DBT Physics Basic to Advanced: Primer On Tomosynthesis

Andrew D. A. Maidment, Ph.D.
University of Pennsylvania
Department of Radiology

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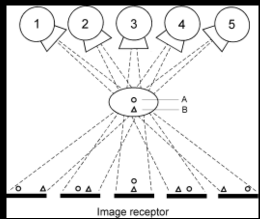
- Dr. Maidment is a scientific advisor to and shareholder of Real Time Tomography, LLC.
- Dr. Maidment is a member of the Scientific Advisory Board of Gamma Medica, Inc.

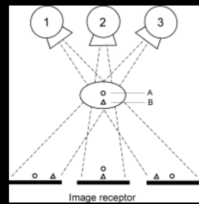
FDA Statement
- This presentation will include off-label uses and applications and devices not yet approved for human use in the United States.

Tomosynthesis Pedigree

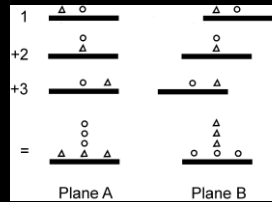
Linear Tomography



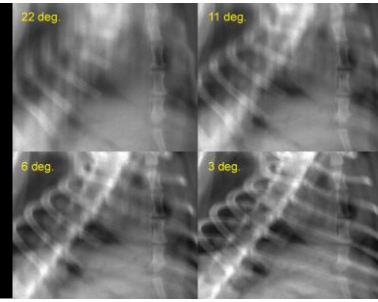
Simple Tomosynthesis

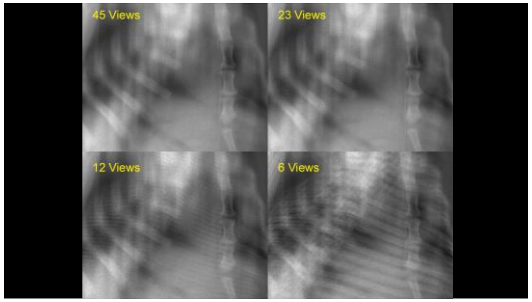


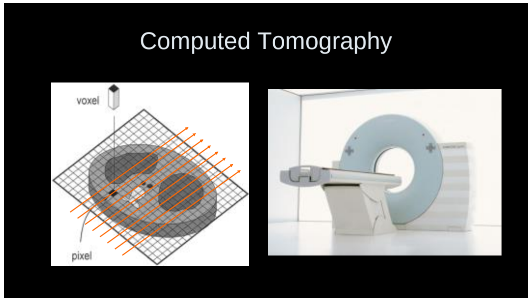
Acquisition geometry

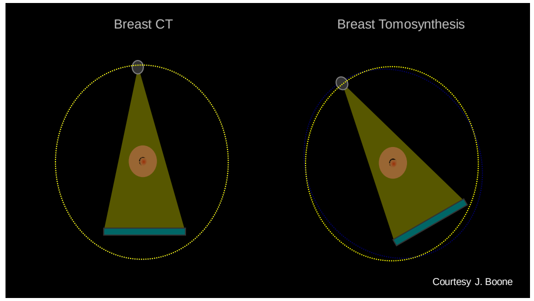


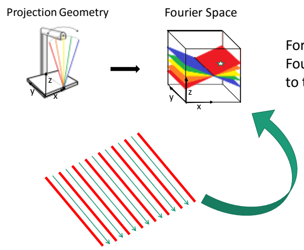
Backprojection image formation



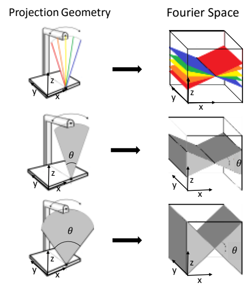

45 Views
23 Views
12 Views
6 Views


Computed Tomography
voxel
pixel


Breast CT
Breast Tomosynthesis
Courtesy J. Boone



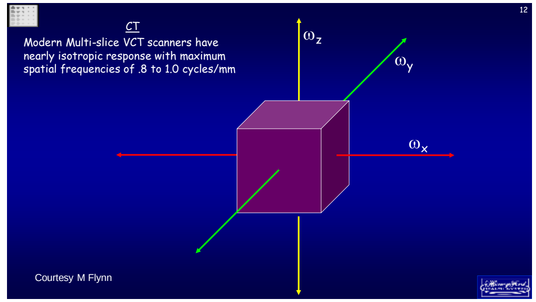
For each projection, the slice in Fourier space is perpendicular to the direction the x-rays travel

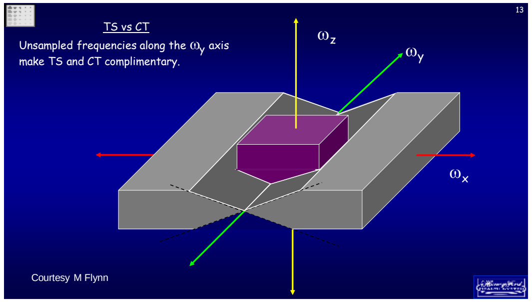


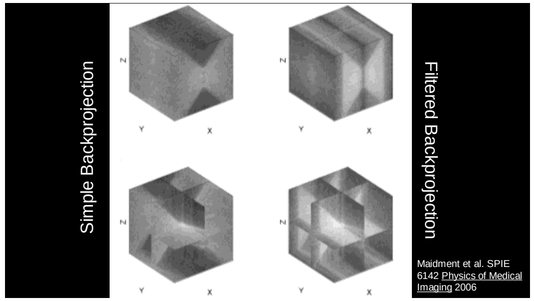
For each projection, the slice in Fourier space is perpendicular to the direction the x-rays travel

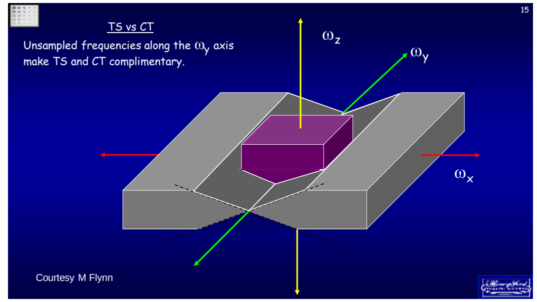
Assuming a parallel beam geometry, one can use central slice theorem to determine how Fourier space would be filled.

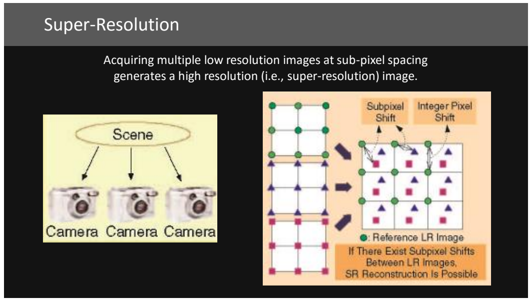
The angular range of the x-ray tube equals the angle of the non-zero region in Fourier space



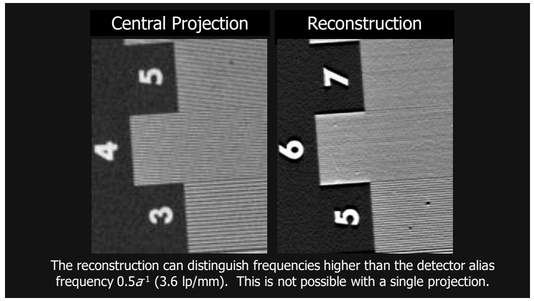

TS vs CT
Unsampled frequencies along the ω_y axis make TS and CT complimentary.
ω_z
ω_y
ω_x
Courtesy M Flynn
13


Simple Backprojection
Filtered Backprojection
Maidment et al. SPIE 6142 Physics of Medical Imaging 2006

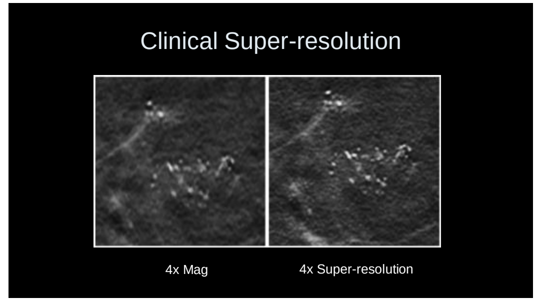

TS vs CT
Unsampled frequencies along the ω_y axis make TS and CT complimentary.
ω_z
ω_y
ω_x
Courtesy M Flynn
15



Super-Resolution
Acquiring multiple low resolution images at sub-pixel spacing generates a high resolution (i.e., super-resolution) image.
Scene
Camera Camera Camera
Subpixel Shift
Integer Pixel Shift
: Reference LR Image
If There Exist Subpixel Shifts Between LR Images, SR Reconstruction Is Possible

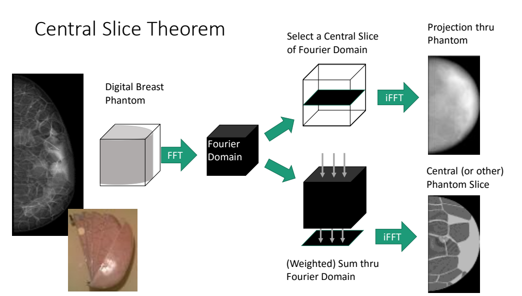


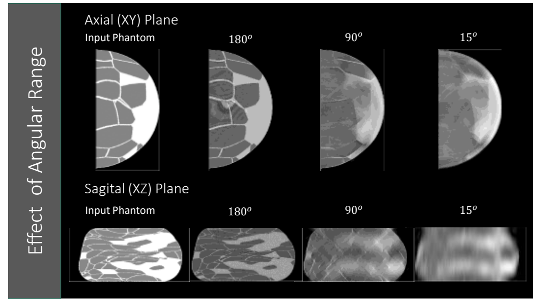
Central Projection
Reconstruction
The reconstruction can distinguish frequencies higher than the detector alias frequency $0.5a^{-1}$ (3.6 lp/mm). This is not possible with a single projection.

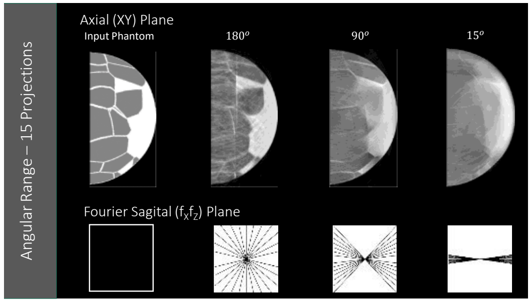


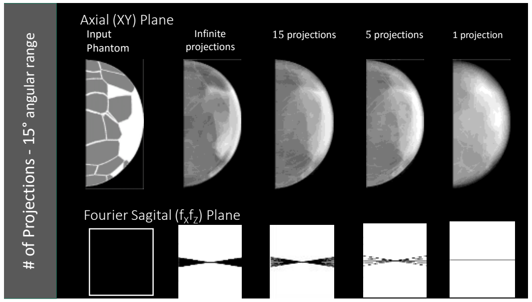
Clinical Super-resolution
4x Mag
4x Super-resolution

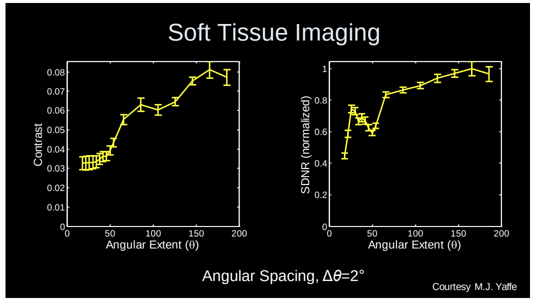

Shimadzu – HD Tomosynthesis

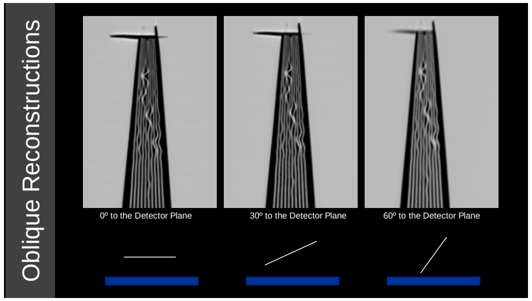

Central Slice Theorem
Digital Breast Phantom
FFT
Fourier Domain
Select a Central Slice of Fourier Domain
iFFT
Projection thru Phantom
(Weighted) Sum thru Fourier Domain
iFFT
Central (or other) Phantom Slice

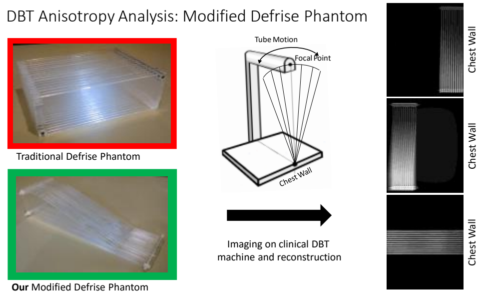

Effect of Angular Range
Axial (XY) Plane
Input Phantom
180°
90°
15°
Sagital (XZ) Plane
Input Phantom
180°
90°
15°

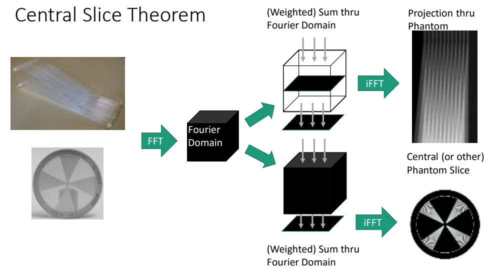

Angular Range – 15 Projections
Axial (XY) Plane
Input Phantom
180°
90°
15°
Fourier Sagital ($f_x f_z$) Plane

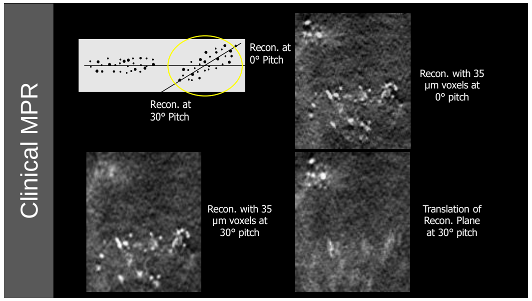

# of Projections - 15° angular range
Axial (XY) Plane
Input Phantom
Infinite projections
15 projections
5 projections
1 projection
Fourier Sagital ($f_x f_z$) Plane

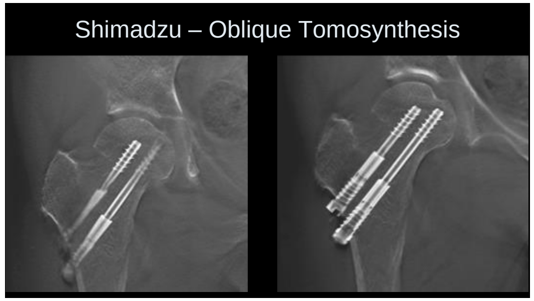

Soft Tissue Imaging
Contrast
Angular Extent (θ)
SDNR (normalized)
Angular Extent (θ)
Angular Spacing, Δθ=2°
Courtesy M.J. Yaffe

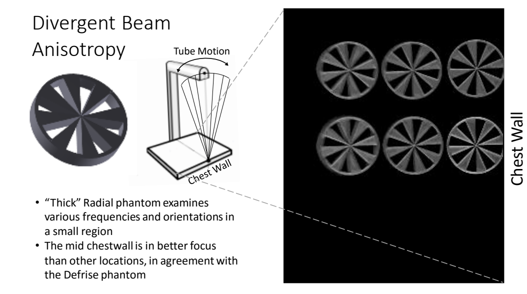

Oblique Reconstructions
0° to the Detector Plane
30° to the Detector Plane
60° to the Detector Plane


DBT Anisotropy Analysis: Modified Defrise Phantom
Traditional Defrise Phantom
Our Modified Defrise Phantom
Tube Motion
Focal Point
Chest Wall
Imaging on clinical DBT machine and reconstruction
Chest Wall
Chest Wall
Chest Wall

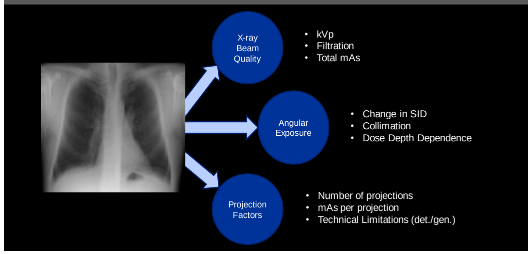

Central Slice Theorem
(Weighted) Sum thru Fourier Domain
Projection thru Phantom
FFT
Fourier Domain
iFFT
iFFT
Central (or other) Phantom Slice
(Weighted) Sum thru Fourier Domain


Clinical MPR
Recon. at 0° Pitch
Recon. at 30° Pitch
Recon. with 35 µm voxels at 0° pitch
Recon. with 35 µm voxels at 30° pitch
Translation of Recon. Plane at 30° pitch

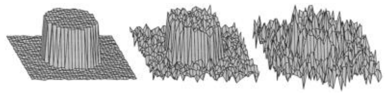

Shimadzu – Oblique Tomosynthesis


Divergent Beam Anisotropy
Tube Motion
Chest Wall
• "Thick" Radial phantom examines various frequencies and orientations in a small region
• The mid chestwall is in better focus than other locations, in agreement with the Defrise phantom
Chest Wall

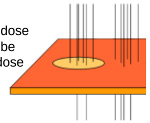
Determinants of Dose

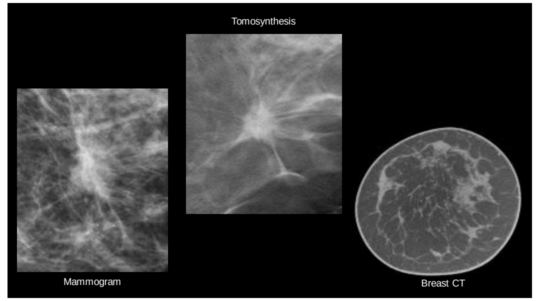


Dose Determines Lesion Detectability



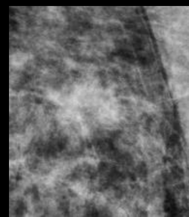
For an ideal detector, the dose for tomosynthesis should be equal to or less than the dose for digital mammography





Clinical Breast Imaging

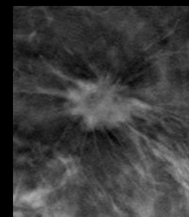
Digital mammography image of an invasive ductal carcinoma.



Rafferty E A et al. Radiology doi:10.1148/radiol.12120674

Radiology

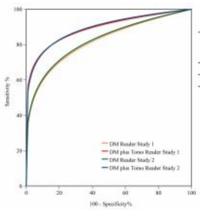
Tomosynthesis image of an invasive ductal carcinoma.



Rafferty E A et al. Radiology doi:10.1148/radiol.12120674

Radiology

Pooled ROC curves for 2 reader studies



Area under the ROC curve

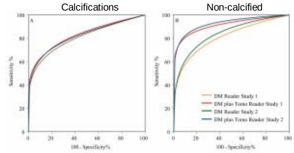
	DM	DM plus Tomo †	Difference	p-value	95% CI
Reader Study 1	82.1	89.4	7.2	<0.001	3.7 , 10.8
Reader Study 2	82.8	89.5	6.8	<0.001	4.1 , 9.5

Using probability of malignancy scores; curves represent average ROC performance for 12 readers in study 1 and 15 in study 2.

Rafferty E A et al. Radiology doi:10.1148/radiol.12120674

Radiology

Pooled ROC by Lesion Type



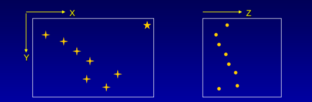
Area under the ROC curve

Case Type	Reader Study	DM †	DM plus† Tomo	Difference	p-value	95% CI
Calcification	1	80.4	84.0	3.3	0.075	-0.4 , 7.4
	2	81.7	83.1	1.4	0.082	-0.2 , 2.9
Non -Calcification	1	80.7	91.2	10.4	<0.001	4.7 , 16.1
	2	84.2	93.0	8.8	<0.001	5.1 , 12.5

Rafferty E A et al. Radiology doi:10.1148/radiol.12120674

Radiology

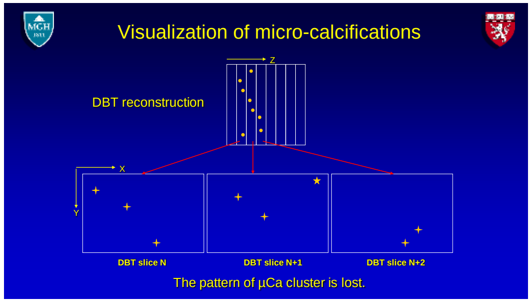
Visualization of micro-calcifications

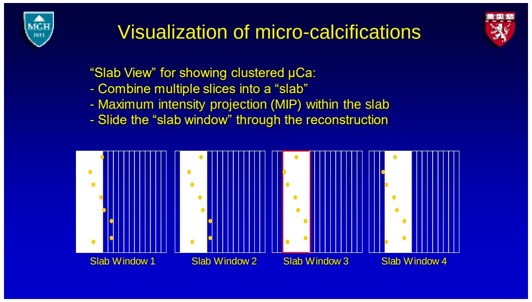


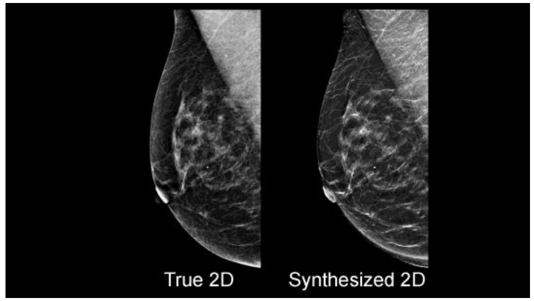
Simulated pattern of clustered µCas (Pattern: Big Dipper and Pole Star)

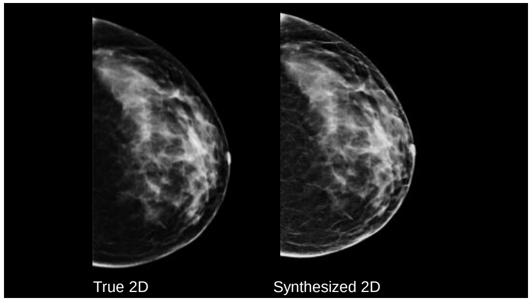
Distribution along z-direction

Conventional mammography:
- Clustered µCa are projected onto a 2-D plane.
- The pattern of µCa distribution is obvious.
- The pattern of µCa distribution contains important diagnostic information.


Visualization of micro-calcifications
DBT reconstruction
z
x
y
DBT slice N
DBT slice N+1
DBT slice N+2
The pattern of μCa cluster is lost.


Visualization of micro-calcifications
"Slab View" for showing clustered μCa:
- Combine multiple slices into a "slab"
- Maximum intensity projection (MIP) within the slab
- Slide the "slab window" through the reconstruction
Slab Window 1
Slab Window 2
Slab Window 3
Slab Window 4


True 2D
Synthesized 2D



JAMA: June 26th, 2014…

Original Investigation

Breast Cancer Screening Using Tomosynthesis in Combination With Digital Mammography

Sarah M. Friedewald, MD; Elizabeth A. Rafferty, MD; Stephen L. Rose, MD; Melissa A. Durand, MD; Donna M. Plecha, MD; Julianne S. Greenberg, MD; Mary K. Hayes, MD; Debra S. Copit, MD; Kara L. Carlson, MD; Thomas M. Cink, MD; Lora D. Barke, DO; Linda N. Greer, MD; Dave P. Miller, MS; Emily F. Conant, MD

Retrospective analysis from 13 centers: 454,850 exams

281,187 DM screens
173,663 DBT+DM screens

Courtesy E. Conant

Friedewald, et al. *JAMA* 2014;311(24):2499-2507

Results: JAMA Tomo Consortium

	DM	DM+DBT	Absolute Difference	Relative Change	P value
Recall Rate	10.7%	9.1%	16/1000	-15%	P<.001
Cancer Detection Rate	4.2/1000	5.4/1000	1.2/1000	+29%	P<.001
Invasive Cancer Detection Rate	2.9/1000	4.1/1000	1.2/1000	+41%	P<.001
PPV1	4.2%	6.4%	2.1%	+49%	P<.001
PPV3	24.2%	29.2%	5.0%	+21%	P<.001

Courtesy E. Conant

Friedewald, et al. *JAMA* 2014;311(24):2499-2507

JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE

Screening Outcomes Following Implementation of Digital Breast Tomosynthesis in a General-Population Screening Program

Anne Marie McCarthy, Despina Kontos, Marie Synnestvedt, Kay See Tan, Daniel F. Heitjan, Mitchell Schnall, Emily F. Conant

University of Pennsylvania Data

Method:

– DM cohort from yr prior to to DBT = 10,728 exams

– DBT cohort 17 months = 15,571 exams

- Complete conversion to DBT for entire screen population
- Patient level data (age, density, race, risk level)
- Same readers across the two time periods

Courtesy E. Conant

McCarthy AM, et al. JNCI. 2014;106(11)

Results for Entire Population

	DM	DBT	change	p-value
Total, N	10751	15633		
Called Back, N	1116	1372		
Called Back %	10.4	8.8	-15.6% (-20% when controlled for variable reader volumes)	<.001
Bx Performed, N	190	315		
Bx Performed %	1.8	2.0		.15
Cancers Detected	47	84		
Cancers per 1000 Screened	4.4	5.4	+19.6%	.26
PPV1 (Cancers/ Callback, %)	4.2	6.1	+40.9	.03
PPV2 (Cancers/ Bx rec 4-5, %)	22.0	24.4		.51
PPV3 (Cancers /Bx Done %)	24.7	25.1		.93

Courtesy E. Conant

McCarthy AM, et al. JNCI. 2014;106(11)

What about Dose?

Combination DBT/DM screening is more than double the xray dose that DM mammography

– Combo phantom dose is less that FDA max allowable

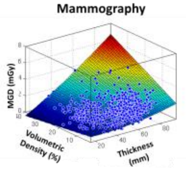
– However, dose increases significantly with increasing breast thickness

Can the DM portion of study be replaced by a reconstructed, "2D" like synthetic image?

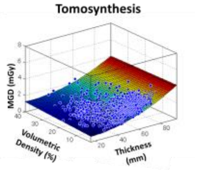
Courtesy E. Conant

Results – MGD and Thickness & Glandularity

Mammography



Tomosynthesis



Digital Mammography:

- MGD is dependent on *both* **thickness** and **glandularity** (**p<0.001**)

Tomosynthesis:

- MGD is dependent on **thickness** (**p<0.001**) but **not glandularity** (**p=0.11**)

Average dose per patient*

Mode	No. Patients	View Position	No. Images Acquired	Average Dose per Patient (mGy)	Average Compressed Breast Thickness (mm)
Tomo Combo (2D)	2,454	CC	5,125	1.84	58.50
		MLO	5,799	2.52	64.54
Tomo Combo (3D)	2,454	CC	4,901	2.16	58.50
		MLO	4,893	2.49	64.54

Mode (Combined MLO and CC)	Average Dose per Patient (mGy and % of total)	Average Compressed Breast Thickness (mm)
Tomo Combo (2D)	4.36 (48.4%)	61.52
Tomo Combo (3D)	4.65 (51.6%)	60.54

The 2D component of the Tomo Combo acquisition accounted for nearly half of the average dose per patient in 2014.

*Information provided by the DICOM header that corresponds to the mean glandular dose in mGy (Organ Dose 0040,0316)

Average dose per patient

Mode	No. Patients	View Position	No. Images Acquired	Average Dose per Patient (mGy)	Average Compressed Breast Thickness (mm)
Tomo Combo (2D + 3D)	2,454	CC	10,026	4.00	58.50
		MLO	10,692	5.01	64.54
Tomo HD (C-View + 3D)	2,064	CC	4,290	2.29	57.60
		MLO	4,427	2.77	63.47

Mode (Combined MLO and CC)	Average Dose per Patient (mGy)	Average Compressed Breast Thickness (mm)
Tomo Combo (2D + 3D)	9.01	61.52
Tomo HD (C-View™ + 3D)	5.06	60.54

- 44% *

The switch to Tomo HD in 2015 eliminated the acquisition of 2D images. This resulted in an overall dose reduction of 44% in our patient population.

* p-value is infinitesimal

Average dose per patient

Mode	No. Patients	View Position	No. Images Acquired	Average Dose per Patient (mGy)	Average Compressed Breast Thickness (mm)
Tomo Combo (3D)	2,454	CC	4,901	2.16	58.50
		MLO	4,893	2.49	64.54
Tomo HD (3D)	2,064	CC	4,290	2.29	57.60
		MLO	4,427	2.77	63.47

Mode (Combined MLO and CC)	Average Dose per Patient (mGy)	Average Compressed Breast Thickness (mm)
Tomo Combo (3D only)	4.65	61.52
Tomo HD (3D only)	5.06 (+9% *)	60.54

In changing from Tomo Combo to Tomo HD, the 3D component of the patient dose is increased by 9%, due to additional images.

* p-value is infinitesimal

s2D Performance metrics continued…

Metric	DM/DBT	s2D/DBT	p value
Recall rate (%)	8.8	7.1	0.001
Biopsy rate (%)	2.0	1.3	0.001
Cancers/1000	5.45	5.03	0.732
in situ	1.48	0.9	0.301
invasive	3.85	4.10	0.840

s2D maintains benefits of DBT:

- Dose reduced by 39%
- Sensitivity and specificity unchanged
  - Slight decrease in *in situ* detection to be monitored…

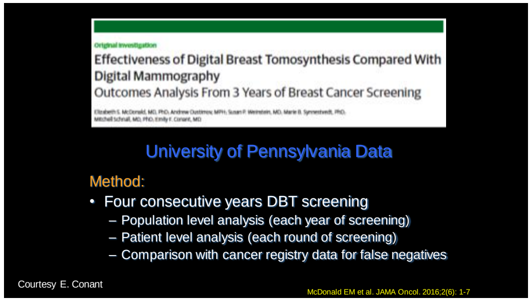
Courtesy E. Conant

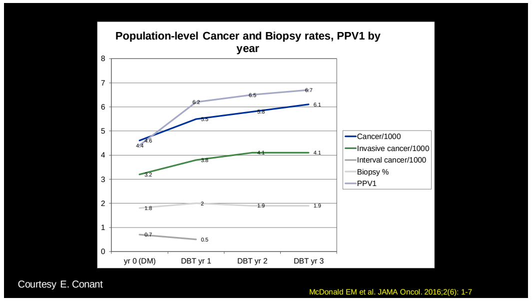
Zuckerman S et al., accepted for publication

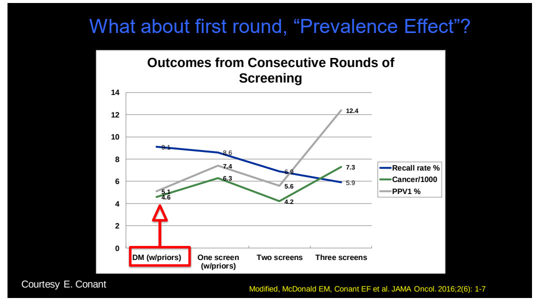
Are DBT outcomes sustainable?

- Consecutive years of screening tomo
  - Impact of learning?
  - Incident versus prevalent screening
- Analysis of false negative studies:
  - Surrogate for mortality benefit
  - Best way to learn is from missed opportunities (mistakes?)

Courtesy E. Conant


Original Investigation
Effectiveness of Digital Breast Tomosynthesis Compared With Digital Mammography
Outcomes Analysis From 3 Years of Breast Cancer Screening
University of Pennsylvania Data
Method:
• Four consecutive years DBT screening
– Population level analysis (each year of screening)
– Patient level analysis (each round of screening)
– Comparison with cancer registry data for false negatives
Courtesy E. Conant
McDonald EM et al. JAMA Oncol. 2016;2(6): 1-7


Population-level Cancer and Biopsy rates, PPV1 by year
8
7
6
5
4
3
2
1
0
yr 0 (DM)
DBT yr 1
DBT yr 2
DBT yr 3
Cancer/1000
Invasive cancer/1000
Interval cancer/1000
Biopsy %
PPV1
4.4
4.6
6.2
6.5
6.7
5.5
5.8
6.1
3.2
3.8
4.1
4.1
1.8
2
1.9
1.9
0.7
0.5
Courtesy E. Conant
McDonald EM et al. JAMA Oncol. 2016;2(6): 1-7


What about first round, “Prevalence Effect”?
Outcomes from Consecutive Rounds of Screening
14
12
10
8
6
4
2
0
DM (w/priors)
One screen (w/priors)
Two screens
Three screens
Recall rate %
Cancer/1000
PPV1 %
9.1
8.6
6.9
5.9
7.4
5.1
5.6
12.4
6.3
4.6
4.2
7.3
Courtesy E. Conant
Modified, McDonald EM, Conant EF et al. JAMA Oncol. 2016;2(6): 1-7

Breast Cancer Research &Treatment (2016)

Breast cancer screening using tomosynthesis in combination with digital mammography compared to digital mammography alone: a cohort study within the PROSPR consortium

Emily F. Conant · Elisabeth F. Beaber · Brian L. Sprague · Sally D. Herschorn · Donald L. Weaver · Tracy Onega · Anna N. A. Tosteson · Anne Marie McCarthy · Steven P. Poplack · Jennifer S. Haas · Katrina Armstrong · Mitchell D. Schnall · William E. Barlow

PROSPR consortium (Brigham-Dartmouth, UVt, UPenn)

- DM and DM/DBT (2011-15): 142,883 DM; 55,998 DBT
- Patient level data
    - 16% reduction in recall (8.7% vs 10.4% p<0.0001)
    - 34% increase in cancer detection (5.9 vs 4.4/1000, p= 0.0026)
      ↑27% invasive cancers
    - Trend in decrease in false negatives (0.46 vs 0.6/1000)

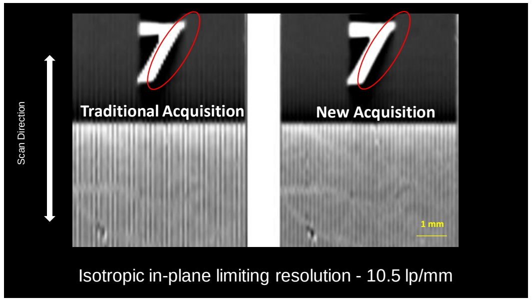
Courtesy E. Conant

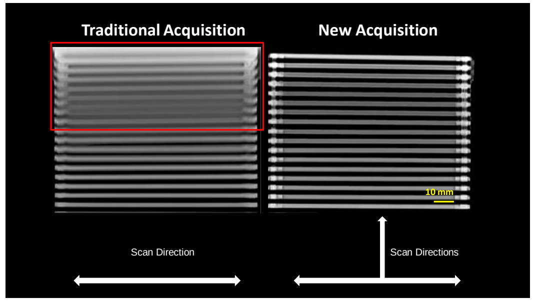
Conant EF et al. BCR&T 2016

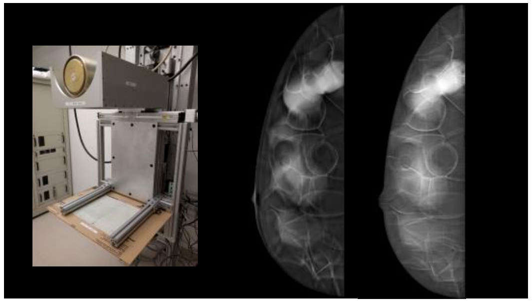
Future Directions

Next-Generation DBT


Next-Generation DBT


Scan Direction
Traditional Acquisition
New Acquisition
1 mm
Isotropic in-plane limiting resolution - 10.5 lp/mm

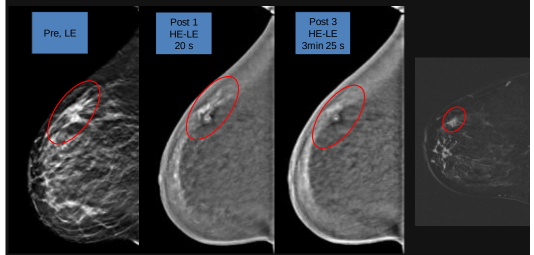

Traditional Acquisition
New Acquisition
10 mm
Scan Direction
Scan Directions



Hologic Prototype CE-DBT System

Target	W
kVp	49 (HE) / 32 (LE)
Filter	Cu (HE) / Al (LE)
SID	70 cm
Detector	3 fps, 2x2 binning
Angular Range	15°
Scan Time	7.3 seconds

- Separate calibrations for LE and HE images
- Manual technique, no AEC
- DE subtraction factor k derived from CIRS Model 20 BR3D phantom



Carton AK, et al. British Journal of Radiology 83(988): 344-350, Apr 2010.

Advantages of tomosynthesis

- Improves conspicuity by removing overlying structures
- Permits section imaging with high resolution in coronal view
- Supports limited multiplanar reconstruction
- Easily performed on the high volume of radiography patients
- Lower radiation dose compared with CT
- Lower cost compared with CT
- Excellent platform for quantitative imaging