



Beth Israel Deaconess  
Medical Center

A TEACHING HOSPITAL OF HARVARD MEDICAL SCHOOL



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# Recurrence Surveillance in Breast Cancer Survivors

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# Agenda

- Patient
  - Presentation
  - Radiological findings
- Breast cancer
  - Staging
  - Treatment
- Recurrence of breast cancer
  - Companion patient
  - Guidelines for surveillance
  - Sensitivity and specificity of modalities
- Take Home Points
- Summary



# Our Patient: Clinical Presentation

- 63 year old female with history of breast cancer (age 47) comes to BIDMC Breast Center 4/2012 to establish care
  - Complained of chronic right chest wall tenderness over the site of her mastectomy scar, worsening over the last 5 months
  - Yearly mammography
    - Last 7/2011 (outside hospital): “BI-RADS 1, negative”
  - Sees her primary care physician regularly



# Our Patient: Medical History

- PMH:
  - At age 47, she was diagnosed with right breast cancer stage IIA, ER-PR+, negative lymph nodes
  - Treatment:
    - Modified radical mastectomy
    - 6 cycles of adjuvant chemotherapy (cyclophosphamide, methotrexate and fluorouracil 5FU)
    - Tamoxifen x 5 years
- Family History
  - Ashkenazi Jewish heritage; refused genetic testing



# Our Patient: Physical Exam

- Breast physical exam:
  - No visible changes: no erythema, rashes, dimpling, or skin lesions; on the left, no nipple discharge, nipple excoriation, or nipple retraction
  - No palpable nodules nor masses bilaterally
  - No axillary lymphadenopathy
  - Tenderness along the length of the surgical scar with deep palpation mainly between the ribs.
- Plan: Reassurance, scheduled for regular yearly mammography

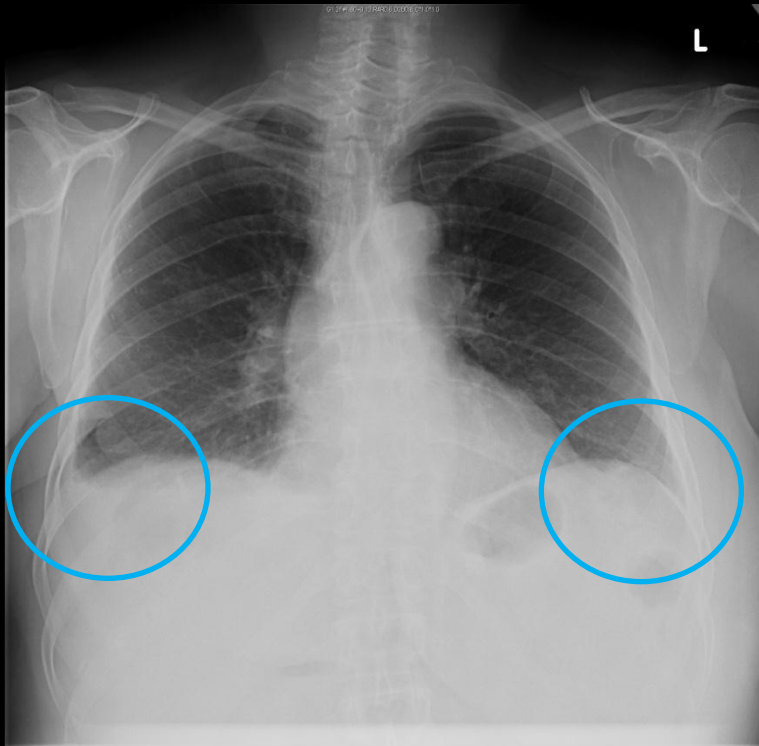


# Our Patient: Primary Care Presentation

- 1 month later:
  - Presents to her primary care physician with a 2 week history of dry cough
  - ROS: denied fever, chills, night sweats or weight loss

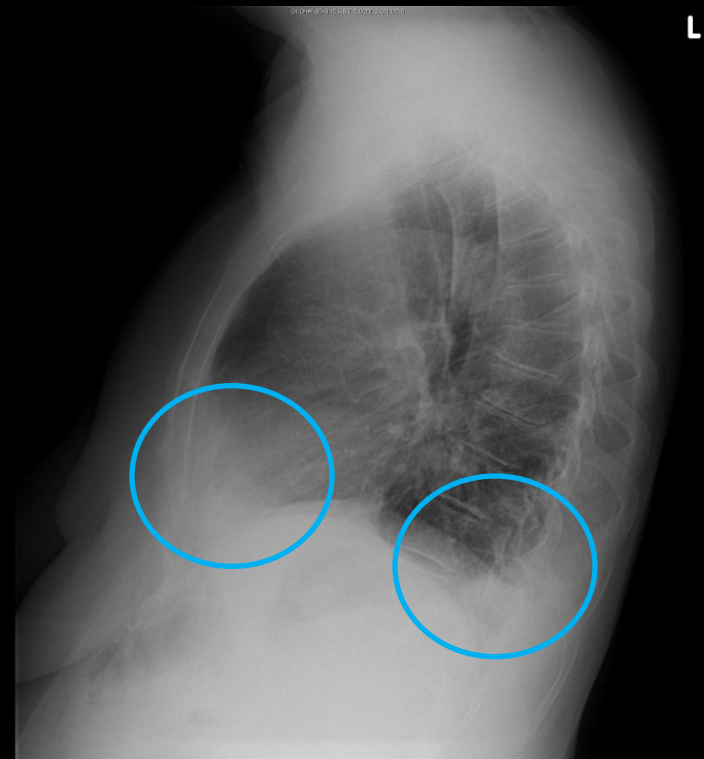
# Our Patient: Pleural Effusion on Plain Film

**Bilateral small pleural effusions and bibasilar opacities**



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Antero-Posterior (AP)  
Upright Chest Plain Film



PACS, BIDMC

AP Lateral Chest Plain Film



# Our Patient: Follow Up

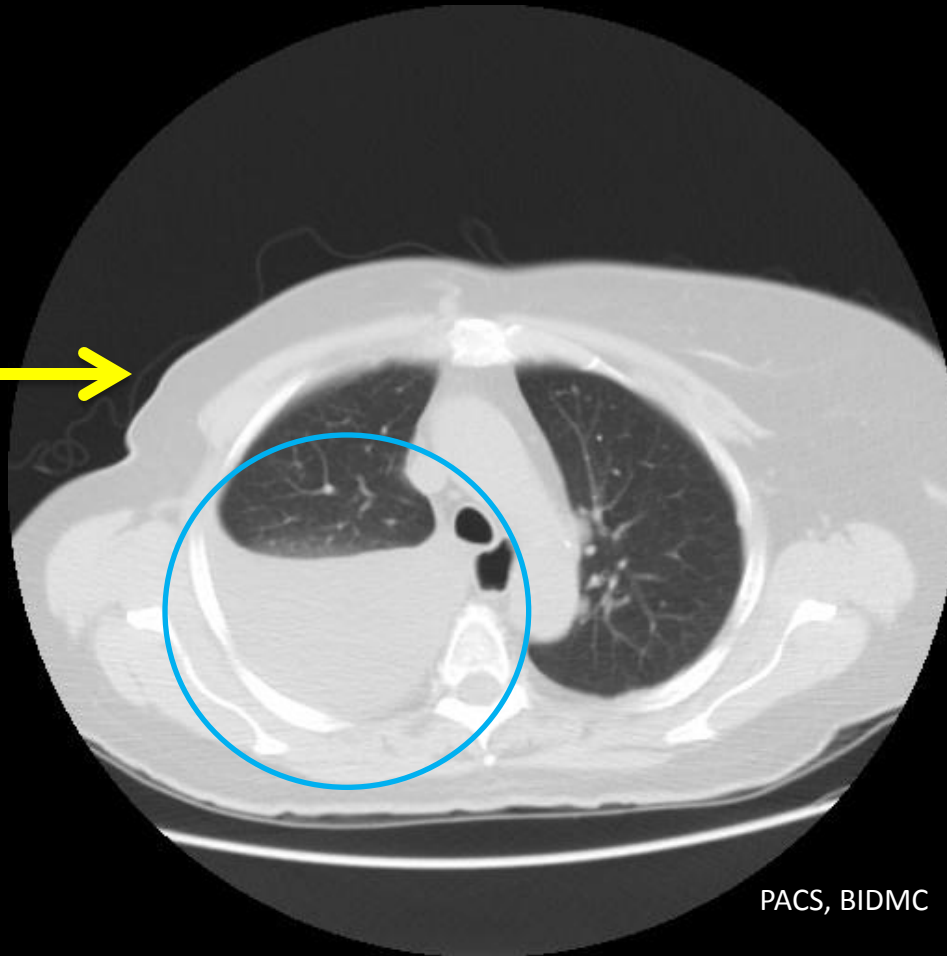
- Despite treatment with azithromycin, levofloxacin and two courses of prednisone, the cough persists for 6 more weeks
- Her primary care physician ordered a chest computed tomography (CT) without contrast



# Our Patient: Pleural Effusion on Chest CT

Moderate – large right sided pleural effusion

Right radical  
modified  
mastectomy



PACS, BIDMC

Axial chest CT without contrast

# Our Patient: Differential Diagnosis

## PLEURAL EFFUSION

<b>Transudate</b>	<b>Exudate</b>
Left ventricular failure	Malignancy
Liver cirrhosis	Parapneumonic effusions
Hypoalbuminemia	Pancreatitis
Peritoneal dialysis	Benign asbestos effusion

Modified from Maskell et al. *Thorax* 2003

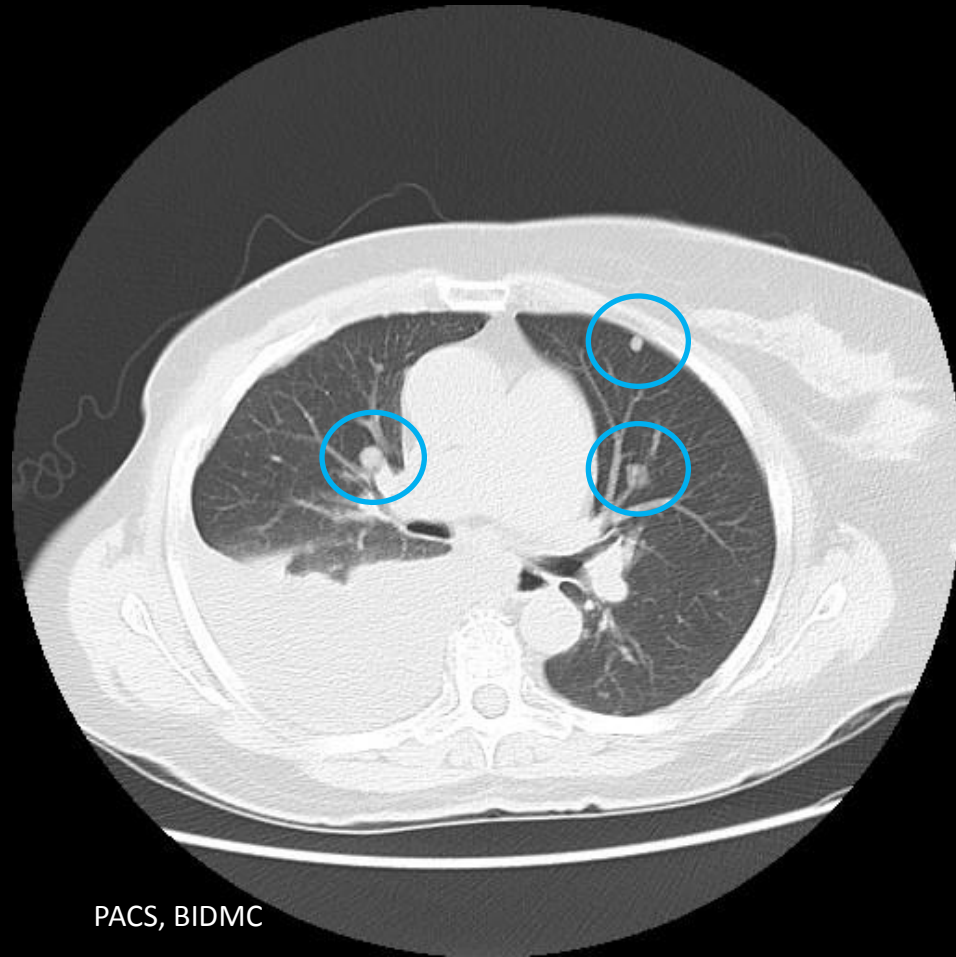
Transudate: balance of hydrostatic and oncotic forces favors pleural fluid accumulation

Exudate: local factors leads to leaky capillaries causing shift of fluids into the pleura.



# Our Patient: Lung Nodules on Chest CT

## Multiple Lung Nodules



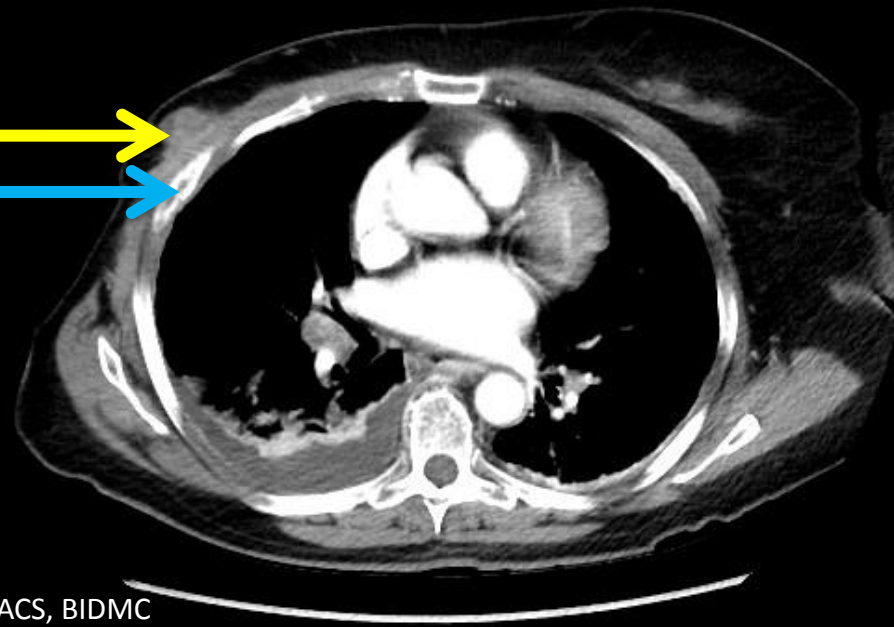
PACS, BIDMC

Axial chest CT without contrast



# Our Patient: Chest Wall Mass on Chest CT

Right Chest  
Wall Mass  
Rib fracture



PACS, BIDMC

Axial Chest CT with Contrast



# Our Patient: Diagnosis and Treatment

- High suspicion for recurrent right breast cancer in the chest wall with metastases to the lungs
- Pleural effusion cytology: + adenocarcinoma
- Core biopsy: invasive carcinoma consistent with breast origin
- Started treatment with chemotherapy for metastatic breast cancer



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# Breast Cancer: Epidemiology

- 12% lifetime risk for average American woman
- Causes 15% of cancer related deaths in women
- Gail model for predicting risk

## Breast Cancer Risk Assessment Tool (Gail Model)

Current Age

Age at menarche

Race

# previous breast biopsies

# breast biopsies showing atypia

Age at first live birth

Number of first degree relatives with history of breast cancer

Fletcher S. Risk Prediction Models for Breast Cancer Screening. *Up-To-Date* 2012



# Breast Cancer: Genetic Risk

- Genetic mutations (BRCA)
  - Mutation carriers have up to 60-80% risk of developing breast cancer in their lifetime
  - Higher prevalence of BRCA gene mutations in Ashkenazi Jews





# Breast Cancer: Staging

Stage	% Diagnosed	% 5 year survival
0	20.8	93
I	38.2	88
II	24.8	74-81
III	8.5	41-67
IV	3.7	14
Unknown	3.9	

Modified from <http://www.facs.org/cancer/ncdb>  
National Cancer Data Base (2001, 2009)



# Breast Cancer: Treatment

- Dependent on the stage
- Equivalent survival benefit:
  - Breast conserving surgery with radiation therapy
  - Mastectomy +/- reconstruction
- Axillary lymph node biopsy + staging
- Adjuvant therapy:
  - Tamoxifen
  - Radiation
  - Chemotherapy



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# Breast Cancer: Recurrence

Term	Definition
Local recurrence	Ipsilateral chest wall (including skin and muscle) or mastectomy scar
Regional spread	Ipsilateral axillary, supraclavicular, infraclavicular or internal mammary lymph nodes
Distant spread	metastases to any other location
Spread to contralateral breast	metastasis versus new primary tumor

- 5-40% risk of locoregional recurrence (average 10%) after invasive breast cancer treatment
- 9-25% of above will have distant metastases
- Majority occur within 5 years of primary treatment



# Breast Cancer: Prognostic Factors for Recurrence

- Influenced by:
  - Tumor size
  - Tumor grade
  - Number of lymph nodes
  - Presence of lymphovascular space invasion
  - Surgical margin status
  - Involvement of fascia or skin
  - Percentage of nodal involvement
- Chest wall recurrence is a poor prognostic factor

Blanco et al. *British Journal of Cancer* 1990

Chagpar et al. *Annals of Surgical Oncology* 2003



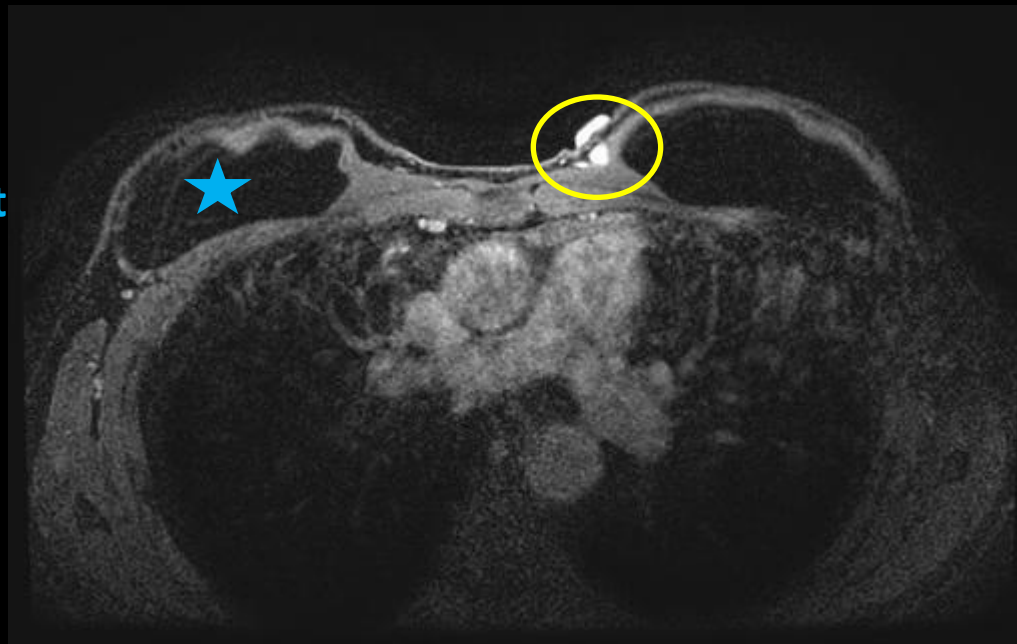
# Companion Patient: Clinical Presentation

- 46 year old female
- Family history: Breast cancer in Mother (age 41), Sister (31)
- BRCA negative
- Age 43 had bilateral prophylactic nipple sparing mastectomy with breast reconstruction
- Pathology from the mastectomy showed DCIS
- Age 46 found a palpable mass
- Breast Magnetic resonance imaging (MRI) ordered

# Companion Patient: Adenocarcinoma on MRI

**Adenocarcinoma**

**Saline  
Implant**



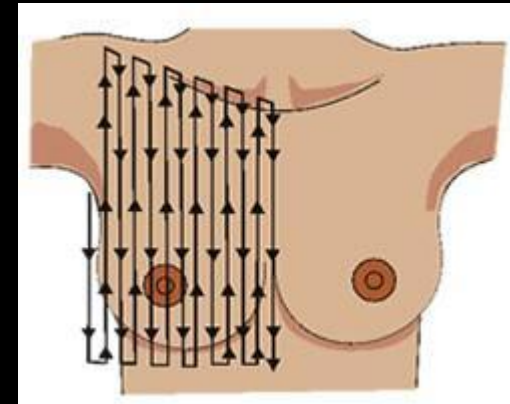
PACS, BIDMC

Axial MRI with Gadolinium enhancement



# Modalities for Surveillance: Clinical Exam

- Clinical Breast Exam



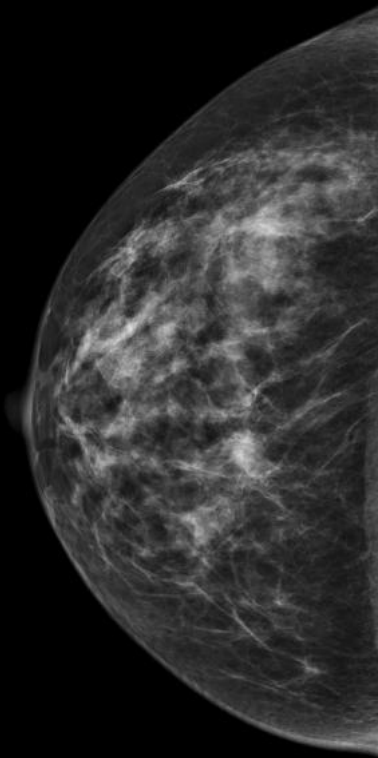
<http://www.siumed.edu/breastcenter/screenings.html>





# Modalities for Surveillance: Mammography

- Clinical Breast Exam
- Mammography
  - Contralateral breast only in patients with mastectomy
  - Both breasts in breast-conserving therapy

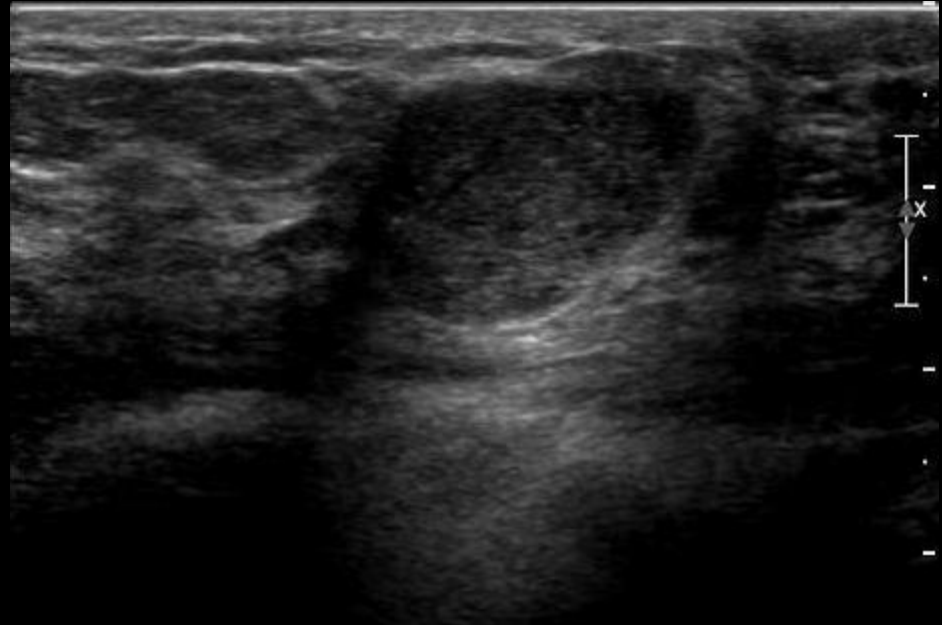


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Craniocaudal  
mammogram

# Modalities for Surveillance: Ultrasound

- Clinical Breast Exam
- Mammography
- Ultrasound



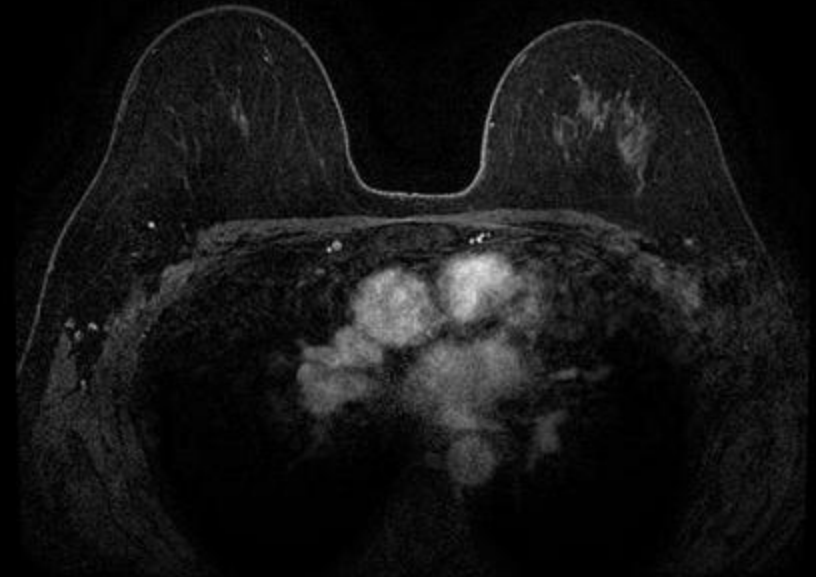
Sagittal ultrasound of right  
breast mass

PACS, BIDMC



# Modalities for Surveillance: MRI

- Clinical breast exam
- Mammography
- Ultrasound
- **MRI**



Axial MRI

PACS, BIDMC



# Modalities for Surveillance: FDG-PET scan

- Clinical breast exam
- Mammography
- Ultrasound
- MRI
- Fluorodeoxyglucose

Positron Emission Tomography  
(FDG-PET scan)



PACS, BIDMC

Transaxial Fusion  
FDG-PET scan

# Breast Cancer Screening: Intermediate Risk

## ACR Appropriateness Criteria

- Compiled by American College of Radiology (ACR)
- Intermediate risk group: personal history of breast cancer, lobular neoplasm, atypical ductal hyperplasia, dense breasts, 15-20% lifetime risk

Radiologic Procedure	Rating	Comments	<u>RRL</u> <sup>+</sup>
Mammography screening	9		☼☼
MRI breast without and with contrast	7	See statement regarding contrast in text under "Anticipated Exceptions."	○
US breast	5		○
FDG-PEM	2		☼☼☼☼
Tc-99m sestamibi BSGI	2		☼☼☼☼
MRI breast without contrast	1		○
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Meiniero et al. ACR Appropriateness Criteria 2012

# Breast Cancer Screening: High Risk

## ACR Appropriateness Criteria

- High Risk Group: BRCA gene mutation, first degree relative with BRCA mutation, history of chest irradiation between ages 10-30, greater than 20% lifetime risk of breast cancer

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
Mammography screening	9	Beginning at age 25-30 or 10 years before age of first-degree relative with breast cancer or 8 years after radiation therapy, but not before age of 25. Mammography and MRI are complementary examinations, both should be performed.	⊕ ⊕
MRI breast without and with contrast	9	Mammography and MRI are complementary examinations, both should be performed. See statement regarding contrast in text under "Anticipated Exceptions."	○
US breast	6	If patient cannot have MRI.	○
FDG-PEM	2		⊕ ⊕ ⊕ ⊕
Tc-99m sestamibi BSGI	2		⊕ ⊕ ⊕ ⊕
MRI breast without contrast	1		○
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

# Recurrence Surveillance: ASCO Recommendations

RECOMMENDED	NOT RECOMMENDED
Clinical Exam	Routine blood tests
Patient education	Imaging studies (CXR, bone scan, liver ultrasound, CT)
Referral for genetic counseling	Tumor markers (CA 15-3, CA27.29, CEA)
Breast self-exam	FDG-PET
Mammography*	Breast MRI
Coordination of care	
Pelvic exam	

Modified from Khatcheressian et al. *Journal of Clinical Oncology* 2006

\*Mammography Recommendations: starting 1 year after initial mammogram that lead to diagnosis (no earlier than 6 months after definitive radiation therapy). Then surveillance mammo every 6-12 months  
- If mastectomy, mammography of contralateral breast

# Recurrence Surveillance: Modality Accuracy

- Review of modality accuracy for detection of ipsilateral breast cancer recurrence

Breast Imaging Modality	Sensitivity range (%)	Specificity range (%)
Mammography (for breast conserving treatment)	64-67	85-97
MRI	86-100	93
Clinical exam	50-89	76
Ultrasound (for symptomatic presentation)	43-87	31-73
PET-CT	96	89
CT	40-92	41-100

Robertson et al. *Health Technology Assessment* 2011

Pennant et al. *Health Technology Assessment* 2010

Pan et al. *Journal of Cancer Research and Clinical Oncology* 2010





# Recurrence Surveillance: MRI

- Very sensitive imaging modality for identifying breast cancer recurrence
- Surveillance must be both clinically effective AND cost effective
  - Debate about reduction of mortality with MRI
  - MRI is 10 x more expensive than mammography
- More data required to determine if MRI is improving outcomes for women with recurrent breast cancer



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# Take Home Points

- Risk of recurrence persists past 5 year disease-free-survival after primary breast cancer treatment
- Screening recommendations depend on risk stratification
  - Intermediate risk: Mammogram with clinical exam
  - High risk: Mammogram + MRI with clinical exam
- MRI has a very high sensitivity but is currently only recommended in high-risk women



# Summary

- Patient with a 16 year disease-free-interval who had recurrent ipsilateral breast cancer
- Breast cancer epidemiology, screening, staging and treatment
- Rates and risk of recurrence
- Surveillance recommendations for breast cancer survivors



# References

1. Bellon JR, Haffty BG, Harris EER et al. Conservation surgery and radiation – Stage I and II breast carcinoma. American College of Radiology ACR Appropriateness Criteria 2011.
2. Blanco G, Holli K, Heikkinen M et al. Prognostic factors in recurrent breast cancer: relationships to site of recurrence, disease-free interval, female sex steroid receptors, ploidy and histological malignancy grading. *British Journal of Cancer* 1990;62:142-146
3. Buchanan CL, Dorn PL, Fey J, et al. Locoregional recurrence after mastectomy: incidence and outcomes. *Journal of the American College of Surgeons* 2006; 203(4):469-474.
4. <http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional>: PDQ Breast Cancer Treatment, 2012, National Cancer Institute; Accessed 9/12/2012
5. Chagpar A, Kuerer HM, Hunt KK et al. Outcome of treatment for breast cancer patients with chest wall recurrence according to initial stage: implications for post-mastectomy radiation therapy. *International Journal of Radiation Oncology, Biology, Physics*. 2003; 57(1):128-35.
6. Chagpar A, Meric-Bernstam F, Hunt KK et al. Chest wall recurrence after mastectomy does not always portend a dismal outcome. *Annals of Surgical Oncology* 2003; 10(6):628-634
7. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005; 366(9503):2087-106.
8. <http://www.facs.org/cancer/ncdb>: National Cancer Data Base (NCDB), 2009, American College of Surgeons, Commission on Cancer; Accessed 9/12/2012
9. Halyard MY, Wasif N, Haffty BG et al. Local-Regional Recurrence (LR) and Salvage Surgery – Breast Cancer. American College of Radiology ACR Appropriateness Criteria 2010.
10. Khatcheressian JL, Wolff AC, Smith TJ, et al. American Society of Clinical Oncology 2006 Update of the Breast Cancer Follow-up and Management Guideline in the Adjuvant Setting *Journal of Clinical Oncology* 2006; 24(31): 5091-5097



# References, continued

11. Maskell NA, Butland RJA. BTS guidelines for the investigation of a unilateral pleural effusion in adults. *Thorax* 2003;58:ii8-ii17.
12. Meiniero MB, Lourenco A, Mahoney MC et al. Breast Cancer Screening. *ACR Appropriateness Criteria* 2012.
13. Moore SG, Shenoy PJ, Fanucchi L et al. Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population *BMC Health Services Research* 2009, 9:9. Accessed 9/13/12.
14. Pan LL, Han Y, Sun XG et al. FDG-PET and other imaging modalities for the evaluation of breast cancer recurrence and metastases: a meta-analysis. *Journal of Cancer Research and Clinical Oncology*. 2010;136(7):1007–1022.
15. Pennant M, Takwoingi Y, Pennant L. A systematic review of positron emission tomography (PET) and positron emission tomography/computed tomography (PET/CT) for the diagnosis of breast cancer recurrence. *Health Technology Assessment* 2010;14(50):1-103.
16. Robertson C, Arcot Ragupathy SK, Boachie C, et al. The clinical effectiveness and cost-effectiveness of different surveillance mammography regimens after the treatment for primary breast cancer: systematic reviews registry database analyses and economic evaluation. *Health Technology Assessment* 2011;15(34):v-vi, 1-322.
17. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *C:A Cancer Journal for Clinicians* 2007; 57(2):75-89.
18. Taghian A, Jeong JH, Mamounas E, et al. Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and without radiotherapy: results from five National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. *Journal of Clinical Oncology* 2004; 22(21):4247-54.
19. Yilmaz MH, Esen G, Ayarcan Y, et al. The role of US and MR imaging in detecting local chest wall tumor recurrence after mastectomy. *Diagnostic and Interventional Radiology* 2007 Mar;13(1):13-8.



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THANK YOU!