

MICHAEL N. LINVER, MD, FACR

EMERGING BREAST IMAGING TECHNOLOGIES

X-Ray Associates of New Mexico, P.C.





NEW TOOLS IN BREAST IMAGING

Full Field Digital Mammography Tomosynthesis, Digital Subtraction Optical Scanning → Thermography, Infrared Imaging, **Opto-Acoustic Imaging** Ultrasound → Elastography, 3D Ultrasound Artificial Intelligence ➡ For Mammography and Tomosynthesis

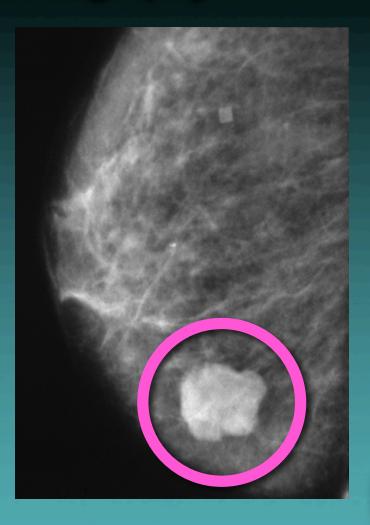


NEW TOOLS IN BREAST IMAGING

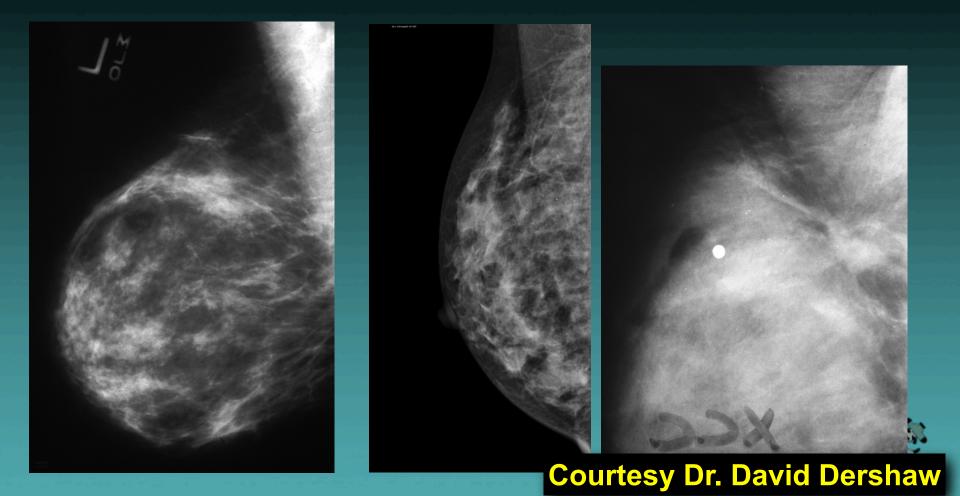
Full Field Digital Mammography Tomosynthesis, Digital Subtraction

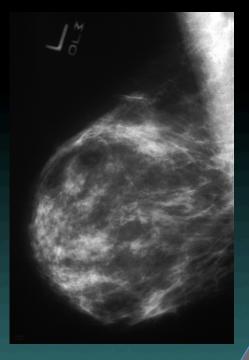


When tumors are in tissue of a different x-ray density, they are easy to see on mammography



 Breasts come in different densities on mammograms, and the denser ones can make it difficult to see some cancers.











10

Compared to mammography with ~85% sensitivity, contrast-enhanced MRI improves sensitivity for invasive cancer, approaching 100%





Inject contrast:

MRI is able to detect close to 100% of invasive breast carcinoma and 40-80% of DCIS.

 Mammography detects no more than 75% of breast cancers and some series suggest less than 50% of DCIS.



MRI is useful in breast imaging due to its ability to map blood flow.

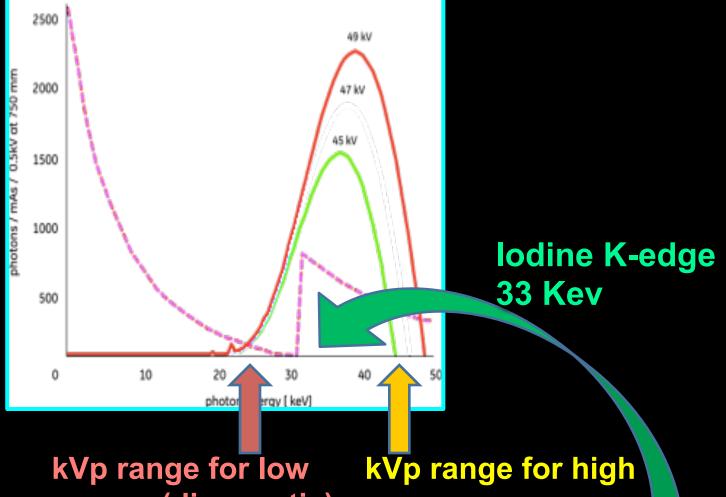
 Could flow maps obtained using digital mammographic technology approach the usefulness of MRI?



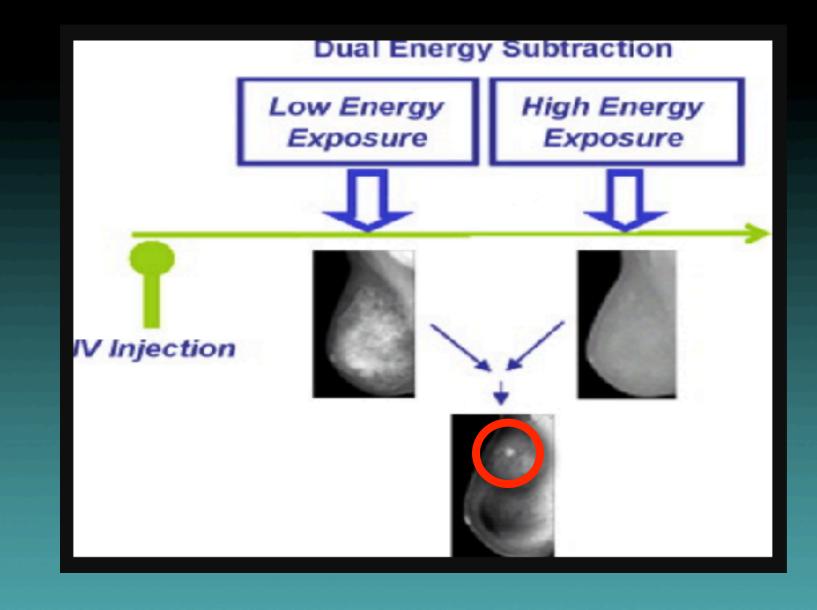


- → BILATERAL STUDY with single MLO and CC image of each breast: dual energy CEDM
 - Each breast imaged at a different time point with high and low kVp.
 - No dynamic information
 - Normal mammogram obtained as part of study

DUAL-ENERY CONTRAST-ENHANCED DIGITAL SUBTRACTION

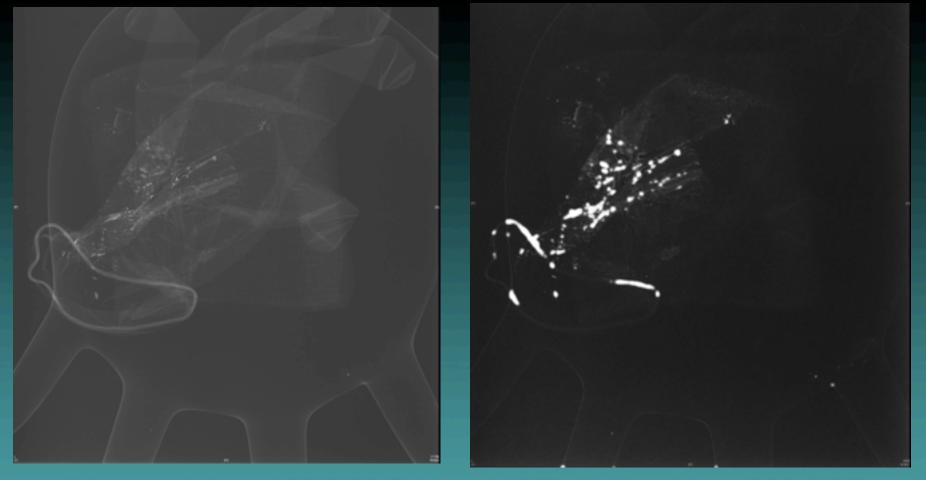


energy (diagnostic) mammography kVp range for high energy mammography





Rubber glove phantom filled with saline and painted with Omnipaque 350



Low energy (25 kV)

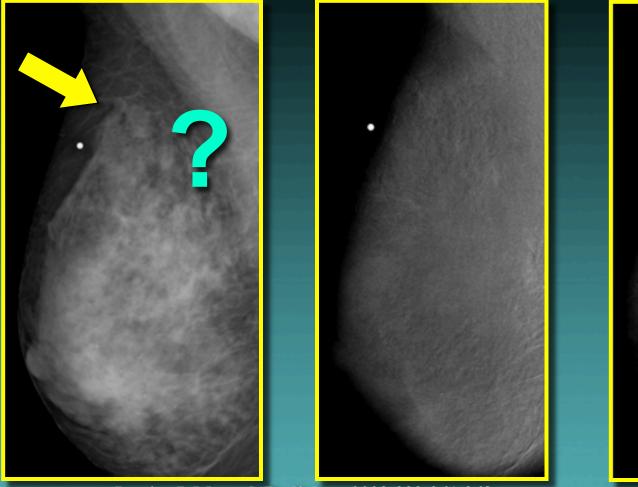


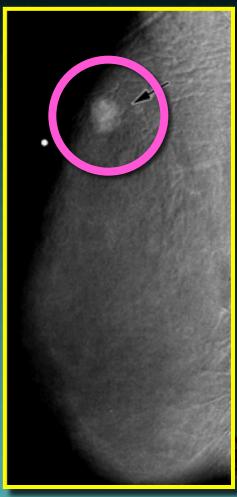
DUAL-ENERY CONTRAST-ENHANCED DIGITAL SUBTRACTION: INVASIVE LOBULAR CARCINOMA

Diagnostic mammogram (lump) dual energy

Pre-contrast

Post-contrast dual energy

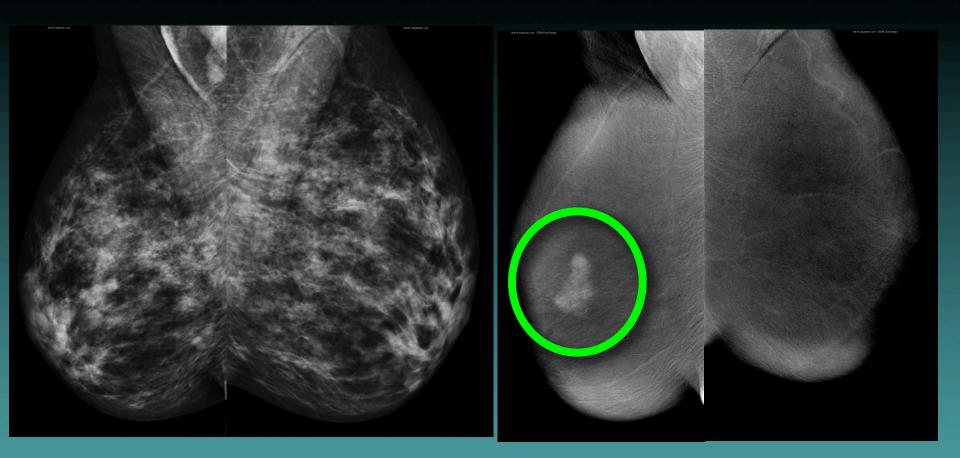




Lewin, J. M. et al. Radiology 2003;229:261-268

SCREENING MAMMOGRAM

CONTRAST ENHANCED







CONTRAST ENHANCED DIGITAL MAMMOGRAPHY: POTENTIAL USES

Workup of indeterminate mammographic lesions

 Pre-op evaluation of extent of disease in pt. newly diagnosed with breast cancer

Assessing response to chemotherapy

Screening



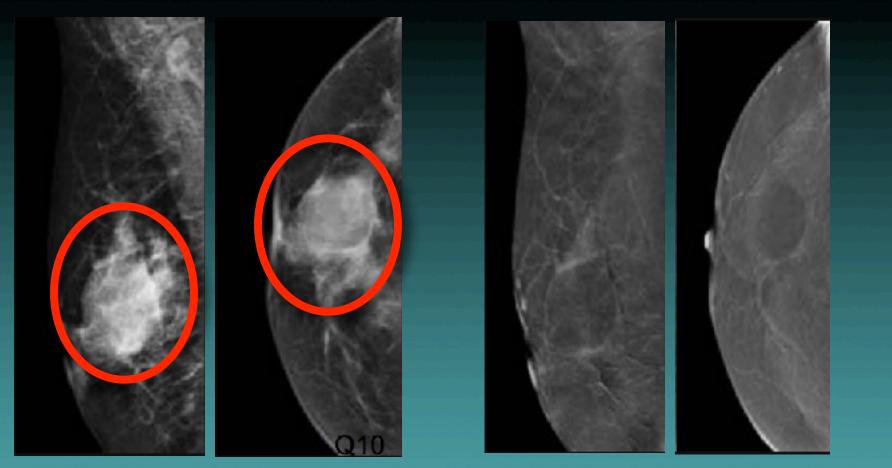
CONTRAST ENHANCED DIGITAL MAMMOGRAPHY: POTENTIAL USES

Workup of indeterminate mammographic lesions



SCREENING MAMMOGRAM

CONTRAST ENHANCED



DIAGNOSIS: BENIGN (CYST)!



SCREENING MAMMOGRAM ENHANCED

CONTRAST









CONTRAST ENHANCED DIGITAL MAMMOGRAPHY: POTENTIAL USES

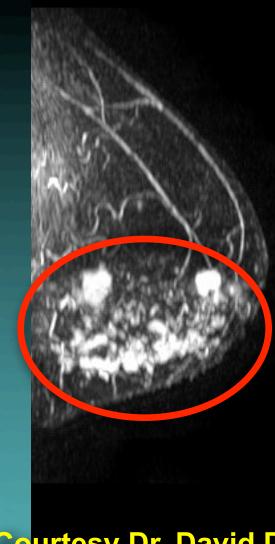
Workup of indeterminate mammographic lesions

Pre-op evaluation of extent of disease in pt. newly diagnosed with breast cancer

EXTENT OF TUMOR IN INVOLVED BREAST

CONTRAST ENHANCED









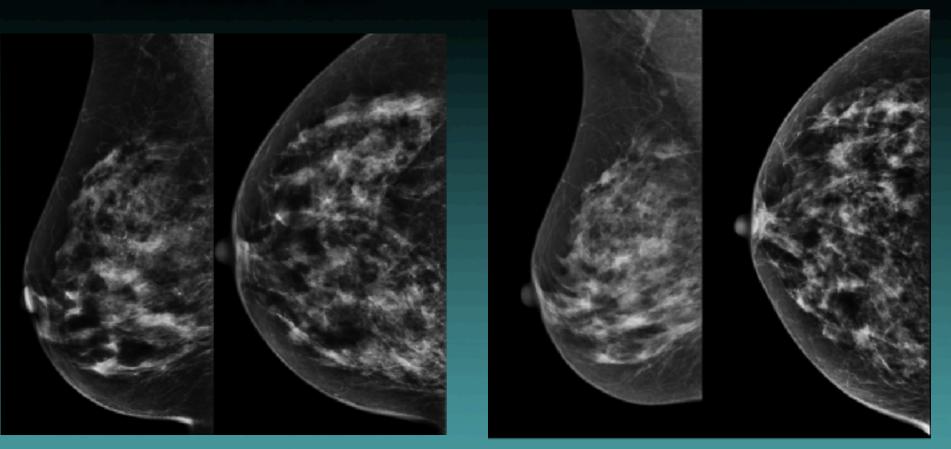
CONTRAST ENHANCED DIGITAL MAMMOGRAPHY: POTENTIAL USES

Workup of indeterminate mammographic lesions

- Pre-op evaluation of extent of disease in pt. newly diagnosed with breast cancer
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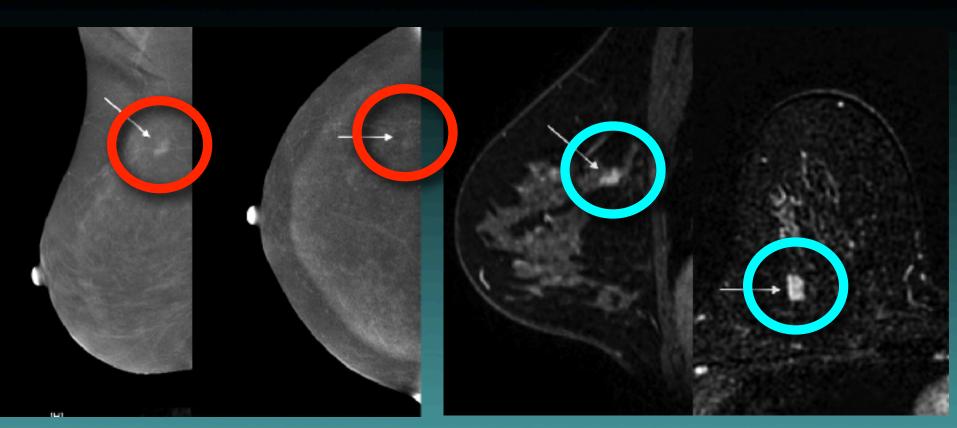
50 y.o. high risk pt (previous LCIS) SCREENING MAMMO PREVIOUS YEAR CURRENT STUDY



NO CHANGE, NO ABNORMALITY SEEN

Jochelson M et al. Europ J Rad 2017;97: 37-43

50 y.o. high risk pt (previous LCIS)SCREENING CEDMSCREENING MRI



INVASIVE LOBULAR CARCINOMA



Jochelson M et al. Europ J Rad 2017;97: 37-43



- Done at same time as routine mammography
- Low cost
- 1.2 x radiation dose
- Improved sensitivity and specificity



CEDM: WHAT ARE THE LIMITATIONS?

- Radiation dose is 20-25% greater than a routine mammogram, the equivalent of one extra image.
- Requires injection of iodinated contrast.
- False positives
- Biopsy of CEDM-only finding:
 Biopsy system now available!!



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IODINATED CONTRAST REACTIONS VS. GADOLINIUM REACTIONS

	lodinated	
		um
Mild	2-	.7-
	31/1000	24/10000
Serious	4/1,000	1.5/1000
Death	1/100,000	1/100,000

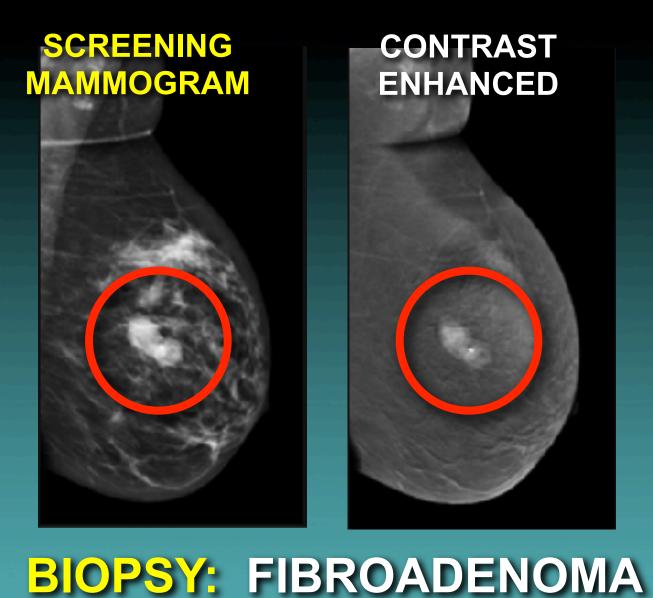




CEDM: WHAT ARE THE LIMITATIONS?

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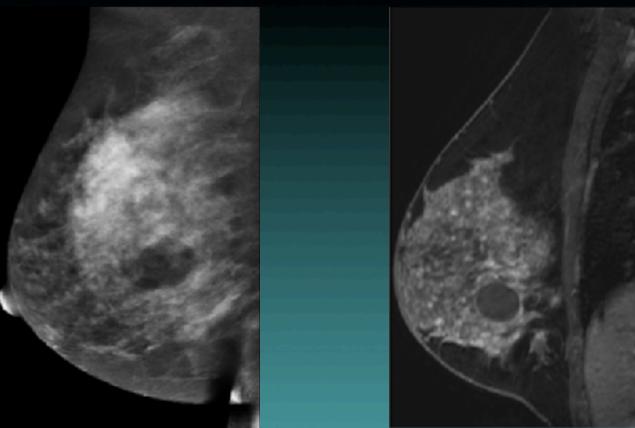
FALSE POSITIVE STUDY





SCREENING MAMMOGRAM

BREAST MRI









CEDM: WHAT ARE THE LIMITATIONS?

- Radiation dose is 20-25% greater than a routine mammogram, the equivalent of one extra image.
- Requires injection of iodinated contrast.
- False positives
- Biopsy of CEDM-only finding Biopsy system now available!!



HOW TO BIOPSY A LESION SEEN ON CEDM

If biopsy guidance system for CEDM is not yet available:

Correlate with mammo/sono

Do "second look" (focused) sono

Do MRI

(After biopsy with clip placement, repeat CEDM is recommended to confirm biopsy accuracy.)

How does CEDM compare with digital mammography in cancer detection?



CANCER DETECTABILITY WITH CEDM

Author # cancer	<u>'s % CEDN</u>	<u>A seen</u>	<u>% m</u>	ammo	<u>% other</u>
Dromain Gustave-Roussey Eur Radiol 2011	80	92% (74/	0)	78%	
Diekman Charite, Berlin Eur J Radiol 2011	30	62%		43%	
Jochelson Sloan-Kettering, NY Radiology 2013	26 (96%		85%	MRI: 96%

CONCLUSION:

CEDM is far superior to digital mammography in the detection and staging of breast cancer



How does CEDM compare with Breast MRI in cancer detection?



BILATERAL CONTRAST ENHANCED DIGITAL MAMMOGRAPHY (CEDM) VS. MRI

	Mammo	MRI		CEDM		
Index CA	42/52 (81%)	50/52 (96%)		50/52 (9	6%)	
Additional ipselat CA		22/25 (88%)		14/25 (5	6%	
Contralateral CA		0/1		0/1		
TOTAL	42/78 (54%)	72/78 (92%) 64/78 (82%)		32%)		
	Mammo	MRI		CEDM		
False positives		13		2		

52 PATIENTS WITH KNOWN CANCER



Jochelson M et al. Radiology 2013;266: 743-751

CONCLUSION:

CEDM is slightly inferior to MRI in the detection of breast cancer and multicentricity, but it is less likely to discover suspicious lesions that require biopsy and are found to be benign (False Positives).





SUMMARY: DIGITAL SUBTRACTION MAMMOGRAPHY

- Finds more cancers than mammography with fewer false positives
- Enhancement of cancers may be less timedependent than on MRI
- Main uses right now: Dx tool after mammo or US; Staging when MRI is not available
- Cannot exclude carcinoma with 100% reliability: perhaps 4-8% false negatives.
- There is now biopsy capability currently available



FUTURE STUDY TOPICS FOR CEDM

Is it worthwhile as a screening tool? If so, at what intervals? (1 yr? 3 yrs?) **Can it replace screening ultrasound?** Can it replace ulltrasound to evaluate lumps? Can it be used for preoperative or posttherapy staging? How good is it in the treated breast? What is the frequency of false positives?

STAY TUNED!



NEW TOOLS IN BREAST IMAGING

Full Field Digital Mammography
 Tomosynthesis, Digital Subtraction
 Optical Scanning



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 Optical Scanning



OPTICAL SCANNING

Infrared scanning- Thermography

Diffuse Optic Tomography
 Laser CT, DOBI Light Scanning

Updated Infrared Imaging

Opto-Acoustics



OPTICAL SCANNING

Infrared scanning- Thermography Found to be worthless for screening



THERMOGRAPHY: Works on distribution of blood flow and attendant heat, detected by infrared light source

No definitive studies showing its benefit to date



Breast Cancer Screening - Thermography is Not an Alternative to Mammography: FDA Safety Communication

Date Issued: June 2, 2011

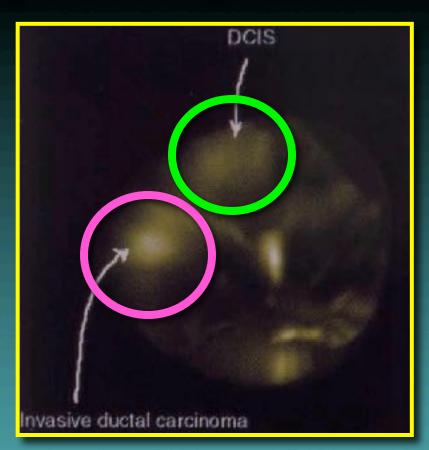




OPTICAL SCANNING

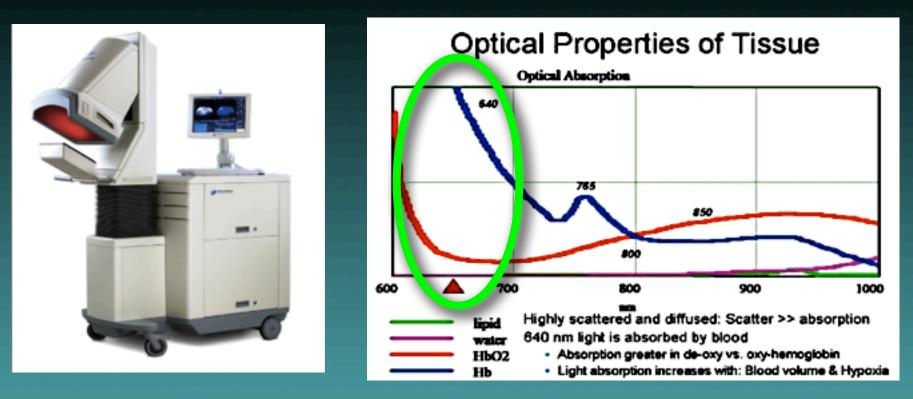
Infrared scanning- Thermography
 → Found to be worthless for screening
 Diffuse Optic Tomography
 → Laser CT, DOBI Light Scanning
 → NOT very successful

LASER DETECTION: Near infrared laser transmitted; reflected & refracted off cancers differently than benign tissue



No definitive studies showing its benefit to date

DOBI (Dynamic Optical Breast Imaging): Diodes emit red light with wavelength of 640 nm through the breast, and light is recorded on CCD camera



No definitive studies showing its benefit to date



OPTICAL SCANNING

Infrared scanning- Thermography
 Found to be worthless for screening
 Diffuse Optic Tomography
 Laser CT, DOBI Light Scanning
 NOT very successful



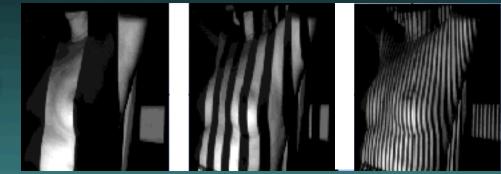
OPTICAL SCANNING

Infrared scanning- Thermography Found to be worthless for screening Diffuse Optic Tomography → Laser CT, DOBI Light Scanning → NOT very successful Updated Infrared Imaging → Now coupled to multiparametric computer analysis

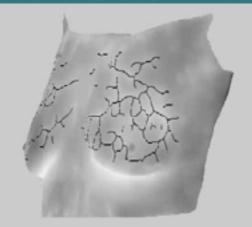
The MIRA System

MIRA utilizes dual-head proprietary *Structured Light Projection* infrared imaging technology to construct 3D vascular maps of the breasts

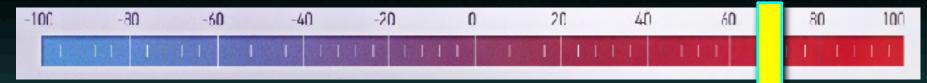




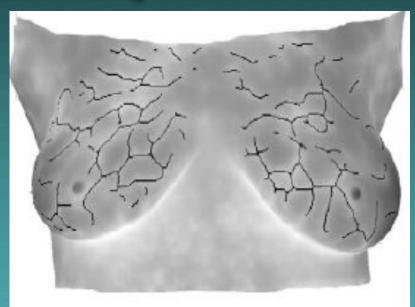
The maps are analyzed to measure vascular asymmetry, vascular density, vessel dimensions, and more



MIRA Score: Overall likelihood of cancer being present in this patient



Hi Resolution Vascular maps and Density scores for each breast



Metabolic analysis I, II Computerized baseline Vascular analysis I, II Morphology analysis I, II Breast density risk factor Structural asymmetry Gradient vector Center of mass

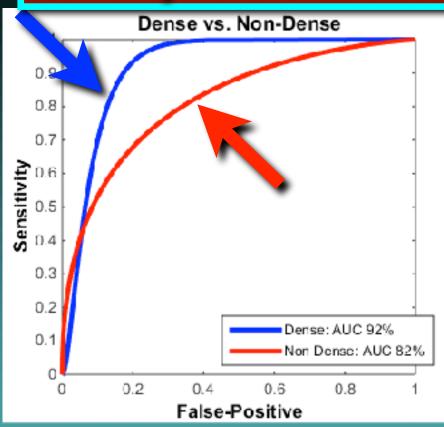
MIRA Scores for individual parameters



Multicenter Prospective Study II

Breast Density Analysis Blind study, 114 subjects (58 verified cancers)

Currently not available due to lack of research funding



	Dense	Non-Dense
Sensitivity	96%	84%
Specificity	76%	64%
PPV	77%	73%
NPV	96%	78%
AUC	92%	82%





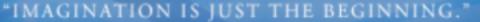
OPTICAL SCANNING

- Infrared scanning- Thermography
 Found to be worthless for screening
- Diffuse Optic Tomography
 Laser CT, DOBI Light Scanning
 NOT very successful
- Updated Infrared Imaging
 - Now coupled to multiparametric computer analysis
- Opto-Acoustics
 - A promising Fusion technology

Opto-Acoustics The Basic Assumptions

> Opto-acoustics - functional imaging

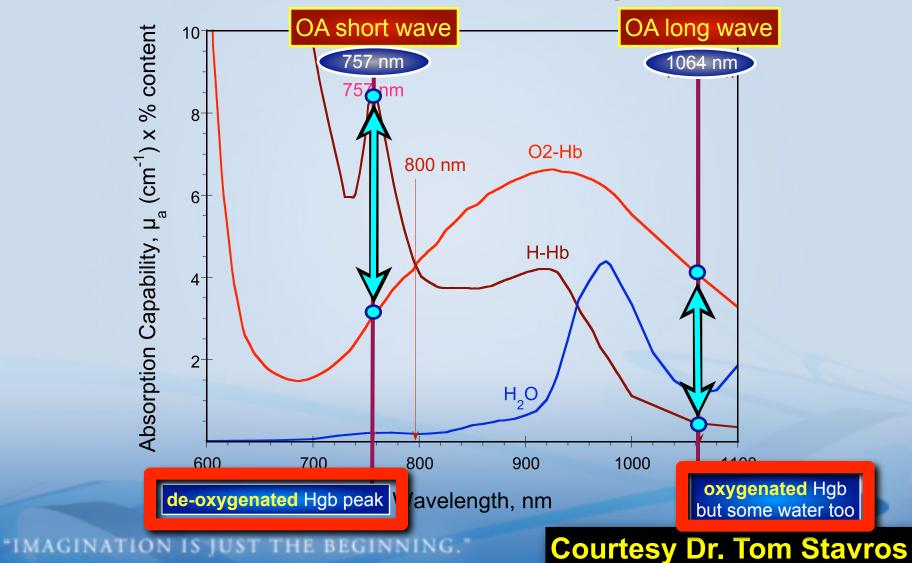
- Cancers are metabolically more active, and therefore, de-oxygenate blood more than either:
 - normal tissues or
 - benign lesions
- Opto-acoustics can demonstrate relatively greater deoxygenation that occurs within malignant lesions





Optical Absorption within Breast Tissues

- at two laser wavelengths



Opto-Acoustics System

Using Opto-Acoustics (OA) gets around limitations of diffuse optic tomography

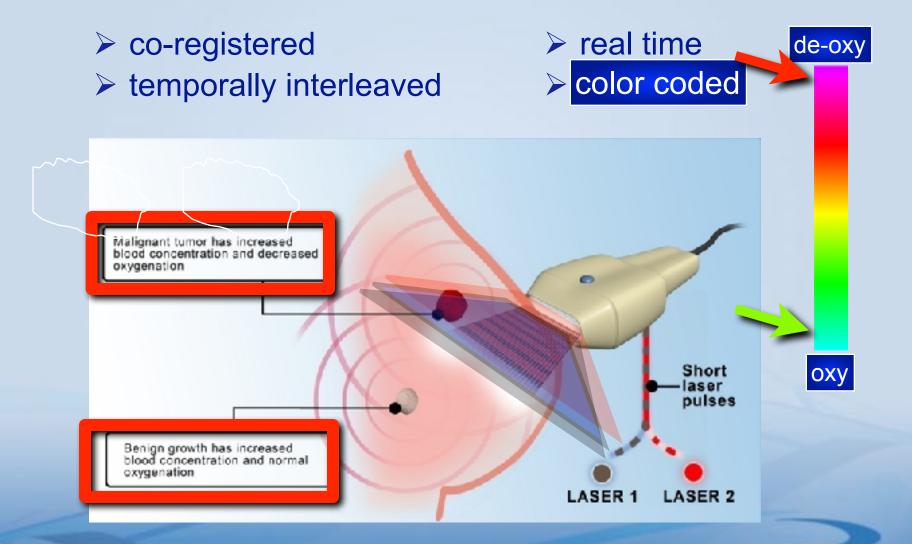
- **Fusion** of function with morphology:
 - function optics, real time dual wavelength laser light
 - morphology OA and real time B-mode gray scale US
- Combines best of optic and US worlds
 - optics high contrast resolution
 - ultrasound high spatial resolution & better penetration

Opto-acoustic approach "light in and ultrasound out"

Courtesy Dr. Tom Stavros

"IMAGINATION IS JUST THE BEGINNING."

Opto-Acoustic (OA) and Ultrasound Images

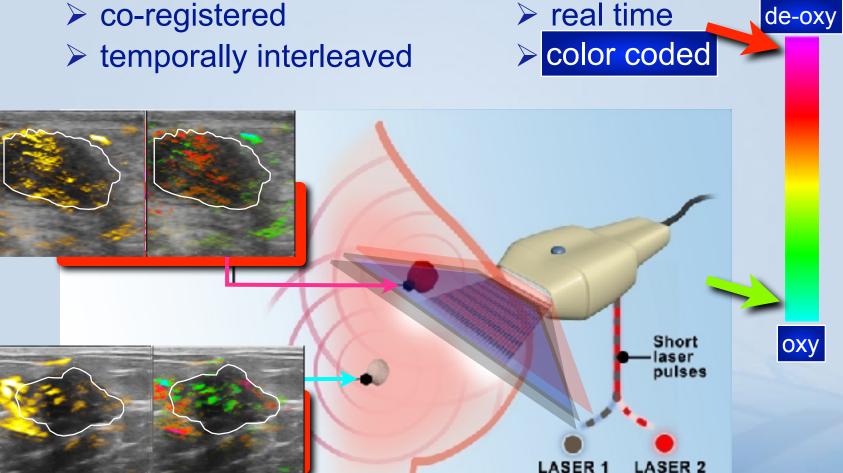


"IMAGINATION IS JUST THE BEGINNING."

Courtesy Dr. Tom Stavros

<u>Opto-Acoustic (OA) and Ultrasound Images</u>

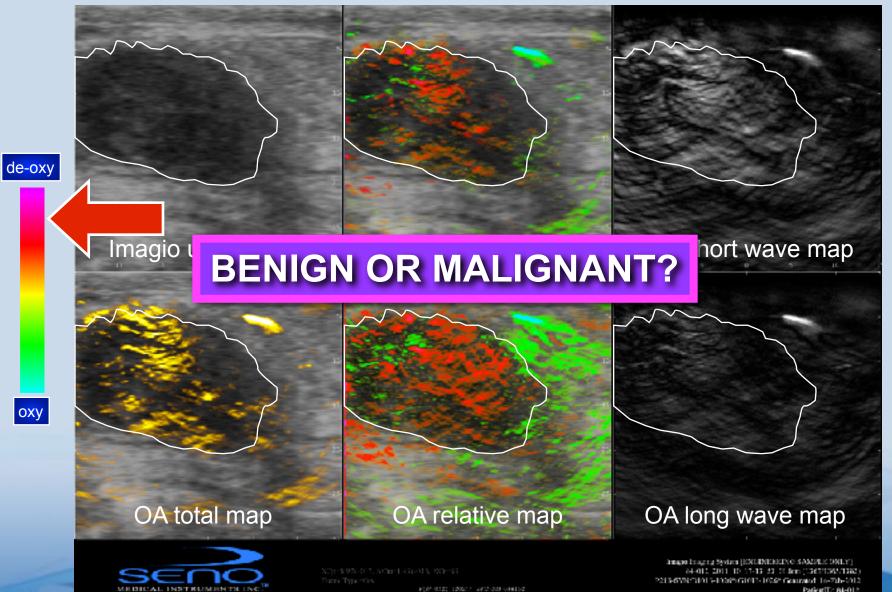
co-registered



"IMAGINATION IS JUST THE BEGINNING."

Courtesy Dr. Tom Stavros

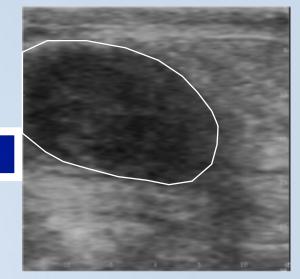
Internal Findings - IDC, gr 3 - OA ff #1

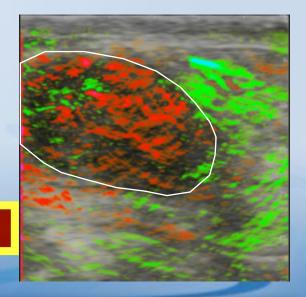


Courtesy Dr. Tom Stavros

"IMAGINATION IS JUST THE BEGINNING."

US appearance overlaps that of benign lesions





Courtesy Dr. Tom Stavros

but the OA appearance does not look benign

"IMAGINATION IS JUST THE BEGINNING."

Thus we need to look at both:

...internal (primarily function) OA findings...

...and...

...external (primarily morphologic) OA findings...

... in order to optimize OA sensitivity

NOW COMMERCIALLY AVAILABLE!



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 Full Field Digital Mammography
 Tomosynthesis, Digital Subtraction
 Optical Scanning
 Thermography, Infrared Imaging, Opto-Acoustic Imaging
 Ultrasound

➡ Elastography, 3D Ultrasound



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Full Field Digital Mammography

 → Tomosynthesis, Digital Subtraction

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➡ Elastography, 3D Ultrasound



BREAST ULTRASOUND: NEW TECHNIQUES

Elastography

• 3-D Ultrasound Imaging





WHAT IS ELASTOGRAPHY?

→ METHODOLOGY:

 Mechanical force induced to tissue (external or internal force)

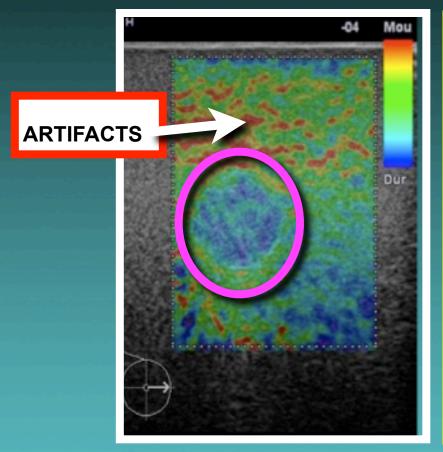
 Measurements of tissue displacements (with US or MRI)

 Estimation of tissue stiffness-Qualitative (strain) or Quantitative (estimation)

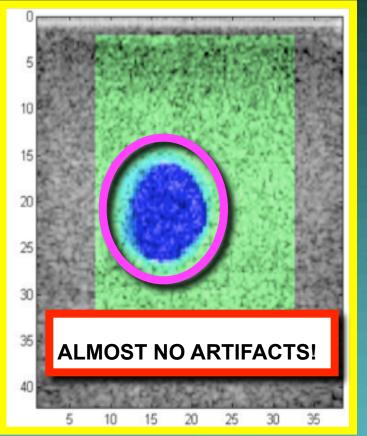


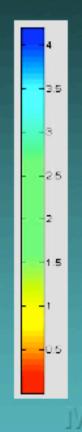
COMPARISON OF ELASTOGRAPHY METHODS

Static vs. Shearwave



Reversed color scale for comparison



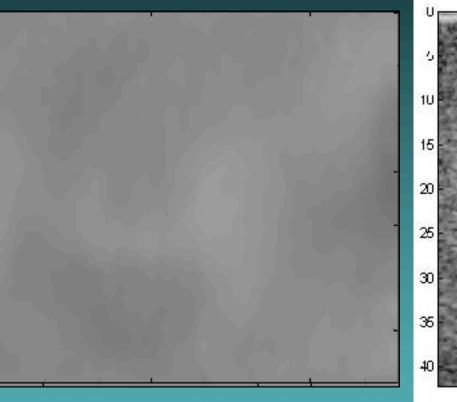


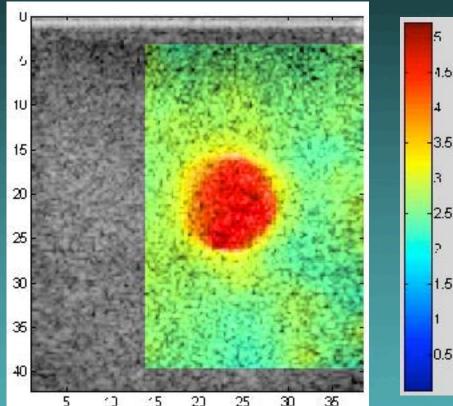
kPa

THE TECHNOLOGY

New ShearWave Elastography Mode

Mechanical constraint generated by acoustic pulse (user-independent and reproducible)





5

4.5

4

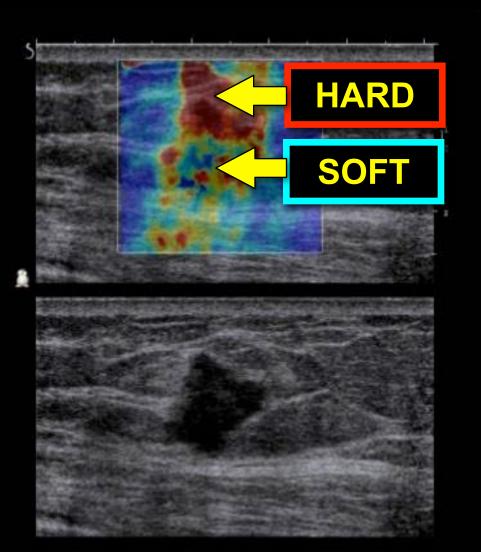
3

2D

Tissue -1 Gen / Gen Map 1 / 52 dB Gain 36 %

.

Gen Map 1 Transp. 35.96 Persist.5 Smooth 4 Gain 75.96



INVASIVE DUCTAL CARCINOMA, GRADE 2



+180 KPa

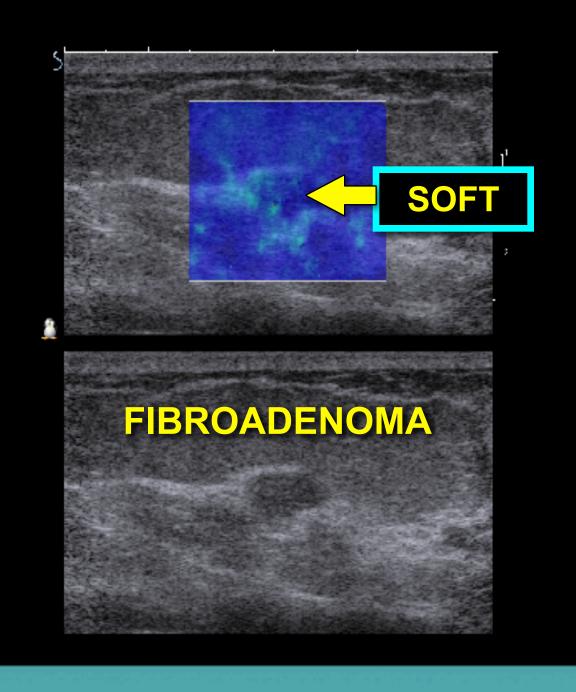
144

108

36

ssue -1 en/ Cor ap 1752 dB a n 48 %

en ap 1 ansp 50.99 ersist G mooth 4 an 75.96





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BREAST ULTRASOUND: NEW TECHNIQUES

• Elastography

3-D Ultrasound Imaging





3D ULTRASOUND: APPLICATIONS

- Showing spiculation better
- Distinguishing artifactual shadowing from a shadowing malignancy
- Showing DCIS components and intraductal components
- Assessing complex cysts
- Identifying anatomy



3D ULTRASOUND: APPLICATIONS

Showing spiculation better

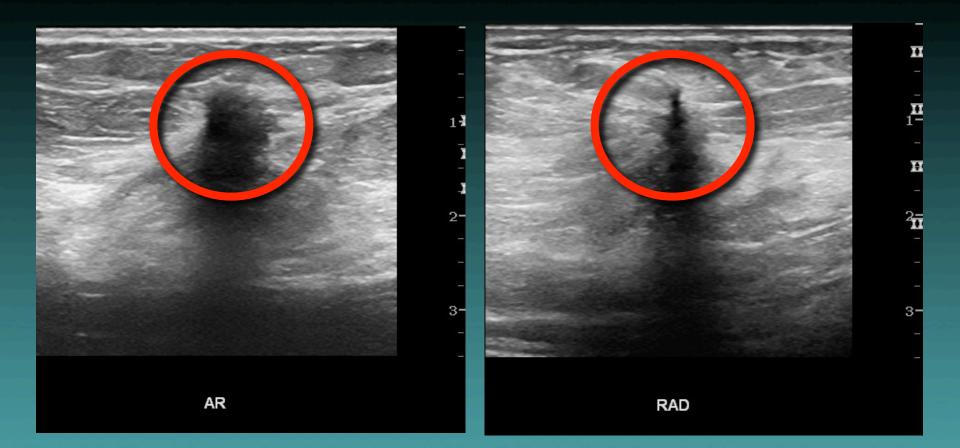




3D ULTRASOUND FOR SPICULATIONS

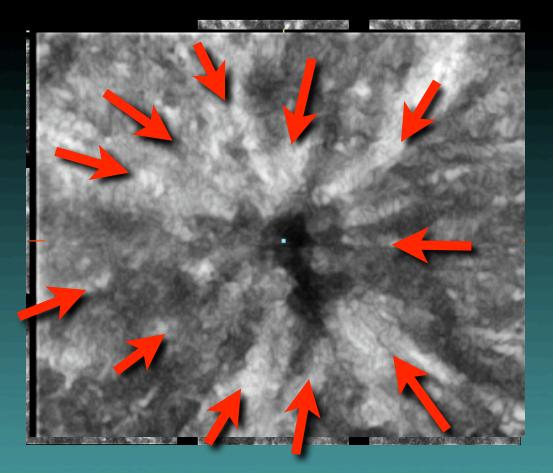
- Spicules are best seen in the CORONAL plane
- The path of low resistance for invasion is the coronal plane
- Spicules more numerous & prominent within tissue planes of the breast, which are coronally oriented
- 3D imaging in the coronal plane shows spicules very well

2D ULTRASOUND





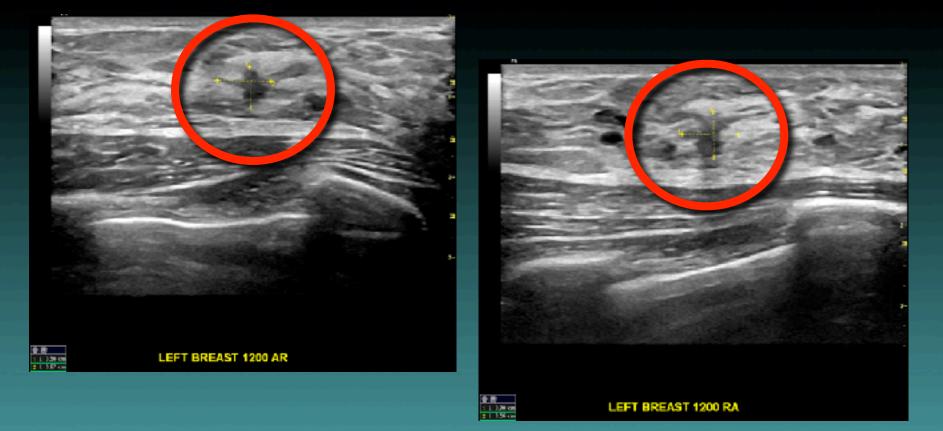
3D ULTRASOUND: SAME LESION



Most spicules hyperechoic & superficial

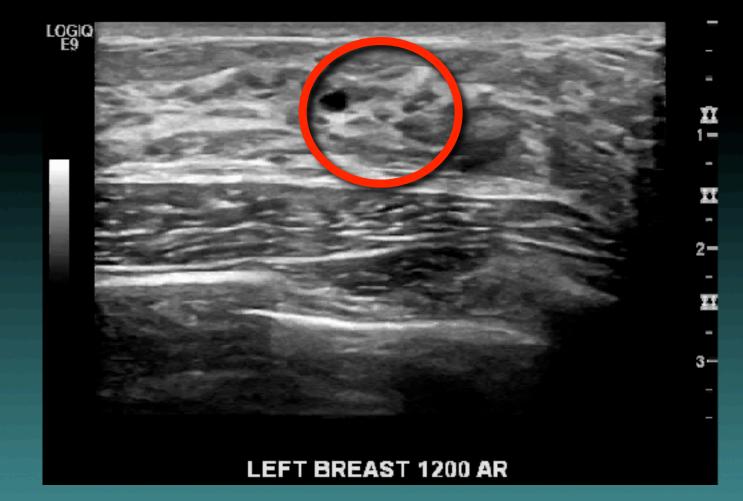


2D: Suggesion of an irregular mass



2D Video Sweep is helpful here





2D Video Sweep shows radiating ducts, & suggests that 3D analysis would be worthwhile



Sometimes, spiculations are seen ONLY on the coronal view: a valid argument for volume imaging!

2D SAGITTAL PLANE

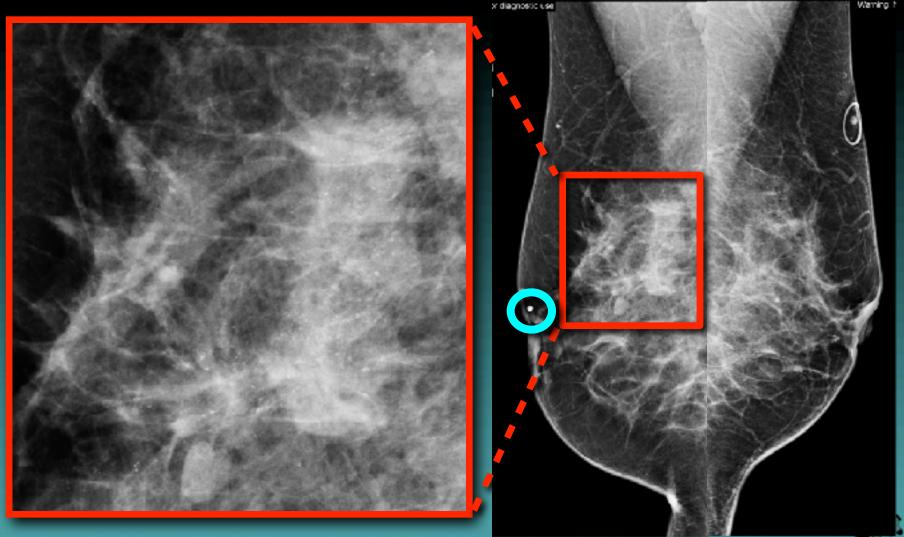
3D CORONAL PLANE



3D ULTRASOUND: APPLICATIONS

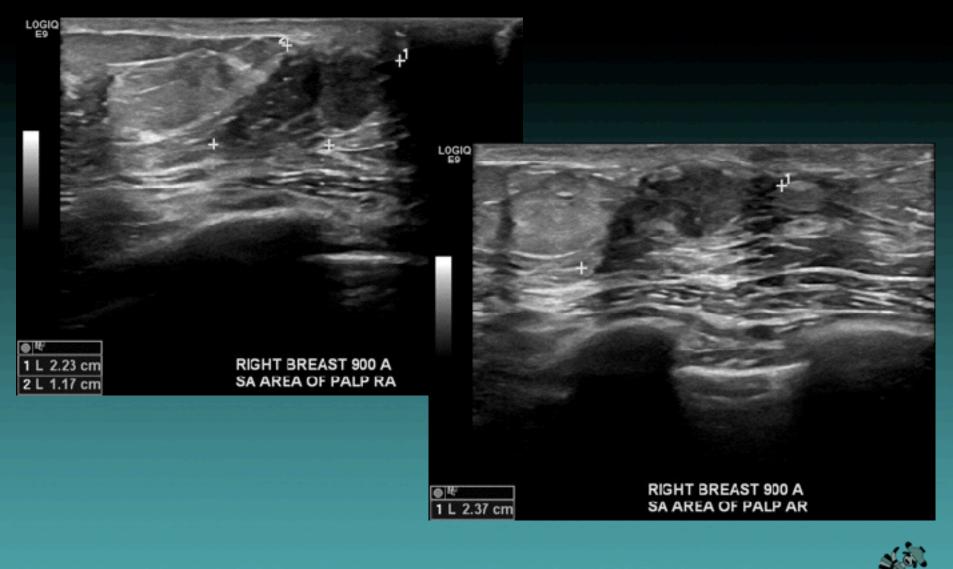
- Showing spiculation better
- Distinguishing artifactual shadowing from a shadowing malignancy
- Showing DCIS components and extensive intraductal components

Palpable lump on Right





Mass seen on 2D Ultrasound







3D: Virtual Rescan Plane

Multifocal IDC with DCIS bridges



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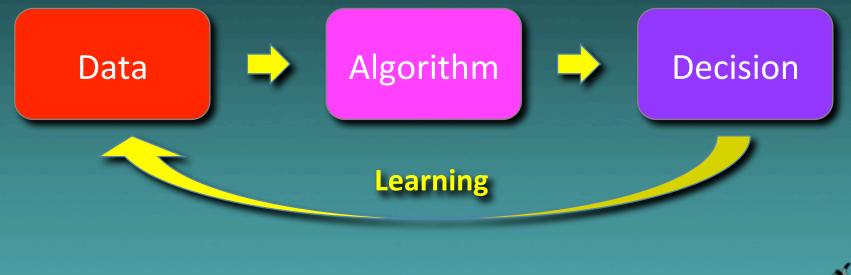


NEW TOOLS IN BREAST IMAGING

- Full Field Digital Mammography
 Tomosynthesis, Digital Subtraction
- Optical Scanning
 Thermography In
 - Thermography, Infrared Imaging, Opto-Acoustic Imaging
- Ultrasound
 - Elastography, 3D Ultrasound
- Artificial Intelligence
 - ➡ For Mammography and Tomosynthesis

WHAT IS AI?

Development of computer systems able to perform tasks that normally require human intelligence





ARTIFICIAL INTELLIGENCE

techniques that enable computers to mimic human intelligence

MACHINE LEARNING

techniques where machines improve at tasks with experience

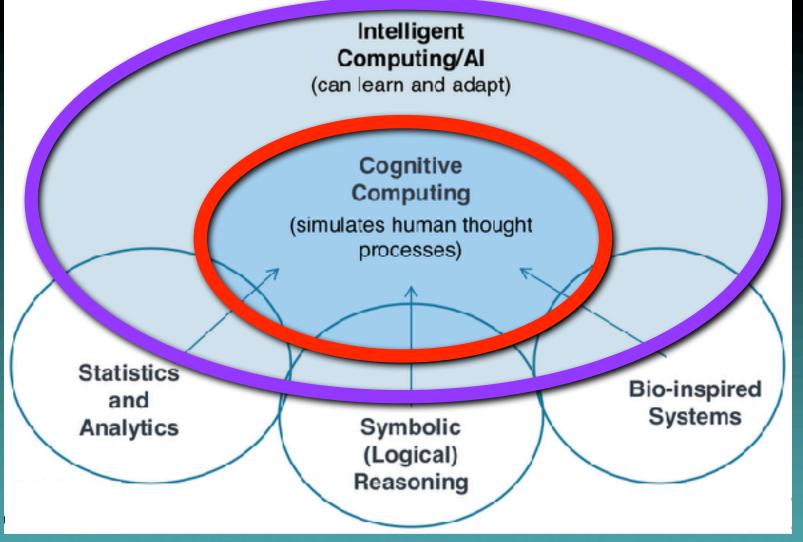
DEEP LEARNING

machine learning using deep neural networks (inspired by human brain architecture)





AI- THE BROADER PICTURE





Improve accuracy of diagnosis, prognosis, and risk prediction. Optimize hospital processes such as resource allocation and patient flow.

Whatcan

machine learning

do for the

healthcare

industry?

Identify patient subgroups for personalized and precision medicine.

Discover new medical knowledge (clinical guidelines, best practices).

Automate detection of relevant findings in pathology, radiology, etc.

Reduce medication errors and adverse events.

Model and prevent spread of hospital acquired infections.

> Improve quality of care and population health outcomes, while reducing healthcare costs.

Automatic **detection** of anomalies and patterns is especially valuable when the key to diagnosis is a tiny piece of the patient's health data.





Detection is also valuable when key patterns of interest are discovered by **integrating** information across many patients, and might not be visible from a single patient's data.

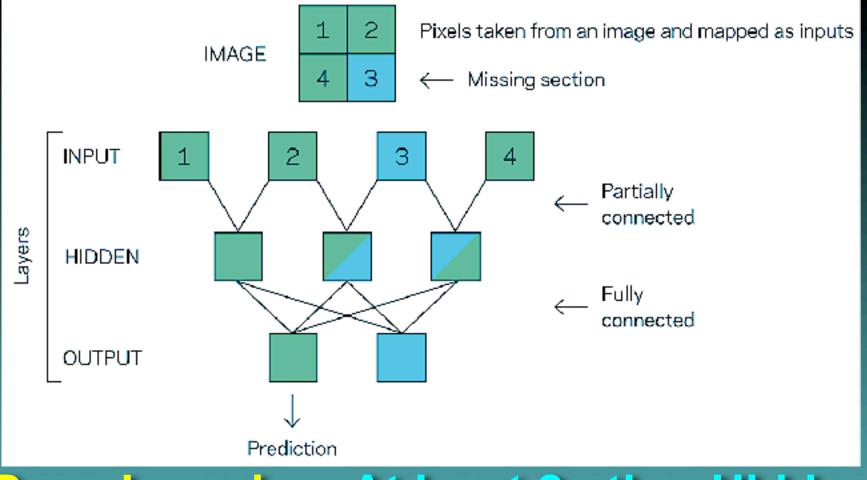


Automate detection of relevant findings in pathology, radiology, etc.

Al and intelligent computing predict we'll see the advances are starting to "singularity" of machine accelerate intelligence in the next few decades Exponential growth: Unpredictable Timing : Will AI take off thanks to Some advances seem to network effects and never arrive (speech disruptive innovations, or recognition), while others will it only make modest come upon us unexpectedly Al Winters: Al has already advances for the next (GPS driving directions) gone through a few phases of cades? hype and troughs of disillusionment (1974-80, and **1987-93**) 5**0s** 60s 70s 80s 90s 2000 2010 2020 2030 2050 2040

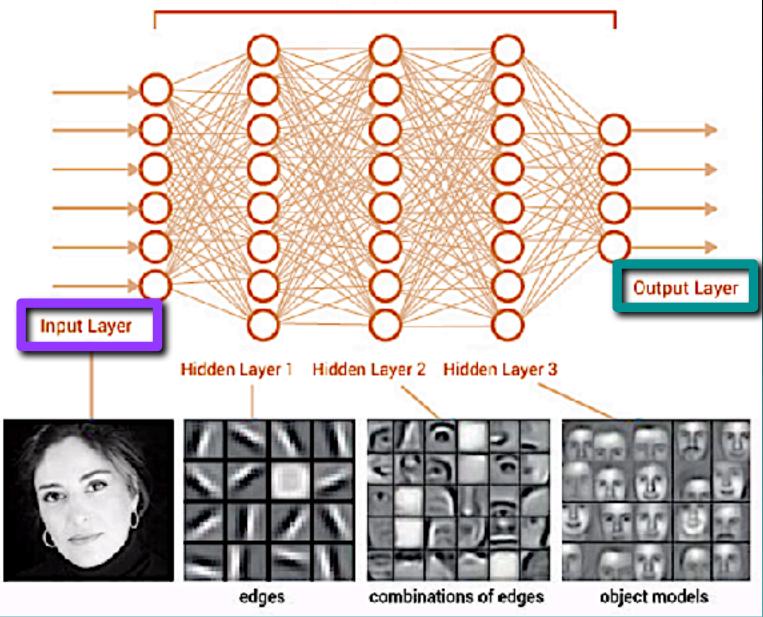
Surpass human intelligence: Some

Machine Learning: Neural Network One input layer, and One Output layer

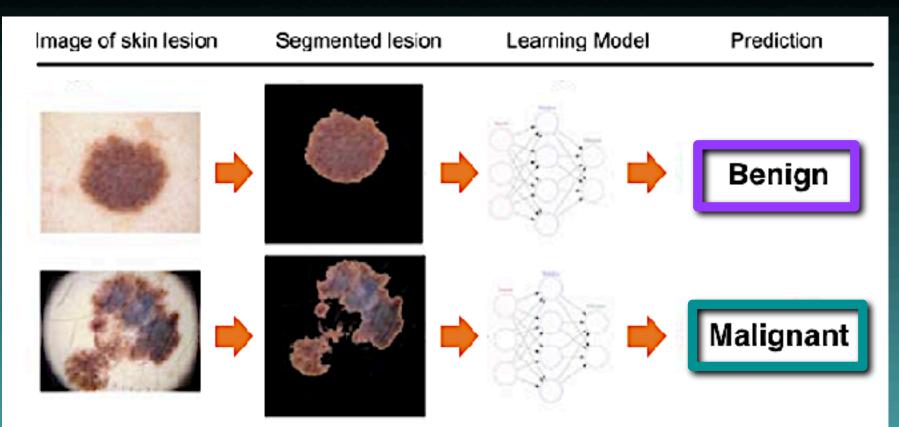


Deep Learning: At least 2 other Hidden Neural Network layers in between

Deep Neural Network



AI APPLICATION FOR SKIN CANCER DETECTION



Kalouche S. Vision-Based Classification of Skin Cancer Using Deep Learning. Stanford University.



AI APPLICATIONS IN BREAST IMAGING

➡ FIRST READ OF SCREENING MAMMOGRAMS

⇒ SYNTHETIC 2D MAMMOGRAPHY

➡ BREAST DENSITY CATEGORIZATION FOR BREAST CANCER RISK

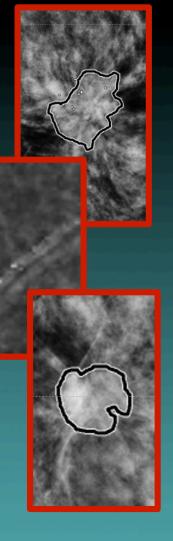


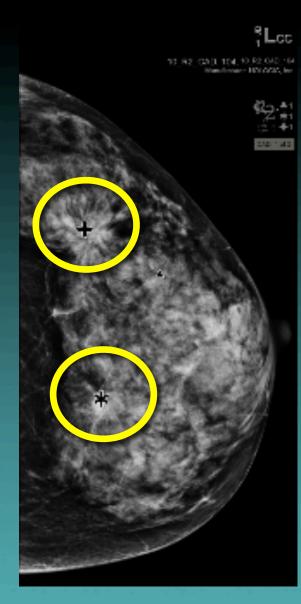
AI APPLICATIONS IN BREAST IMAGING

 → CAD
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AI APPLICATIONS IN BREAST IMAGING

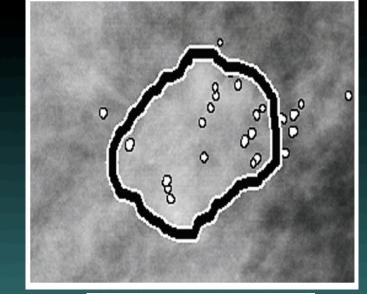
CAD systems-Constantly improving over the past 20 years

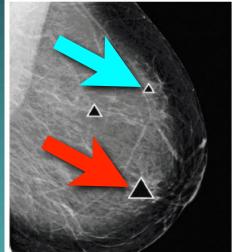






AI APPLICATIONS IN BREAST IMAGING





CAD systems- Now very sophisticated:

Markings are sized according to the likelihood of malignancy!

Left MLO

Right MLO SCREENING CASE:

62 months prior to diagnosis

COURTESY LASZLO TABAR

SCREENING CASE:

Right CC

Left CC

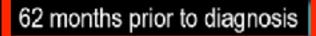
62 months prior to diagnosis

COURTESY LASZLO TABAR

SCREENING CASE:

Al





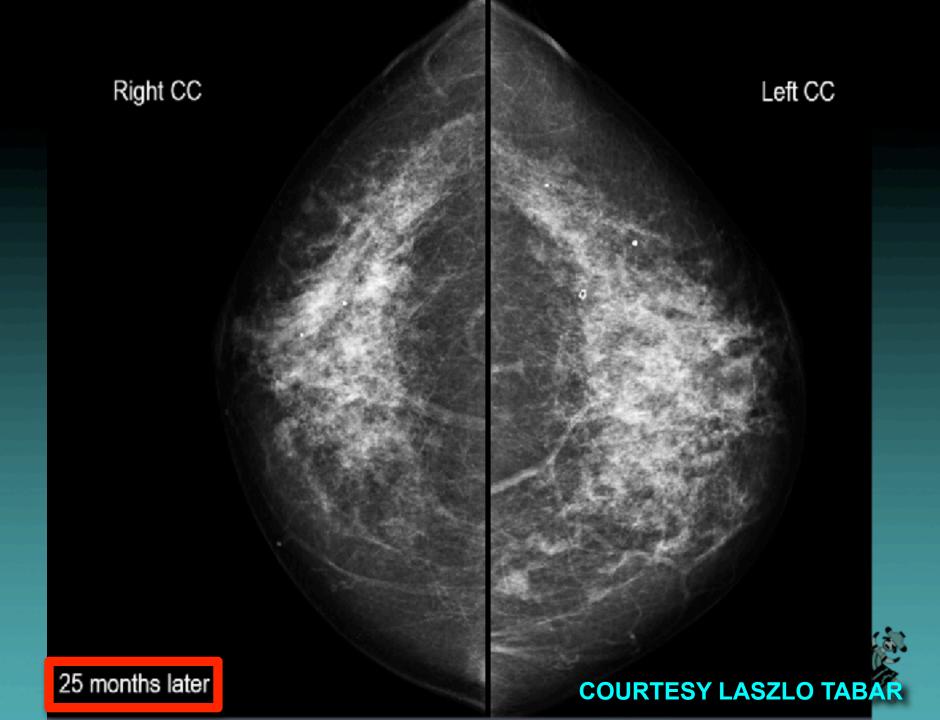


Right ML



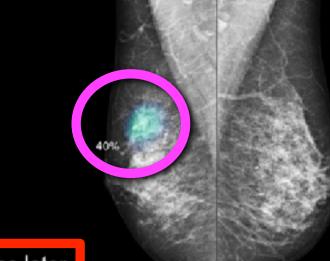
25 months later

COURTESY LASZLO TABAR



WITH AI

COURTESY LASZLO TABAR



24

25 months later

Al

Right MLO



At the time of diagnosis and treatment





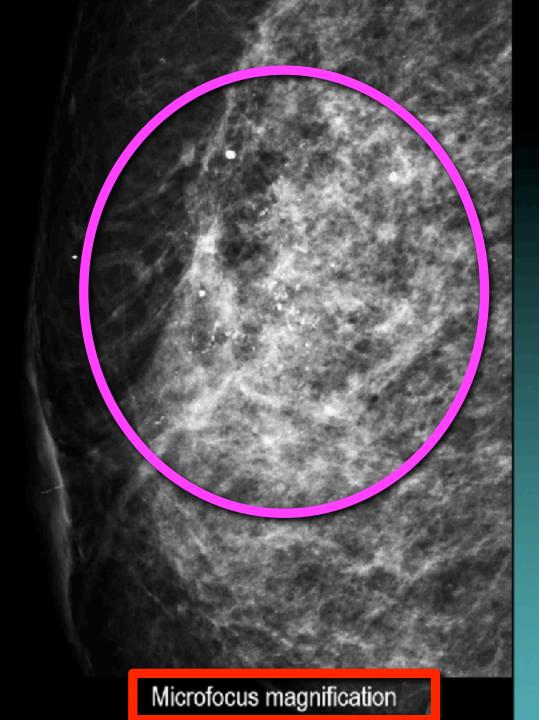
98%

999

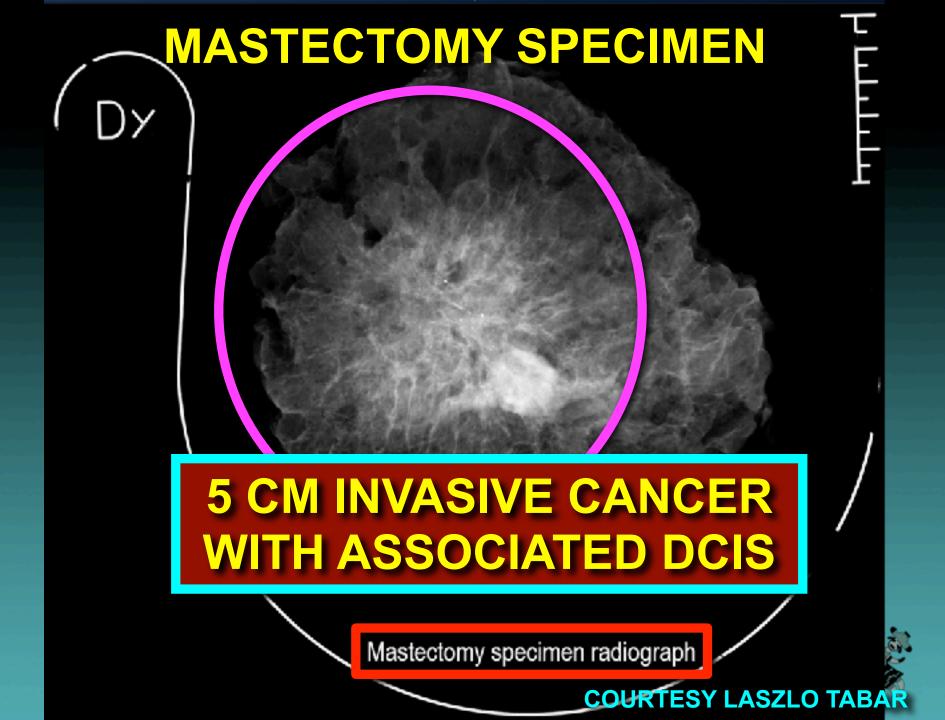
AI

COURTESY LASZLO TABAR

Right MLO









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AI APPLICATIONS IN BREAST IMAGING Direct interpretation of screening mammograms!

Stand-Alone Artificial Intelligence for Breast Cancer Detection in Mammography: Comparison With 101 Radiologists

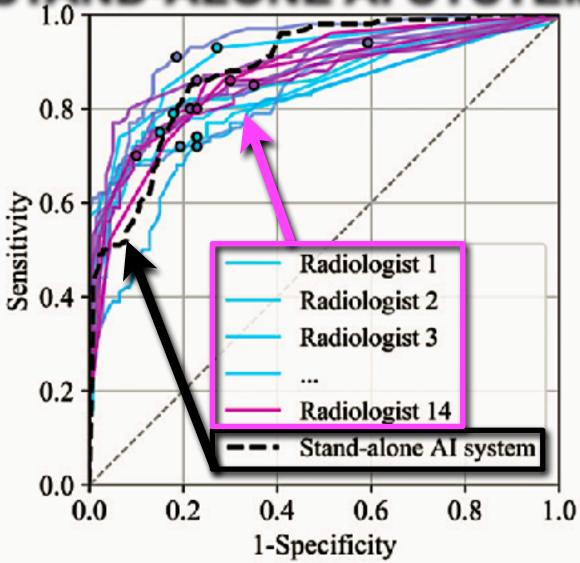
Alejandro Rodriguez-Ruiz Kristina Lång Albert Gubern-Merida Mireille BroedersGisella Gennaro Paola Clauser Thomas H Helbich Margarita Chevalier Tao TanThomas Mertelmeier Matthew G Wallis Ingvar Andersson Sophia ZackrissonRitse M Mann Ioannis Sechonoulos JNCI: Journal of the National Cancer Institute, djy222, <u>https://doi.org/10.1093/jnci/djy222</u> Published:



STUDY IN JNCI ON DIRECT AI INTERPRETATION OF MAMMOGRAMS

- 101 radiologists interpreted 2652 mammograms (653 malignancies), as did Al
- Each exam given score of 1 to 10 level of suspicion by AI & by radiologists, independently
- ROC Area under curve (AUC, accuracy) HIGHER FOR AI (.84 versus .81) than for radiologists
- Al had higher sensitivity than 58% of rads!
- Al had higher AUC than 62% of radiologists
- HOWEVER, Al's performance was consistently LOWER than the best radiologists

ROC CURVES OF RADIOLOGISTS VS. STAND-ALONE ALSYSTEM



RAMMOGRAM FROM THIS STUDY:



STUDY IN JNCI ON DIRECT AI INTERPRETATION OF MAMMOGRAMS

- These findings suggest that AI could be utilized in situations where there is a lack of experienced or specialized breast imagers
- Findings also suggest that Al tuned to a high sensitivity could be utilized to "pre-screen" and eliminate studies deemed to have a very low likelihood of malignancy

 This could reduce radiologists' workload of cases to be interpreted without impacting their accuracy



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AI APPLICATIONS IN BREAST IMAGING

Synthesized 2D Image

How does it work?

 Perform a standard tomosynthesis scan (existing system)

 Reconstruct tomosynthesis slices (existing system)

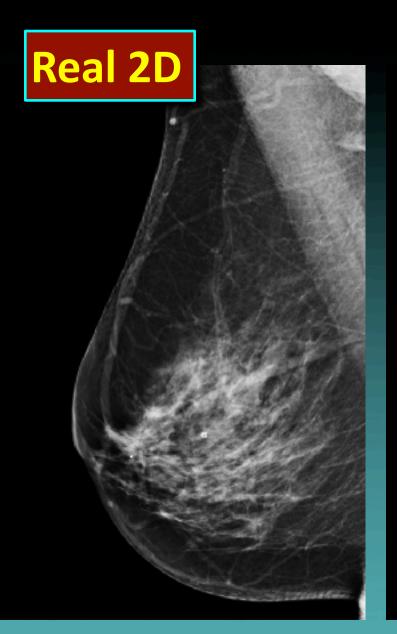
Synthesize 2D image (C-View)

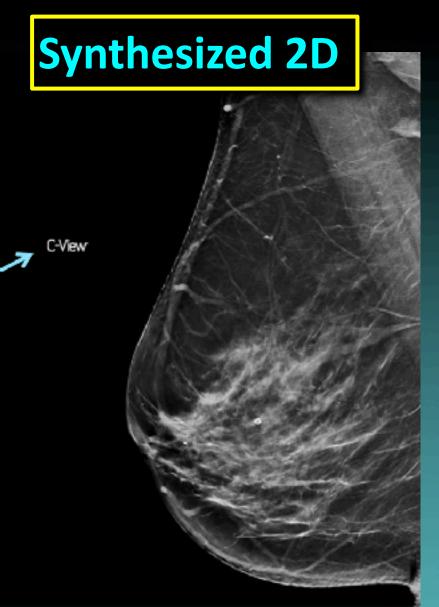
 Similar to Maximum Intensity Projection (MIP) as done with MRI images Image Summation



Synthesized

AI APPLICATIONS IN BREAST IMAGING

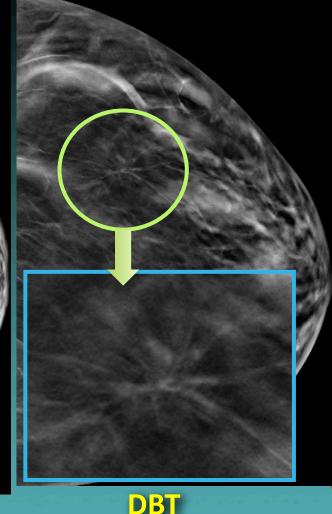


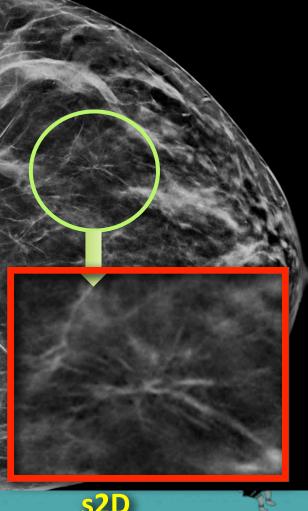


AI APPLICATIONS IN BREAST IMAGING Arch. Distortion on s2D and DBT

51 yo architectural distortion seen well only on s2D/DBT

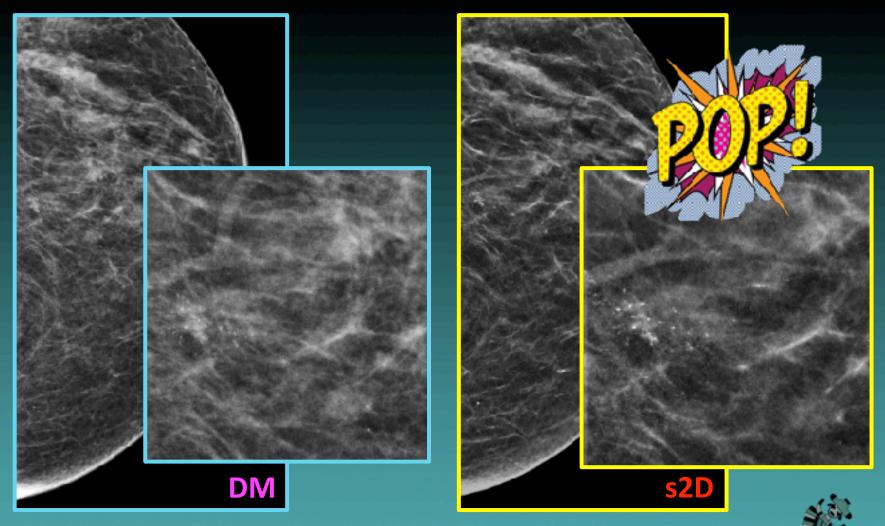
Pathology: invasive ductal carcinoma.





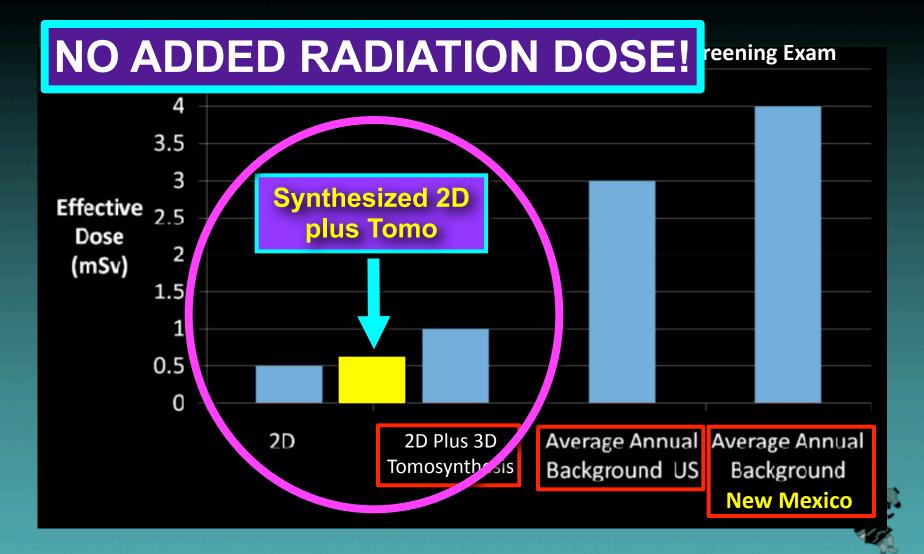


AI APPLICATIONS IN BREAST IMAGING Synthetic 2D with Tomosynthesis



Pathology: Ductal Carcinoma in situ (DCIS)

RADIATION DOSE WHEN SYNTHETIC VIEW IS ADDED TO TOMOSYNTHESIS VIEW:





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AI APPLICATIONS IN BREAST IMAGING

Breast density categorization

Quantra Breast Density Assessment Software

 Patient Name
 21462864

 Patient ID
 21462864

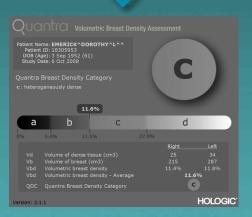
 DOB
 1 Jan 1962

 Study Date
 12 Apr 2016

 Process Date
 21 Nov 2017

Version: 2.2.2

QDC





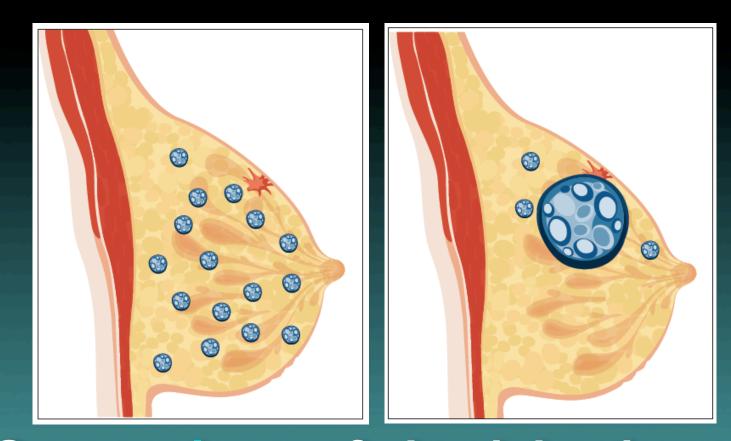
QDC

AI APPLICATIONS IN BREAST IMAGING Al can measure actual DISPERSION of dense breast tissue, not just volume!

Same volume of confetti, but different dispersions-DIFFERENT SIGNIFICANCE!



AI APPLICATIONS IN BREAST IMAGING



Same volume of glandular tissue, but different dispersions-DIFFERENT BREAST CANCER RISK!

SUMMARY OF AI APPLICATIONS IN BREAST IMAGING

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- ⇒ SYNTHETIC 2D MAMMOGRAPHY
- ➡ BREAST DENSITY CATEGORIZATION FOR BREAST CANCER RISK
- ➡ MUCH, MUCH MORE: Device optimization analytics, positioning & motion algorithms, "smart" machines for further analyses, etc.

AI IS OUR FUTURE!

THE FUTURE LOOKS BRIGHT AND INTERESTING FOR BREAST IMAGING!

IT IS A PRIVILEGE & A PLEASURE TO BE PART OF IT, AS WE CONTINUE SKYWARD!

