Breast Cancer Screening

Steven Stanten MD

Rupert Horoupian MD

AltaBates Summit Medical Center

Oakland, California

Breast cancer incidence and mortality

	Incidence	Mortality
	n	n
ENGLAND	34,176	10,846
FRANCE	35,726	10,811
GERMANY	48,098	17,692
Total EU	210,631	73,592
USA	211,300	39,800

Jemal A et al. CA Cancer J Clin 2003; 53: 5–26;
Cancer Research UK. Cancer Stats – Incidence & Mortality UK, April 2003;
Ferlay et al. IARC Press, 1999

Incidence

- USA - 2008
  - 184,450 new cases of invasive ca
  - 40,930 deaths
  - 3 decade increase
  - Wide spread screening
  - Increased dx of non-invasive and pre-malignant lesions

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

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

Signs and Symptoms

- The earliest sign is an abnormality that shows up on a mammogram before it can be felt by the woman or health care provider.
- Early stages of breast cancer usually do not produce symptoms.

Signs and Symptoms

- When breast cancer grows to the point where physical symptoms exist, these may include:
  - A painless mass (up to 10 percent of patients have breast pain and no mass).
  - Breast changes: thickening, swelling, and skin irritation or distortion.
  - Nipple changes: discharge, erosion, inversion, or tenderness.

Treatment

- Treatment

  - most successful when the cancer is detected early, before it has spread.

- Treatment

  -depends on the situation and the patient's choices.

- Surgery

  - Breast conservation surgery (lumpectomy) removes the tumor and surrounding tissue.

  - Mastectomy removes the breast.

Treatment

- Radiation therapy
- Chemotherapy
- Hormone therapy
- Monoclonal antibody therapy
- Often, two or more methods are used in combination with each other.

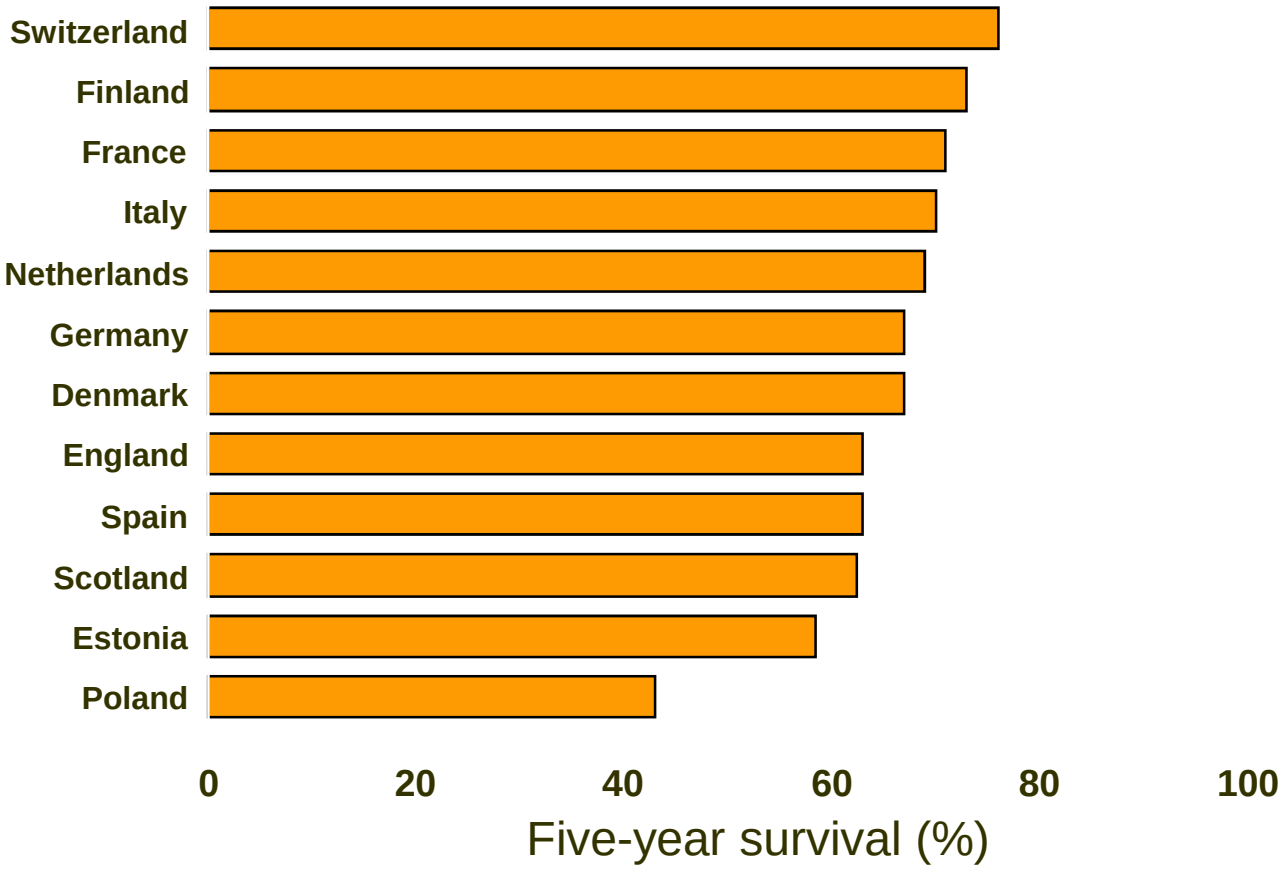
Mortality

- One in six diagnosed with breast cancer will die from it
- Directly related to stage of disease
- Varies according to geography, culture, ethnicity, race, and socioeconomic status

Deaths

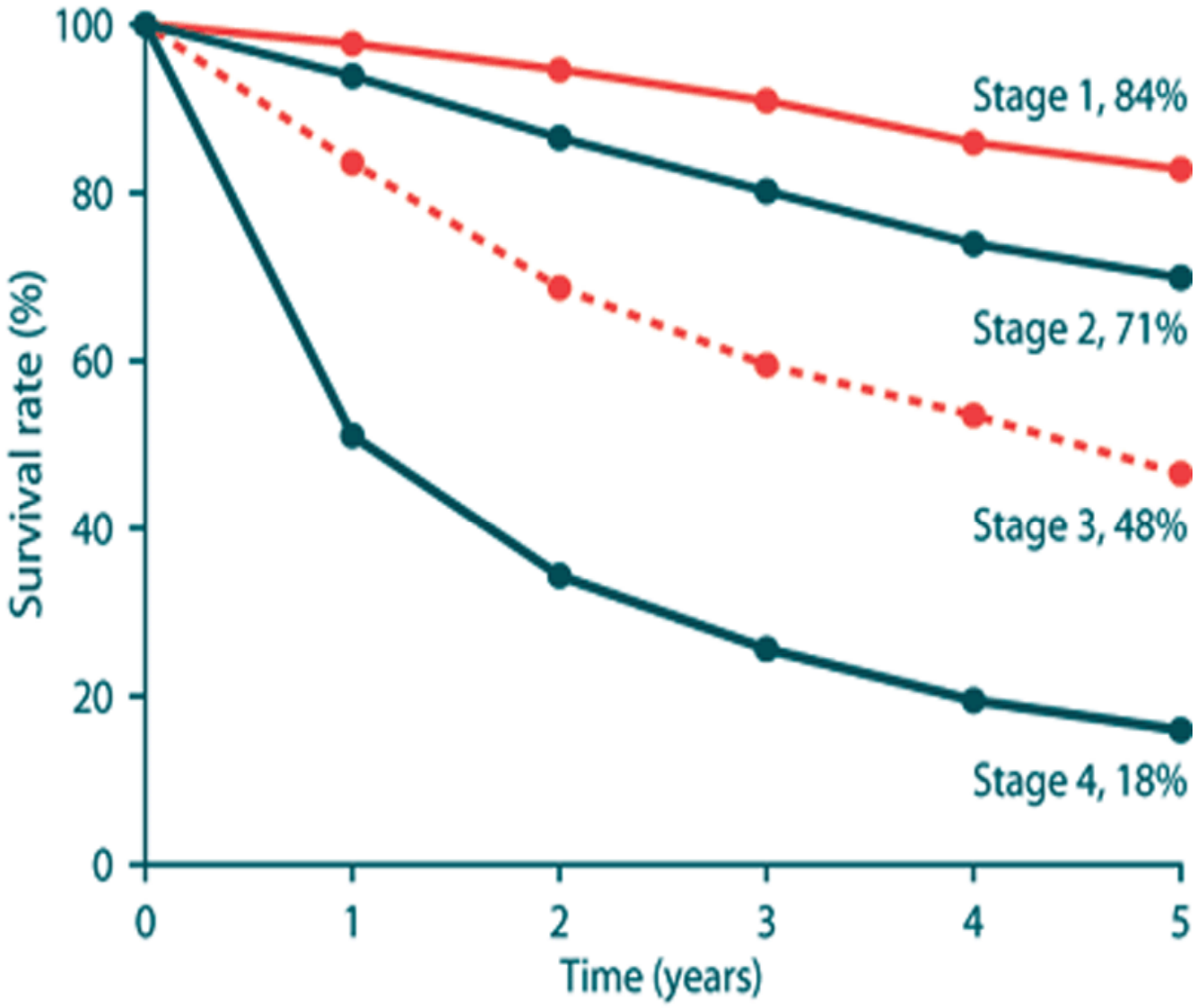
- An estimated 40,200 deaths will occur from breast cancer in 2003.
- More than 39,000 of these deaths will be among women.
- Only lung cancer accounts for more cancer deaths in women.

Survival



	5-year survival (%)	No. of patients
Switzerland	75.7	2,243
Finland	73.5	11,123
France	71.4	2,498
Italy	70.8	3,595
Netherlands	69.9	2,653
Germany	68.4	3,359
Denmark	68.1	17,498
England	62.5	60,390
Spain	62.5	1,043
Scotland	61.8	11,261
Estonia	58.8	2,387
Poland	43.9	1,089

J Nat Cancer Inst 1995; 87: 1209



Reference: Cancer Research Campaign Fact Sheet 6.2 (1991)

Survival

- Five-year localized survival rate.....97%
- Five-year regional survival rate.....78%
- Five-year distant survival rate.....21%
- Five-year overall survival rate.....86%
- Ten-year overall survival rate.....76%

Risk Factors

- Direct
  - Age
  - Family hx
  - Early menarche
  - Late 1st birth
  - Proliferative benign breast disease
  - Thoracic radiation

Risk Factors

- As age increases, so does risk. Of all the women with breast cancer, 77% are 50+ years old.
- Genetic risk factors/personal or family history.
- Early menarche (< 12 years) or late menopause (>55 years)
- Late age at first full-term pregnancy (> 30 years).

Risk Factors

- No children/not breast feeding = slight risk.
- Oral contraceptives use or hormone replacement therapy = slightly greater risk.
- Risks increase with alcohol consumption.
- Even moderate physical activity can decrease risk.
- Obesity = increased risk in post-menopausal women.

Risk Factors

- Associations
  - Radiographically dense breasts
    - Obesity
    - Alcohol intake
    - Menopausal hormone use

Risk Factors for Breast Cancer

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

Risk Assessment

- 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

Risk Assessment

- 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

Risk Assessment

- LIMITATIONS OF GAIL MODEL –

  MAY OVERPREDICT RISK IN PRE-MENOPAUSAL WOMEN WHO DO NOT ADHERE TO GUIDELINES FOR ANNUAL SCREENING

Risk Assessment

- 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

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

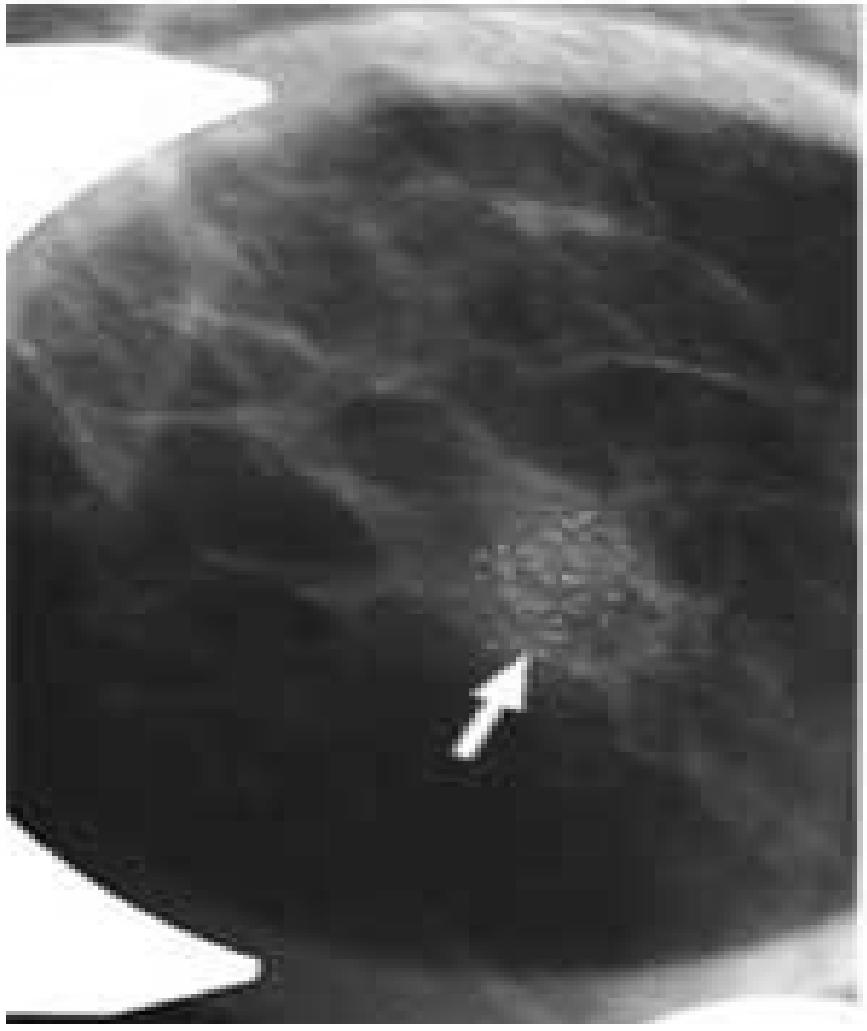
RCT

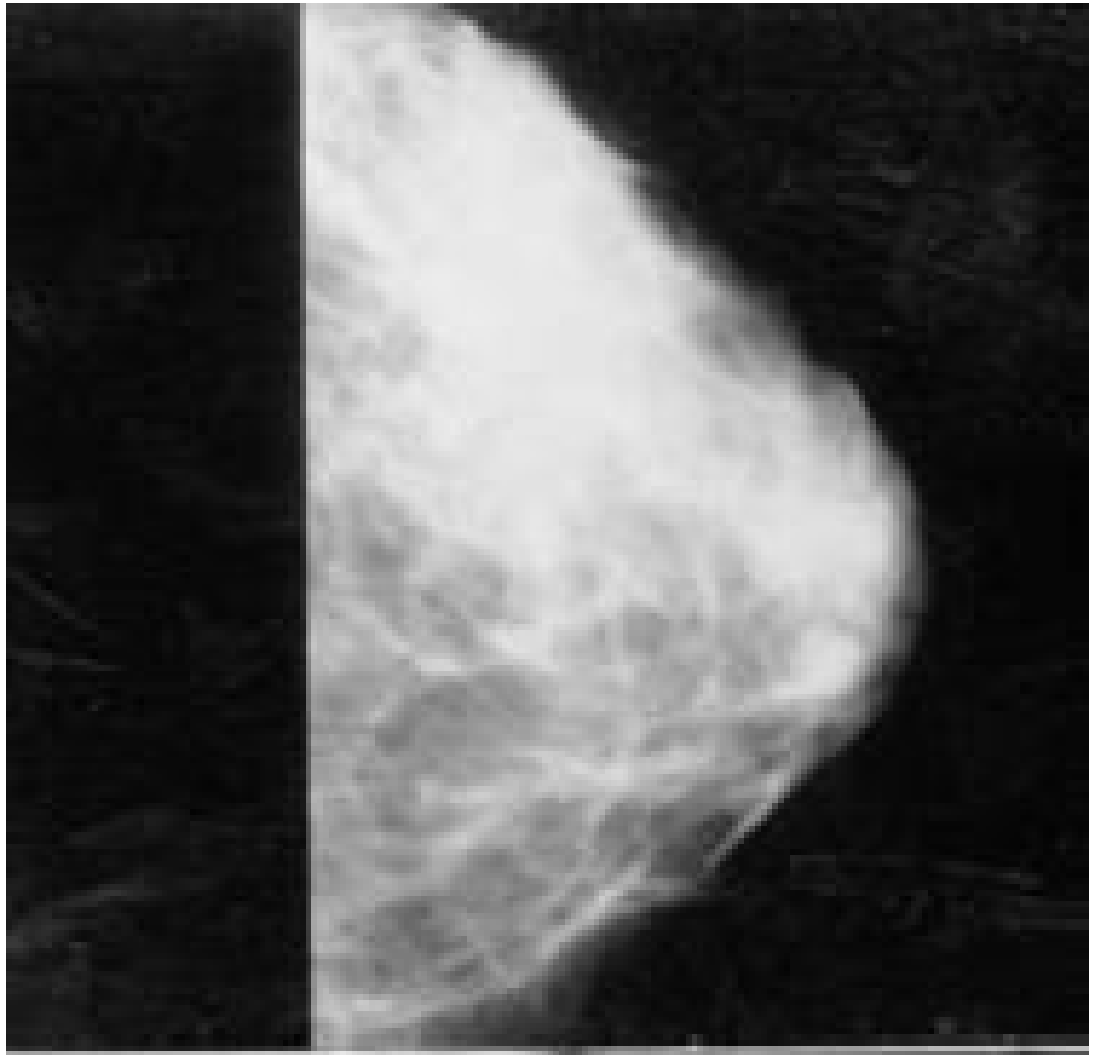
The statistical power of the RCT is crucial.

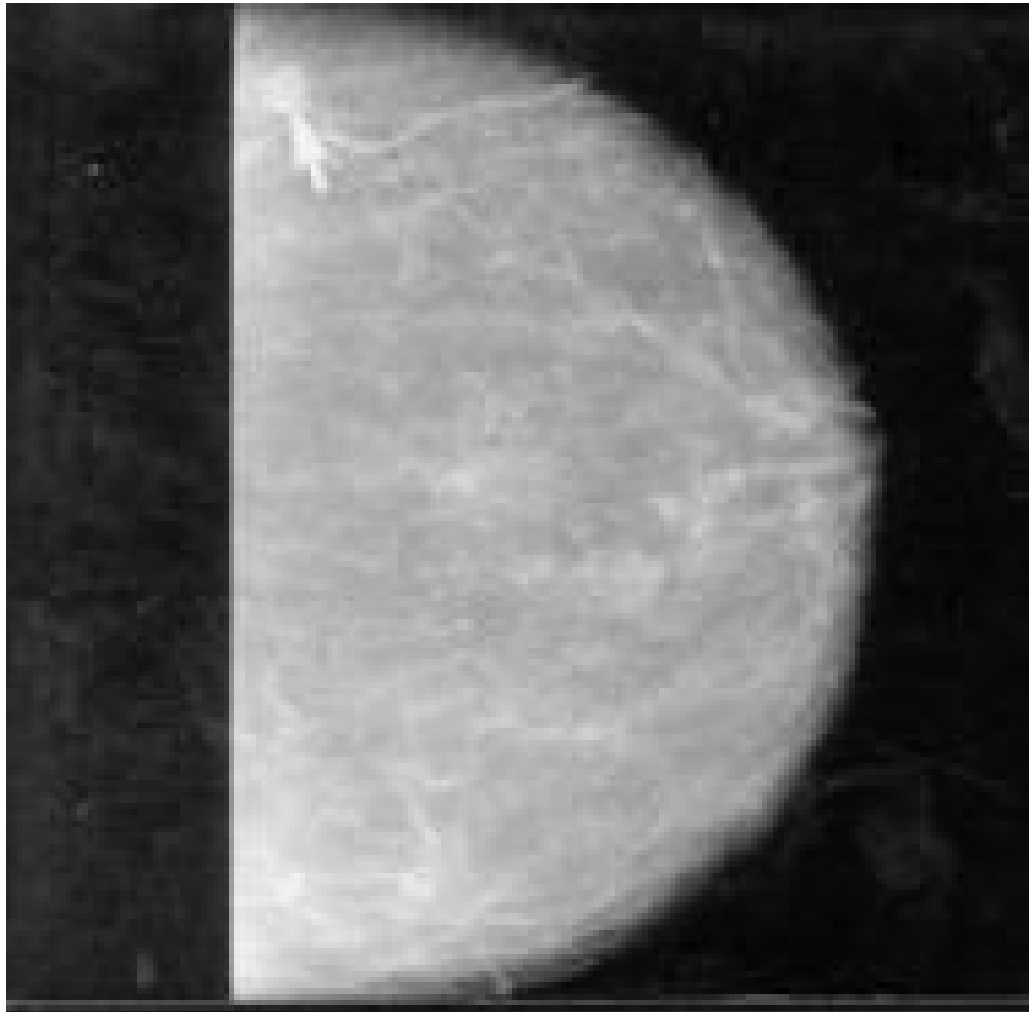
Screening

Current screening methodologies rely heavily on imaging with proof from RCTs

Calcifications







Screening

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

Sojourn Time

- The period of time during which a cancer is detectable by a test before it is clinically evident is called the ‘sojourn time’.

Sojourn Time

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

Screening Mammography

- Basic definitions
- Uses
- Specificity
- Sensitivity

Mammography

- Basics
  - Identify breast cancer too small to palpate
  - Identify non-invasive and pre-malignant lesions
  - Ionizing radiation
  - Medial-lateral oblique view
  - Cranial-caudal view
  - Nipple to pectoralis
  - FDA approved sites
  - Screen film vs. digital

Mammography

- Category Assessment Follow-up
- Breast Imaging Reporting and Database System (BI-RADS)

Mammography

- BIRADS
  - 0 – more info
  - 1 – normal
  - 2 – benign
  - 3 – probably benign
  - 4 – suspicious
  - 5 - malignant

Mammography

- Uses
  - Diagnose small, early stage breast ca
  - Favorable clinical course
  - Better cancer related survival
  - Interpreting studies has some biases
    - Lead-time bias
    - Length bias
    - Overdiagnosis bias
    - Healthy volunteer bias

Mammography

- CAD – computer aided diagnosis
  - -Aids radiologist in detecting abnormalities
  - -3 available commercial systems
  - -500 CAD systems in US

  Clinical Trial –

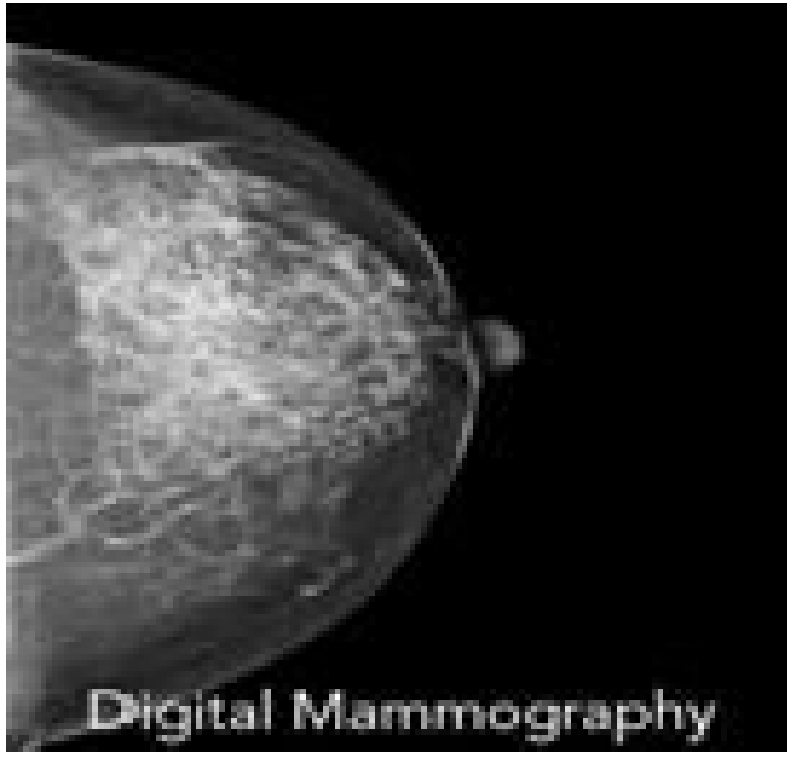
  Increase overall recall rate

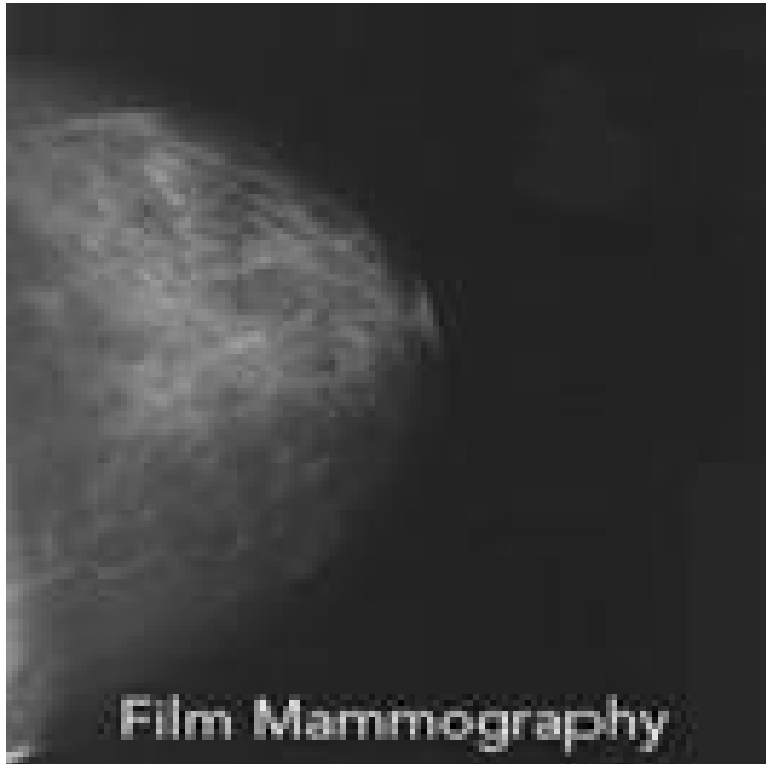
  Increase in # of detected cancers

Considerations in Choosing a Mammography Site

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

MAMMOGRAPHY
DIGITAL VS FILM





Mammography

- Specificity
  - Likelihood of test being normal when cancer is absent
    - We want this high
    - If low then false positives lead to unnecessary tests.
    - Exceeds 90%
    - BIRADS categories

Mammography

- Sensitivity
  - Proportion of breast cancer detected when cancer is present
    - Lesion size
    - Lesion conspicuity
    - Breast tissue density
    - Patient age
    - Hormone status of tumor
    - Image quality
    - Skill of radiologist

Mammography

- Sensitivity

  Overall 75%

  54-58% in age <40

  81-94% in age >65

Mammography

- Factors influencing Specificity and Sensitivity
  - Radiologist interpretation
  - High breast density
  - Centralized screening systems
  - National QA programs
  - Interval between mammograms
  - Post-menopausal hormone use
  - Prior breast surgery
  - BMI

Mammography

- Evidence of Benefit
  - Randomized controlled studies
  - 4 countries
  - 500,000 women
  - 9 studies
  - Different designs
  - Effect on mortality
  - Conflicting results

Mammography

- Harms of screening
  - False negatives
  - False positives
  - Radiation exposure
  - Anxiety
  - Over diagnosis

Mammography

Cochrane Review

- Review of 7 trials
- Screening mammography likely reduces breast cancer mortality
- magnitude uncertain
- ~20% reduction – or 15% relative risk reduction
- screening leads to over diagnosis and over treatment

Mammography

- For 2000 women invited to screening for 10 years
  - 1 will have her life prolonged
  - 10 will be treated unnecessarily
  - Conclusion – “It is thus not clear whether screening does more good than harm. Woman invited to screening should be fully informed of both benefits and harms.”

UTZ

- As adjunct to mammography
- Inexpensive
- Widely available
- Targeted evaluation
  - Solid vs. cyst
  - Benign vs. malignant

UTZ

- Image guided biopsy
- Limited screening use
  - Needs a skilled operator
  - Lack of standard exam techniques
  - Lack of standard interpretation criteria
  - No microcalcifications

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

Background: What is MRI?

- Uses magnetic fields to produce detailed cross- sectional images of tissue structures
- Uses injected contrast agents to distinguish fat, glandular tissue, lesions, etc. in the breast
- Different factors contribute to the measured signal that determines the brightness of the tissues in the image
- Contrast agent provides reliable detection of cancers and other lesions.
- Screening MRI requires appropriate techniques and equipment (including dedicated breast MRI equipment) and experienced staff

MRI

- MRI is not a screening technique for average risk patients

MRI

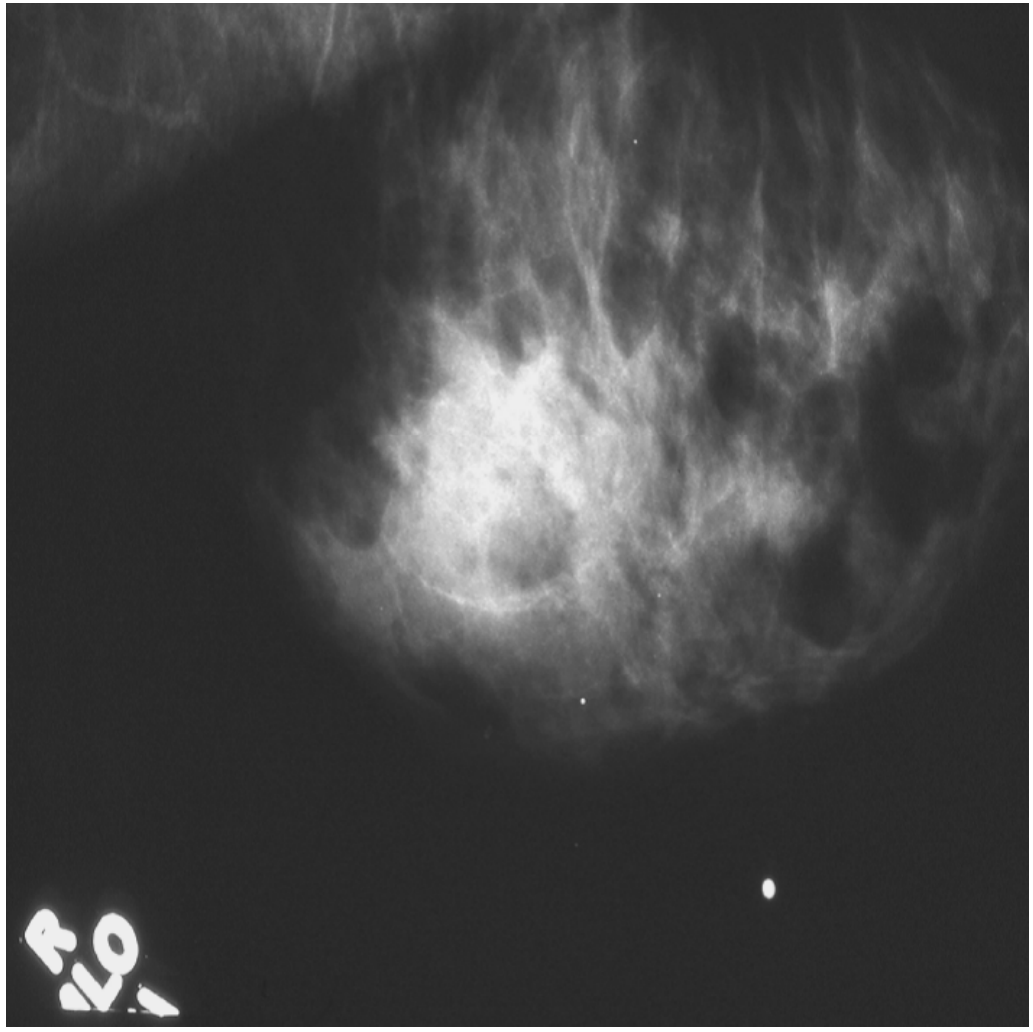
- With IV gadolinium
  - 83-100% sensitive with cancer above a few mm
  - Average 96% sensitive

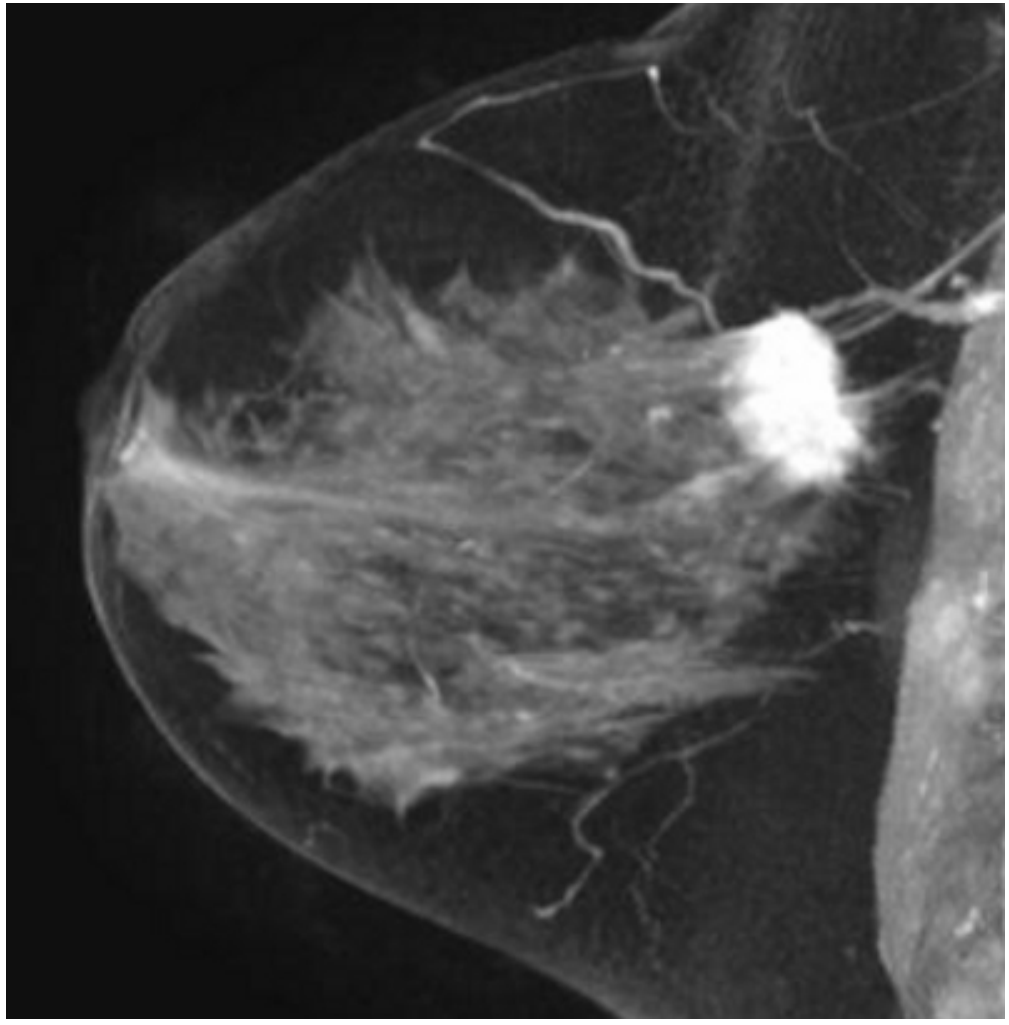
MRI

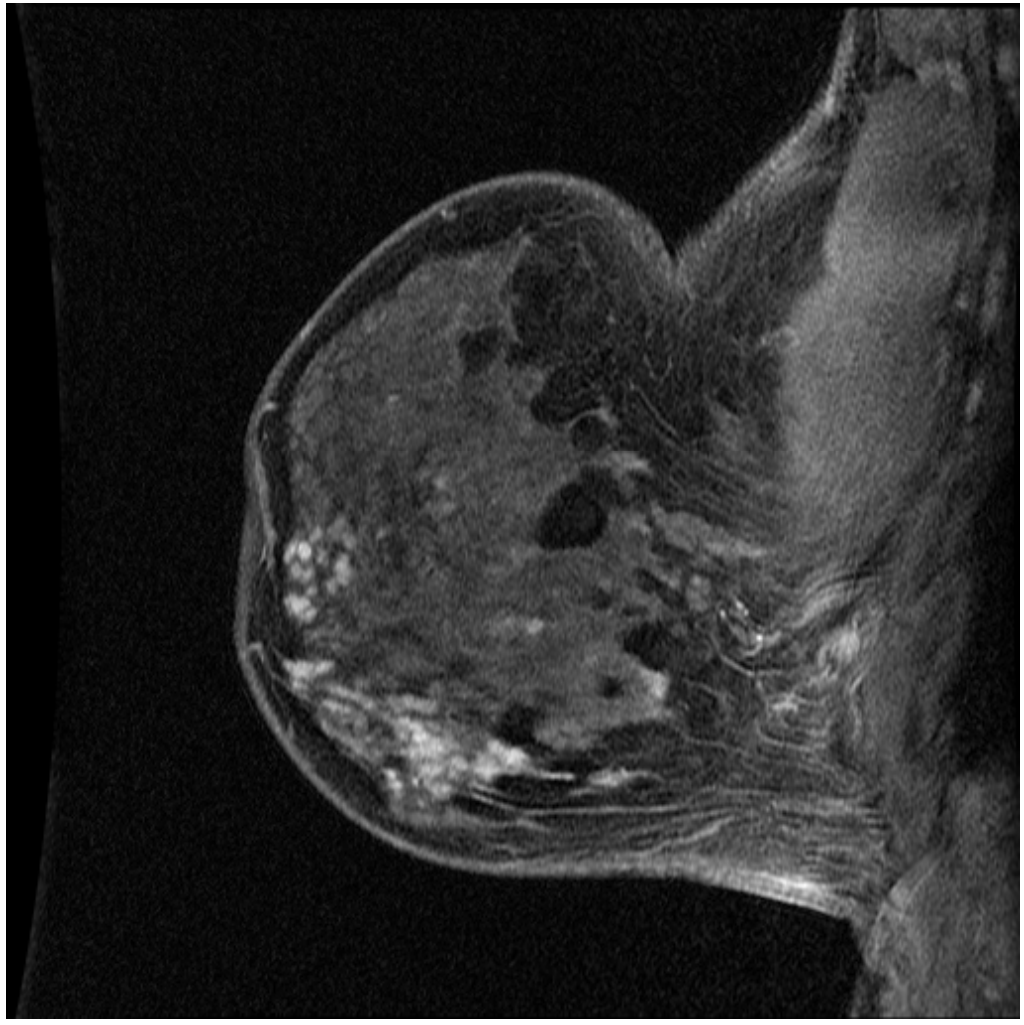
- Pros and cons
  - Cost
  - Lack of standard exam
  - Lack of standard interpretation criteria
  - No micro Ca++
  - Variability of equipment
  - Increase in false + rate
  - Availability of equipment

MRI

- Sensitivity - 71-100%
- Specificity - 37 - 97%
- Not recommended for screening
  - Breast implants
  - Masses after surgery or XRT
  - Occult lesions with metastasis
  - Pre-operative planning?







Rationale

- New evidence supporting MRI screening
- Ability of MRI to detect cancers is much higher (double) than mammography
- MRI plus mammography detects more cancers than MRI alone
- High false positive rate of MRI makes it inappropriate for screening women at average risk
- Strong evidence for MRI screening of women at increased risk based on family history/genetics
- Insufficient evidence to recommend for or against MRI screening of women at moderately increased risk based on clinical factors
- Insufficient evidence for other technologies

Limitations and Potential Harms

- False negatives
- False positives
- Anxiety, psychological distress
- More call-backs
- More biopsies
- Cost
- Limited access to high quality MRI screening and MRI-guided biopsies
- Variation in performance, interpretation, recall rates, and expertise
- Little or no data on recurrence, survival rates, age, when to start and stop screening, screening intervals
- Variation in insurance coverage

BREAST CANCER SCREENING WITH 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

Other modalities

- Not FDA-approved for screening
  - Ductoscopy/ductal lavage
  - Tomography
  - Scinitimammography
  - PET
  - Elastography
  - Spectroscopy
  - Optical imaging
  - Electrical impendence measurements
  - Thermography
  - Etc.

Ductoscopy/Lavage

- 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.

Ductal Lavage

- Asymptomatic women
- High risk
- Use alone or in combination with mammography

High Risk Patients

- Identify High Risk patients

  2 or more relatives with breast or ovarian ca

  Breast ca before age 50 in a relative

  Male relative with breast ca

  Genetic profiles

  Chest radiation

Who is at High Risk?

- Three approaches:

#1 - Family history suggestive of inherited gene mutation; risk is calculated by assessment models/tools

#2 - Genetic testing for mutation in BRCA1/2, TP53, or PTEN

#3 - Review of clinical history
- Treated for Hodgkin disease
- LCIS, ALH
- ADH, DCIS
- High mammographic density
- Personal history of breast cancer

High Risk

- Screening options

  Initiate screening at age 30

  Shorter intervals

  MRI

  UTZ

  Insufficient evidence exists

High Risk

- Who is at high risk?
- Family History
- Clinical Indicators
- MRI screening studies
- Evidence of efficacy
- Benefits, limitations, and potential harms

Evidence

- Since the 2003 guideline, at least 6 prospective, non-randomized studies were conducted, in 6 different countries
- All studies measured benefit of adding annual MRI to mammography
- All study participants had either a BRCA mutation or a strong family history
- Some studies included women with a personal history of breast cancer
- Some studies also included ultrasound and/or CBE
- All 6 studies reported significantly higher sensitivity for MRI compared to mammography (and US, CBE), and lower specificity (i.e. more false positives)

High Risk

- Current ACS Recommendation for Women at Increased Risk for Breast Cancer (2003)

-In the absence of sufficient evidence to recommend specific screening strategies that might benefit women at increased risk, options are provided:

-earlier initiation of screening (30 years or younger)

-the addition of MRI and/or Ultrasound to screening mammography and physical examination.

Early Detection

- There is no certain way to prevent breast cancer.
- The best plan for women at average risk is to follow the American Cancer Society guidelines for early detection.
- Nine out of 10 women can survive breast cancer simply by detecting it early

Bottom Line

- Age and gender are the main risk factors.
- Early detection increases survival and treatment options.
- All women 40+ should talk to their doctors about annual mammograms and CBEs. They can also perform monthly BSEs.
- Mammograms can save lives.

Early Detection/Guidelines

- Age 40+: Annual mammogram, annual clinical breast exam (CBE) by a health care professional, and an optional monthly breast self-exam (BSE).

- Ages 20-39: Every three years a CBE by a health care professional and an optional monthly BSE.

- Women with a family history of breast cancer should talk to their doctor about when to start screening

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%.