Application of computer models for advancement of X-ray breast imaging techniques

Grand Hotel Santa Lucia Napoli

Phase contrast mammography with synchrotron radiation

Alberto Bravin

European Synchrotron Radiation Facility (Grenoble, France)
THANKS

To MAXIMA organizers for their kind invitation

To all collaborators

A special thanks to:
- Prof. Paola COAN, LMU, Munich
- Dr. Alberto MITTONE, ESRF
- Prof. T. Peters, London, Canada
WHAT IS A SYNCHROTRON?

“A very large microscope to see deep inside matter”

- A source of X-rays produced by relativistic electrons of special characteristics:
  - Extremely intense: the most intense on earth
  - Highly collimated
  - Brilliant
  - Tunable in energy
Why is SR interesting for imaging and therapy?

- $\sim 10^6/10^8$ more intense than medical X-ray generators or LINACS
- tunable monochromatic energy
- parallel beam
- (sub)micrometric spatial resolution
SR is produced by electrons with relativistic energies circulating in a ring.

Synchrotron machine scheme:

1 injector  2 transfer line  3 booster  
4 storage ring  5 beamline  6 exp. station

SR is a very intense source of radiation from Infra Red to hard X-rays.
3 larger facilities
5 with dedicated medical beamlines
Breast cancer: First mortality cause for women in western countries

Diagnosis is simple in a fatty breast (radiotransparent)

Fat - Glandular tissues

90%/10%  10%/90%

Tumors in dense breasts are masked by tissues
Challenges in mammography

“~10% of palpable malignant tumours are not visible in mammography (dense breast, infiltrating tumors etc)”

- High radiosensitive organ
  --> Possible radio-induced tumors --> Risk benefit evaluation

- Small difference in contrast between tumor and normal tissues
  --> need more images, higher doses

- Need of resolutions better/\= 40 microns (microcalcifications)
  --> doses increase with the $1/\text{pixel}^2$

- Need of better identification of the lesion (2.5D – 3D imaging)
  --> higher doses
• **Improve contrast formation**: from absorption to phase contrast imaging
  -- > use improved source or setup (Olivo, Longo, Bravin, Paterno…)

• **Move from 2D to 2.5 and 3D**: vision in depth
  -- > tomosynthesis or CT (K. Bliznakova)

• **Improve detectors**  -- > higher efficiency of used dose
  -- > single photon counting (Kalender, Boone, Esposito..)

• **Improve image reconstruction** technique to use fewer X-rays and reduce dose
  -- > use improved reconstruction algorithms (This talk)
A software platform for phase contrast x-ray breast imaging research

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In-line phase-contrast breast tomosynthesis: a phantom feasibility study at a synchrotron radiation facility

K Bliznakova\textsuperscript{1}, P Russo\textsuperscript{2}, Z Kamaranianakis\textsuperscript{4}, G Mettivier\textsuperscript{2}, H Requardt\textsuperscript{3}, A Bravin\textsuperscript{3} and I Buliev\textsuperscript{1}

PHC IN THE 90IES: FROM NYLON WIRES TO FIRST MAMMOGRAPHIES

Conventional radiography

Phase contrast

Elettra synchrotron 1997-1998

F. Arfelli, A. Bravin et al, Physics in Medicine and Biology 43, 1998

“Yes, but it can work only in simple objects”

First demonstration of phase contrast imaging in a full human organ

F. Arfelli, A. Bravin et al, Radiology 215, 2000
Optimal radiation is monochromatic collimated, and coherent X-rays, presently available only at synchrotron radiation sources.
Analyzer-Based Imaging (ABI)

 Analyzer: acts as a perfect and extremely narrow slit

 Rocking curve width Si (333)
 ~ 3.0 μrad at 25 keV
 ~ 1.3 μrad at 50 keV
 ~ 0.9 μrad at 60 keV

 Bragg’s law: 2dsinθ = nλ
Diffraction Enhanced Imaging: an algorithm for ABI

\[ I_L = I_R \left( R(\Theta_L) + \frac{\partial R}{\partial \Theta} (\Theta_L) \Delta \Theta_z \right) \]

\[ I_H = I_R \left( R(\Theta_H) + \frac{\partial R}{\partial \Theta} (\Theta_H) \Delta \Theta_z \right) \]

\[ I_R = \text{apparent absorption image} \]

\[ \Delta \Theta_z = \text{refraction image in the plane of the object} \]

\[ \Delta \Theta = \frac{I_H \cdot R(\Theta_L) - I_L \cdot R(\Theta_H)}{\left| \frac{dR}{d\Theta}_{\Theta_H} \right| - \left| \frac{dR}{d\Theta}_{\Theta_L} \right|} \]
Carcinoma Medullare

- 1 Siemens Mammomat 3000 -23 kVp
  5.6 mAs
  MGD=0.4 mGy

- 2 ABI 25 keV minus 0.7 μrad Si(333)
  MGD= 0.6 mGy

- 3 Histology

Breast cancer

- 1 Hospital scanner
- 2 SR technique
- 3 Histology (reality)

Conventional

MGD = 6.9 mGy

Phase contrast (ABI)

MGD = 1.9 mGy

Full breast: 8 cm
33 keV

Keyriläinen et al. Radiology, 2008
Breast-CT: PCI-CT vs conventional CT vs histology

PCI CT outperforms conv. CT and it is in strong correlation with histology

A. Sztrokay et al *Physics in Medicine and Biology*, 57(10) 2931 - 2942, 2012
High-resolution, low-dose phase contrast X-ray tomography for 3D diagnosis of human breast cancers

Yunzhe Zhao¹,², Emmanuel Brun³,⁴, Paola Coan⁵,⁶, Zhifeng Huang⁷, Aniko Sztrókay⁸, Paul Claude Diemoz⁹, Susanne Liebhardt⁴, Alberto Mittone⁹, Sergei Gasilov⁹, Jianwei Miao¹,², and Alberto Bravin³,⁴

Phase contrast CT + iterative reconstruction method

Dose = 2.0 ± 0.1 mGy
25 times dose saving vs clinical breast CT at same resolution
CT BASIC PRINCIPLES

Rotating sample

Detector

X-rays

Computing (reconstruction algorithms)

Sinogram

3D image

0°

360°
LOW DOSE CT

Combination of 3 ingredients:

- "Phase contrast imaging"
- Advanced CT reconstruction algorithms
- High X-ray energies

Resulting in:

- Highly sensitive imaging techniques
- Iterative algorithms for CT reconstruction - less projections than normally used
- Tissues more radio-transparent -> less dose
- Breast imaging needs high resolution
  - High number of projections for CT (Shannon Nyquist criterion):
    \[ \text{Proj} = \frac{D \pi}{p \cdot 2} \]
    - D: sample thickness
    - P: pixel size

- Can we reduce the number of projections?

2 possible strategies:

- To reduce the number of projections for a CT data set:
  - Shannon-Nyquist criterion not valid anymore

- To reduce the number of photons onto the detector per each angular projection
REDUCING THE NUMBER OF PROJECTIONS OF A CT DATA SET

Using FBP: prone to the appearance of artefacts
REDUCING THE NUMBER OF PROJECTIONS

- **Filtered Back Projection (FBP)**
- Simultaneous Iterative Reconstruction Technique (SIRT)
- Simultaneous Algebraic Reconstruction Technique (SART)
- Conjugate Gradient Least Squares (CGLS)
- Total Variation (TV) minimization
- Iterative FBP algorithm based on the image histogram updates
- **Equally Sloped Tomography (EST)**

*S. Pacile et al, Biomed Opt Express. 2015 Aug 1; 6(8): 3099–3112*
REDUCING THE NUMBER OF PROJECTIONS

Table 4. Qualitative assessment of the considered images performed by expert supervisors.

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Radiol. 1</th>
<th>Radiol. 2</th>
<th>Radiol. 3</th>
<th>Pathologist</th>
<th>Mean Score</th>
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<tbody>
<tr>
<td>FBP</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>FBP-ITER</td>
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<td>SIRT</td>
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<td>1.75</td>
<td>1.43</td>
</tr>
<tr>
<td>SART</td>
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<td>1.75</td>
<td>1.5</td>
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<tr>
<td>CGLS</td>
<td>1</td>
<td>1.25</td>
<td>1.5</td>
<td>1.5</td>
<td>1.31</td>
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<tr>
<td>EST</td>
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<td>1.25</td>
<td>1.5</td>
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<td>1.31</td>
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<tr>
<td>phr FBP-ITER Epan17</td>
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<td>phr FBP-ITER Susan5</td>
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<td>2.5</td>
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<td>2.68</td>
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<tr>
<td>phr TV-MIN</td>
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<td>2.43</td>
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<td>phr FBP</td>
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<td>2.75</td>
<td>2.75</td>
<td>3.5</td>
<td>2.81</td>
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<tr>
<td>phr SIRT</td>
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<td>3</td>
<td>3</td>
<td>3.25</td>
</tr>
<tr>
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<td>2.93</td>
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<tr>
<td>phr EST</td>
<td>3.5</td>
<td>3.25</td>
<td>3.5</td>
<td>3</td>
<td>3.43</td>
</tr>
</tbody>
</table>

0: worst case; 4: best image

All algorithms available in X-TRACT software: http://www.ts-imaging.net/Services/SignUp.aspx

Observation:

- Real space image is in Cartesian grid while the Fourier space data is in Polar Grid

- There is no exact and direct FFT between polar and Cartesian Grid [1]

Idea: “a polar like” grid that enables direct and exact Fourier transform

=> PSEUDO POLAR GRID

- Grid points in the Fourier domain are lying on the equally-sloped lines instead of equally-angled lines
- N*N Cartesian grid -> 2N*2N Pseudo polar grid (PPG) points
- There exist a PPFFT between PPG and Cartesian Grid
  - algebraically exact
  - geometrically faithful
  - Invertible


PNAS, Zhao, Brun, Coan et al., 109 (45) 6 Nov 2012

Slides provided by Prof. P. Coan
Idea: “a polar like” grid that enables direct and exact Fourier transform

=> PSEUDO POLAR GRID

EST iterative algorithm

Starts with the conversion of the projections to Fourier slices in the pseudo polar grid fractional FFT

Iterative process is initiated:

• Inverse PPFFT is applied to the frequency data
• A new object is obtained through constraints. Forward PPFFT onto modified image
• Frequency data is updated with the measured Fourier slices

Real domain constraints:

• Minimization of the coefficients
• Real values as result

Iterations are monitored by an error function
WE TESTED EST ON DIFFERENT CASES

→ On both synthetic and experimental data

→ Different Phase Contrast Imaging techniques Propagation-based
   - Propagation based imaging
   - Analyzer based imaging

→ Different clinical cases (FULL JOINTS or ORGANS):
   - Breast imaging
   - Musculoskeletal imaging

Slides provided by Prof. P. Coan
The raw data

The sinogram
Visual Comparison

Zoomed view in a 92 µm thick slice an excised full human tumor bearing breast

- FBP - 512 exhibits high noise degraded features and blurred boundary of the tumour

FBP

2000proj = 7.7mGy

512proj = 1.7mGy

Prof. P. Coan

_PNAS_, Zhao, Brun, Coan et al., 109 (45) 6 Nov 2012
Result of reconstruction by EST 512 projections

MGD 1.7 mGy
Blind Test made by 5 radiologists (Radiology department of Ludwig Maximilians University)

Radiologist were asked to mark form 1 (worst) to 5 (best) on the following criteria

<table>
<thead>
<tr>
<th></th>
<th>FBP 512</th>
<th>EST 200</th>
<th>FBP2000</th>
<th>EST512</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image quality</td>
<td>2.2 ± 0.4</td>
<td>2.7 ± 0.9</td>
<td>4.3 ± 0.9</td>
<td>4.5 ± 0.5</td>
</tr>
<tr>
<td>Sharpness</td>
<td>3.3 ± 0.0</td>
<td>2.2 ± 0.8</td>
<td>4.0 ± 0.7</td>
<td>4.3 ± 0.5</td>
</tr>
<tr>
<td>Contrast</td>
<td>3.0 ± 0.7</td>
<td>3.4 ± 0.9</td>
<td>4.0 ± 0.5</td>
<td>4.8 ± 0.4</td>
</tr>
<tr>
<td>Evaluation of different structure</td>
<td>2.7 ± 0.5</td>
<td>2.9 ± 1.0</td>
<td>4.1 ± 0.6</td>
<td>4.8 ± 0.4</td>
</tr>
<tr>
<td>Noise</td>
<td>1.8 ± 0.7</td>
<td>3.3 ± 0.8</td>
<td>4.2 ± 0.7</td>
<td>4.8 ± 0.3</td>
</tr>
</tbody>
</table>
3D CT breast tumor detection at high resolution and at a dose even lower than conventional 2D mammography (~3.5 mGy)!

Fourier based iterative Equally Slopped Tomography (EST) algorithm

Conventional CT
Dose 49 ± 1 mGy

Phase contrast CT + EST
Dose = 2.0 ± 0.1 mGy

25 times dose saving vs clinical breast CT at same resolution

PNAS, Zhao, et al., 109 (45) 6 Nov 2012
Summary

- 3D information of soft tissues at higher resolution and better contrast, but also deliver less radiation doses to the sample

- A step towards the clinical application of PCT for 3D screening and diagnosis of human breast cancer

- Very low dose (<1mGy) 3D imaging is possible if one is ready to loose a bit of spatial resolution and noise

PNAS, Zhao, Brun, Coan et al., 109 (45) 6 Nov 2012
Sparsity

image is intrinsically sparse when it can be approximated as a linear combination of a small number $n$ of basis functions, with $n=N$, where $N$ is the image dimensionality.

Good case: when image has large constant parts: the basis can be small pieces varying only on the borders.
RECONSTRUCTION USING A PRIORI INFORMATION

How many patches?

\( mxm<< NxN \) (pixel size)
- Fast calculation
- Image not well reproduced
- Very low noise (noise has little sparsity)

\( mxm>> NxN \) (pixel size)
- Heavy computation
- Image well reproduced
- Very smooth transition at the patches borders if the patches are overlapping
- Also noise is reproduced, to be treated with a denoisy method

Submethods:
- Dictionary learning
- Total Variation penalization (TV): introduces a regularization parameter

All mathematics can be found in
A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Dictionary Learning reconstruction

• Idea of the method:
  – To create a database of patchworks starting from images close to the images to be reconstructed
  – To decompose the slice to be reconstructed in a patchwork of sub-images
  – To express a given sub-image at position “r” as a linear combination of the basis patches
  – To find the solution which gives the maximum Likelihood by minimizing the number of entries in the dictionary
  – Minimization is done toggling between slice and sinogram
  – A regularization included to assure fidelity

Dictionary “learnt” from Lena image and used for reconstructing the image of interest

Noisy image

Denoised image

Prof. P. Coan

A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Reconstructing Lena

- **Experiment:**
  - 512*512 pixel Lena image
  - 80 projections

- **Remark:**
  - To avoid aliasing 800 projections should be used (Nyquist-Shannon sampling criterion)

Prof. P. Coan

A. Mirone, E. Brun, P. Coan. *PlosOne, 9*(12) e114325
Results

NO noise

80 projections
Zoom views in two different image regions

FBP  EST  TV  DL  Original

A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Results

Noisy data

Additive White Gaussian Noise = 0.3% max of sinogram

80 projections
Zoom views in two different image regions

Additive White Gaussian Noise = 0.3% max of sinogram

Prof. P. Coan

A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Direct comparison

FBP

EST

DL

No Noise

Noise

No Noise

Noise

A. Mirone, E. Brun, P. Coan. *PlosOne, 9*(12) e114325
THE IMPORTANCE OF THE FAST CONVERGING
APPLICATION ON EXPERIMENTAL DATA
Reconstructing phase gradient images

Sample imaged with the analyzer set at two points of its rocking curve may yield to obtain two images of the 2 phase gradient in the reconstructed plane.

The two phase gradients are linked each other.

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Diameter: 7 cm

Shannon criterion: 2335 projections (pixel: 47 microns)
Vectorial Set of Patches

Set of 2* 7*7 pixels patches learnt from another breast sample

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Phase Contrast Reconstruction using DL

Analyzer Based Imaging of a full (7cm) human tumor bearing breast tumor

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A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Small Structures are preserved in the Dictionary Learning reconstructions. Global Image quality is higher in DL.

A. Mirone, E. Brun, P. Coan. PlosOne, 9(12) e114325
Phase retrieval converting the problem to Poisson equation, robust to noisy data

Application of a finite element technique to solve the boundary value problem in phase retrieval

PhC vs conventional CT: accuracy in refraction Index calculation in noisy data

Fast and low dose phase retrieval using a single Image dataset
The problem of the radiation delivered
How to perform fast dose simulations?

Conventional Monte Carlo
Long computational time

• The track-length estimator (TLE)
• Electrons production cut
How to perform fast dose simulations?

Conventional Monte Carlo
Long computational time

- The track-length estimator (TLE)
- Electron energy is deposited locally and are not tracked

Local deposition
vs
continuous deposition

\[ D = \Phi E \frac{\mu_{en}}{\rho} \]

- It requires fewer particles to converge
- Works when electron range is < spatial resolution (<100 keV)
- No significative energy escape (radiative, atomic deexcitation): Z<20; E<1 MeV

The TLE code (C++) has been integrated in GATE (Geant4)
COMPARISON WITH STANDARD MONTE CARLO METHOD

10^7 events on segmented CT data of experimental **breast sample**

TLE Method\(^8,9\)

**Standard Monte Carlo**

- Statistical error TLE: \( \sim 1.5\% \)
- Statistical error MC: \( \sim 50\% \)

To obtain the same statistics with MC \( \sim 2 \) orders of magnitude more time!

Estimation of the average dose in a breast (monochromatic radiation):

- Range of energy: 15-100 keV
- Different geometries (thickness)
- Different compositions (fraction of glandular tissue)

Y. Zhao, E. Brun, *PNAS* 2012, November 6, vol. 109, no. 45, 18290–18294
J. Keyrilainen, A. Bravin, *Acta Radiologica* 2010 51 (8) 866-884
A. Mirone, E. Brun *PLOS ONE* 2014 vol.9, art 0114325. DOI:10.1371/journal.pone.0114325
S. Gasilov, A. Mittone, *Biomedical Optics Express* 2013 Vol. 4, No. 9 1512-1518