

US Screening in the USA: Technologist-Performed HHUS

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Disclosures

- Nothing to disclose

Objectives

- Discuss outcomes from screening HHUS after 2D mammography
- Discuss outcomes from HHUS after DPT
- Describe issues in implementing HHUS
- Interesting cases

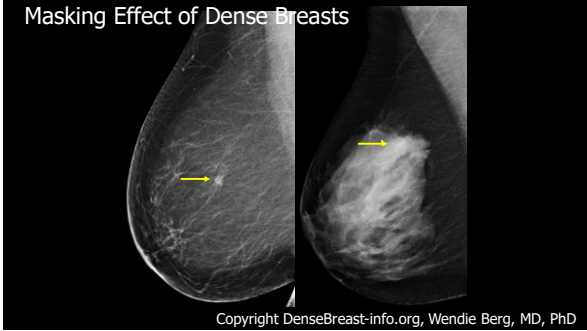
Mammography Works

- Coldman A et al JNCI 2014;106:epub
- 40% (95% CI 33 to 48) reduction in mortality from participation in screening
 - Annual 40-49; biennial 50-79 yrs
 - Ranged from 44% (entry at 40-49 yrs) to 35% (entry at 70-79 yrs)

Failure Analysis

- Webb ML et al Cancer 2013, epub 9/11/13
- 7301 invasive breast cancer dx 1990-1999 f/u 2007
 - 609 breast cancer deaths; median age 49 yr at dx
 - 29% cancer deaths were among women screened
 - 19% screen detected
 - 10% interval cancers
 - 71% deaths among unscreened women

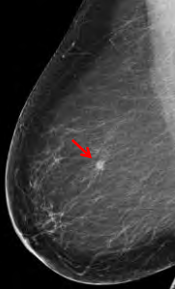
- But, mammography does not benefit all women equally



Masking Risk

Destounis S et al AJR 2017;208:222-227

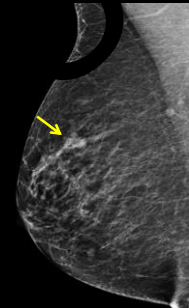
- 652 screen-detected, 119 interval cancers 1/09-12/12
- Breast density only independent factor predicting interval cancer
 - OR 3.54 BI-RADS density
 - OR 4.68 automated density grade (Volpara)
- Sensitivity drop with density: 95, 81, 83, 65% across automated density vs. 82, 90, 87, 71% for BI-RADS



Almost entirely fatty

- 13% of women
- 86-98% of cancers present are detected on mammography

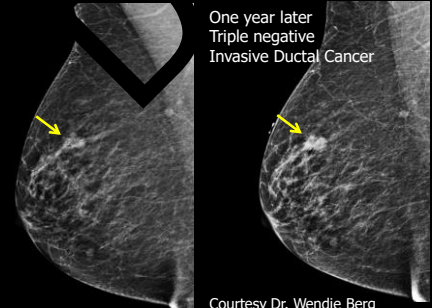
Courtesy Dr. Wendie Berg
 Courtesy DenseBreast-info.org



Scattered Areas of Fibroglandular Density (Tissue)


- 43% of women
- 78-90% of cancers present are detected on mammography
- Cancer can still be missed if it lacks calcifications and is in an area of tissue

Courtesy Dr. Wendie Berg



One year later
 Triple negative
 Invasive Ductal Cancer

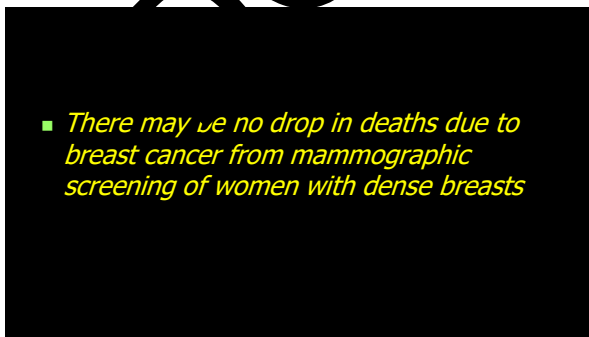
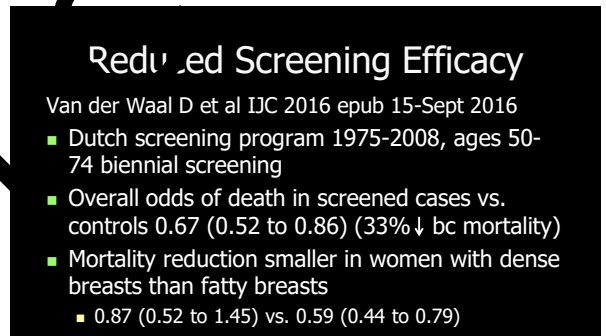
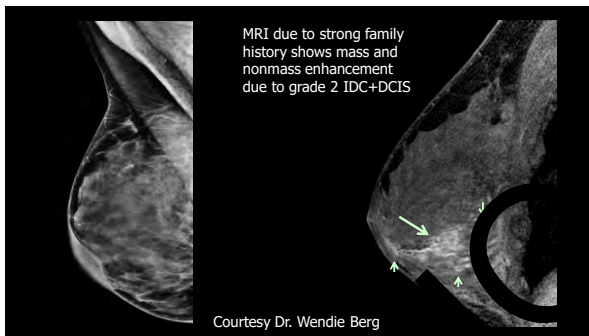
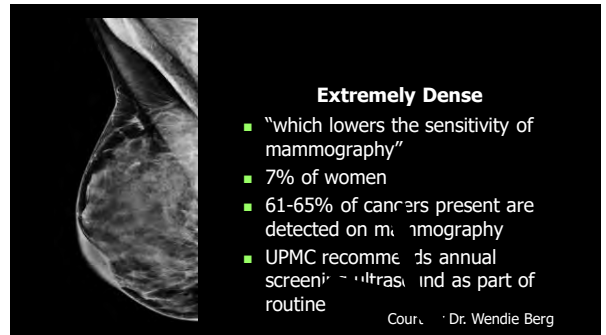
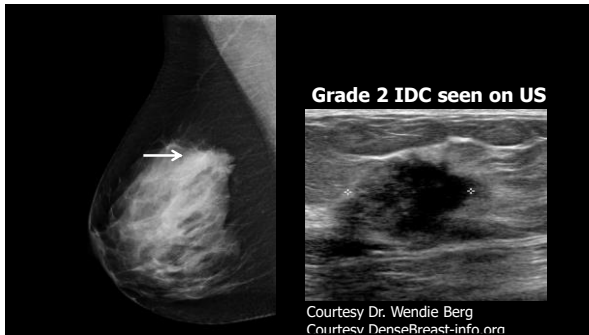
Courtesy Dr. Wendie Berg



Heterogeneously Dense

- "which may obscure small masses"
- 36% of women
- 70-83% of cancers present are detected on mammography

Courtesy Dr. Wendie Berg
 Courtesy DenseBreast-info.org



Possible tests to add to mammography

Modality vs. Mammography alone	Absolute ↑ Cancer Detection per 1000 screens
Clinical breast exam	0.3
Double Read or CAD	1
Tomosynthesis	1-2
Ultrasound	3-4
Molecular Breast Imaging	7-8
MRI, CEDM	10

Copyright Wendie Berg, MD, PhD

Evidence Supporting Screening

- Disease-specific mortality reduction
 - Only studied for mammography
- Reduction in node-positive disease
 - Increase in node-negative invasive cancers
- Reduction in interval cancers
 - Fewer than 10% of all cancers diagnosed

Interval Cancer

- Cancer dx by clinical symptoms in interval between recommended screenings
- Worse prognosis and worse outcome
- ~1/2 deaths in screened women diagnosed in their 40s are due to interval cancers

Interval Cancers and Breast Density

Density	Odds Ratio	95% CI
< 10%	1.0	-
10-24%	2.1	(0.9, 5.2)
25-49%	3.6	(1.5, 8.7)
50-74%	5.6	(2.1, 15.3)
≥ 75%	17.8	(4.8, 65)

Boyd NF, et al. NEJM 2007;356:227-36

Dense Breasts: Physician Performed US Multicenter Results

Author	N screens	ICDR per 1000	Recall Rate (%)	Bx Rate (% women)	PPV3 Bx Performed
Corsetti	9157	4.0	NS	449 (4.9)	50/623 (8.0)
Berg yr1	2659	5.3	401 (15.1)	207 (7.8)	14/264 (5.3)
Berg yr2-3	4841	3.7	356 (7.4)	242 (5.0)	21/276 (7.6)
TOTAL	16,657	4.4	10%	898 (5.4)	85/1163 (7.3)

4.9% of women had biopsies for benign findings

Interval Cancer Rate Italy

Corsetti V et al. Cancer 2011;47:1021-6

- Interval cancer rate in fatty breasts
 - 1.0 per 1000
- Interval cancer rate in dense breasts after adding screening US
 - 1.1 per 1000

Interval Cancer Rate: ACRIN 6666

Yr	N Interval	N Cancers	(%)
1	2	36	5.6
2	4	29	14
3	3	46	6.5
All	9	111	8.1

Interval Ca Rate: 9/7473 screens = 1.2 per 1000
8% of all cancers

Berg WA et al JAMA 2012;307:1394-404

CAN WE TRAIN OUR TECHNOLOGISTS TO PERFORM HANDHELD ULTRASOUND?

Japan

Tohno E et al Breast Cancer 2012;19:138-146

- 2-day educational program; results of training/testing for 415 technologists and 422 physicians
- Observers worse with experience < 100 cases
- Video sensitivity, still image sensitivity, and disease agreement for technologists is greater than for MDs

J-START

Ohuchi N et al Lancet 2015, epub 11/4/2015

- Asymptomatic women aged 40-49 at 42 sites
- Randomized to M+US or M alone twice in 2 years
- 36,869 to intervention and 36,139 to control group
- Mostly performed by trained technologists

'Dense' breasts: Results J-START first round

	Intervention	Control	P-value
Sensitivity	91.1 (87.2-95.0)	77.0 (70.3-83.7)	.0004
Specificity	87.7 (87.3-88.0)	91.4 (91.1-91.7)	<.0001
% Stage 0, I	144/184 (71.3)	79/117 (52.0)	.019
Interval Cancers	18 (0.05%)	35 (0.10%)	.034

Ohuchi N et al Lancet 2015, epub 11/4/2015

J-START 7: US Results

Ohuchi N et al Lancet 2015, epub 11/4/2015

- 1932/36,752 (5.25%) women recalled
- 67/36,752 (1.8 per 1000) ICDR from US
- 55/67 (82.1%) cancers invasive
- 47/55 (85.5%) node negative

Tech-Performed US (USA): Prevalent Screens

Author	N	ICDR per 1000	Recall Rate (%)	Bx Rate (%)	PPV/Bx Performed
Kaplan, 2001	1,862	2.7	176 (9.5)	97 (5.2)	6/96 (6.3)
Hooley, 2012	648*	4.6	154 (23.8)	46 (7.1)	3/58 (5.2)
Weigert, 2012	8,647	2.8	1,196 (13.8)	429 (5.0)	25/418 (6.7)
Parris, 2012	5,519	1.8	680 (12.3)	185 (3.3)	10/181 (5.5)
Overall	16,676	2.5	2,206 (13.2)	757 (4.5)	47/753 (6.2)

*analysis presented for women with negative screening mammograms

Berg WA and Mendelson EB. Radiology 2014;272:12-27

Recalls: Tech-Performed HHUS

- 2,206/16,676 (13.2%) test positive on prevalence screen
 - 1,399 (8.4%) all women BI-RADS 3
 - 757 (4.5%) all women BI-RADS 4
 - 44/753 (5.8%) found to have cancer
- Only 43/16,676 (0.3%) recalled for additional evaluation (BI-RADS 0) prior to final assessment

Berg WA and Mendelson EB. Radiology 2014;272:12-27

Technologist-Performed US

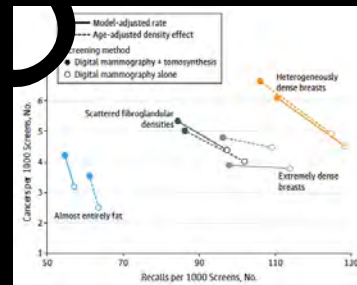
Weigert Breast J (2017) 23:34-9

- Incidence screen ICDR: 30/10,810 (2.8/1000)
- 1073/10,810 (9.9%) recall rate
 - Vs. 325/2706 (12.0%) for prevalence screens
- 30/379 (7.9%) PPV3
 - Vs. 11/151 (7.3%) for prevalence screens

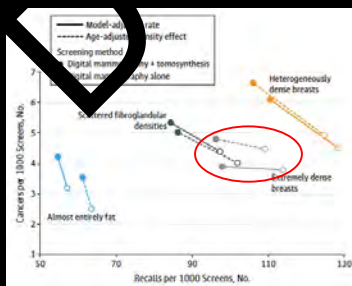
Tomosynthesis and Dense Breasts

Rafferty EA et al JAMA 2016;315:1784-6

- Data from 13 institutions
- Historical control DM alone: 278,906
- 173,414 DM+DBT
- 2157 cancers diagnosed
- Recall rate, CDR per 1000, PPV recall
- Subsets by breast density



Rafferty EA et al JAMA 2016;315:1784-6



Rafferty EA et al JAMA 2016;315:1784-6

ASTOUND-1 trial

Tagliafico AS et al JCO 2016;epub 3/9/2016

- 3231 women with dense breasts, negative mammogram, 5 centers in Italy
- Prevalent screening DBT (3D)
- Mostly incidence screening US (physician-performed HHUS)

Cancer Detection Rates

- DBT (3D): 13 cancers (ICDR 4.0/1000, 95%CI 1.8 to 6.2)
- US: 23 cancers (ICDR 7.1/1000, 95%CI 4.2 to 10.0, p=0.006)
- Only 1 cancer seen only on DBT (3D)

Tagliafico AS et al JCO 2016; epub 3/9/2016

ASTOUND-2

Tagliafico AS Eur J Ca 2018;104:39-46

- 5300 participants with dense breasts DBT and US after mammography
- 29 additional cancers; 27 invasive; 6 N+
- 12 on both US and DBT; 3 DBT only; 14 on US only (4.9 per 1000 US vs. 2.8 per 1000 DBT, p=.015)
- FP rate 1.0% for US, > 0.5% for DBT

IMPLEMENTATION

Technique: HHUS Screening

- Transverse and sagittal scanning survey
 - Radial and antiradial images of lesions
 - With and without calipers if other than simple cysts
 - With and without power Doppler*
- *(Not possible with automated approaches)

Scanning Technique

- 12 MHz or higher frequency linear array transducer, 5 cm footprint usual
- Gentle pressure
- TGC: gradually increases with depth
- Focal zone(s)
 - Broad when surveying
 - Set at lesion when documenting lesions
- Glob of gel for very superficial lesions

FOV

- Depth: breast only, not lungs!
- 94% of breasts < 4 cm thick
 - Berg WA et al JAMA 2008, ACRIN 6666
- Better detail with narrower focal zone at lesion

Cover the Entire Breast!

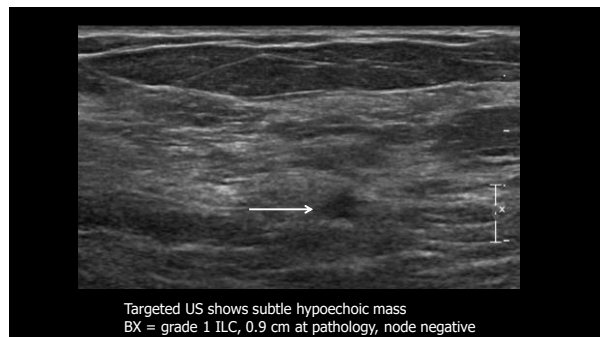
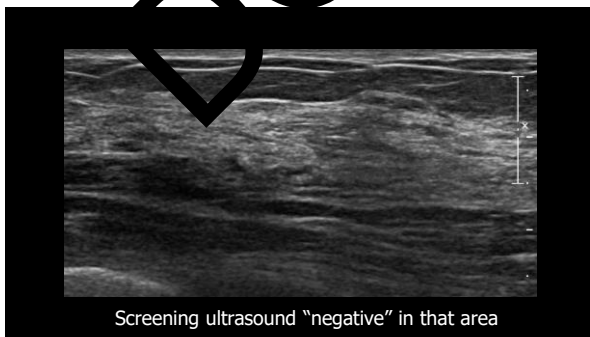
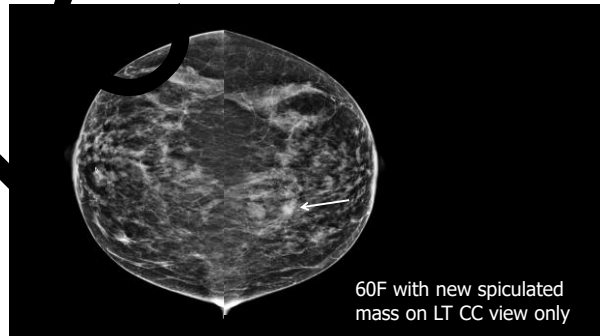
- 58% of all cancers are in the UOQ
- US not limited by positioning: most important to get the "edges" of the breast that may be excluded from mammography FOV

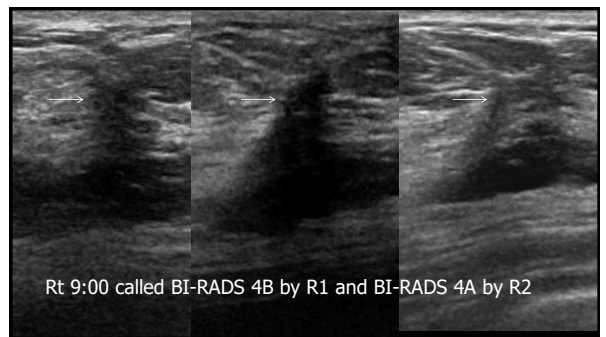
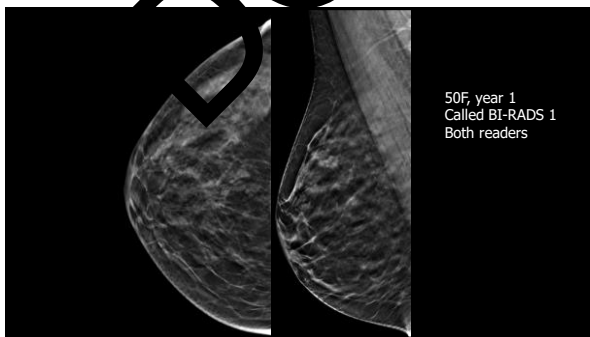
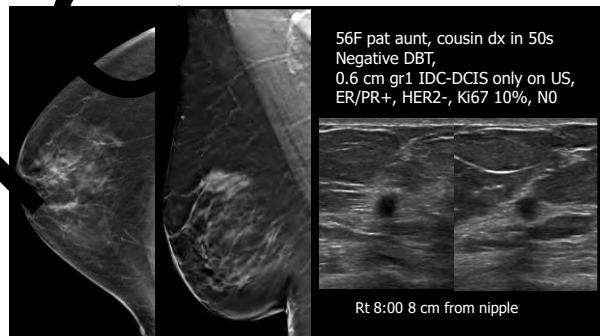
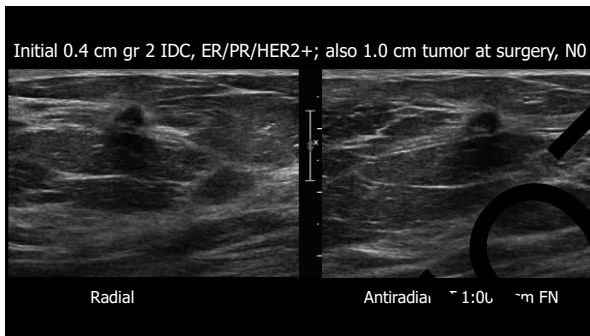
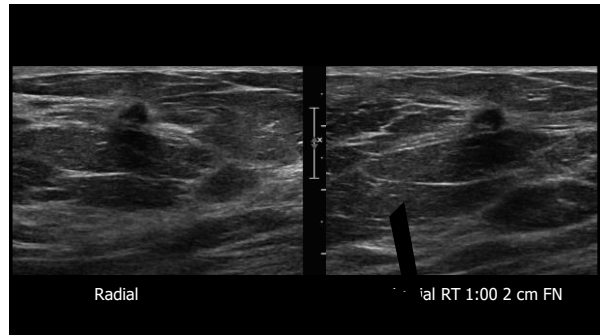
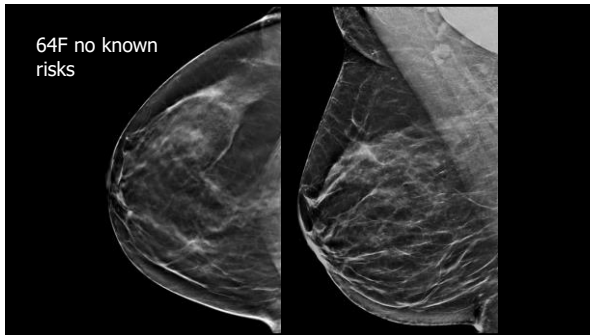
DBTUST

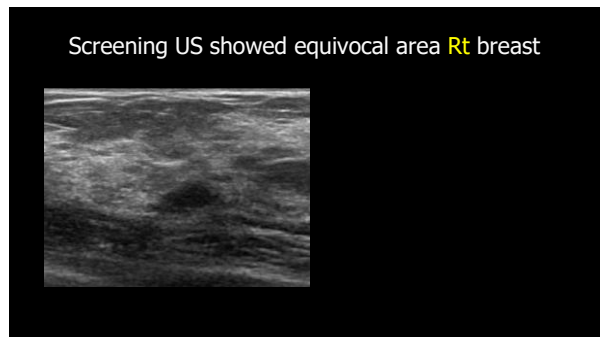
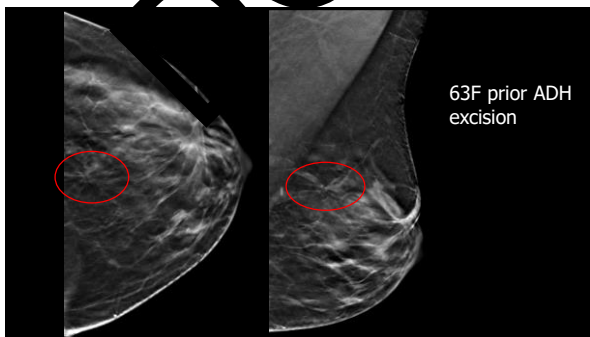
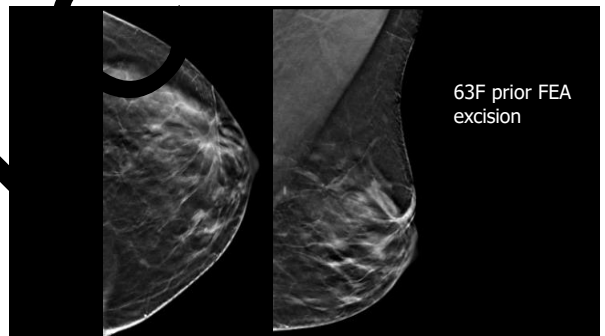
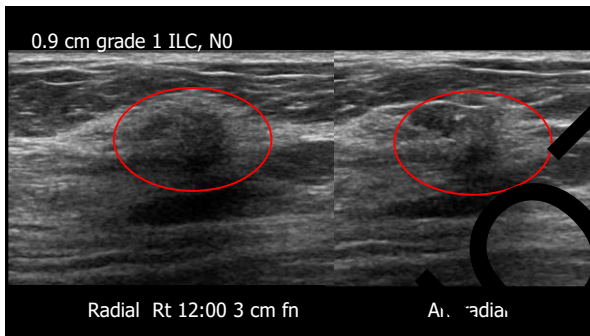
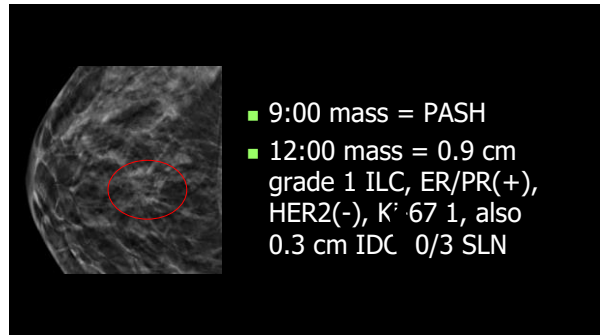
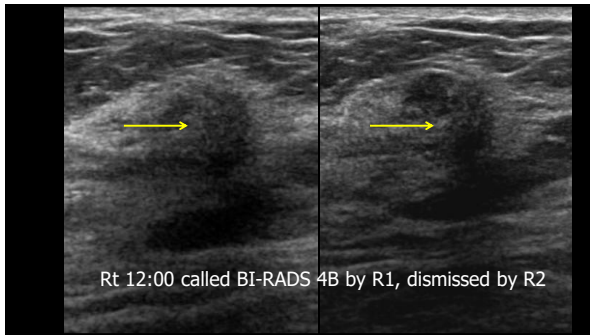
- Digital Breast Tomosynthesis Ultrasound Screening Trial
- 3 Centers in Western PA: UPMC Pittsburgh, Weinstein Imaging, UPMC Erie
- 6200 women 3 rounds of DBT and 1 technologist-performed screening US
- Accrual completed in February 2019

Technologist Training DBTUST

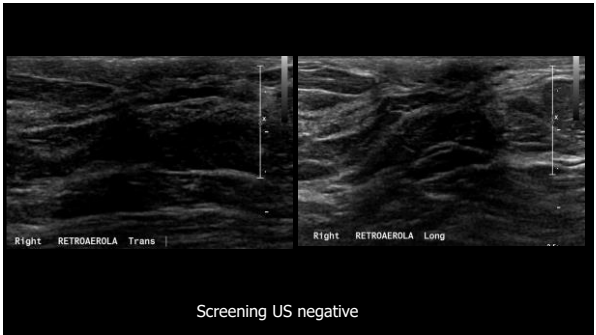
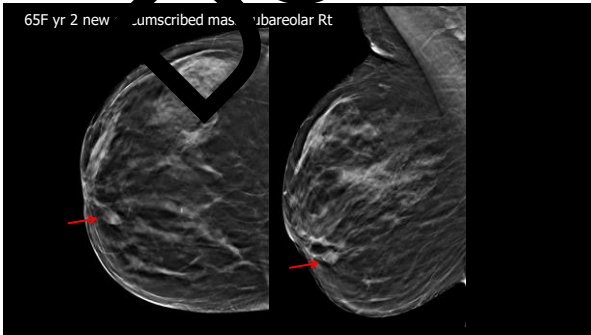
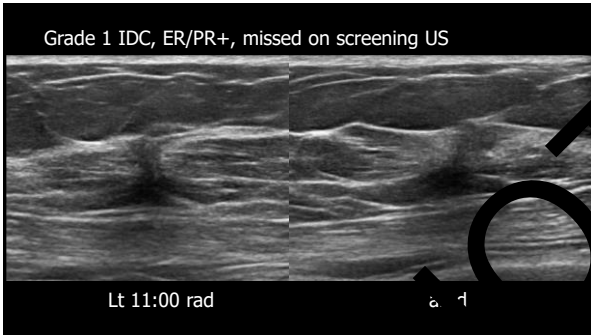
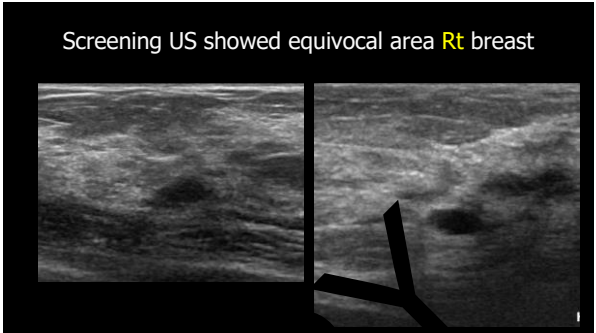
- Mammographic technologists
- 3 months as apprentice on diagnostic service under supervision of experienced technologist
- Total 12 months' minimum on diagnostic breast imaging—immediate feedback
- At least 1000 exams
- Registry in breast US

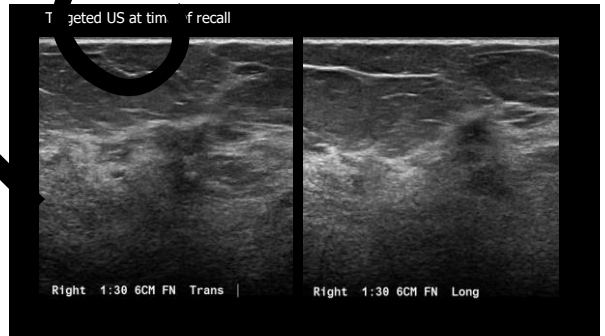
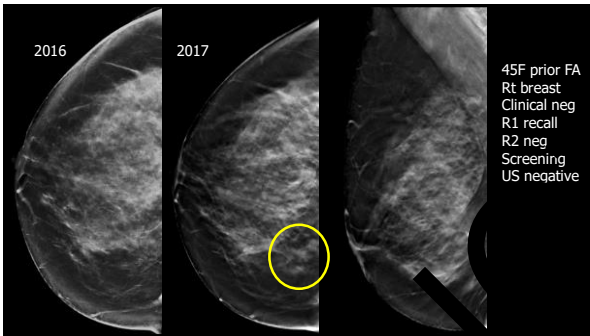
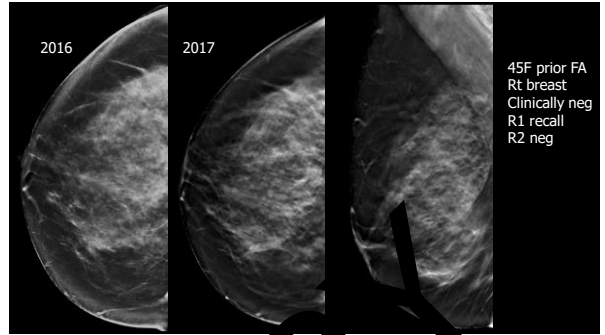
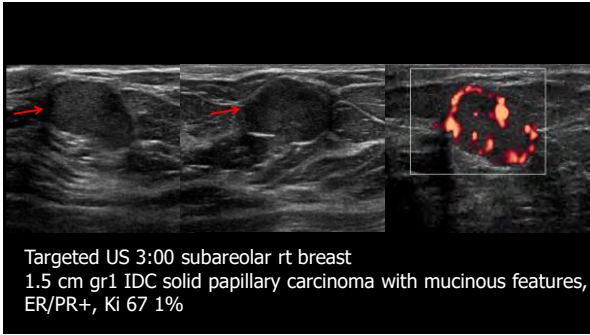




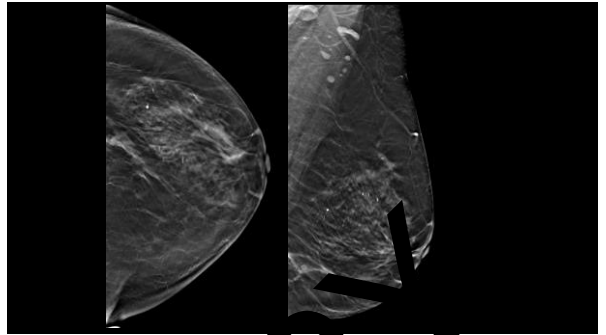
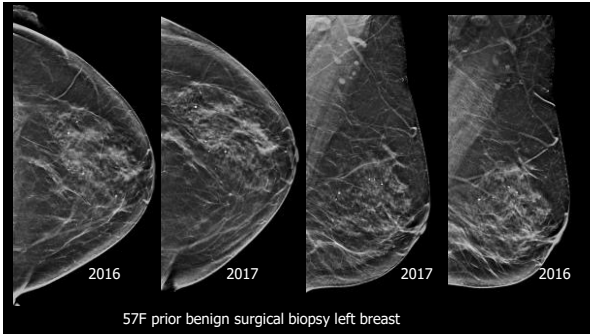


- Screening US of the left breast was normal: patient recalled for additional testing bilaterally

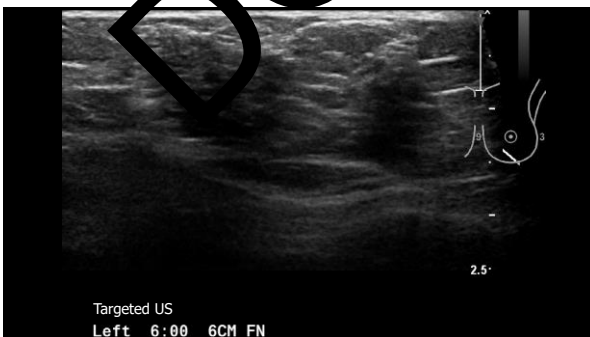
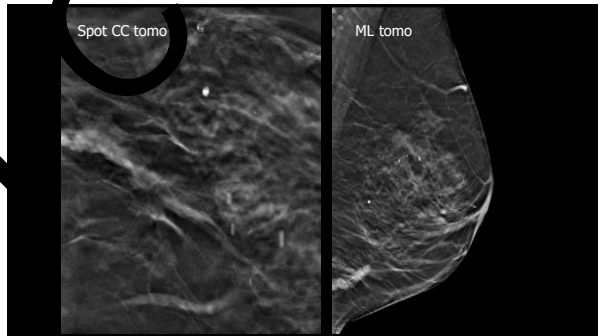




- Rt 1:30 mass grade 1 IDC, tubular features, ER/PR(+), HER2(-), Ki-67 2%, 0.7 cm
- Rt 2:00 mass grade 2 ILC, ER/PR(+), HER2 equivocal by FISH, Ki-67 3%, 1.8 cm (mastectomy), 0/2 SLN
- Lt mastectomy LCIS, ADH



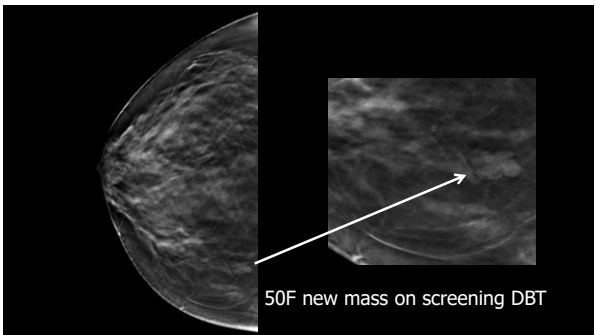
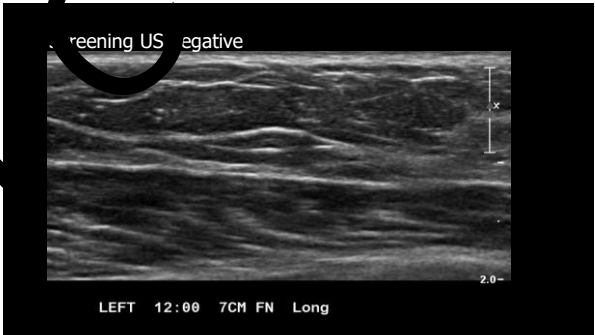
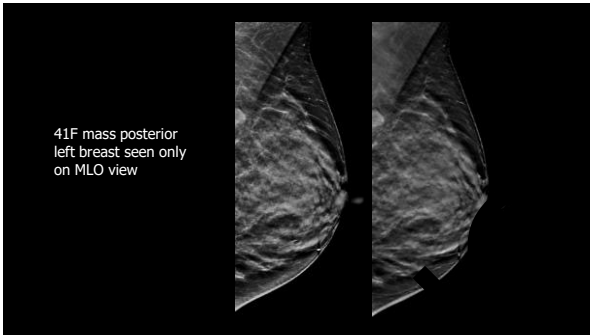
- Screening ultrasound bilateral cysts



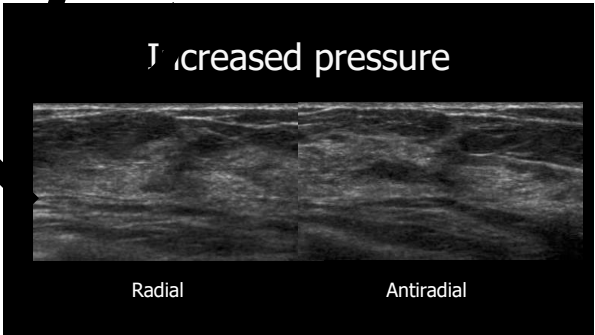
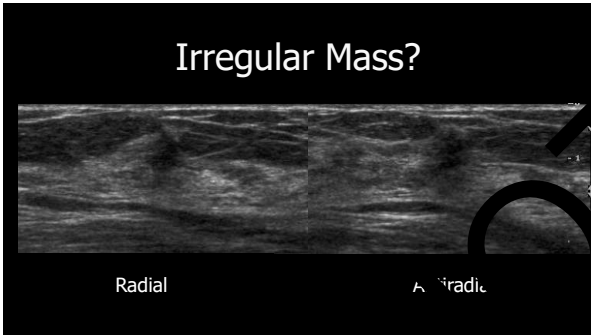
- US-bx 2 masses = grade 2 DCIS with comedonecrosis



- Lt mastectomy = 4.0 cm gr 2 IDC, ER/PR(+), HER2(- by FISH), Ki-67 12%, 5.5 cm DCIS, 0/1 SLN
- Rt mastectomy (after MR bx = ALH) = FCC



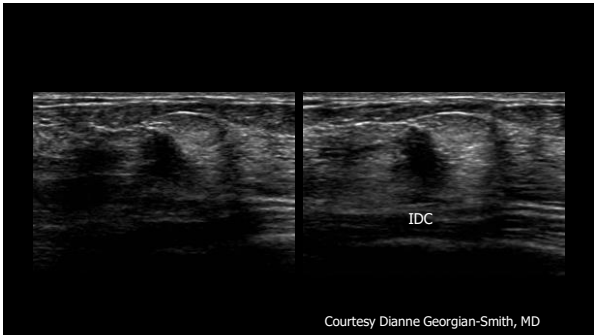
Screening US normal, pt recalled for further imaging



Posterior Shadowing



- Malignancy
- Fibrosis
- Refractive Edge
- Artifact
 - Esp. at edge of adjacent fat lobules

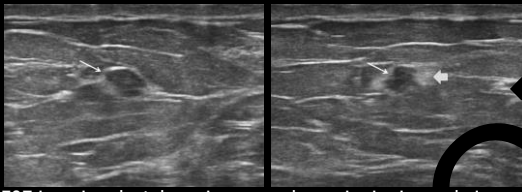


Documentation

- Negative exam
 - At least one image per quadrant and one behind the nipple = 5 images per breast
- Findings other than simple cysts
 - With and without calipers, along long axis of lesion (usually radial)
 - Orthogonal set of images
 - With and without power Doppler
 - Consider harmonics: Reduce artifact; bring out posterior shadowing; increase conspicuity of ~isoechoic masses

Orthogonal Views

- Required for any mass for which future comparison is desirable
 - Not necessary for simple cysts
- Incomplete characterization without this
 - Does not constitute a "positive test"



50F invasive ductal carcinoma; echogenic rim in all view only

Courtesy of Ellen Mendelson

Berg WA and Mendelson EB Radiology 2014; 29(11):2621-2626

Positive Test

- Generally can give a final assessment on HHUS
- BI-RADS 3 or higher assessment, or recommendation for further imaging
- BI-RADS 0, "technical recall"

Batch vs. Online Screening US

- We read in batch mode together with DBT
- If online, and you rescan the patient, this "counts" as a recall
 - Technical recall
 - Positive test

Technical Recalls; 12,264 reads

- 31 (0.25%) for DBT
- 147 (1.2%) for US
 - Finding or lumpectomy scar not included
 - Probable fat lobule measured
 - Artfactual shadowing
 - Possible intraductal mass vs. artifact
 - Likely cyst or clustered cysts but deep/not certain
- Final assessment on 98.8% of screen US

Berg WA et al RSNA 2017 DBTUST

True Recall, Bill Targeted US

- If additional evaluation is needed prior to making a final assessment
- RARELY needed with HHUS
- **Routinely needed with ABUS**

Billing

- CPT codes
 - 76641, unilateral complete right
 - 76641, unilateral complete left
 - Medicare reimbursement averages \$165
 - Subject to deductible and copays

Billing

- ICD-10 92.2
 - "Inconclusive mammogram"
 - Applicable to dense breasts, NOS
 - Inconclusive mammogram due to dense breasts

<http://www.icd10data.com/ICD10CM/Codes/R00-R99/k.../R94/k.../922>

Insurance Laws Dense Breasts

- IL, NY, LA, IN, AR, VT, DC require insurance to fully cover screening US with no out of pocket cost to woman
- NJ requires in women with extremely dense breasts
- CO as of 1/1/21 "noninvasive" testing covered
- CT copay limited to \$20

DenseBreast-info.org/legislation.aspx

Overall Performance

	Cancers	N Women	ICDR per 1000	Added Recalls	PPV3
Physician-Performed HHUS	738	361,562	2.0	7.6%	10.8%
Tech HHUS	144	64,018	2.7	7.5%	9.0%
AUS	69	27,163	2.5	10.6%	8.5%

Berg and Vourtsis J Breast Imaging, epub 10/31/19

Cancers Detected

	N Cancers	N Invasive (%)	N Node Negative Invasive (%)*
Physician-performed HHUS	719	631 (87.8)	457/554 (89.7)
Tech HHUS	144	124 (86.1)	102/123 (82.9)
AUS	69	63/69 (91.3)	36/40 (90.0)

* Where reported

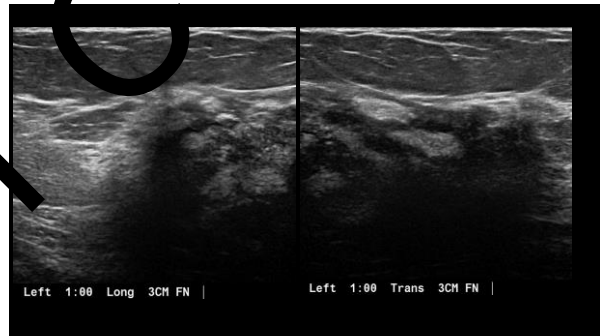
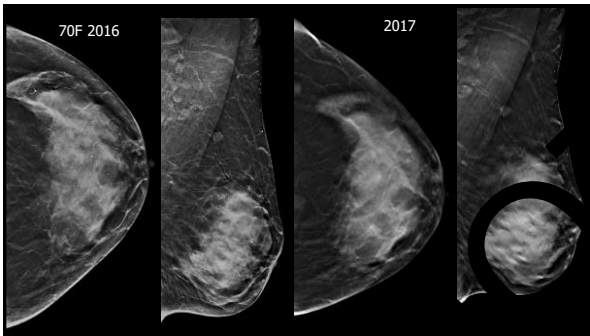
Berg and Vourtsis J Breast Imaging, epub 10/31/19

Efficacy of Screening

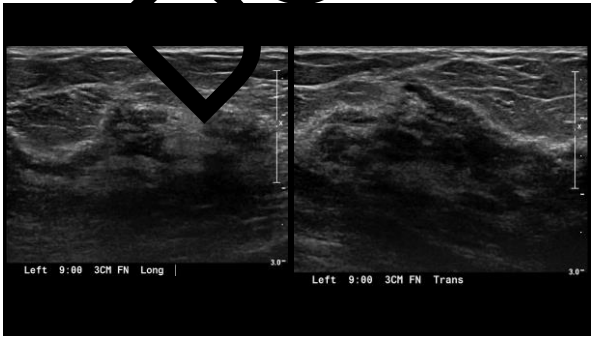
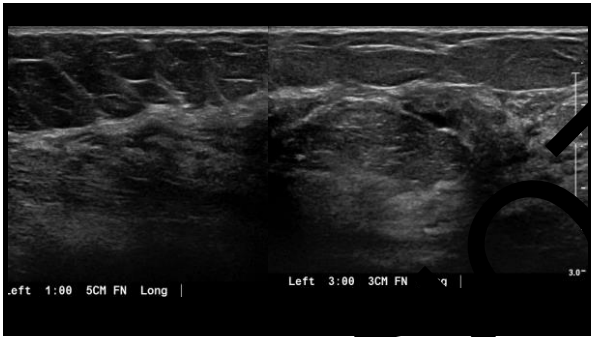
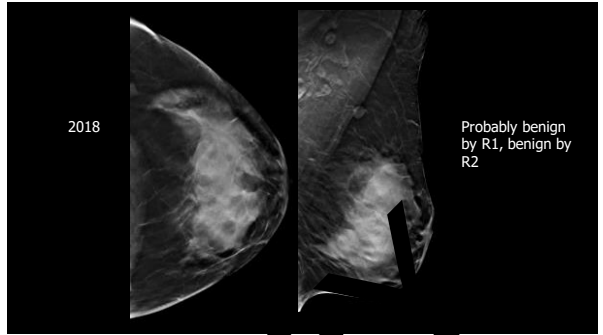
	Mammo	DBT	US	MRI
Reduced Breast Cancer Mortality	✓			
Reduced Interval Cancers	referent		✓	✓
> Stage 0, I disease	referent	✓	✓	✓
< Stage II-IV disease	referent			✓

Summary

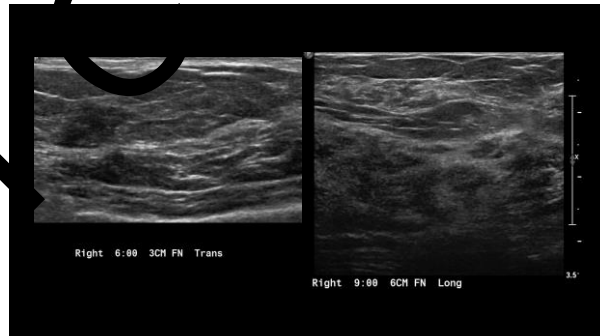
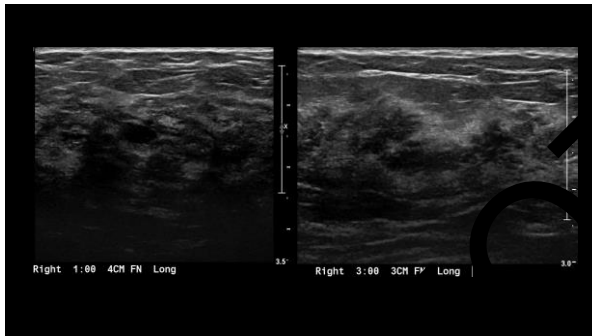
- DBT does not solve masking issues in dense breasts, esp. extremely dense breasts
- Screening US can be implemented, is fully covered by insurance in some states
- Audit your practice, regular feedback, minimize false positives and false negative



- Recalled on DBT in 2017, dismissed as normal on US



DO NOT COPY



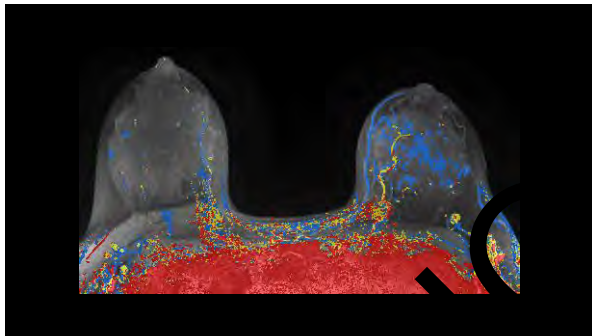
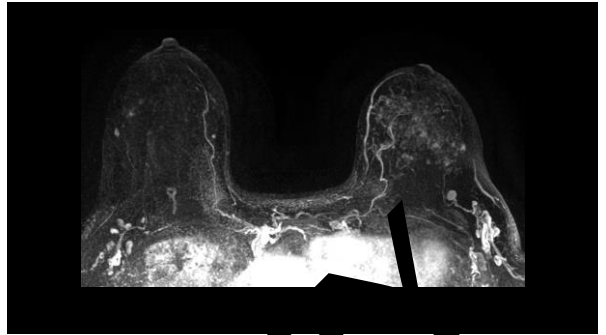
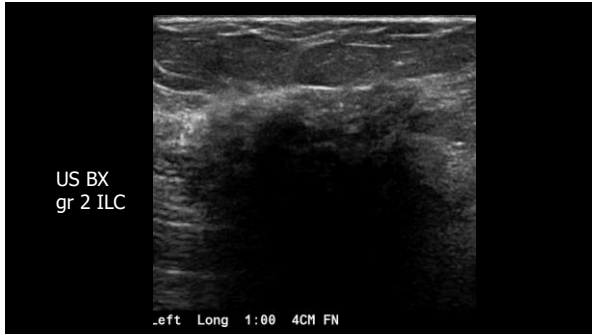
■ Screening US interpreted as normal





CIBC 2019

Chicago International Breast Course
The Westin Chicago River North
November 1-3, 2019



- 8.5 cm gr 2 ILC, ER/PR(+), HER2(-)
- Ki-67 10%
- 2/3 left axillary nodes had isolated tumor cells

