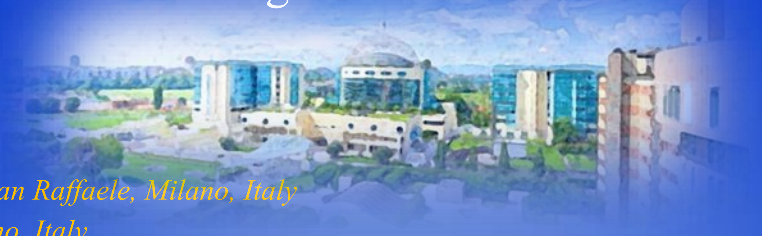
I.R.C.C.S. Ospedale San Raffaele
Gruppo San Donato

State of art and optimization perspectives for breast imaging

R. Calandrino+, A. Loria+, P. Panizza#, A. Taibi*, A. del Vecchio+

Advanced Medical Imaging with Synchrotron and Compton sources
Bologna 21- 22 Nov 2019



+ Medical Physics Department IRCCS San Raffaele, Milano, Italy
 # Breast Unit IRCCS San Raffaele, Milano, Italy
** Dipartimento di Fisica e Scienze della Terra ; Universita' degli Studi di Ferrara*

Breast CA Screening

The meaning of the screening test

Screening for the early diagnosis of breast cancer is applied to women between the ages of 50 (45) and 69 and is performed with a mammogram every 2 years. In some regions effectiveness is being tested in a broader age range, between 45 and 74. According to the ATS(1, the frequency could also be annual for women under 50 or for high risk patients (i.e. previous surgery or familiarity).

A large study published in September 2012 in the Journal of Medical Screening where published research on breast cancer screening programs active in Europe have been reviewed, showed that mortality is reduced by 25% for women who undergo the screening.
For every 1,000 women aged between 50 and 69, who are regularly screened and followed up to 79 years of age, screening can save between 7 and 9 lives.

1: Azienda di Tutela della Salute =: Regional Public Health System

Ref. WEB Site of the Italian Ministry of Health update :8/03/2016

The Screening Protocol

Age	45 - 49	50 - 74
Frequency	Annual/Biennal	Biennal

2 radiograms at the 1° exam and 1 radiogram at subsequent examinations

Results for the age classes 50 -74

The data tell us that out of 100,000 women aged 0-100 in the absence of screening there would be 12,289 diagnoses of breast cancer.
Of these 4330 would be fatal. In Italy, every year, the number of new patients increases of about 5000 new cases. The screening prevents 26% of these deaths for the 50 - 74 group with biennial exams, causing 1.6 extra cancer deaths in the group (with DGM equal to 1.3 mGy).

Thus the ratio between mortality without screening and the cases of fatal cancer induced by radiation with screening would be equal to 2706.
The ratio between prevented deaths and induced deaths is 704.

Dati da R. Gelder et al ; Population based mammography screening below age 50:…;

British Journal of Cancer (2011)

Results for the age classes 40 -74

Including the decade 40-49 with an annual screening frequency (at the same MGD of 1.3 mSv) we have 7.4 extra cancer deaths.
Consequently the ratio between prevented and induced deadly cancers is reduced to 175: 1 (prevention would rise to 29.9)

The risk-benefit ratio tends to decrease if MGD were to rise, as it happens when working with thicker breasts.

Dati da R. Gelder et al ; Population based mammography screening below age 50:…;

British Journal of Cancer (2011)

I risultati del programma italiano (publ Impatto 2011)

Cosa è cambiato in Italia dopo l'avvio dei programmi di screening? Una valutazione di impatto

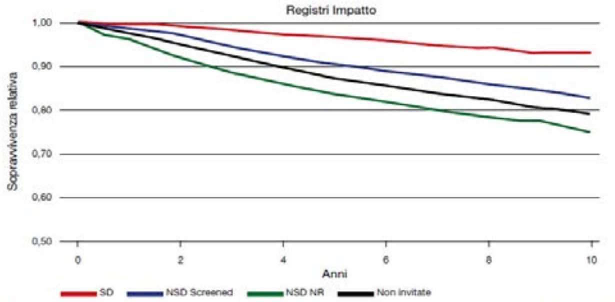


Figura 6a. Sopravvivenza relativa per modalità diagnostica: SD = Screen detected; NSD Screened = Screened (ma) non screen detected; NSD NR = Non screen detected non responders; Non invitate.

la stima della riduzione della mortalità attribuibile all'invito allo screening, che è risultata pari al 33% (36% nello studio citato[8]).

Dose & Related Risk

Tabella di riferimento AGD *Linee Guida Europee - IV ed*	
Desirable (mGy)	Acceptable (mGy)
0,6	1
1	1,5
1,6	2
2	2,5
2,4	3
3,6	4,5
4,3	6,5

2-view FFDM

- *Average Mean Glandular Dose: 3,7 mGy*
- *LAR 1,3 per 100 000 women aged 40 y (at time of exposures)*
- *1 case per million women aged 80 years (at time of exposures)*

Radiation Doses and Cancer Risks from Breast Imaging Studies - R. Edward Hendrick – Radiology (2010)

Dati ottenuti in modalità STD; in modalità DOSE si ottengono valori mediamente inferiori del 25%

Lowering the doses (DBM)

SECTRA MICRODOSE L30			**Tabella di riferimento AGD** *Linee Guida Europee - IV ed*	
Spessore fantoccio PMMA (mm)	Spessore equivalente mammella (mm)	Average Glandular Dose (mGy)	Desirable (mGy)	Acceptable (mGy)
20	21	0,4	0,6	1
30	32	0,6	1	1,5
40	45	0,6	1,6	2
45	53	0,6	2	2,5
50	60	0,8	2,4	3
60	75	0,9	3,6	4,5
70	90	0,8	4,3	6,5

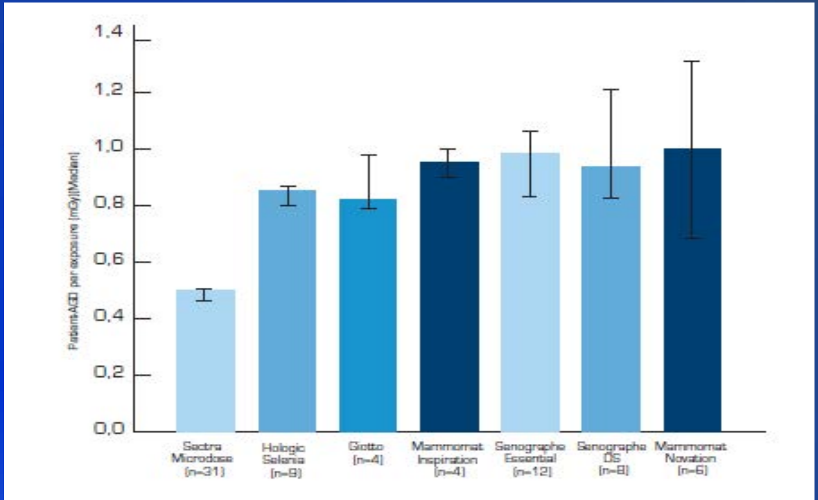
Dati mediamente inferiori del 60% rispetto alla mod STD e del 40% rispetto alla mod DOSE

Lowering the doses (DBM)

Patient AGD per exposure (mGy) for different digital systems

Sectra – Report 2010

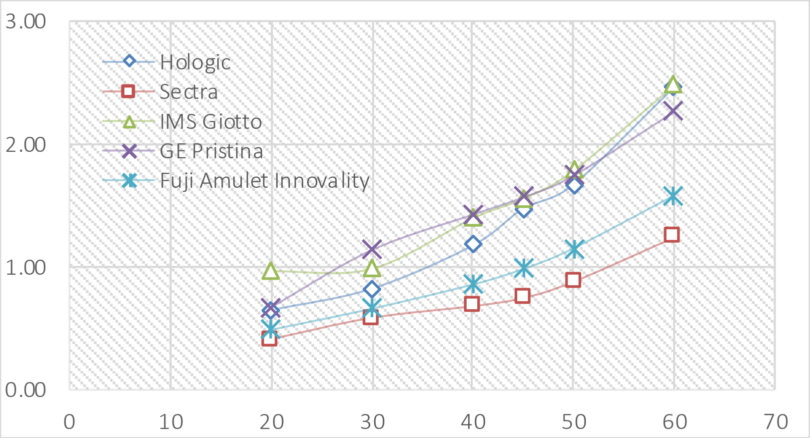
Swedish Radiation Safety Authority



Experimental measurements

Medical Physics Dept.

San Raffaele Scientific Institute



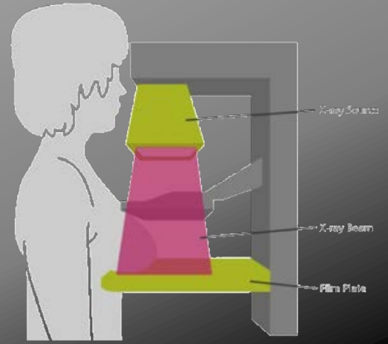
A way to improve diagnostic power of the screening

Breast screening with mammography is the most effective method of detecting early-stage breast cancer and reducing breast cancer mortality.

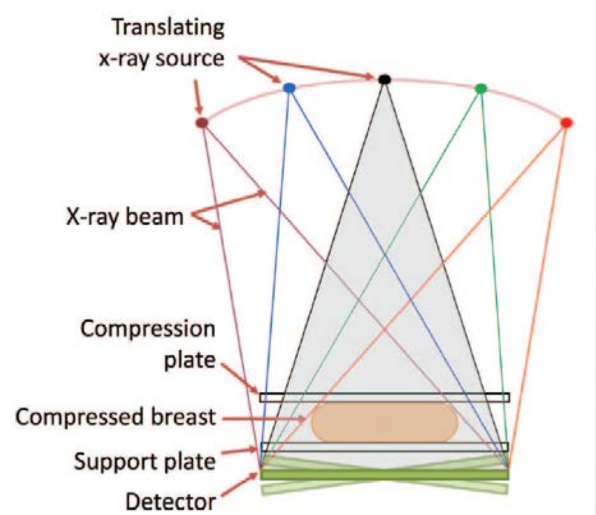
The intrinsic limits of mammography → overlapping of normal and pathological tissues

Digital Breast Tomosynthesis (DBT) is expected to overcome this limitation:

- quasi-three-dimensional (3D) image;
- reducing overlapping shadows;
- small size lesions could be more readily detected ;
- women with radiologically dense breast;
- decrease of false-positive recalls.



The Digital Breast Tomosynthesis



The same basic components as a digital mammography system:

- a full field digital detector;
- a breast support;
- a compression plate;
- an x-ray tube.

\+

- the ability of the x-ray tube to rotate around a point;
- the presence of a fast readout detector;
- different x-ray spectrum filtration;
- pixel binning.

The Digital Breast Tomosynthesis

The **detector** technologies

- Energy Integrating (EI);
- Photon Counting (PC).

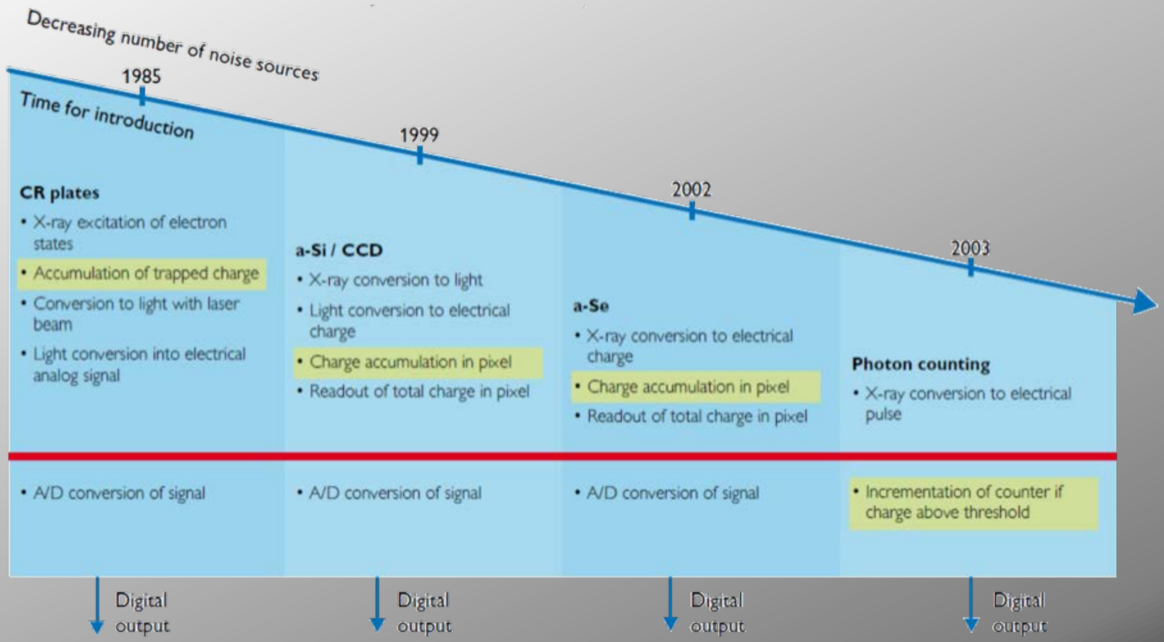


Image courtesy of Philips

The Digital Breast Tomosynthesis

DBT system typically uses a **limited number of angled projections** of the breast.

The **image quality** depends on:

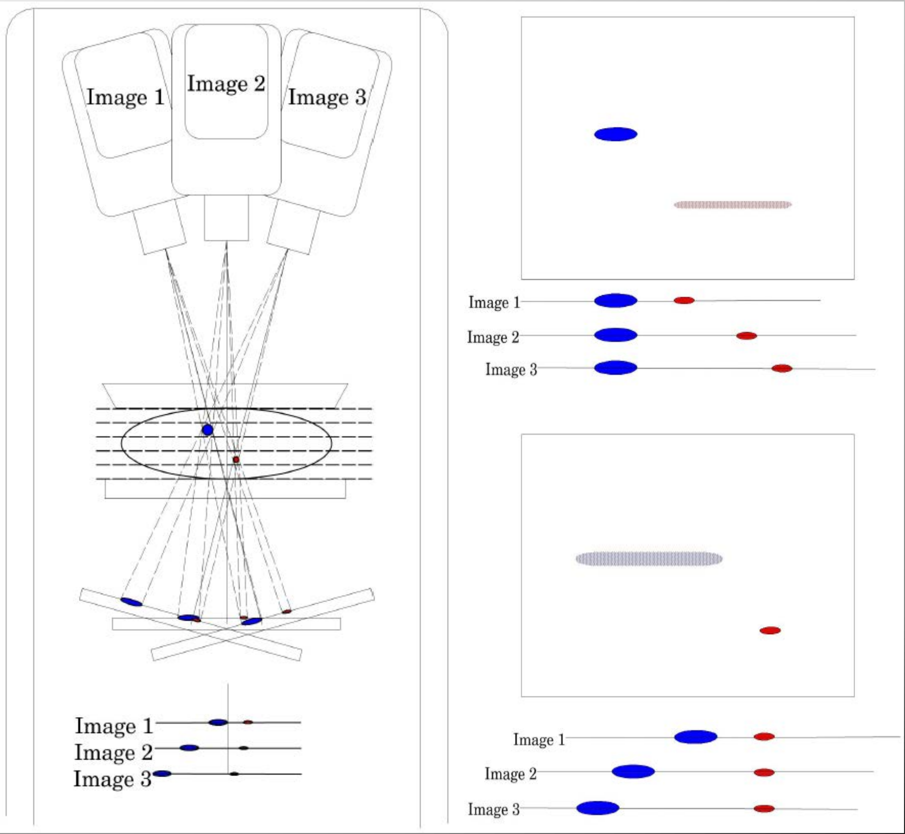
- the number of projections;
- the total projection angle.

\+ better the 3D resolution

− increased total scan time

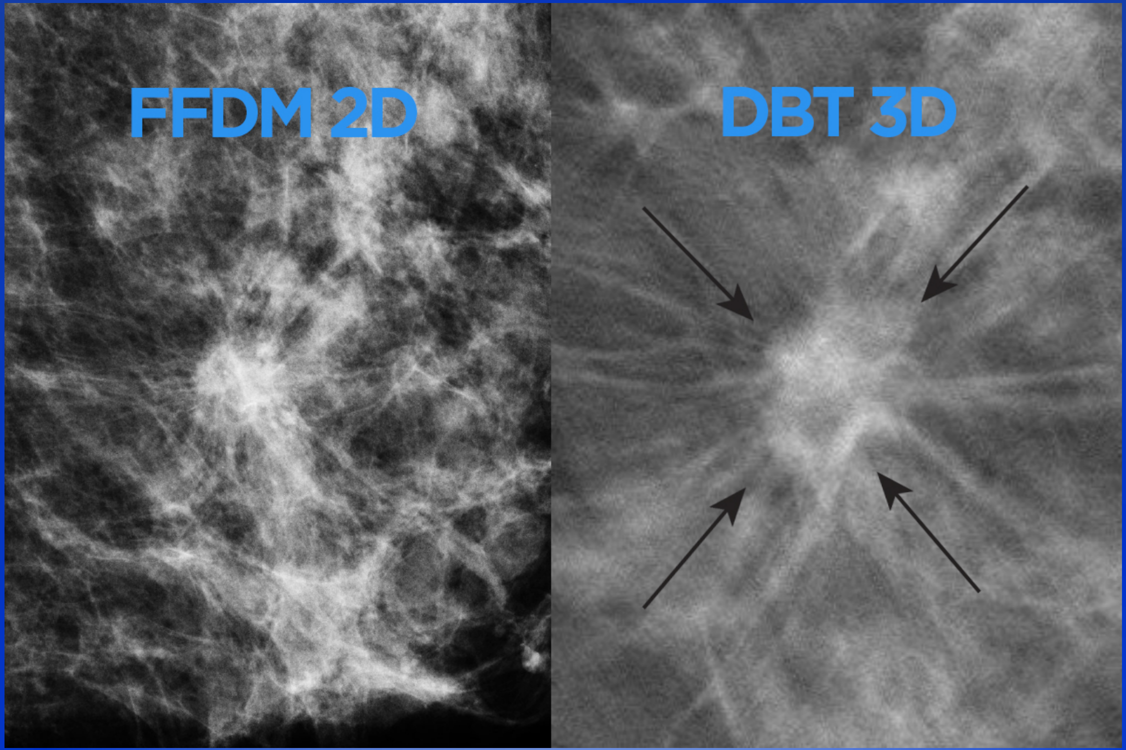
− increased motion blurring

− artifacts



Images courtesy of The Phantom Laboratory

Quality of the images 2D vs 3D



Diagnostic improvement

DBT combined with mammography allows a better diagnostic performance than mammography alone

Study	FFDM	DBT (one view)	FFDM+DBT
OTST trial	FPR: 6.1% CDR: 6.1‰		FPR: 5.3% CDR: 8‰
STORM trial	FPR: -		FPR: + 17%
Malmo	CDR: 6.3‰	CDR: 8.9‰	
Rose	RR: 8.7%		RR: 5.5%
Friedewald	RR: 10.7% CDR: 4.2‰		RR: 9.1% CDR: 5.4‰

Coupling FFDM with DBT decreases the FPR and increases the CDR

CDR: cancer detection rate per 1000 screens;
FPR: false positive rate;
RR: recall rate

Diagnostic Improvement

DBT combined with mammography allows a better diagnostic performance than mammography alone

	FFDM	DBT
Equipment cost (Euro)	35.000***	60.000**
Exam SSN reimbursement (Euro)	1-view: 25,5* 2-view: 44,87*	Not included

**Regione Lombardia*
***Prezzo unitario da gara Consip 2017*
**** Costo acquisto 2019 GSD*

DBT and Screening

DBT is not yet used in mammographic screening because:

- Higher dose
- Longer examination time (+135%)
- Less radiologists experience (need of specific courses)

⇓

Increase of biologic and economic costs

Dose ratio between DBT and FFDM

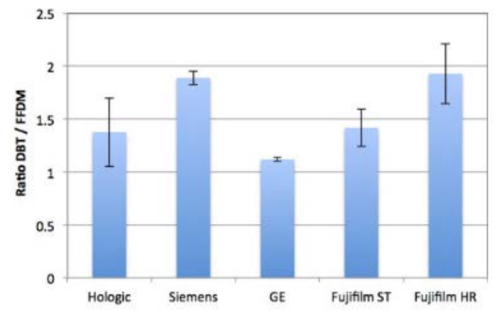


Fig. 2. Mean ratio between DBT and 2D FFDM AGDs for the investigated systems. Error bars represent the standard deviation of this ratio across different thickness.

Digital breast tomosynthesis: Dose and image quality assessment

A. Maldera[a,c,*], P. De Marco[b,c], P.E. Colombo[a], D. Origgi[b], A. Torresin[a]

The DBT devices

Flat Panel

Direct

Hologic

Selenia Dimension

- (a-Se) detector;
- square pattern;
- 70µm binned pixel;
- angle: 15°;
- 15 projection;
- FBP.

Fujifilm

Amulet Innovality

- (a-Se) detector;
- hexagonal pattern;
- 100µm (ST)/ 50µm (HR) binned pixel;
- angle: 15°(ST)/40°(HR);
- 15 projection;
- FBP.

IMS

Giotto Tomo

- (a-Se) detector;
- square pattern;
- 85µm;
- angle: 40°;
- 13 projection;
- Iterative.

Siemens

Mammomat Ins.

- (a-Se) detector;
- square pattern;
- 85µm;
- angle: 50°;
- 25 projection;
- FBP.

Indirect

General Electric

Senographe Pristina

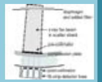
- scintillator (CsI) detector;
- square pattern;
- 100µm pixel;
- angle: 25°;
- 9 projection;
- iterative.

Photon counting

Philips

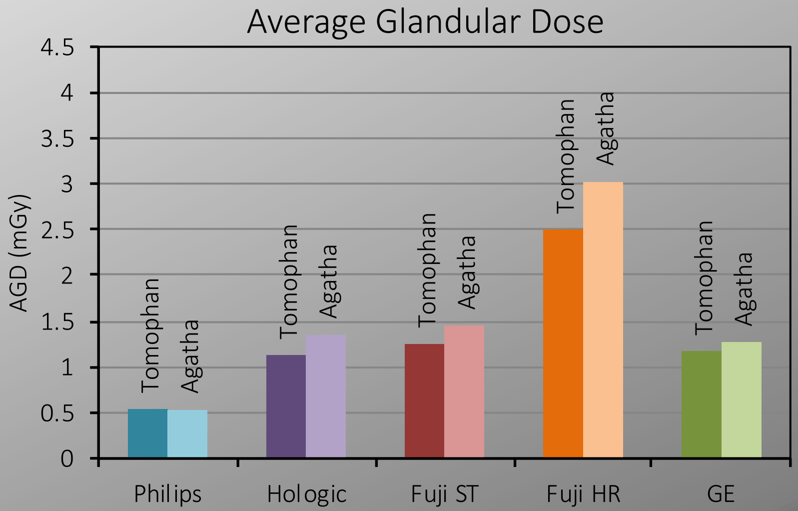
MicroDose Mammography S0 (Prototype)

- photon counting detector;
- linear slit scan-spectral pattern;
- 50µm binned pixel;
- angle: 11°;
- 25 projection;
- iterative.



AGD in AEC mode in phantom exposures in DBT

		Philips	Hologic	Fuji ST	Fuji HR	GE
Tomophan	Voltage (kV)	32	29	31	31	34
	Current (mAs)	10.3	41	30.1	58.5	23.1
	Anode	W	W	W	W	Rh
	Filter	Al	Al	Al	Al	Ag
	AGD (mGy)	0.54	1.13	1.29	2.51	1.18
Agatha	Voltage (kV)	32	30	31	31	34
	Current (mAs)	10.5	44	35.4	73.3	29.7
	Anode	W	W	W	W	Rh
	Filter	Al	Al	Al	Al	Ag
	AGD (mGy)	0.53	1.35	1.45	3.02	1.27



Strategy Madness

Even if the advantage in image quality and dose sparing is well known
Photon Counting technology will be no longer used in 2D and neither in 3D, why ?   Too expensive

R&D on improvement of existing detector is more convenient!

A Clinical Judgment on tomosynthesis (MSK)

Instead of capturing a picture of the entire breast at once, tomosynthesis generates an image using multiple very thin pictures or slices of tissue that build the view of the breast. The approach is so effective because it avoids clouding the image with overlapping tissue.

Studies indicate the technique is 30% more accurate in finding early breast changes than digital mammography, and also greatly reduces the number of distressing false-positive readings. It's effective for people at all levels of risk, regardless of the density of the breast tissue.

What is expected by the senologist in a short term

Radiologist's opinion (by Pietro Panizza)

Photon Counting Technology

Our experience with Philips Tomosynthesis confirmed that this technology performs high quality images, which are not inferior to traditional technology, with about 50% dose reduction.

Photon Counting demonstrated very low dose and high quality in all the fields where it was used: 2D FFDM, Tomosynthesis , Density Measurement with Spectroscopy as well as first evaluations with CESM.

This is the best technology we have so far, so it is difficult to understand the reason why it has been abandoned.

Photon Counting technology could offer the best examination tool in comparison with traditional FFDM, with one shot acquisition and subtraction of the two energies obtained with post-processing elaboration with a quarter of dose reduction.

What is expected by the senologist in a short term

Radiologist’s opinion (by Pietro Panizza)

CEDM

Currently, there are some FFDM Units with devices and software able to perform breast examinations after contrast medium i.v. injection, subtracting the high and low energy acquisition mammograms - CESM or CEDM (contrast enhanced digital mammography)

In some cases, this technique might replace Breast MRI exam at a lower cost and logistic advantage

What is expected by the senologist in a short term

Radiologist's opinion (by Pietro Panizza)

ARTIFICIAL INTELLIGENCE

To date, highly specialized software has been developed which is able to detect suspicious mammographic findings.

This technology is very interesting especially in the screening field, in fact there are multiple ongoing studies evaluating the use of AI as a second reader.

Contrast-enhanced spectral mammography (CESM)

- CESM is a novel breast imaging technique that combines standard full field digital mammography (FFDM) with contrast-enhanced high- and low-energy images.
- The iodinated contrast agent tends to highlight regions with vasculature that is increased and leaky—two characteristics of early neoplasm.
- The low-energy image provides detail of soft tissue and calcifications similar to standard FFDM,
- Digitally subtracted images remove the normal mammary glandular tissue and highlight areas of angiogenesis to help detect breast malignancies

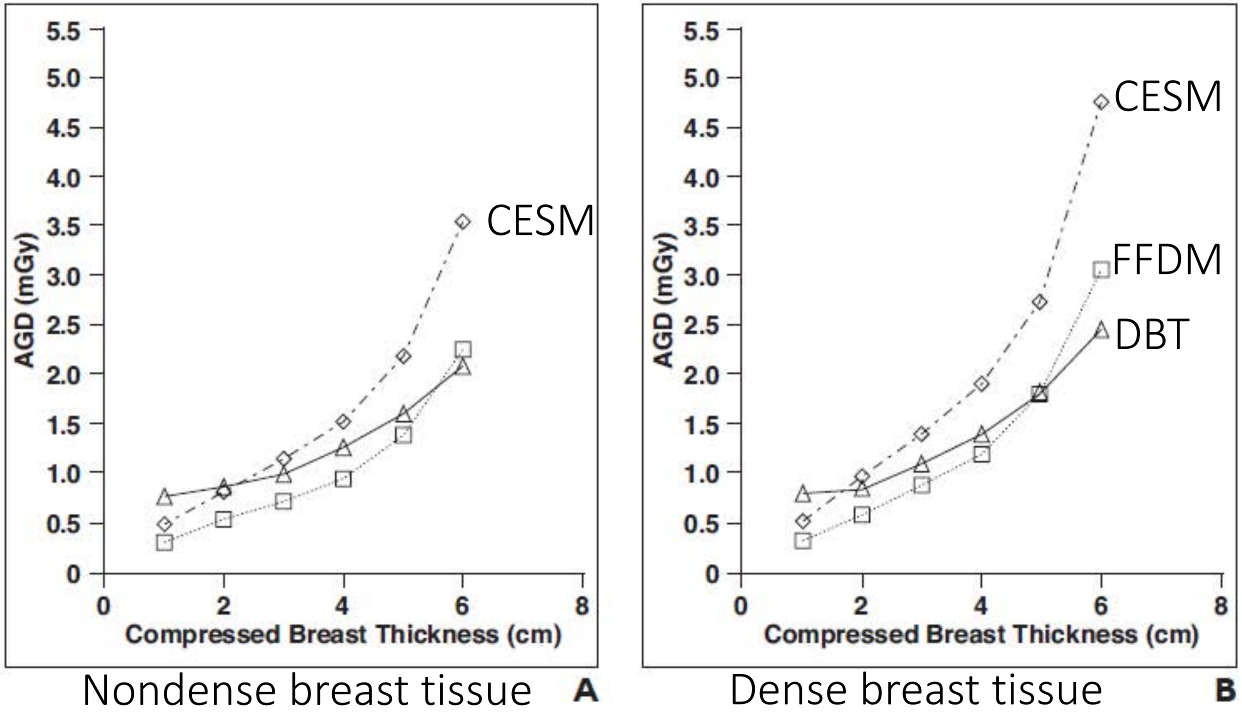
TABLE 1: Radiation Exposure Settings for 2D FFDM, 3D Tomosynthesis, and CESM Studies of Nondense Breast Tissue–Mimicking Phantoms

Imaging Technique	Phantom Thickness (cm)	Scanner Reported Thickness (cm)	Filter Type	Tube Voltage (kVp)	Tube Current–Time Product (mAs)	Half-Value Layer (mm)
CESM						
Low energy	1.0	1.1	Rh	26	23	0.497
	2.0	2.1	Rh	26	39	0.497
	3.0	3.1	Rh	26	68	0.497
	4.0	4.0	Rh	28	83	0.529
	5.0	5.0	Ag	29	97	0.575
	6.0	6.0	Ag	31	142	0.608
High energy	1.0	1.1	Cu	45	29	3.130
	2.0	2.1	Cu	45	46	3.130
	3.0	3.1	Cu	45	57	3.130
	4.0	4.0	Cu	45	90	3.130
	5.0	5.0	Cu	49	82	3.386
	6.0	6.0	Cu	49	138	3.386

Anode: tungsten

Reference:
Breast Radiation Dose With CESM Compared With 2D FFDM and 3D Tomosynthesis Mammography
Judy R. James,William Pavlicek, James A. Hanson, Thomas F. Boltz, Bhavika K. Patel-Medical Physics and Informatics (2016)

Contrast-enhanced spectral mammography (CESM)



Reference:
Breast Radiation Dose With CESM Compared With 2D FFDM and 3D Tomosynthesis Mammography
Judy R. James, William Pavlicek, James A. Hanson, Thomas F. Boltz, Bhavika K. Patel-Medical Physics and Informatics (2016)

Fig. 5—Average glandular dose (AGD) results for 2D full field digital mammography (*line with squares*), 3D tomosynthesis (*line with triangles*), and contrast-enhanced spectral mammography (*line with diamonds*).
A, Nondense breast tissue–mimicking phantom. Each slab contained tissue-equivalent materials mimicking 100% fatty and 100% glandular tissues in ratio of approximately 50:50 (nondense) by weight.
B, Dense breast tissue–mimicking phantom. Each slab contained tissue-equivalent materials mimicking 100% fatty and 100% glandular tissues in ratio of approximately 70:30 (dense) by weight.

Contrast-enhanced spectral mammography (CESM)

Reference:
Comparison between Breast MRI and ContrastEnhanced Spectral Mammography - Elżbieta Łuczyńska, Sylwia Heinze-Paluchowska, Edward Hendrick,…. - Medical Science Monitor (2015)

Table 1. Distribution of benign and malignant lesions in the study cohort.

Lesion	Cancer	Q-ty	Percent [%]
Infiltrating cancer	Invasive ductal carcinoma	58	49
	Invasive lobular carcinoma	5	4
	Apocrine carcinoma	1	1
	Papillary and micropapillary carcinoma	2	2
	Tubular carcinoma	1	1
	Mixed cases	5	4
Non-infiltrating cancer	Ductal carcinoma *in situ*	8	7
	Lobular carcinoma *in situ*	1	1
Benign lesions	Fibroadenoma	14	12
	Radial scar	4	3
	Intraductal papilloma	3	2
	Atypical ductal hyperplasia	1	1
	Inflammation	1	1
	Fibrosclerosis and fibrocystic lesions	14	12

Table 2. Distribution of lesions visible in MRI and CESM.

Number of lesions per patient	Lesion	Number of lesions	MRI – no enhancement	MRI – enhancement	CESM – no enhancement	CESM – enhancement
1	Benign	29	4	25	12	17
	Cancer	59	4	55	0	59
2	Benign	8	1	7	0	8
	Cancer	16	1	15	0	16
3	Benign	–	–	–	–	–
	Cancer	6	1	5	0	6
Total		**118**	**11**	**107**	**12**	**106**

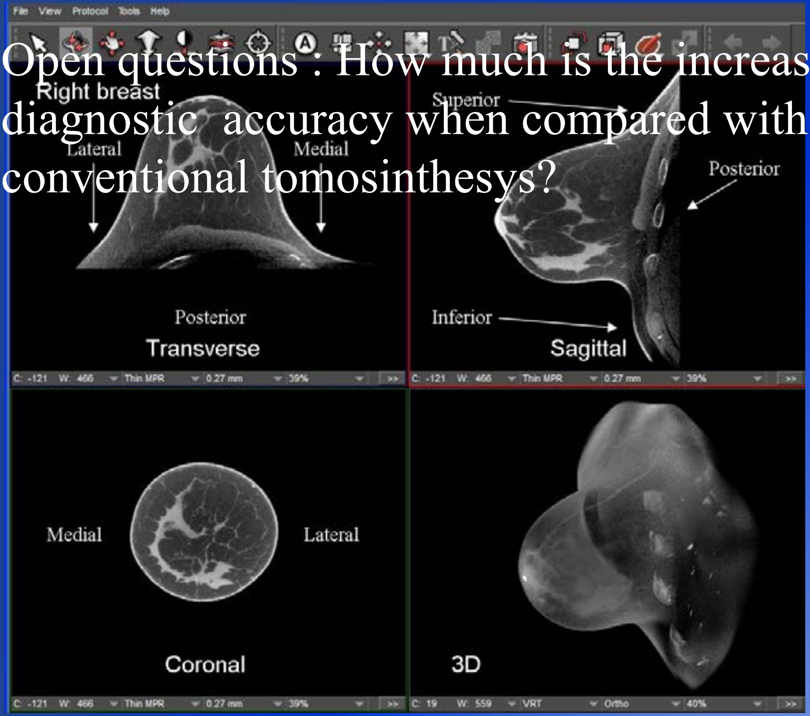
Table 3. Sensitivity, accuracy, PPV and NPV according to BI-RADS assessment. Brackets indicate 95% confidence intervals. P-values assess the significance of differences between MRI and CESM by variable.

	Sensitivity	Accuracy	PPV	NPV
MRI	93%	73%	74%	65%
	[85%; 97%]	[64%; 81%]	[65%; 82%]	[38%; 86%]
CESM	100%	79%	77%	100%
	[96%; 100%]	[69%; 86%]	[67%; 84%]	[74%; 100%]
p value	0.04	0.29	0.72	<0.001

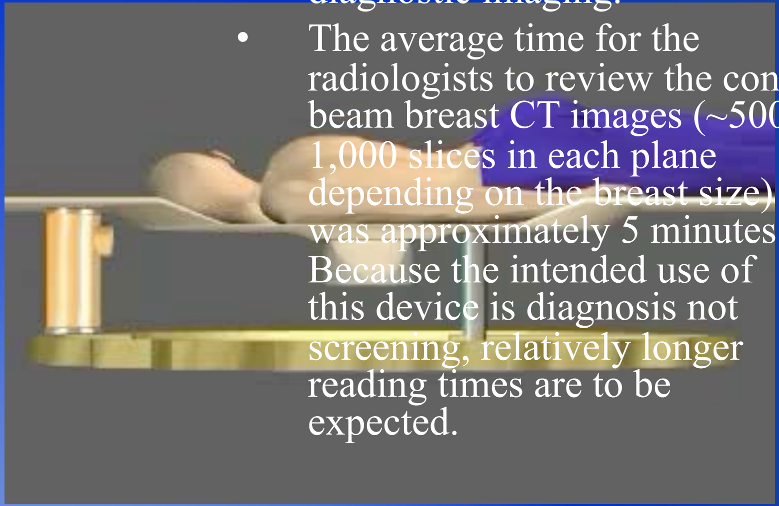
A thought on the future from the Academy

University Researcher opinion (by Angelo Taibi)

The Cone Beam Breast CT

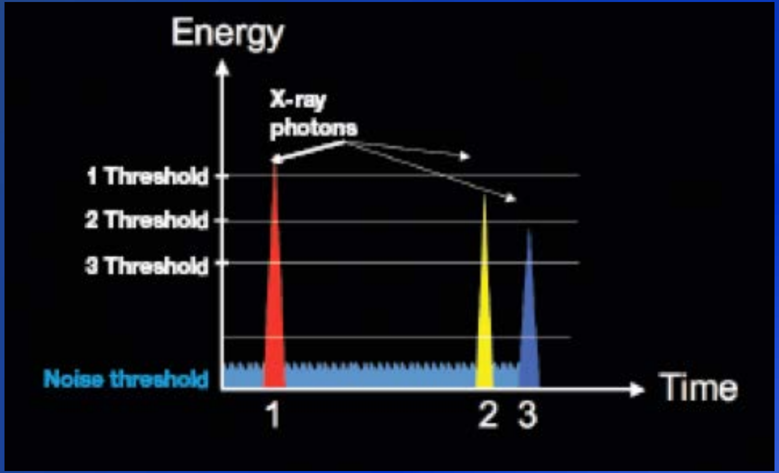


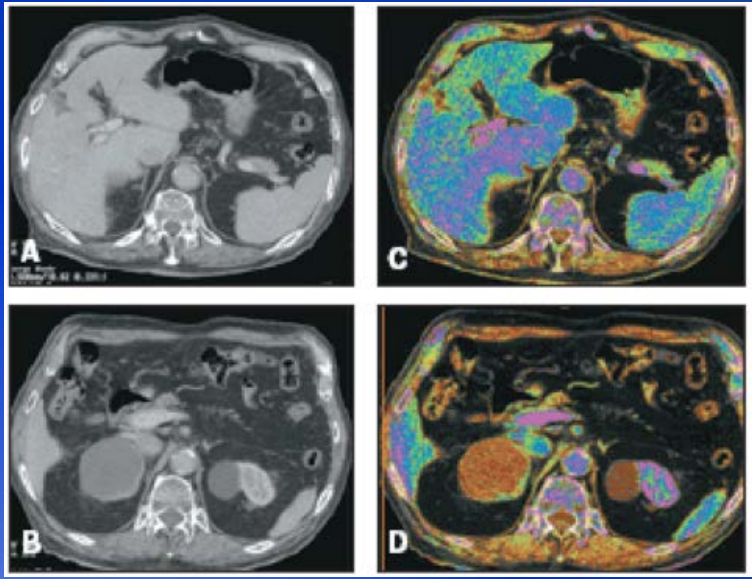
Open questions : How much is the increase in diagnostic accuracy when compared with conventional tomosinthesys?



- This dose range for cone-beam breast CT is acceptable [4-12.8 mGy …] because the intended use of cone-beam breast CT is diagnostic imaging.
- The average time for the radiologists to review the cone-beam breast CT images (~500–1,000 slices in each plane depending on the breast size) was approximately 5 minutes. Because the intended use of this device is diagnosis not screening, relatively longer reading times are to be expected.

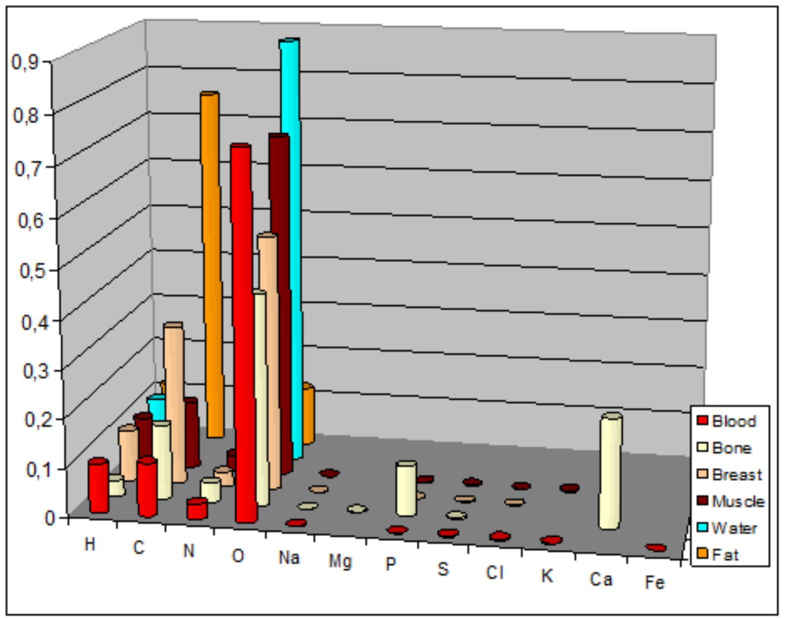
Spectral Imaging (Photon Counting o Multienergy Mono X rays)

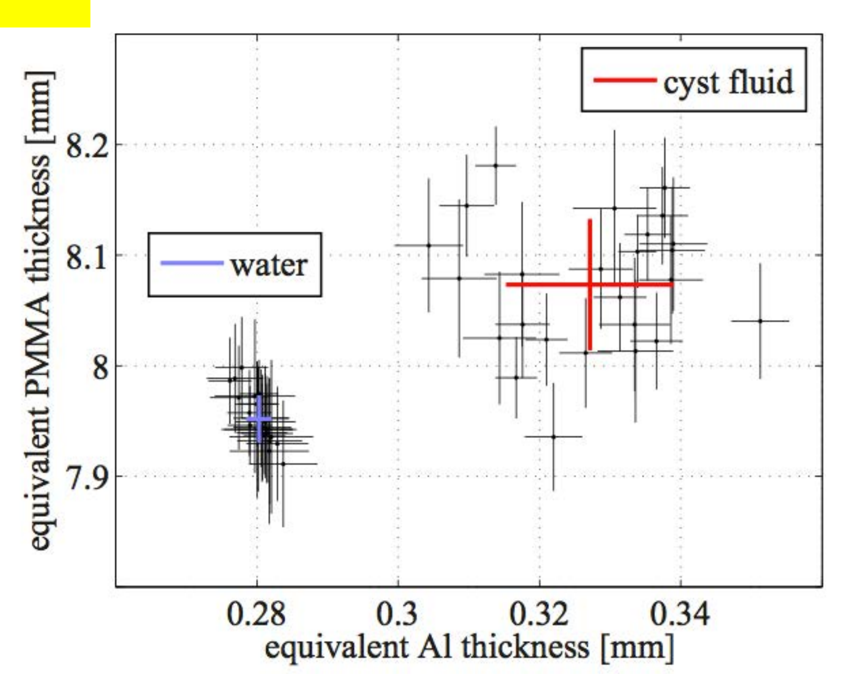




Aslund et al "Detectors for the future of X-ray Imaging", Rad. Prot. Dos. 139, 2010

“X-ray attenuation is material specific and information about the object constituents can be extracted by spectral imaging”





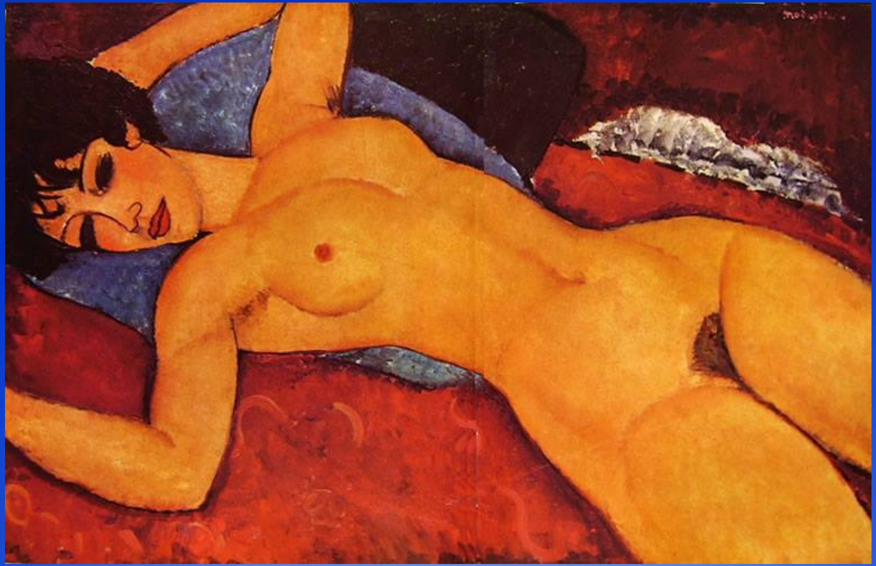
Fredenberg et al, SPIE Proc 8668, 2013

A thought on the future from the Academy (in short)

The methodological evolution will be towards   multi energy diagnostics obtained by means of a tunable monochromatic source or by means of a Photon Counting detector equipped with a variable energy window, and a polichromatic source.

Multienergy, made in one way or another, becomes the key to characterize tissue parameters, that is to improve the diagnostic accuracy.

Thank you for your attention



Appendix

Digital Breast Tomosynthesis (DBT)

Principio:

- Con diverse angolazioni del tubo radiogeno vengono acquisite una serie di immagini non direttamente utilizzabili clinicamente.
- I dati acquisiti vengono ricostruiti in una serie di strati sottili ad alta risoluzione

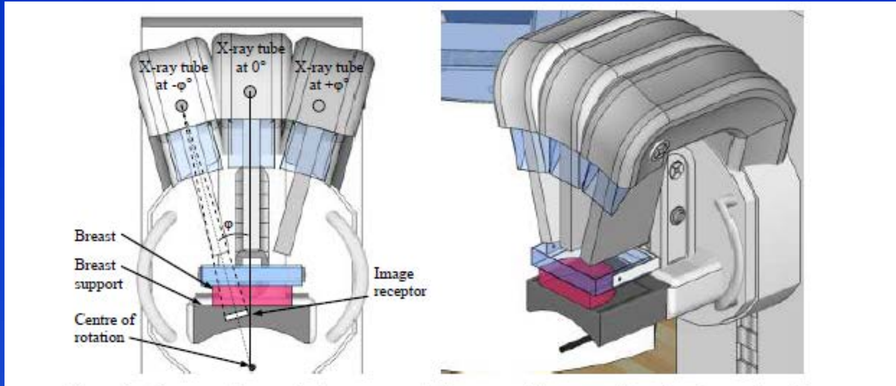


Figure 2 Geometry of a scanning breast tomosynthesis system with a narrow X-ray beam (currently under development) showing three positions of the X-ray tube (not to scale). In this system both the X-ray tube and image receptor rotate. The X-ray field is collimated to the image receptor. The limits of the X-ray field and the ray passing through the centre of rotation are shown.

The Digital Breast Tomosynthesis

The **detector** technologies

- **Energy Integrating (EI);**

- indirect conversion:

<u>scintillator</u> (CsI:Tl) in optical contact with a plate of amorphous silicon (a-Si)

- direct conversion:

generates an image without intermediate conversion of x-rays to visible light,
a-Se semiconductor

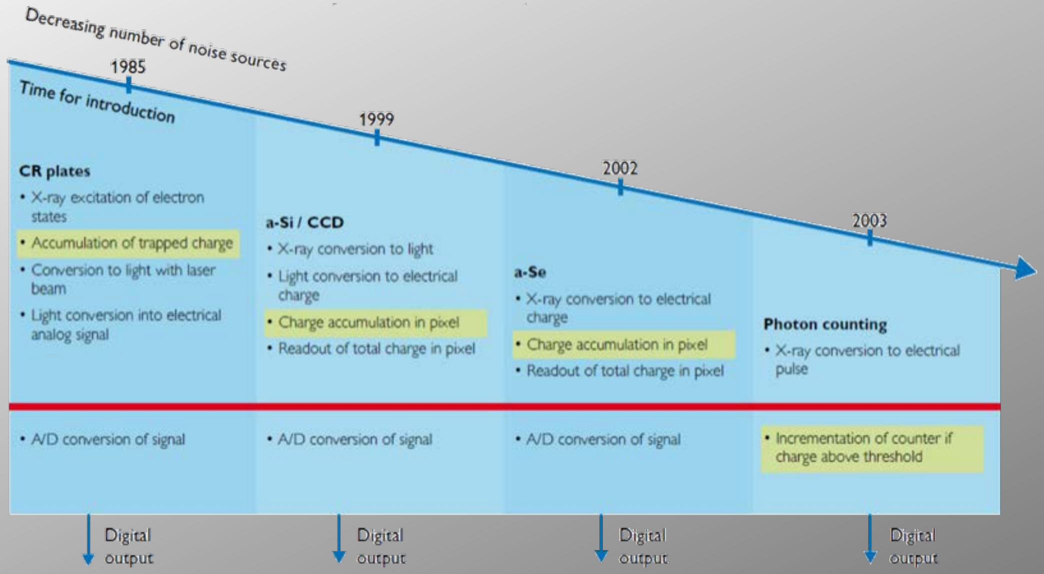


Image courtesy of Philips

The Digital Breast Tomosynthesis

The **detector** technologies

- Energy Integrating (EI);
- **Photon Counting (PC).**

Read the <u>single incident x-ray quanta </u>as discrete event.

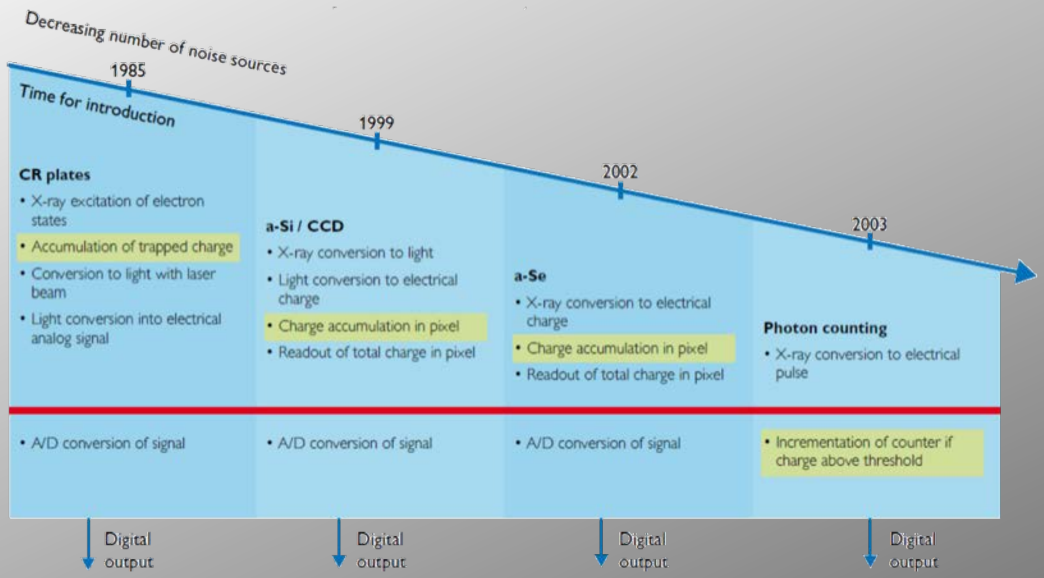


Image courtesy of Philips

Photon Counting Technology

The **detector** technologies

- Energy Integrating (EI);
- **Photon Counting (PC).**

Read the single incident x-ray quanta as discrete event.

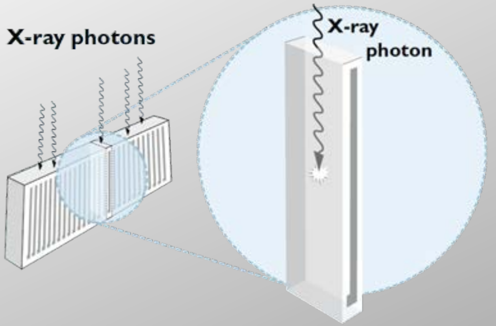


Image courtesy of Philips

Thin silicon strip detectors with long axis parallel to the x-ray beam.

+ path length of absorption

+ quantum efficiency

3.6 eV to generate a single electron-hole pair

Photon Counting Technology

The **detector** technologies

- Energy Integrating (EI);
- **Photon Counting (PC).**

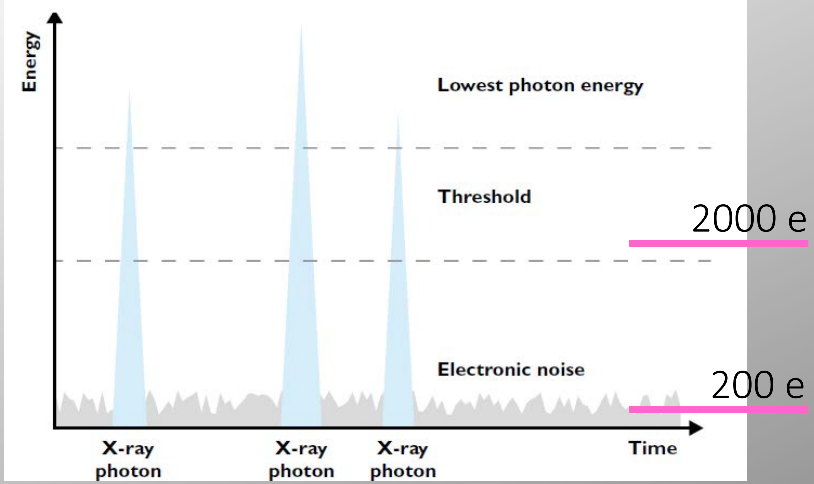
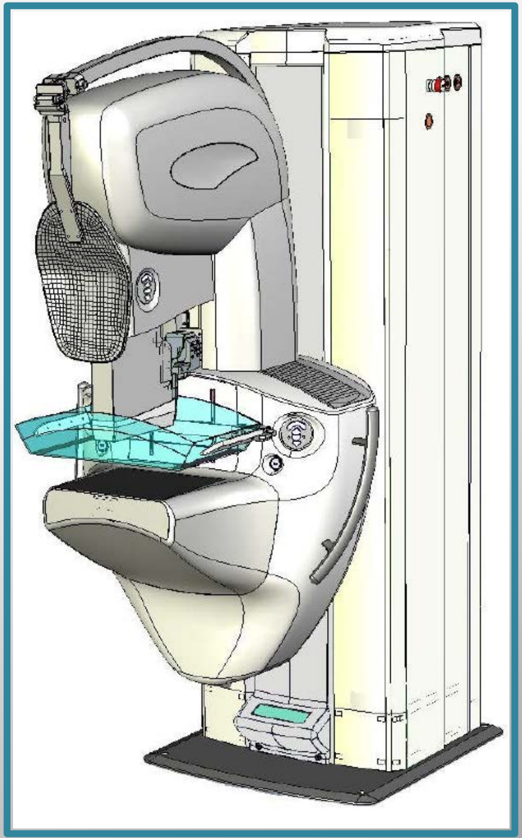


Image courtesy of Philips

every x-ray produce **thousands** of electron-hole pairs

It is possible to completely **remove** the background noise from the image

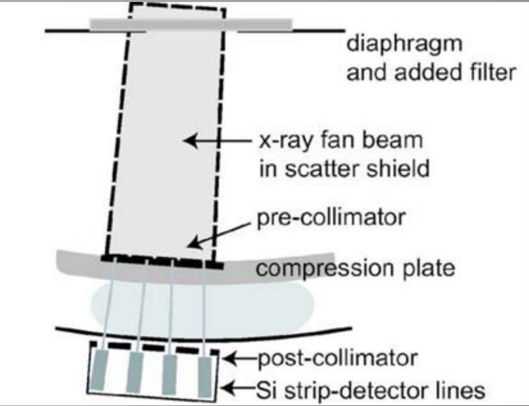
The DBT devices



Philips MicroDose Mammography S0 (Prototype)

Highlights:

- photon counting detector;
- linear slit scan-spectral pattern;
- 24x29cm detecting area: 21 line detectors each 24cm long ;
- 50μm binned pixel;
- tube moves continuously;
- angular range: 11°;
- projection images: 25;
- detector – CoR: 40cm;
- reconstruction method: iterative.



Even if the advantage in image quality and dose sparing is well known
Photon Counting technology will be no longer used in 2D and it has been never used in 3D.
Too expensive

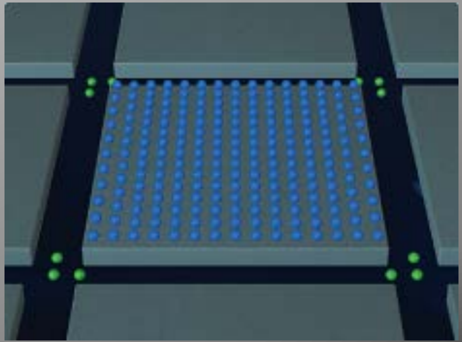
R&D on improvement of existing detector is more convenient!

Generator & Tube

- **New** Generator fully integrated a more robust (CESM)
- Dual Track tube Mo/Rh with optimal dense breast penetration thanks to RH (unique to GE)
- Dual Filtration with Mo and **New** filter Ag replacing Rh filter contributing to reduced acquisition times
- Combined with AOP to deliver optimized patient dose
- Ready right after boot

Detector & Grid

- High DQE at low dose in 2D, DBT, CESM
- Large FOV: 24 cm x 29 cm – Robust CsI scintillator 100µ and **New** Grid compatible for 2D, DBT and CESM
- No daily calibration required nor need for a cooling liquid – ready right after boot
- DBT: allows the visualization of small objects such as µcalcs **(no binning)**



Courtesy GE

The Digital Breast Tomosynthesis

The **volume reconstruction algorithm** in tomosynthesis can be divided into:

- back-projection algorithm (BP);
- filtered back-projection algorithm (FBP);
- iterative algorithm (derived from CT).

Post-processing

- 2D: eContrast a variety of 6 flavors (incl. implants)
- DBT: **ASIR** for µcalcs visibility and minimize artifacts & High IQ for the 3 reading formats (**New** V-Preview 3)

1.Tomo planes

2.Tomo slabs
= 1cm thick planes

3.V-Preview
Synthetic 2D

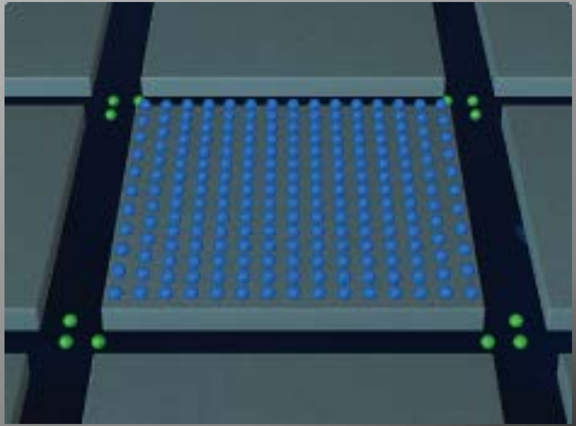
Courtesy GE

The DBT devices

Hologic Selenia Dimension

Highlights:

- direct capture Thin Film Transistor (TFT) based coupled with an amorphous selenium (a-Se) detector;
- square pattern;
- 24x29cm detecting area;
- 70µm binned pixel;
- tube moves continuously;
- angular range: 15°;
- projection images: 15;
- detector – CoR: 0 cm;
- reconstruction method: Iterative/FBP.

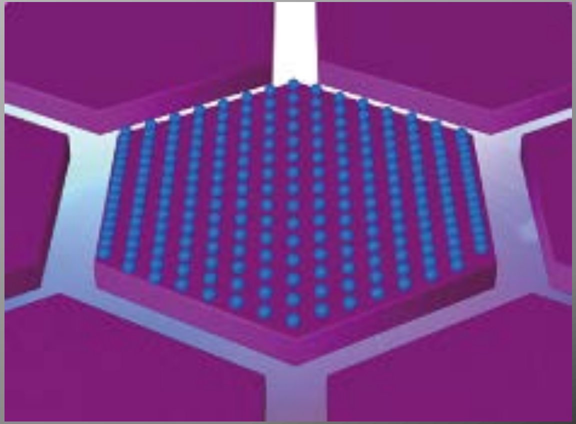


The DBT devices

Fujifilm Amulet Innovality

Highlights:

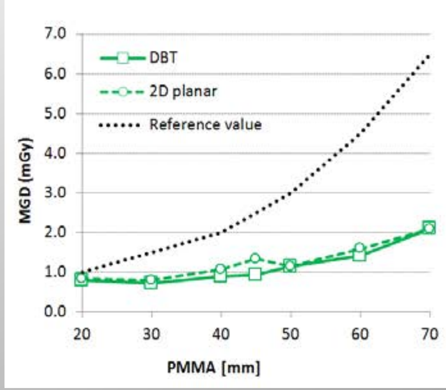
- direct capture Thin Film Transistor (TFT) based coupled with an amorphous selenium (a-Se) detector;
- hexagonal pattern;
- 24x30cm detecting area;
- 100µm (ST)/ 50µm (HR) binned pixel;
- tube moves continuously;
- angular range: 15°(ST)/40°(HR);
- projection images: 15;
- detector – CoR: 4cm;
- reconstruction method: FBP.

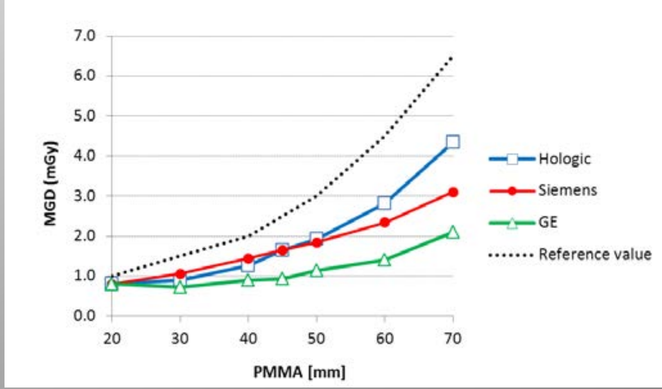


Pristina 3D A new detector Designed for a low dose DBT

Target Dose

- Low dose technology combined with **New** compression tools contributing to low dose performance in 2D, DBT and CESM
- DBT: the only FDA approved DBT @ isodose





Reference value = EUREF limits

N.W. Marshall and H. Bosmans, Medical Physics UZ Leuven, Application of the draft EUREF protocol for Quality Control of digital breast tomosynthesis (DBT) systems", BHPA 2014.