Effective Breast Ca Detection and Treatment: Big Picture of Physicists

Dianne Georgian-Smith, MD
Associate Professor Radiology
Harvard Medical School
Brigham and Women's Hospital

Breast Ca Detection & Treatment

- Mammography
- Magnetic Resonance Imaging (MR)
- Ultrasound
- Tumor Histologies
- Treatment
- New Devices under Investigation

Breast Cancer Detection: Mammography

Benefits of Screening for early forms of breast cancer has been proven by randomized controlled trials.

- Only imaging modality to be so rigorously tested
  - Prevalence rates ~ 5/1000
  - Incidence rates ~ 2/1000
  - Autopsy prevalence rates ~ 20/1000

Breast Cancer Detection: Mammography

- Swedish Two-County 20 yrs later (Tabar L et al. Lancet 2003 ; 361 (9367):1405
  - Compared deaths 20yrs before (1858-1977) and after (1978-1997) screening
    - Marked reduction in death from Br Ca in women 40-69 yrs

Breast Cancer Detection: Mammography

- Deaths before (1858-1977) "not exposed" and after (1978-1997) "exposed" screening (Tabar L- Lancet)
    - 40-69 yrs: 44% reduction "exposed"
    - 41% in all population (exposed and not)
      - 40-69 yrs not exposed- 16% reduction
      - 20-39 yrs never screened- 27% reduction
    - ~18% reduction changes in treatment, awareness, management indpt of Screen

Breast Cancer Detection: Magnetic Resonance Imaging

- ACS Guidelines for Br Screening with MRI as an Adjunct to Mammography (CA Cancer J Clin 2007; 57: 75-89)
  - Recommended for Women >,=20-25% lifetime risk of breast cancer: strong fam history or ovarian Ca and Tx'd Hodkins Lymphoma
  - Insufficient data: personal h/o Br Ca, DCIS, ADH, extremely dense breasts

Breast Cancer Detection: Magnetic Resonance Imaging

- 6 RCT Prospective MR Screening Trials starting in late 1990's
  - Populations differed definition of high risk
    - All BRCA mutation carriers or very strong fam hy
    - Some personal history breast ca
  - Sensitivty: MR 71%-100% ; Mam 16-40%
  - US Screening in 3 studies: similar to Mam
  - Specificity: MR 90-99%; Mam 95-99 %

Breast Cancer Detection: Sonography

- American College of Radiology Imaging Network (ACRIN) 6666: US Screening Trial
  - High risk population US vs Mam Independently evaluated by two radiologists; 3 intervals of Screening; Data final late 2008
  - Accrued 2800 pts; now in follow up
  - Added MR

Breast Cancer Detection: Sonography

Kaplan – (2001 Rad)- 6/ 1862 (0.3 %)

Kolb – (2002 Rad;)- 37/ 13,547 (0.27 %)

Leconte- (June 2003 AJR)- 16/ 3084 (0.5%)

Crystal – (July 2003 AJR)- 7/ 1517 (0.46%)

Breast Cancer Detection:

Do these studies "prove" that Screening works?

To PROVE effectiveness, one must study the affect of the test on MORTALITY; not all Cances kill.

The test must be evaluated INDEPENDENT of other tests

even if clinically adjunctive

Breast Cancer Detection:

For any Screening Test:

Know your False Positive Rate

Know your False Negative Rate

Asymptomatic, healthy people-

- DO NO HARM!
- Will the “cure” be very risky to the patient?
  - E.g Are you subjecting pt to chemo Tx unnecessarily?

Breast Cancer Detection: Histologies

- Ductal Carcinoma
  - Invasive (IDC)
  - In situ (DCIS)
- Lobular
  - Invasive (ILC)
  - In site (LCIS)- considered benign, high-risk marker
- Less common
  - Colloid (Mucinous); Medullary; Inflammatory
  - Phyllodes (15%); Tubular
  - Lymphoma
  - Metastases- other breast, lung, melanoma

Detection on Digital Mammograms:

- Mammographic detection of Breast Cancer basic 3 types of findings:
  - Masses
  - Architectural Distortion
  - Calcifications
    - Superior contrast to film-screen;? Greater detection
    - Hampered by digital noise; difficult to discern the amorphous calcification from pixels

Mastectomy:

Technique 26 kVp/ 50 mAs

Mastectomy:
Technique 30 kVp/ 70 mAs
Mastectomy:
Technique 36 kVp/ 100 mAs

High Noise Low Noise

Purpose

To evaluate effects of radiation techniques on conspicuity of magnified calcifications as measured by confidence in determining extent and morphology/ number.

Hypothesis: Increasing x-ray technique decreases noise on digital magnification; greater confidence in determining extent / morphology of calcifications with a lower noise technique.

Results

Results

Results

Per case, assessment of <u>extent</u> was better with the low noise (high technique) in <u>all cases</u>.

Per case, the <u>morphology</u> was most of the time better with low noise technique, but not always. Why?

- Density and Size of the calcifications

Results- Equal in Morphology

#1: **A**: 35 kVp/97 mAs; **B**: 27 kVp/ 62.5 mAs

Results- Low Noise Better

#12: **A:** 31 kVp/ 79 mAs; **B:** 35 kVp/ 97.3 mAs

Results- Equal in Morphology

#17: **A**: 26 kVp/ 48.7 mAs; **B**: 35 kVp/ 97.3 mAs

Results- Low Noise Better

#10: **A:** 35 kVp/ 92.5 mAs; **B:** 29 kVp/ 53.6 mAs

Conclusion

Diagnostic evaluation of calcifications on magnification views with a low noise technique (higher kV and mAs) improves visualization.

- Best applied to faint, amorphous calcifications
- One higher dose magnification view may be lower in exposure than

multiple, “noisy” images.

– Discriminantly applied by radiologist depending on clinical history

Detection on Digital Mammograms:

- “Dose Creep in Digital Radiography and its Prevention” (p379 Williams et al. Digital Radiography Image Quality: Image Acquisition. J Am Coll Radiol 2007; 4: 371-388)
  - “Only the noise in the image changes with the exposure. Radiologists react negatively to digital images with excessive noise….Technologists recognize this…This leads to the potential for dose creep.”

Detection on Digital Mammograms:

- “Dose Creep in Digital Radiography and its Prevention” (p379 Williams et al. Digital Radiography Image Quality: Image Acquisition. J Am Coll Radiol 2007; 4: 371-388)
  - “One way to eliminate..validated radiographic technique charts…as a function of patient size.”
  - But also the size and density of the object!
  - Education of physicians and technologists.
  - One technique is not good for all situations!
  - Radiation MUST be used judiciously!

Breast Cancer: Treatment

- Surgical Excision
  - Lumpectomy vs Mastectomy
- Radiation
  - Whole breast vs Partial
- Chemotherapy
- Hormonal Tx
  - Tamoxifen; aromatase inhibitors

Breast Cancer: New Devices under Investigation

- Electrical Impedence
- Optical Imaging
- Tomosynthesis

Investigative Techniques

“Z-Tech”

– All tissues have electrical properties in which the fluids and cell membranes act like resistors and capacitors.

– By passing electrical current through pair of electrodes, one measures impedence of flow

– Hypothesis: decrease impedence in malignant tissues.

Electrical Impedence

Results from HEDA study

- Not yet published or made public
- Is FDA approved

Optical Imaging

1. Absorption and Scattering
2. Chromophores

Optical Imaging

Measure:

- blood volume- Hgb concentration (micromoles per liter blood)
- Oxygenation of tissues

Quantify by measuring the absorption and scatter of light

- 1 source; 3 detectors; 8 separate wavelengths

- Boas D, Ang L, Chaves T. Applied Optics 2003; 42:5181

Optical Imaging: Chromophores

Molecules containing chromophores designed to be split by specific enzymes

Optical Imaging

A chromophore is a molecule that gives off light when stimulated by incident energy (eg. other light). When two chromophores are linked and hit by UV light they cancel each other out and no light is emitted from the molecule. When the molecule is split by an enzyme (one that is more abundant in a tumor than normal cells) the separate pieces give back light and the tumor "lights up".

OPTICAL IMAGING

Molecules containing chromophores designed to be split by specific enzymes

Case 1
Case 1
Case 2
Case 2
Case 3
Case 3
Case 4
Case 4
Case 5

Breast Cancer Detection: Summary

- Detection
  - Mammography; MR; Sonography
- Histologies
- Calcifications vs Noise
- Treatment
- New Modalities