Martin J. Yaffe, PhD
Senior Scientist, Imaging Research Program, Tory Family Chair in Cancer Research
Sunnybrook Health Sciences Centre
University of Toronto

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Prof Harold E. Johns, OC
What HEJ taught us

• If you have an idea, question it, pull it apart, look at it from all sides until you’re sure it’s right
  – “Mene, mene, tekel, upharsin” – Writing on the wall
    Daniel: 5
    (“judged in the balance and found wanting”)

• Once you believe in it, pursue it with vigour and make it happen
  – In that quest, don’t tolerate, mediocrity, procrastination or red tape
How do you reduce mortality and suffering from cancer?

- Prevention – must understand causes
- Earlier detection – find the cancer at a point when therapy can be effective
- Better treatments – tailor the treatment to the individual and the cancer

Imaging can have an important impact in all of these areas
Improvements in breast cancer imaging
Mammogram, circa 1978

- “Fuzzy”
- Poor contrast
- High radiation dose
Improvements in Mammography

• Working with Dr Johns, Ken Taylor and industry, we made some evolutionary developments to improve mammography
  – Sharper images, reduced dose
• Stimulated introduction of Ontario legislation to mandate standards for medical imaging – qualifications and quality control
Where we are today - Effect of screening mammography

Stage distribution of breast cancers in screened vs un-screened British Columbia women aged 40-49

<table>
<thead>
<tr>
<th>STAGE</th>
<th>SCREENED (%)</th>
<th>UNSCREENED (%)</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>62</td>
<td>39</td>
</tr>
<tr>
<td>II</td>
<td>30</td>
<td>46</td>
</tr>
<tr>
<td>III</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>IV</td>
<td>0.3</td>
<td>7</td>
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Mortality reduction demonstrated in BC of screened vs unscreened women - 25% (Coldman et al)
Accuracy of mammography is limited in the dense breast
Could the use of electronic x-ray detectors and computer processing improve mammography – i.e. digital mammography?

• Capitalize on technological advances arising from:
  – Space and military research (microelectronics, precision motors, fast computers, image processing)
  – Home entertainment (CCDs, high resolution flat-screen displays)
Digital Mammography

• 1985 – 1990 preliminary science and technology at PMH (supported by Canadian grants)

Bob Nishikawa
Andrew Maidment
Rebecca Fahrig
Digital Mammography

- 2000 Funding of $26.5 M US to conduct full clinical assessment – The DMIST Study.

- Requires signing of a special bill by Bill Clinton.

- 2001-2005 Recruiting of 50,000 women (3100 in Toronto), imaging and data analysis. (911 / SARS)
Digital Mammography: More accurate acquisition, image processing, reduced radiation dose
DMIST Study - Digital vs Film Mammography

- 50,000 women in US and Canada
  - Received both exams
- 2005 - Publication of positive results:
- Compared to film mammography, digital mammography finds substantially more cancers in
  - women with dense breasts
  - women under the age of 50
- 2008 - 38% of mammography in US is now digital; 80% by 2012.
Breast MRI for High-Risk Women

• There is a group of women (many positive for breast cancer gene mutations) who are at high risk for breast cancer (80% lifetime risk) and for whom mammography does not work well.

• These women tend to develop these cancers earlier in life.

• Lacking an accurate screening method, many of these women opt for prophylactic mastectomy.

• Plewes, Warner, Causer and colleagues at Sunnybrook developed breast MRI techniques.
Magnetic resonance imaging

1 cm

0.5 cm

Courtesy of Dr. E. Ramsay
Warner, Plewes et al. Sensitivity for breast cancer detection in high risk women

Sensitivity by Modality (n=19)
Conventional mammogram
Cancer not seen on Conventional Mammography
The Future
(could be closer than we think)
• Up to now, we have mainly been detecting cancer on the basis of changes in structure – feeling lumps, seeing masses on an x-ray image.

• Develop cancer imaging techniques that are specifically targeted to changes in function or molecular characteristics associated with cancer - biomarkers
Ontario Institute for Cancer Research

- “The 1 mm Cancer Imaging Challenge” – Program in Earlier Detection and Diagnosis
- Support for new personnel, infrastructure and operation ~ $35M 2007-2010

Tom Hudson, President OICR
Biomarker

- Something that provides information about the disease state
  - Disease is present or not
  - Level of aggressiveness
  - Responsiveness to a particular treatment
- Biomarker can be
  - a molecule on the surface of a cancer cell
  - a change in temperature or acidity, etc.
Imaging Angiogenesis

- Tumour induces angiogenesis
- Resulting vessels are of poor quality & leaky
- These vessels are a biomarker for cancer

Vascularized tumour penetrated by capillaries

Melissa Hill
Dual Energy CEDM

Screening Mammography
• Potential architectural distortion on right breast (CC view)

• Physical examination normal

Courtesy: Dr Clarice Dromain, Institut Gustave Roussy – Villejuif, France, GE Healthcare, Buc, France
Improved Pathology To Validate New Imaging Techniques

Gina Clarke
Chris Peressotti

Greg Czarnota
Claire Holloway
Eg Diffuse Optical Tomography - LABC

SoftScan® image acquired 5 days before surgery

Wholemount section with highlighted inset
Tumour Stem Cells

CD-24 (Negative Staining)  CD-44 (Positive Staining)
OICR Earlier Detection and Diagnosis Program (1mmCC)

- Molecular Imaging – Identify the fingerprints of breast cancer
  - Create new probes for targeted imaging
Cancer Imaging with Ultrasound probes
Peter Burns

- US (targeted microbubble, nanodroplets)

- Targeted microbubbles, nanodroplets

Naomi Matsuura
Rajiv Chopra
Quantitative Classification

Case-Control Studies

Boyd (1982)
Brisson (1982)
Brisson (1984)
Brisson (1989)
Maskarinec (2000)
Thomas (2002)
Ursin (2003)
Van Gils (1998)
Van Gils (1999)
Van Gils (2000)
Wolfe (1986)

Case-Control Summary

Cohort Studies

Boyd (2003)
Boyd-computer (1995)
Boyd-radiologist (1995)
Byrne (2001)
Byrne (1995)
Saftlas (1991)

Cohort Summary

All Studies Summary

Risk Estimate

1 5 10
Volumetric Density From Film Mammography

kVp 26, mAs 59.6, thickness 3.6 cm, VBD=34%
The Promise of Imaging

• Detect the cancers that will progress and kill
  – earlier, more accurately
• Provide individualized treatment based on characteristics of the cancer
• Identify and validate biomarkers that can be used for cancer screening
• Practical imaging “probes” that provide molecular and functional information