Project proposal for INFN CSN5 - Bando n. 21188
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AGATA

Advanced GeAnt4-based platform for virtual clinical Trials in X-ray breAst imaging

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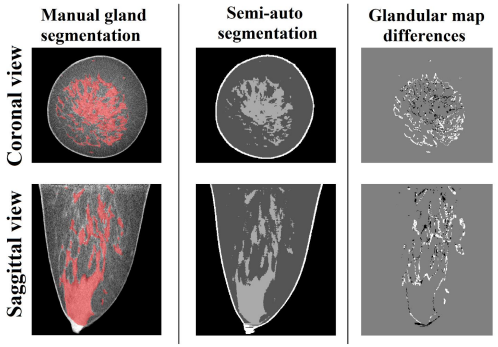
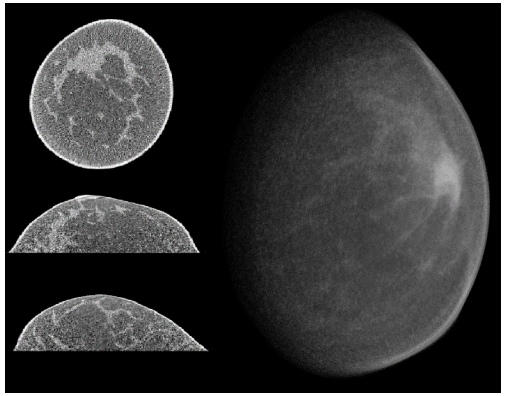
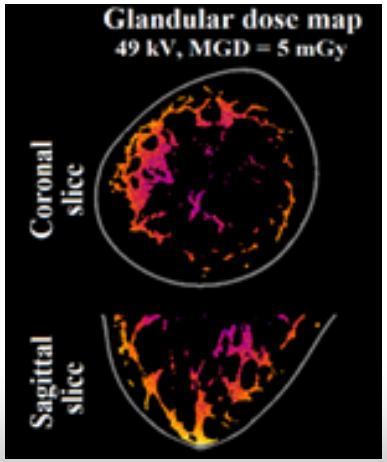
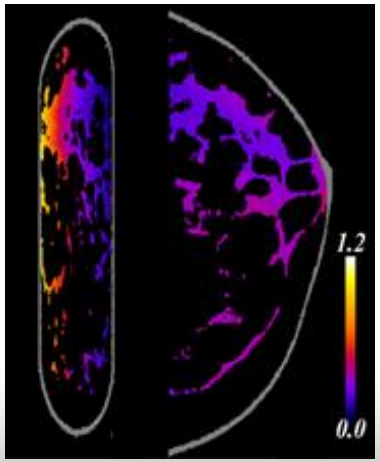
AGATA

- Introduction
- Breast imaging tecniques
- Digital Breast Phantoms for dosimetry
- Heterogenous breast models
- The AGATA Platform
  - Database of patient derived breast phantoms
  - The simulation platform for bCT
  - The simulation platform for DM/DBT
- Discussion

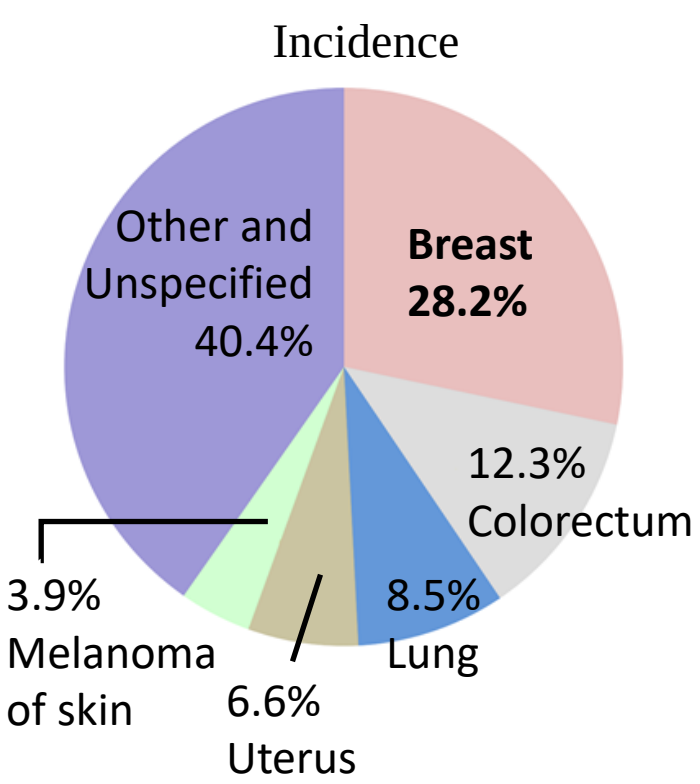


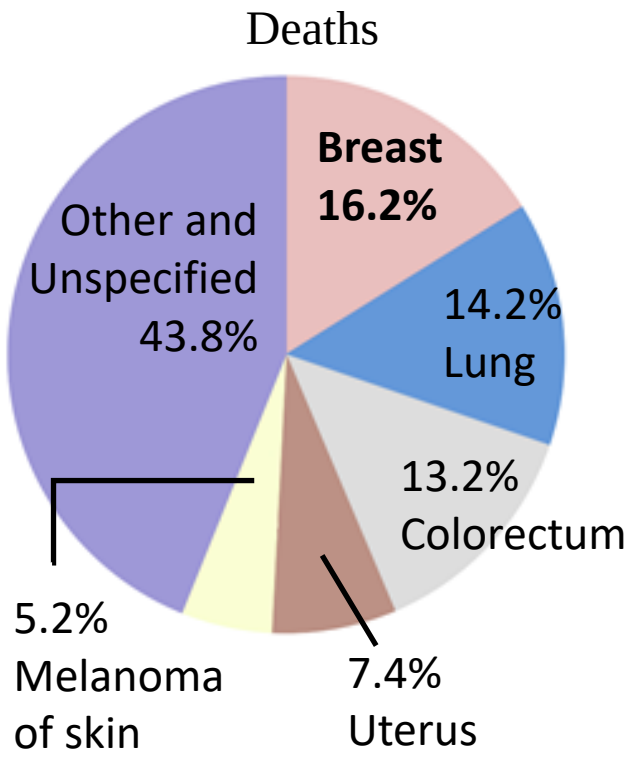






Breast Cancer





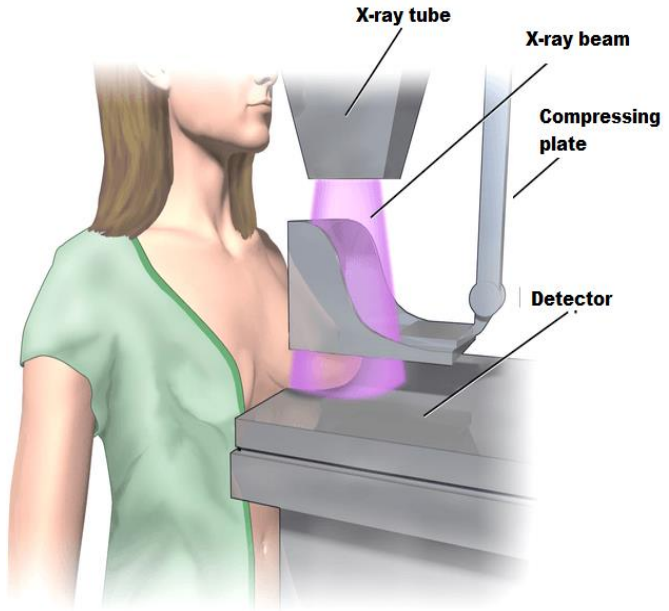
Worldwide, in female subjects, breast cancer is the most commonly diagnosed cancer, accounting about 2.1 million newly diagnosed breast cancer (1 in 4 cancer cases among women) and the leading cause of cancer death, followed by colorectal and lung cancer for incidence, and vice versa for mortality. In 2018, among European females, breast cancer was by far the most frequently diagnosed neoplasm (522,500 , 28.2% of the total), followed by colorectal (228,000 , 12.3%), lung (158,000 , 8.5%) and corpus uteri (122,000 , 6.6%) cancers.

As suggested by the WHO, to improve breast cancer outcomes and survival, early detection is critical. There are two prerequisites for reducing the rate of death: early diagnosis and mass screening procedures. Screening consists of testing women to identify cancers before any symptoms appear.

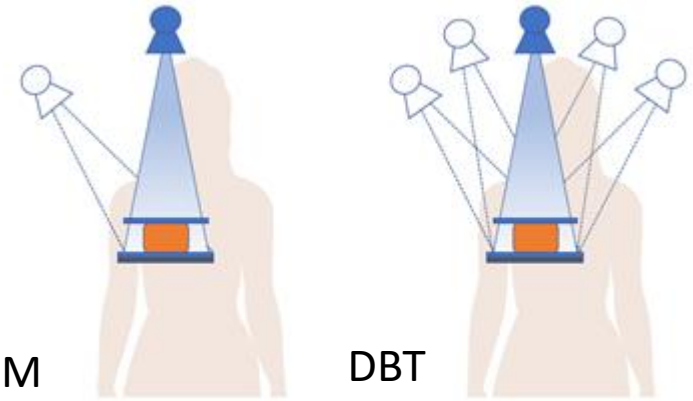
F. Bray, J. Ferlay, I. Soerjomataram, R. L. Siegel, L. A. Torre, and A. Jemal, 'Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries', *CA. Cancer J. Clin.*, vol. 68, no. 6, pp. 394–424, 2018, doi: 10.3322/caac.21492

Breast screening tecniques

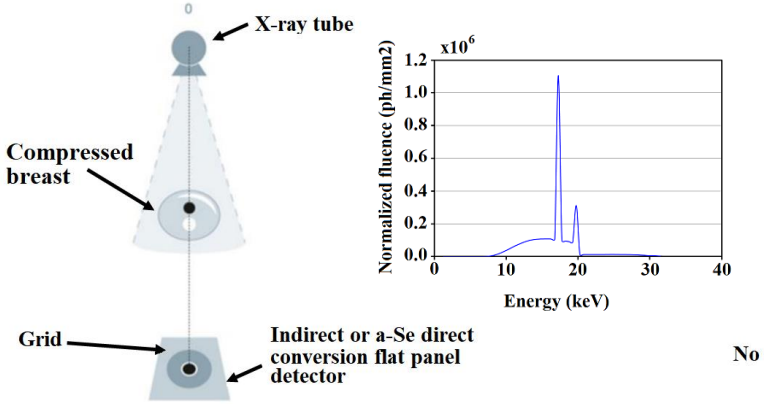
Breast cancer screening programs have been introduced by public health services of many countries. Early detection and accurate diagnosis are carried out with X-ray Digital Mammography (DM) and, in the last few years, with Digital Breast Tomosynthesis (DBT).

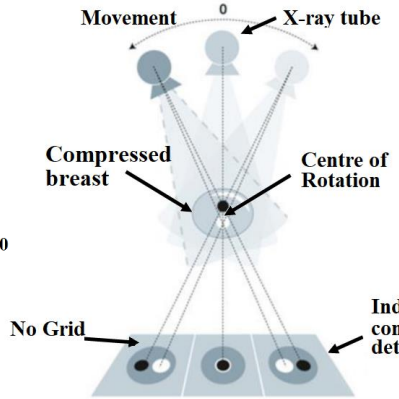


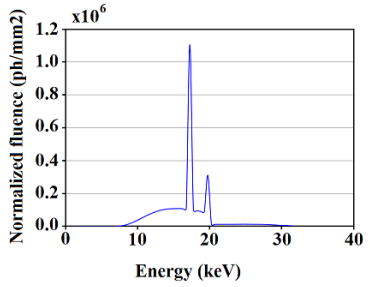
DM and DBT provide radiographic images of the compressed breast. In the first case two images for each breast are acquired (CC and MLO views), while in DBT the X-ray tube moves in an arc over the compressed breast and multiple projections are acquired and then reconstructed by a computer, forming pseudo-three-dimensional images.

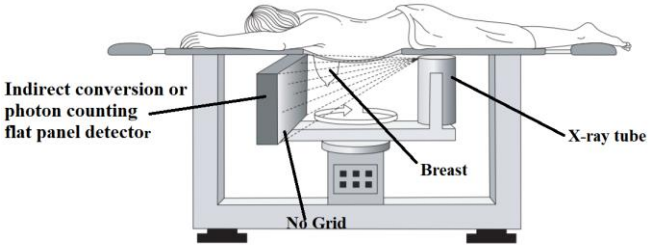


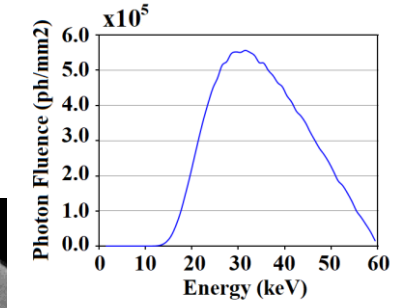
DBT and BCT: the advent of 3D x-ray breast imaging



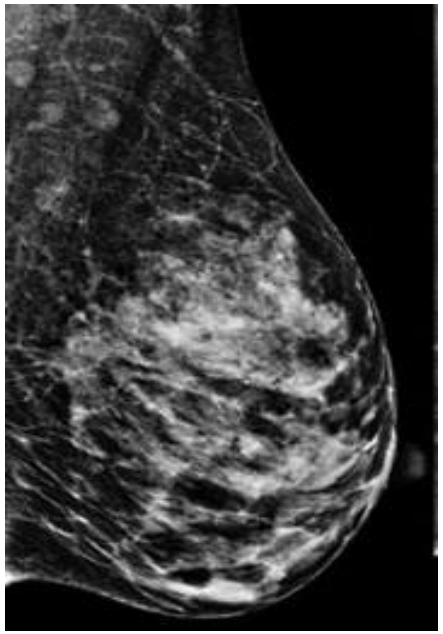






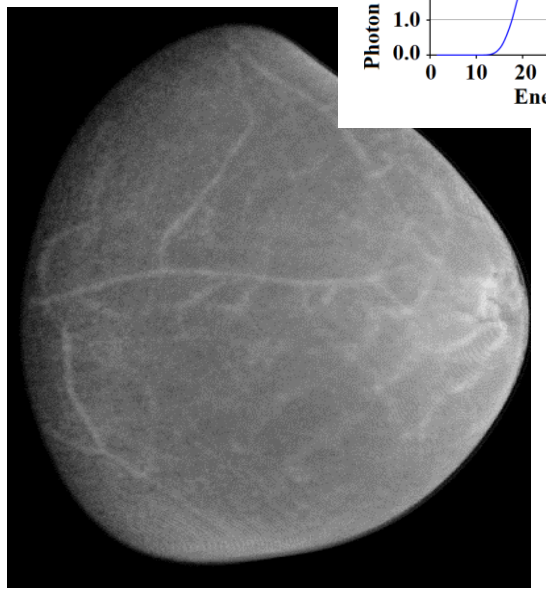


Mammo



DBT

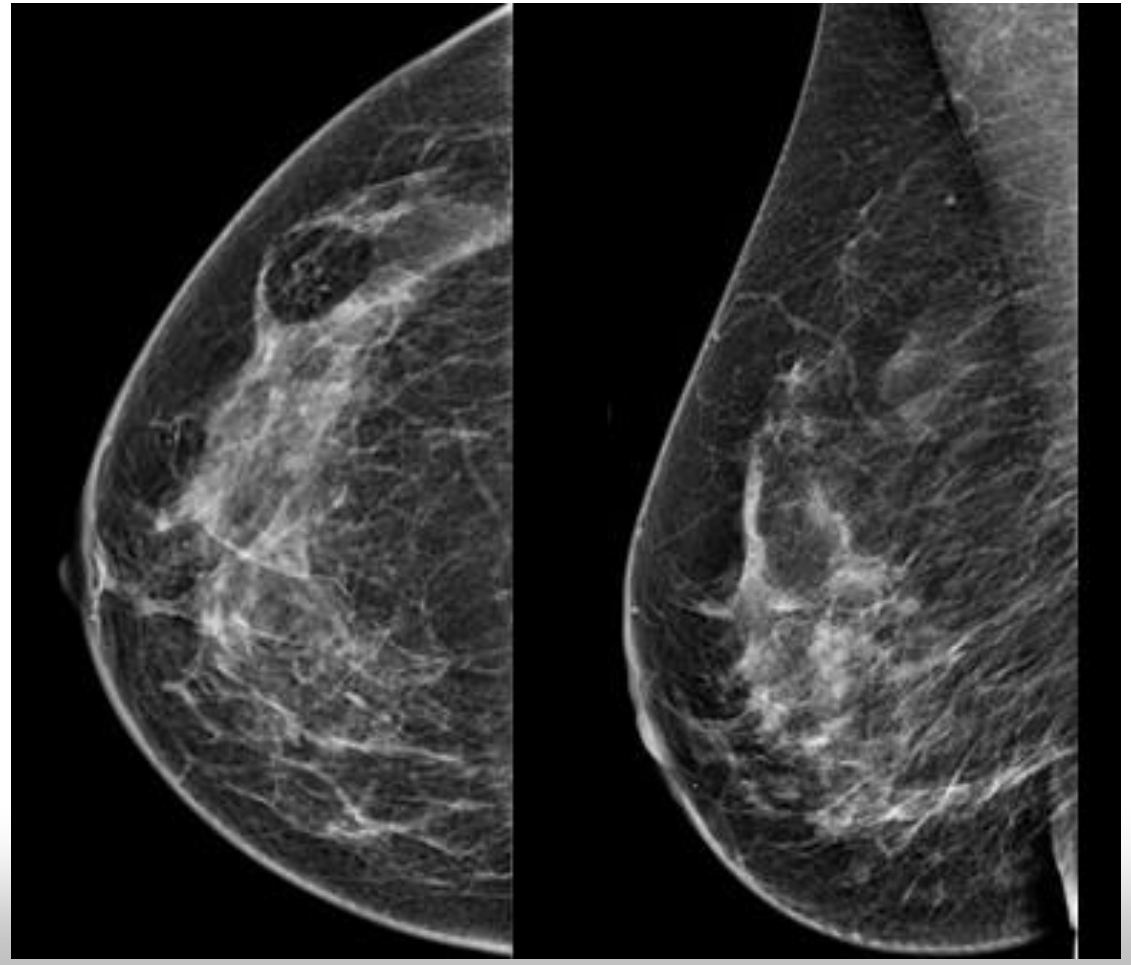
Breast CT



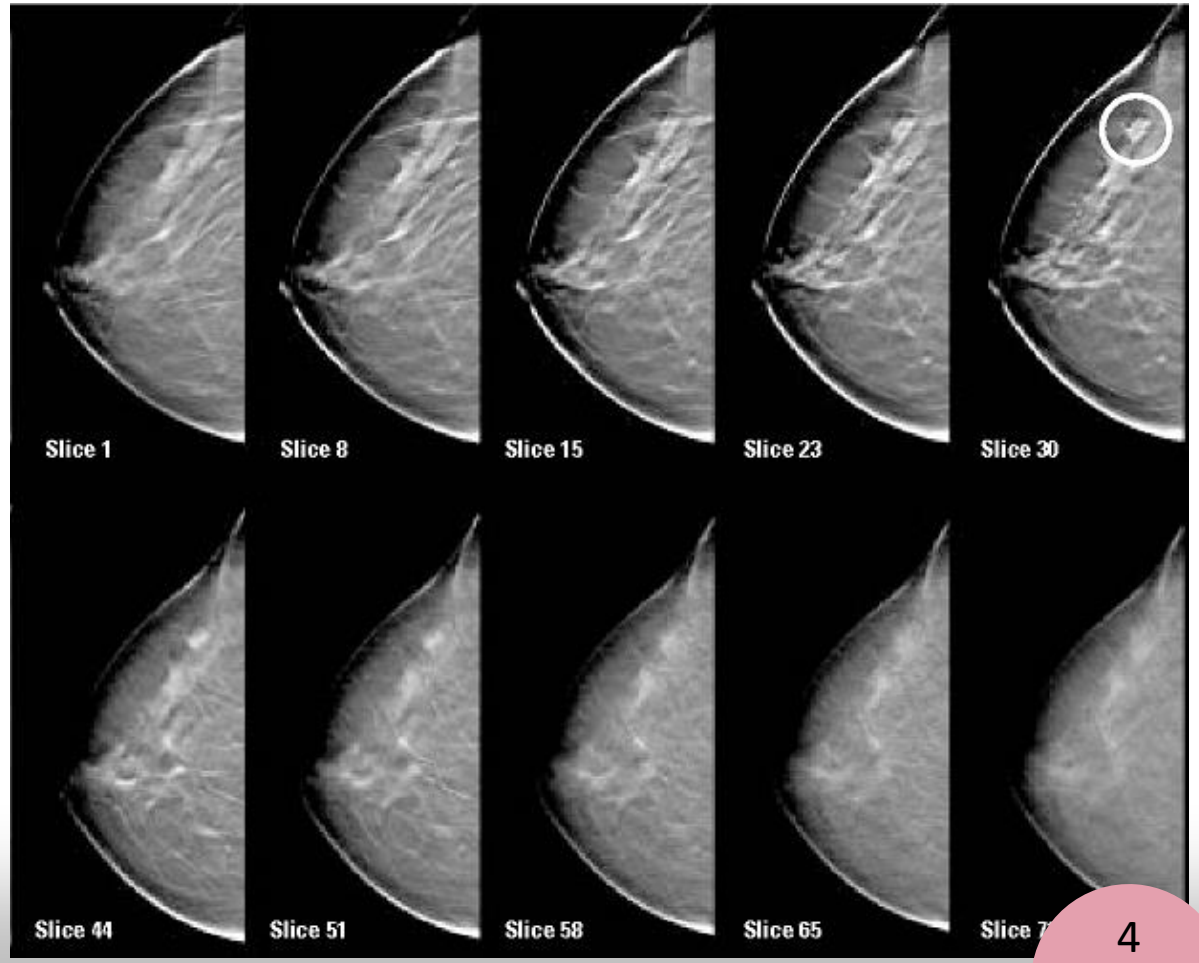
2D — pseudo-3D — 3D

Advantages of Digital Breast Tomosynthesis

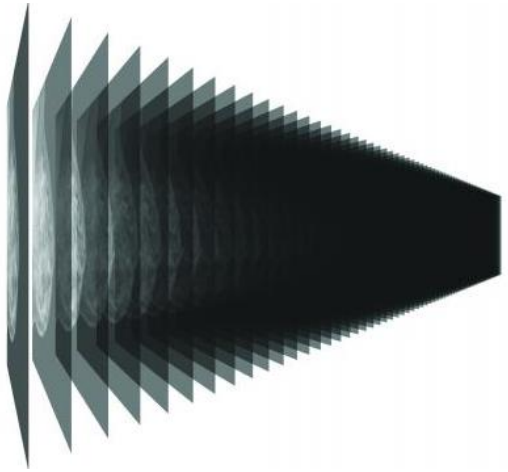
(2D) Digital Mammography

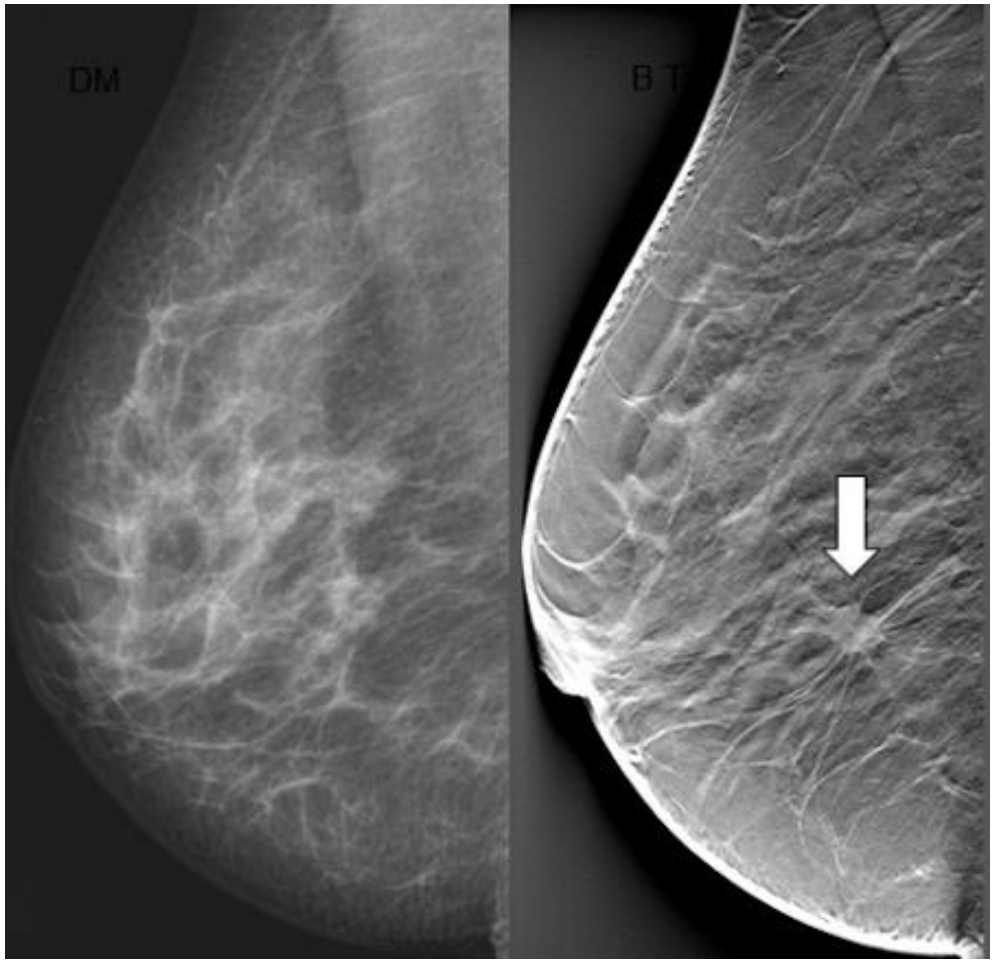


(pseudo-3D) Digital Breast Tomosynthesis



Advantages of Digital Breast Tomosynthesis





In this screening case, an asymptomatic woman has a tumor that is not discernible on digital mammography (left) but appears as a clearly visible spiculated lesion on digital breast tomosynthesis (white arrow), which shows the slice where the lesion is in focus. The lesion is a 13-mm invasive ductal carcinoma, grade 2. *Images courtesy of Dr. Sophia Zackrisson.*

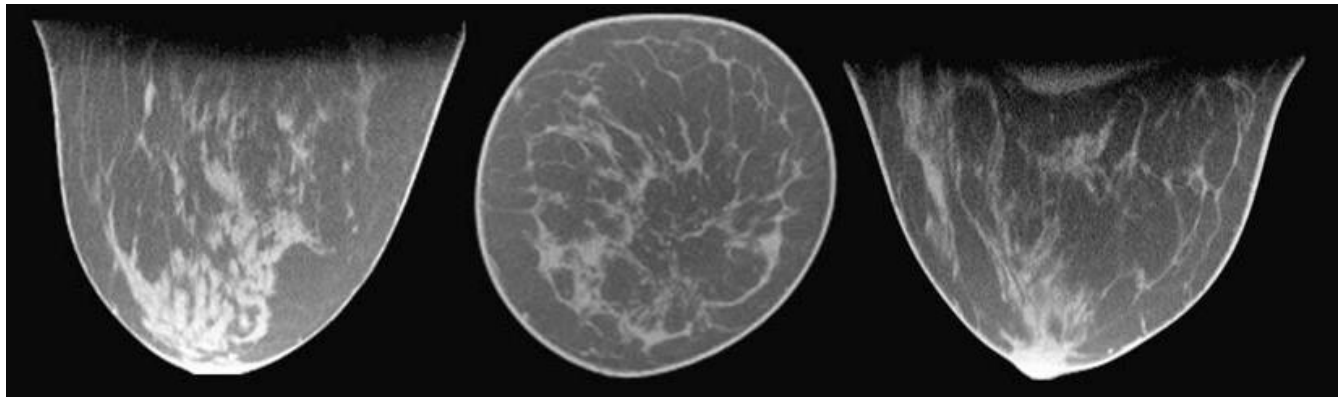
Breast Computed Tomography (bCT)

A breast CT scanner with the patient in prone position with one breast being imaged at a time (typically 10 seconds or less) and without compression. Image courtesy of Dr. Willi Kalender

In bCT the uncompressed breast hangs at the scanner isocenter in pendant geometry and the gantry rotates over 360 degrees around a vertical axis of rotation.

Higher x-ray beam energy (49–80 kVp) than mammography
~500 frames or projection images are acquired over about 16 seconds acquisition sequence

512 × 512 pixels reconstructed images are produced

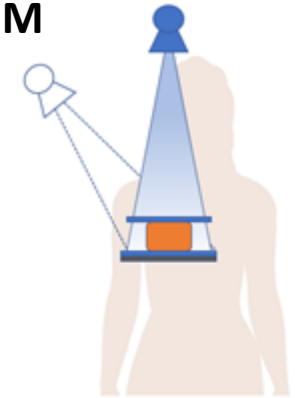


Example of reconstructed bCT slices. Courtesy of J.M. Boone

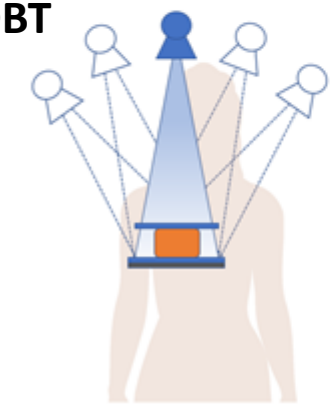
Sarno, A., Mettivier, G. and Russo, P. (2015), Dedicated breast computed tomography: Basic aspects. Med. Phys., 42: 2786-2804. doi:10.1118/1.4919441

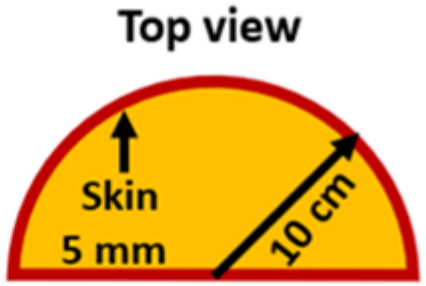
Digital breast phantom for dosimetry in DM and DBT

DM



DBT



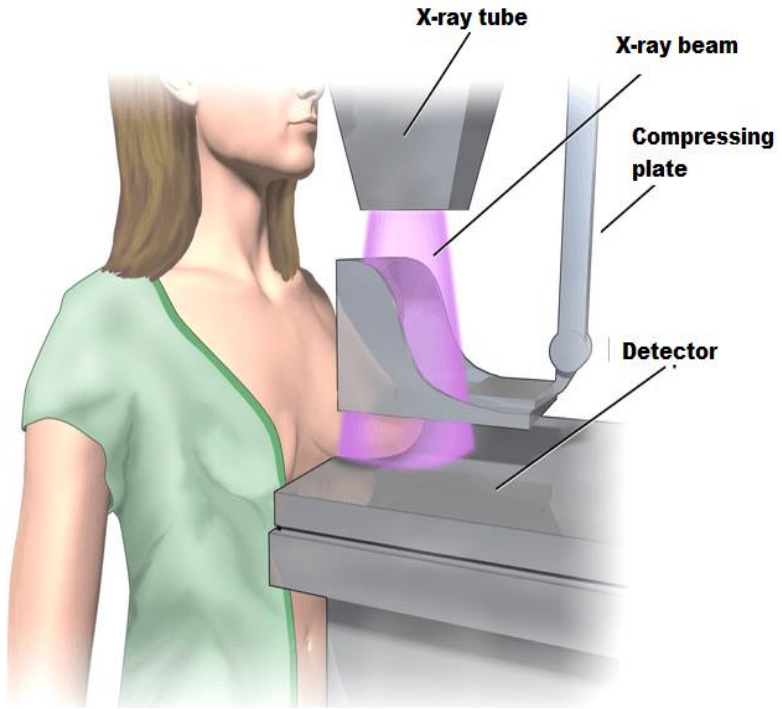


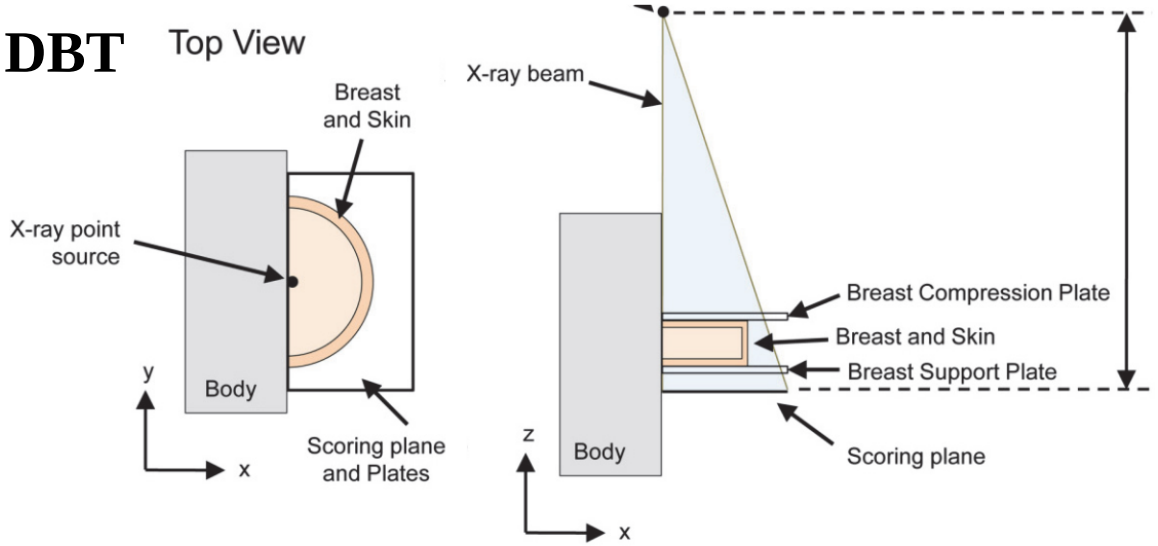
Elemental composition and density for glandular and adipose tissues.

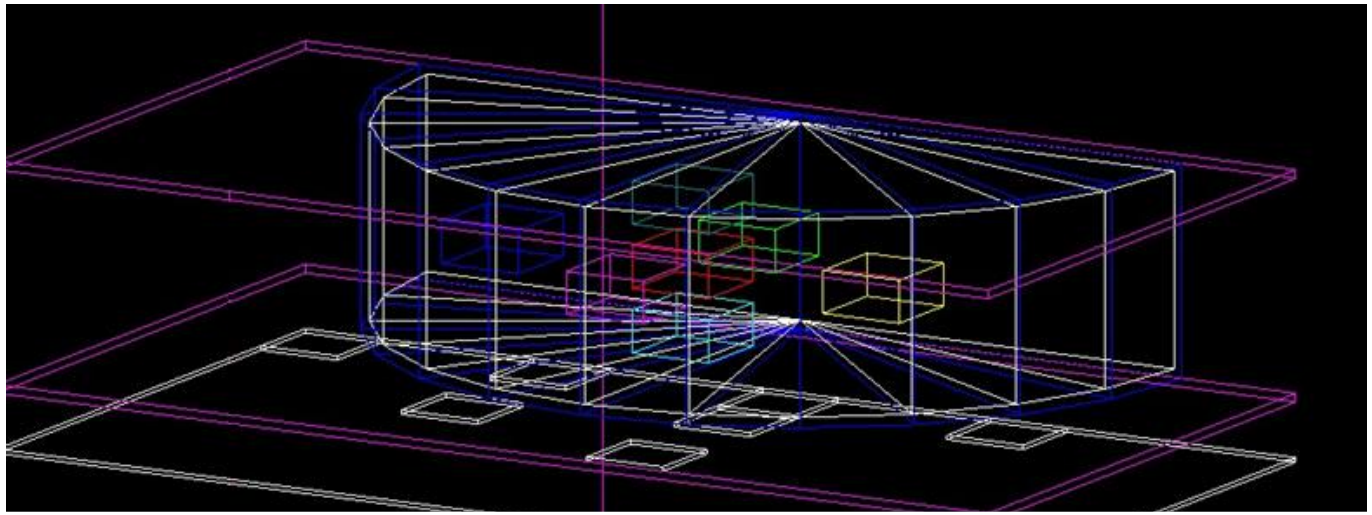
Tissue	H	C	N	O	P	density (g/cm^3)
glandular	0.102	0.184	0.032	0.677	0.005	1.04
adipose	0.112	0.619	0.017	0.251	0.001	0.93

In Monte Carlo (MC) models, the breast digital phantom is modelled as a semi-cylinder with an outer layer of skin made by adipose tissue while the inner part is a homogeneous mixture of adipose and glandular tissues. Glandularities ranging from 0 to 100% are composed by mixing properly glandular and adipose tissues.
The glandular tissue is the radiosensitive tissue in the breast. Thus, Mean Glandular Dose (MGD) is the parameter used to assess dose delivered to the gland.

Digital breast phantom for dosimetry in DM and DBT



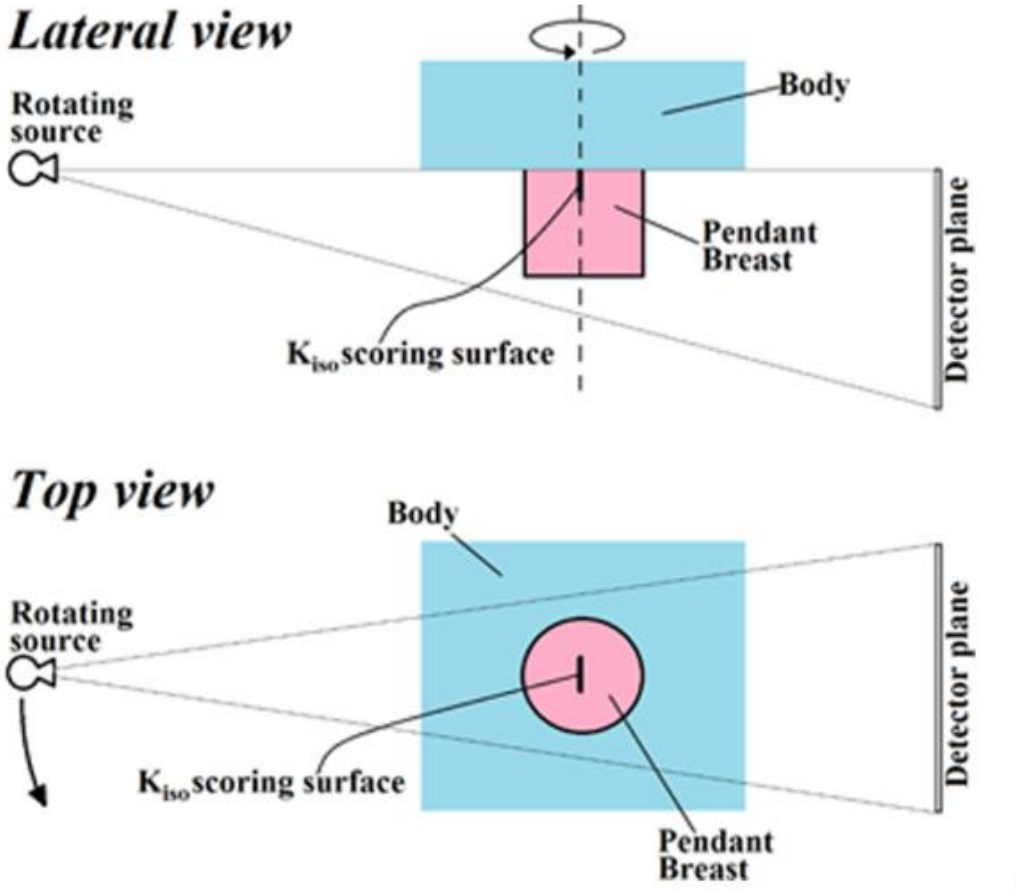




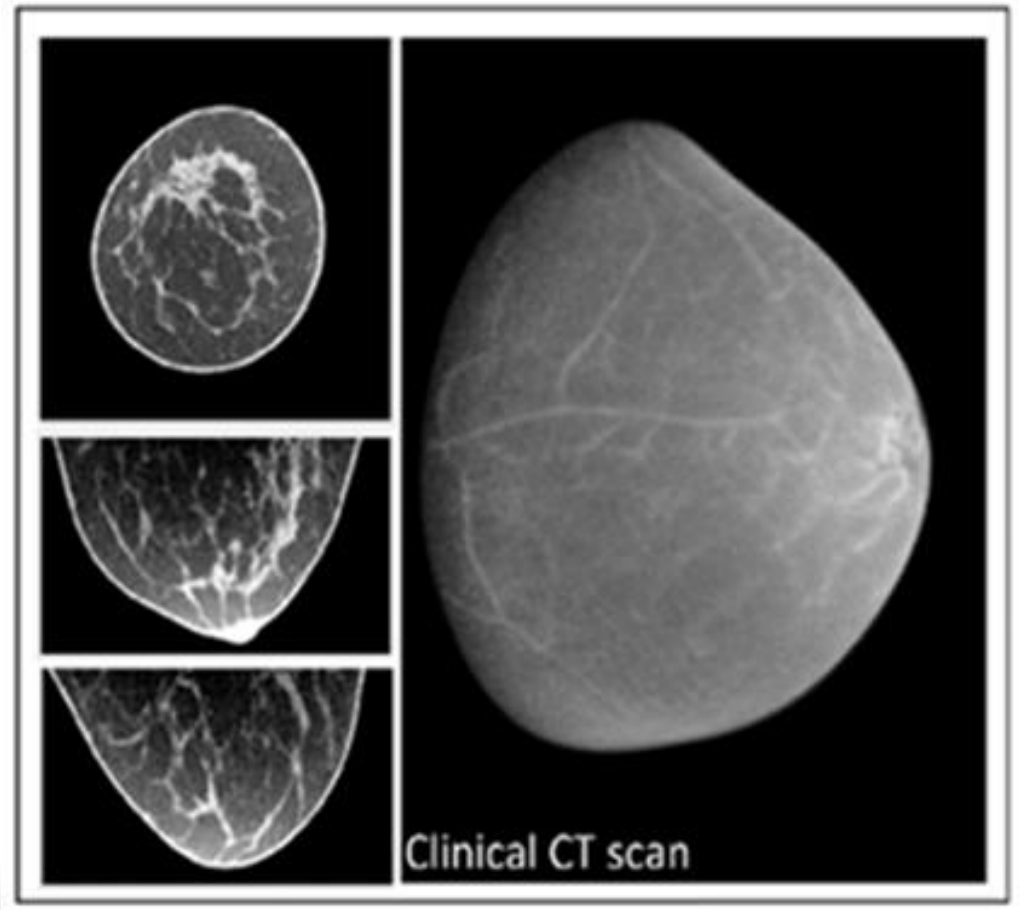
Report No. 195 - Monte Carlo Reference Data Sets for Imaging Research: The Report of AAPM Task Group 195 (2015)

Digital breast phantom for dosimetry in bCT

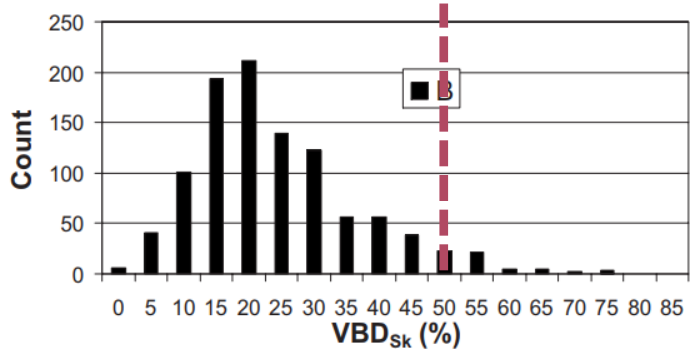
Homogeneous phantom for dosimetry

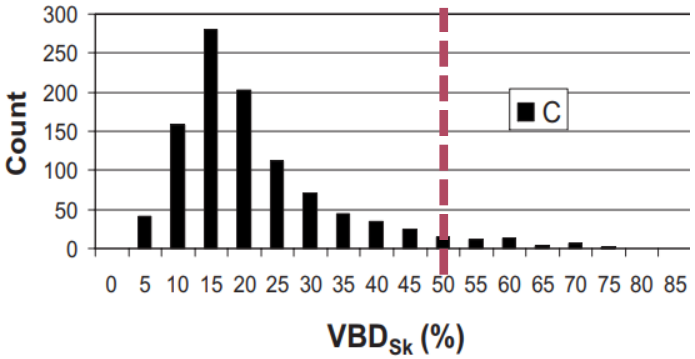


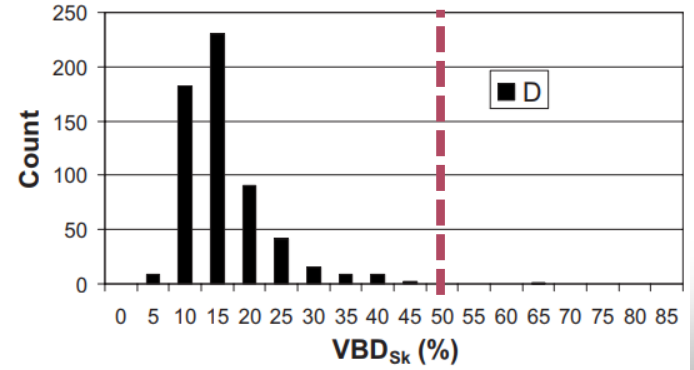
Heterogeneous phantom



Literature updates based in bCT







Medical Physics
The International Journal of Medical Physics Research and Practice

The myth of the 50-50 breast

M. J. Yaffe, J. M. Boone, N. Packard, O. Alonzo-Proulx, S.-Y. Huang, C. L. Peressotti, A. Al-Mayah, and K. Brock

2831 bCT patient exams have been analyzed and the Volume Breast Density (VBD) has been evaluated. **The mean VBD was found to be 14.3%** by volume with a standard deviation of 10.3% with skin excluded.

TABLE I. Characteristics of the four groups for whom density was measured. For each group the mean and standard deviation ( ) of VBD are given both for the "skin-included" and "skin-excluded" conditions. The difference between these means, the mean compressed breast thickness and the mean total breast volumes are also given.

Group	N	Mean age (Range)	Mean breast volume (cm^3)	VBD_{Sk} (%) (σ)	VBD_{NSk} (%) (σ)	ΔVBD (%)	Mean compressed thickness (mm) (σ)
A	191	53.8 (35–82)	769	25.6(12.6)	14.3(10.3)	11.3	N/A
B	1029	N/A	512	21.7(12.8)	16.8(11.5)	4.9	56(19)
C	1020	59.2 (40–85)	720	18.9(12.3)	14.2(11.1)	4.7	57(14)
D	591	61.4 (50–76)	755	13.7(7.5)	9.9(6.7)	3.8	65(11)
All groups	2831			19.3(12.1)	14.3(10.7)	5.0	

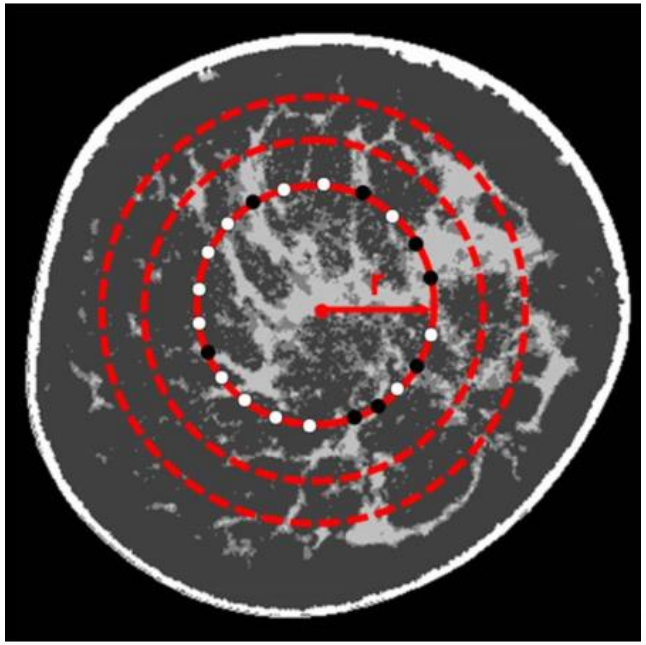
Literature updates based in bCT

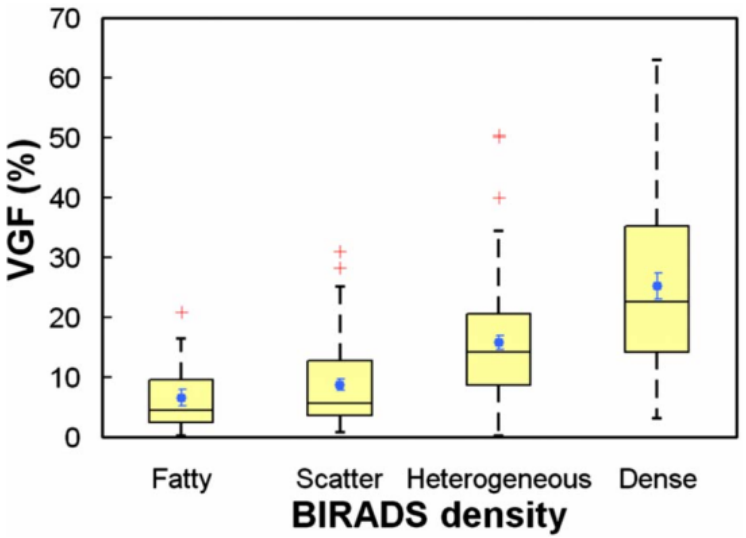
Medical Physics
The International Journal of Medical Physics Research and Practice

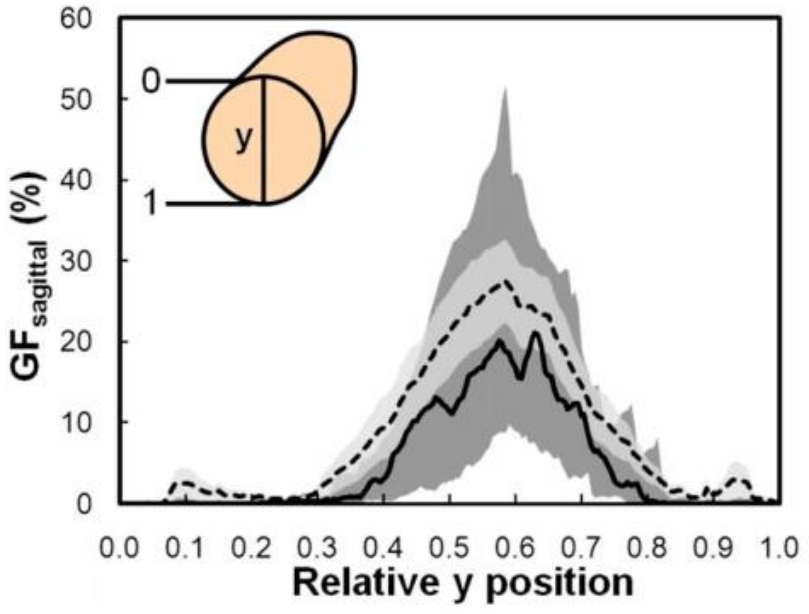
The characterization of breast anatomical metrics using dedicated breast CT

Shih-Ying Huang, John M. Boone, Kai Yang, Nathan J. Packard, Sarah E. McKenney, Nicolas D. Prionas, Karen K. Lindfors, and Martin J. Yaffe

Among 219 bCT data sets, the volume glandular fraction VGF was examined in coronal and sagittal planes of the breast, and the radial distribution of breast glandular fraction within a coronal bCT image was examined for three breast regions.







Literature updates based in bCT

Medical Physics

The characteriz

Shih-Ying Huang, J
K. Lindfors, and Ma

Among 219 bCT data sets, the volume glandular fraction VGF was examined in coronal and sagittal distribution of nal bCT image

Breast dose in mammography is about 30% lower when realistic heterogeneous glandular distributions are considered

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J. Anthony Seibert and John M. Boone
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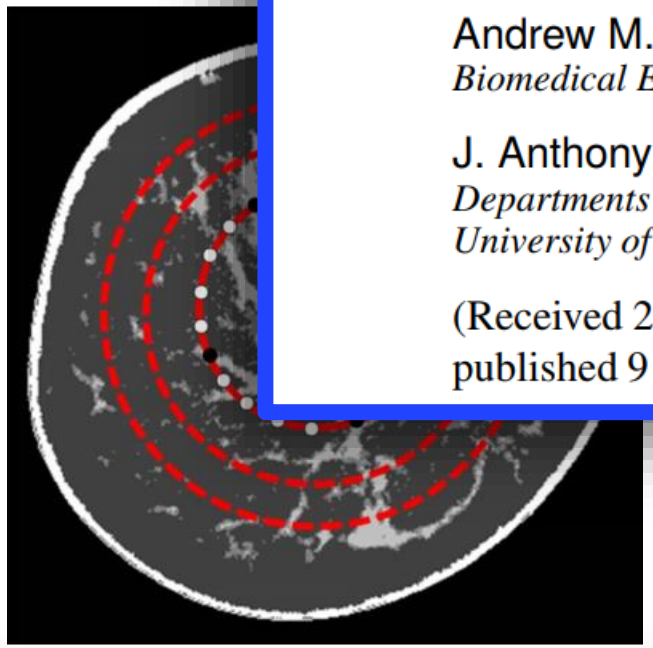
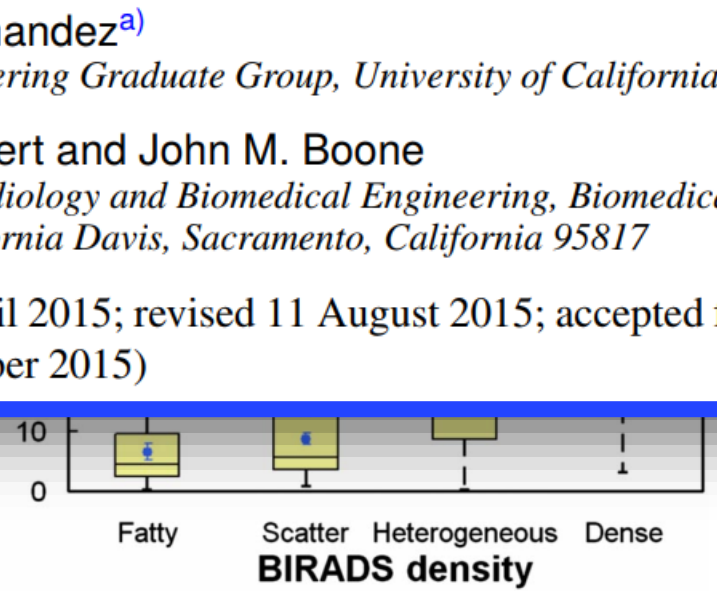
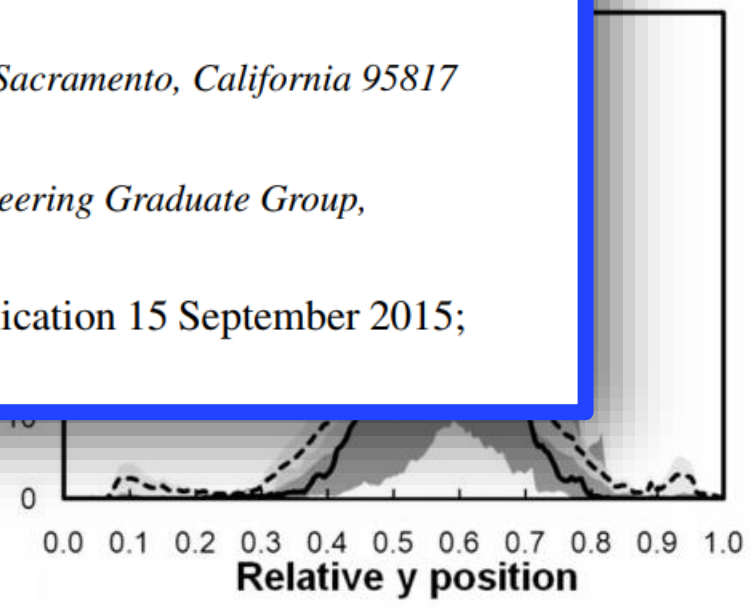
(Received 22 April 2015; revised 11 August 2015; accepted for publication 15 September 2015; published 9 October 2015)







Virtual clinical trials

7 March 2019

Virtual clinical trial for task-based evaluation of a deep learning synthetic mammography algorithm

Andreu Badal; Kenny H. Cha; Sarah E. Divel; Christian G. Graff; Rongping Zeng; Aldo Badano

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https://doi.org/10.1117/12.2513062

International Workshop on Breast Imaging
IWDM 2016: Breast Imaging pp 145-151 | Cite as

Evaluation of the *BreastSimulator* Software Platform for Breast Tomography: Preliminary Results

Authors | Authors and affiliations

Giovanni Mettivier, Kristina Bliznakova, Francesca Di Lillo, Antonio Sarno, Paolo Russo

Development and validation of a modelling framework for simulating 2D-mammography and breast tomosynthesis images

Premkumar Elangovan[1], Lucy M Warren[2,3], Alistair Mackenzie[2,3], Alaleh Rashidnasab[1], Oliver Diaz[1], J Strudley[2] and Kevin Wells[1]

g in Medicine

Original Investigation | Imaging

Evaluation of Digital Breast Tomosynthesis as Replacement of Full-Field Digital Mammography Using an In Silico Imaging Trial

Aldo Badano, PhD; Christian G. Graff, PhD; Andreu Badal, PhD; Diksha Sharma, MSc; Rongping Zeng, PhD; Frank W. Samuelson, PhD; Stephen J. Glick, PhD; Kyle J. Myers, PhD

Towards 4D dedicated breast CT perfusion imaging of cancer: development and validation of computer simulated images

Marco Caballo[1], Koen Michielsen[1], Christian Fedon[1,2] and Ioannis Sechopoulos[1,3,4]

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Physics in Medicine & Biology, Volume 64, Number 24

VIRTUAL CLINICAL TRIALS OF BREAST TOMOSYNTHESIS

Predrag R. Bakic
University of Pennsylvania, Philadelphia, PA, USA.

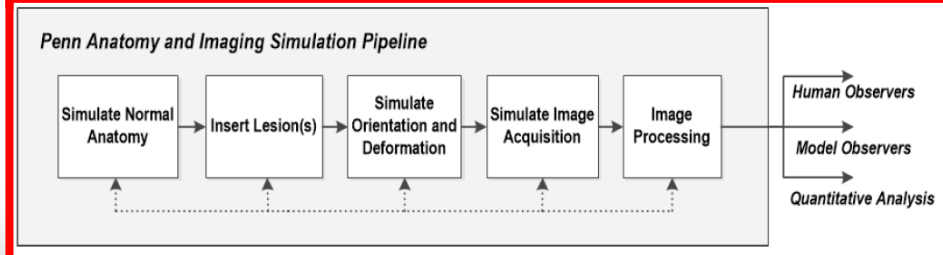

Figure 1 – Flowchart of a virtual clinical trial of breast imaging.

...validation of a method to simulate the acquisition of mammographic images with different techniques

Joana Boita; Alistair Mackenzie; Ioannis Sechopoulos

Author Affiliations +

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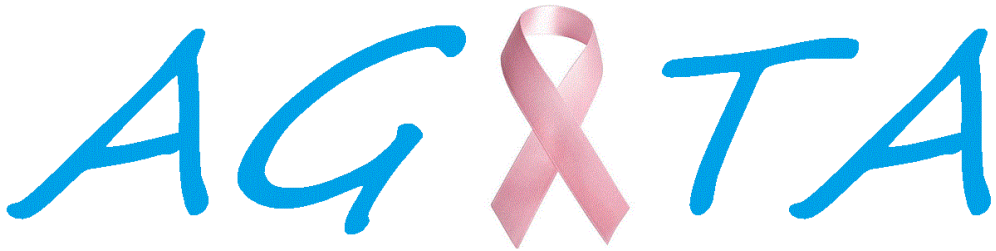
https://doi.org/10.1117/12.2513393
Event: SPIE Medical Imaging, 2019, San Diego, California, United States

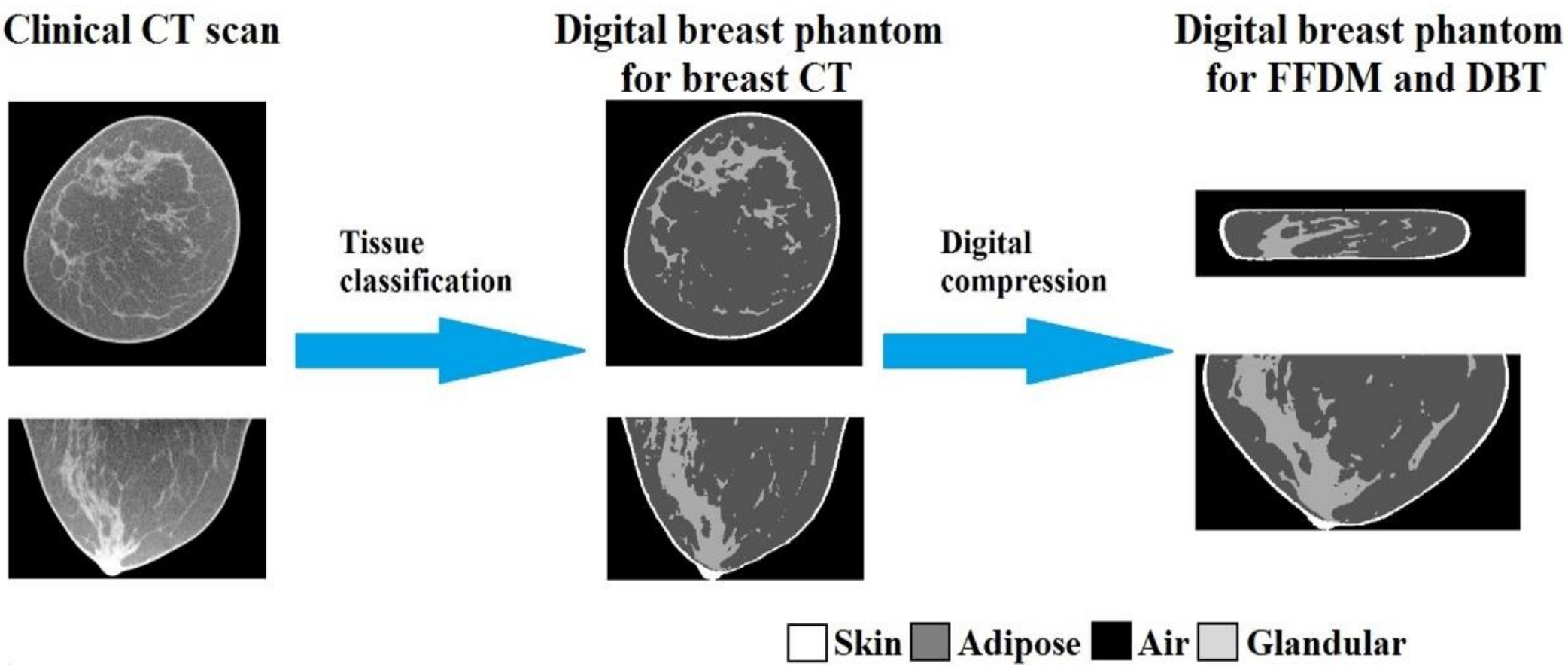


***A**dvanced **G**eant4-based **A**pplication for in-silico clinical **T**rial in x-ray bre**A**st imaging*

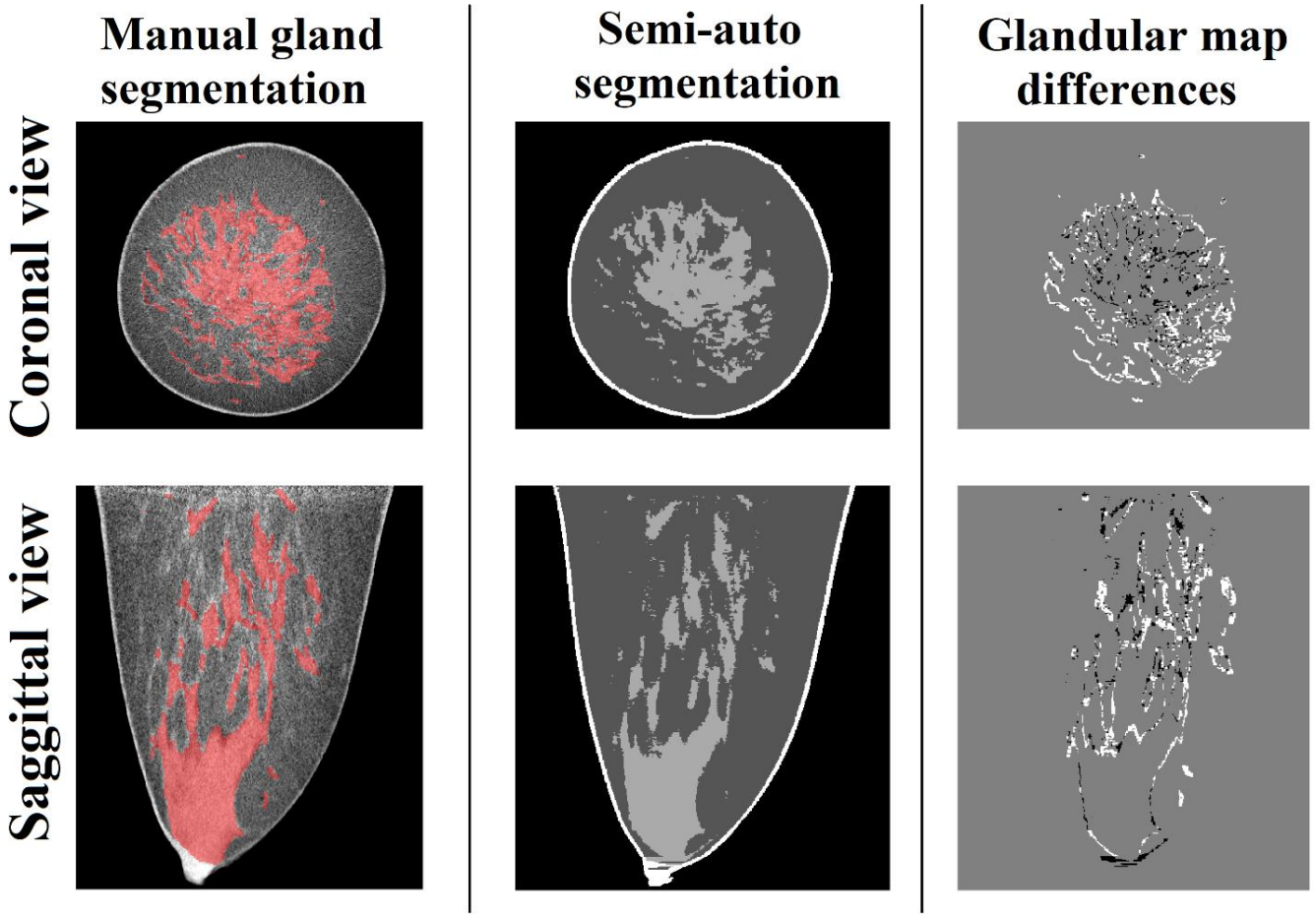
The **first platform** for virtual clinical trials in **2D and 3D** (2D mammography, DBT and BCT) x-ray based breast imaging based on a **Monte Carlo** software and **patient-derived** digital breast models.

Patient derived digital breast phantoms

Up to 300 cases provided by UC Davis



Segmentation process evaluation

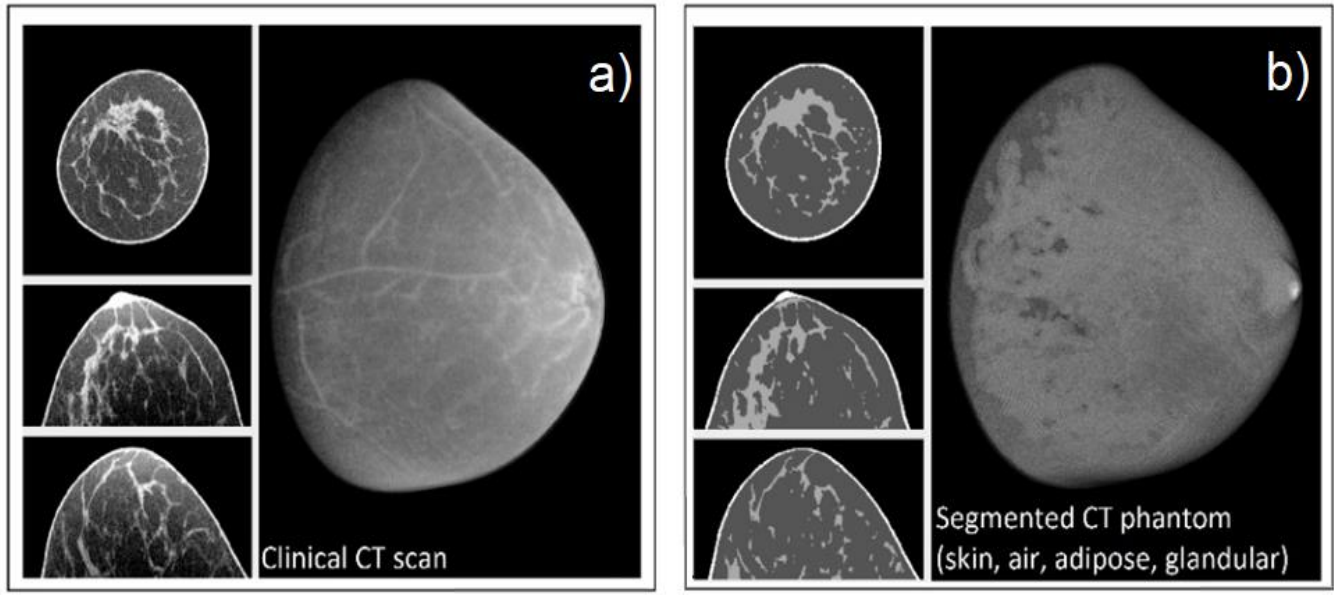


$$\frac{\#different\ voxel}{\#total\ voxel}$$

0.023

0.028

Database of uncompressed breast phantoms

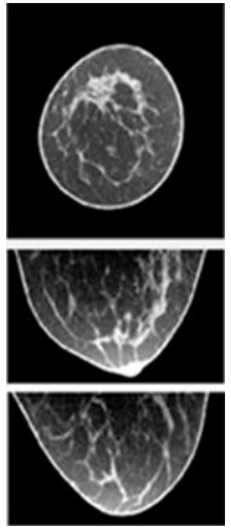


85 digital breast phantoms from 85 unaffected breast acquired with the UC Davis BCT scanner

	Mean	Std. Dev.	Min.	Max.
Glandular fraction by mass	0.13	0.10	0.01	0.59
Glandular fraction by volume	0.11	0.10	0.01	0.53
Breast volume – skin excluded (cm^3)	513.83	198.24	139.36	880.25
Breast length from chest wall to nipple (mm)	84.29	12.93	49.85	104.14
Equivalent diameter at the center of mass (mm)	105.87	14.66	57.13	136.23

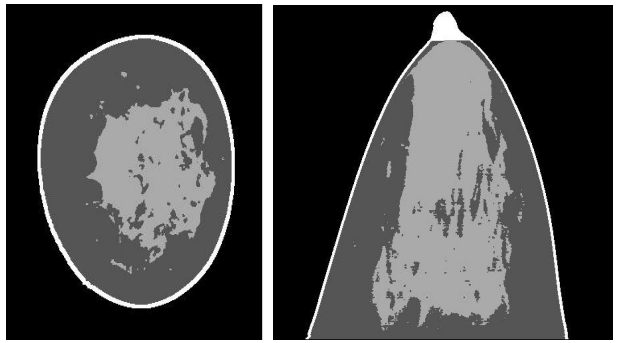
The simulation platform for bCT

Clinical CT scan

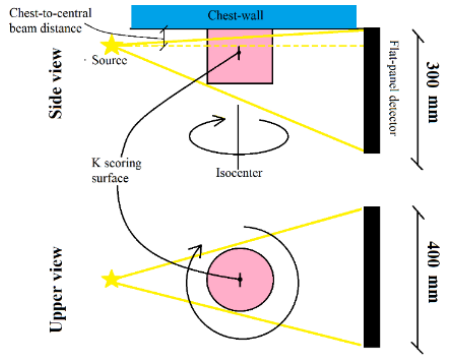


INPUT

Segmented Digital Breast Phantoms



Scanner specifications



Monte Carlo based on GEANT4

OUTPUT

Dose map

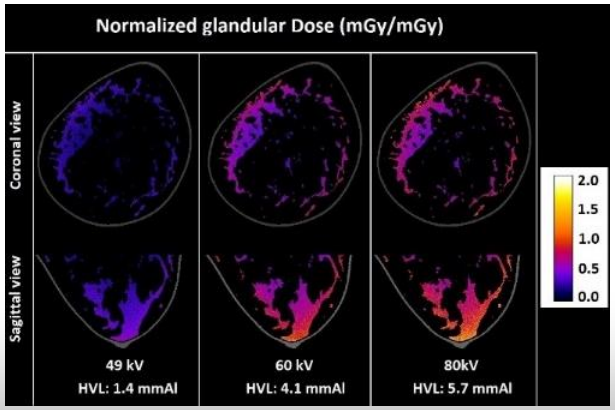
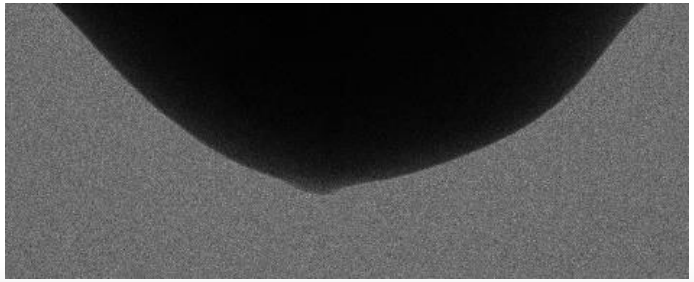
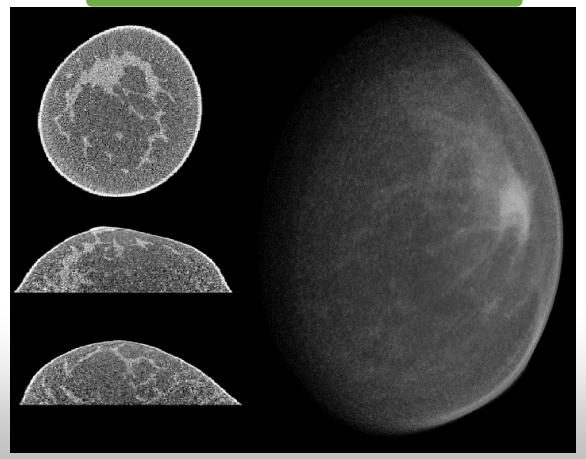


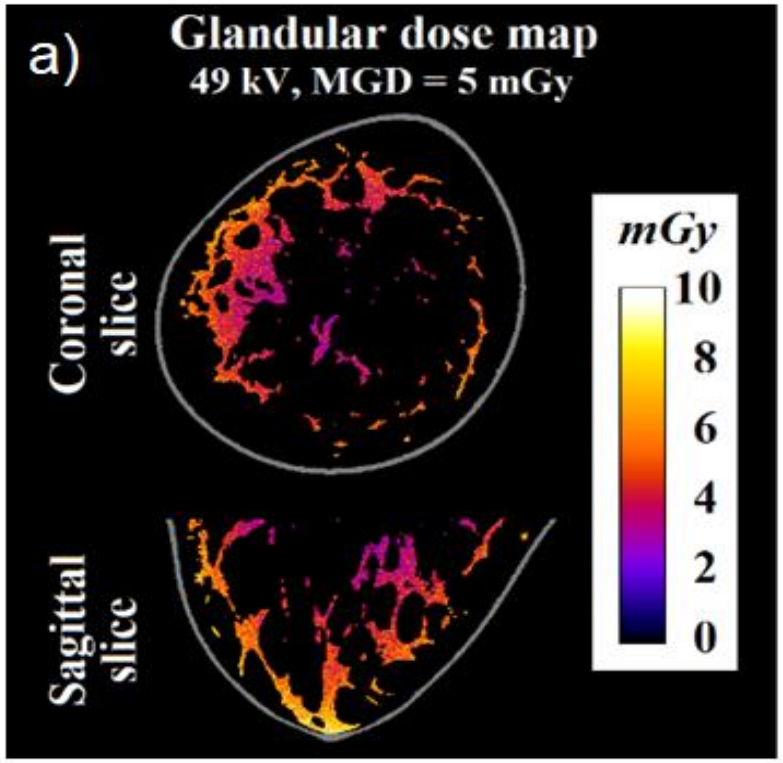
Image projections

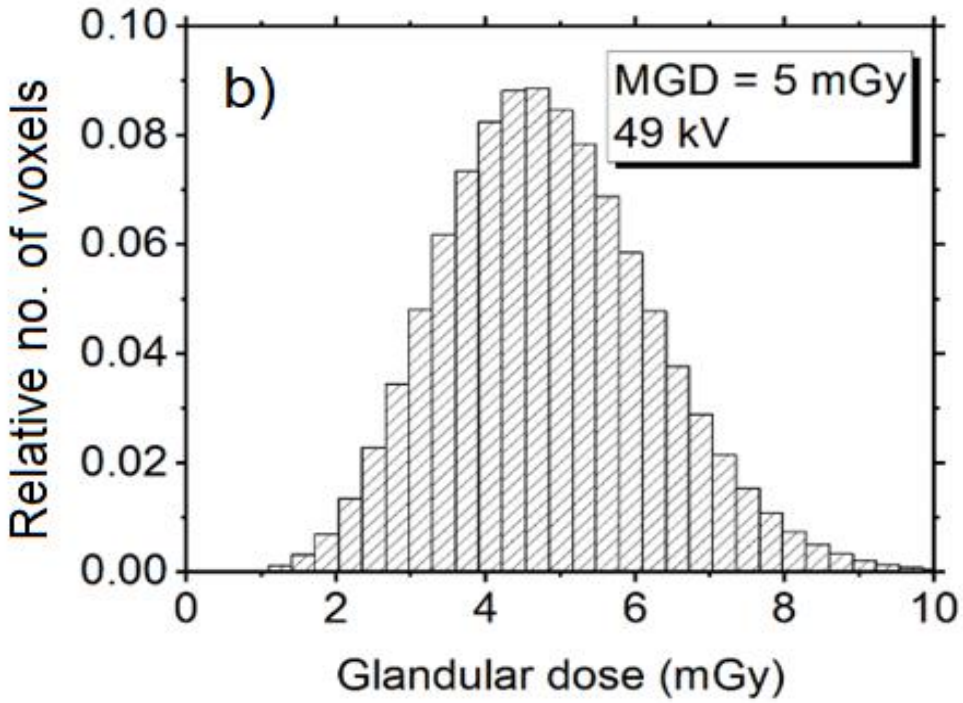


Post processing



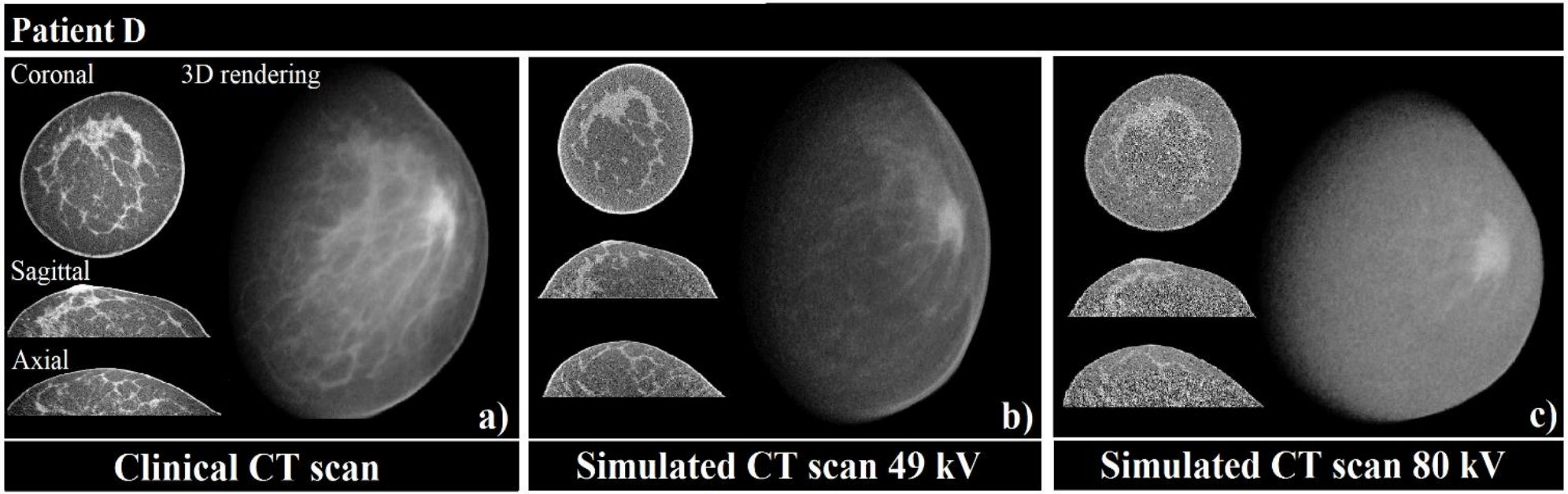
Breast CT exam





Dose distribution assesment with patient derived digital breast phantoms can help in evaluating peak doses and validating homogeneous breast models for average glandular dose estimates.

Simulated dedicated breast CT

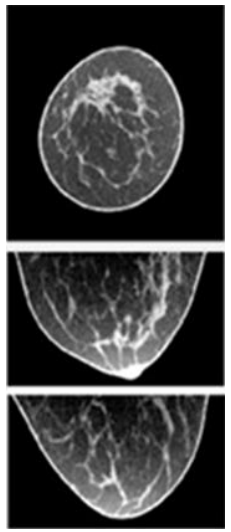


MGD = 5.0 mGy **MGD = 0.5 mGy** **MGD = 0.5 mGy**

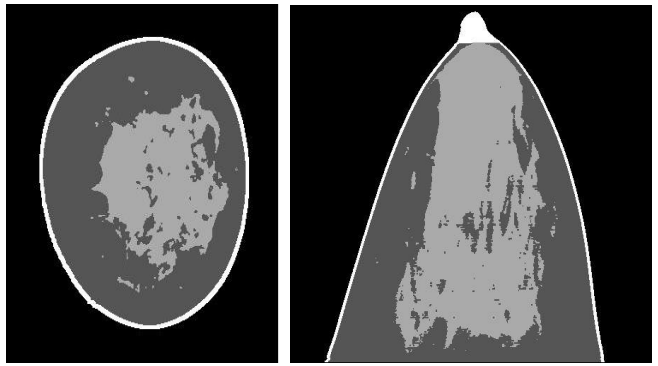
Comparison of clinical and simulated CT dataset
Multiscale structural similarity index – **MS-SSID: 0.88 @ 49 kV, 0.84 @ 80 kV**

The simulation platform for DM / DBT

Clinical CT scan



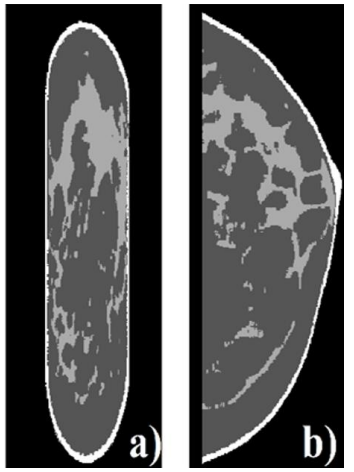
Segmented Digital Breast Phantoms



INPUT

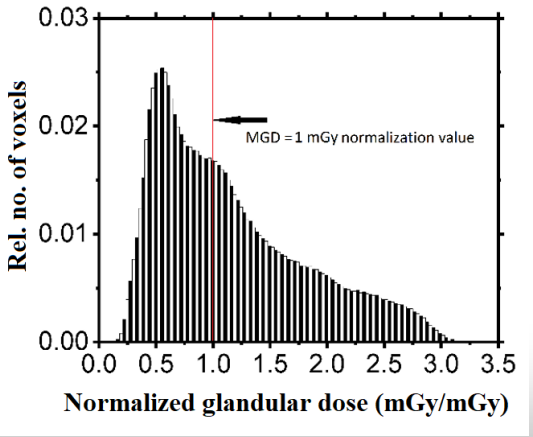
Compressed Digital Phantoms

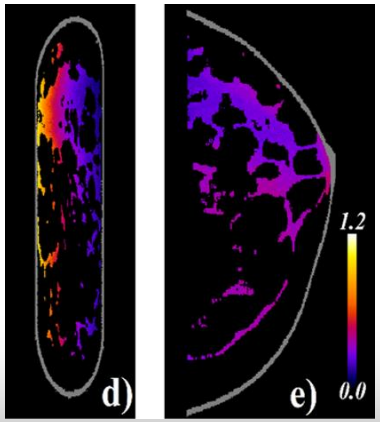
a), b) coronal and axial slices of a compressed breast phantom

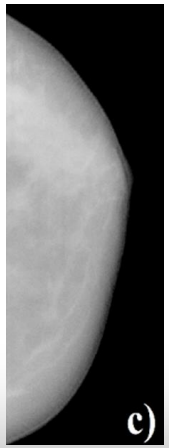


Monte Carlo based on GEANT4

Dose map







c) Simulated mammogram using

28 kV W/Al;
HVL = 0.486 mmAl;
MGD = 0.01 mGy

What will the Agata platform permit?

The **AGATA platform** will constitute an **engaging proposal to a broad community**, also including those people involved in R&D of applications and scanners **which have not easy access to clinical data**.

THE PLATFORM WILL PERMIT:

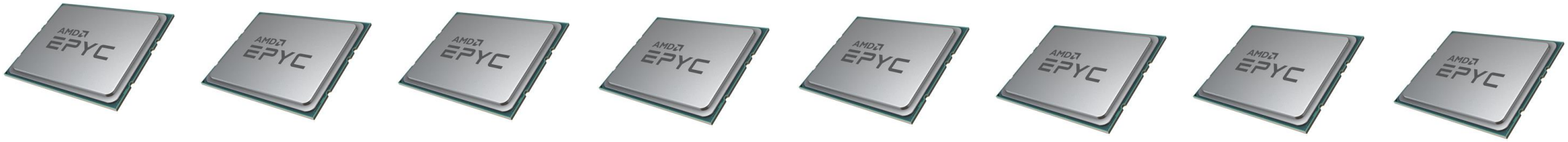
1) comparison of breast imaging modalities and technical solutions;
2) development of scanners on the basis of comparison between several solutions;
3) refinement of imaging protocols and dose optimization;
4) developing of software which needs the knowledge of the ground truth (organ state and morphology)
5) comparison of artifacts removing algorithms;
6) development of scatter correction algorithms;
7) development and feasibility studies of new technologies
8) teaching and divulgation support

Ongoing work

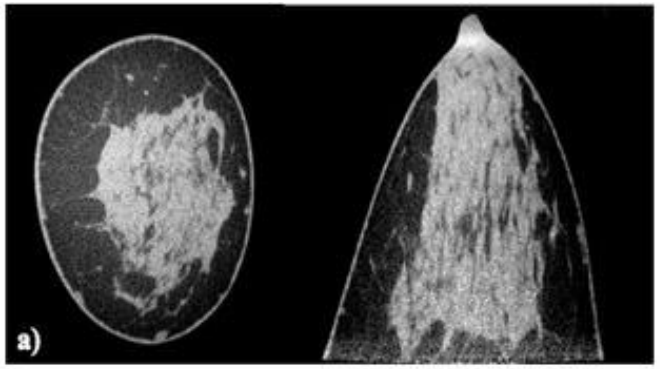
- ➢Validation of the segmentation and compression processes
- ➢Extention of the uncompressed digital breast phantoms to 300 cases
- ➢Generation of compressed phantoms for all the uncompressed ones
- ➢Development of the Monte Carlo code for DM and DBT → ***Pisa***

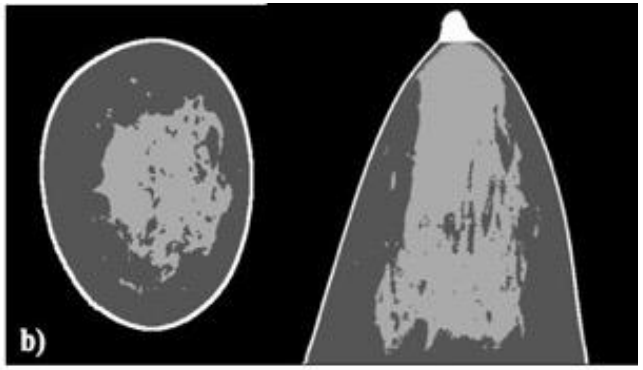
Computing Power

4 x Server DELL EMC PowerEdge R7425 with
8 x AMD EPYC™ 7281 (16 core, 32 working threads)

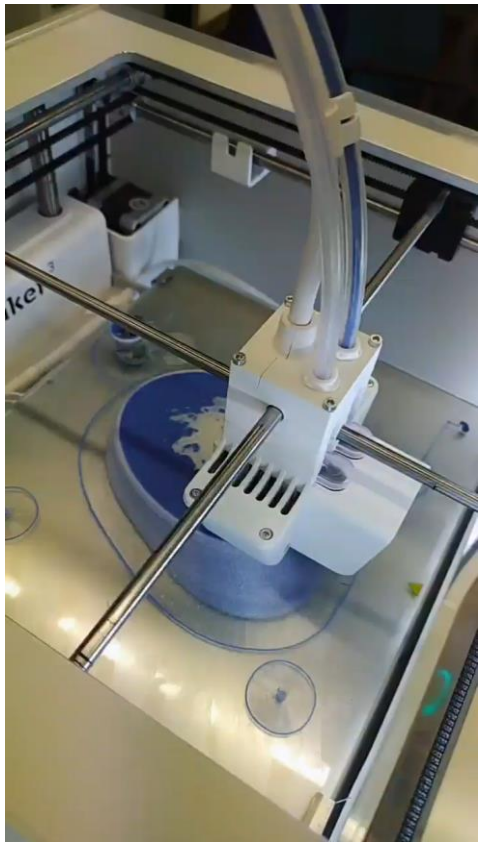


…and a little treat

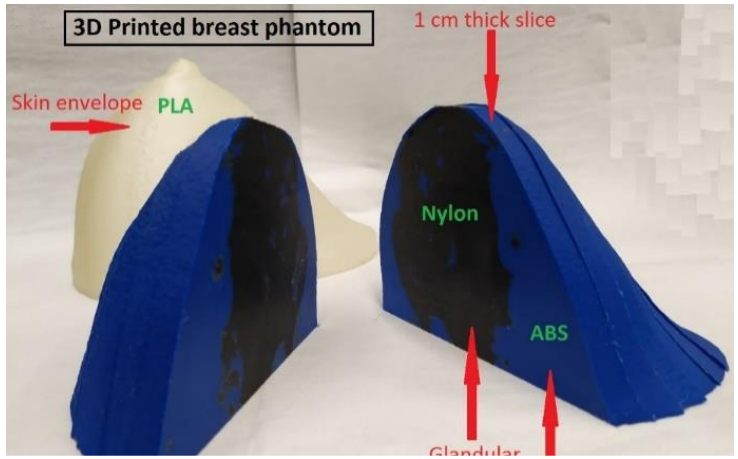




3D printing @INFN Napoli



Physical breast phantom



Istituto Nazionale di Fisica Nucleare

Thank you for your attention!

AGATA

Advanced GeAnt4-based platform for virtual clinical Trials in X-ray breAst imaging