Screening Mammography:

Exploring the impact of the USPSTF recommendations

Susann E. Schetter, DO,
Chief, Division of Breast Imaging, Department of Radiology
Penn State Hershey Medical Center
Co-Medical Director, Penn State Hershey Breast Center

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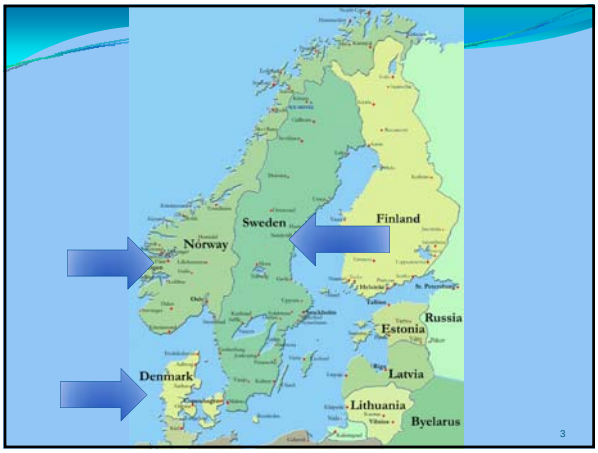

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- Who is the USPSTF?
- What were the recommendations, why?
- How does this impact women's health?
- What has been the impact of screening mammography on breast cancer?
- What is recommended by Breast Disease specialists and why?
- What are the strengths and weaknesses of screening mammography?
- What other tools are available to identify breast cancer at earlier stages?

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USPSTF

- Independent panel of non-government experts, first convened in 1984.
- Since 1988 sponsored by the Agency for Healthcare Research
- Mission: evaluate the benefits of individual services based on age, gender and risk factors for disease and make recommendations about which preventive services should be incorporated routinely into primary medical

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USPSTF

- 16 primary care physicians and public health specialists
- Supported by the Evidence Based Practice Center
  - Institutional partners in US and Canada

No Breast Disease experts.

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November, 2009

- USPSTF recommends:
  - Screening every 2 years for women ages 50 – 74 (Grade B)
  - Finds that there is no evidence to screen routinely before age 40, recommends individual decision based on person's values regarding specific benefits and harms (Grade C)
  - Current evidence insufficient to assess additional harms and benefits of screening over age 75 (Grade C)
  - Current evidence is insufficient to assess additional benefits and harms of CBE
  - Against teaching self breast examination (Grade D)

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Rationale

- "Breast cancer is the second-leading cause of cancer death among women in the United States. Widespread use of screening, along with treatment advances in recent years, have been credited with significant reductions in breast cancer mortality."

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USPSTF

- Life yrs. gained vs. # mammograms/1000 women
- looked at 6 "best" models: Life-years Gained
- Results: For 25,000 mammograms/1000 women (this is the increase in number from biennial to annual)
  - Average Life-years Gained = 79 years
  - Proportional increase in Life-years = 72%

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USPSTF Recommendations

- Acknowledge a statistically significant 15% reduction in mortality from breast cancer in women 40 – 49 yrs.
- State that the "harms" associated with screening: anxiety, false +, need for additional testing, possibility of overdiagnosis and treatment outweigh the benefit.
- Women should consider their personal risk before entering into screening.

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USPSTF recommendations

- Bad timing and poorly communicated
  - Politicians and public assumed it was a result of new Healthcare Reform bill.
  - Chair, "meant to say that limited clinical evidence supports the test for women younger than 50."
- Social Media - irresponsible
- Lasting Effects
  - Healthcare reform Bill AND many states coverage use USPSTF grade A and B recommendations to guide reimbursement
  - DHHS Secretary Kathleen Sebelius states that she could use her authority to require plans to cover treatments with lower grades.

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- Dr. Ned Calonge, Chairman of the Preventive Services Task Force:
  - "If I take 1,000 women age 40, over their lifetimes, 30 of them will die from breast cancer if we do no screening," he says. "If I screen every one of those women beginning at age 50 until she's 74, we reduce the deaths from 30 to 23. And if I reach down and screen them in their 40s, I can increase that by one additional life saved — at best." (NPR Interview, Monday, October 11, 2010)
- US population: 308.4 million - 80 million women eligible for screening (estimate)
- Total lives saved per million = 7,000 or 8,000 if screening > age 40.
- Total lives saved per 80 million = 560,000 or 640,000 lives saved
- Start screening at 40 = save an additional 80,000 lives
- Reading pop. 81K, Bethlehem pop. 73K, Scranton pop. 72K, Lancaster pop. 55K

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USPSTF Recommendations

- Ignoring fact that '50' has no meaning
- No direct evidence that screening women based on their individual risk factors would have same impact on mortality
  - **NONE of the RCT's randomize women according to risk**

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USPSTF recommendations

- Confusion for patients
- Challenges physicians
  - Valuable counseling – not reimbursed
  - Primary care physicians

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Fallout of USPSTF

- "Women cancel appointments in wake of recommendation"
- Several states discontinue support for coverage of mammograms for women ages 40 - 49

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- **AAFP, Others Defend USPSTF, Breast Cancer Screening Recs in Letter to HHS**
  - May 26, 2010
  - …level C recommendation, which means that although the USPSTF recommends against routinely providing the service and there is at least moderate certainty that the net benefit is small, there may be considerations that support providing it in an individual patient.
  - …false-positive results are more common among women ages 40-49 than those in older age groups.
  - task force's statement was published Nov. 17 in the *Annals of Internal Medicine*. The same issue includes a study that concluded that biennial screening intervals "are more efficient and provide a better balance of benefits and harms than annual intervals."

Confused?

What is the goal of breast cancer screening?

- Reduce deaths due to breast cancer by detecting them early, when treatment is more effective and less harmful
- Palpable lumps – larger, greater likelihood of node positive disease or distants mets (especially true in pre-menopausal women)

How good is my mammogram?

- How do we measure quality?

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BCSC

- Sensitivity represents the proportion of women who truly have breast cancer who have been identified as such by a positive mammogram (“true positives”).

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BCSC

- Specificity represents the proportion of women who truly do not have the disease who have been identified as such by a negative mammogram (“true negatives”).

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BCSC

- Positive predictive value (PPV) represents the likelihood that a woman has breast cancer, given a positive mammogram.

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BCSC

- Recall rate represents the proportion of women who are recommended for further follow-up evaluation because of an abnormality detected in a mammogram.

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BCSC

- Cancer detection rate represents the proportion of mammograms in which cancer is found through a positive mammogram among all women undergoing mammography.

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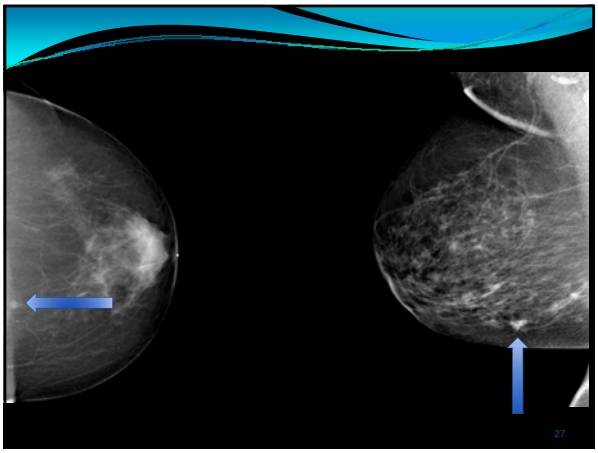
Screening goals

- Mean tumor size when screen detected (high quality 2 view mammo) is 1.0 – 1.5 cm

- 10% of invasive cancers 1 cm or smaller have spread to nodes
- 35% of cancers 2 cm in size
- 60% of tumors 4 cm

Screening goals

- 2 cm or smaller cancers – Stage I has a 5 year survival rate of >98%



Mammography is the mainstay of screening for the detection of clinically occult disease

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	Number of screening mammography examinations[1]	Number of cancers[2]	Cancer rate (per 1,000 examinations)[3]	Cancer detection rate (per 1,000 examinations)[4]
Total	3,884,059	19,146	4.92	4.00
Age 40-44	534,324	1,260	2.35	1.69
Age 45-49	625,930	2,146	3.42	2.60
Age 50-54	677,991	2,755	4.06	3.23
Age 55-59	552,900	2,811	5.08	4.20
Age 60-64	426,096	2,477	5.81	4.70
Age 65-69	365,536	2,300	6.29	5.25
Age 70-74	313,809	2,227	7.09	5.95
Age 75-89	387,473	3,170	8.18	6.96

Breast Cancer Surveillance Consortium, NCI, NIH

Mammography at age 40

- Randomized control trials in Europe and NA including nearly 500,000 women.
  - Overall – 26% reduction in mortality
  - study of women "invited" to screening - does not imply compliance

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Mammography at age 40

- More recent studies show greater benefit
  - Duffy et al – 39% reduction in breast cancer mortality compared to period before advent of screening.
    - 75% of this reduction due to screening and early detection.

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Screening Mammography

- NEJM, Kalager, et al. Compared breast cancer death rates for women who are screened vs. those not screened. New Eng J Med 2010. 363:1203-1210

  Title: Effect of Screening Mammography on Breast Cancer Mortality in Norway.

- Conclusion: The availability of screening mammography was associated with a reduction in the rate of death from breast cancer, but the screening itself accounted for only about a third of the total reduction. (Funded by the Cancer Registry of Norway and the Research Council of Norway.)

  Followup: Mean 2.2 yrs. Maximum 8.

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Screening Mammography

- **Swedish Study** – looks at the screening data from the entire country.
  - 16 yrs of average followup
  - Addressed the 40 – 49 age group (not offered screening in Norway)
    - Death rate decreased by 29% for women in their 40's who actually HAD mammograms

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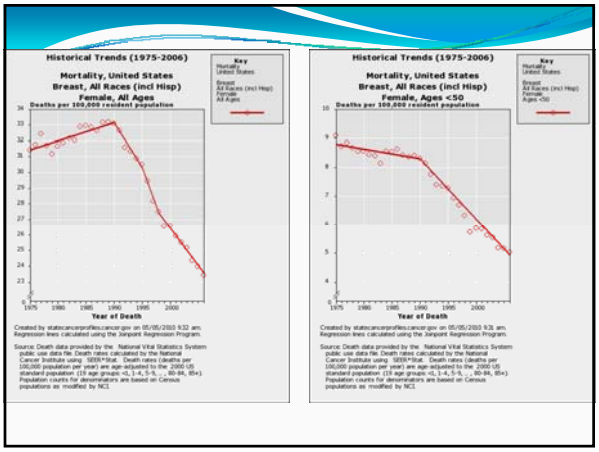

What's the risk?

- For a woman in her 40's – 1 in 69 will be diagnosed with Breast Cancer
- Incidence increases with age
- Incidence is very low in under 30 yr olds.

Mammography at age 40

- MGH - retrospective review of breast cancer deaths (extrapolated to 2009)
- 192,370 Invasive cancers expected
  - 25% deaths in 80% screened = 4.7% mortality
  - 75% deaths in 20% unscreened = 56% mortality

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QUIZ!
Those advocating screening at age 50 assume:

1. Age 50 is a surrogate for menopause
2. Women at that point are too weak to fight back
3. There is a mysterious biologic switch that flips at age 49

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Age 50?

- Originally chosen by researchers as a surrogate for menopause
- RCT's did not have statistical power to allow for subgroup analysis of the 40 – 50 yr. group
- Data actually show that the same benefits exist for the 40 – 49 yr. women.

Kopans DB. Informed decision making: age of 50 is arbitrary and has no demonstrated influence on breast cancer screening in women. AJR Am J Roentgenol 2005;185:177-82.

Kopans DB, Moore RH, McCarthy KA, et al. Biasing the interpretation of mammography screening data by age grouping: nothing changes abruptly at age 50. Breast J 1998;4:139-45.

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Annual vs. Biennial screening

	Yearly 10 - 14 mo interval	Every 2 years 22 - 26 mo interval
Screen detected Invasive Cancer	84%	74%
Mean Diameter	12.6 mm	15.4 mm
Median diameter	10.0 mm	13.0 mm
+ nodes	13%	17%
Stage > or = 2	15%	21%
Interval Invasive Cancer	16%	26%
Mean diameter	17.1 mm	25.4 mm
Median diameter	15.0 mm	23.0 mm
+ nodes	20%	40%
Stage > or = 2	30%	60%

Hunt, Rosen, Sickles *AJR* 1999

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In the US

30% decrease in Breast Cancer mortality since 1990

no change in the mortality for 50 yrs prior

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Mammographic screening should begin at age 40.

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QUIZ!

The majority of women who develop breast cancer:

1. Have at least one family member with the disease
2. Have had a prior benign biopsy
3. 70 – 80 % have no identifiable risk factors
4. Are nulliparous
5. Have early menarche and late menopause

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- Risk factors have been identified
- Most women (70% - 80%) that develop Breast cancer have **NO** identifiable risk factors

- Main risk factors:
  - **Being a woman**
  - **Getting older**

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What are the facts about the "harms" of screening?

- For every 1000 women screened – approx 100 (76 at PSHBC)
- few extra images, possible ultrasound
- Nothing wrong in over half
  - these are the false + studies
  - some may return in 6 months
  - 15 require biopsy
  - 5 will have cancer

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National Consortium of Breast Centers

- quality of life has significant value, not just survival
- Discontinuation of screening in women 40 - 49 will result in larger cancers, more aggressive surgery and more chemotherapy
- Lives will be at risk if recommendations are implemented

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Breast Cancer rates continue to increase

- *USPSTF statement*
- "Widespread use of screening mammography has been the mainstay of breast cancer prevention in the US for the past 25 years"
- Be careful to discuss this intelligently - Screening mammography does not PREVENT cancer!!!!!

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one size does not fit all

- modifications to screening protocols SHOULD be based on risk
- Women of significantly higher risk will require a different schedule for screening.

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Mammography's weakness?

- 20 – 30% of breast tumors are found during the time interval between regular screenings.
  - Technical
  - Interpretive error
  - Some have aggressive biology

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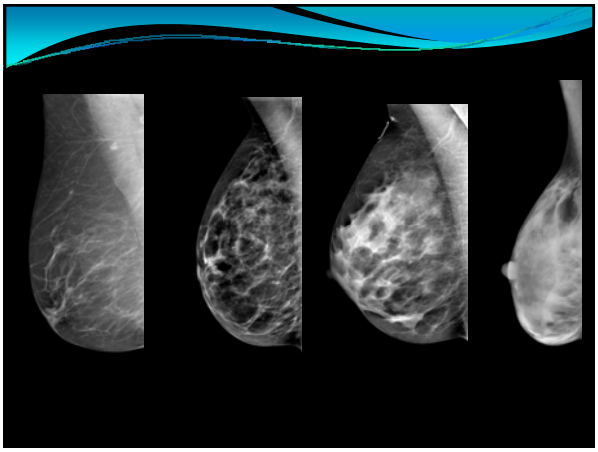
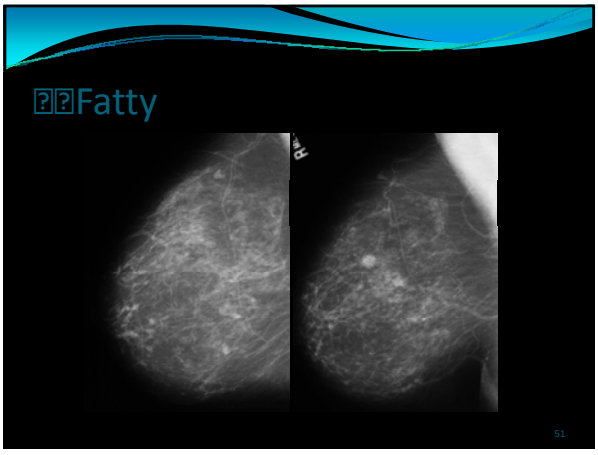


??Fatty



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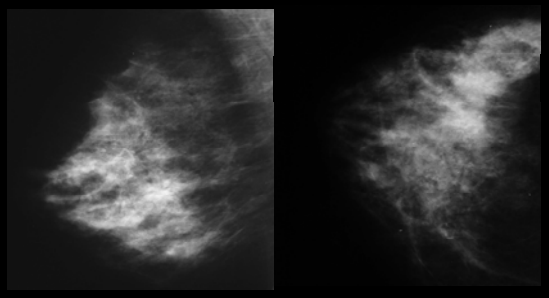
Dense



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Group Health Cooperative: mammography failures…

- In women:
  - Under 50 yrs
  - Increased breast density
    - ?effect of Digital mammo
- Tumors with:
  - Mucinous histology
  - High proliferation
  - Aggressive features (receptor -)

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Increasing the potential of screening

- matching mammography to Breast cancer **Biology**

Age	Sojourn Time	% progression Grade 1,2,to 3	Proposed schedule
40 - 49	2.46 yrs	47%	q 6 mo
50 - 59	3.75 yrs	12%	q year
60 - 69	4.23 yrs	15%	q 2 yrs
> 70	?	?	q 3 yrs

Data from Tabar 54

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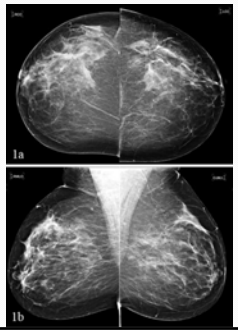
Increasing the potential of screening



imagingeconomics.com/issues/articles/2005-12_04

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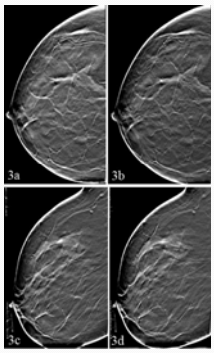
Digital breast tomosynthesis



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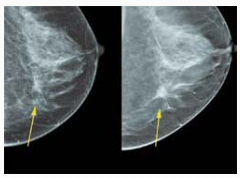

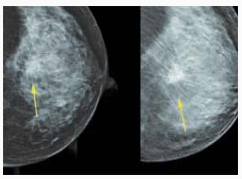

european-hospital.com, 2/29/2008

What about women of increased risk for developing breast cancer?

QUIZ!

Women with a first degree relative with BRCA1 or BRCA 2 mutations or 20% chance of developing Breast Cancer should be screened:

1. With MRI
2. Mammograms starting at age 40
3. Ultrasound starting at age 30
4. 1 & 2
5. All of the above

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- No data to support optimal screening in high risk women
- recommendations are based on CONSENSUS opinions of the fellows of the SBI and members of the ACR Breast Imaging Commission

60 60

Recommendations for women with 20% risk of developing breast cancer:

mammographic screening annually starting at age 30,

but not before age 25.

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For women of **significant elevated risk** of malignancy (and their physicians):

- Appropriate experts in breast cancer genetics or high risk management should be consulted

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recommendations

Women with mothers or sisters with PRE menopausal breast cancer

yearly, starting at age 30, not before age 25, or 10 years earlier than the age of the diagnosis of the youngest affected relative - whichever is later.

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Women with history of biopsy proven **lobular neoplasia** (lobular carcinoma in situ (LCIS) and **atypical lobular hyperplasia** (ALH), **atypical ductal hyperplasia** (ADH), **ductal carcinoma in situ** (DCIS), **invasive breast cancer or ovarian cancer**

- **yearly, REGARDLESS OF AGE**

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QUIZ!

Women who should begin screening prior to age 40 include:

1. women with mothers and sisters with BRCA mutations.
2. women with history of biopsy histology of ALH, ADH or LCIS
3. women with history of mantle radiation
4. a and c
5. all of the above

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Special circumstances

- Women with history of breast cancer and breast conservation therapy
- Recurrence rate 0.5 - 1% per year
- Risk for all women with hx of Br cancer - any age, of developing second cancer is 5 - 10% in the first decade after their diagnosis
- Recommendation: Annual

66 66

Special circumstances

- Women with history of ovarian cancer have a 3 - 4 fold increased risk for the subsequent development of breast cancer
- Recommendation: Annual screening from the time of diagnosis

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Special circumstances

- Mediastinal radiation - scatter to the breasts increases risk of breast cancer development
  - Largest group: Hodgkins
    - one study - 35% of all treated pts. developed breast ca by age 40
  - relative risk: 4 - 75 times - higher end when radiation is delivered between 10 - 30 yrs of age
  - As early as 10 yrs. following cure for Hodgkin's -
  - Recommendation: 8 - 10 years after treatment, but not before age 25.

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Special circumstances

- Genetic mutations - rare
  - PTEN - associated with Cowden's syndrome
  - tumor suppressor gene
    - CS: multiple non-cancerous tumors, hamartomas
    - usu assoc with skin and mucous membranes (oral and nasal mucosa and GI tract)
  - BRCA I - 19% risk of malignancy by age 40, lifetime risk as high as 85%
  - BRCA2 - similar lifetime risk, but develops later

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high risk screening

- Risk assessment models
  - Gail, Claus, Tyrer-Cusick, BRCAPRO, Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BODAICEA)

When do you stop recommending mammography?

- Life expectancy less than 5 – 7 yrs based on comorbidities and age
- Results of screening would not be acted upon

>74 yrs

- sensitivity and PPV of mammo in diagnosing breast cancer increases with increasing age
- >690,000 women aged 66 - 79 yrs
  - incidence of metastatic breast cancer decreased by 43% in screened population.

Smith-Bindman R, Kerlikowske K, Gebretsadik T. Is screening mammography effective in elderly women? Am J Med 2000;108:112-119.

>74 yrs

- Women of average health aged 75 - 79 yrs is approximately 10 years,
- nearly 8 yrs for women aged 80 - 84
- 6.6 yrs for women aged >85

- morbidities must be considered
- woman's interest in continuing screening should also be taken into account - implies interest in undergoing treatment for disease.

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>74 yrs

- Recommendations: woman has a life expectancy of 5 - 7 yrs on the basis of age and health status
- is willing to undergo additional testing including biopsy
- would be treated for cancer if diagnosed

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Screening with MRI

- Women with highest risk
- ACS recommendations - endorsed by the College of Breast Surgeons, SBI

- Many prospective studies: all suggest higher sensitivity
- Recommendation: Annual if lifetime risk is >20%

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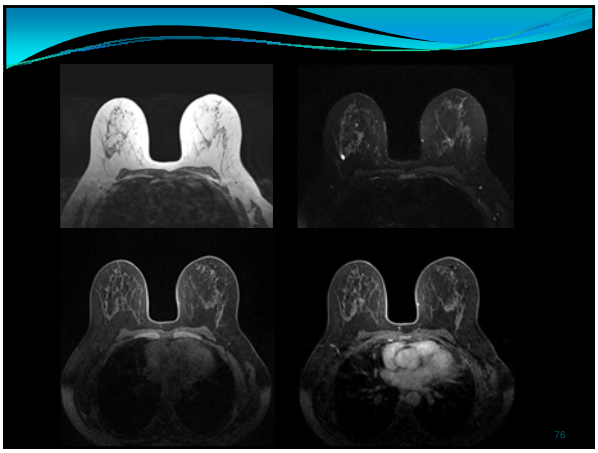

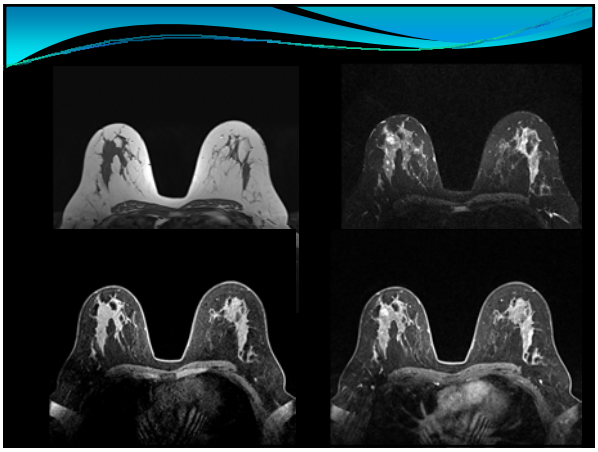

Screening with MRI

- Highest sensitivity for the detection of occult cancer
- Recommended in conjunction with annual Screening mammography for women with >20% lifetime risk for development of breast cancer.

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MRI screening

- Adds considerable cost
- BRCA 1 mutation carriers –
  - Increases costs by $50K per cancer
  - Also as women with decreasing risk undergo MRI, will increase False + biopsy rate

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MRI screening

- Screening for high risk biopsies has not yet been recognized as useful
  - Not recommended for or against by ACS
  - Individual clinical decision
- Screening with MRI – Inappropriate for women with less than 15% life time risk
  - Tyrer-Cusick , etc.

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Screening with Ultrasound

- Incremental cancer detection rate of 2.8 to 4.6 cancers per 1,000 women
- ACRIN 6666 – multi-institution
  - Women with dense breasts and also those with increased risk of breast cancer.
  - Results similar to single institution studies 4.2 per 1000 patients scanned.
  - All small invasive cancers, node negative

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Screening with Ultrasound

- More attention to screening of women with dense breasts
- Most studies have reported high false + rates
  - Dedicated breast imagers, with standard protocol, positive biopsy rate 8.8% -
    - 6.7% if cyst aspirations are included.

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Ultrasound screening as an adjunct to mammography

- Can be considered in:
  - High Risk women in whom MRI would be recommended, but not feasible.
  - Dense breast tissue

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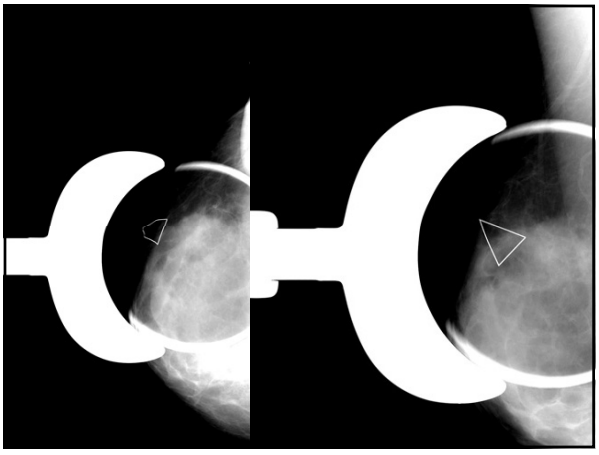

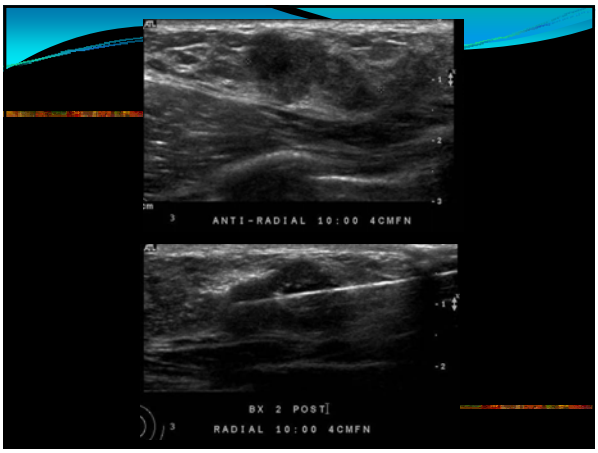

Screening with Ultrasound

- Adds no additional benefit over mammo + MRI in high risk women
- Difficult to imagine feasibility of widespread screening with US
  - Reproducibility
  - High false + rates
  - Low PPV
  - Operator dependency
  - Inability to image DCIS

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USPSTF

- Kathleen Sebelius
- August 2010 – reverted back to the 2002 recommendations:

"The USPSTF recommends screening mammography for women, with or without clinical breast examination, every 1-2 years for women aged 40 and older."

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ACS Recommendations

- For women of Average Risk:

- Yearly mammograms are recommended starting at age 40 and continuing for as long as a woman is in good health
- Clinical breast exam (CBE) 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 look and feel and report any breast change promptly to their health care provider. Breast self-exam (BSE) is an option for women starting in their 20s.

Thank You

sschetter@psu.edu

Susann E. Schetter, DO,
Chief, Division of Breast Imaging, Department of Radiology
Penn State Hershey Medical Center
Co-Medical Director, Penn State Hershey Breast Center

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