



Clinical Mammography With Synchrotron Radiation And The New Digital Development

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Compton Sources for X/ γ Rays: Physics and Applications
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Hospital

Health
Physics

University

INFN

Elettra

Outline

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- SYRMEP (SYnchrotron Radiation for MEDical Physics)
- The mammography clinical program
 - Motivations
 - Material and methods
 - Results
- The digital development
 - PICASSO (Phase Imaging for Clinical Application with Silicon detector and Synchrotron radiation)
- Conclusions and Outlook

Outline

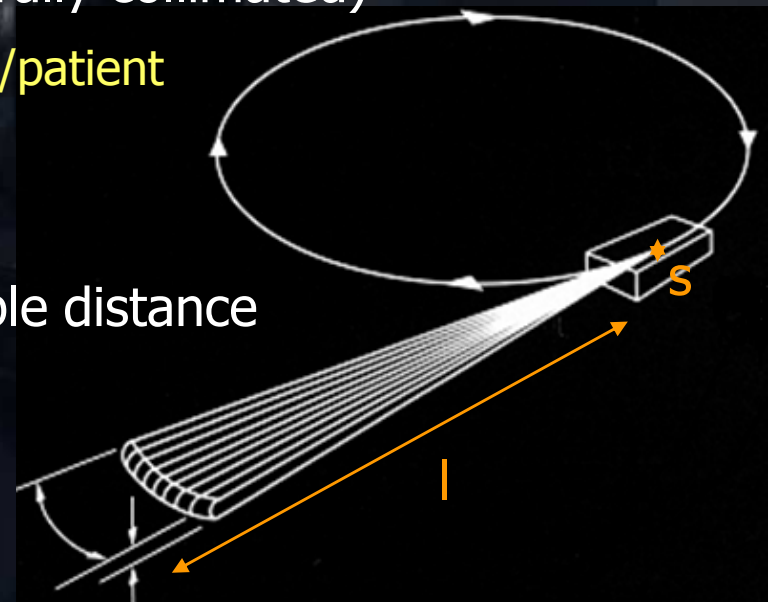
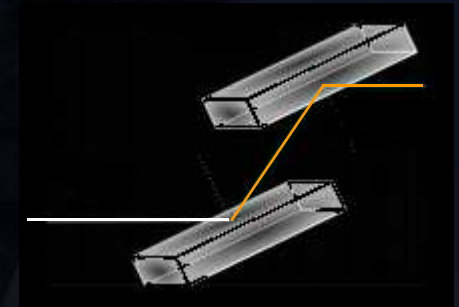
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Characteristics of synchrotron radiation (SR)

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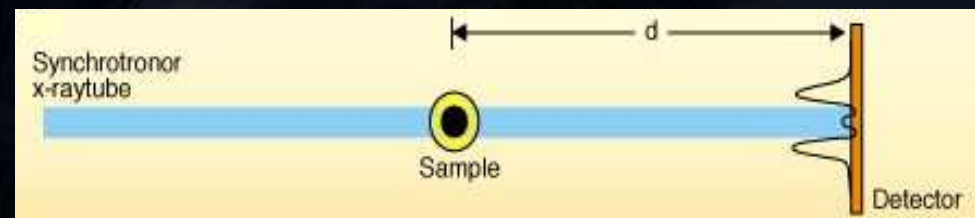
- High x-ray intensity on a broad energy range
 - Tunable monochromatic beam
 - Choose the optimum energy for a specific examination
 - Dose optimization/reduction
 - Allow double energy subtraction techniques
 - No beam hardening effects or artifacts (tomography)
- Laminar beam geometry (the beam is naturally collimated)
 - Images are acquired by scanning the object/patient through the fan beam
 - High scattering rejection
- Small source size and large source-to-sample distance
 - High degree of lateral coherence
 - Phase contrast (PhC) imaging



Phase Contrast (PhC)

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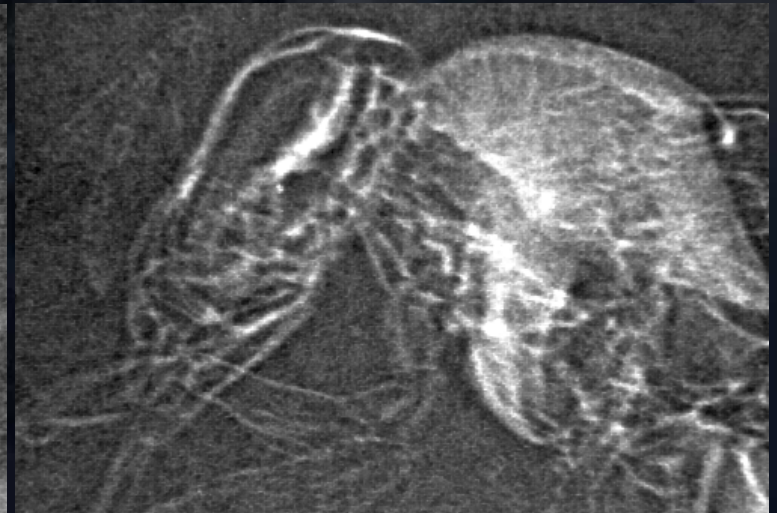
- Phase effects → Modulation of X-ray intensity on the detector
- PhC is the simplest way
 - In line propagation
 - Edge enhancement ($\nabla^2 \Phi(x, y)$)



- Example:



absorption



phase contrast

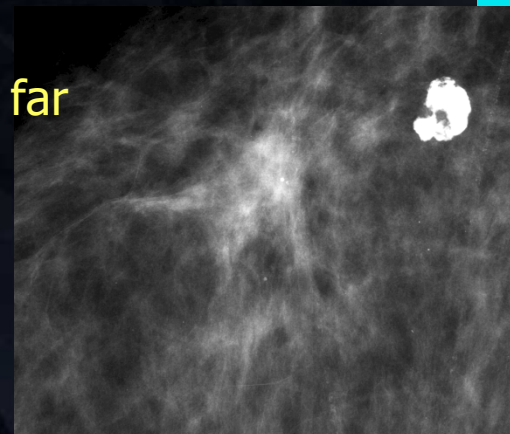
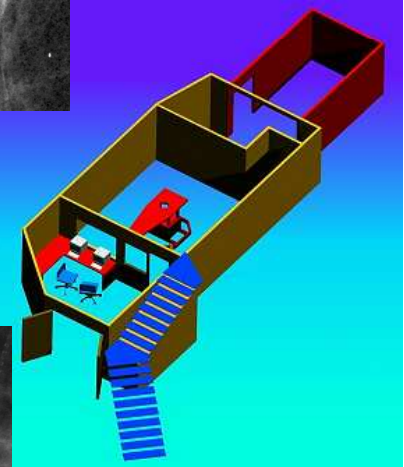
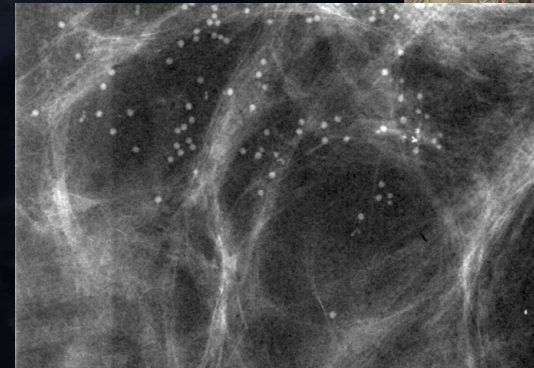
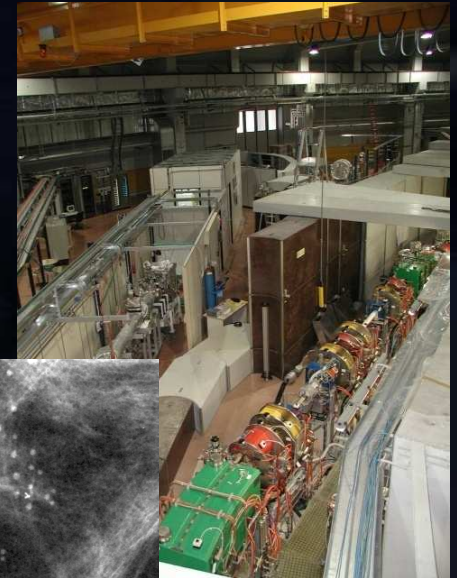
SYRMEP (SYnchrotron Radiation for MEdical Physics)

- Since 1993 the SYRMEP group (Trieste, Italy) has been investigating the applications of Synchrotron Radiation in Medical Imaging, and in particular to Mammography
- The SYRMEP project included:
 - **BEAMLINE**
 - Design and construction of a bending magnet beamline at the ELETTRA Synchrotron Light Source
 - **DETECTOR**
 - Design and construction of a Silicon microstrip detector equipped with a single photon counting read-out electronics



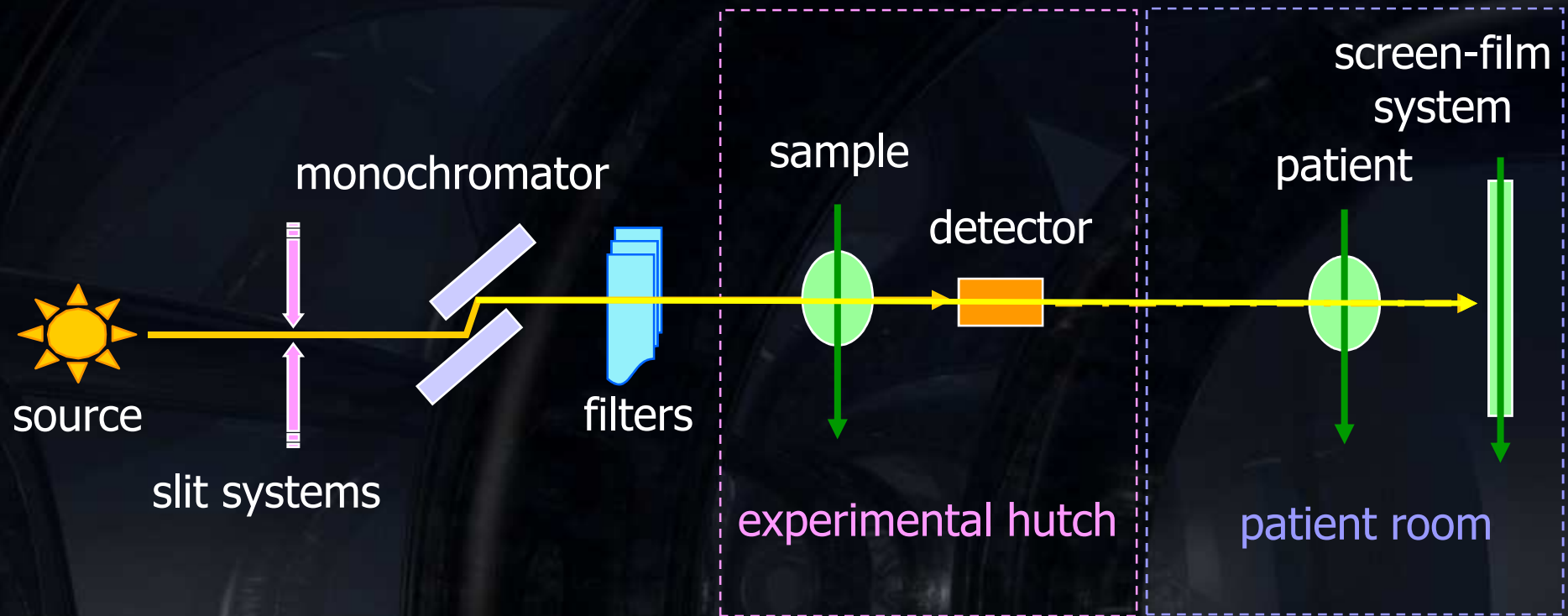
Beamline, A brief history of

- 1996 First Photons
 - The SYRMEP beamline is devoted to *in vitro* medical imaging
- 1998 First low-dose PhC
- 2002 Upgrade beamline
 - A dedicated mammographic station is developed for the clinical program
- 2006 Clinical Program
 - 53 patients have been examined so far with promising results



The SYRMEP Beamline (I)

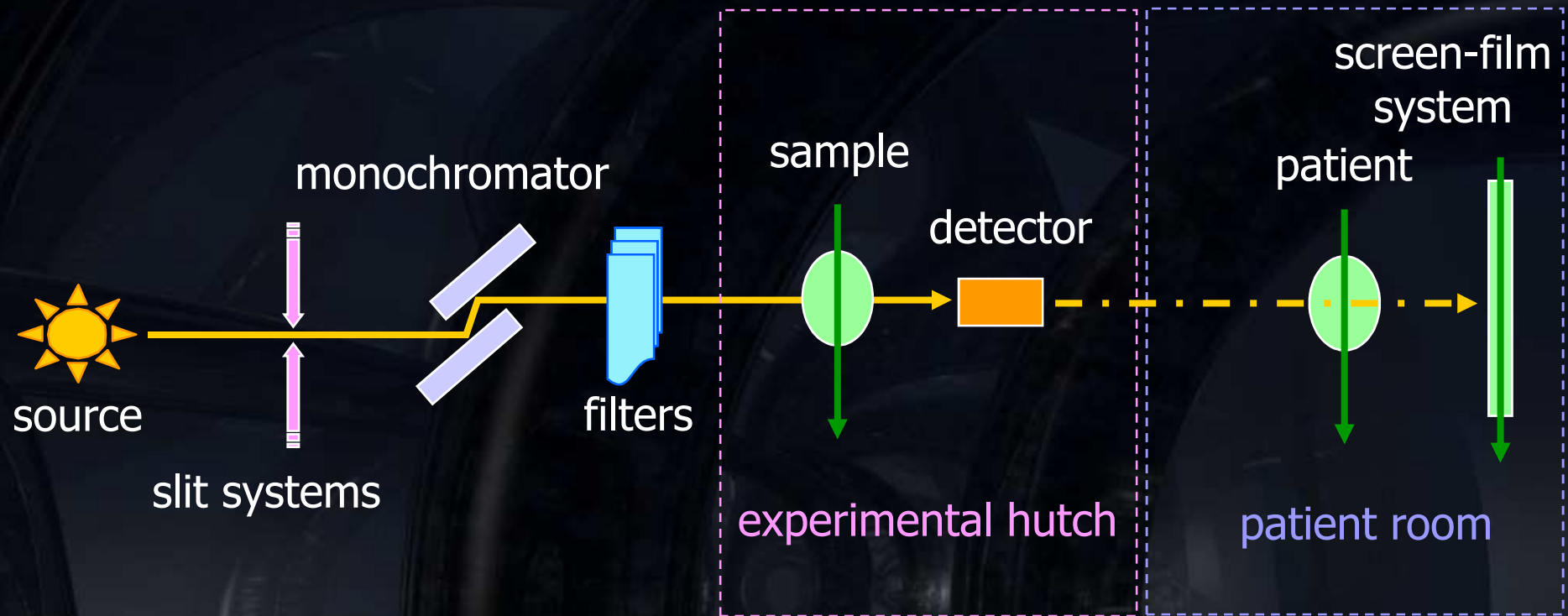
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- Bending Magnet Source
- Source size ~ 1.1 (horizontal) $\times 0.1$ (vertical) mm^2
- Monochromatic beam with tuneable energy (8.5 - 35 keV)
- Bandwidth: $\Delta\lambda/\lambda \sim 2 \times 10^{-3}$
- Divergence: ~ 7 mrad (horizontal) $\times 0.2$ mrad (vertical)

The SYRMEP Beamline (II)

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- Source-to-Sample distance: ~ 23 m
 - Laminar beam cross section: 4×150 mm²
 - Flux available at 17 keV (Elettra operated at 2.4 GeV, 140 mA ring current): $6 \cdot 10^8$ ph/mm²/s
 - Transverse coherence length at 17 keV ($L_c = \lambda R_1 / 2s$): 8 μ m
- ~ 32 m
 4×210 mm²
 $2 \cdot 10^8$ ph/mm²/s
 11 μ m

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Motivations

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- Mammography must fulfill extreme requirements on the X-ray source as well as on the detection system
- Possible indicators of early breast cancer
 - Micro calcifications (high spatial resolution)
 - Nodules - masses (high contrast resolution)
- Breast is one of the most radiosensitive organs
 - Low dose
- Clinical Mammography is far from being perfect
 - sensitivity 75% - 90%
 - specificity 90% - 95%
- The energy of X-rays available at our beamline (8.5 – 35 keV) is particularly suited for mammography

Objectives

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- Our goals
 - Improving the diagnostic quality
 - Reducing the dose delivered to the patient
- Instruments and Methods
 - Use of a synchrotron radiation X-ray source
 - Novel imaging techniques based on phase effects (PhC)
 - Digital imaging using a silicon micro-strip detector operated in single photon counting
 - High efficiency
 - Good spatial resolution
 - High contrast resolution
 - Wide dynamic range

The clinical program

- 3 Phase program
 - Phase I: PHC radiography with conventional film screen system
 - » Clinical trial has started in 2006
 - » 53 patients so far
 - Phase II: PHC radiography with digital detector
 - » Feasibility study by using FUJIFILM Fuji CR for Mammography PROTECT ONE
 - » Development and construction of a custom digital detector (PICASSO)
 - Phase III: new techniques (CT and/or tomosynthesis)
 - » R&D

Patient recruitment (I)

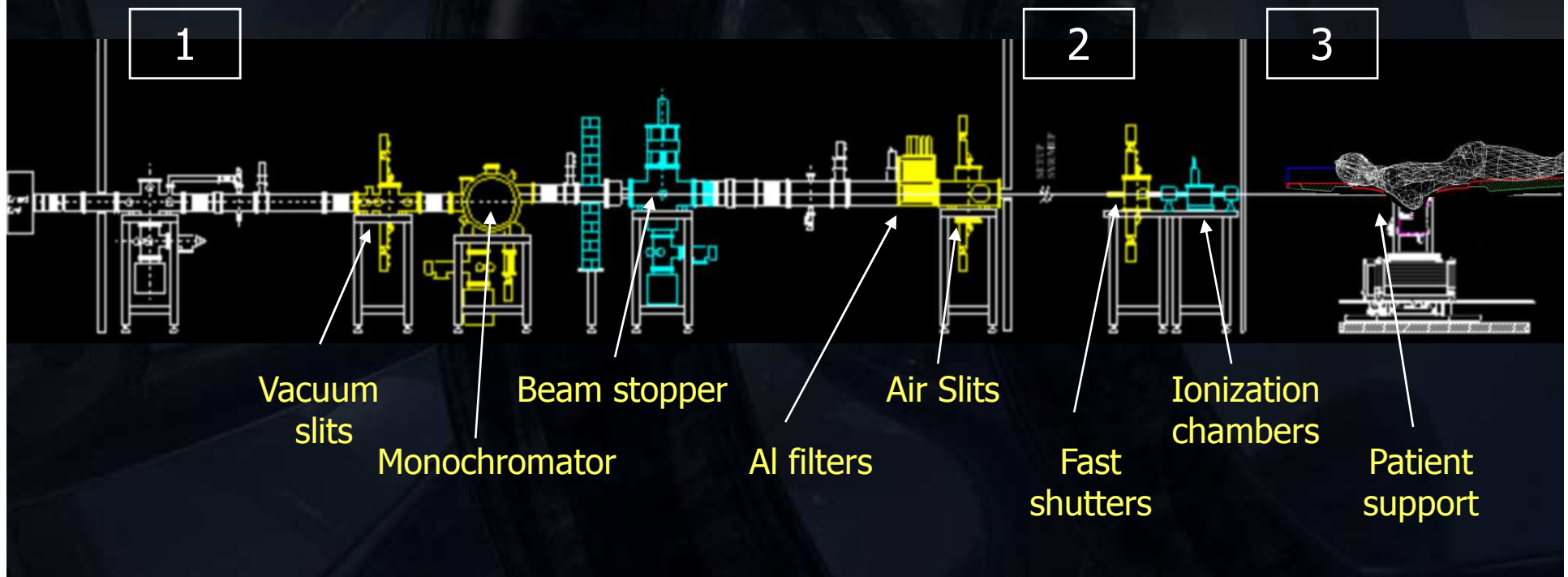
- Patients
 - Volunteers: informed consent is obtained
 - Selected by the Radiologist on the basis of BI-RADS classification (ACR, accepted by European screening guide lines) after conventional mammography and ultrasonography
- Target
 - Uncertain diagnosis of conventional examination
 - Suspicion of false positives
 - Dense breasts
- Typical cases
 - Mammography shows a dense disomogeneous breast and ultrasonography does not solve the problem
 - Mammography shows asymmetry of the two breasts and ultrasonography does not solve the problem
 - Both mammography and ultrasonography are uncertain

Patient recruitment (II)

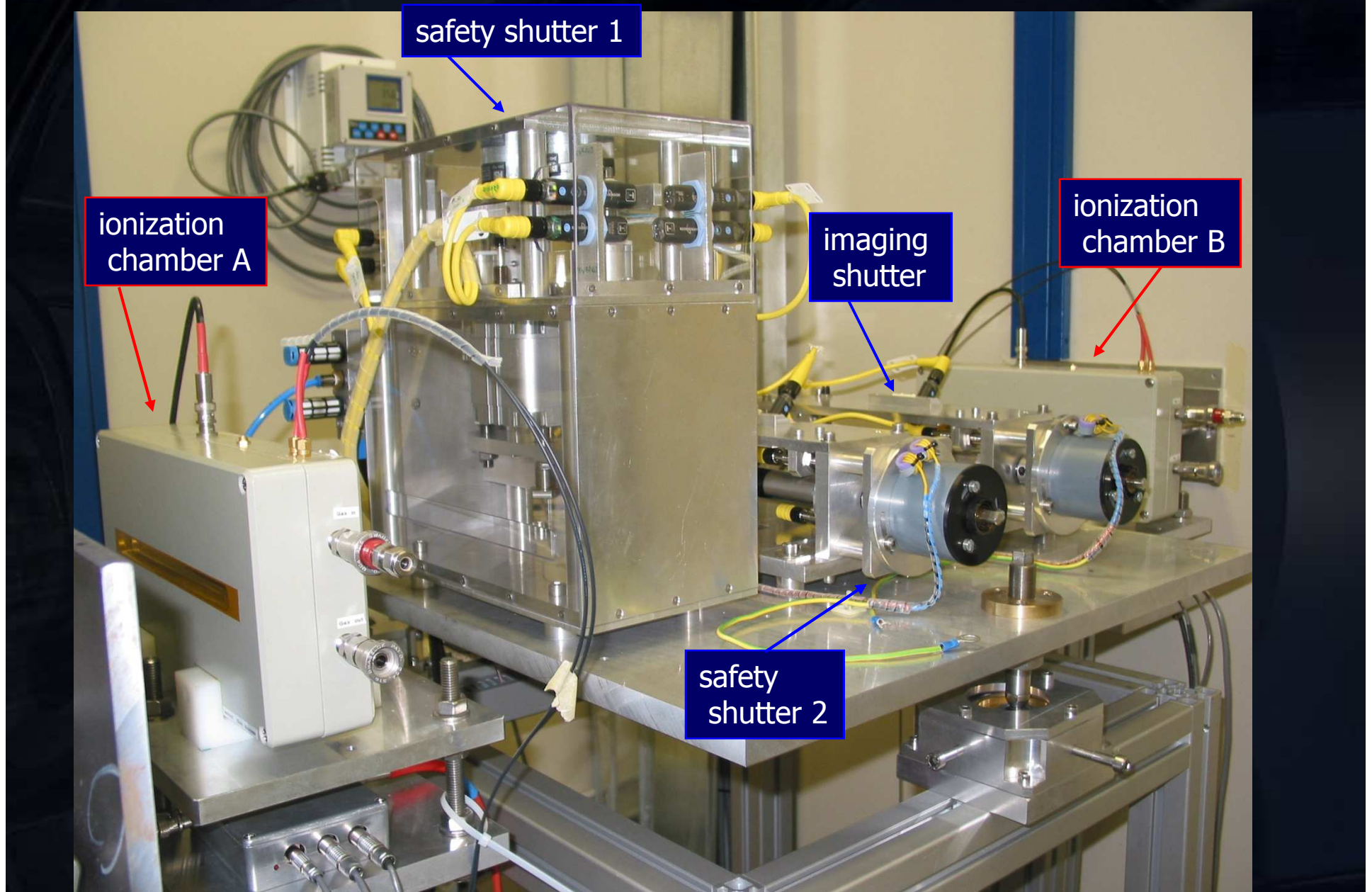
- We expected 70-100 patients/year fulfill our selection criteria
- Only 55 have been examined in more than 2 years. Main causes:
 - For ethical reasons, the patient should undergo mammography at SYRMEP within 1 week from conventional mammography and/or ultrasonography
 - Shifts dedicated to patients require Elettra is operated at 2.4 GeV and cannot be scheduled every week
 - Elettra activity was stopped for 5 months due to a major upgrade (booster)
 - Onset of a screening mammographic program in our region
 - Our recruitment center at the hospital acted as a second level test for this program
- We have now
 - Extended our recruitment pool including the other main hospital in Trieste
 - Allocated dedicated 2.4 GeV shifts once a month in the Elettra calendar
- We aim to reach 70 patients by the end of the year

The patient beamline layout

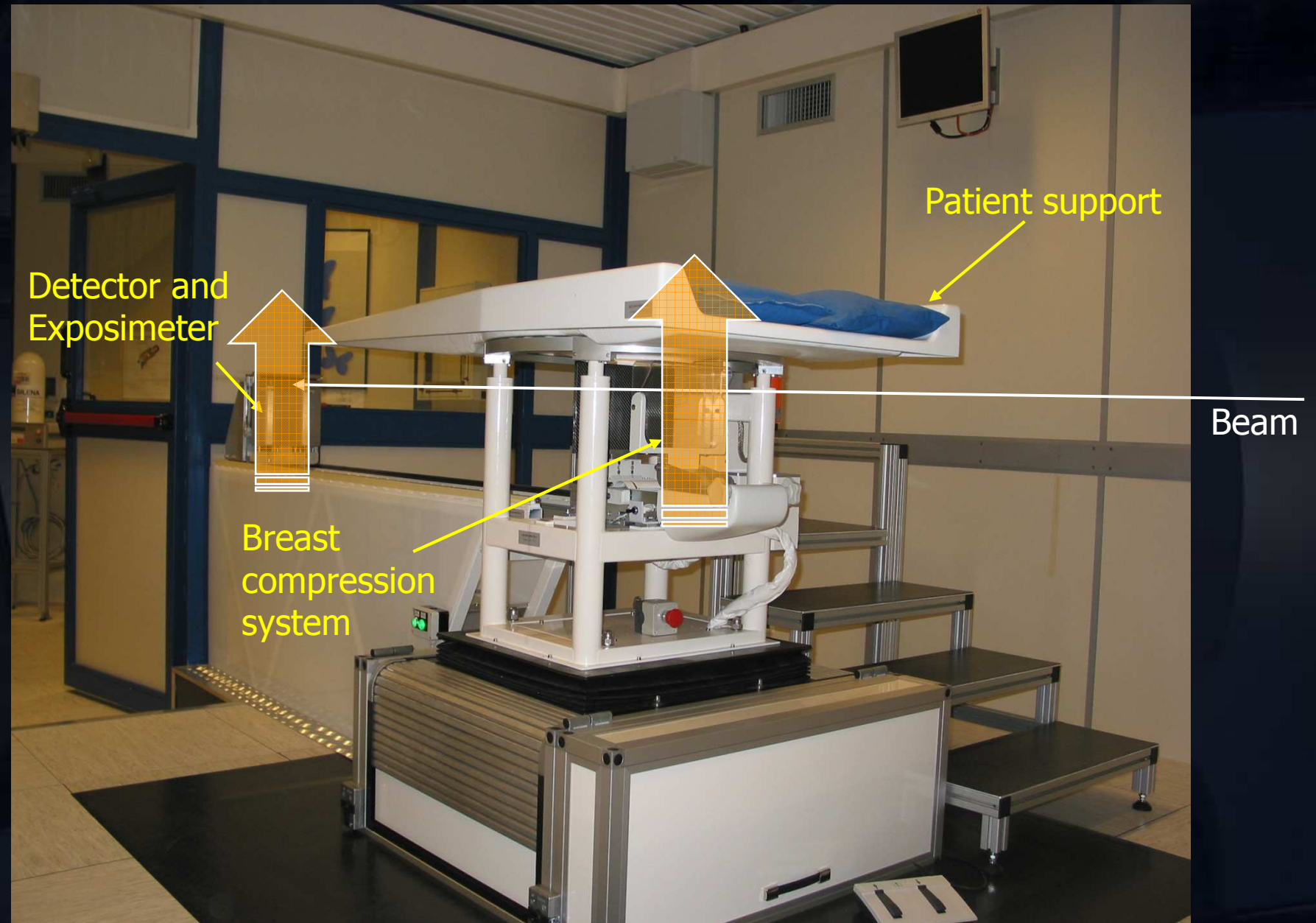
- 1 Beam preparation (energy, flux, geometry)
- 2 Beam monitoring (dose, exposure time, safety system)
- 3 Patient exposure



Dose control and safety system

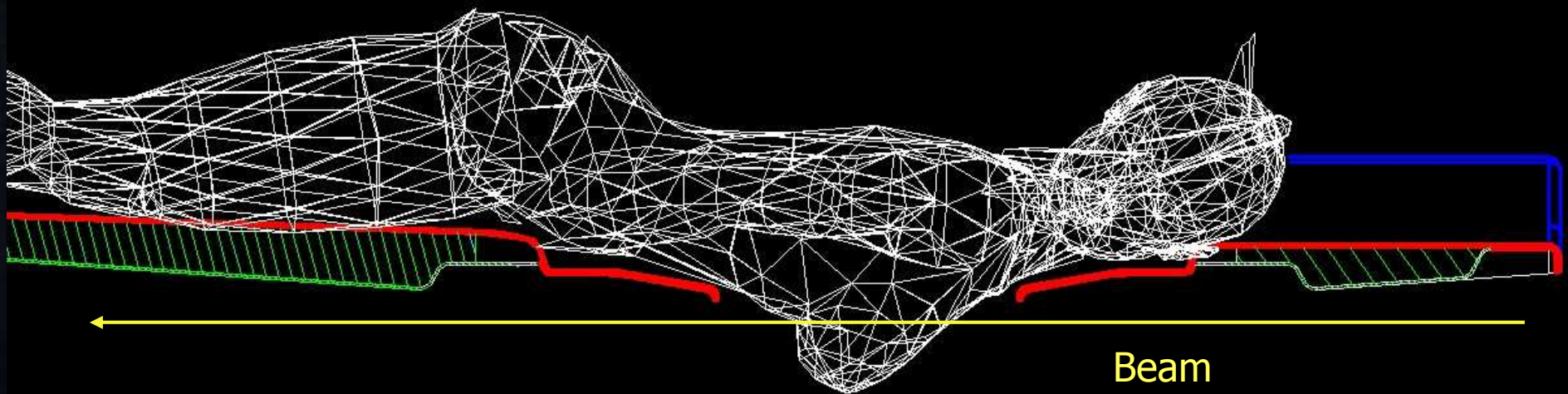


Patient Room



Patient support (I)

- Prone position as used in stereotactic biopsy tables
 - Full Field Digital Biopsy system Giotto Image (IMS, Bologna, Italy)
- Size and shape of the opening are consistent with the chest anatomy
 - Good patient comfort



Patient support (II)



Carbon fiber
support

26 cm Ø

Clinical Program Results

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- 53 patients have undergone Synchrotron Mammography (SYM) so far
- A comparison with conventional mammography is performed
 - The conventional system is a state-of-the-art Full Field Digital Mammography (FFDM) GE Senographe DS
 - An expert Radiologist compared SYM and FFDM images and evaluated them in terms of
 - Visibility of the lesion
 - Visibility of the glandular structure relevant to the diagnosis
- The results are evaluated by means of a Wilcoxon signed rank test

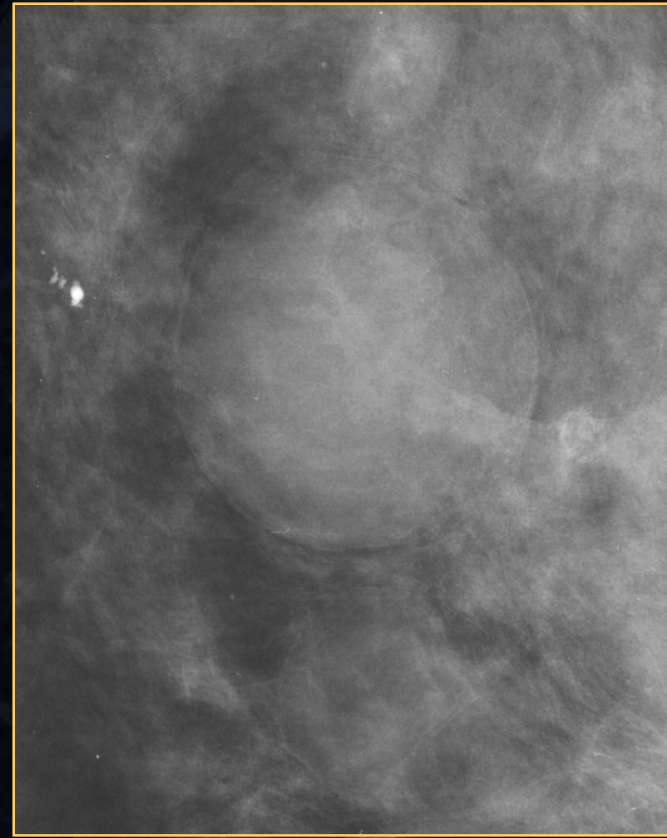
Conventional (FFDM) Vs Synchrotron (SRM)

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FFDM



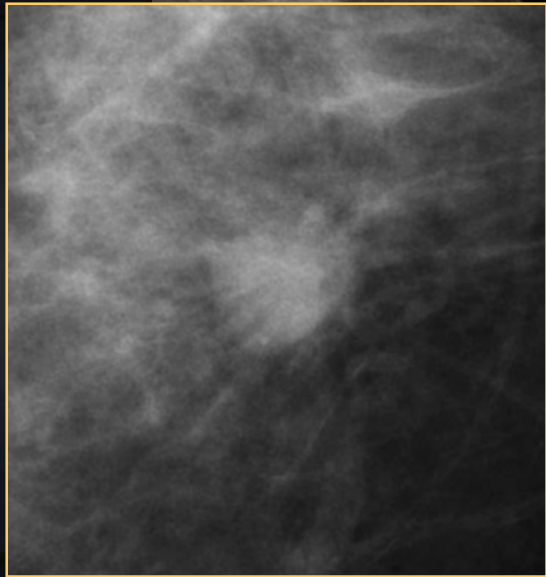
SRM



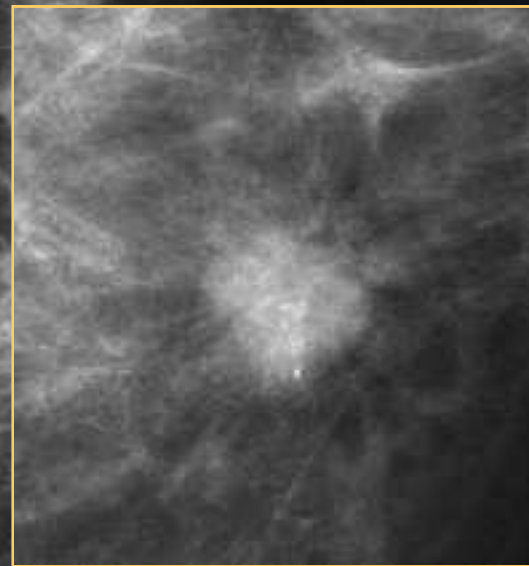
Conventional (FFDM) Vs Synchrotron (SRM)

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FFDM



SRM



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PICASSO Digital Detector Requirements

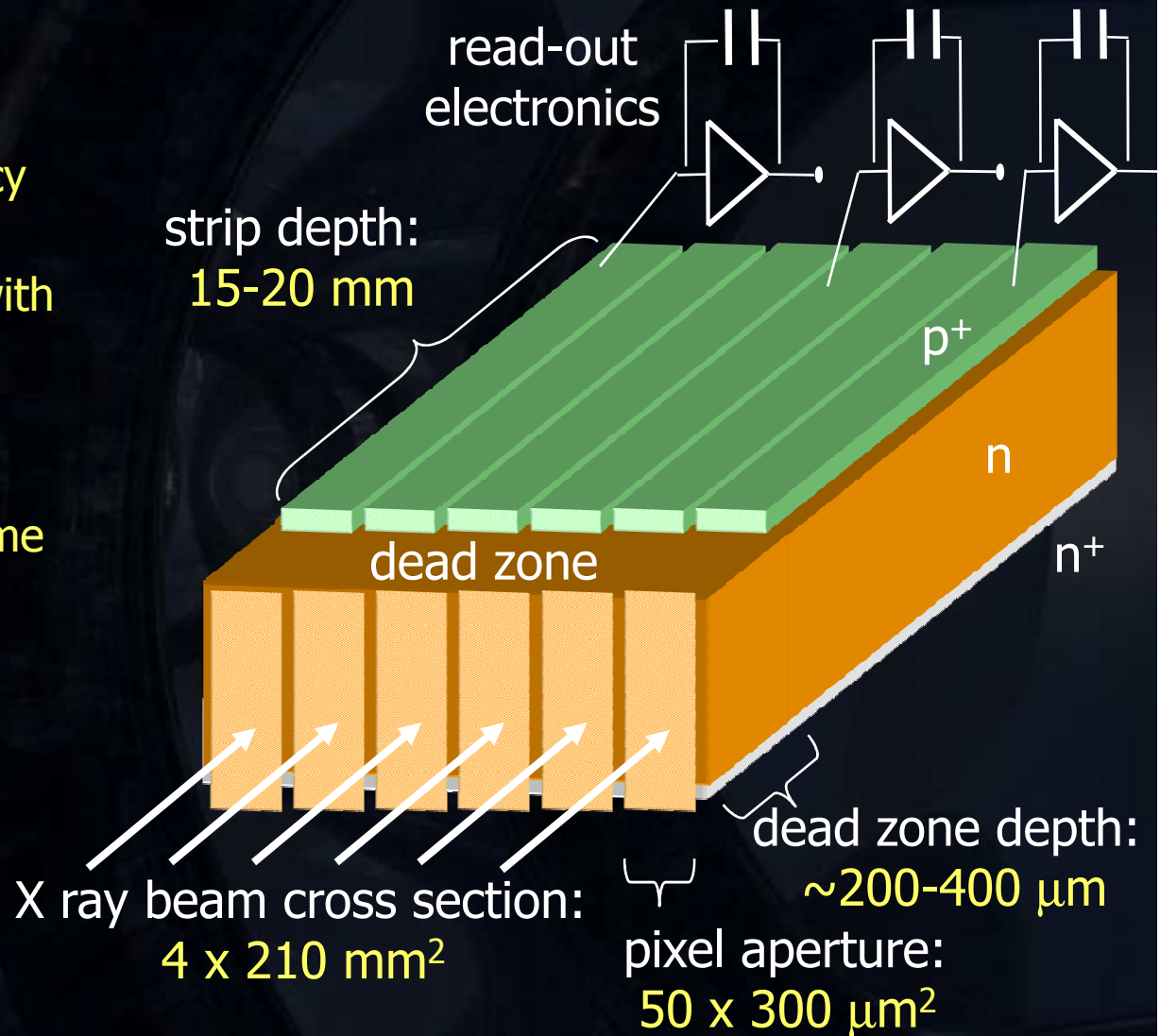
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- Laminar geometry
 - Scatter Rejection
 - Matching beam cross section
- High efficiency
 - Low dose
- High spatial/contrast resolution
 - Detect micro-calcifications/nodules
- Wide dynamic range
- Fast Rate Capabilities and Read-Out
 - Take a mammogram in a few seconds



The silicon micro-strip detector: "edge-on" geometry ²⁸

- Advantages of "edge-on" geometry:
 - High absorption efficiency
 - Matching the laminar geometry of the beam with a natural pixel array
- Problems:
 - Dead (undepleted) volume in front of the sensitive region that reduces the detection efficiency (~70-85% @20keV)

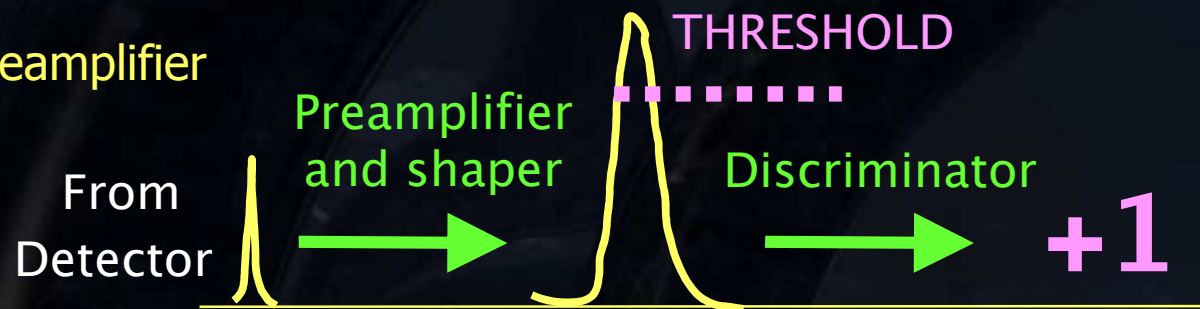


Single Photon counting

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- Each strip is bonded to a channel of the read-out electronics. Each channel features:

- Charge sensitive preamplifier
- Shaper
- Discriminator
- Counter



- Advantages
 - The quantum nature of the information carried by the photon beam is preserved (no quantization error typical of charge integration devices)
 - High (virtually infinite) dynamic range
- Challenges
 - Can we have a uniform response over all channels?
 - Can we have a low noise AND high acquisition speed (\sim MHz)?
 - Can we have all channels (pixels) counting simultaneously at full rate (when contrast is in the order of 1%)?

Detector, A brief history of

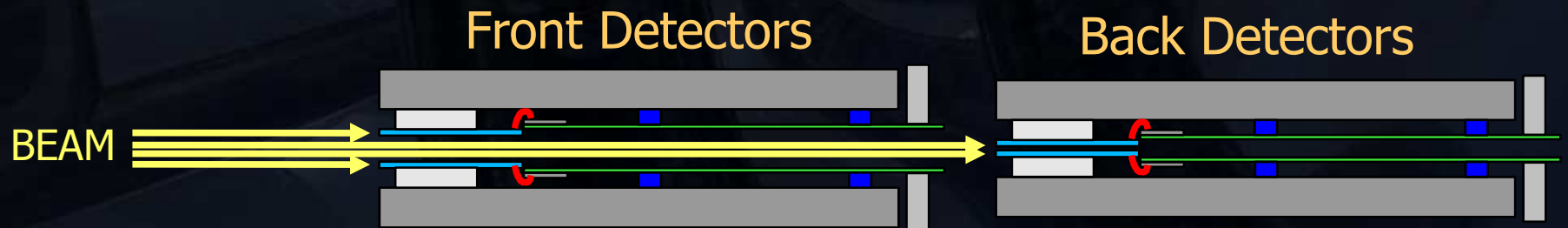
- 1994-1998 SYRMEP
(SYnchrotron Radiation for MEdical Physics)
- 1999-2002 FRONTRAD
(FRONTier RADiology)
- 2003-2006 MATISSE
(Mammographic and Tomographic Imaging with Synchrotron light Source at Elettra)
- 2007-2009 PICASSO
(Phase Imaging for Clinical Application with Silicon detector and Synchrotron radiation)

A decade of single photon counting

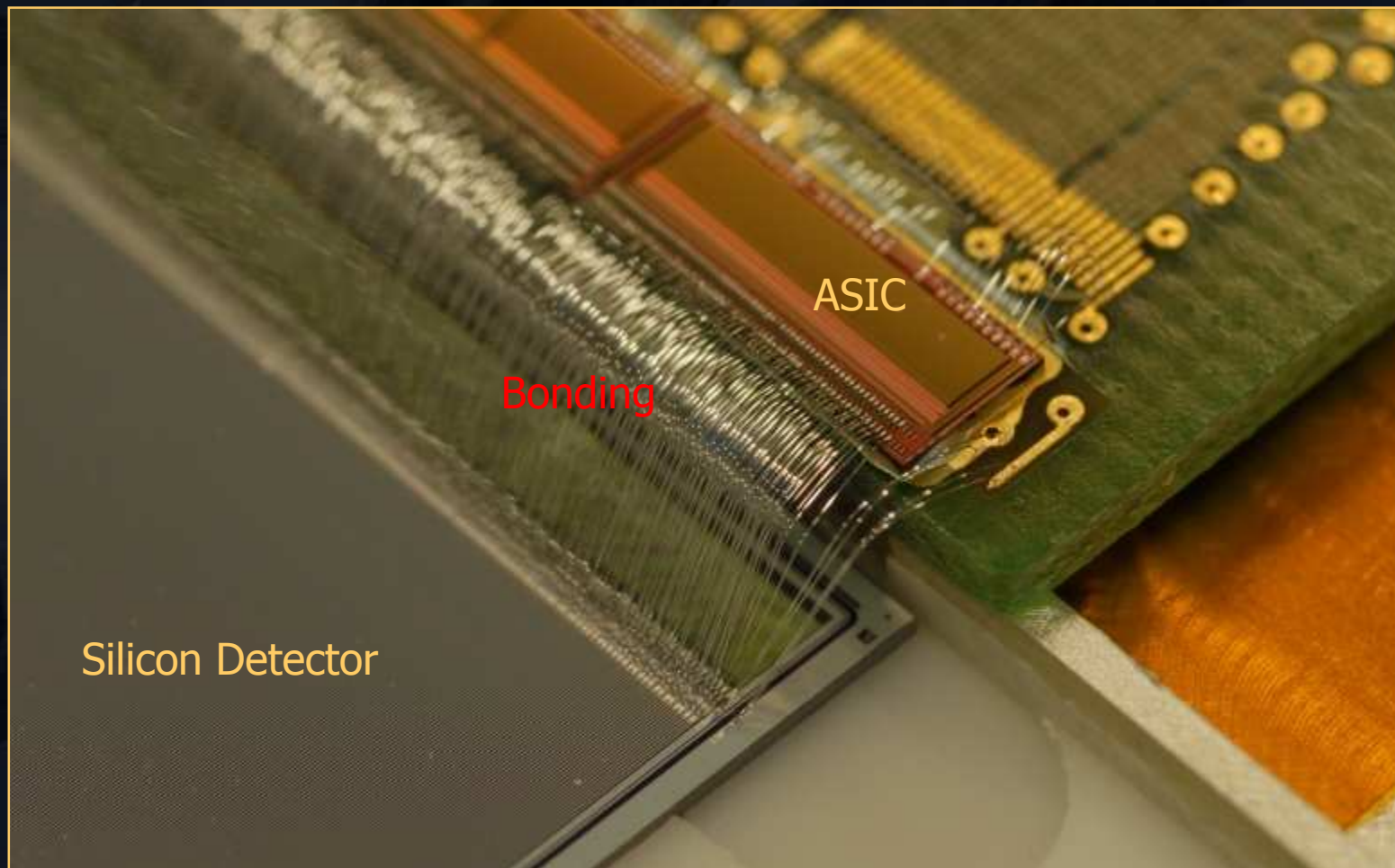
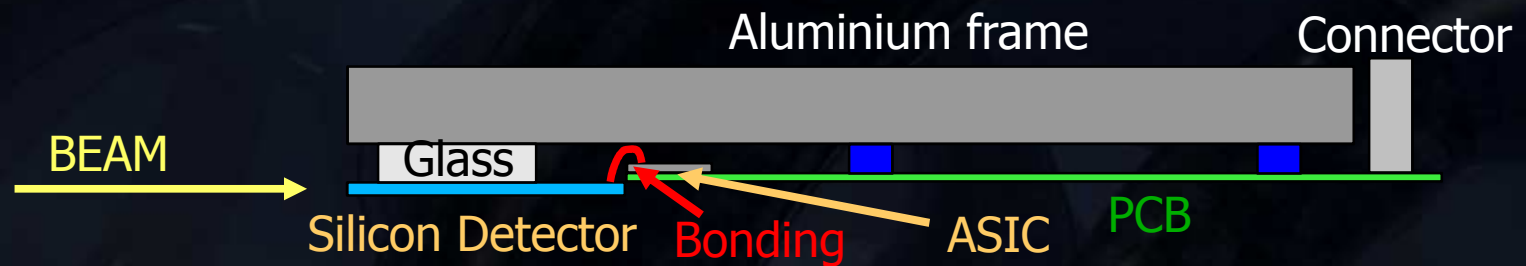
	ASIC	Channels	Pitch μm	Pixel Size $\mu\text{m} \times \mu\text{m}$ h x v	Gain mV/fC	Noise e- RMS	Max Rate MHz
SYRMEP 	CASTOR (Lepsi)	32	200	200 x 300	200	250	0.01
FRONTRAD 	FROST (Caen)	64	200	100 x 300	130	800	0.1
MATISSE 	VA64_TAP +LS64 (Ideas)	64	100	100 x 300	100	500	1
PICASSO 	Mythen II (PSI)	128	50	50 x 300	110	240	1

The PICASSO detector assembly

- A 4-layer detector to successfully exploit the beam size
- Tight requirements
 - very small spacing between layers
 - no aligned dead pixels
 - coverage of the beam width (210 mm)
 - silicon detector planarity about 10-20 μm
- Our solution
 - displacement of the modules along the beam propagation direction
 - PCB supported by an Aluminum frame and shielded from direct beam

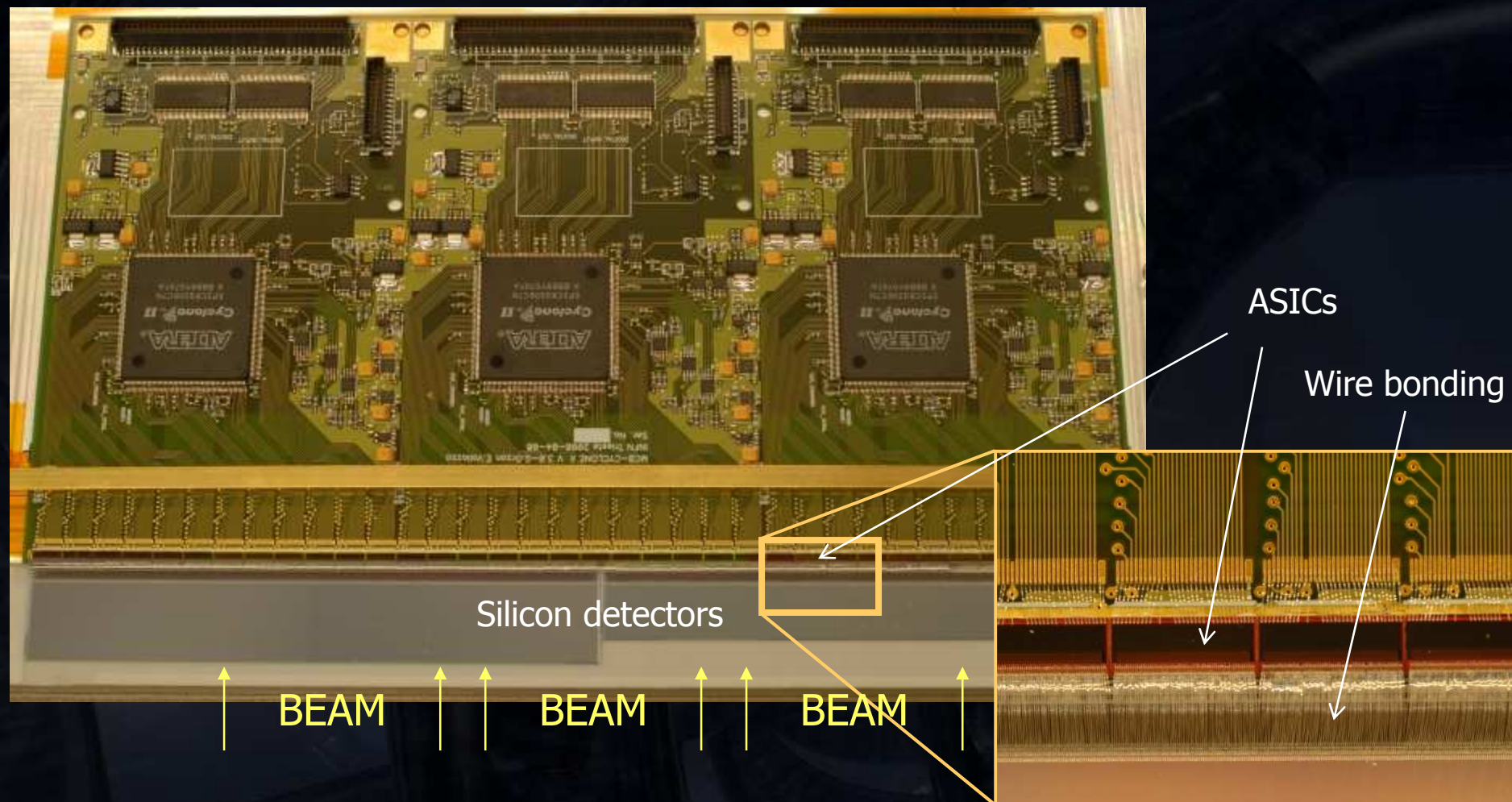


Modular design



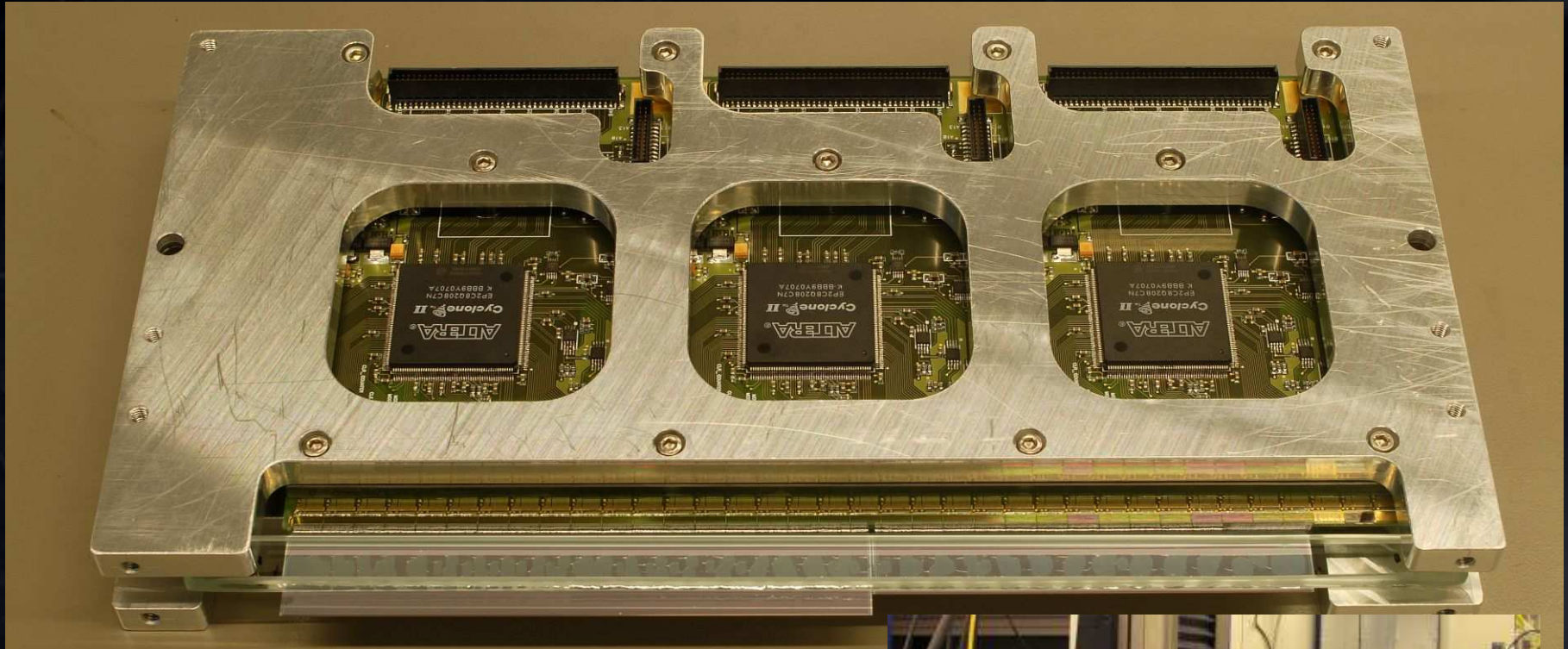
Single layer full size prototype

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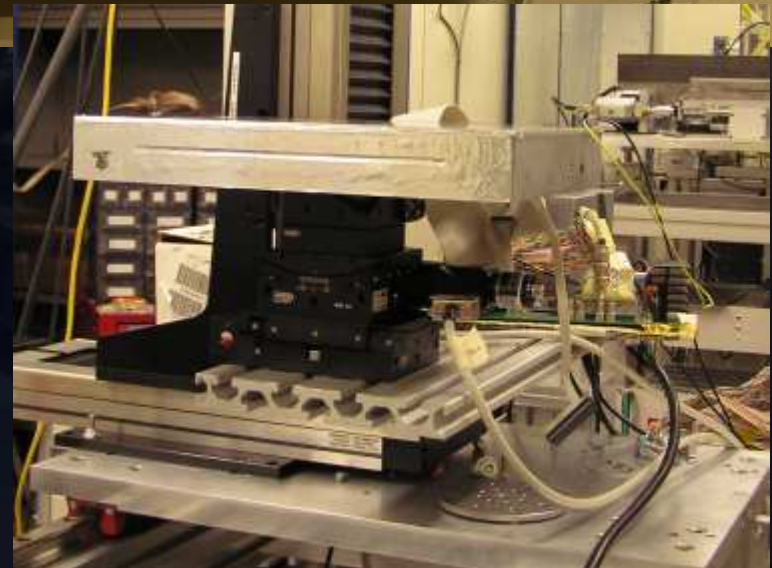


- Single layer 210 mm silicon detector
 - Use of two modules (120 mm+90 mm), 33 ASICs (4224 channels)
 - PCB hosts 3 Altera Cyclone-II FPGA for ASIC control
 - Assembled and bonded at Mipot SpA (Cormons, Italy)

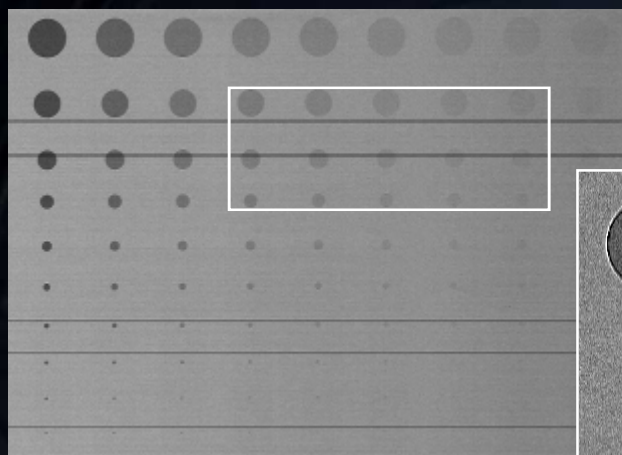
Double layer prototype



- Double layer 210 mm silicon detector
 - Assembly system developed by the mechanical workshop of INFN
 - Detectors glued to a glass bar to ensure good planarity ($\sim 20 \mu\text{m}$)
 - Tested at the SYRMEP beamline

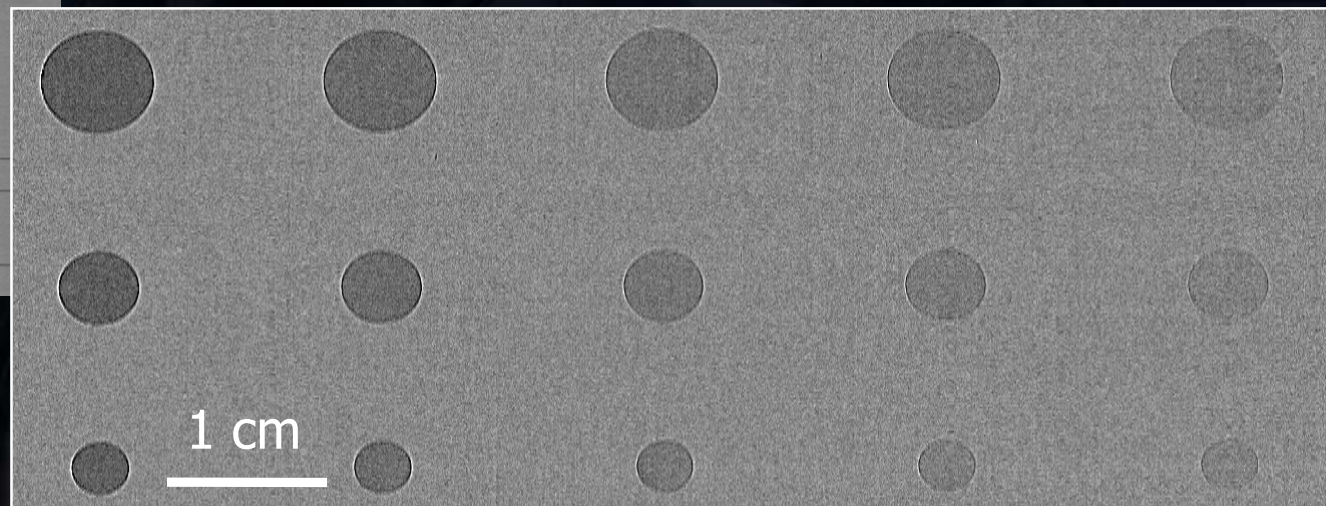


Experimental results: CD Phantom detail

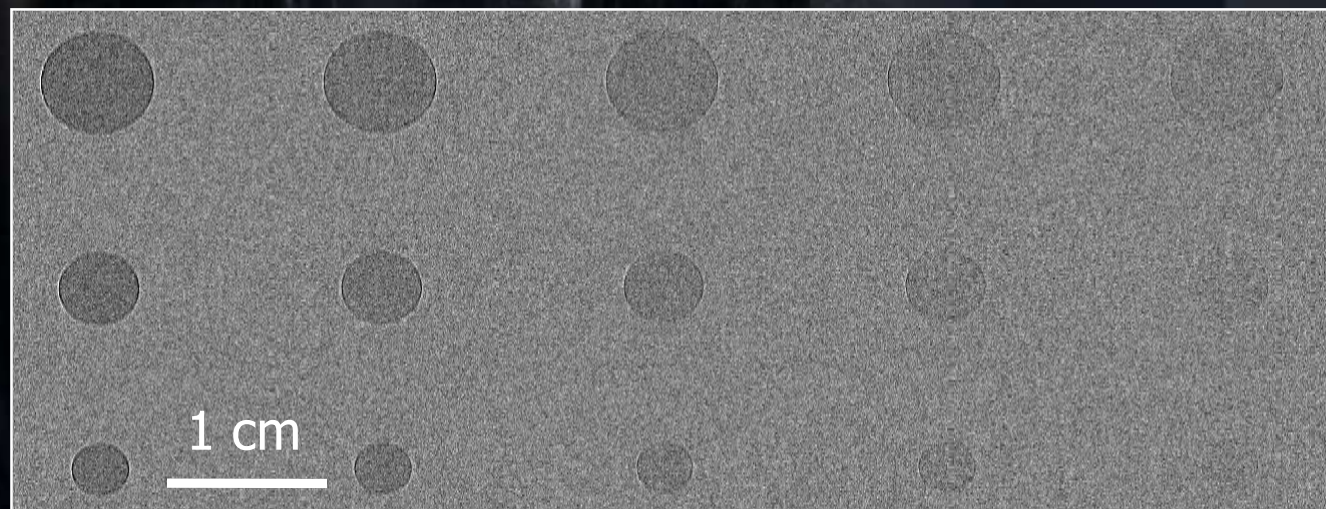


19 keV
Scanning step 100 μm , 0.015 s per step

Air Entrance dose
1.35 mGy



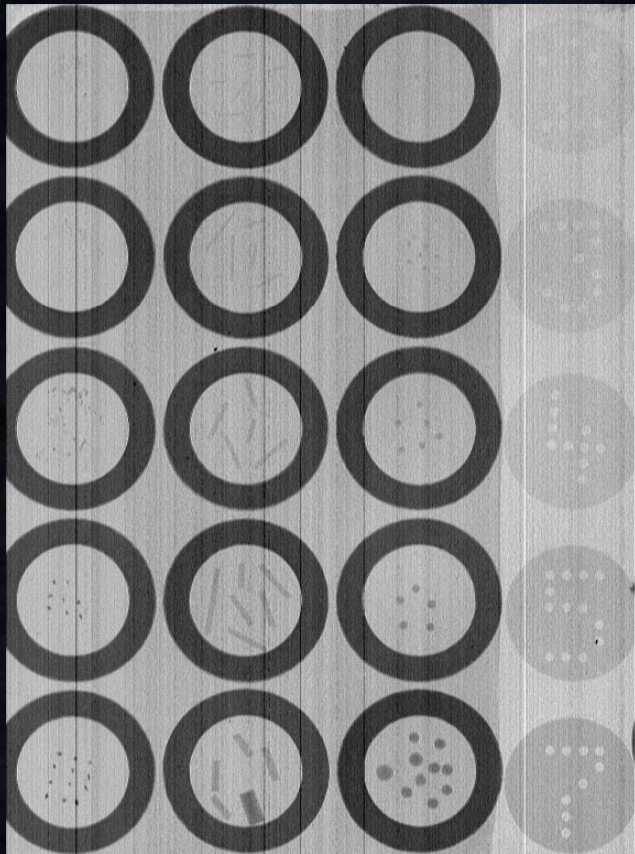
Air Entrance dose
0.18 mGy



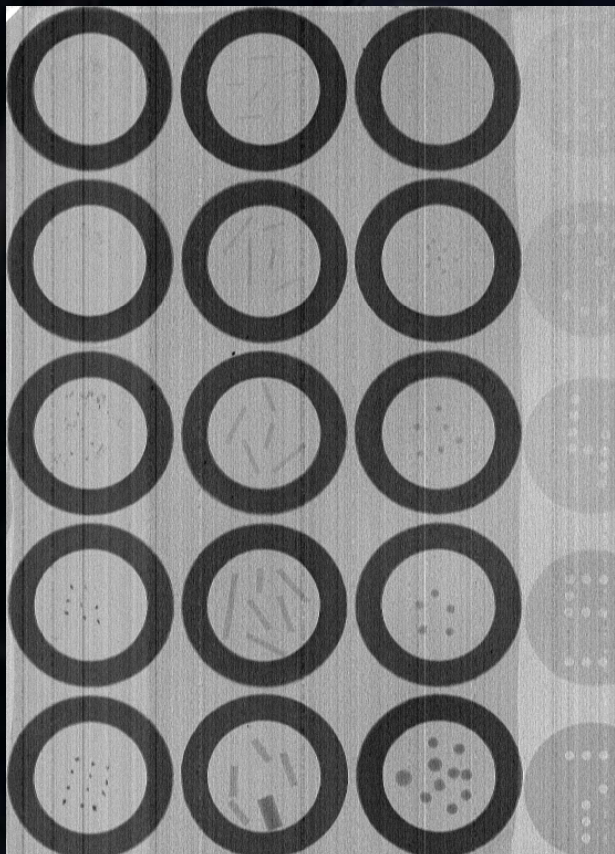
Gammex RMI 160 "Ackermann" Phantom detail

- Phantom + 30 mm Plexiglas acquired at 19.5 keV
 - Scanning step 100 μm , 0.100 s per step
 - Air Entrance dose 1.75 mGy

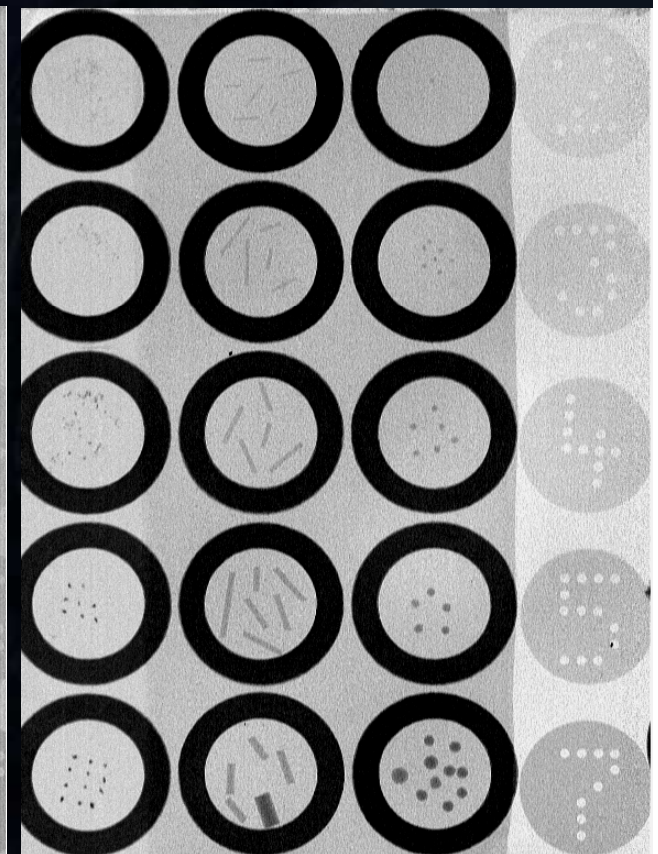
1 cm

Top layer
Raw image



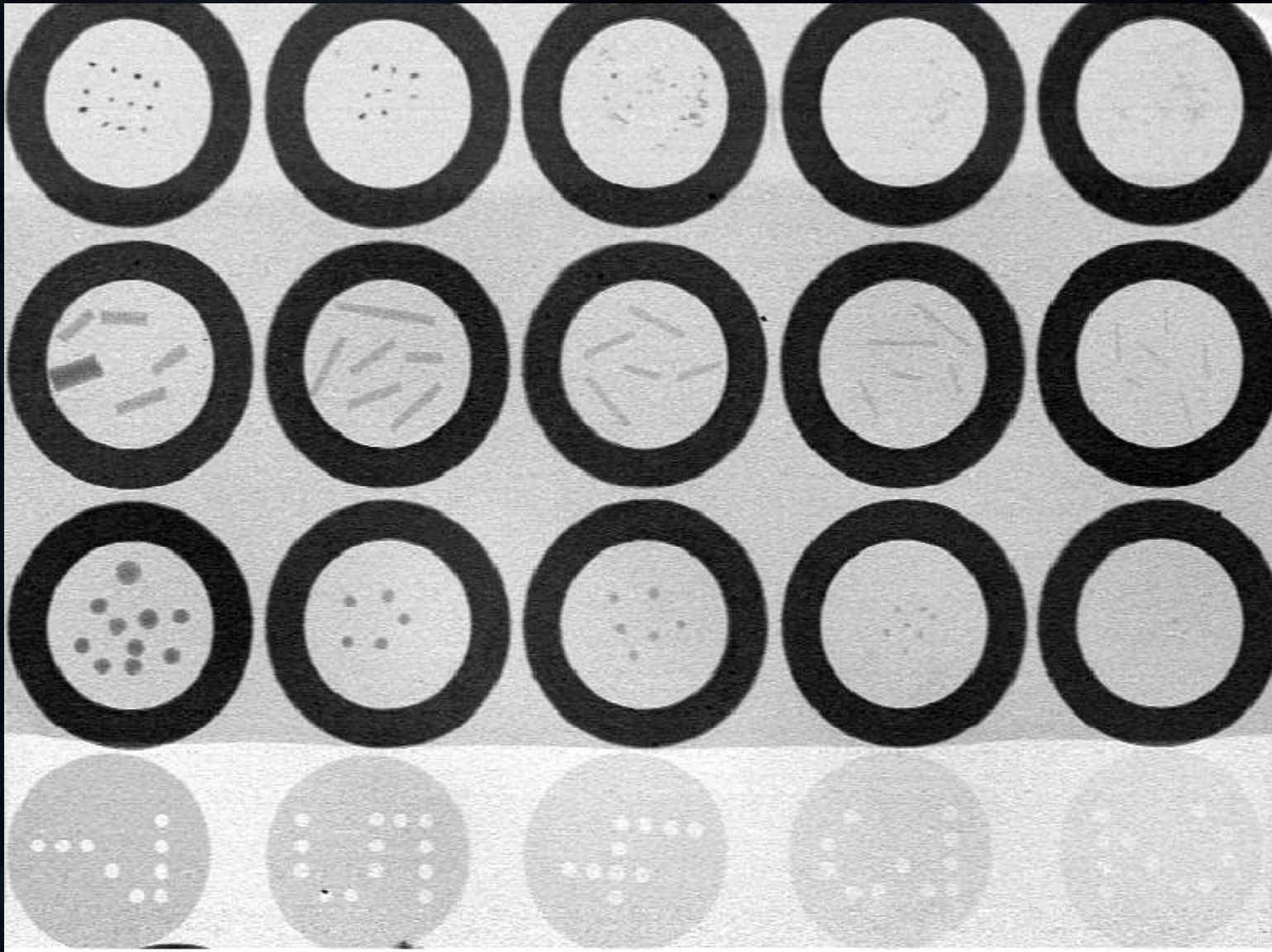
Bottom layer
Raw image



Summed and normalized
image

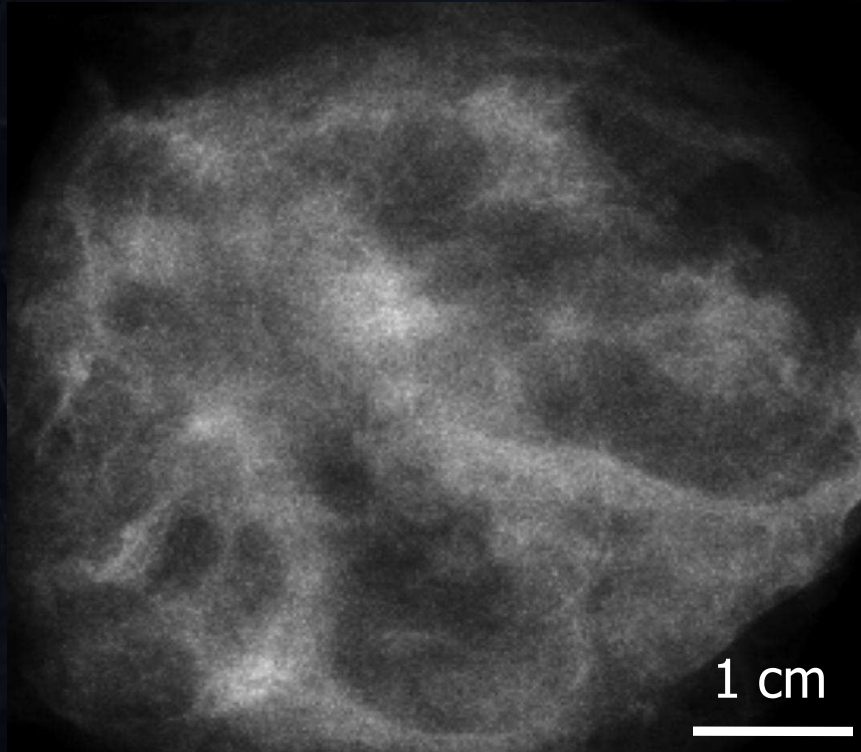
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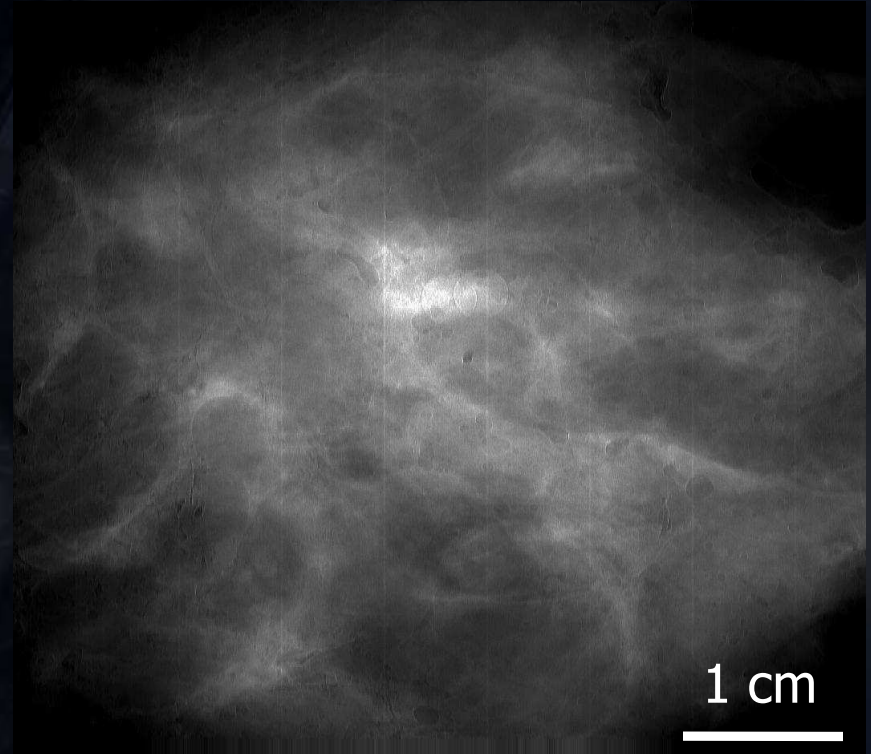
In vitro breast tumor tissue

Agfa Image Plate mammographic system



Ro/Ro Anode/Filter
7 mAs, 28 kVp
Air entrance dose ~ 0.6 mGy

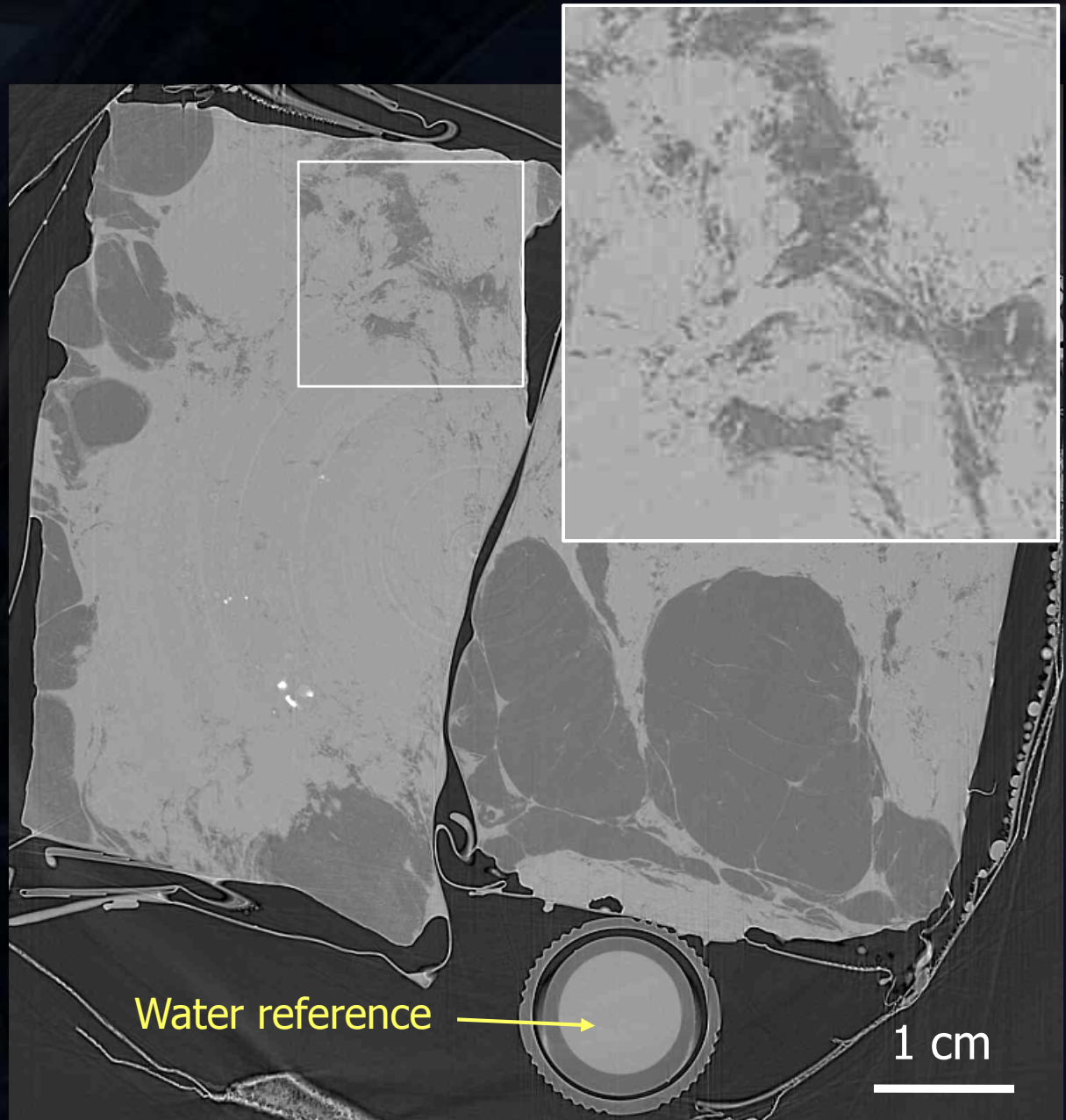
PICASSO single layer detector



Energy 23 keV
Scanning step 200 μ m
Exposure time 80 ms/step
Air entrance dose ~ 0.4 mGy

Breast Tissue Tomography

- Accurate measure of linear attenuation coefficient of breast tissue
- Slice reconstructed from 2400 projections on 180° (angular step 0.075°)
- Energy 23 keV
- Exposure time 1s per projection
- High dose



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Concluding Remarks

- The SYRMEP group is operating a beamline dedicated to *in vivo* mammography at ELETTRA
- The clinical mammography project started in 2006
 - 55 patients have been examined so far using a conventional screen-film system
 - clear evidence that SYM outperforms FFDM in visualizing
 - lesions
 - glandular structure relevant for the diagnosis
- A very promising detection system based on a silicon microstrip detector and the Mythen-II ASIC has been developed, showing:
 - High efficiency
 - Remarkable spatial and contrast resolution
 - Single photon counting capability up to ~ 1 MHz
 - Excellent uniformity over $\sim 2 \times 4200$ channels counting simultaneously

Future Work

- A more extended statistics could lead to a more comprehensive study
- We plan to reach ~ 70 patients by the end of the year, increasing
 - the recruitment pool
 - the shifts dedicated to the patients program
- In 2009 we aim at tackling the digital program, possibly using the PICASSO detector



Thank you!

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