Bone repair and ultrasound stimulation: an insight into the interaction of LIPUS with the bone through a multiscale computational study

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Ultrasound waves and living tissues

UltraSounds (US) interact with living tissues : destroy (HIFU) and repair (LIPUS)

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LIPUS stimulates bone healing :

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But how ?
Open question !
(*Claes et al. 2007, Padilla et al. 2014*)

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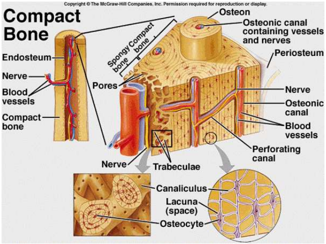
How is cortical bone tissue organized ?



- Multiscale porosity :
  - vascular porosity (HV) :
    Havers and Volkman canals (Ø$\simeq$ 100 μm)
  - lacuno-canalicular network (LCN) :
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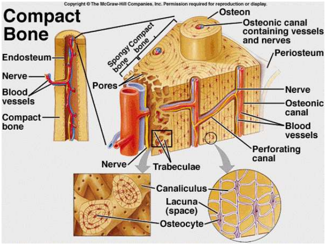

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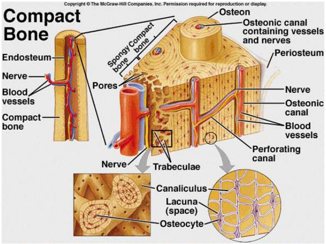

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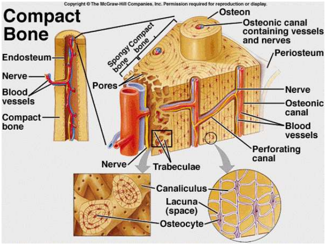

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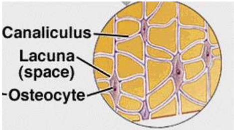

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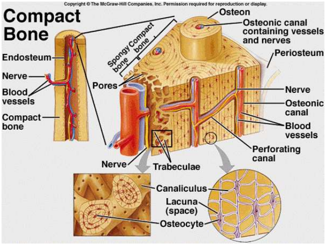

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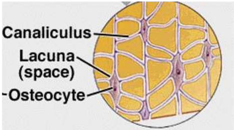
Bone mechanotransduction under physiological loading

(Cowin et al. 1991, Weinbaum et al. 1994, Klein-Nulend et al. 1995, etc.)

Interstitial fluid (IFluid) shear stress on **osteocytes**

$\Rightarrow$ bone remodelling



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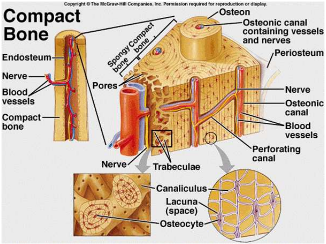

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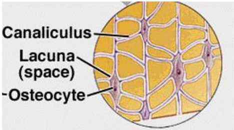

Cortical bone = double-porosity medium

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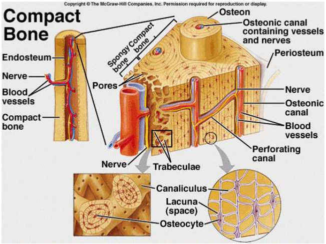

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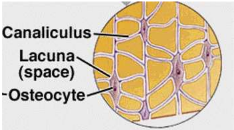

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Biphasic medium 2D-model + US

- Vascular pores (HV) = fluid phase $\approx$ water
  HV pores reconstructed from binarized μCT images (22.5 μm)

RX image

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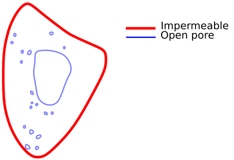

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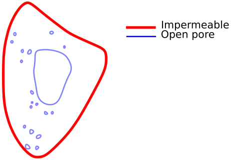

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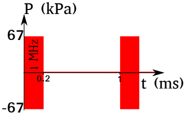


FE simulation

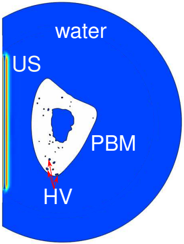
Interaction between ultrasound waves and double-porosity medium in water

<u>Software</u> : Comsol Multiphysics

- Time-dependent problem

  $\Rightarrow$ Weak form of wave equation in poroelastic medium + boundary conditions *(Nguyen et al. 2010)*

  $\triangle x \leq \lambda/5$, and $\triangle t = 0.1\mu s$ (CFL) $\rightarrow$ 24h to simulate a single cycle propagation.



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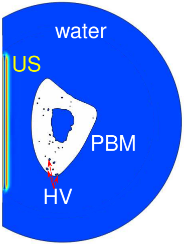

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    (Goulet et al. 2008)

τ : wall shear stress (Pa)
μ : dynamic IFluid viscosity (Pa.s)
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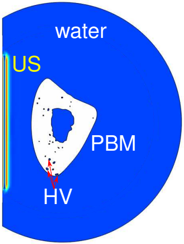

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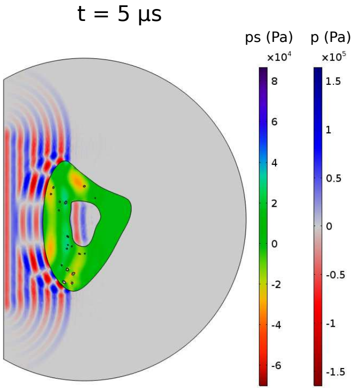

p : fluid pressure
ps : IFluid pressure

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3 models :

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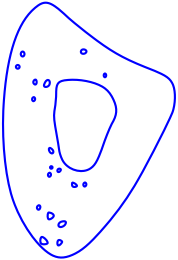

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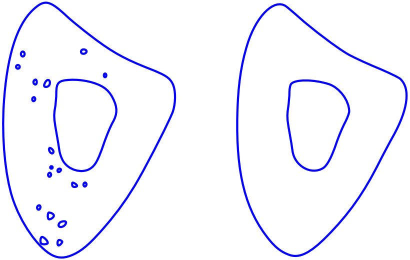

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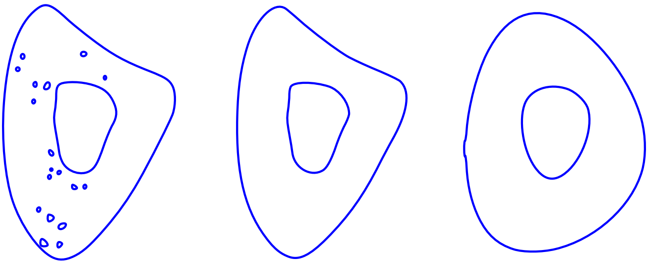
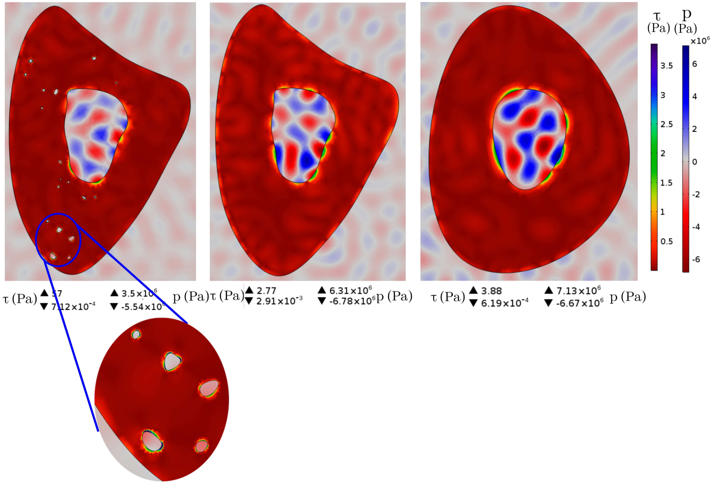
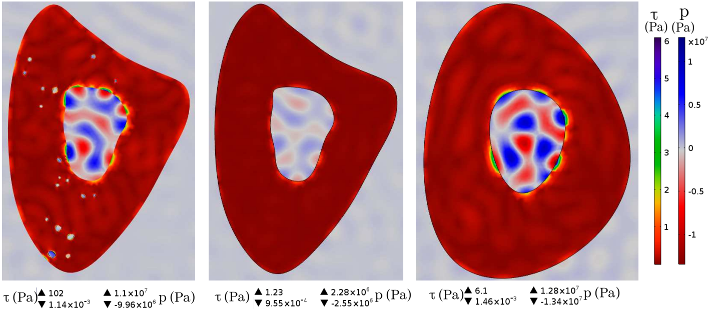


Results

IFluid shear stress and fluid acoustic pressure maps at 200 μs



IFluid shear stress and fluid acoustic pressure maps at 1 ms



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- IFluid shear stress localized around medullar canal and vascular pores

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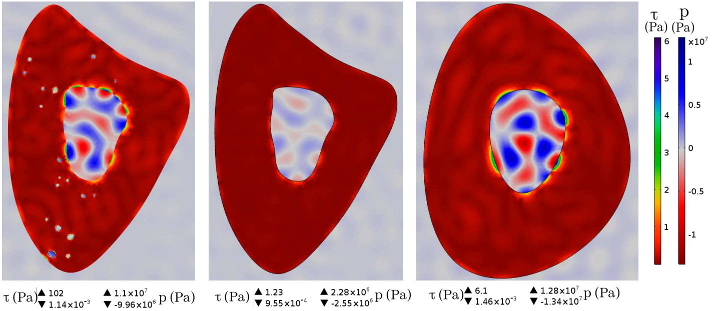

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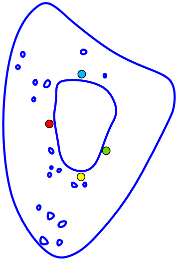

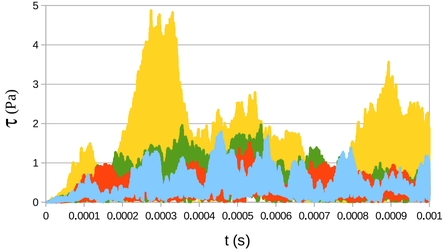

- Average IFluid shear stress : [0.4 - 1.2] Pa

- Prediction interval of osteocyte activation under physiological loading : [0.3 - 8] Pa

(Weinbaum et al. 1994)

Conclusion and Perspectives

2-scale numerical model to investigate the mechanical effects of LIPUS on osteocytes.

⇒ IFluid shear stress level locally in the range of the prediction interval ([0.8-3] Pa) given in literature for physiological loading *(Weinbaum et al. 1994)*

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⇒ Influence of the geometry and of the vascular pores

Poroelastic model and US

- LCN permeability 2.2×10^{-22} m^2 *(Cowin et al. 2009)*
- treatment duration (15 min) vs 1 cycle (1 ms) : cumulative effect to investigate
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- stimulation frequency higher than physiological loading (1 - 100 Hz)
- loading direction
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(Cardoso et al. 2013)

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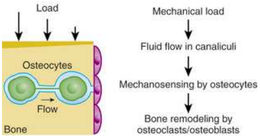

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Questions :

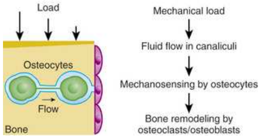
- fluid shear stress ?
- osteocytes ?

Other physical phenomena :

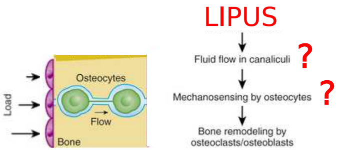
- Microstreaming ?
  Force radiation ?
  Piezoelectricity ?
- vascular porosity : osteoblasts / lining cells ?
  (Kwon et al. 2010, 2012)

→ LIPUS on culture cells : cells = osteoblasts
(Doan et al. 1999, Gleizal et al. 2010, Puts et al. 2016)

[1-100] Hz

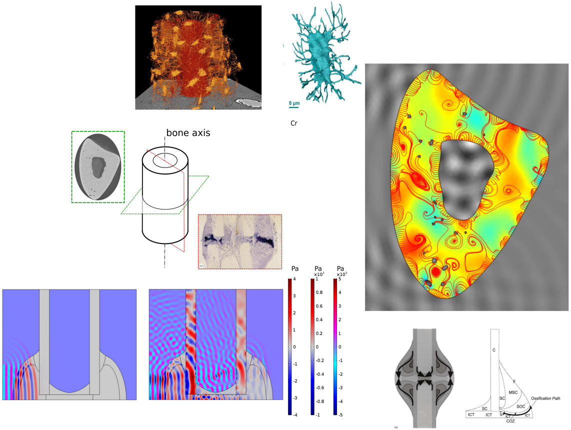


>1 MHz



Thank you for your attention.

Any questions (or answers) ?



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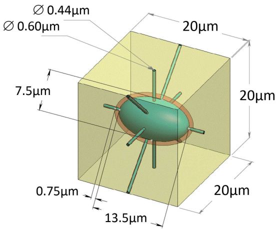
Models

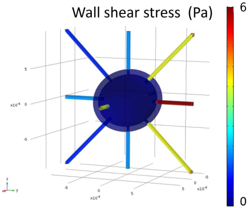
Osteocyte Model



IFluid domain : ρ=997 kg/m^3, μ=885$\times$ 10^{-4} kg.m^{-1}.s^{-1}

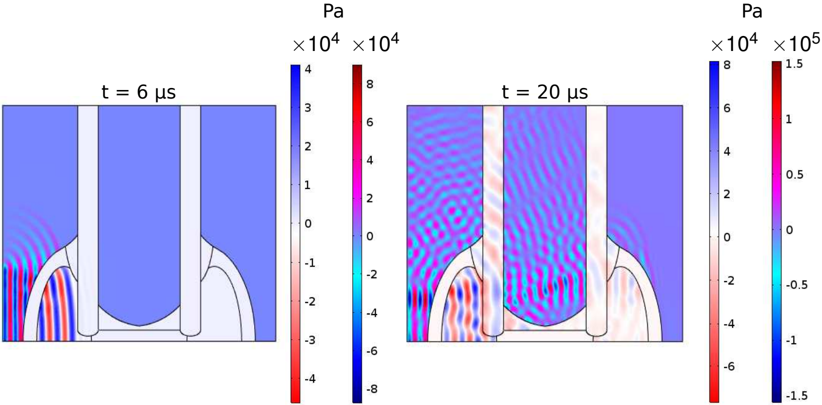
ECM : E=16.6 GPa, ν=0.38
osteocyte : E=4.47 kPa, ν=0.3

- input parameter :
  IFluid P gradient : 30 Pa$/\mu$m
- output parameter :
  fluid shear stress on osteocyte : τ



Limitations of the study

- a realistic model of the bone callus ?

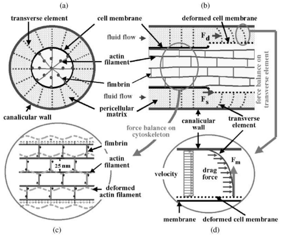


Conclusion and Perspectives

2-scale numerical model to investigate the mechanical effects of LIPUS on osteocytes.

Osteocyte process model

- Zoom on the osteocyte process into the canaliculi
  $\rightarrow$ GAG fibers $\rightarrow$ **strain amplification**



You et al. 2001

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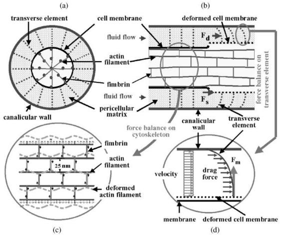

You et al. 2001

Drag forces F_d

$$F_s = 2\pi a L \tau \approx 16.10^{-12}\mathrm{N} \Rightarrow F_d \approx 330.10^{-12}\mathrm{N}$$

a = 0.22 μm : process radius ; L = 20 μm : process length.

Equations

- Wave propagation in the anisotropic poroelastic matrix (from *Nguyen et al. 2012*)

The constitutive equations for the anisotropic linear poroelastic material are given by

$$\boldsymbol{\sigma} = \mathbb{C} : \boldsymbol{\epsilon} - \boldsymbol{\alpha}\, p \,, \tag{7}$$

$$-\frac{1}{M}\, p = \nabla \cdot \boldsymbol{w} + \boldsymbol{\alpha} : \boldsymbol{\epsilon} \,, \tag{8}$$

where $\mathbb{C}(\boldsymbol{x})$ is the elasticity fourth-order tensor of drained porous material; $\boldsymbol{\alpha}$, which is a symmetric second-order tensor, is the Biot effective tensor; M is the Biot scalar modulus; $\boldsymbol{\epsilon}(\boldsymbol{x}, t)$ is the infinitesimal strain tensor, which is defined as the symmetric part of $\nabla \boldsymbol{u}^s$.

$\boldsymbol{w} = \phi(\boldsymbol{u}^f - \boldsymbol{u}^s)$

- boundary conditions : pressure and stress fields continuity + *open pore* condition (continuity of the normal relative velocity between fluid and solid)

Poroelastic cortical bone properties

Transverse isotropic extralacunar matrix

$$\begin{pmatrix} 22.88 & 10.14 & 0 \\ 10.14 & 29.60 & 0 \\ 0 & 0 & 6.98 \end{pmatrix} (GPa)$$

(Scheiner et al. 2015)

Mass density : ρ=1.9 g/cm^3
Isotropic LCN permeability : 2.2×10^{-22} m^2 *(Smith et al. 2002, Cowin et al. 2009)*
Other Biot's parameters from *NGuyen et al. 2016*
ϕ=5%, α_1=0.11, α_2=0.15, M = 35.6 GPa.

Poroelastic healing tissues properties

4 weeks_ Isotropic solid matrix

- Granular tissue

$$\begin{pmatrix} 2.502 & 2.5 & 0 \\ 2.5 & 2.502 & 0 \\ 0 & 0 & 0.001 \end{pmatrix} \text{(GPa)}$$

ϕ=90%
α_1=0.98
α_2=0.96
M = 2.2 MPa
ρ= 1.01 g/cm^2

- Cartilage

$$\begin{pmatrix} 5.98 & 5.3 & 0 \\ 5.3 & 5.98 & 0 \\ 0 & 0 & 0.34 \end{pmatrix} \text{(GPa)}$$

ϕ=80%
α_1=0.98
α_2=0.96
M = 2.4 MPa
ρ= 1.04 g/cm^2

- Woven bone

$$\begin{pmatrix} 17.1 & 12.9 & 0 \\ 12.9 & 17.1 & 0 \\ 0 & 0 & 2.1 \end{pmatrix} \text{(GPa)}$$

ϕ=50%
α_1=0.976
α_2=0.955
M = 2.55 MPa
ρ= 1.25 g/cm^2