BREAST CANCER SCREENING

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BREAST CANCER SCREENING IS AN INTEGRAL PART OF WOMEN'S PREVENTATIVE HEALTH

BREAST CANCER BURDEN

Breast cancer is the most common malignancy diagnosed in women (excluding cancers of the skin) In the United States breast cancer is the second most common cause of death from cancer

LESSONS FROM MAMMOGRAPHY DEBATES

Concepts of Screening

- Merely finding a cancer earlier does not mean the patient will benefit
- A different level of proof is required for a screening test as compared to applying a test to someone who is already ill
- Because the vast majority of those who will be screened will not have the disease most will not benefit from the test, but many may have false positives studies which may 'harm them'
- Since there are cancers that never kill and cancers that are destined to kill before they can be discovered only a randomized control trial (**RCT**) in which one group is screened and the other has the 'usual' care can prove a screening test is efficacious

The period of time during which a cancer is detectable by a test before it is clinically evident is called the '**sojourn time**'

In order to intercept the most cancers earlier, the screening interval should be less than half the sojourn time

Cancers detected by periodic screening are likely to be slower growing, more indolent cancers. Faster more aggressive cancers become clinically evident between screens.

The statistical power of the RCT is crucial.

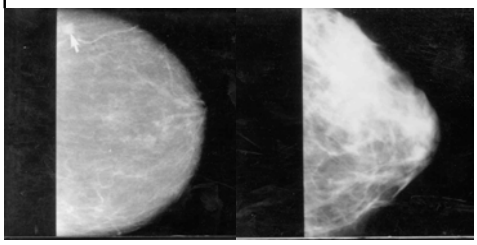
American Cancer Society
GUIDELINES FOR THE EARLY DETECTION OF CANCER

- Yearly mammograms are recommended starting at age 40 and continuing for as long as a woman is in good health.
- Clinical breast exam (CBE) should be part of a periodic health exam, about every 3 years for women in their 20s and 30s and every year for women 40 and over.
- Women should know how their breasts normally feel and report any breast change promptly to their health care providers. Breast self-exam (BSE) is an option for women starting in their 20s.
- Women at high risk (greater than 20% lifetime risk) should get an MRI and a mammogram every year. Women at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram. Yearly MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%.

Risk Factors for Breast Cancer

- Family History/genetic factors
- Reproductive/hormonal
- Proliferative benign breast disease
- Mammographic density

BREAST DENSITY



FACTORS USED IN NCI BREAST CANCER RISK PREDICTION MODEL

- Age
- Number of 1st degree female relatives with a history of breast cancer
- Number of breast biopsies
- Age at first live birth or nulliparity
- History of atypical hyperplasia
- Age at menarche
- Race

ORIGINAL GAIL MODEL

- Gail *et al* Journal National Cancer Institute 1989; 81: 1879-1886
- Model based and derived from extremely large data sets
- Estimates the risk of:
  - invasive
  - *in situ* (DCIS)
  - or lobular carcinoma in situ (LCIS)

  over a defined interval in women having annual screening

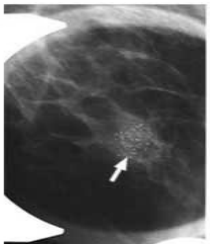
LIMITATIONS OF GAIL MODEL

MAY OVERPREDICT RISK IN PREMENOPAUSAL WOMEN WHO DO NOT ADHERE TO GUIDELINES FOR ANNUAL SCREENING

CLAUS MODEL

The Claus model takes into account 1st and 2nd degree relatives effected by breast cancer and accounts for their ages at the time of diagnosis

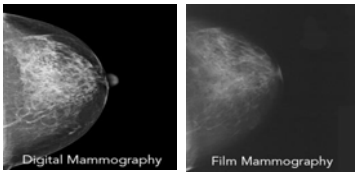
Current screening methodologies rely heavily on imaging



Considerations in Choosing a Mammography Site

- FDA certification
  technician, medical physicist, radiologist
- BIRAD reporting
- CAD system
- Digital Mammography

MAMMOGRAPHY DIGITAL VS FILM



Breast Imaging Reporting and Database System (BI-RADS)

Category	Assessment	Follow-up
0	Need additional imaging evaluation	Additional imaging needed before a category can be assigned
1	Negative	Continue annual screening mammography (for women over age 40)
2	Benign finding	Continue annual screening mammography (for women over age 40)
3	Probably benign	Receive a 6-month follow-up mammogram
4	Suspicious abnormality	May require biopsy
5	Highly suggestive of malignancy (cancer)	Requires biopsy
6	Known biopsy—proven malignancy (cancer)	Biopsy confirms presence of cancer before treatment begins

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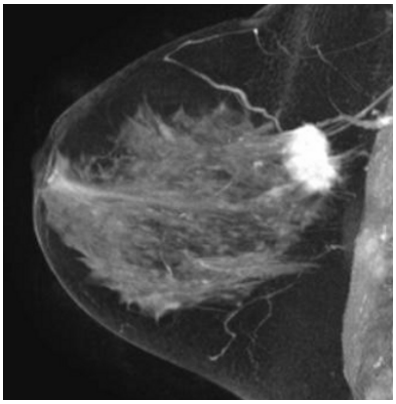
BREAST MRI

THE BASIC STRENGTH OF BREAST MRI LIES IN THE DETECTION OF CANCER THAT IS **OCCULT** ON CONVENTIONAL IMAGING SUCH AS MAMMOGRAPHY AND SONOGRAPHY

MAGNETIC RESONANCE IMAGING (MRI) IN BREAST CANCER SCREENING

THE PERFORMANCE AND CLINICAL USE OF BREAST MRI ARE NOW MUCH MORE DEFINED THAN SEVERAL YEARS AGO



BREAST CANCER SCREENING use of MRI

- Individuals with BRCA1 or BRCA2 mutation
- Individuals with a 1st degree relative of a BRCA1 or BRCA2 carrier- but have not been tested
- Individuals with a lifetime risk of breast cancer of >20%
- Individuals that have had radiation therapy to the chest between the ages of 10 and 30 years old
- Breast cancer in a male relative
- One first degree relative with bilateral breast cancer
- Individuals consider at high familial risk:
  - -Two or more first degree relatives with breast cancer **or**
  - - One 1st degree relative and two or more 2nd or 3rd degree relatives with breast cancer **or**
  - - One 1st degree relative with breast cancer before the age of 45 years and one other relative with breast cancer **or**
  - - One first degree relative with breast cancer and one or more relatives with ovarian cancer

MRI is not a screening technique for average risk patients

FUTURE SCREENING TOOLS

- Gene expression profiling
- Ductal lavage/ ductoscopy
- Blood markers for auto antibodies
- Electrical Impedance Scanning
- PET Scanning

Gene Expression Profiling

Using DNA microarrays; immunohistochemical markers have been used as biomarkers to identify altered cellular phenotypes.

By studying gene expression profiles of early lesions of the breast such as atypical ductal hyperplasia and ductal carcinoma in situ new biomarkers of risk and response may be identified.

Nipple aspirate fluid (NAF) can be analyzed for biomarkers or cellular atypia….

a technique pioneered by Dr. Susan Love

DUCTAL LAVAGE, DUCTOSCOPY, and
MOLECULAR ANALYSIS of DUCTAL FLUID

The majority of breast cancers originate in the breast duct system so evaluating this system visually with ductoscopy
or studies to evaluate the cells from the ducts may help detect transformation from healthy to malignant cells.

Breast cancer mortality rates have been declining since 1990 at an average rate of 2.3% with larger percentage declines in recent years