MASSACHUSETTS GENERAL PHYSICIANS ORGANIZATION

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

Artificial Intelligence in Breast Imaging: Image Interpretation and Clinical Implementation

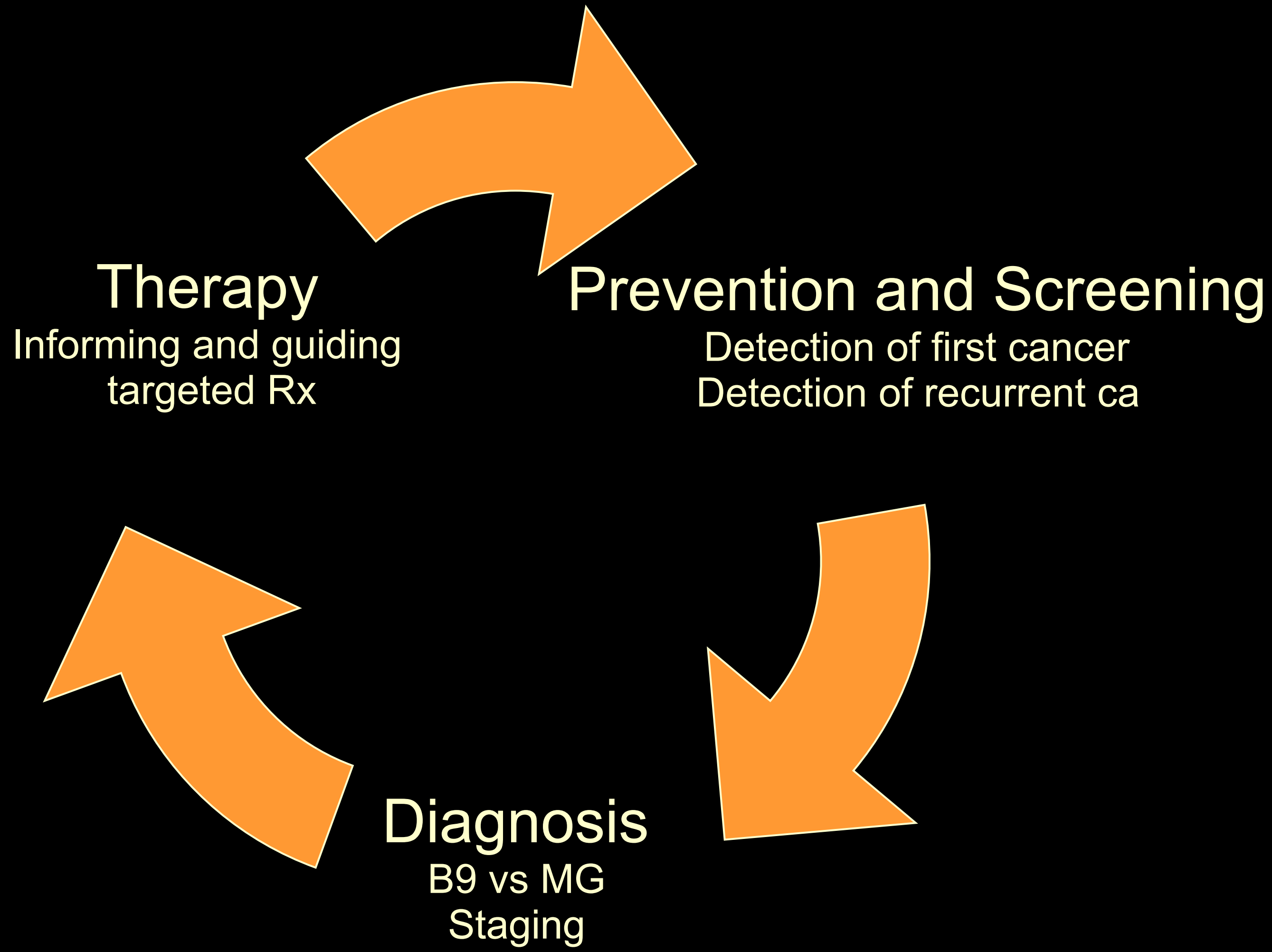
Connie Lehman MD PhD

Breast Cancer: Most Frequent Cancer in Women Worldwide

Every Year:

- Of 3.8 billion women in the world, > 2 million diagnosed with breast cancer each year
- > 40,000 deaths in the US alone
- > 600,000 deaths in the world

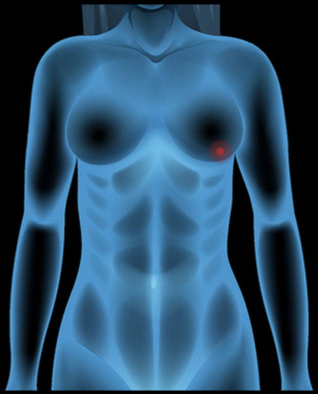
Precision Medicine/Risk Assessment Supports All Levels of Care Pathway



Our Challenge

Screening/early detection is key to cure

- Effective screening programs require:
  - accurate risk assessment tools
  - effective screening tests

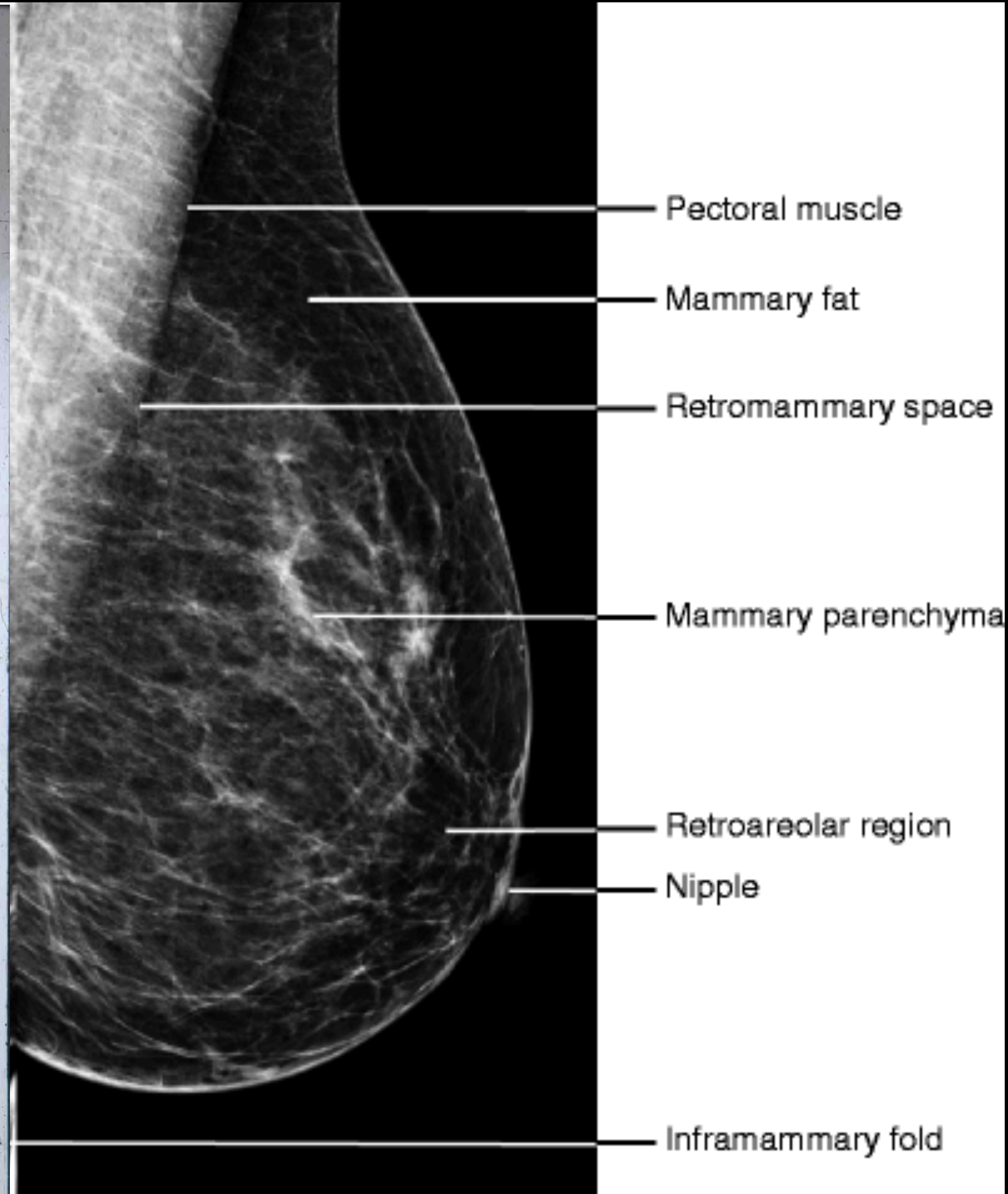


Mammography as a Screening Examination in Breast Cancer[1]

JOHN N. WOLFE, M.D.[2]

[1] Presented at the Fiftieth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 29–Dec. 4, 1964.
Supported by grants from the Michigan Cancer Foundation and Woman's Hospital Research Fund.
[2] Associate Radiologist, Woman's Hospital, Detroit, Mich.

The tedious task of examining about 250 women to detect one cancer seems relatively unrewarding unless it is realized that the cancer found is most likely to be in a curable stage. If left until it is clinically evident, the likelihood of salvage diminishes rapidly.



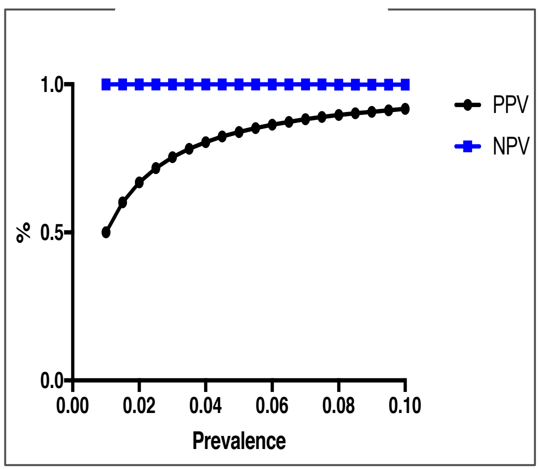
https://link.springer.com/chapter/10.1007/978-3-642-23893-2_15

AI and Screening Mammography

- Problems to address
  - No risk assessment models that predict individual risk with any accuracy
  - Human variation in interpretation (quality)
  - Lack of human breast imaging specialists to support screening mammography expansion (access)

Our Challenge

- In order for screening tests to be effective, essential to screen an <u>at-risk population</u>
- False positives are decreased when prevalence is increased through <u>risk assessment</u>



CANCER CARE

By Mei-Sing Ong and Kenneth D. Mandl

DOI: 10.1377/hlthaff.2014.1087
HEALTH AFFAIRS 34,
NO. 4 (2015): 576–583

National Expenditure For False-Positive Mammograms And Breast Cancer Overdiagnoses Estimated At $4 Billion A Year

Impact of False High Risk Assessment on Patients and Systems

- Anxiety, unnecessary tests, interventions
  - MRI or US screening
  - Chemoprevention
  - Mastectomy
  - Costs

American Cancer Society 2007

"Based on the evidence from studies of MR screening high risk women, and the limitations of mammography and CBE alone, the American Cancer Society recommends annual MR screening in conjunction with mammography in women at significantly increased risk of breast cancer."

American Cancer Society®

NCCN National Comprehensive Cancer Network®

EUSOBI european society of breast imaging

SBI ACR Breast Imaging Symposium 2 0 1 7

Original Investigation

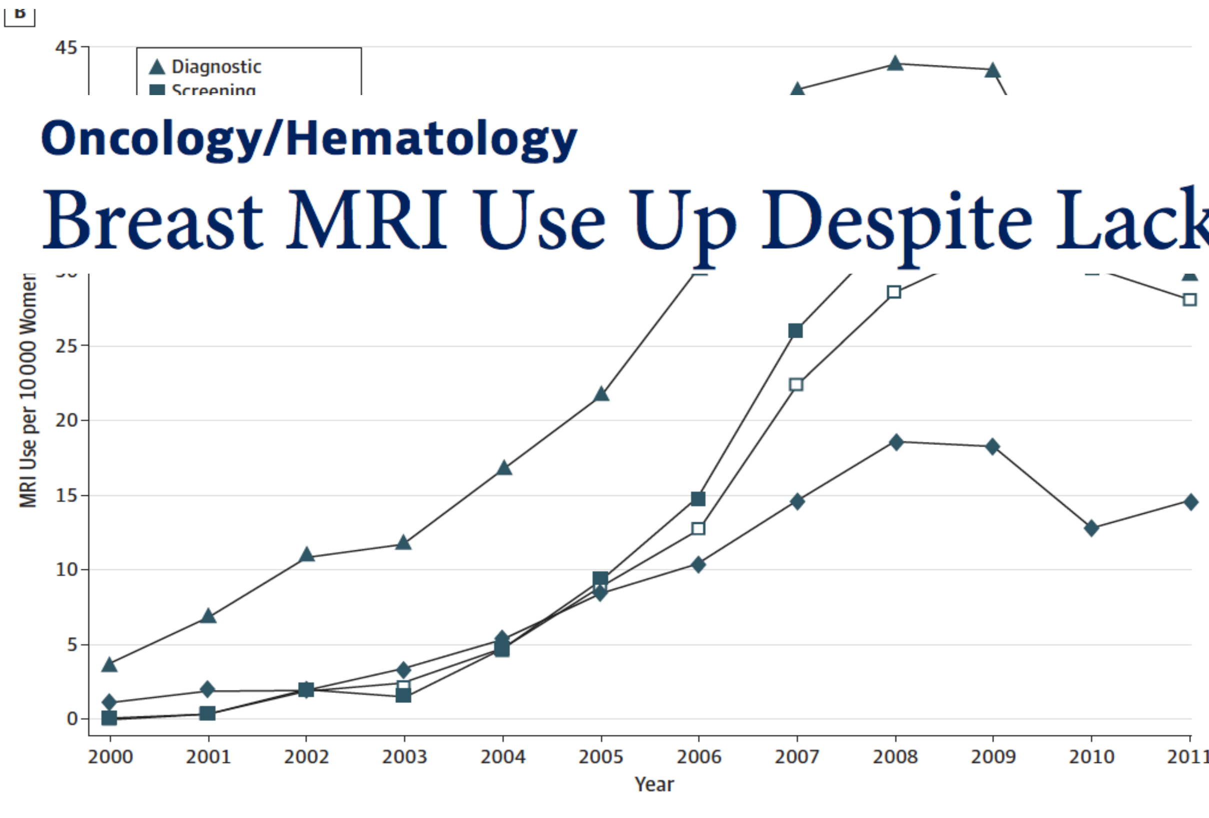
Rapid Increase in Breast Magnetic Resonance Imaging Use

Trends From 2000 to 2011

Breast MRI use grows, but does it benefit the right women?

Oncology/Hematology

Breast MRI Use Up Despite Lack of Indications



A, Age-specific rates. Each bar within an age group represents a calendar year. B, Indication-specific rates for 4 primary indications: screening, diagnostic, staging or treatment, and surveillance.

Table 4. Breast Cancer Risk Assessment Tool (BCRAT) Scores for Lifetime Breast Cancer Risk for Women Screened With Breast Magnetic Resonance Imaging (MRI) and Women Screened With Mammography Alone, 2005 Through 2009

BCRAT Lifetime Risk Score	Year, No. (%) 2005	2006	2007	2008	2009	Total
Examinations of women who received breast MRI for screening[a]						
<15%	57 (74)	147 (50)	227 (55)	194 (53)	202 (50)	827 (53)
15%-20%	13 (17)	85 (29)	84 (20)	79 (21)	87 (21)	348 (22)
>20%	7 (9)	60 (21)	101 (25)	96 (26)	119 (29)	383 (25)
Examinations of women who received screening mammography only						
<15%	234 209 (92)	229 157 (92)	228 708 (92)	222 685 (92)	216 402 (92)	1 131 161 (92)
15%-20%	15 120 (6)	14 480 (6)	14 590 (6)	14 560 (6)	13 657 (6)	72 407 (6)
>20%	5153 (2)	5110 (2)	5033 (2)	5021 (2)	4920 (2)	25 237 (2)

[a] Test for trend comparing total proportion at higher than 20% (high) risk to 20% risk or lower (P <.001).

- 75% of all screening MRIs performed were in women with less than 20% lifetime risk
- Of women at greater than 20% lifetime risk, less than 2% had received an MRI

Classical Risk Models

Age

Family History

Prior Breast Procedure

Parity

Breast Density

Risk

AUC: **0.631**

AUC: 0.607 without Density

J Natl Cancer Inst. 2006 Sep 6;98(17):1204-14.

Prospective breast cancer risk prediction model for women undergoing screening mammography.

Barlow WE[1], White E, Ballard-Barbash R, Vacek PM, Titus-Ernstoff L, Carney PA, Tice JA, Buist DS, Geller BM, Rosenberg R, Yankaskas BC, Kerlikowske K.

Screening Mammography Interpretation and AI

- Breast Density?
- Normal or Not?

VOL. 89 NO. 2

Radiology

AUGUST 1967

a monthly journal devoted to clinical radiology and allied sciences

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, INC.

A Study of Breast Parenchyma by Mammography in the Normal Woman and Those with Benign and Malignant Disease[1]

JOHN N. WOLFE, M.D.[2]

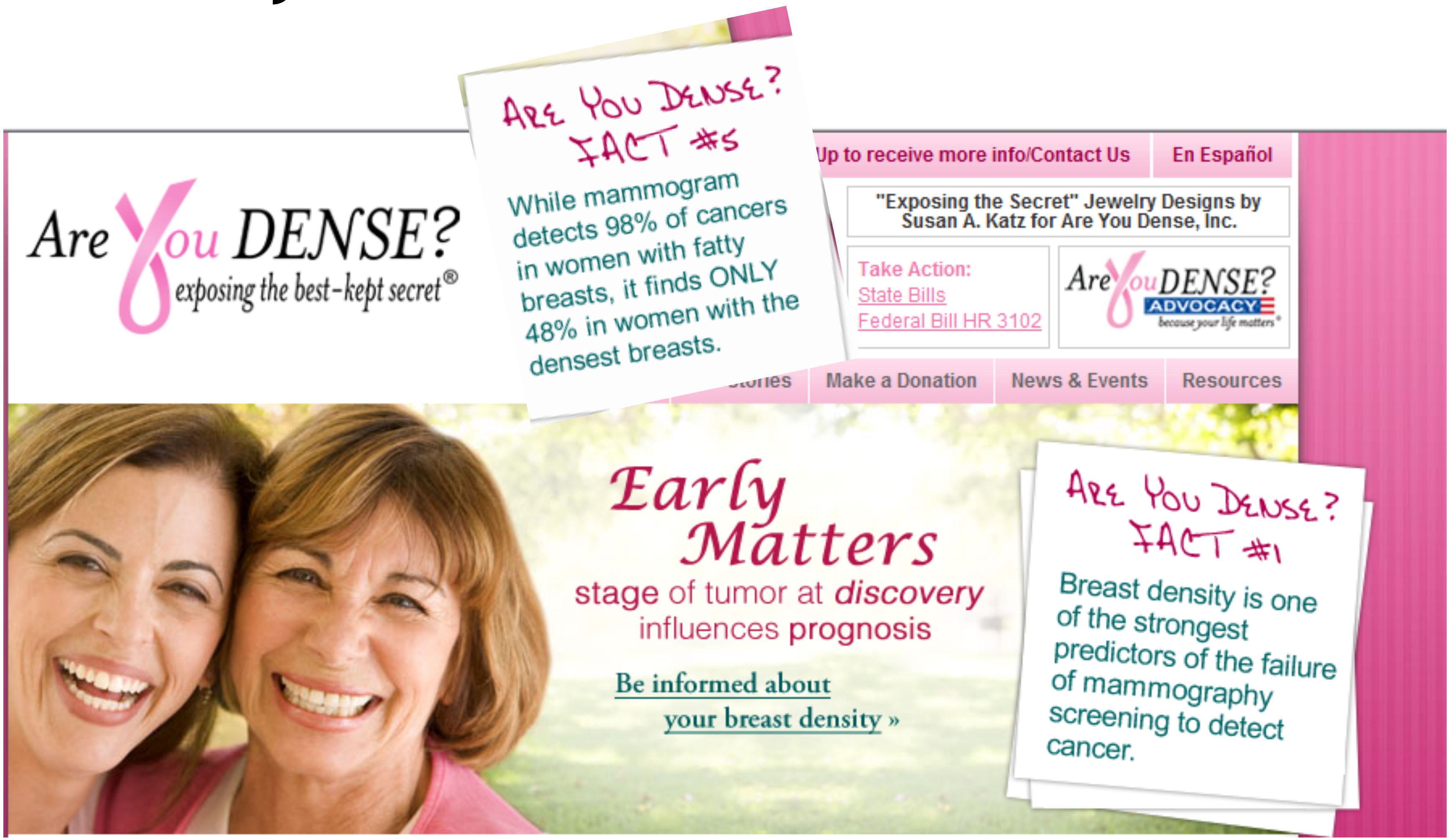
All normal and abnormal parenchymal elements were noted, but the main emphasis was on assessment of the alveolar tissue and ducts; their presence or absence, amount, and distribution. This material was coded and later subjected to analysis by computer.

Breast Composition

- “visually estimated content of fibroglandular-density within the breasts”

Breast Composition Categories
a. The breasts are almost entirely fatty
b. There are scattered areas of fibroglandular density
c. The breasts are heterogeneously dense, which may obscure small masses
d. The breasts are extremely dense, which lowers the sensitivity of mammography

Advocacy efforts to inform women



Breast Density Law

Nancy Cappello
1952-2018

- Diagnosed: 2003, stage III
- Her last mammogram was false negative
- She lobbied for supplemental screening law in Connecticut
- The law was enacted in 2005

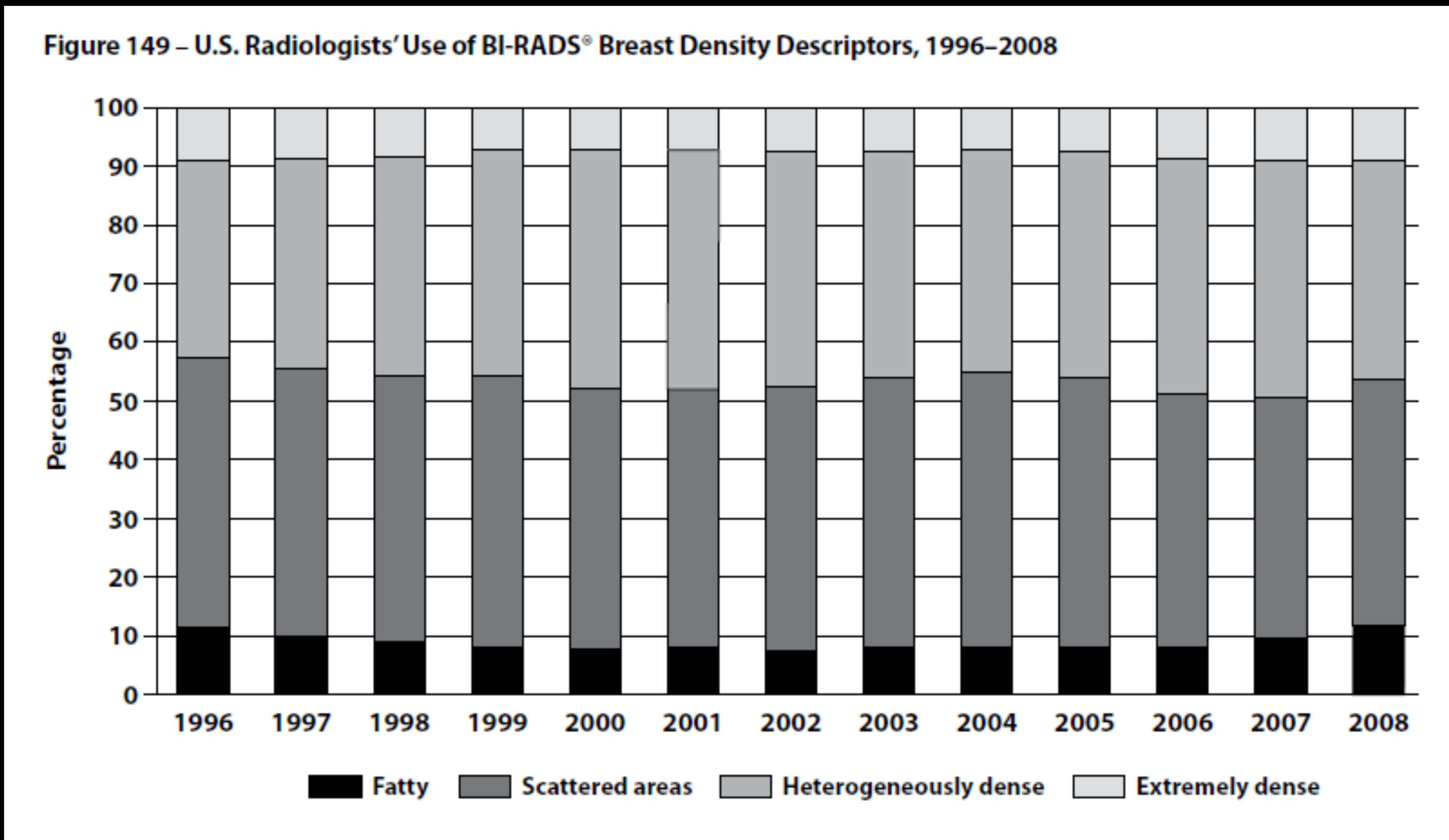
New federal law requires mammography providers to send breast density notifications

February 19, 2019 | Michael Walter | Policy

When President Donald Trump signed a federal funding bill into law on Feb. 15, it included text that said that all mammography providers must include updated information about breast density in reports sent to both patients and their physicians.

The notifications sent out to patients will inform them about their own personal breast density and explain the importance of that information. More than 30 states currently require such information to be shared with patients after they undergo a mammogram, a number that has been rising steadily for years.

Breast Cancer Surveillance Consortium data from over 3.8 million screening mammograms in U.S. community practice: over 50% of women told they have dense tissue



Quartile ranges introduced

Wide Variation in Radiologists' Assessment of Mammograms as "Dense"

Ann Intern Med. 2016 Oct 4;165(7):457-464. doi: 10.7326/M15-2934. Epub 2016 Jul 19.

Variation in Mammographic Breast Density Assessments Among Radiologists in Clinical Practice: A Multicenter Observational Study.

Sprague BL[1], Conant EF[1], Onega T[1], Garcia MP[1], Beaber EF[1], Herschorn SD[1], Lehman CD[1], Tosteson AN[1], Lacson R[1], Schnall MD[1], Kontos D[1], Haas JS[1], Weaver DL[1], Barlow WE[1]; PROSPR Consortium.

83 radiologists:
6% to 85% of large (>500) number of mammograms read as "dense"

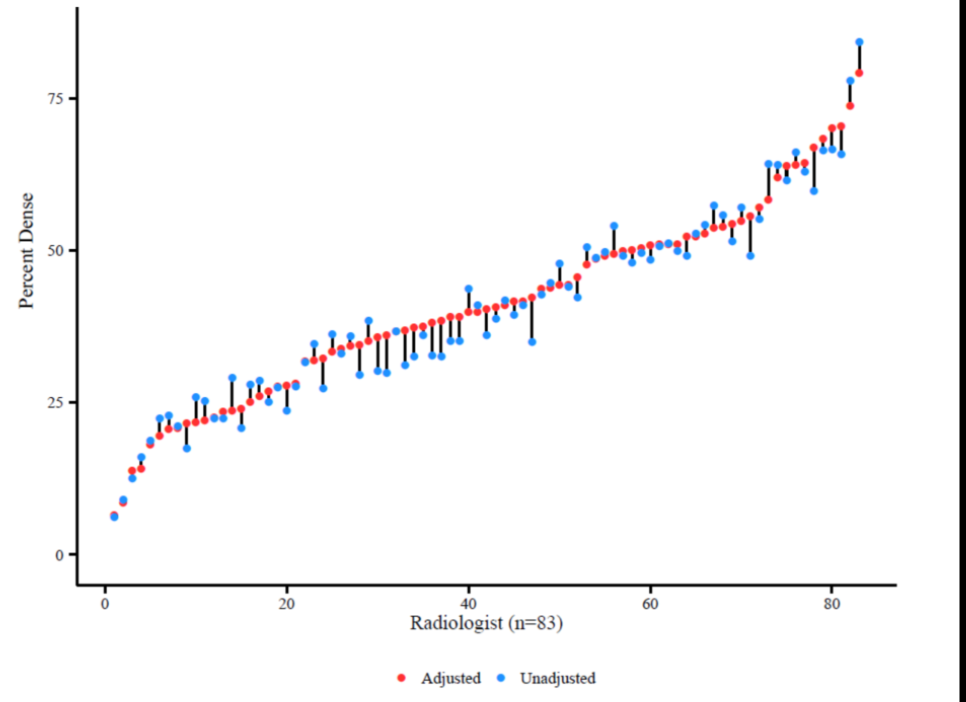
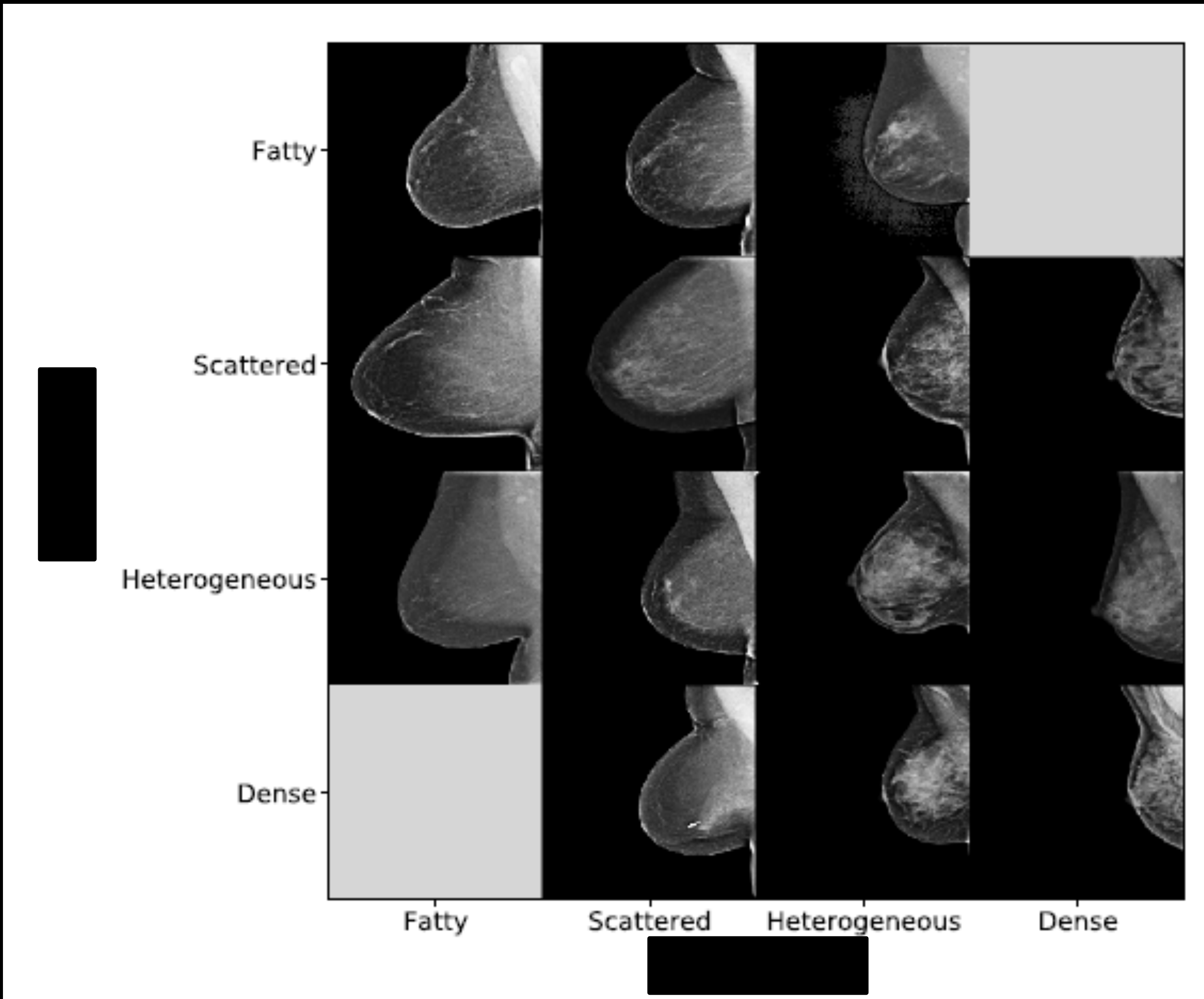


Figure 2. Paired unadjusted and multivariable-adjusted percent of patients with dense breasts (heterogeneously or extremely dense), by radiologist.

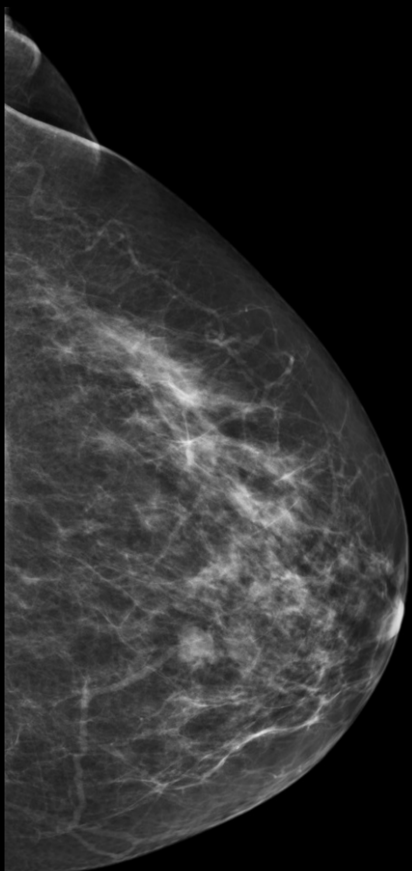

Fatty
Scattered
Heterogeneous
Dense
[redacted]
Fatty
Scattered
Heterogeneous
Dense
[redacted]

Screening Mammography Interpretation and AI

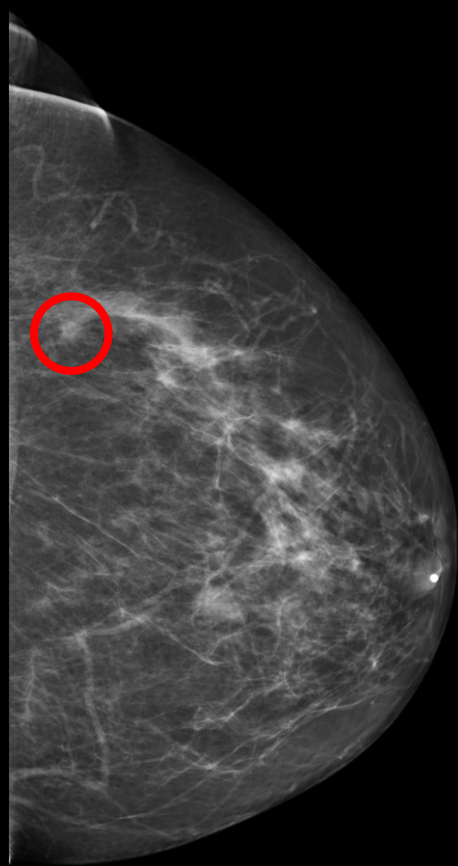
- Breast Density?
- Normal or Not?

Interpretation: Normal or Not?

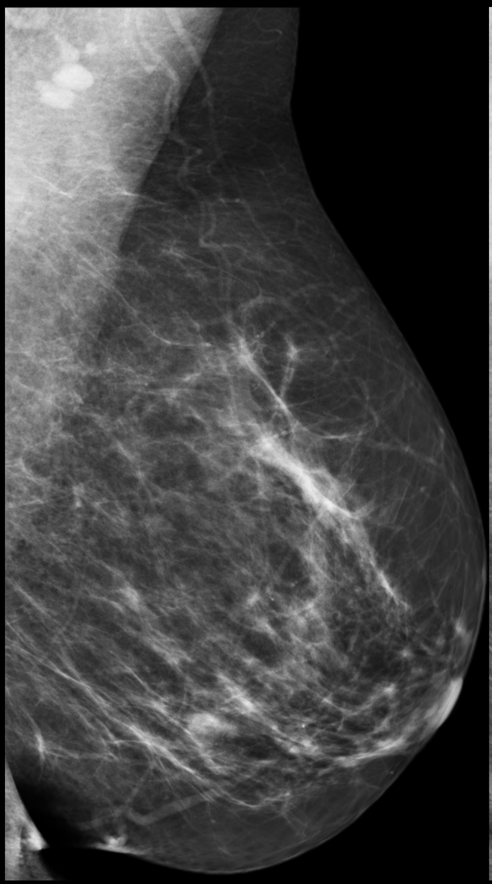
Prior



Current



Prior

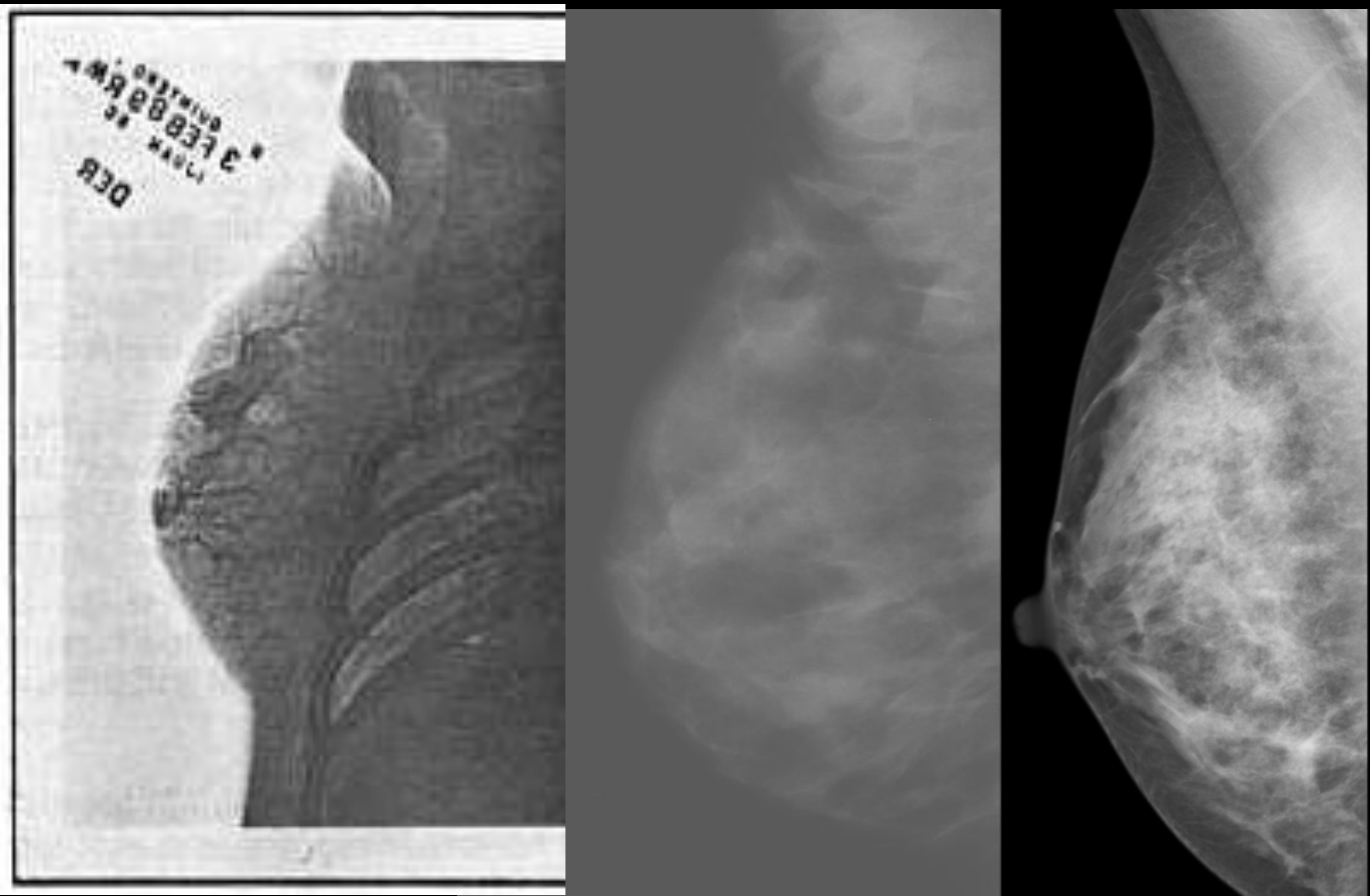


Current

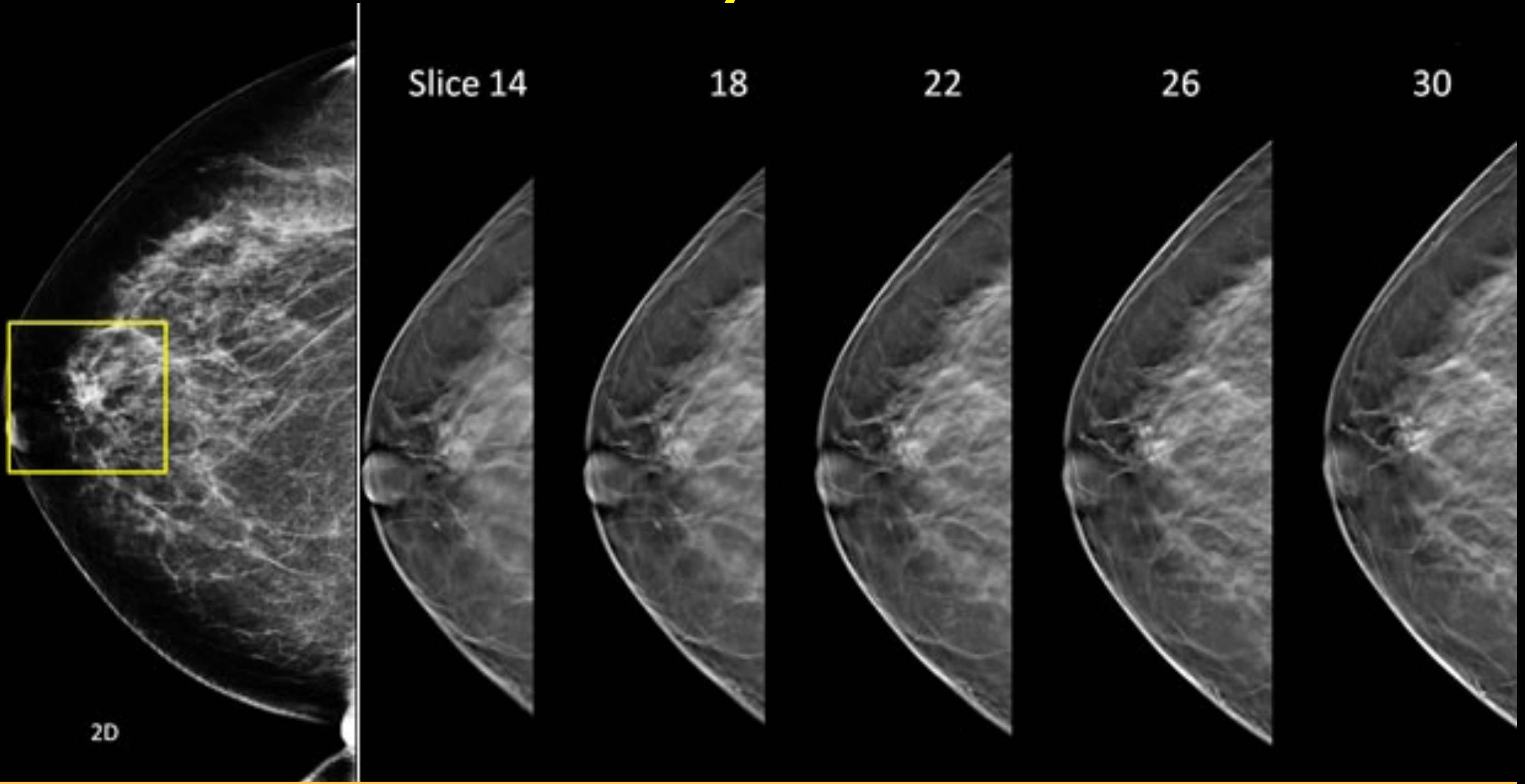
Challenges

- Our imaging screening tests depend on highly specialized human expertise
  - Human variation in performance of tasks

Advances in imaging technology have outpaced human performance in interpreting mammograms accurately

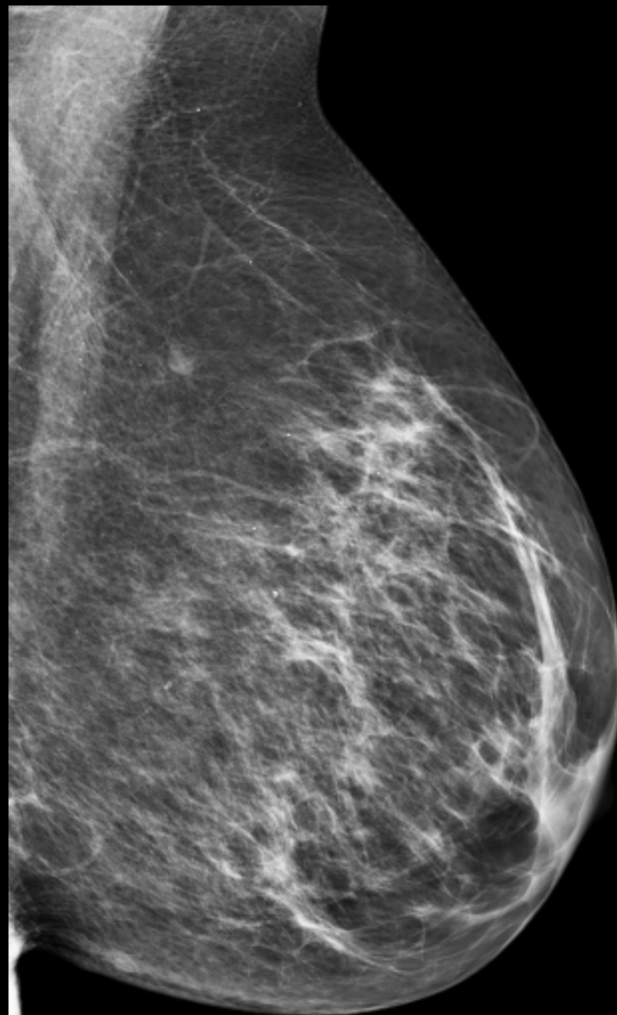


Tomosynthesis

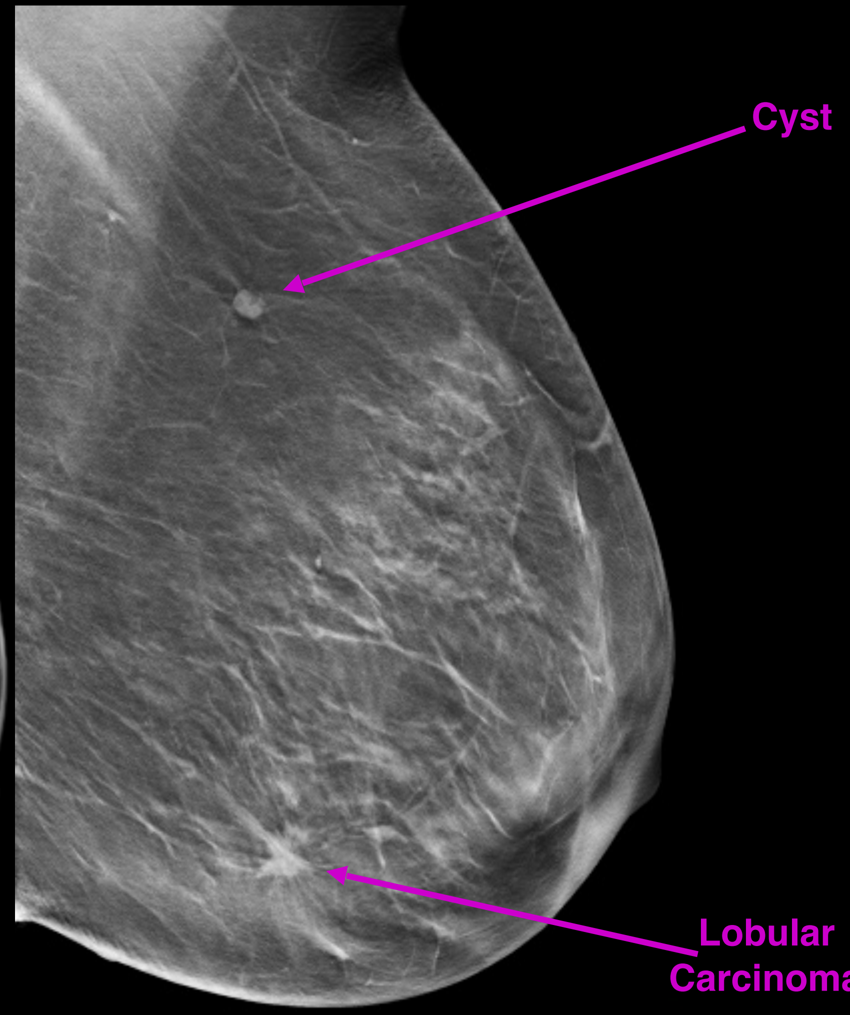


DBT Reveals Occult ILC

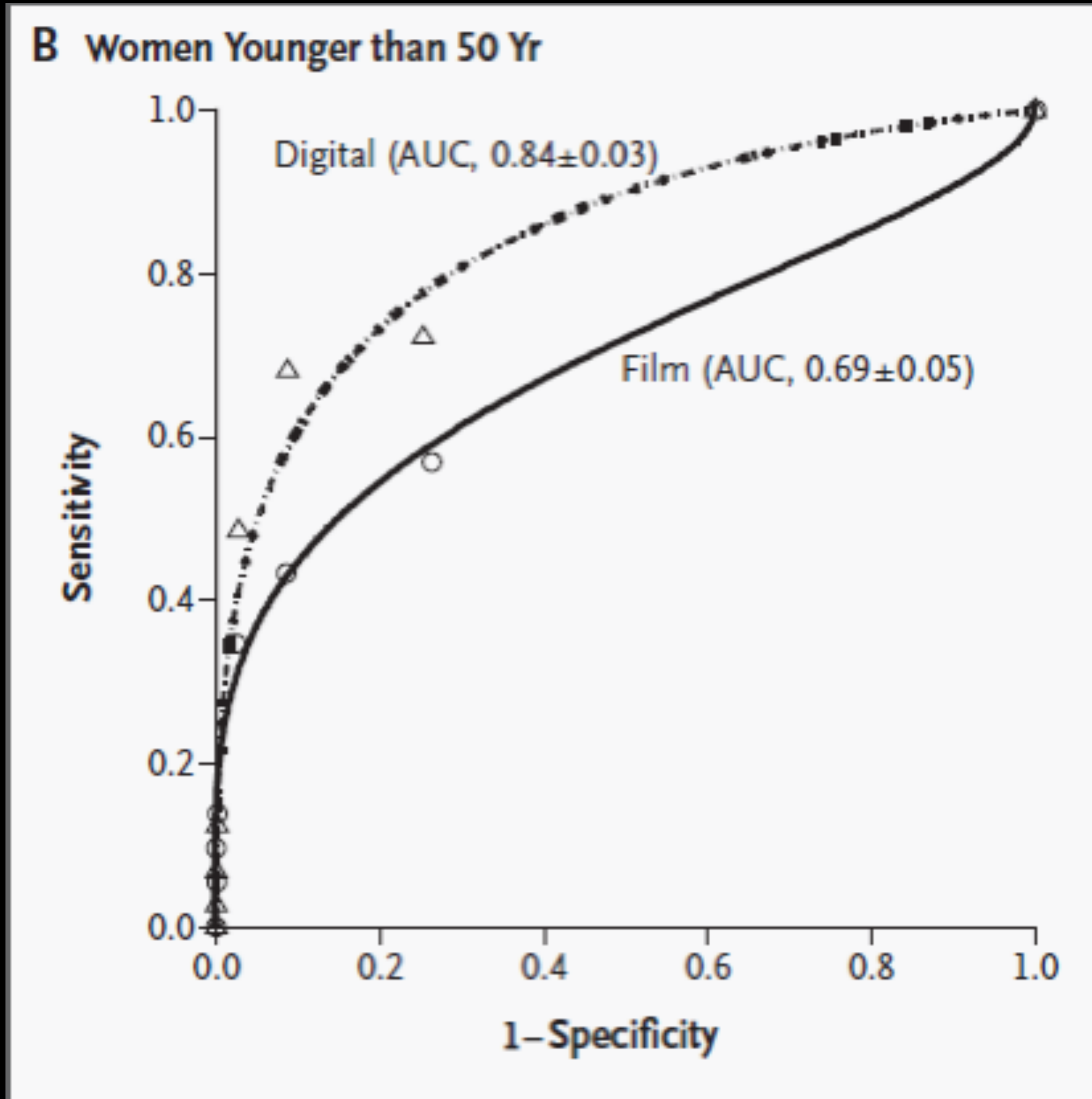
2D FFDM



Tomosynthesis Slice



Images courtesy of Drs. Di Maggio & G Gennaro,
Istituto Oncologico Veneto I.R.C.C.S. - Padova, Italia


B Women Younger than 50 Yr
Digital (AUC, 0.84±0.03)
Film (AUC, 0.69±0.05)
Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.2
0.4
0.6
0.8
1.0
1–Specificity

$P < 0.002$

Radiology

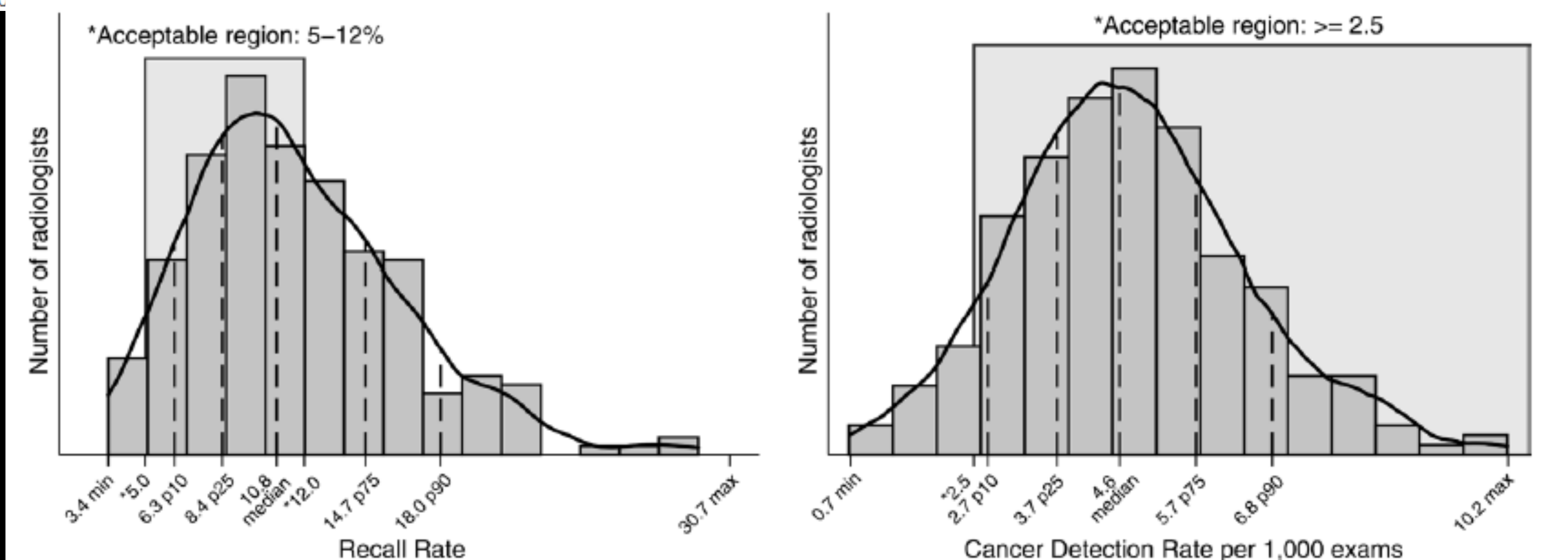
ORIGINAL RESEARCH ■ BREAST IMAGING

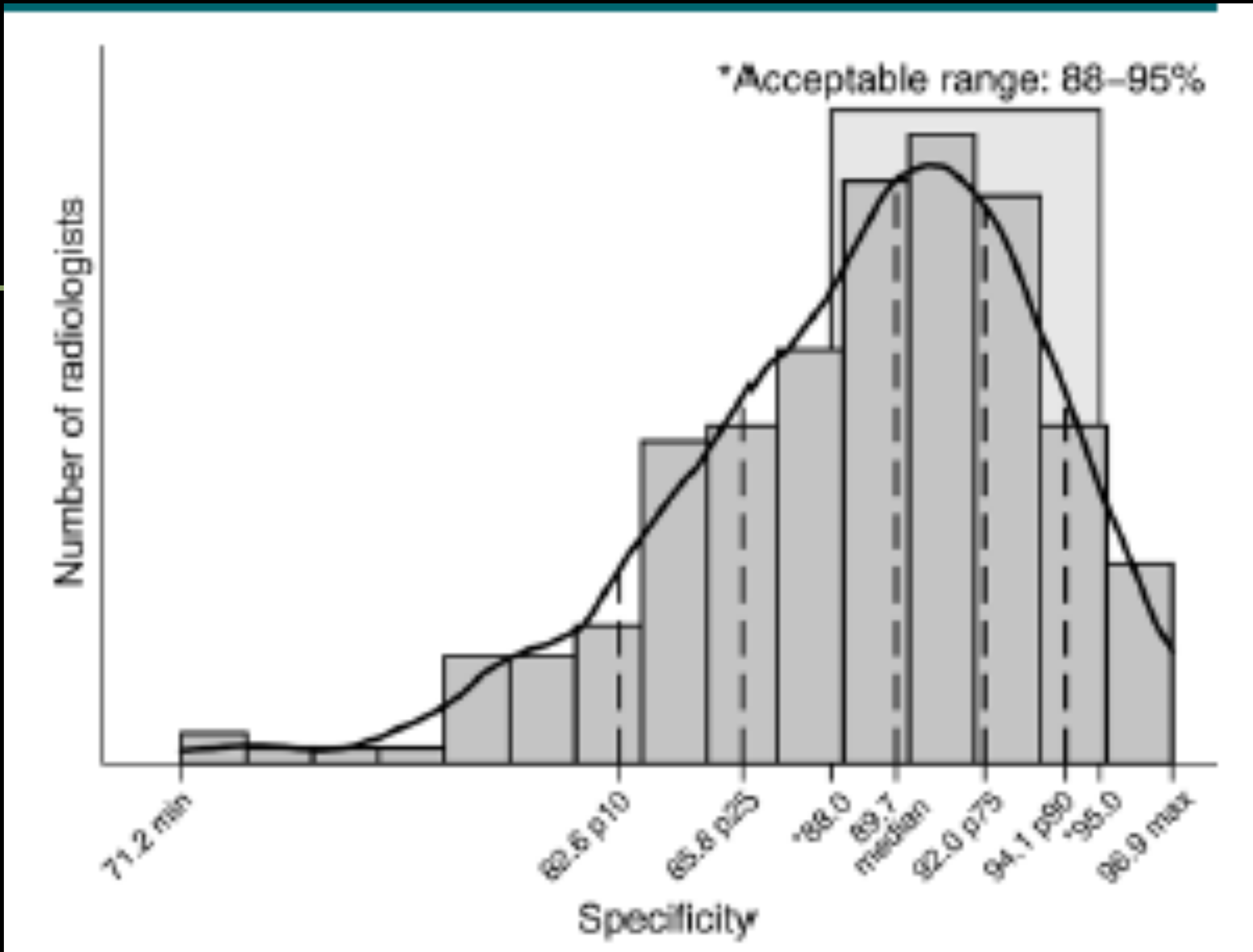
National Performance Benchmarks for Modern Screening Digital Mammography: Update from the Breast Cancer Surveillance Consortium[1]

Constance D. Lehman, MD, PhD
Robert F. Arao, MPH
Brian L. Sprague, PhD
Janie M. Lee, MD, MSc
Diana S. M. Buist, PhD, MPH
Karla Kerlikowske, MD
Louise M. Henderson, PhD, MSPH
Tracy C

Purpose: To establish performance benchmarks for modern screening digital mammography and assess performance trends over time in U.S. community practice.

Materials and Methods: This HIPAA-compliant, institutional review board–approved study measured the performance of digital screening mammography interpreted by 359 radiologists across 95 facilities





Breast Cancer Surveillance Consortium
BCSC
Working together to advance breast cancer research

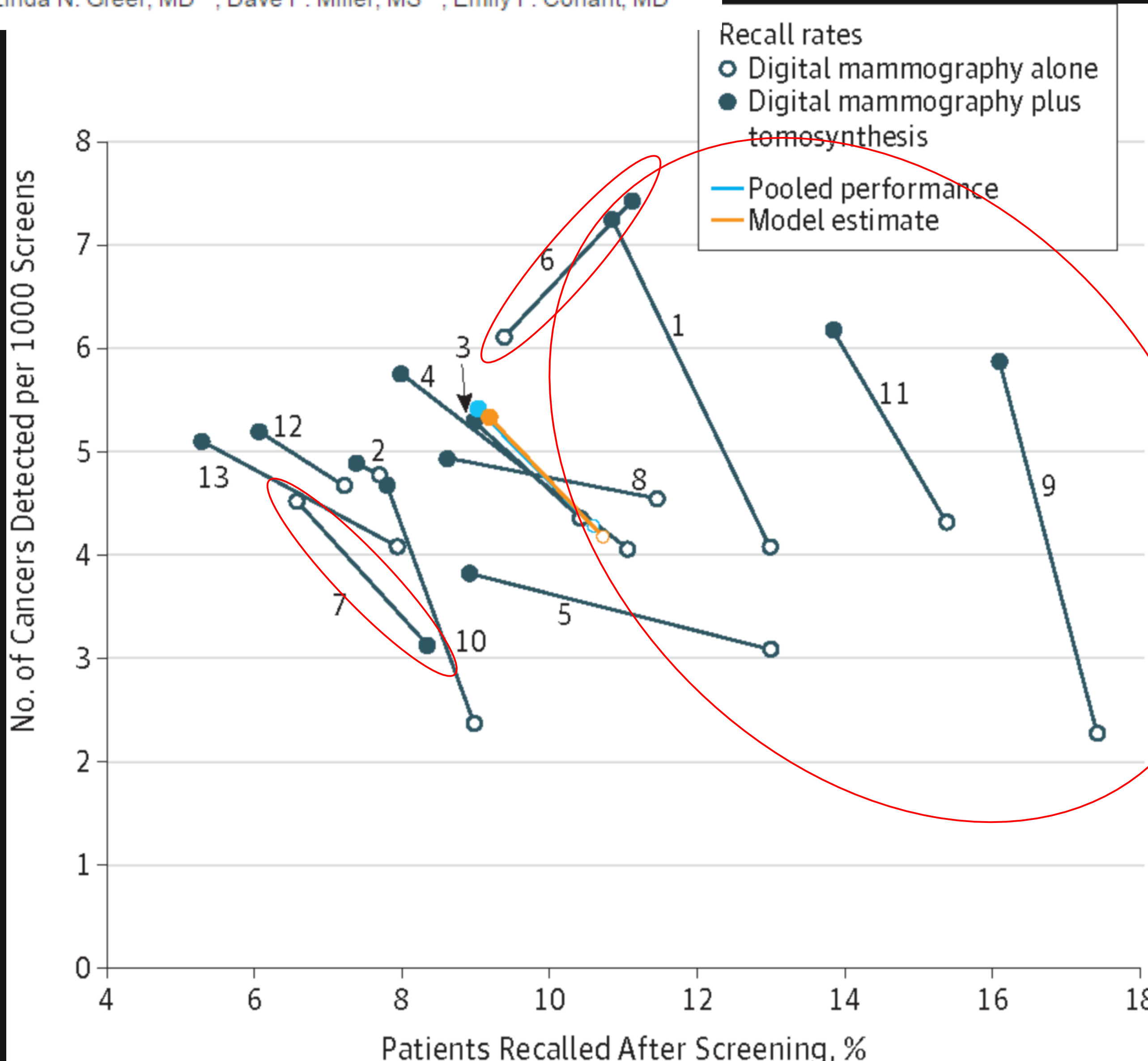
- More than 40% of radiologists have AIRs outside the recommended ranges, and more than 37% fall below recommended ranges for specificity.

Lehman et al ***Radiology*** April 2017

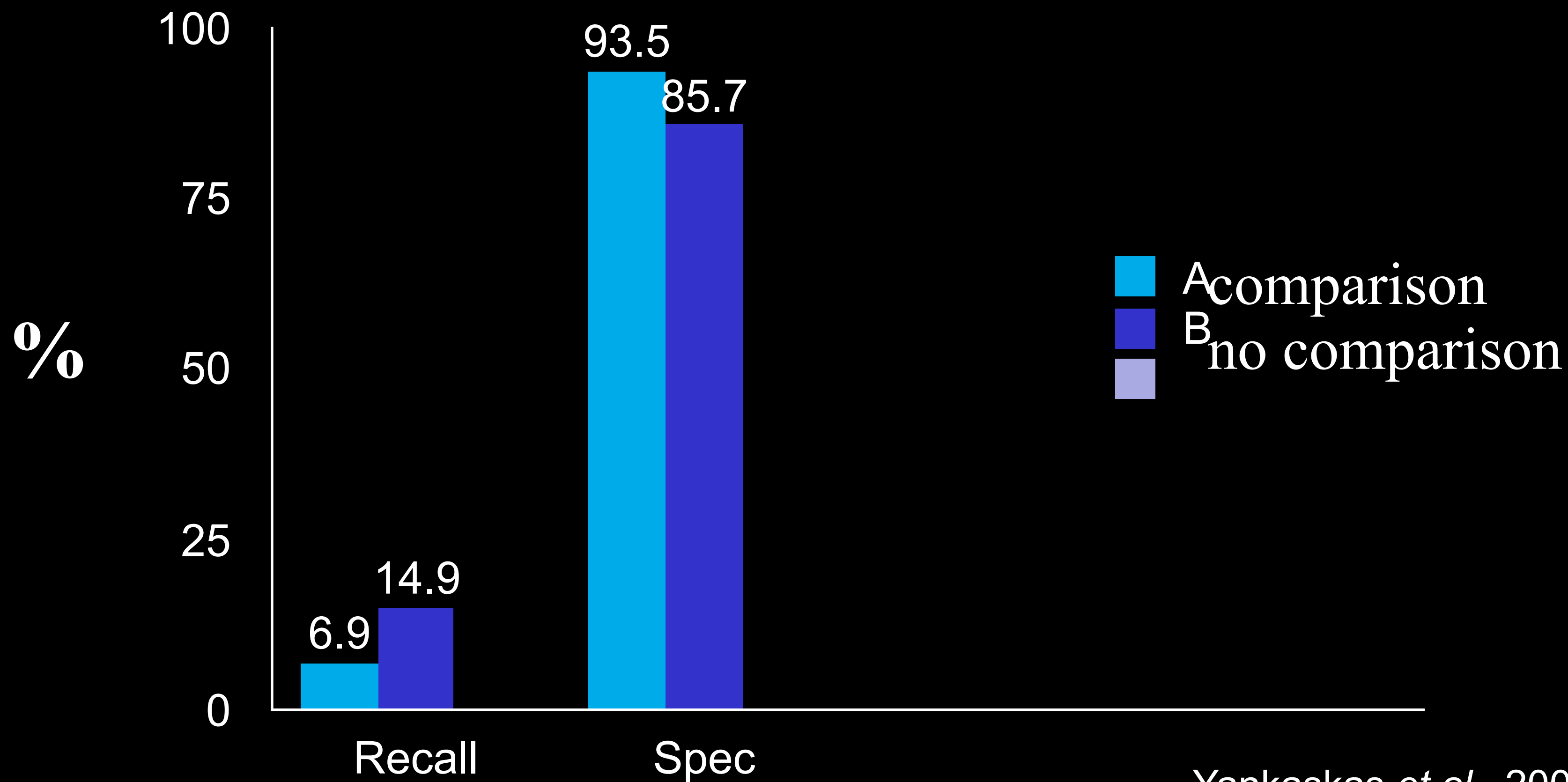
Breast Cancer Screening Using Tomosynthesis in Combination With Digital Mammog / FREE

Sarah M. Friedewald, MD[1]; Elizabeth A. Rafferty, MD[2]; Stephen L. Rose, MD[3,4]; Melissa A. Durand, MD[5]; Donna M. Plecha, MD[6]; Julianne S. Greenberg, MD[7]; Mary K. Hayes, MD[8]; Debra S. Copit, MD[9]; Kara L. Carlson, MD[10]; Thomas M. Cink, MD[11]; Lora D. Barke, DO[12]; Linda N. Greer, MD[13]; Dave P. Miller, MS[14]; Emily F. Conant, MD[15]

Modern technology is better but wide variation across radiologists

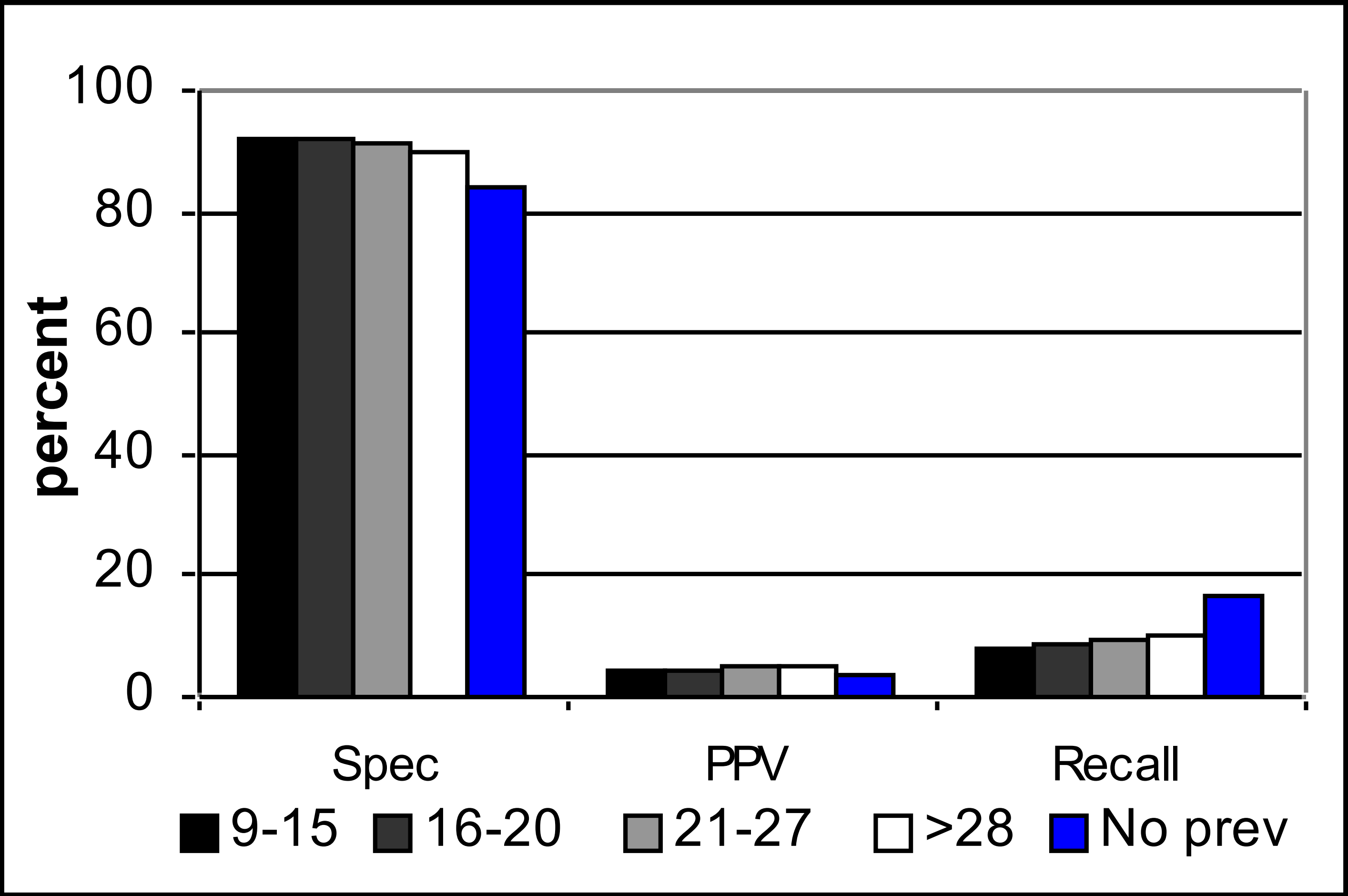


Performance of screening test influenced by group (> 1 million cases)

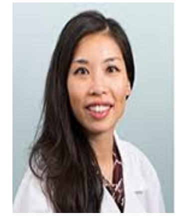


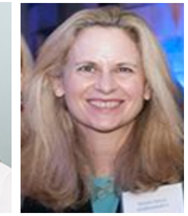
Yankaskas *et al.*, 2005

“No Comparison Mammogram” strongest predictor of “harms”



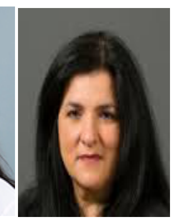
Yankaskas *et al.*, 2005

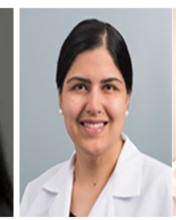


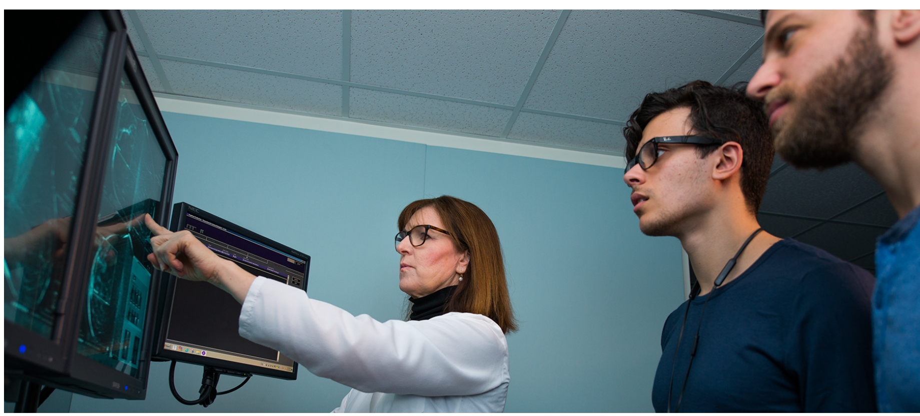


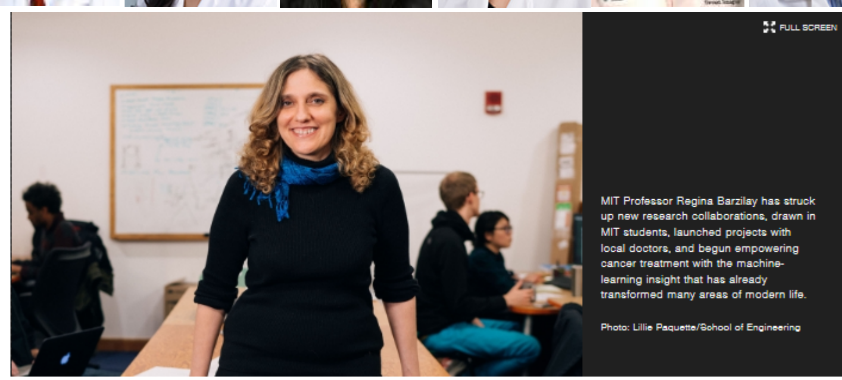
MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL









Putting data in the hands of doctors

Computer scientist Regina Barzilay empowers cancer treatment with machine learning.

First LOOK

PARTNERS HEALTHCARE

Knowledge of effective strategies for clinical implementation essential

- Breast density DL platform in place now at MGH and implemented in routine clinical care
  - 50,000 screening mammograms/year performed/processed
- 1 (triage), 2 and 5 year risk assessment DL model platform in place at MGH and under evaluation for performance

ORIGINAL RESEARCH ■ BREAST IMAGING

Radiology

High-Risk Breast Lesions: A Machine Learning Model to Predict Pathologic Upgrade and Reduce Unnecessary Surgical Excision[1]

Manisha Bahl, MD, MPH
Regina Barzilay, PhD
Adam B. Yedidia, MEng
Nicholas J. Locascio, MEng
Lili Yu, PhD
Constance D. Lehman, MD, PhD

Purpose: To develop a machine learning model that allows high-risk breast lesions (HRLs) diagnosed with image-guided needle biopsy that require surgical excision to be distinguished from HRLs that are at low risk for upgrade to cancer at surgery and thus could be surveilled.

ORIGINAL RESEARCH • BREAST IMAGING

Radiology

Mammographic Breast Density Assessment Using Deep Learning: Clinical Implementation

Constance D. Lehman, MD, PhD • Adam Yala, MEng • Tal Schuster, MSc • Brian Dontchos, MD • Manisha Bahl, MD, MPH • Kyle Swanson, BS • Regina Barzilay, PhD

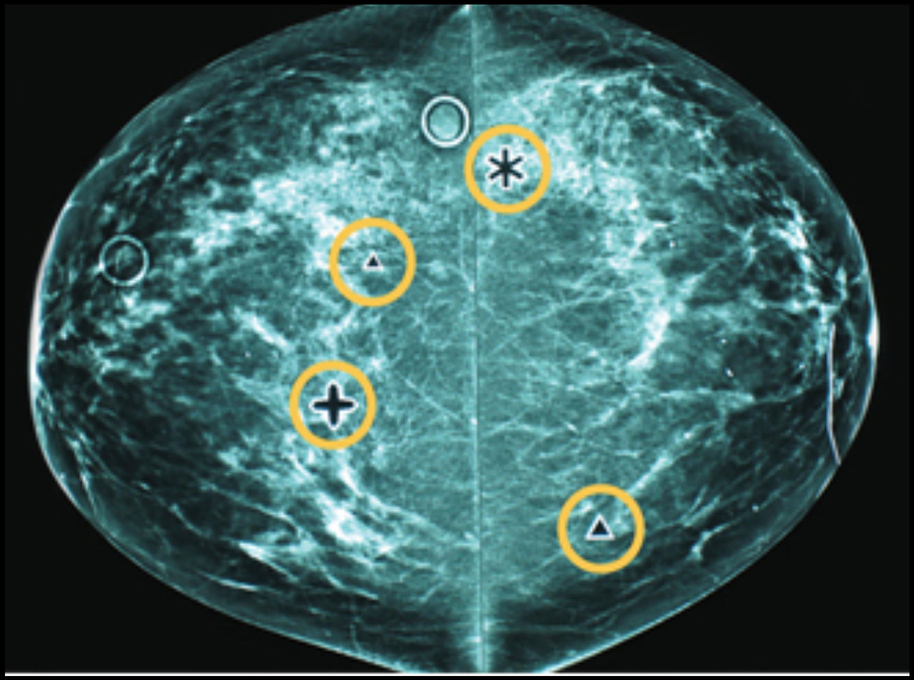
From the Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Avon Comprehensive Breast Evaluation Center, 55 Fruit St, WAC 240, Boston, MA 02114-2698 (C.D.L., B.D., M.B.); and Massachusetts Institute of Technology, Cambridge, Mass (A.Y., T.S., K.S., R.B.). Received March 24, 2018; revision requested May 14; revision received August 21; accepted August 27. **Address correspondence to** C.D.L. (e-mail: *clehman@partners.org*).

- Rigorous peer reviewed original scientific publications

Culture and Resistance to Change

"I'll be happy to give you innovative thinking. What are the guidelines?"

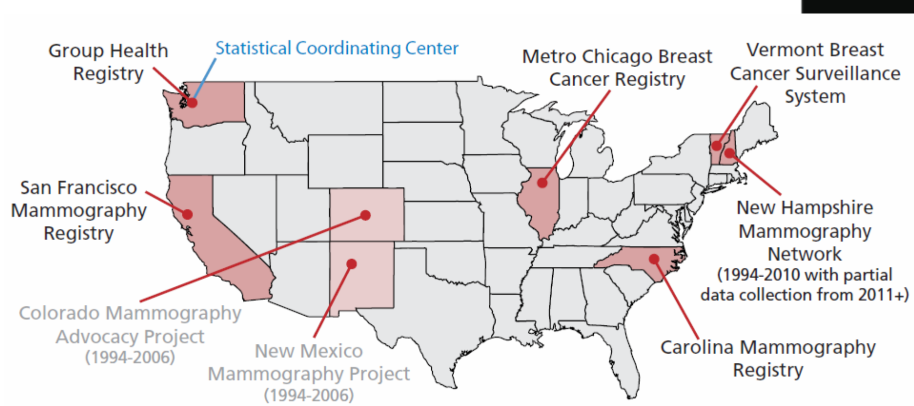
Brief History of Past Traditional CAD Methods in Mammography

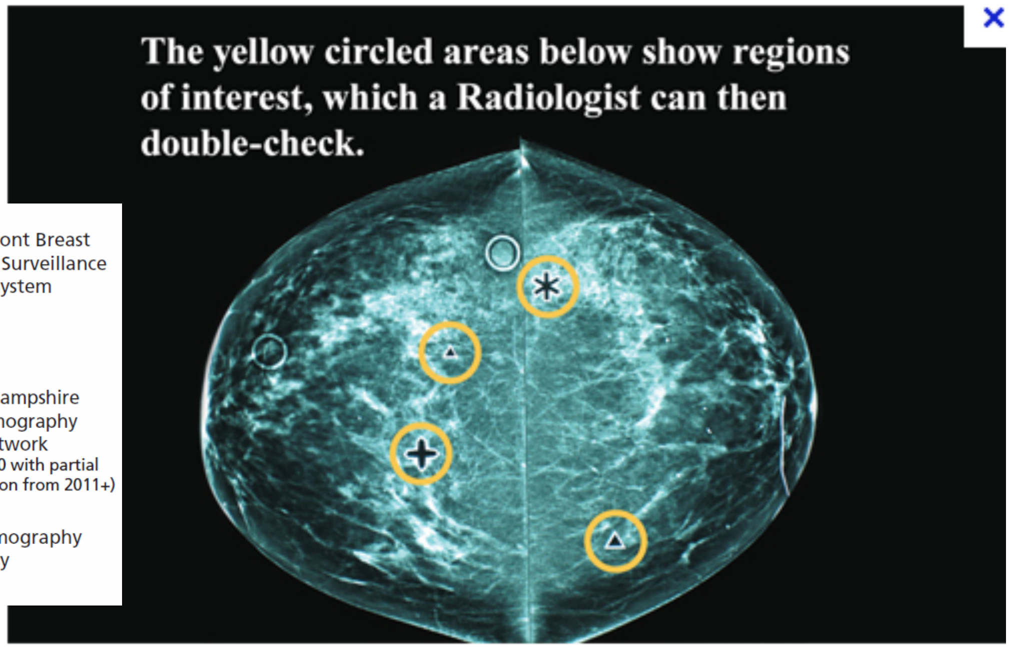


Overview

Breast Cancer Surveillance Consortium
BCSC
Working together to advance breast cancer research

- CAD applied to mammography approved by FDA in 1998
- With reimbursement, use rapidly increased across the U.S.
- Multiple study designs in early phases: retrospective, reader studies, prospective small single site, etc. with mixed results on impact of CAD on accuracy of mammographic interpretation





Background

Breast Cancer Surveillance Consortium
BCSC
Working together to advance breast cancer research

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Influence of Computer-Aided Detection on Performance of Screening Mammography

Joshua J. Fenton, M.D., M.P.H., Stephen H. Taplin, M.D., M.P.H., Patricia A. Carney, Ph.D., Linn Abraham, M.S., Edward A. Sickles, M.D., Carl D'Orsi, M.D., Eric A. Berns, Ph.D., Gary Cutter, Ph.D., R. Edward Hendrick, Ph.D., William E. Barlow, Ph.D., and Joann G. Elmore, M.D., M.P.H.

N Engl J Med 2007; 356:1399-1409 | April 5, 2007 | DOI: 10.1056/NEJMoa066099

- 1998-2002 at 43 BCSC facilities (GHC Seattle, New Hampshire, Colorado)
- Conducted early in adoption (7 of 43 facilities implemented CAD during the study)

The NEW ENGLAND JOURNAL of MEDICINE

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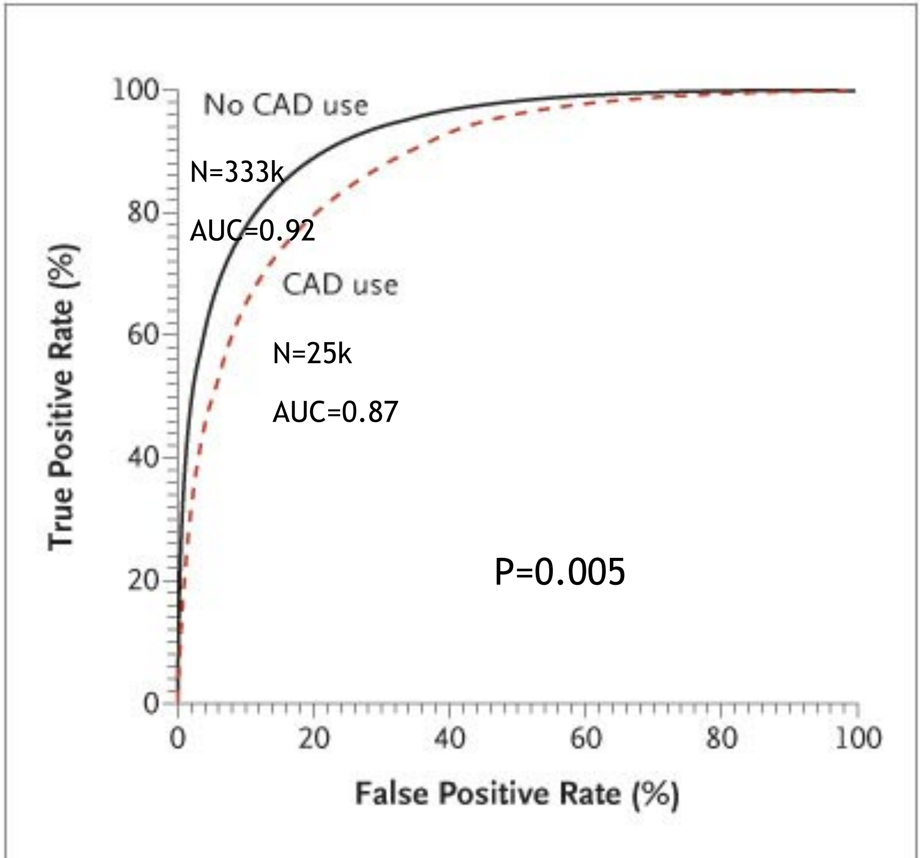
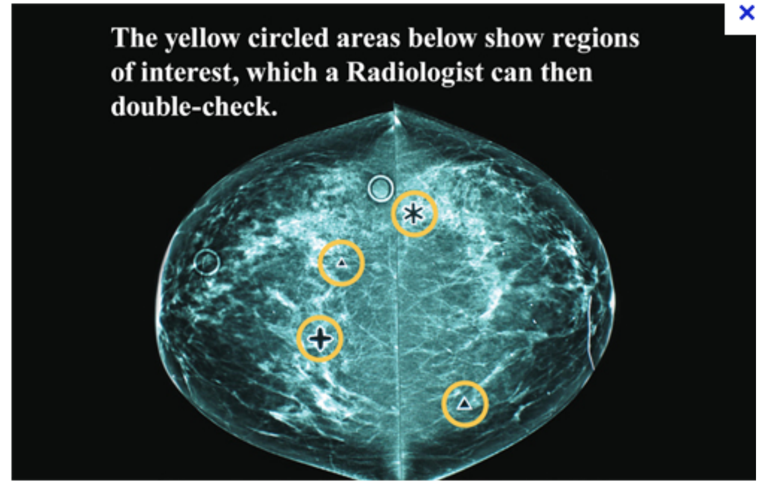
ORIGINAL ARTICLE

Influence of Computer-Aided Detection on Performance of Screening Mammography



Fenton, et al. April 5, 2007
Data source: BCSC



Study Limitations

- Data from early years of CAD integration (1998-2002)
- Didn't control for learning curve (weeks to a year to learn to use CAD)
- Outdated "obsolete" technology (film screen CAD)
- Low numbers (25k CAD exams)

Research

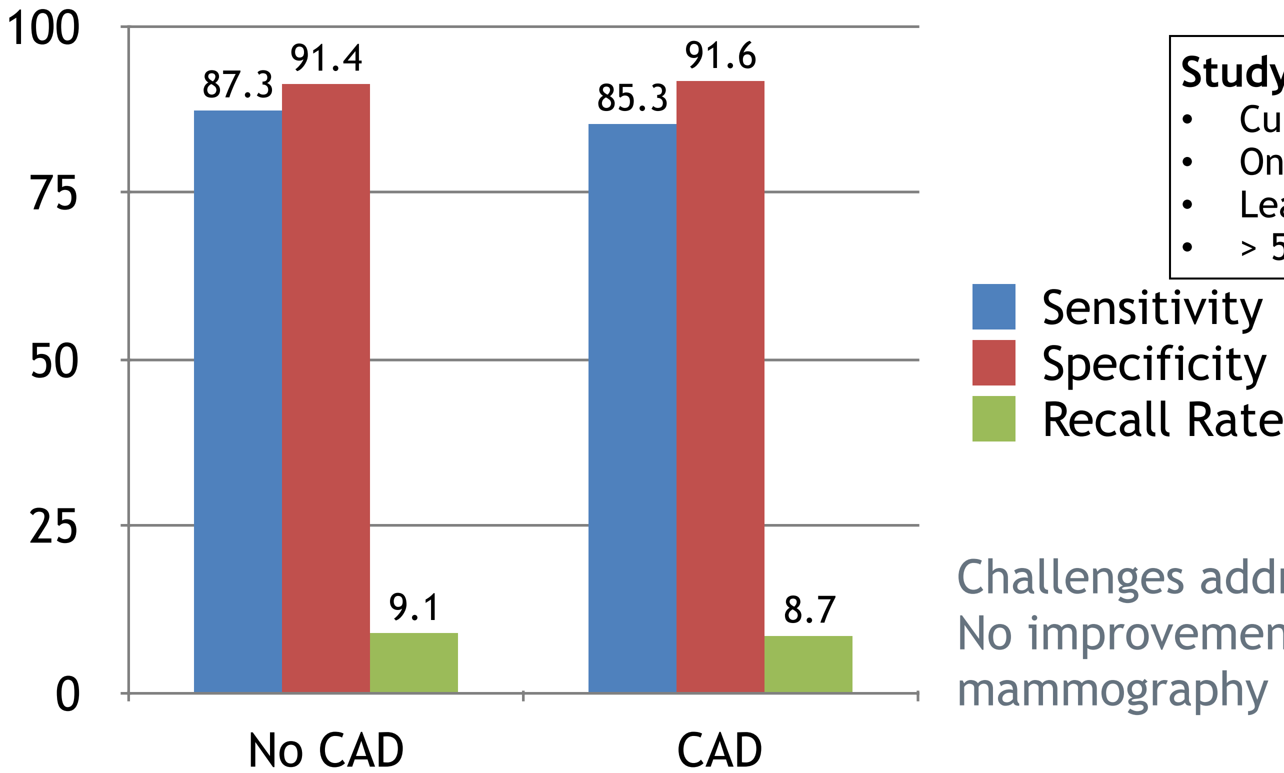
Original Investigation | LESS IS MORE

Diagnostic Accuracy of Digital Screening Mammography With and Without Computer-Aided Detection

Constance D. Lehman, MD, PhD; Robert D. Wellman, MS; Diana S. M. Buist, PhD; Karla Kerlikowske, MD; Anna N. A. Tosteson, ScD; Diana L. Miglioretti, PhD; for the Breast Cancer Surveillance Consortium

Breast Cancer Surveillance Consortium
BCSC
Working together to advance breast cancer research

JAMA Intern Med. 2015;175(11):1828-1837. doi:10.1001/jamainternmed.2015.5231



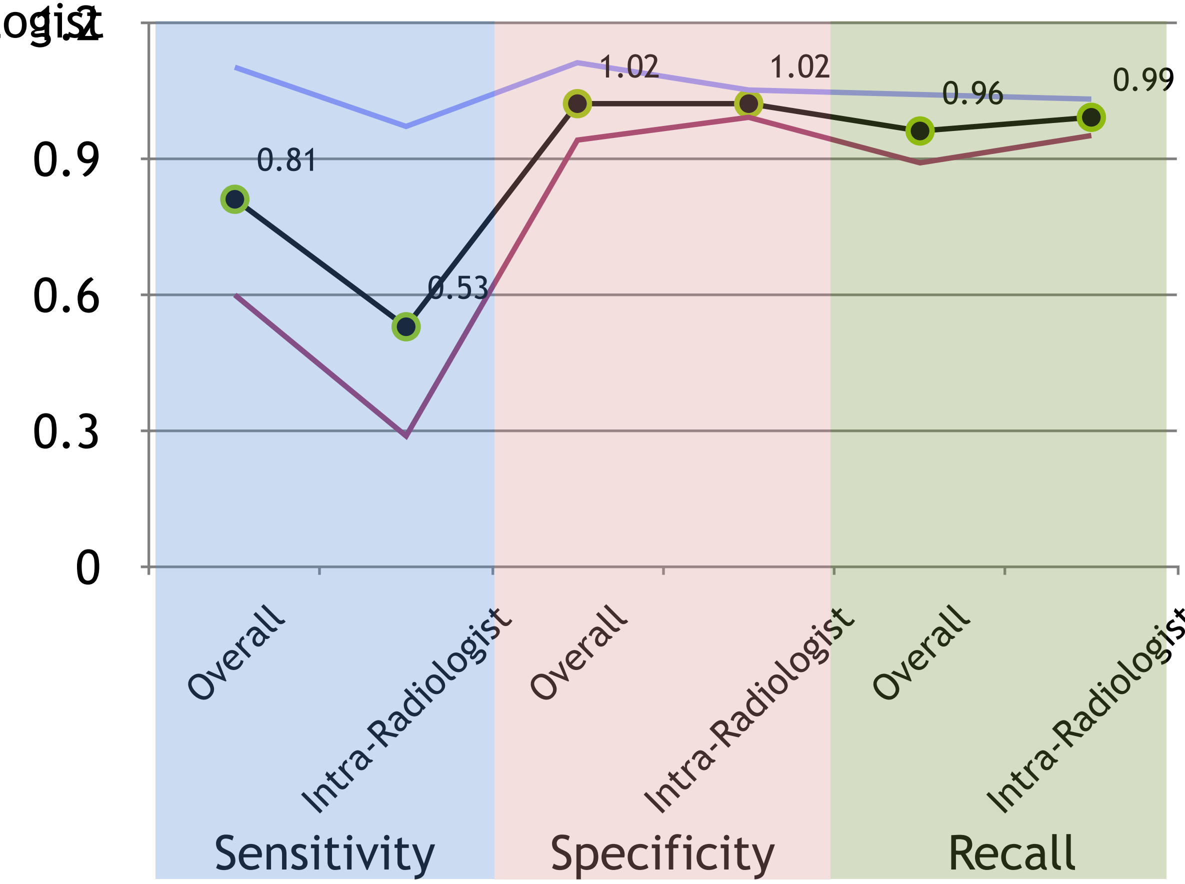
Study Strengths
- Current performance 2003-09
- Only digital mammo with CAD
- Learning curve addressed
- > 569k CAD exams

Challenges addressed by BCSC:
No improvement of digital mammography performance with CAD

Odds ratio for CAD vs. No CAD adjusted for site, age, race, time since prior mammogram and calendar year of exam using mixed effects model with random effect for exam reader and varying with CAD use found no significant difference in sensitivity, specificity or recall rate.

Intra-radiologist analysis: Mammography performance not improved with CAD—sensitivity trended to worse with CAD

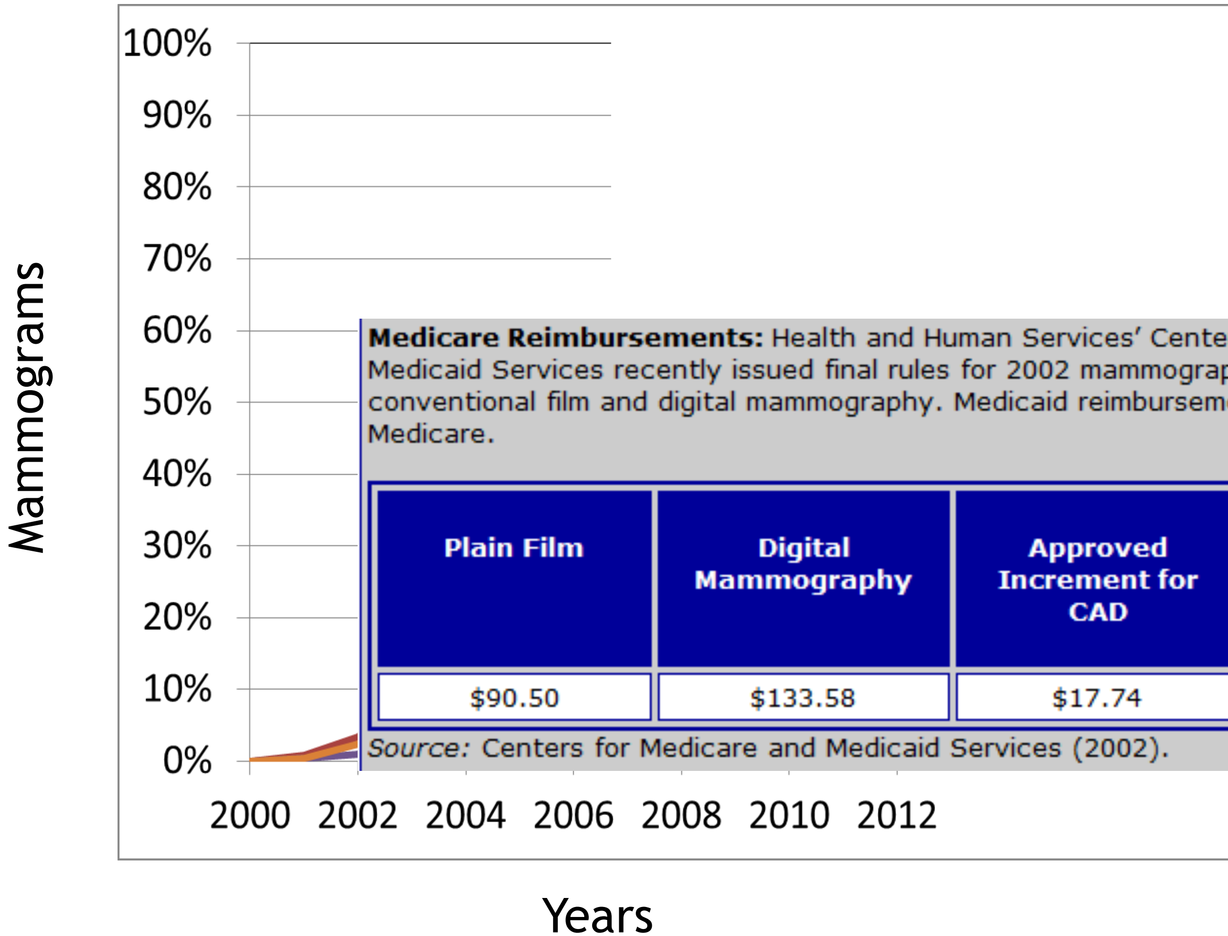
Odds ratios comparing CAD use versus no CAD, both overall and intra-radiologist



110/271 radiologists read with and without CAD

Drivers of Practice: Science and Reimbursement

Breast Cancer Surveillance Consortium
BCSC
Working together to advance breast cancer research



1998. FDA approves CAD
2002 CMS ⬆ payment
2005 NEJM DMIST
2007 NEJM CAD

Medicare Reimbursements: Health and Human Services' Centers for Medicare and Medicaid Services recently issued final rules for 2002 mammography reimbursements for conventional film and digital mammography. Medicaid reimbursements tend to follow Medicare.

Plain Film	Digital Mammography	Approved Increment for CAD	Digital Mammography CAD Plus
$90.50	$133.58	$17.74	$151.32

Source: Centers for Medicare and Medicaid Services (2002).


MGH
1811
MASSACHUSETTS
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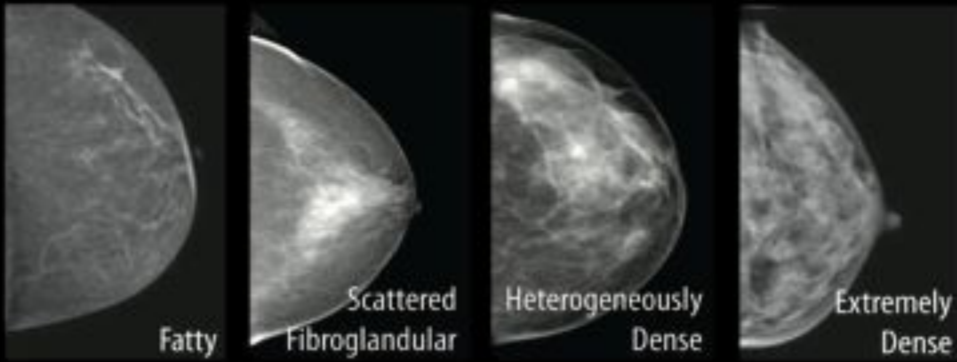
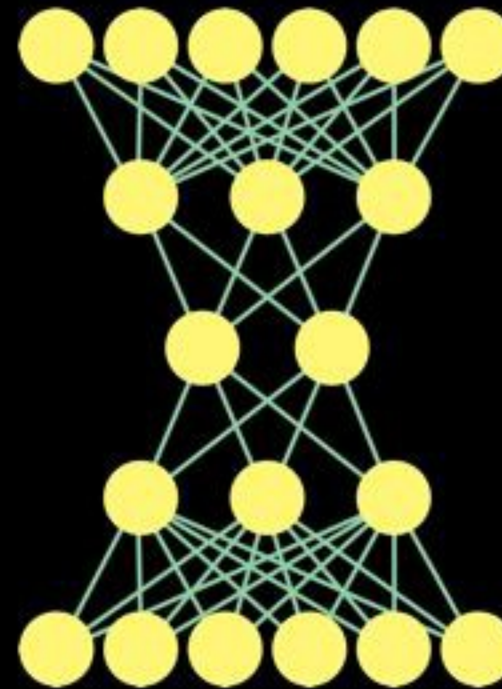


Density



88% binary accuracy on previous logs
97% agreement with an expert radiologist

In clinical implementation in first year at MGH:

Human Agreement: 94%

>40K mammograms read by the machine

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MIT

ORIGINAL RESEARCH • BREAST IMAGING
Radiology

Mammographic Breast Density Assessment Using Deep Learning: Clinical Implementation

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IMAGING

REFRESH DATA

MRN	Age	Study Date	Accession	TC Life	NCI Life	BRCA Life	MGH/MIT 1yr	MGH/MIT 2yr	MGH/MIT 5yr

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IMAGING

		count	percent			count	percent			count	percent
	TRIAGE hi risk >.0156	172	16%	>0.125	5 year hi risk	91	8%	0.05	2 year hi risk	107	10%
REFRESH DATA	TRIAGE low risk < .00156	206	19%		5 year intermedi	368	33%		2 year intermediate	535	48%
				<0.05	5 year low risk	645	58%	0.01	2 year low	462	42%

43545.51 5/30/2018

1104

MRN	Age	Study Date	Accession	TC Life	NCI Life	BRCA Life	MGH/MIT 1yr	MGH/MIT 2y	MGH/MIT 5yr	INIT BIRADS	FINAL BIRADS . highest order SCREEN:TN FP TP FN

AI and Breast Cancer: Phase 1

- Problem to address
  - No risk assessment models that predict individual risk with any accuracy
  - Human variation in interpretation (quality)
  - Lack of human breast imaging specialists to support screening mammography expansion (access)
- Large quality databases with known outcomes
  - > 250,000 modern digital consecutive mammograms at MGH linked to tumor registries
  - Partnerships with other institutions outside MGH
- AI expertise: MIT
- Clinical expertise and engagement: MGH

Future

- Machine Learning is a tool to address our greatest challenges for our patients worldwide and amplify our impact
  - Workflow
  - Image acquisition
  - Risk assessment
  - Image interpretation
  - Lesion and patient management
- Clinical implementation of discoveries critical

Thank you

Integration of DBT at MGH