ClearPEM-Sonic: a multimodal PET-ultrasound mammography system

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on behalf of the ClearPEM-Sonic Collaboration

Outline

- Introduction
- ClearPEM
- Aixplorer
- Multimodality
- First clinical results
- Conclusions

Introduction

- **ClearPEM-Sonic**: an international project developed in the frame of **CERIMED**, with the co-operation of the **Crystal Clear Collaboration:**
  - **Academic partners**: CERN, Univ. Aix-Marseille II, Univ Milano-Bicocca, VUB-Brussels, LIP-Lisbon, LMA-CNRS
  - **Industrial partners**: PETsys, SuperSonic Imagine
  - **Clinical partners**: AP-HM Marseille, Cancerpole PACA, Inst. Paoli Calmettes Marseille

- Aim to develop an imaging tool that can **improve the diagnosis of breast cancer**

- **CERIMED**, European Centre for Research in Medical Imaging:
  - A center of excellence for the development of molecular imaging technologies
  - A multidisciplinary community involving medical doctors, biologists, chemists, physicists and industry representatives
  - *http://cerimed.web.cern.ch/*

Motivation

Breast Cancer

- High incidence rate, about 1 every 8 women affected during lifetime
- Second cause of cancer death among women
- Early detection greatly improve survival rates
- Screening recommended starting at 50 years old

Standard diagnosis

- High rate of false positives (especially for MRI)
- Xray and US issues (e.g. dense breasts)
- Large number of unnecessary biopsies (60-85%), high costs and risks for the patient
- Metabolic information is needed!

Whole-body PET

- High specificity but poor spatial resolution
- Open geometry, very sensitive to background from chest
- Low sensitivity for mammography
- Expensive and bulky, not adapted to systematic screening

Clear need for a dedicated device that combines **morphological** and **metabolic** information, in order to get good **sensitivity** and **specificity**

ClearPEM-Sonic

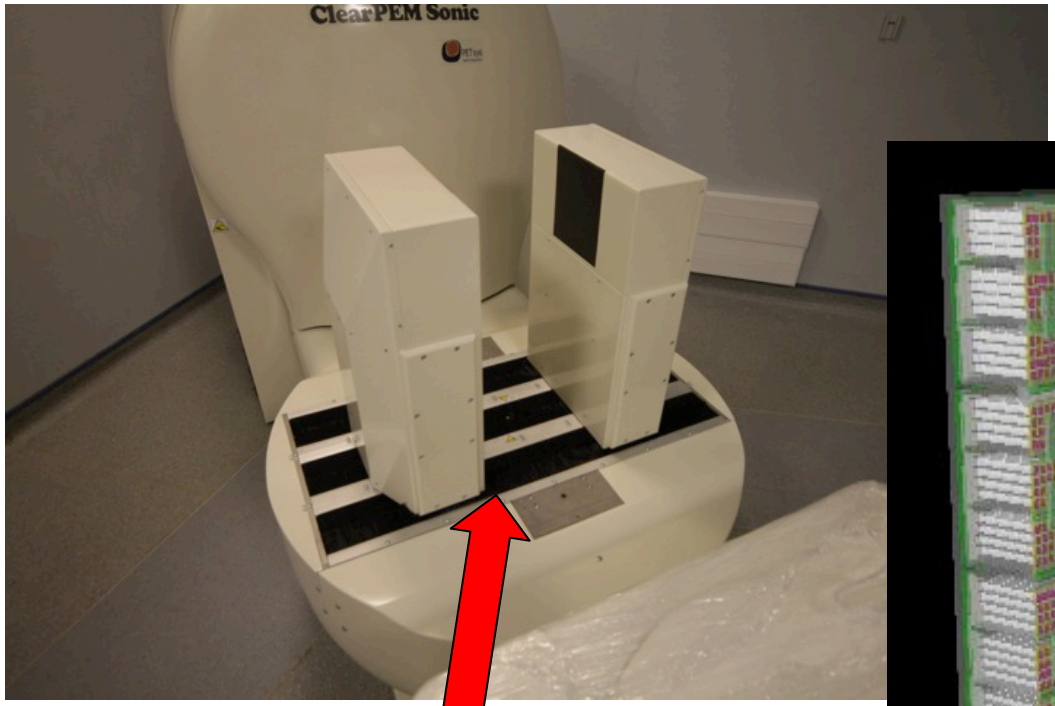
ClearPEM

- Metabolic information (specificity)
- Possibility to perform axillary exams
- High system sensitivity
- Very good spatial resolution

SuperSonicImagine Aixplorer

- Morphological information
- Conventional 3D Ultrasound imaging
- Real time ShearWave Elastography
- Local and global elasticity (specificity)
- Acoustic signature and vascularization

ClearPEM detector



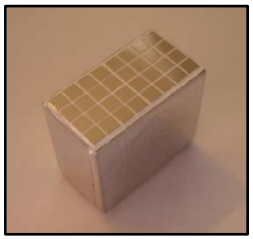
The ClearPEM detector **heads**

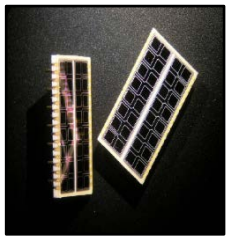
ClearPEM

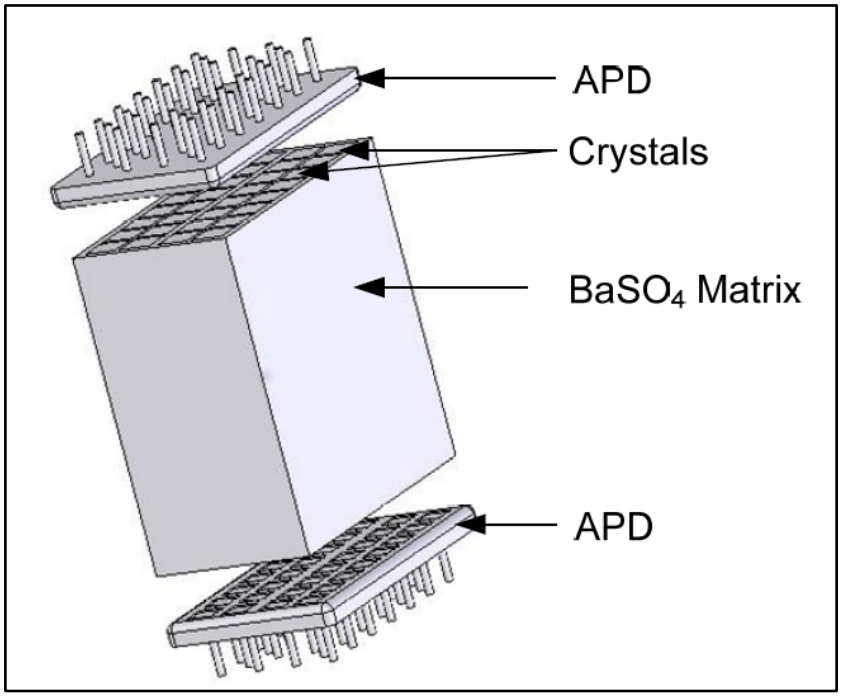
- Developed by the **Crystal Clear Collaboration** → know-how of HEP (CMS-ECAL) applied to medical imaging

- Two prototypes: **ICNAS** – *Coimbra*, and **Hopital Nord** – *Marseille*

- **Detector Design**:
  - 6144 2x2x20 mm^3 **LYSO** crystals
  - 192 **matrices** of 4x8 crystal
  - **$BaSO_4$** acting as matrix structure and reflector
  - For each matrix, 2 Hamamatsu S8550 4x8 **APD** matrices → each crystal has double readout for depth of interaction
  - 8 **supermodules** (4 for each plate)
  - Packing fraction about **52%**
  - **Fast front-end readout** with dedicated ASICs



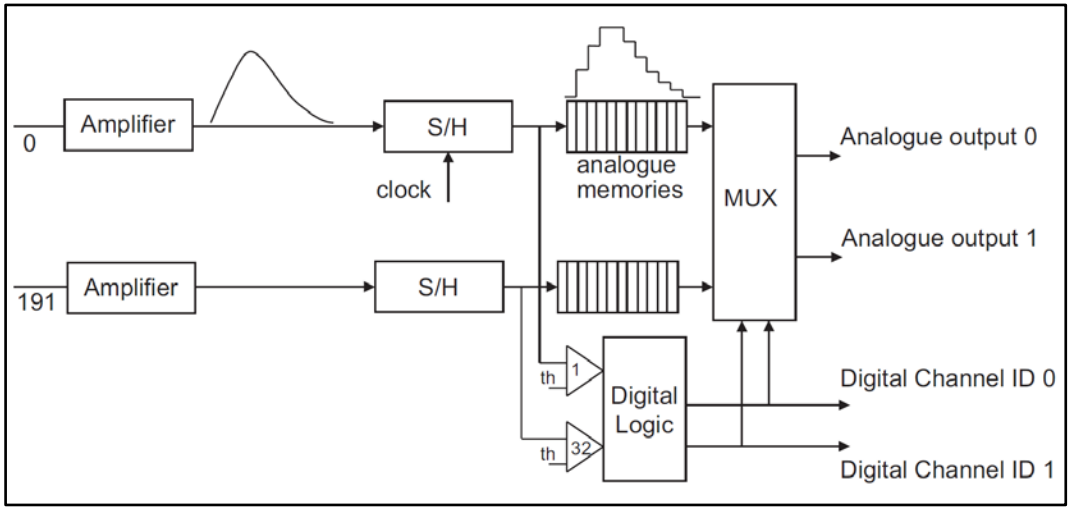




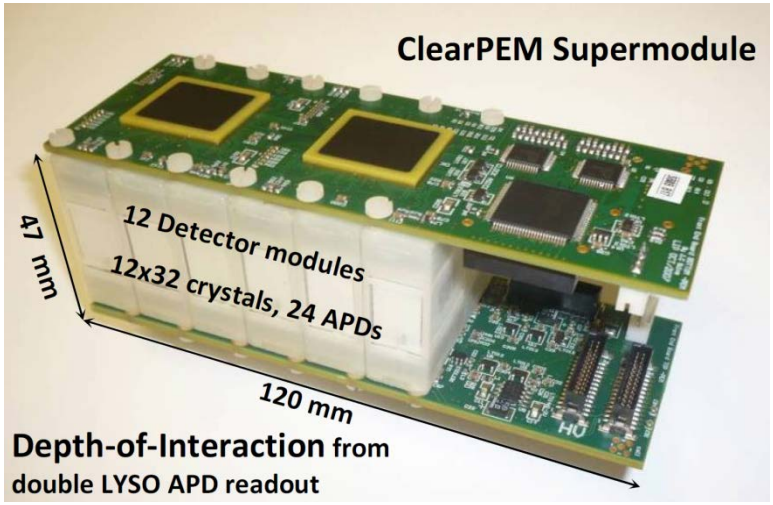
- Image reconstruction through **2D-OSEM**, **3D-OSEM** and **ML-EM** algorithms

Front-end electronics

- Developed by **Laboratório de Instrumentacão e Física Experimantal de Partículas** (LIP)
- Signal amplification, channel selection and analog multiplexing, analog to digital conversion, parallel to serial translation
- Requirements of **low noise** (input ~30fC) and **low power** dissipation



E. Albuquerque *et al,* NIM A 598 (2009) 802



Front-end ASIC:

- Technology: AMS 0.35 µm CMOS, 70 mm^2 area
- Input: 192 APD channels
- Output: 2 highest channels
- Clock frequency 30-120 MHz
- 3.2-3.6 mW/channel

Front-end Electronic Boards:

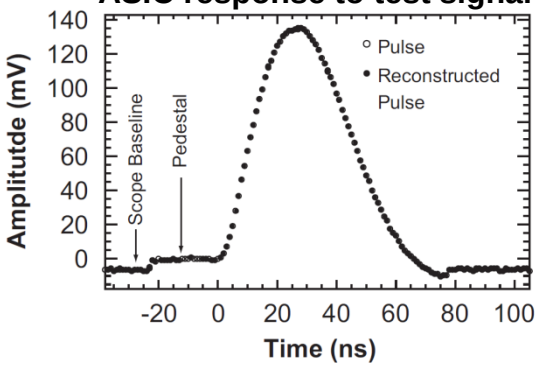
- 2 Front-end ASICs (50 MHz)
- 2 free sampling dual 10-bit ADC (50 MHz)
- 1 LVDS ChannelLink transmitter (2.4 Gbps)

Detector performance

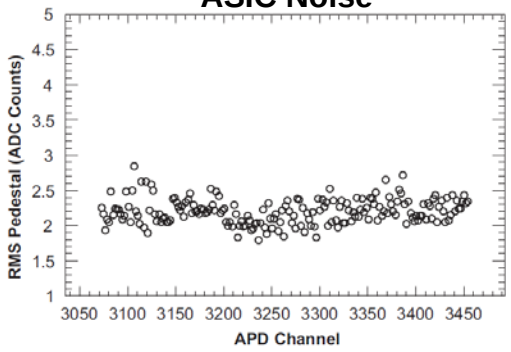
Front end electronics:

- Amplifier rise time = 30ns
- Shaping time = 60ns
- Very low baseline variation
- Low noise (~2% @ 511 KeV)

ASIC response to test signal



ASIC Noise

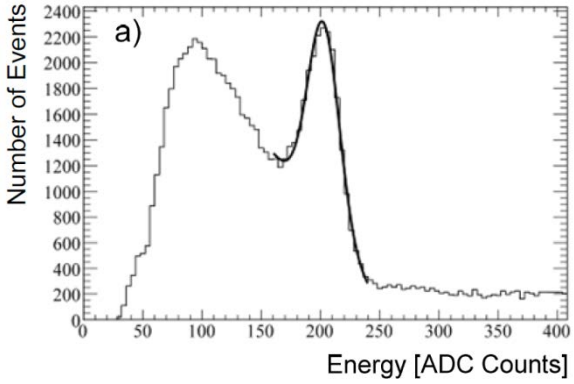


E. Albuquerque *et al,* NIM A 598 (2009) 802

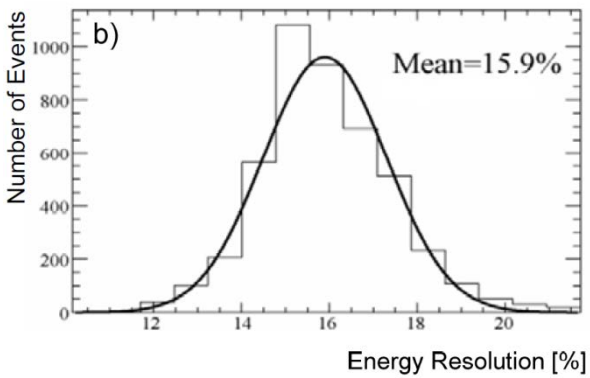
Overall performance:

- Large solid angle coverage **+** high photon interaction prob. **= high system sensitivity**
- Crystal segmentation (2x2mm) **+** Depth Of Interaction **= good spatial resolution**
- Average energy resolution of 15.9%
- Coincidence time resolution 5.2 ns FWHM

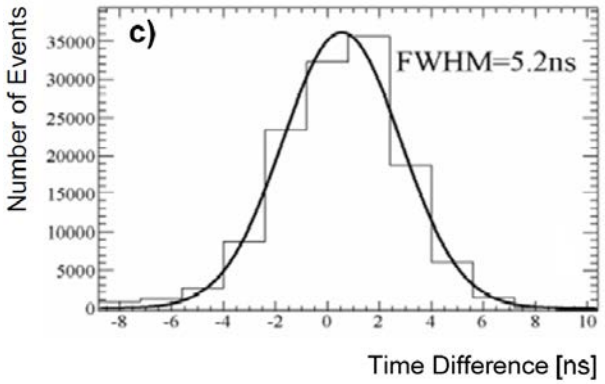
Tipical 511 KeV peak



Mean Energy Resolution



Mean time coincidence resolution



E. Albuquerque *et al,* NIM A 598 (2009) 802

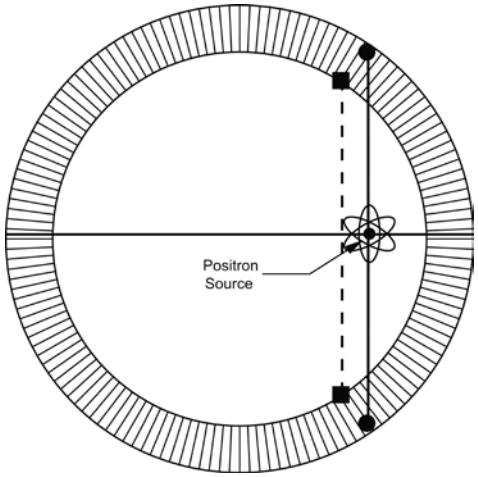
Depth Of Interaction

Depth of interaction (DOI) affects image reconstruction:

- Parallax error for photons not parallel to scintillator main axis
- Degrades spatial resolution!
- Asymmetry in light yield at both extraction surfaces allow determination of interaction point

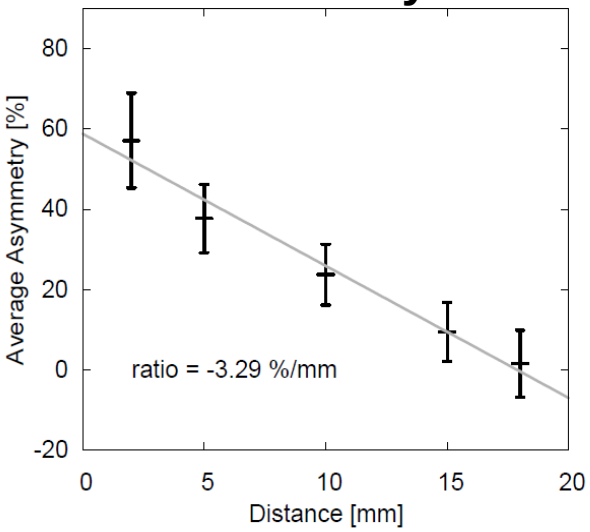
$$Asymm. = \frac{A_1 - A_2}{A_1 + A_2}$$

A_1 = pulse area on face 1
A_2 = pulse area on face 2

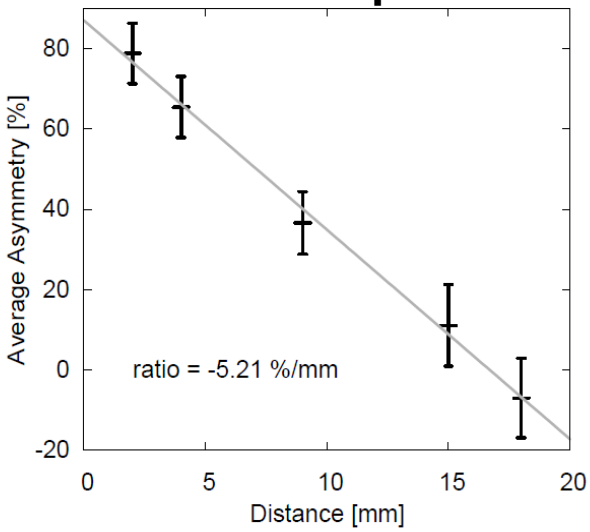


=> DOI improvement **depolishing** one lateral crystal surface

Polished crystal



One face depolished



B. Frisch, PhD Thesis, Technische Universitaet Wien, Vienna, 2012

- Depolishing improves DOI without affecting too much Light Yield

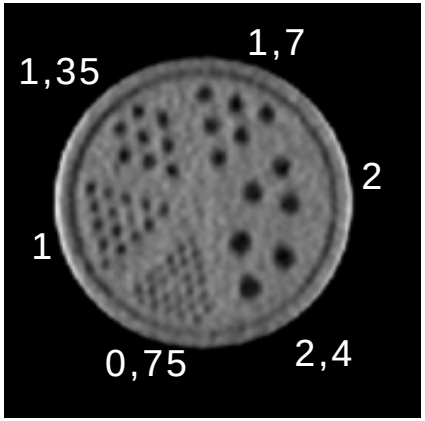
	LY (Ph/MeV)	α_{DOI} (%/mm)
Polished	18600	3.29
Depolished	17500	5.21

=> DOI resolution **~3mm**

Spatial Resolution

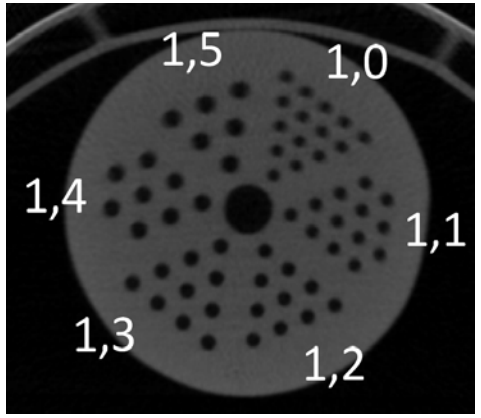
Derenzo-type phantoms used to asses the spatial resolution of ClearPEM

Ultra Micro Hotspot Phantom
CT image

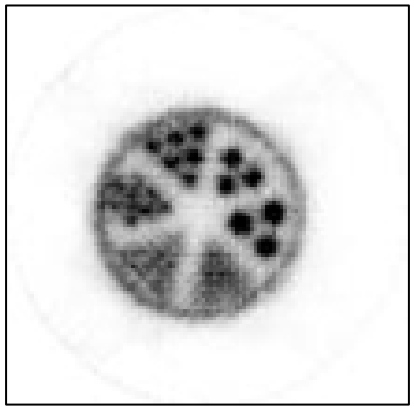


- Phantoms filled with ^{18}F-FDG
- Distance between center of 2 rods is equal to twice the rod diameter
- 20 minutes acquisition, 50 MBq

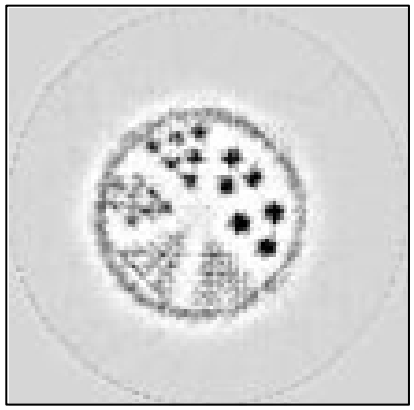
Bioscan mini-Jaszczcak Phantom
CT image



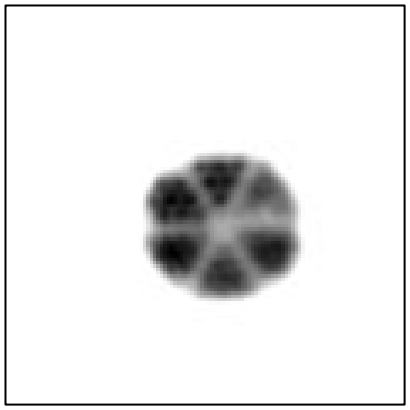
ClearPEM Raw image



ClearPEM high contrast image



ClearPEM Raw image



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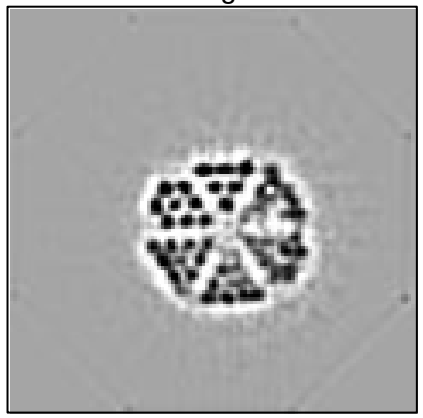

B. Frisch, PhD Thesis, Technische Universitaet Wien, Vienna, 2012

Spatial Resolution

Derenzo-type phantoms used to asses the spatial resolution of ClearPEM

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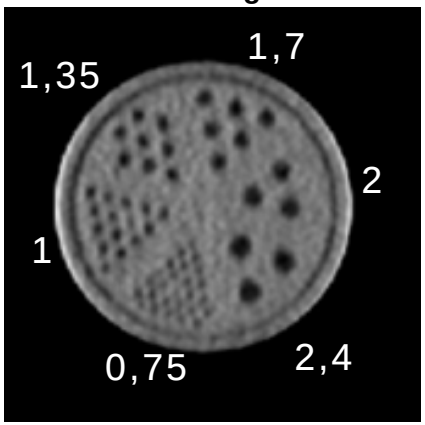
CT image

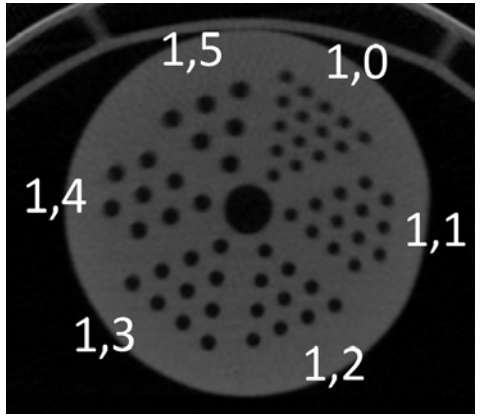


- Phantoms filled with ^{18}F-FDG
- Distance between center of 2 rods is equal to twice the rod diameter
- 20 minutes acquisition, 50 MBq

- Confirmed spatial resolution:

1.4 mm

Bioscan mini-Jaszczcak Phantom
CT image



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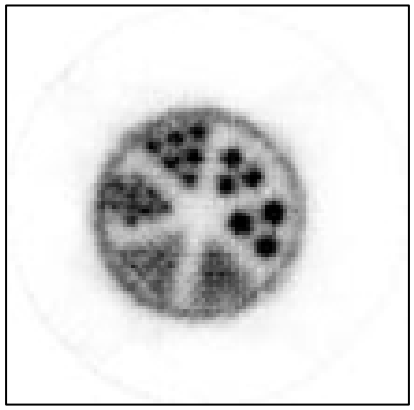

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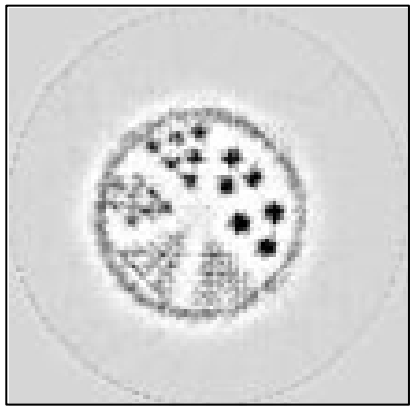

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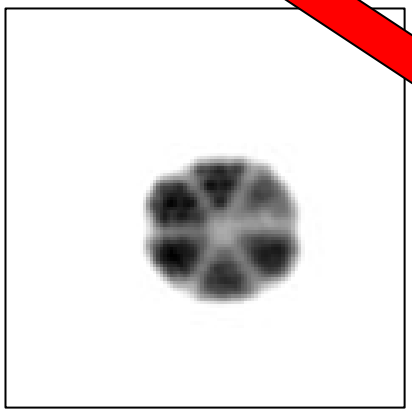
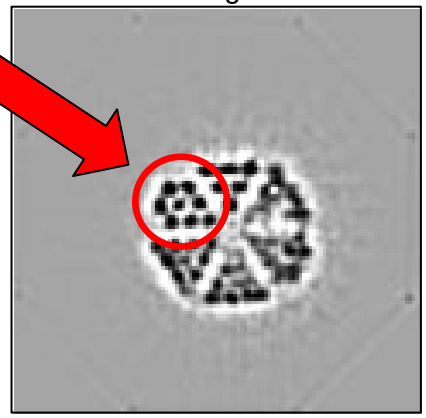


ClearPEM high contrast image



B. Frisch, PhD Thesis, Technische Universitaet Wien, Vienna, 2012

Elastography

- B-mode US → density, variations within few %
- Elastography → Young's modulus

$$E \overset{\text{def}}{=} \frac{\sigma}{\varepsilon}$$

σ = *uniform compression*
ε = *tissue deformation*

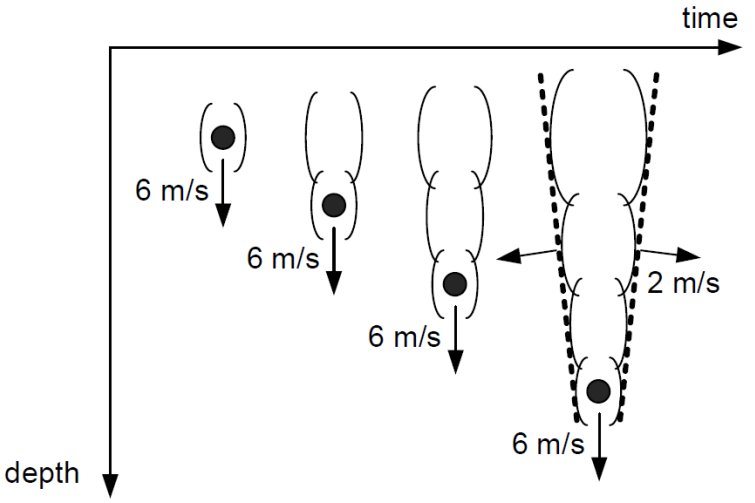
Tissue type	Young's mod. (kPa)	Density (g/dm³)
Normal Fat	18-24	1000 ± 8%
Normal Glandular	28-66	
Fibrous Tissue	96-244	
Carcinoma	22-560	

Great stiffness variation, important diagnostic value → **specificity**

Elastography principle:

- US beam focused at a certain depth in the tissue
- Dipolar source of shear waves (mainly transverse)
- Shear source moved at supersonic speed
- Share wave interfere constructively, Mach cone

- Quasi-planar shear wave deformed by regions of varying stiffness
- US waves used to register this deformation
- Elasticity map is computed



B. Frisch, PhD Thesis, Technische Universitaet Wien, Vienna, 2012

Aixplorer

SuperSonic Imagine Aixplorer

- **B-mode**:
  - linear array of transducers mechanically moved to get a 3D image volume
- **Elastographic mode**:
  - share wave created in 2ms
  - imaging of share wave in 18ms
- Acquisition volume **40x40x40 mm³** in 20 seconds
- Voxel size **100x100x75 µm³**

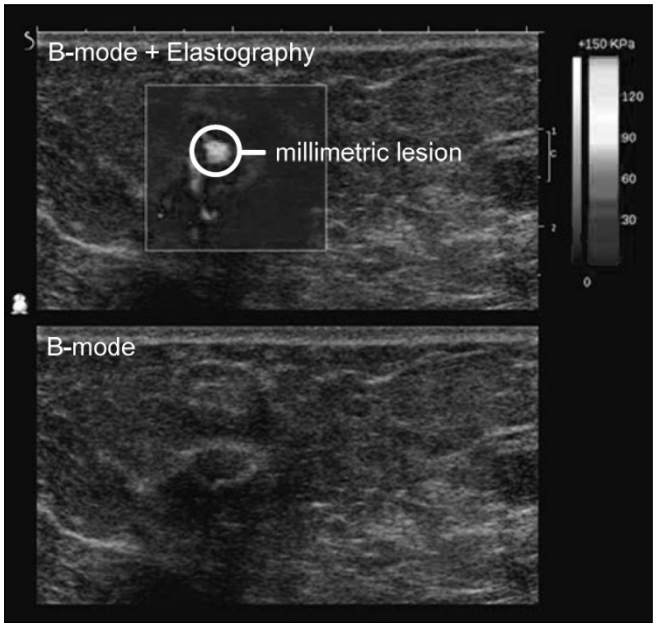


**Image courtesy of SuperSonic Imagine*

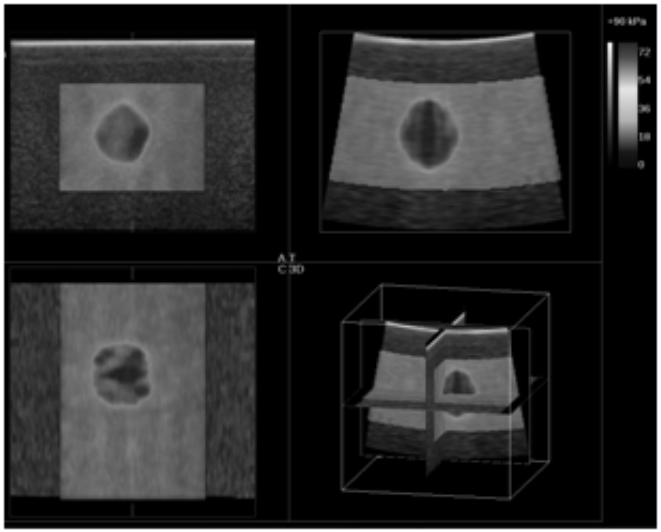


**Image courtesy of SuperSonic Imagine*

Image acquired in clinical test:

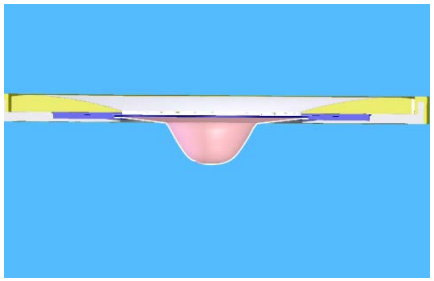
- Standard B-mode does not show any anomaly
- Elastography reveals a **spot of hard tissue**
- Biopsy confirms **malignant lesion**

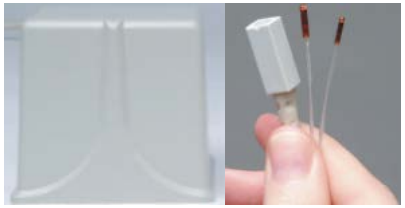
Multimodality

ClearPEM and Aixplorer are integrated into a **single multimodal imaging system**

Technical solutions

- Conical breast contention
- US probe fixed to a mechanical arm
- Spatial localization of the US probe with a magnetic tracking system

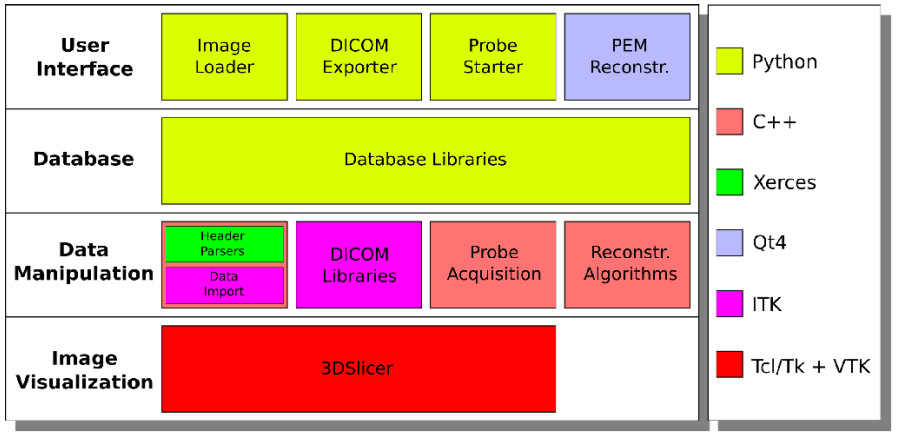




B. Frisch, IEEE NSS/MIC 2011 Conference Record, pp. 2267–2272

Software solutions

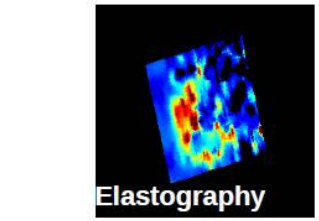
- Control of tracking system
- Monitoring of PEM image reconstruction
- Database manipulation
- Co-registration of volumes from different modalities, image visualization
- User-friendliness
- Compliance with medical imaging standards



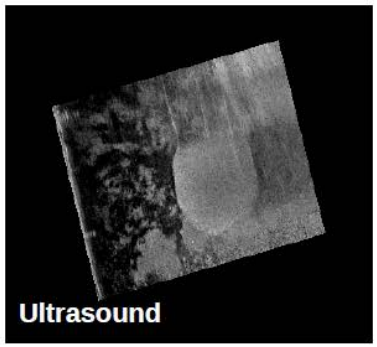
M. Pizzichemi et al, 13th ICATPP Conference Record, 2011

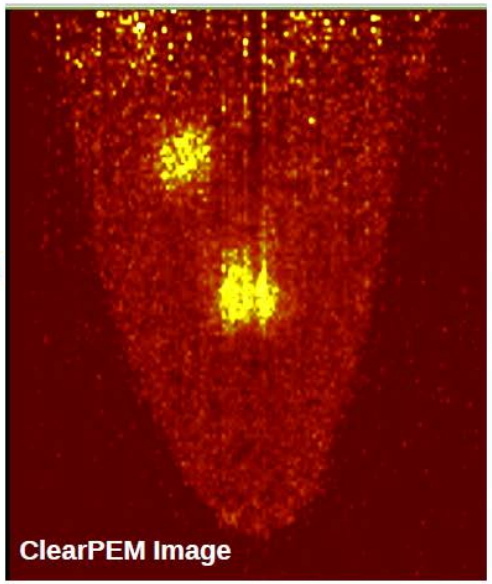
Multimodality

- Multimodal images acquired on Agar-Agar gelatin Phantom with hot lesions
- Proof of automatic co-registration



OR





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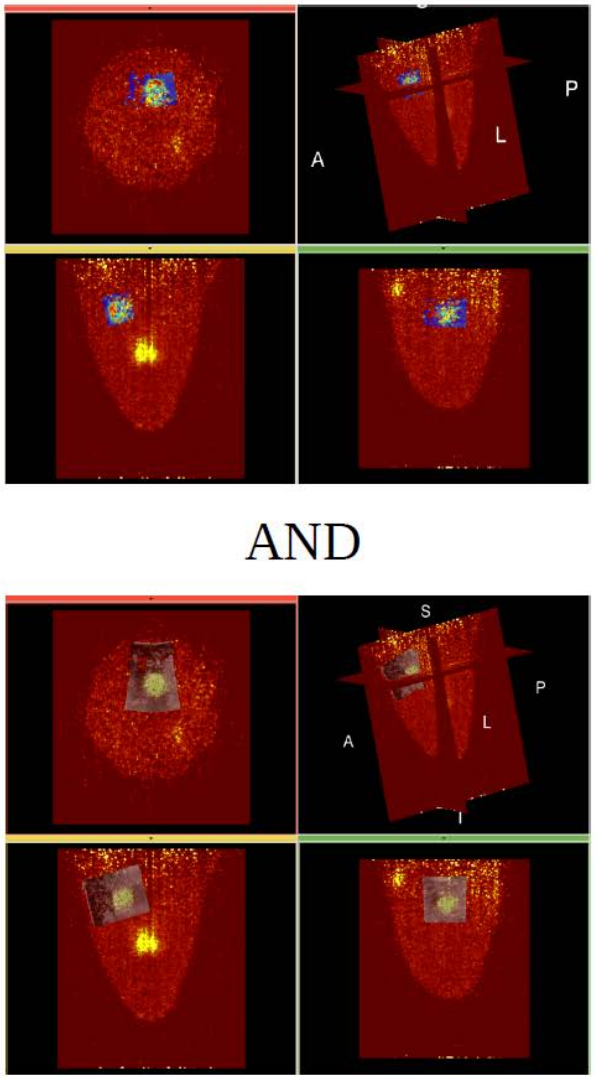
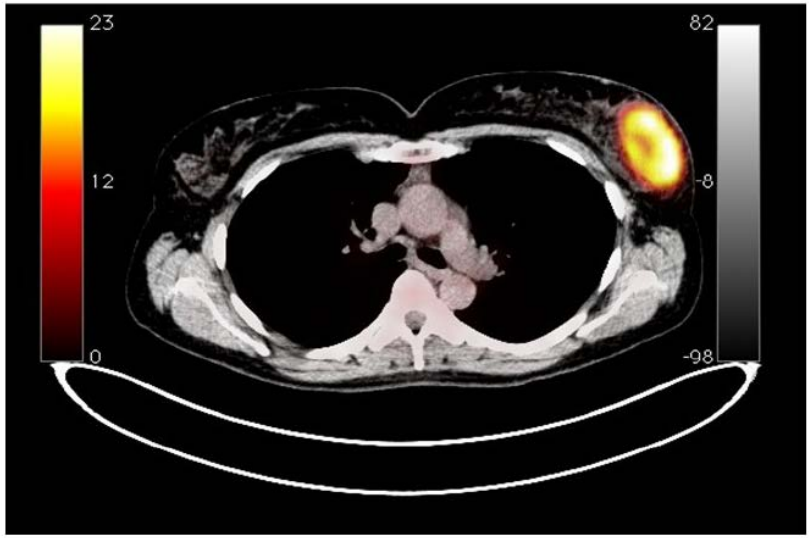


B. Frisch, IEEE NSS/MIC 2011 Conference Record, pp. 2267–2272

First clinical results

First **clinical trial** on 20 patients is ongoing at Hopital-Nord, Marseille:

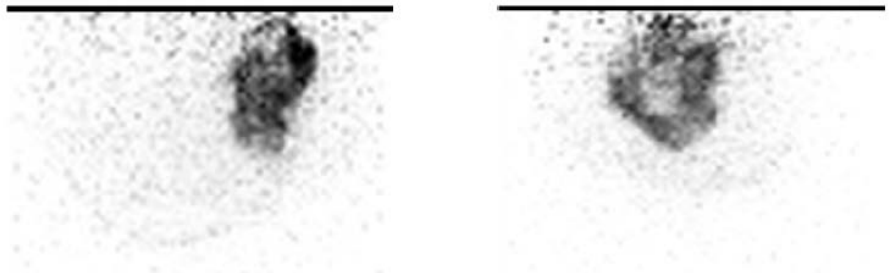
- Compare results with other modalities (US, CT, WB-PET, MRI)
- Evaluate how the patient tolerates the exam
- Optimize acquisition protocol
- Biopsy as a gold standard



Whole-body PET/CT

Infiltrating Ductal Carcinoma

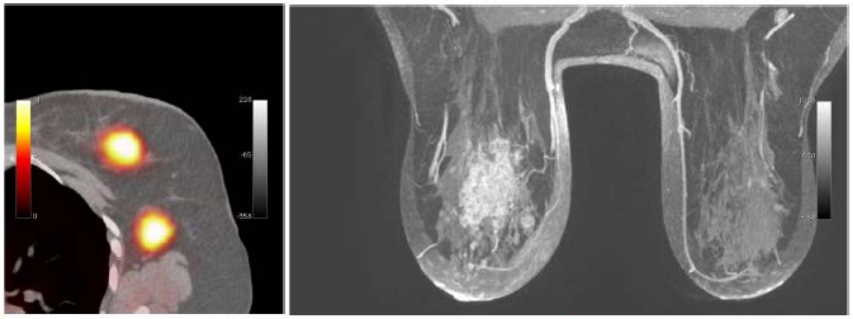
- Left breast carcinoma visible in WB-PET as well as in ClearPEM-Sonic
- Breast tumour of sufficient size to be seen on whole-body PET is also seen in ClearPEM-Sonic


Sagittal ClearPEM-Sonic Coronal ClearPEM-Sonic

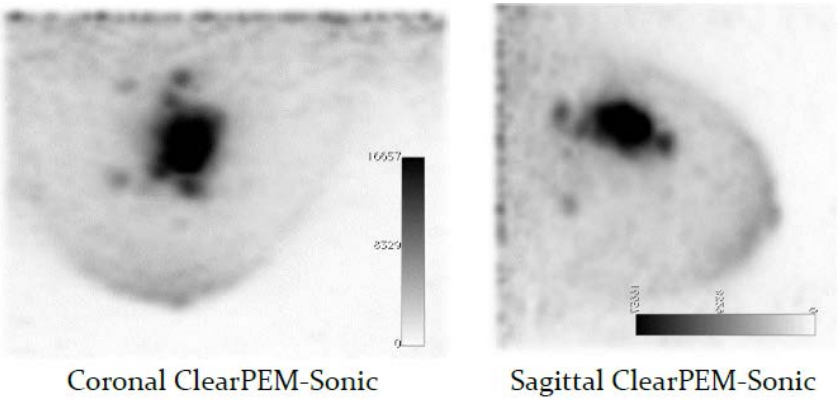
B. Frisch, IEEE NSS/MIC 2011 Conference Record, pp. 2267–2272

First clinical results

Multifocal Breast Cancer



Whole-body PET/CT MRI



Coronal ClearPEM-Sonic Sagittal ClearPEM-Sonic

B. Frisch, M. Pizzichemi *et al*., "Towards Multimodal Positron Emission Mammography and Ultrasonography: the ClearPEM-Sonic Project" IEEE Transaction on Medical Imaging, *in review*

- MRI exam shows small lesions around main lesion in left breast
- Whole-body PET/CT not able to distinguish small lesions
- Multifocal lesions are clearly seen in ClearPEM-Sonic

Compared to Whole-body PET, ClearPEM has

- Better spatial resolution
- Higher sensitivity

Conclusions

- ClearPEM-Sonic: multimodal mammography scanner that combines morphological and metabolic information, aiming towards the improvement of breast cancer diagnostic
- Development of High Energy Physics research (CMS-ECAL) applied to medical imaging
- ClearPEM results:
  - Spatial resolution = 1.4 mm
  - Average energy resolution = 15.9%
  - DOI resolution = 5.2 %/mm
- Airxplorer results:
  - 3D B-mode and Elastography
  - Acquisition volume = 40x40x40 mm^3
  - Voxel size = 100x100x75 μm^3
- PET and Ultrasound integrated into a single multimodal imaging system
- First clinical results show better sensitivity and specificity when compared to whole-body PET
- ClearPEM-Sonic about to be moved to San Gerardo Hospital, near Milano, to complete the clinical tests
- Development of an improved version of ClearPEM-Sonic has started