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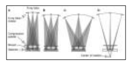
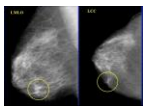
Digital Breast Tomosynthesis, VCT Research at the FDA

Stephen J. Glick, PhD
FDA/CDRH/OSEL/DIDSR
Silver Spring, MD





1

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Research Team/Collaborators

CDRH

OSEL/ DIDSR
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University of Massachusetts
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University of Texas
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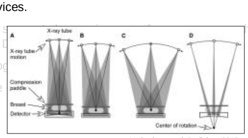
INTRODUCTION

- Currently three FDA approved DBT systems (Hologic 2011, GE 2014, Siemens 2015)
- No standard DBT system (different detectors, acquisition geometries etc.). Continue to see submissions for design changes to approved DBT devices.
- Industry s... ny (FFDM) towards D...
  - Holog...
  - Role...



Vedantham et al, Radiology 2015

3

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INTRODUCTION

- ❑ Currently three DBT (Hologic 2011, GE 2014, Siemens 2014) and one BCT (Koning Inc.) systems approved FDA
- ❑ No standard DBT system (different detectors, acquisition geometries etc.). Continue to see submissions for design changes to approved DBT devices.
- ❑ Industry seems to be moving away from mammography (FFDM) towards DBT
  - Hologic (3D + C-view), Siemens (solely 3D)
  - Role of synthetic mammography

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FDA REGULATORY LANDSCAPE
CURRENT ASSESSMENT OF BREAST IMAGERS

- ❑ Clinical Study (Pre-Market Approval - PMA)
  - Multiple breast radiologists reading large number of clinical cases
  - Rigorous multi-reader, multi-case ROC analysis
  - Expensive, time-consuming, and radiation risk
- ❑ Clinical Data (510k)
  - Limited number of clinical cases
  - Subjective assessment of diagnostic image quality
  - Limited ability to predicate
- ❑ Non-clinical, physics based phantom testing
  - MTF, NPS, DQE, SNR or CNR
  - Use simple unrealistic phantoms, might not apply for non-linear reconstruction, don't evaluate objective task performance

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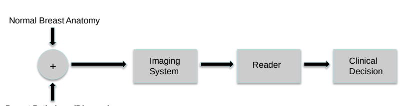
ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS



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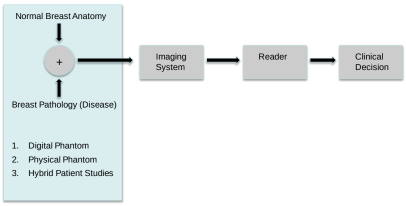
ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS



7

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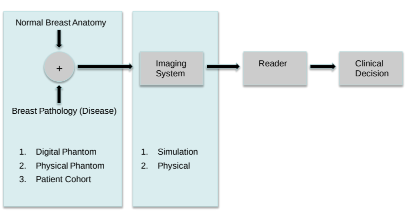
ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS



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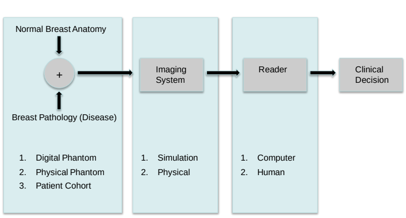
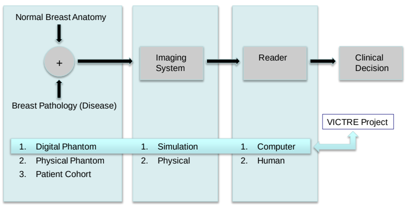
ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS



9

ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS



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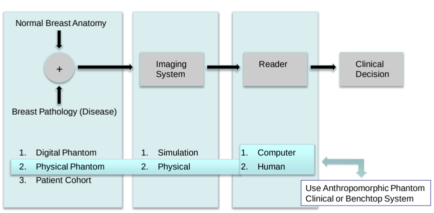
ALTERNATIVE APPROACHES FOR ASSESSING DIAGNOSTIC ACCURACY OF BREAST IMAGING SYSTEMS - VCT



11

Limited use of “virtual clinical trial” approach in FDA submissions

- BARCO Mammo/Tomosynthesis display. Temporal response claim cleared using a combination of bench testing and modeling using a computational reader approach
- GE ASiR-V image reconstruction. CT dose reduction claim in CT cleared using a homogeneous physical phantom and computational models of low-contrast detectability.

12

Virtual Imaging Clinical Trials Regulatory Evaluation (VICTRE) - Goals

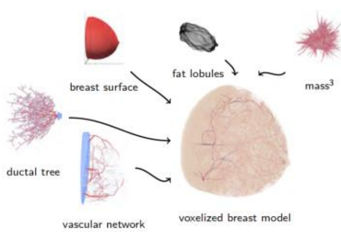
- To perform a complete in silico clinical study for a DBT device and compare the results to those in an existing FDA submission using patients and clinicians
- To develop, validate, and distribute an open-source code that will include the complete computational imaging pipeline
- To develop draft guidelines and guidance on virtual imaging clinical trials.

Research Team:

- Aldo Badano (lead)
- Andreu Badal (physics)
- Stephen Glick (physics/regulatory)
- Christian Graff (breast models)
- Anita Nosratieh (regulatory)
- Frank Samuelson (reader studies)
- Diksha Sharma (pipeline)
- Rongping Zeng (recon and readers)

13

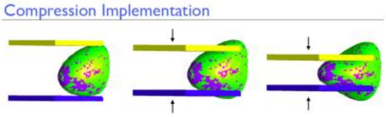
Variable and realistic model of breast anatomy

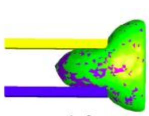


- C.G. Graf, "A new open-source multi-modality digital breast phantom," Proc SPIE 9783, 2016.
- L. Sisternes, "A computational model to generate simulated 3D breast masses," Med Phys 2015.

14

Compression Implementation





compressed to 5 cm

- elastic deformation run until desired compression
- occasionally can fail due to mesh behavior

15

Simulation of the imaging process

FDA/DIDSR has developed open-source freely available and widely used software to simulate physics of the imaging system

- ❑ MC-GPU[1] - GPU-accelerated x-ray transport code to simulate clinically realistic images
- ❑ MANTIS[2] - Monte Carlo x-ray electron and optical imaging simulation tool

1. A. Badal and A. Badano, "Accelerating Monte Carlo simulations of photon transport in a voxelized geometry using a massively parallel graphics processing unit," Med Phys 2009
2. A. Badano and J. Sempau, "MANTIS: combined x-ray, electron, and optical Monte Carlo simulations of indirect radiation imaging systems," Phys Med Biol, 2006.

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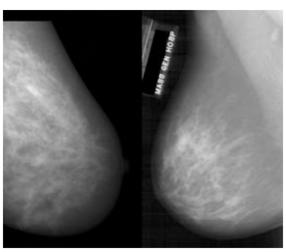

Simulated Real

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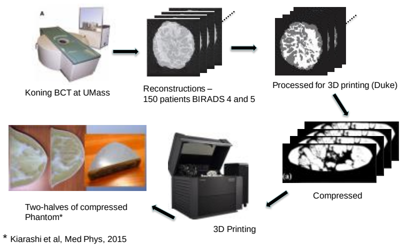
Model Observers for VICTRE Project

Draw on breast imaging model observer research at FDA

- Zeng R, Park S, Bakic P, and Myers KJ, "Evaluating the sensitivity of the optimization of acquisition geometry to the choice of reconstruction algorithm in digital breast tomosynthesis through a simulation study," Phys Med Biol, 2015.
- Park S, *Zhang G**, and Myers KJ, "Comparison of channel methods and observer models for the task-based assessment of multi-projection imaging in the presence of structured anatomical noise," in press, *IEEE Transactions on Medical Imaging*, 2016.
- *Young S* , Bakic P, Jennings R, Myers KJ, and Park S, "A virtual trial framework for quantifying the detectability of masses in breast tomosynthesis projection data," *Medical Physics*, 40 (5), p. 051914, 2013 * Italicized with * are the names of students and postdoctoral fellows who I have mentored.
- Park S, "Spatial domain model observers for optimizing tomosynthesis," in *Tomosynthesis Imaging*, edited by I. Reiser and S. Glick, Taylor and Francis Books, Inc., 2014.
- Ikejimba L, Glick SJ, Samei E, and Lo JY, "Comparison of model and human observer performance in FFDM, DBT, and synthetic mammography," SPIE Medical Imaging 2016, Proc SPIE 9783, 2016

ANTHROPOMORPHIC BREAST PHANTOMS 3D PRINTING (Collaboration with Duke)



* Kiarashi et al, Med Phys, 2015

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ANTHROPOMORPHIC BREAST PHANTOMS 2D INKJET PRINTING

Ikejimba et al, IWDM 2016

20

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Validation - FFDM

Tissue equivalent chips of known glandularity

21

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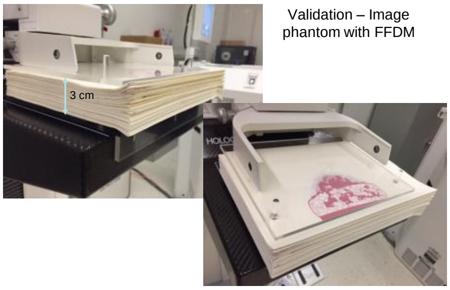

Validation – Image phantom with FFDM

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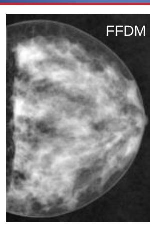
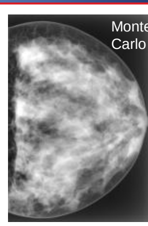
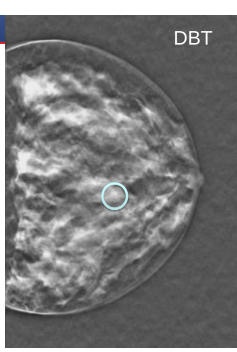




Phantom Study
Hologic Selenia FFDM

Monte Carlo Simulation
- Ideal detector
- Ideal focal spot

23



- DBT acquisition on clinical system
- Lesion inserted in virtual model
- Slices reprinted and replaced

24

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COMPARISON OF MODEL AND HUMAN PERFORMANCE IN FFDM, DBT, AND SYNTHETIC MAMMOGRAPHY*

- Compare model and human observers in reader study using anthropomorphic breast phantom and inserted low-contrast signals.
- Task-based performance of FFDM, DBT, and synthetic mammography (SM)
- Variable tasks with uniform and structured backgrounds

* Ikejimba L, Glick SJ, Samei E and Lo JY, Proc SPIE 9783, 2016.

25

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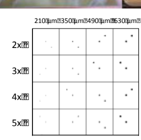
COMPARISON OF MODEL AND HUMAN PERFORMANCE IN FFDM, DBT, AND SYNTHETIC MAMMOGRAPHY

Iodine Contrast Agent



4 contrast levels (CL)
4 disk diameters

26

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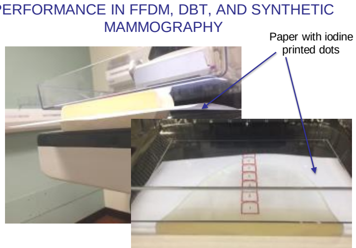
PROJECT 2 - COMPARISON OF MODEL AND HUMAN PERFORMANCE IN FFDM, DBT, AND SYNTHETIC MAMMOGRAPHY



27

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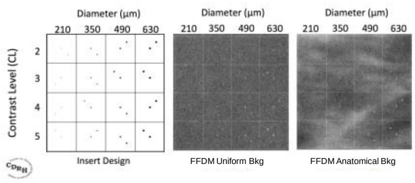
COMPARISON OF MODEL AND HUMAN PERFORMANCE IN FFDM, DBT, AND SYNTHETIC MAMMOGRAPHY



28

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Image Acquisition

Clinical Hologic System

	FFDM	DBT and SM[1]
Detector pixel size, x-y plane (mm)	0.07	0.07 (2x2 binning)
Image pixel size, x-y plane (mm)	0.07	0.09
Target/Filter	W/Rh	W/Al
Tube voltage (kV)	28	29
Tube load (mAs)	80	42
AGD at AEC (mGy)	1	1.4

29

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Human and Model Observer Study

- 4 alternative forced choice (4AFC)
- Human readers: Six non-radiologists
- Model Observers
  - Nonprewhitening with eye filter (NPWE)
  - Channelized Hotelling observer (CHO)
    - Gabor channels
    - Laguerre-Gauss (LG) channels

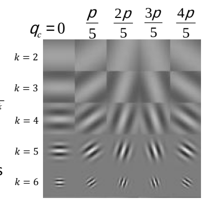
30

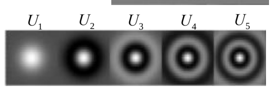
2D Observer Models

- NPWE[2] $E(f) = f^{n_1} e^{cf^{n_2}}$
  - Fixed viewing distance 500 mm
  - Field of view 23.9 mm
  - Display size 338 mm
- Gabor CHO (Gb-CHO)
  - DBT – 5 frequencies, 5 orientations, 2 phases
  - FFDM, SM – 7 frequencies, 7 orientations, 2 phases
- Laguerre-Gauss CHO (LG-CHO)
  - 5 channels
  - Gaussian width ∝ task diameter

Gabor Channels

$f_c = \frac{3}{2^k}$

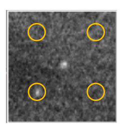




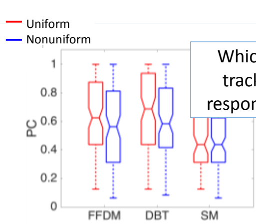
LG Channels

Reader Study

- Model Observer
  - Apply template matching to each corner
  - Select corner of maximum response
- Performance: Proportion Correct (PC)
  - PC = X/n
  - X = number of successes
  - n = number of trials
  - 0 ≤ PC ≤ 1



Human Scores



Which model tracks these responses best?

Overall PC differs by phantom and modality

PC for nonuniform phantom, DBT

Contrast Level \ Disk Diameter (μm)	210	350	490	630
2	0.18	0.32	0.46	0.69
3	0.35	0.44	0.58	0.86
4	0.39	0.49	0.71	0.92
5	0.46	0.75	0.86	1.00

-Wide range of PC
-Varies by size, contrast

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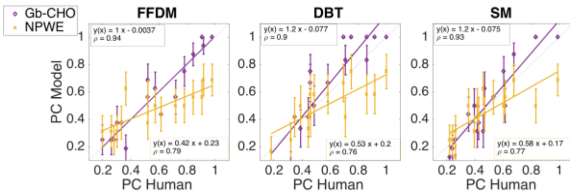
Effect of modality on model accuracy



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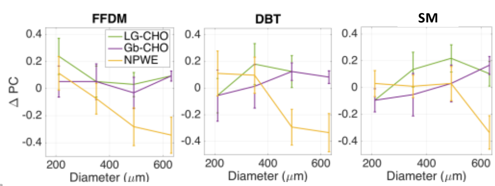
Effect of size on model accuracy

ΔPC = PC(Model) – PC(Human)

ΔPC > 0, Model score higher than human

ΔPC < 0, Model score lower than human



Disk contrast level = 3

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DISCUSSION

- Results of task-based analysis can be impacted by phantom type and model observer
- Readers scored higher with FFDM and DBT than SM, in uniform and nonuniform backgrounds
- Gabor-CHO and LG-CHO matched well with humans, in uniform and nonuniform backgrounds
  - Gabor-CHO matched human scores more closely than LG-CHO
  - LG-CHO overperformed relative to humans

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SUMMARY AND FUTURE WORK

- Anthropomorphic Breast Phantoms
  - Continue to investigate 2D and 3D printing of phantoms. Investigate new materials, new breast models, reproducibility, spatial resolution, and phantoms for dynamic imaging.
- Using new phantoms, continue to explore methodologies for assessing diagnostic task-performance that can be used to support PMAs.
  - VICTRE project (simulated objects and imaging systems)
  - VCT using physical phantoms and real imaging systems
  - Contribute to the down-classification of DBT devices (III -> II), decrease time to market
- Continue investigating new breast imaging applications including spectral imaging, material decomposition, and new detectors

37

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Thank you

Disclosure: The mention of commercial products herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services

38

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39

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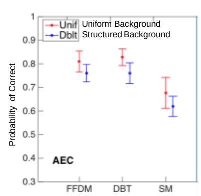
HUMAN OBSERVER RESULTS



41

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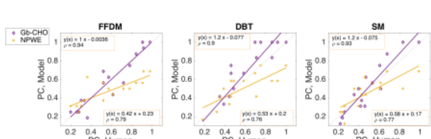
RESULTS
HUMAN VS MODEL OBSERVER



42

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Spectral Analysis

- High purity germanium energy discriminating photon counting detector
- Source and detector collimation
- Calculated μ as a function of keV

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Results

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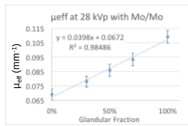
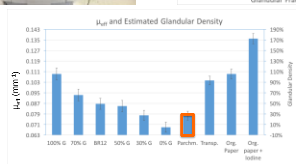
Material Validation





6

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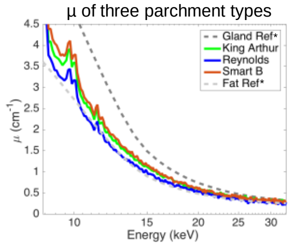
Spectral Analysis

μ of three parchment types



- Low material separation
- Reynolds lower μ
- KA sheets flat

47

*Hammerstein et al., Radiology 1979

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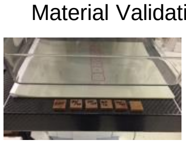
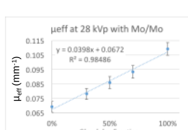
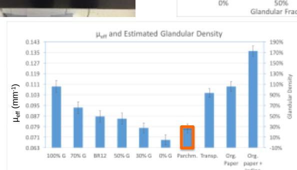
Material Validation







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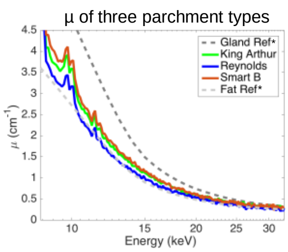
Spectral Analysis



- Low material separation
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49

*Hammerstein et al., Radiology 1979

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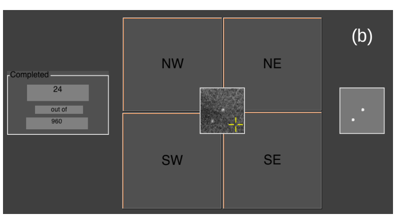

-Supervised training with easy, medium, difficult tasks

-All Modes x Tasks x Trials x Phantoms = 1536 ROIs

50