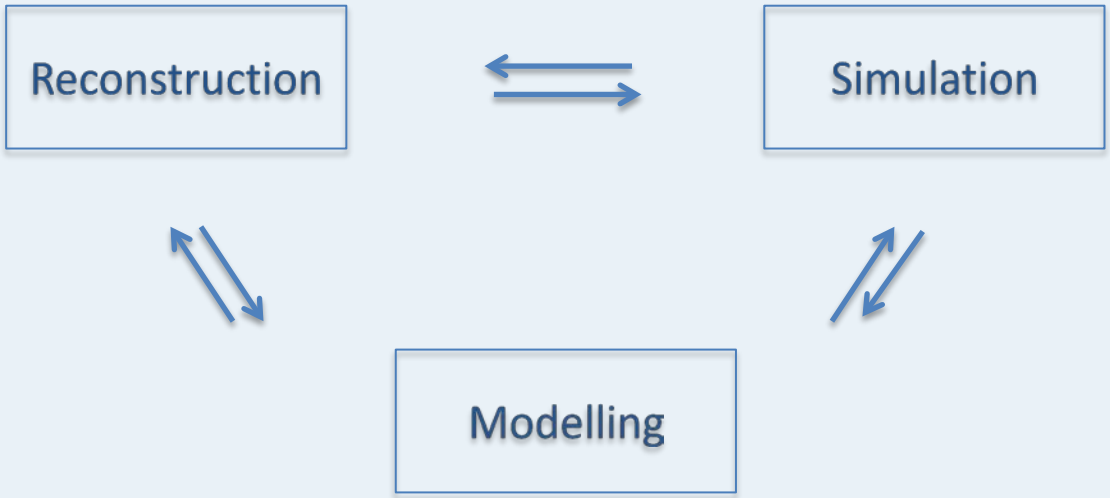
Reconstruction, Simulation & Modelling for the multiscale assessment of organs

- Research in different pathologies, different image modalities
- Multiscale Assessment : from the organ to the tissue level
- Examples : cardiac and bone imaging



Tomographic reconstruction

- **Background**
  - Problem : reconstruction of an image from its line integrals
  - Analytic versus iterative approaches
  - New progresses in sparse reconstruction and L1 regularizations

- **Issues**
  - New emerging modalities raising more complex inverse problems

- **Research topics**

• X-ray Phase CT	non linear ill posed problem
• Compton CT	integrals over cones not lines
• Fluorescent Diffuse Optical CT	complex direct problem, ill posed
• 3D cardiac rotational angiography	limited number of projections

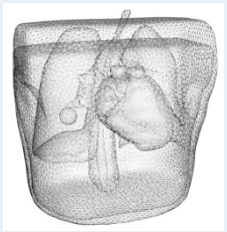
Simulation

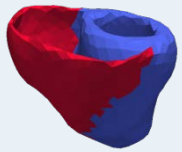
- **In-silico simulation in radiation and particle therapy**
  - Main Goals
    - Dose in Radiation therapy,
    - Simulation in X-ray imaging (CBCT)
    - Dose in Proton therapy, Prompt-gamma (dose monitoring)
  - Methods
    - Monte-Carlo. GATE plateform (international opengate collaboration)
    - High performance computing (GateLab, related to VIP project)
    - Hybrid approach: mixing analytical and MC methods

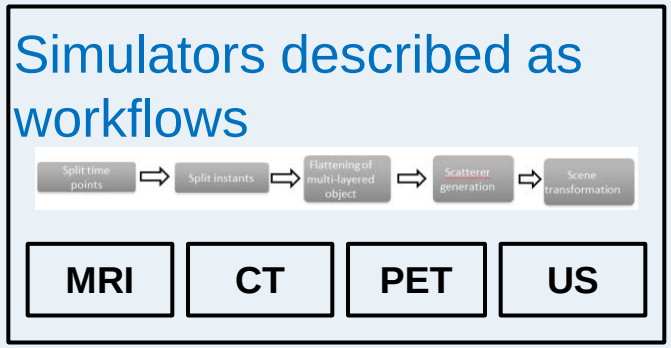
- **In-silico image simulation**
  - Goal : Simulation of imaging modalities
  - Methods :
    - VIP platform (integrated simulation, various modalities)
    - Dedicated simulations (given medical application/ given modality)

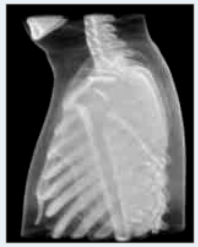
Virtual Imaging Platform : VIP

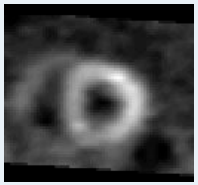
- **A grid enabled, multimodality, web accessible simulation platform**
- **Integration of existing software (NO simulation development)**

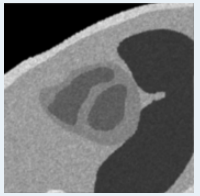


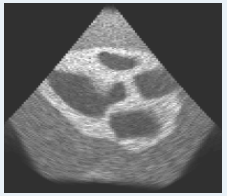




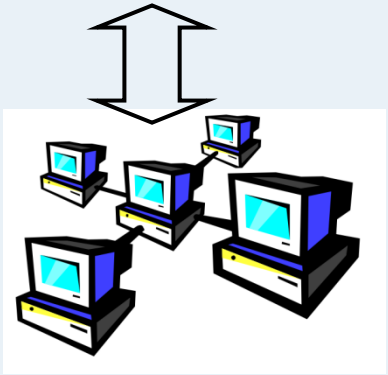








Simulated images



Models repository:

Geometry and physical parameters (proton density, echogenicity, radioactivity, etc.)

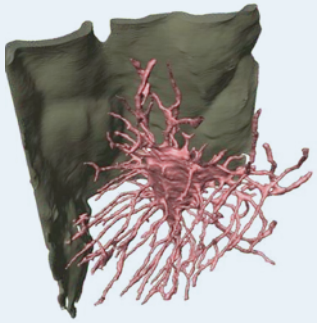
Grid access :

- **European Grid Infrastructure (EGI)**
- **Biomed Virtual Organization**

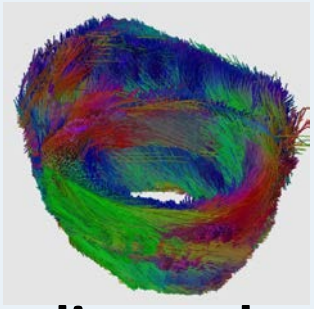
[Glatard et al IEEE TMI 2013]

Reconstruction, Simulation & Modelling for the multiscale assessment of organs

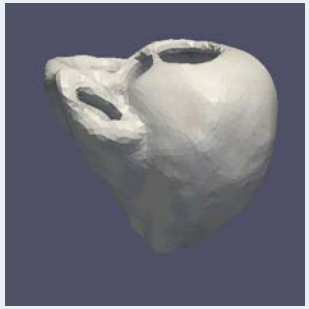
- **Bone Imaging and X-ray phase CT**
  - Presented by Max Langer, Team 4



- **Multiscale modeling, simulation and reconstruction of 3D fiber architectures of the human heart**
  - Presented by Yue Min Zhu, Team 1



- **Ultra realistic simulation of 3D echocardiography**
  - Presented by Olivier Bernard, Team 2



Bone Imaging and X-ray phase CT

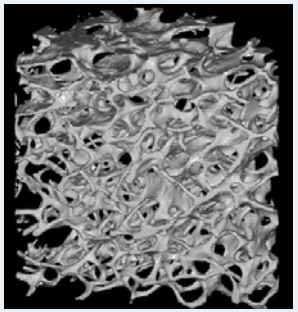
Max Langer

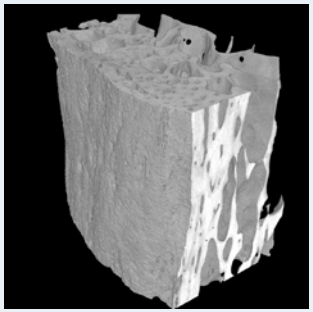
Bone Imaging and X-ray phase CT

- **Medical context : Osteoporosis**
  - Bone fragility disease increasing with aging *[Kanis, 2006]*
  - Definition : Bone loss and modification of bone micro-architecture

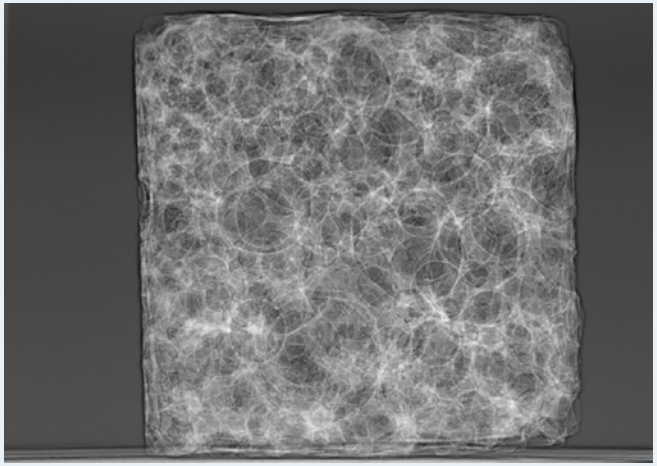
  ➔ Goal : understand bone fragility and the risk of fracture

  ➔ Requires a multi-scale investigation of bone



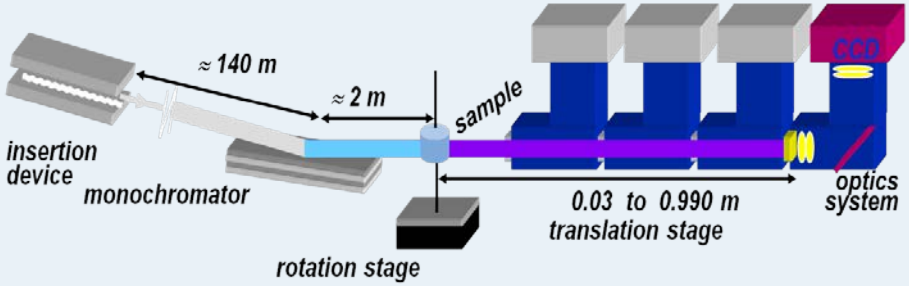


- **X-ray imaging techniques**
  - Clinical X-ray CT : at the organ scale
  - X-ray micro-CT : at the microscopic scale
  - New developments with Synchrotron CT
    - Synchrotron micro-CT
    - X-ray Phase CT :
      - Hard and Soft tissue imaging
      - Propagation-based Phase CT
      - Phase contrast radiograph

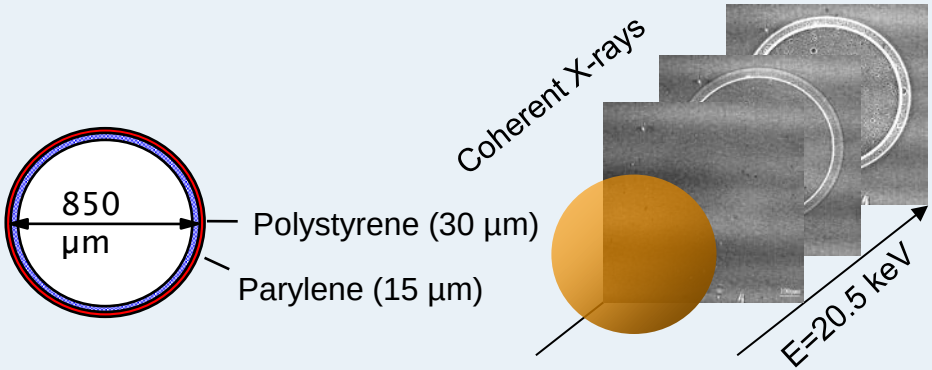


X-ray phase contrast

- **Free space propagation is the simplest phase contrast mechanism**



- **Several orders of magnitude increase in sensitivity**



Phase tomography

- **Inverse problem to be solved**
  - Direct problem

$$n(x,y,z) = 1 - \delta_n(x,y,z) + i\beta(x,y,z),$$

$$B(\mathbf{x}) = \left(\frac{2\pi}{\lambda}\right)\int \beta(x,y,z)\,dz \quad \varphi(\mathbf{x}) = -\left(\frac{2\pi}{\lambda}\right)\int \delta_n(x,y,z)\,dz$$

$$T(\mathbf{x}) = A(\mathbf{x})\exp[i\varphi(\mathbf{x})] = \exp[-B(\mathbf{x})]\exp[i\varphi(\mathbf{x})].$$

$$u_D(\mathbf{x}) = P_D(\mathbf{x}) * u_0(\mathbf{x}) \quad P_D(\mathbf{x}) = \frac{1}{i\lambda D}\exp\left(\mathrm{i}\frac{\pi}{\lambda D}|\mathbf{x}|^2\right)$$

$$I_D(\mathbf{x}) = |u_D(\mathbf{x})|^2,$$

  - Phase retrieval : find φ from $I_D(\mathbf{x})$
  - Phase CT : Tomographic reconstruction of $\delta(x,y,z)$
- **State of the art : Linear algorithms and homogeneous object prior**
- **Aim: improve resolution, more general object priors**

Non-linear phase retrieval

- Most linear algorithms limited to slowly varying phase
- Aim: improvement of resolution (PhD V. Davidoiu)
- Frechet derivative of data term

$$I_D(\varphi+\varepsilon) = I_D(\varphi) + G(\varepsilon) + O(\varepsilon^2)$$

- Landweber iteration

$$I_D'(\varphi_k)^* \left[I_D(\varphi_k) - I_D^{\delta_n} \right] - \alpha \Delta \varphi_k = 0$$

$$\varphi_{k+1} = \varphi_k - \tau_k \left\{ I_D'(\varphi_k)^* \left[I_D(\varphi_k) - I_D^{\delta_n} \right] - \alpha \Delta \varphi_k \right\}$$

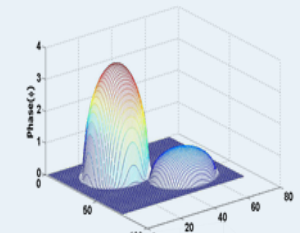
[Davidoiu et al Opt Express 2011]

[Davidoiu et al Opt Lett submitted]

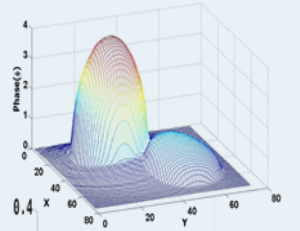
Results

- Simulated data : 2D phase retrieval

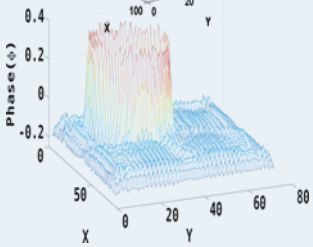
Ideal



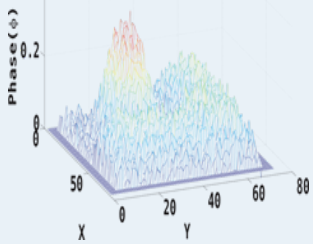
NL



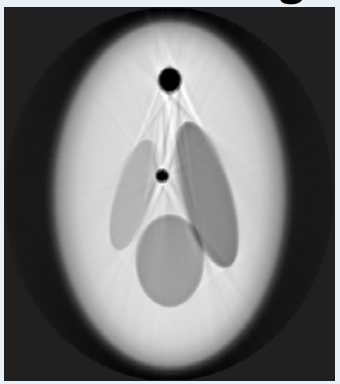
Error mixed

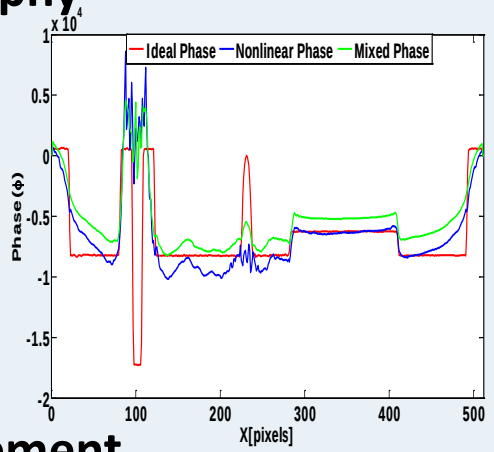


Error NL



- Phase tomography

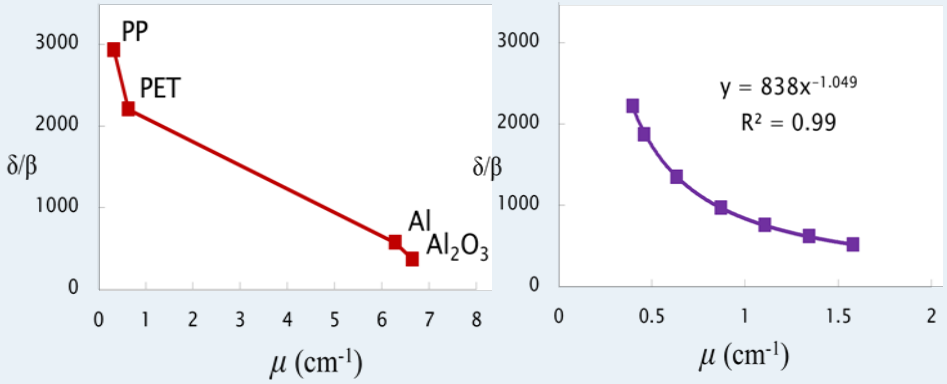




- Global improvement
- Regularization parameter?

Regularization

- Previous methods require homogeneity, ie δ/β constant (cf Paganin's method)
- Aim: reduction of LF artifacts without homogeneity prior
- Idea: use a priori information from attenuation
- Introduce in object domain
- δ/β as function of μ

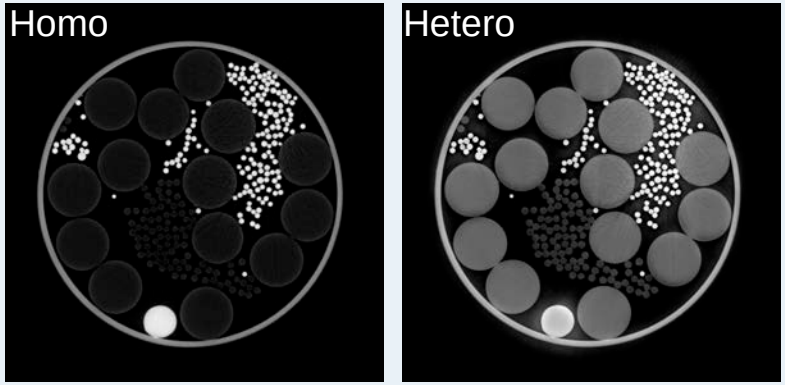


[Langer et al Opt Lett 2012]

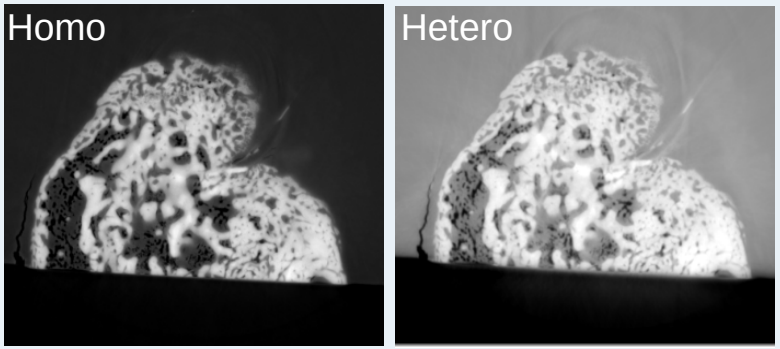
[Langer et al Phil Trans A in press]

Results

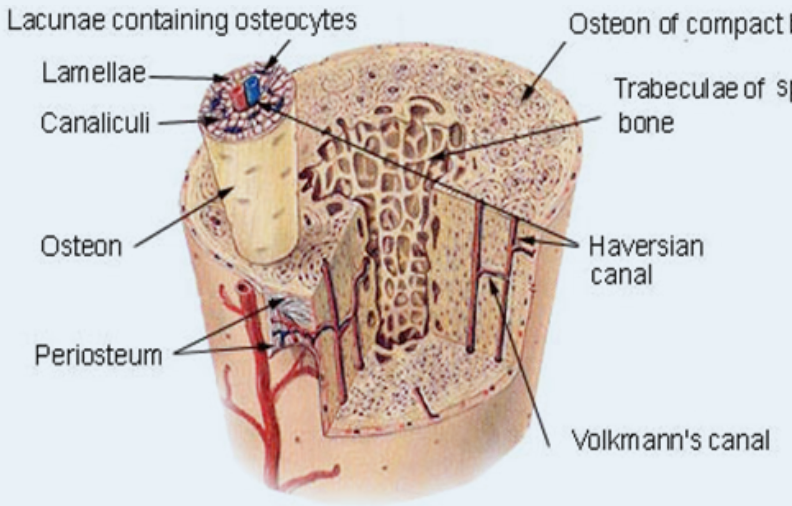
- Experimental data

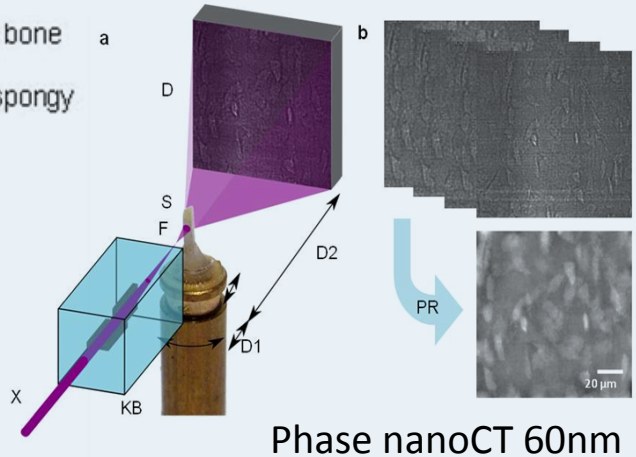


- High accuracy/precision
- Loss of resolution - deconvolution
- Not possible on truncated data
- Mineralization gradient in bone :

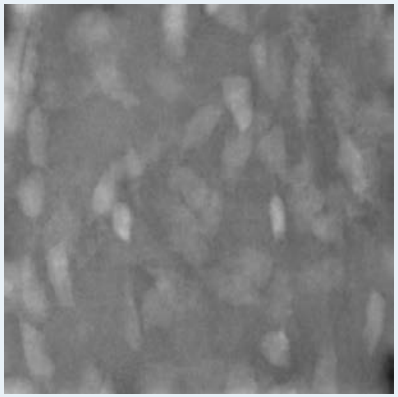


Bone ultrastructure by SR Phase Nano-tomography

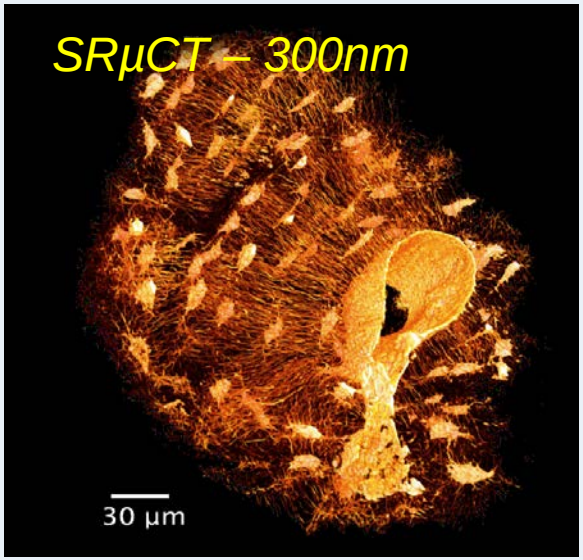


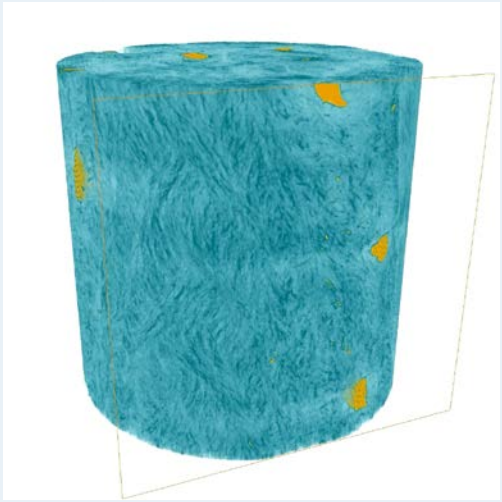


Phase nanoCT 60nm

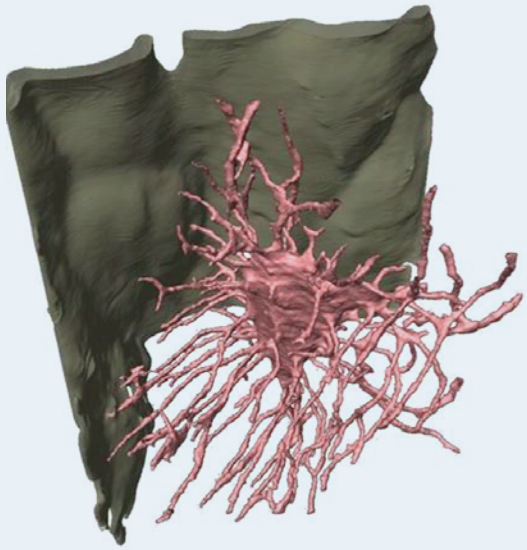


Phase maps





Volume rendering



Lacunae and matrix morphology

[Pacureanu et al Med Phys 2012]

[Langer et al PLoS One 2012]

Perspectives : X-ray phase tomography

- **3D phase retrieval**
  - Aim: weaker assumptions on object, avoid need to measure attenuation, simultaneous attenuation and phase retrieval, …
  - Idea: other priors in object domain (Piecewise constant, piecewise smooth, parcimony, …)
- **Bone ultrastructure imaging**
  - Aim: 3D Imaging of bone cells in situ at <50 nm resolution
  - Very challenging sample environment, dose sensitivity, …

  - First direct 3D imaging of collagen in bone *[Varga et al Acta Biomat 2013]*
  - Future: Quantitative investigation at Multiple sites
  - Aim: elucidate role of collagen organization with mechanical simulations

Perspectives in Tomographic reconstruction

- **Tomographic Reconstruction**

• X-ray Phase CT	non linear ill posed problem
• Compton CT	integrals over cones not lines
• 3D cardiac rotational angiography	limited number of projections
• Proton –CT	curved path
• Spectral-CT	multi-energy bands
• High Resolution pQCT	super resolution
• Motion Compensated CT	respiratory motion
• Cone Beam CT	truncated projections, scattering

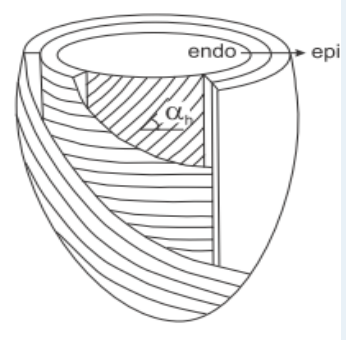
Some Publications in Phase Imaging

- *Inverse Problems and Imaging*, vol. 60, pp. 1693-1701, 2013
- *Applied Optics*, vol 52(17), pp. 3977-3986, 2013
- *Acta Biomaterialia*, vol 9(9), pp. 8118-8127, 2013
- *Molecular Imaging in Biology*, 2013
- *Phil Trans A*, 2013
- *Stem Cells Transational Medicine*, vol. 2, pp. 316-324, 2013
- *Med Phys*, *vol. 39(4), pp. 2229-2238, 2012*
- *Optics Express*, *vol. 20, pp. 27670-27690, 2012*
- *Signal Proc Letters*, *vol. 54, pp. 1435-1456, 2012*
- *Optics Letters*, *vol. 37(11), pp. 2151-2153, 2012*
- *PLoS One*, *vol 7(8), 2012*
- *Optics Express*, *vol. 19(23), pp. 22809-22819, 2011*
- *IEEE TIP*, *vol 19, pp. 2428-2436, 2010*

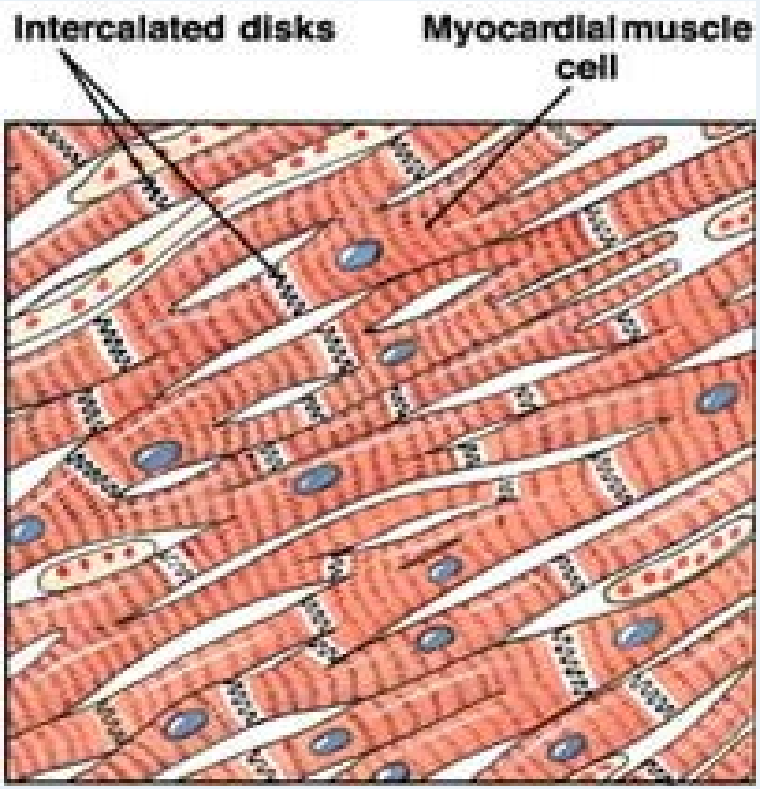
Multiscale modeling, simulation and reconstruction of 3D fiber architectures of the human heart

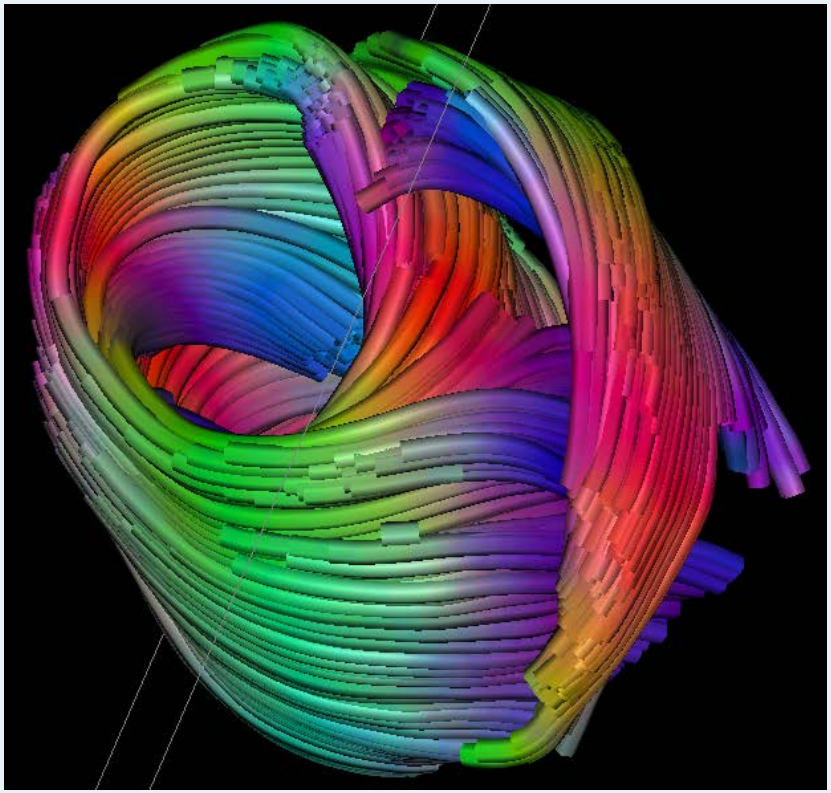
Yue min Zhu

Multiscale modeling and simulation of 3D fiber architectures of the human heart



What is 3D fiber architecture of the heart ?





Myofibers are in spirals in the myocardium

Why 3D fiber architecture ?

- Fiber orientation underlies electrical propagation and mechanical properties of the heart
- Fiber orientation is altered in the case of cardiac disease
- The helical fiber structure is responsible for the twisting motion of the left ventricle

Techniques for investigating cardiac fiber structure

Dissection and histology

☹ Distortion and misalignment
☹ Don't allow for 3D reconstruction

dMRI or more exactly
DTI (diffusion tensor imaging):
the new and perhaps the only way to access 3D fiber architecture of the in vivo human heart

Diffusion MRI (dMRI)

☺ 3D entire heart
☺ *Ex vivo* and *In vivo*
☺ Non destructive et non invasive

Our objective

know about 3D in vivo fiber architecture of the heart using dMRI

Bottlenecks

- ☹ Motion problem: in vivo DTI is sensitive to cardiac and/or breathing motion
- ☹ Bad image quality: low spatial resolution and low SNR
- ☹ Missing of ground-truth on 3D fiber architecture of the heart

Our approaches

- ➢ Combine acquisitions with post-processing for in vivo DTI
- ➢ Develop appropriate post-processing techniques for diffusion tensor data
- ➢ Model cardiac fibers and simulate dMRI (DTI, Q-ball imaging, etc.), at various scales, in 3D, and at different cardiac phases

Recent representative works on dMRI

- *IEEE Trans. Medical Imaging,* **2013.**
- *IEEE Trans. Biomedical Engineering*, **2013.**
- *Medical Image Analysis*, **2013.**
- *Investigative Radiology*, **2012.**
- *IEEE Trans. Biomedical Engineering*, **2012.**
- *Medical Image Analysis*, **2012.**
- *Physics in Medicine and Biology*, **2011.**
- *MRM*, **2010.**
- *Medical Image Analysis*, **2009.**
- *Physics in Medicine and Biology*, **2009.**
- *ISMRM, 2013, 2013.*

From
acquisition
to
fiber tracking,
including
preprocessing
(reconstruction,
denoising,
interpolation, etc.)
of *diffusion tensor data*

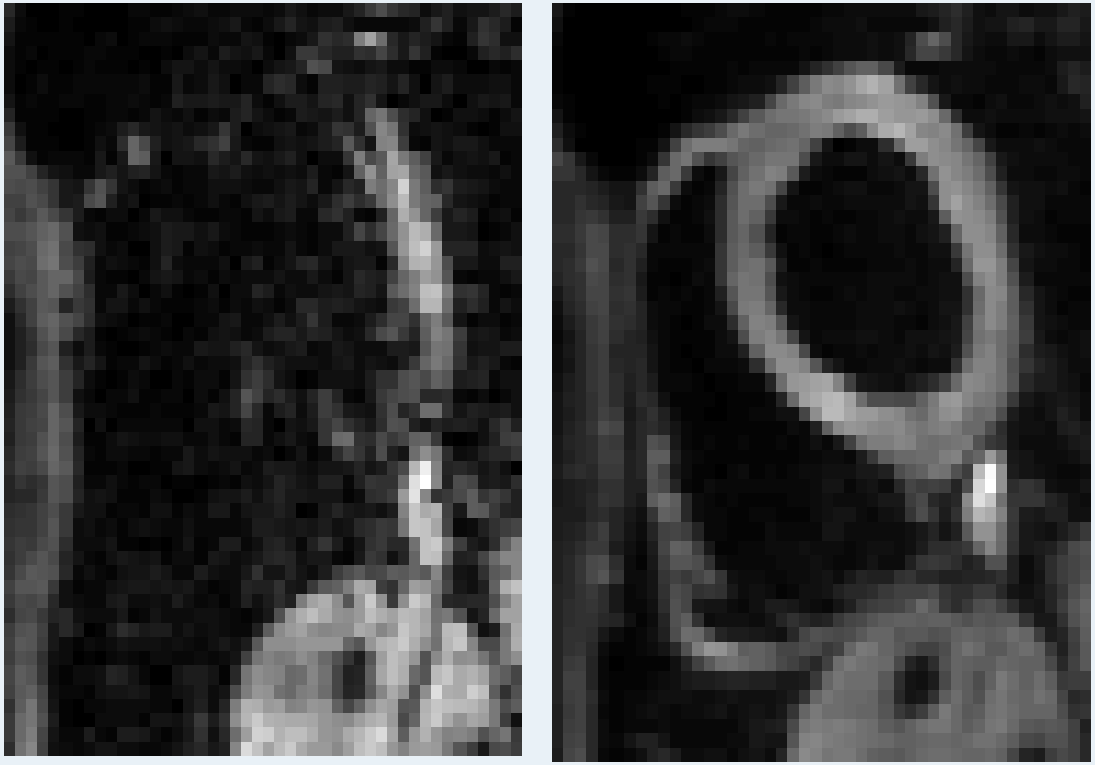
Project highlights:

In vivo cardiac DTI

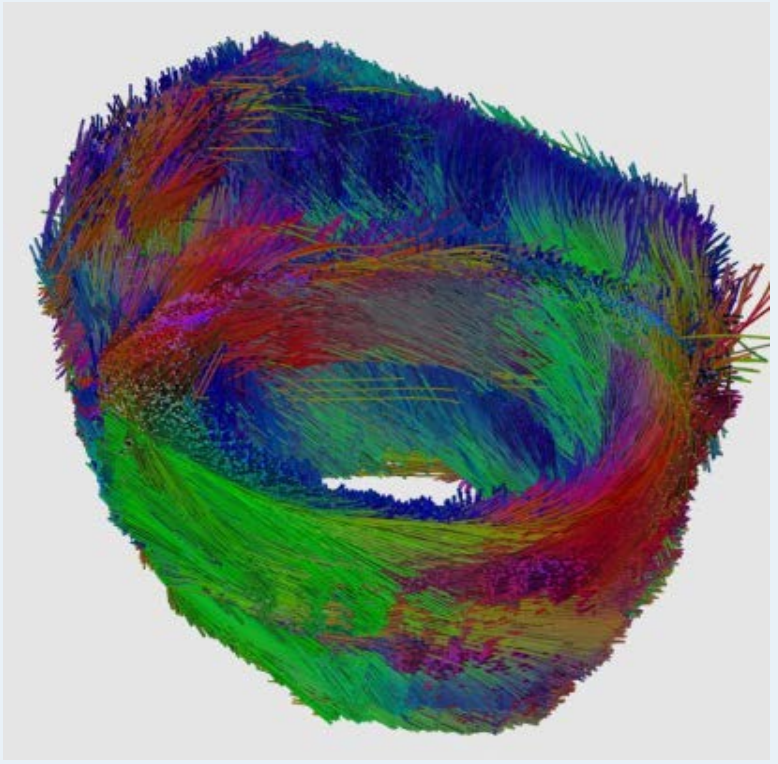
Fiber tracking and diffusion property study under free-breathing conditions and without respiratory gating

(IEEE TMI 2013, ISMRM 2013, SCMR 2013)

Before (left) and after (right) processing



3D fiber architecture in vivo



Project highlights:

Nonstationarity adaptive filtering (NAF) for DTI (IEEE TBME 2013):

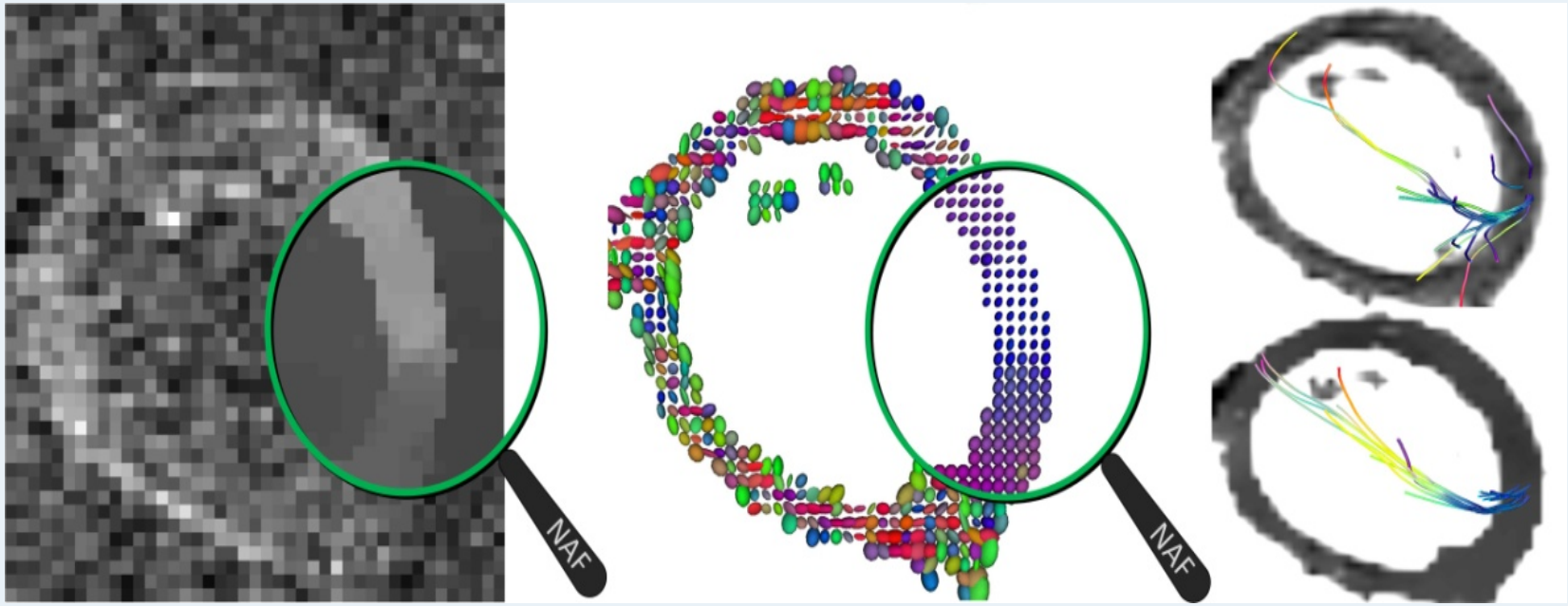
- Cover page of IEEE TBME in June 2013
- «Featured article » of IEEE TBME 2013

Adaptive neighborhood based on NonStationarity Measure (NSM) :

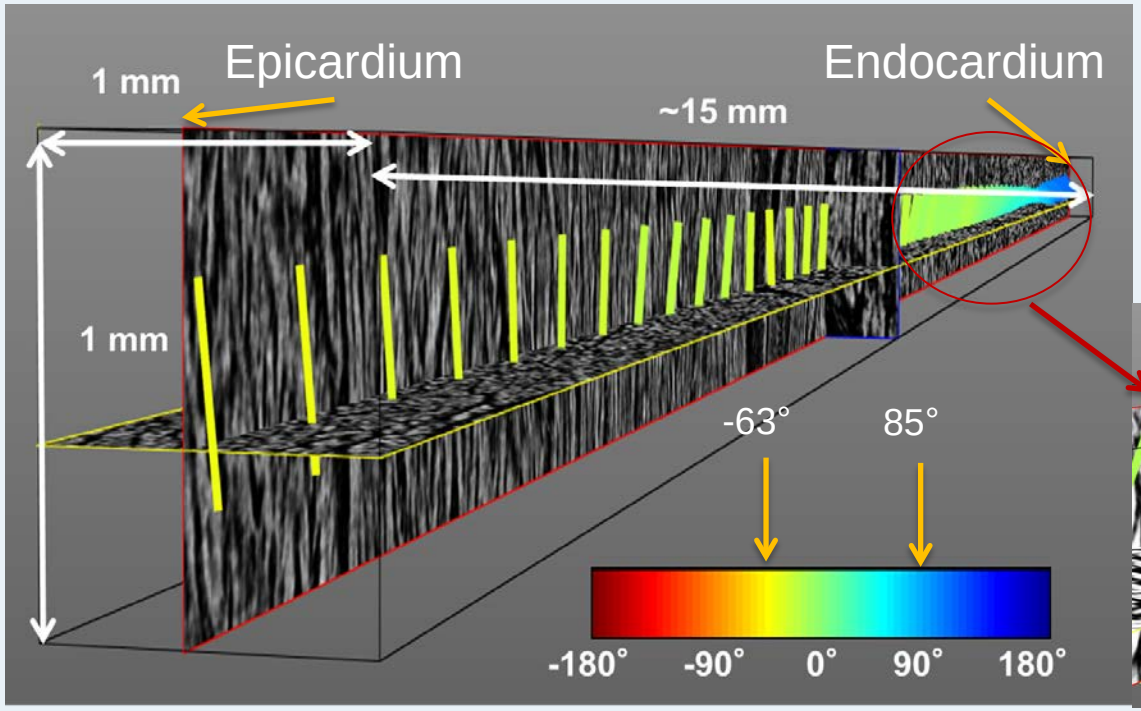
$$\mathbf{N}(\boldsymbol{x}) = \{\boldsymbol{y} : R(\boldsymbol{x}, \boldsymbol{y}) \le T, \boldsymbol{x}, \boldsymbol{y} \in \Omega\}$$

$$R(\boldsymbol{x}, \boldsymbol{y}) = \sum_{i=1}^{n} \left[\left\| \boldsymbol{y}_{i-1} - \boldsymbol{y}_i \right\|_2 + nsm(\boldsymbol{y}_i) \cdot \left| f(\boldsymbol{y}_{i-1}) - f(\boldsymbol{y}_i) \right| \right]$$

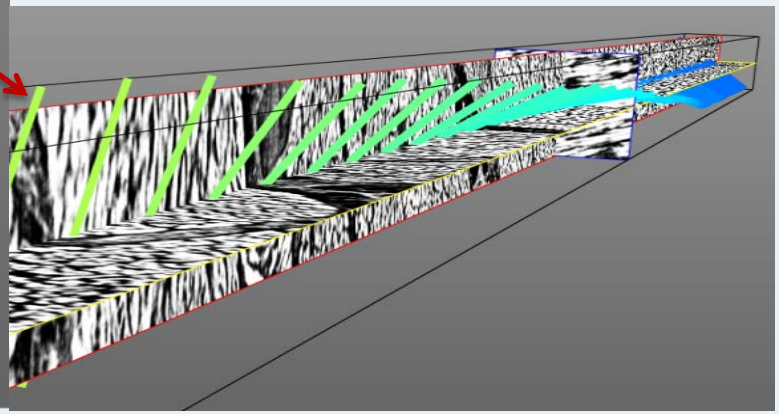
$nsm = g * (h * f)^2 - (g * h * f)^2$ with weighting function *g* and parameter estimation function *h*



Future work



Synchrotron monochromatic X-ray imaging [FIMH 2013]:
very high isotropic resolution of 3.5 µm x 3.5 µm x 3.5 µm.



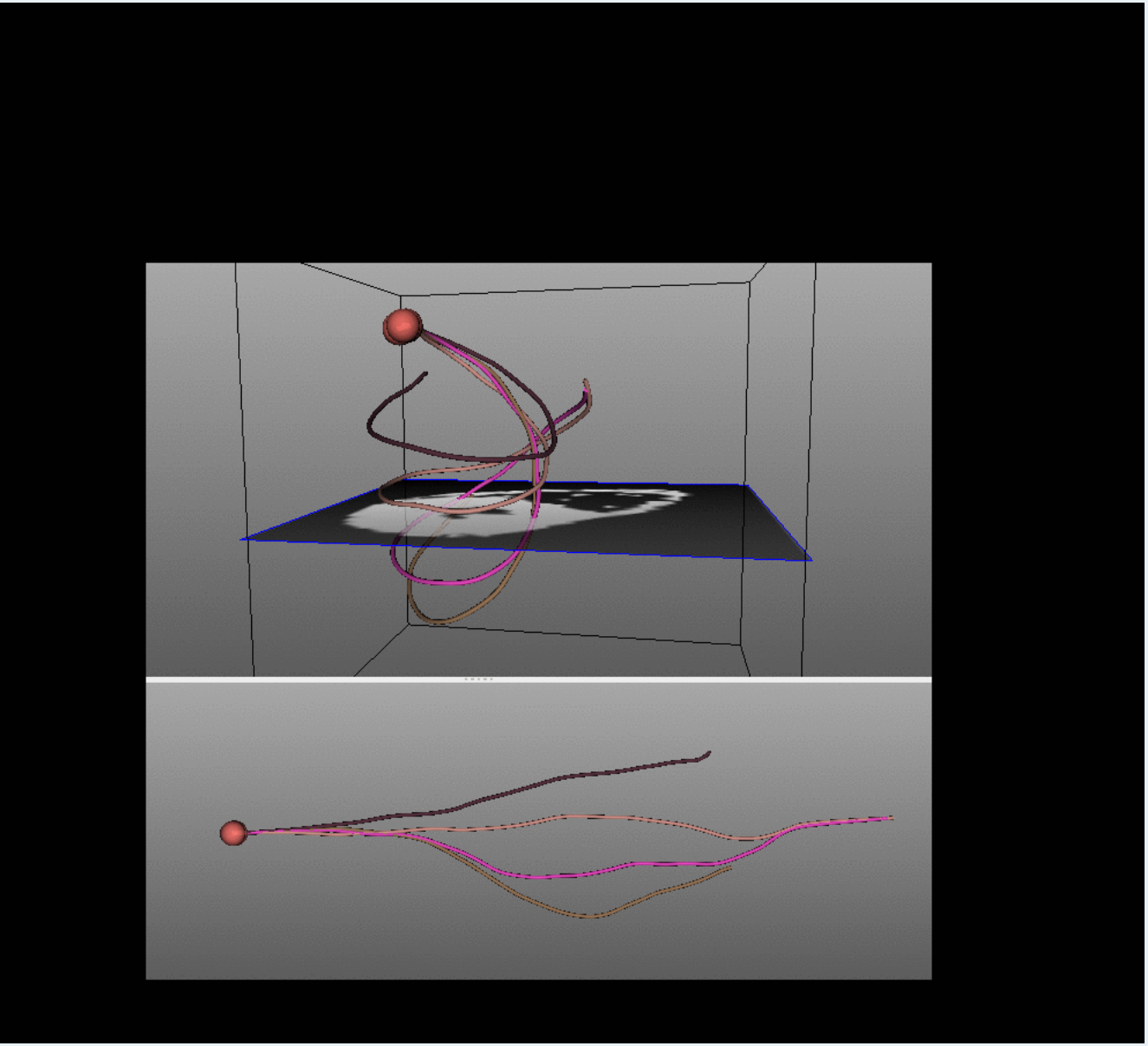
Multiscale modelling and simulation:

- **Realistic fibers and diffusion images, from a few microns to a few millimeters using data from dMRI, PLI and synchrotron**
- **Dynamic 3D in vivo DTI**
- **Multiscale and probabilistic fiber architecture atlases**

Project ANR MOSIFAH (2013-2017)

(Consortium with TIMC-IMAG and INRIA Athena)

Unfold 3D fibers for description



Fibers in 3D

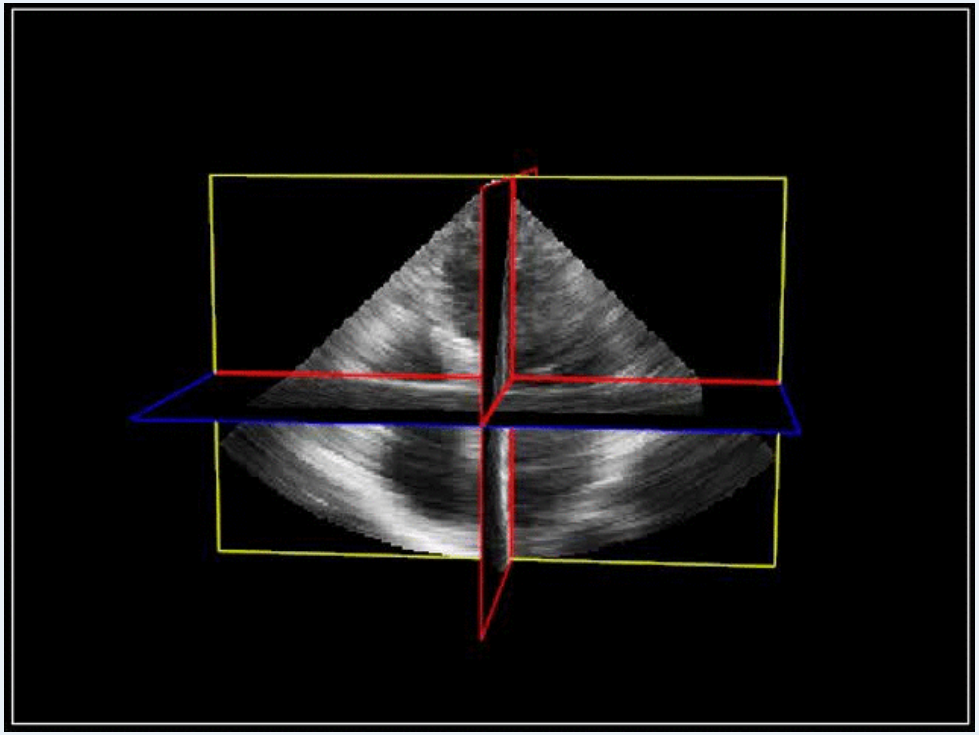
Unfolded fibers in 2D

Ultra realistic simulation of 3D echocardiography

Olivier Bernard

Context: 3D echocardiography

- Allows assessing mechanical properties of the heart such as the strain in real time
- Image quality => no real concensus on the accuracy of what we can extract from this modality

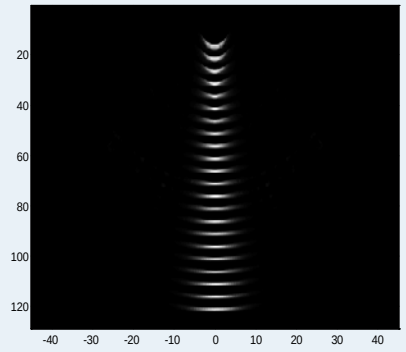


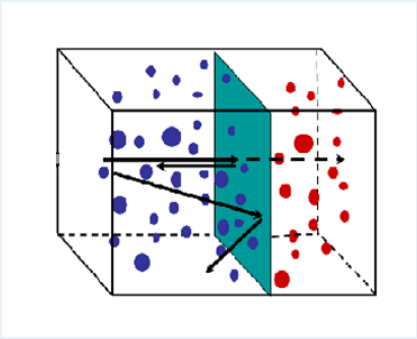
Problematic

- **Create numerical phantoms for quality assurance of algorithms applied to echocardiographic sequences for :**
  - **Segmentation**
  - **Motion analysis**
  - **Tissue characterisation based on strain estimation**

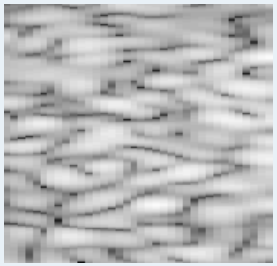
Simulator principle

Simulate a realistic point spread function that characterises the ultrasound probe



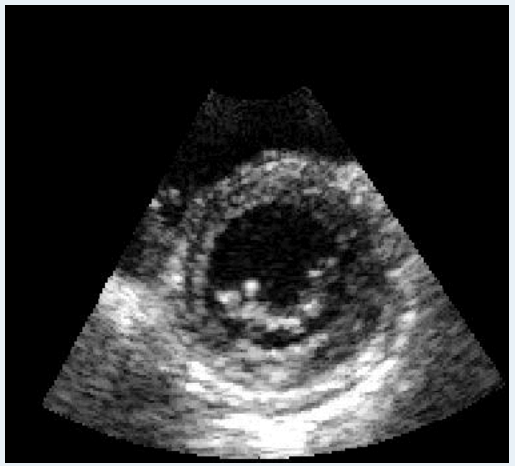


*



Speckle pattern

?



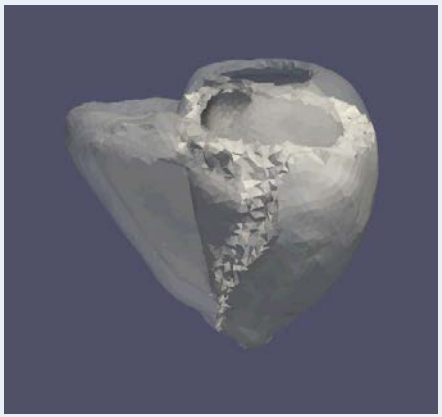
- **How many scatterers ?**
- **Which positions ?**
- **Which amplitudes ?**
- **Which motion ?**

Simulate a medium from a set of scatterer points with specific backsctarred amplitude

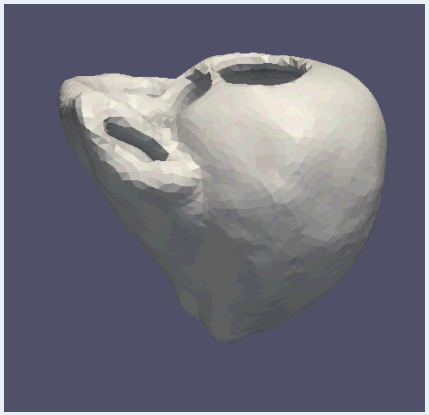
More advanced simulations in the litterature

Anatomical model → Electromechanical motion model → Ultrasound simulator

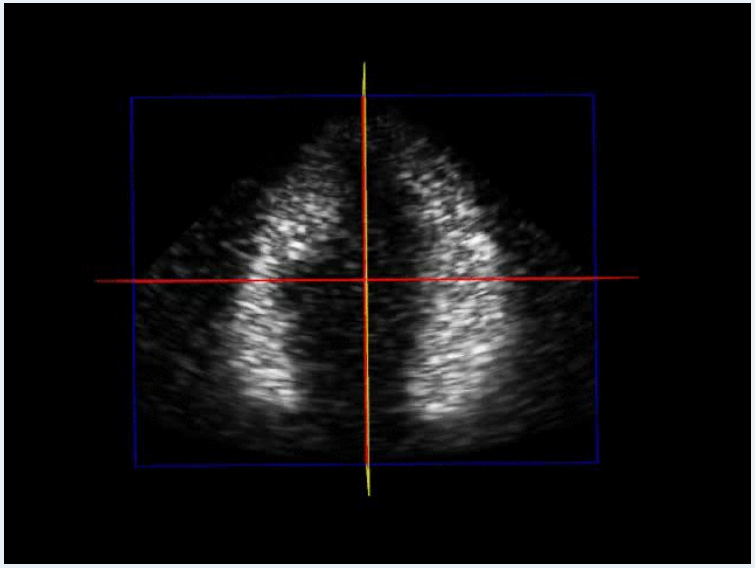
- *Inside myocardium: motion derived from the EM model*
- *Outside myocardium: random scatterers position and motion*
- *Scatterers amplitudes: simple gaussian distribution*



Obtained from MR segmentation



Contractility Activation



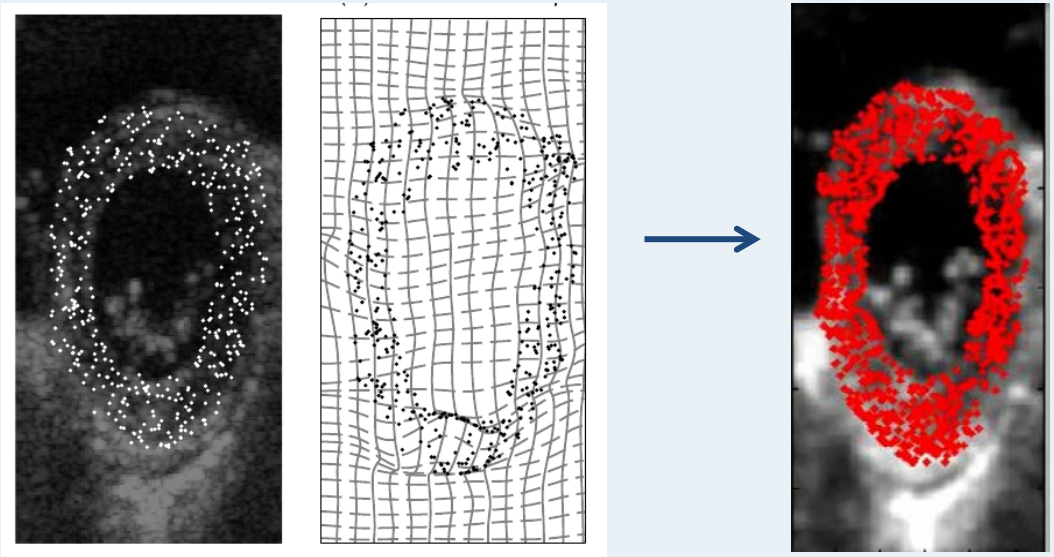
- **Properties**
  - Realistic motion model
  - Need to improve image quality

Our contributions [Alessandrini *et al.*, *ICIP*, 2012]

- Improvement of image quality
  - ➢ We propose an image-based simulation
  - ➢ Main idea: create a simulation getting inspired by a real clinical sequence

---

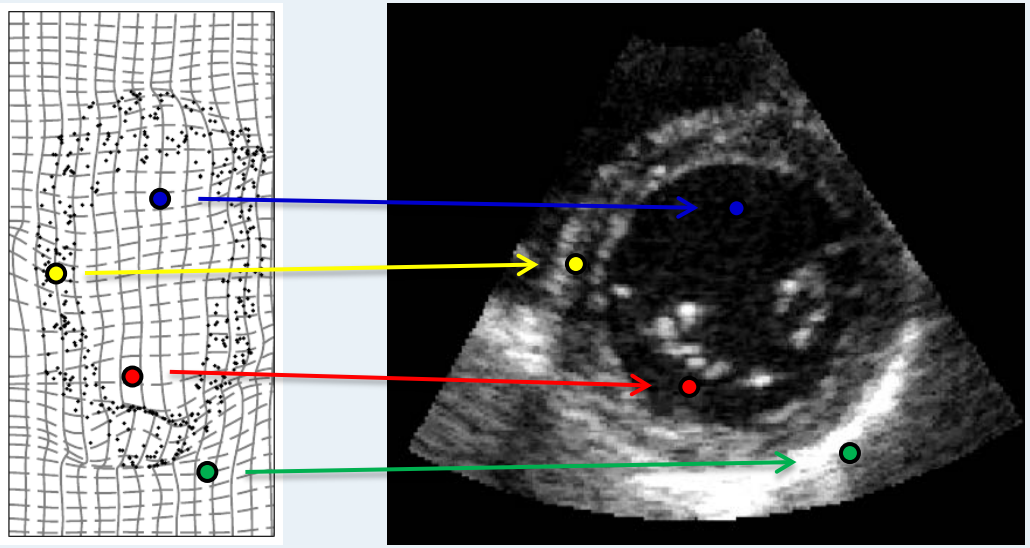
- Learn the motion to apply to the scatterers inside the myocardium from the real sequence



Our contributions [Alessandrini *et al.*, *ICIP*, 2012]

- **Improvement of image quality**
  - ➢ **We propose an image-based simulation**
  - ➢ **Main idea: create a simulation getting inspired by a real clinical sequence**

- **Learn the scatterers amplitudes from the real sequence**



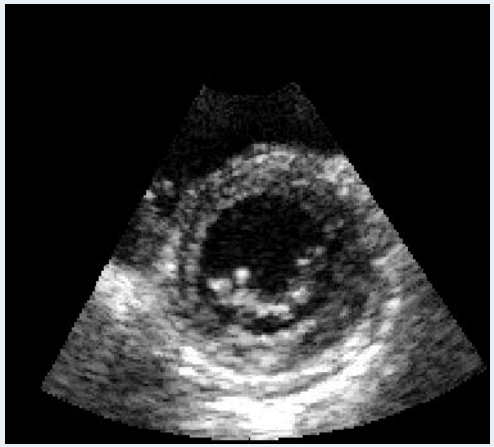
$$A = 10^{\frac{K}{20}} \left(\frac{I}{I_{MAX}} - 1 \right)$$

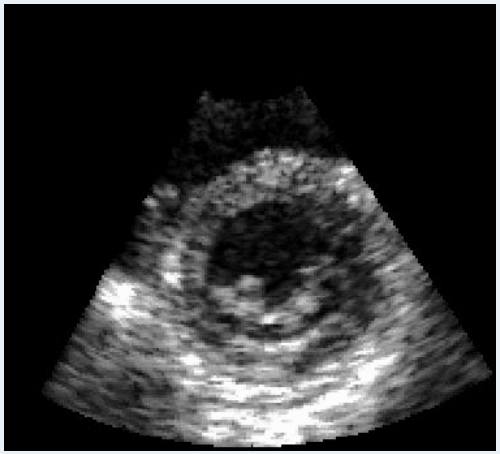
- **A: scatterers amplitude**
- ***I* : real image intensity**
- **K: parameter that controls the dB range of the resulting image**

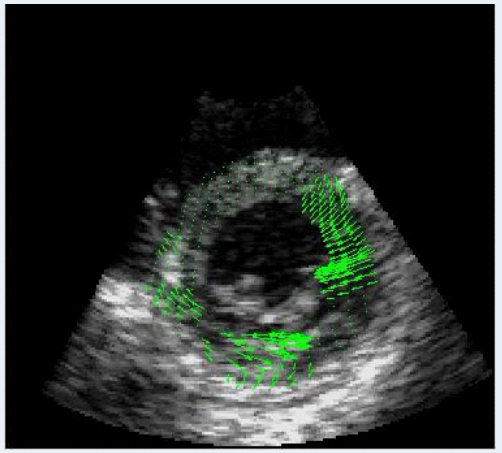
Our contributions

[Alessandrini *et al.*, *ICIP*, 2012]

Real clinical recording → Simulated sequence → Reference motion







- **Properties**
  - Simulation of surrounding structures
  - Simulation of image artifacts
  - No motion model
  - Only implemented in 2D

On going work

- **How to improve the simulation ?**

  - ***Main idea*: merge the model-based simulation with the image-based one**

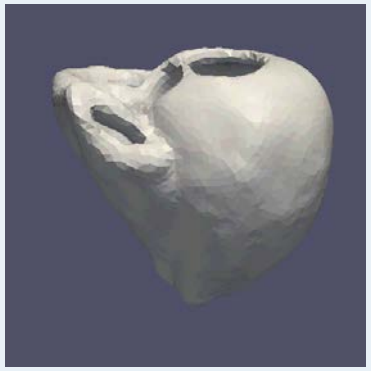
  - **Develop a specific registration between a model and a real 3D ultrasound sequence**

    - ✓ **Derivate a motion strategy for the scatterers inside the myocardium**

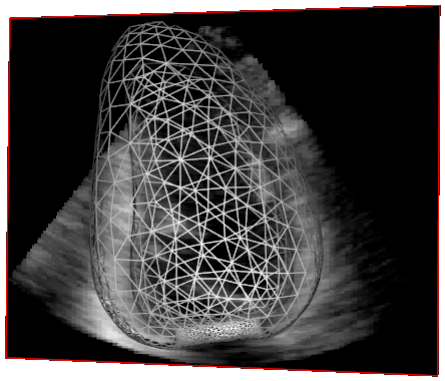
    - ✓ **Derivate an amplitude strategy for all the scatterers using our image-based phylosophy**

On going work

Anatomical + Electromechanical motion models



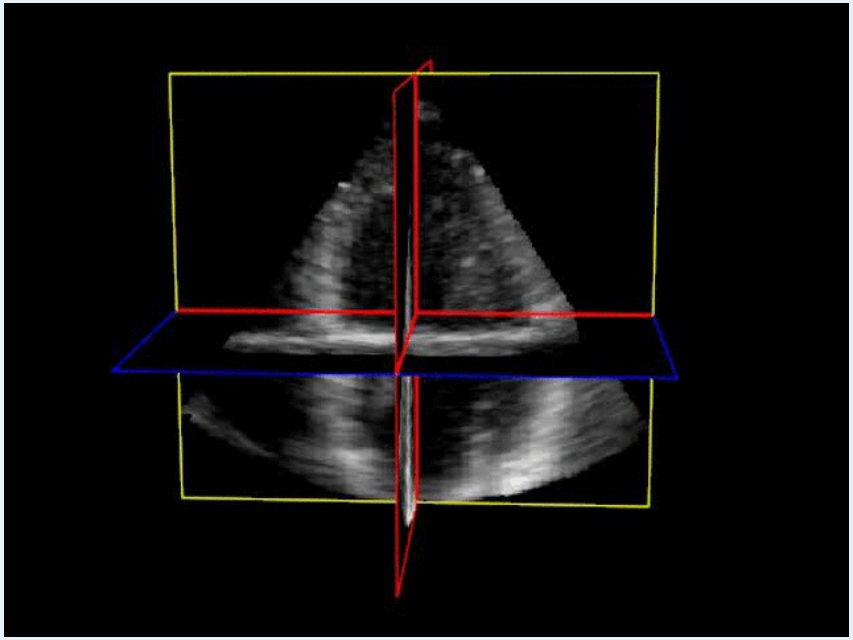
Real clinical recording



Dedicated registration algorithm

Ultrasound simulator

- ***Outside myocardium: random scatterers position and motion***
- ***Inside myocardium: motion from the EM model***
- ***Scatterers amplitudes: derived from the image-based strategy***



Conclusions

- We are developing a pipeline based on synthetic sequences for the quality assessment of segmentation / motion / strain estimation techniques

- This can be used to simulate both 2D and 3D US sequences

- Improve the realism of the simulations by:

  - Including surrounding structures and US realistic artifacts having major impact on the performance of algorithms

  - Making the motion fully controlled by an E/M model capable of modeling pathological conditions

  - Making the speckle texture appearance realistic

Future developments

- **Quantitative comparison of existing 3D strain estimation techniques**

- **Improving the E/M model for the generation of a set of controled pathological cases**

- **Creation of a publicly available library of sequences including clinically relevant cases and distributed through the VIP platform**

Conclusion

- **A better understanding of living functions (heart, bone …)**

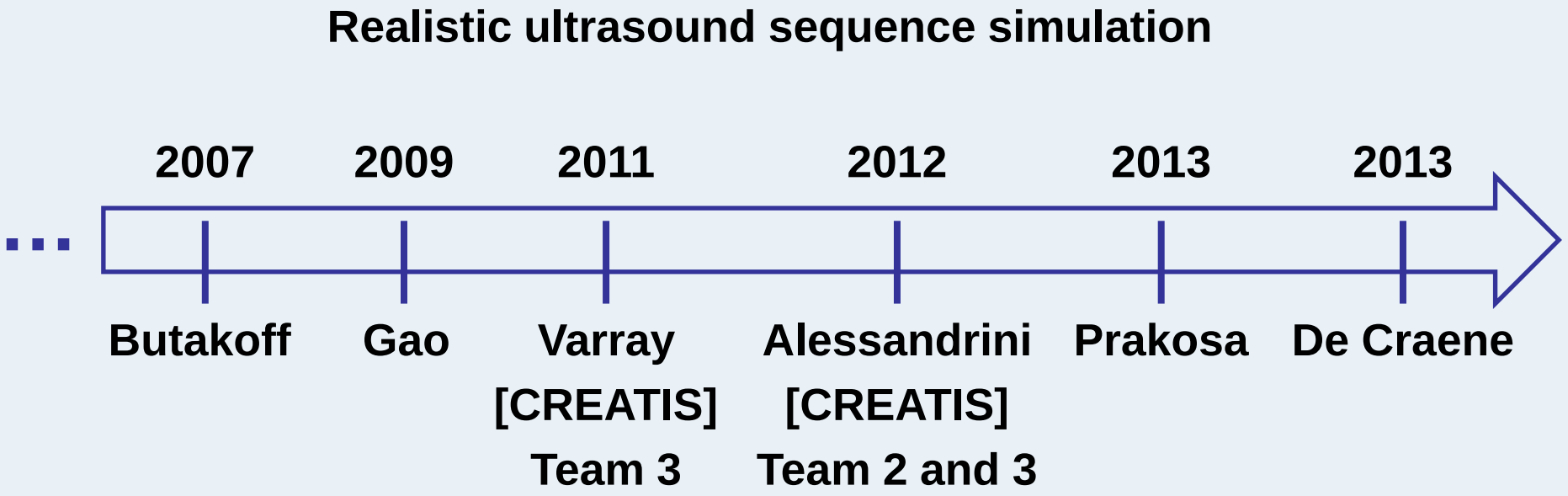
  ⇒ Imaging is a privileged tool

- **Challenges**
  - *In-vivo* imaging
  - Improvement of spatial resolution : from macro to nano
- **Perspectives**
  - Reconstruction : new imaging modalities
  - Models :
    - Improvement of the models with information at various scales
    - Progresses in various aspects of modelling : geometric modelling, motion modelling, distributed computing modelling …
  - Simulation :
    - Image, dose
    - High performance computation

Appendices

State of the art in ultrasound sequence simulation

- **Continuous effort to make simulation more realistic both in terms of simulator and numerical phantoms**



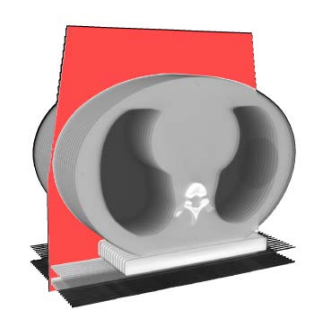
In-silico simulations in radiation and particle therapy

- **Issues**
  - Accurate and fast dose prediction
  - Design of new imaging devices
  - Improved reconstruction by integrating physics properties (scatter)

- **Methods**
  - Monte-Carlo. GATE plateform (international opengate collaboration)
  - High performance computing (GateLab, related to VIP project)
  - Hybrid approach: mixing analytical and MC methods

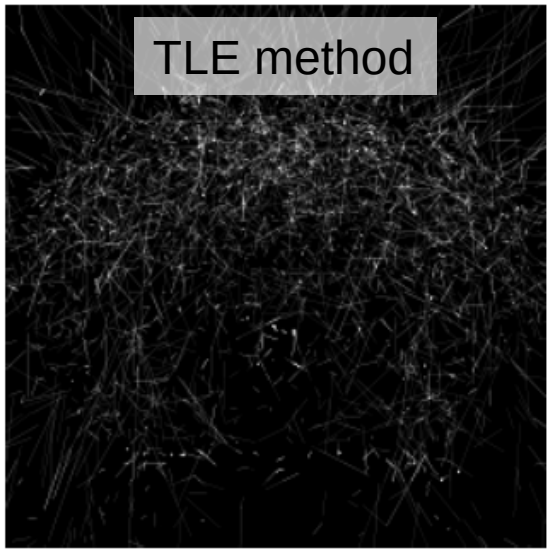
- **Applications**
  - Dose in radiation therapy (high E for patient and low E for small animals)
  - Dose in X-ray imaging (CBCT)
  - Dose in proton therapy
  - Prompt-gamma (dose monitoring in protontherapy)

In-silico simulations in therapy : one example

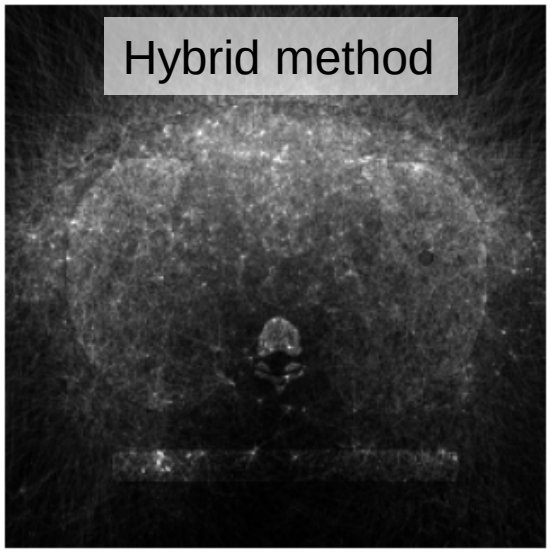


- Dose computation in X-ray imaging (CBCT), 80 kV
- Very slow MC convergence
- x100 faster with TLE approach (published PMB)
- x700 faster with hybrid approach (in progress)

reference



~100 x faster

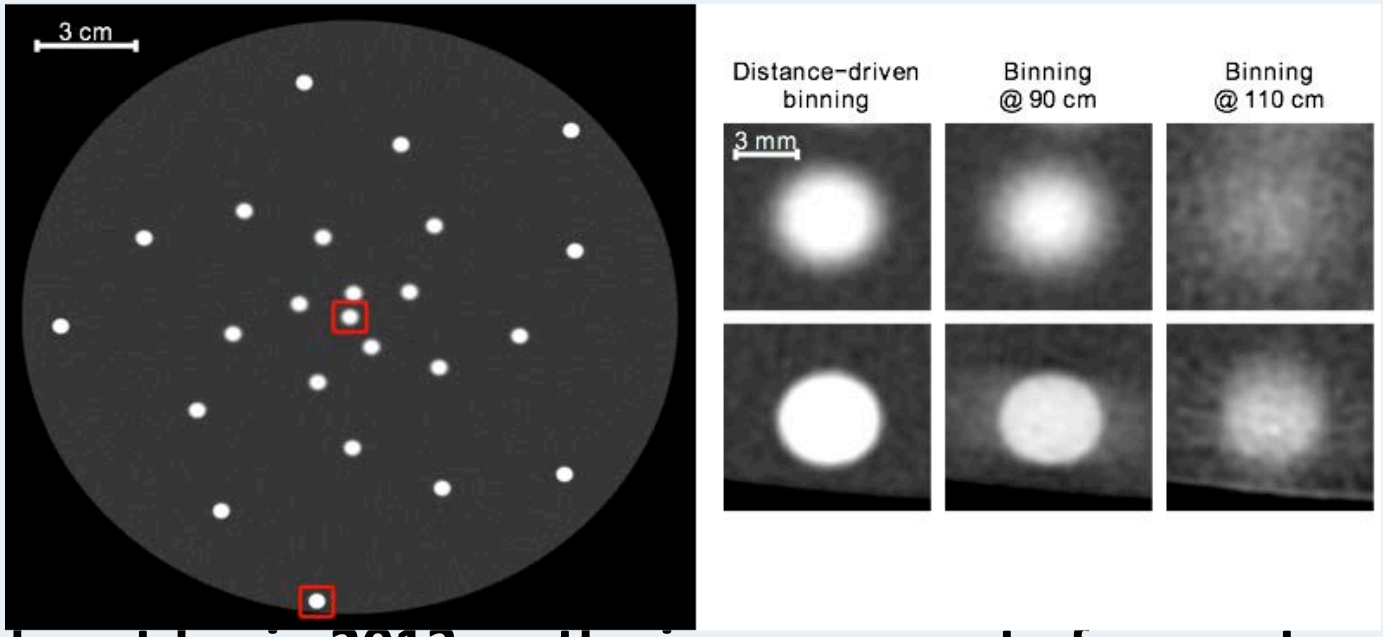


~700 x faster

Perspectives : Proton-CT

- **Protons lose energy along curved paths**

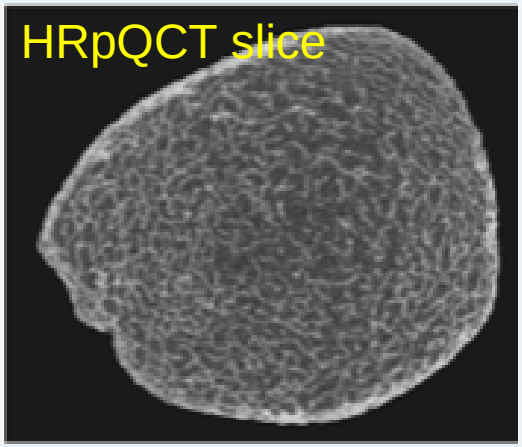
➔ **Distance driven binning for improved spatial resolution**
[Rit et al, Med Phys, 2013]

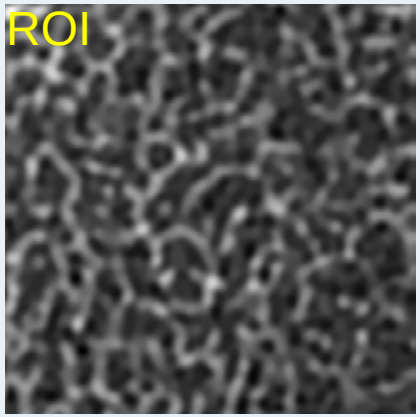


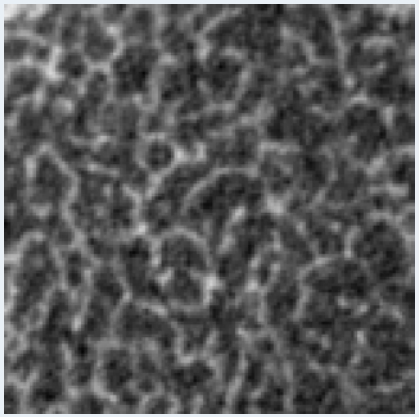
PhD and postdoc in 2013 on the improvement of reconstruction algorithms and the simulation-based design of a prototype.

Perspectives : HR pQCT

- **High Resolution Peripheral CT :** In vivo imaging of bone µ-architecture
- **Aim :** super resolution techniques (PhD Alina Toma)



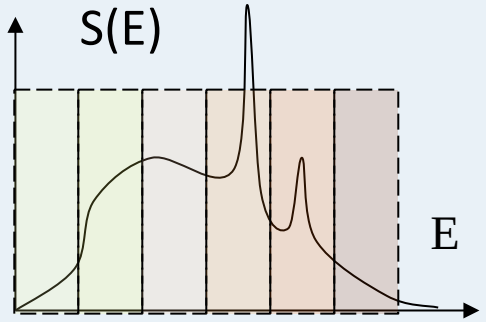




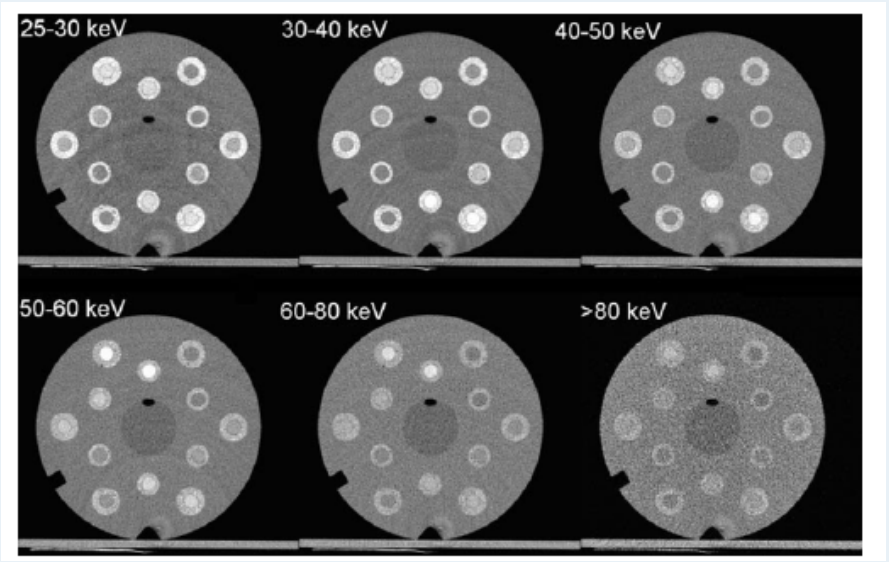
- **Methods**
  - TV-based regularization methods
  - Challenges
    - identification of PSF, variant noise…
    - Automatic choice of the regularization parameter
    - Handle the segmentation problem
    - Application to real data : 3D, large data sets

Perspectives : SPECTRAL CT

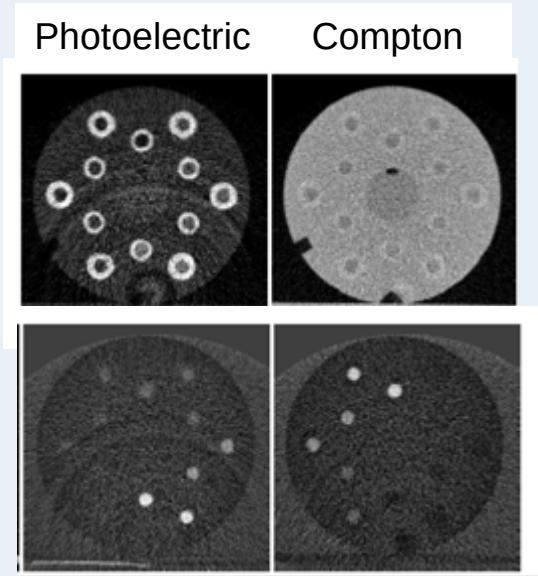
- **Spectral CT**
  - Idea : Divide the spectrum in energy bands
  - Systems with energy sensitive detectors are developed
  - Raise new problems for data processing (coll CEA-LETI)



X-ray energy spectrum



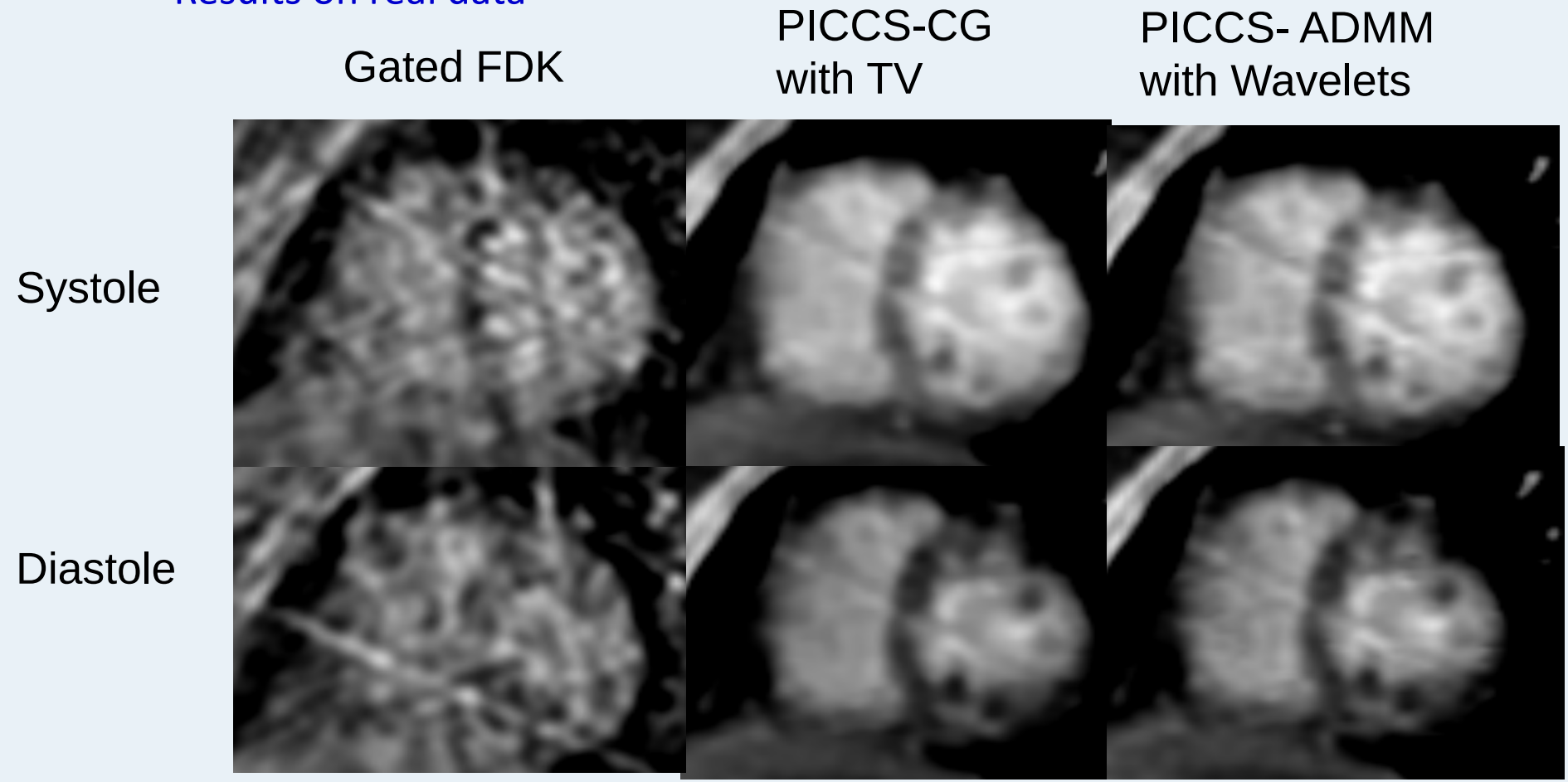
[from Schlomka PMB, 2008]



Concentration Io, Gd (umol ml^{-1})

Cardiac imaging in Rotational Angiography

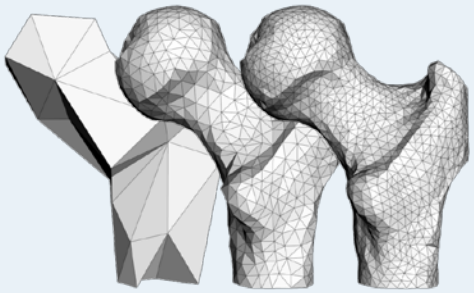
- **Prior Image Constrained Compressed Sensing :**
  - Results on real data



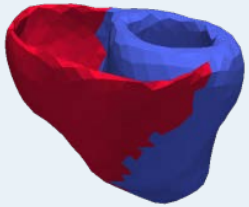
PhD Cyril Mory, coll Team 1

Modelling

- Modelling the physics of imaging
- Geometric Modelling



- Motion Modelling
- Deformable Modelling



- Models for distributed computing