L.I.P. Laboratoire d'Imagerie Paramétrique

Quantitative ultrasound techniques using axial transmission to assess bone fragility

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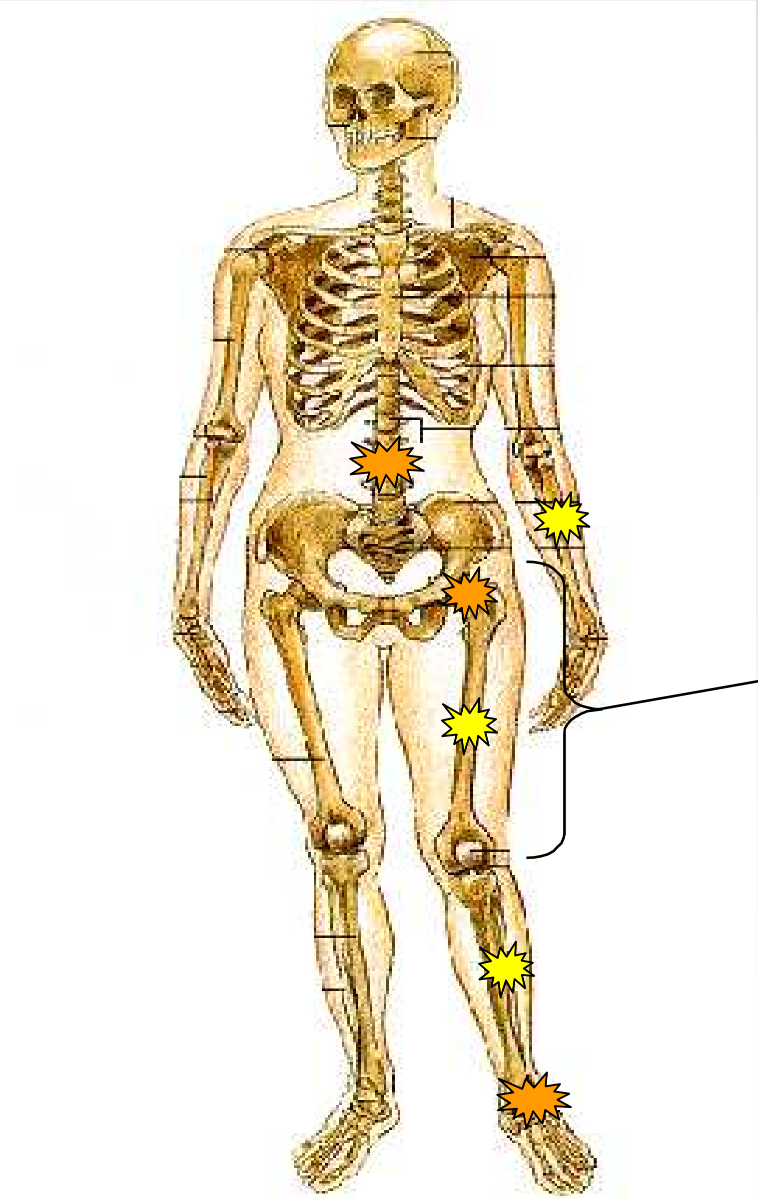
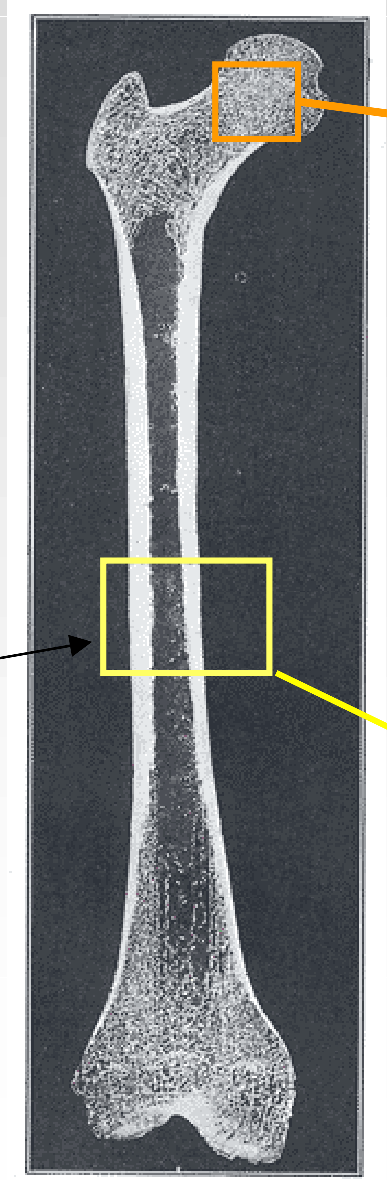
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE

Why Should We Care About measuring Bone?

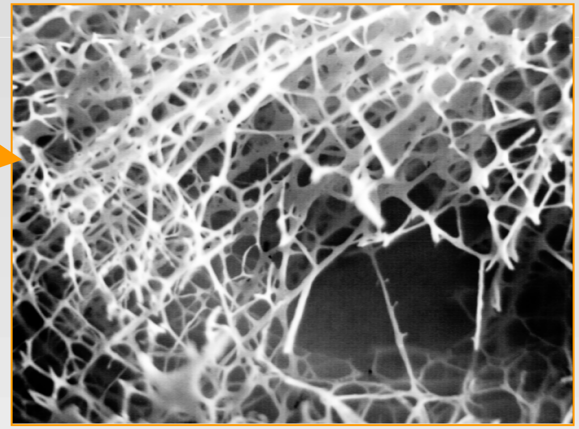
- Prevention of osteoporosis has been recognized as a major priority
- One in three women over the age of 50
- Osteoporotic fractures cause increased morbidity and mortality (hip fracture)
- Treatments are available that reduce fracture risk by 50%
- Other bone diseases associated with bone fragility can benefit from non invasive ultrasonic testing (adult secondary osteoporosis, pediatrics, orthopedics)

Architecture of bone





Cancellous bone



Cortical bone

Why Should We Care About measuring Bone?

- Quantitative ultrasound (QUS) : an alternative approach to X-ray bone densitometry testing
- Objective : assessment of bone fragility (prediction of fracture risk)
- Unlike X-ray densitometry, which determines the amount of mineralized tissue (BMD) in the bone volume, we assume that bone quantitative ultrasound (QUS) parameters will reflect skeletal factors other than BMD and be markers for whole bone strength
- Applied to cancellous bone or cortical bone

Introduction

Long list
Multiscale

Short list
Macroscopic
Poorly defined

Long list
Multiscale
Well defined

Bone properties

- BMD
- Structure (macro, micro)
- Damage
- Osteocytes
- Bone composition
- Collagen cross-links
- Crystal orientation
- …

***In vivo* QUS variables**

- Attenuation (BUA)
- Sound speed (SOS)

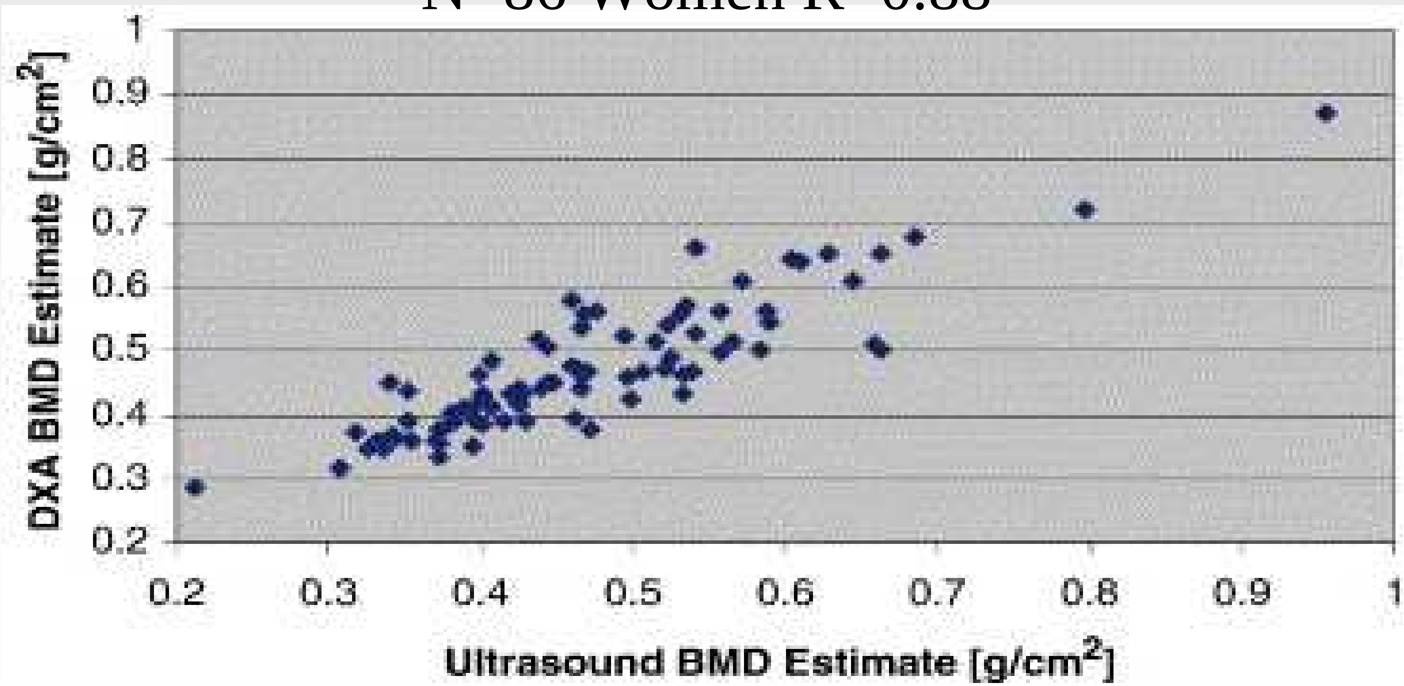
Measured at cortical or cancellous peripheral skeletal sites

Mechanical properties

- Stiffness
- Anisotropy
- Yield strain/strength
- Ultimate Strain/strength
- Energy to failure
- Toughness
- …

- Heel QUS is the best validated technique
- At the heel, QUS results are good proxy for BMD at the QUS measurement site

N=86 Women R=0.88



Siffert RS, Kaufman JJ.Bone. 2006 Aug 31

Question

Is it possible to identify new QUS measurement modes that could potentially quantitatively assess BMD-unrelated bone strength factors?

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- Stiffness
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- Toughness
- …

+ a few …

Model-based (backscatter)	or	empirically defined variables
→ US estimated Tb.Th, Tb.Sp Jenson et al. 2005, Pereira et al. 2005		Barkmann et al. 2000

Objectives

- To clearly state what can be measured
- Focus on SOS measurements in cortical bone

What is needed?

- As opposed to empirical methods developed so far, model-based methods are needed
- It requires solving the direct problem,

  i.e., predicting :
  - the measured signal field when the bone material properties and structure are known
  - Predicting the outcome of the measured variables
- *Expected result*
  - a clear identification of the different waves and their exact propagation path that contribute to the analyzed signals
  - a solution to the inverse problem (i.e., determining material or structural properties from multiple measurements).

An example : *in vitro* characterization

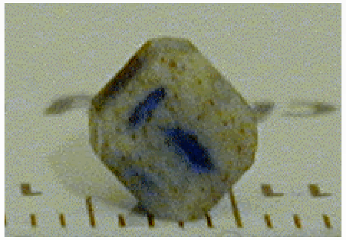
- Ideal experimental conditions in which the size and shape of the specimens is controlled
- The propagating waves (pure bulk shear or compression wave) are usually well identified
- Well established theory
- Material properties can be recovered from QUS measurements.

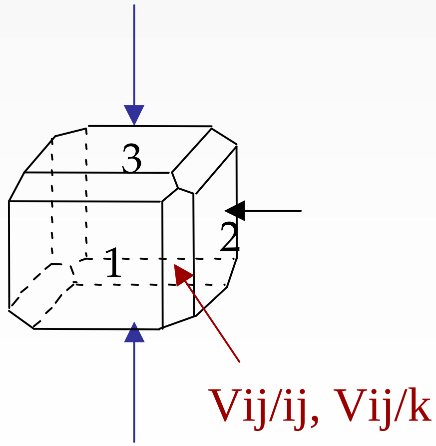
Bone is isotropic transverse

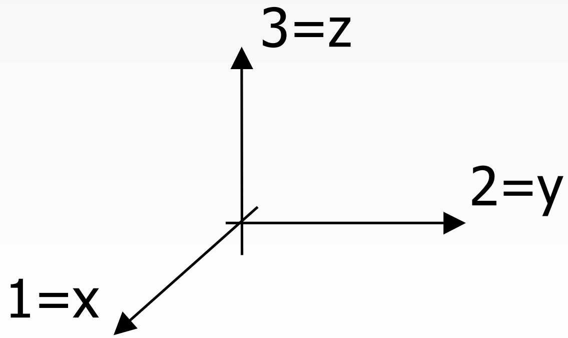
5 independent stiffness coefficients

$$[C_{ij}] = \begin{bmatrix} C_{11} & C_{12} & C_{13} & 0 & 0 & 0 \\ C_{12} & C_{11} & C_{13} & 0 & 0 & 0 \\ C_{12} & C_{13} & C_{33} & 0 & 0 & 0 \\ 0 & 0 & 0 & C_{44} & 0 & 0 \\ 0 & 0 & 0 & 0 & C_{44} & 0 \\ 0 & 0 & 0 & 0 & 0 & \dfrac{C_{11}-C_{12}}{2} \end{bmatrix}$$

Ultrasound can be used to derive the stiffness coefficients or the elastic moduli by sound speed measurements along multiple test axes

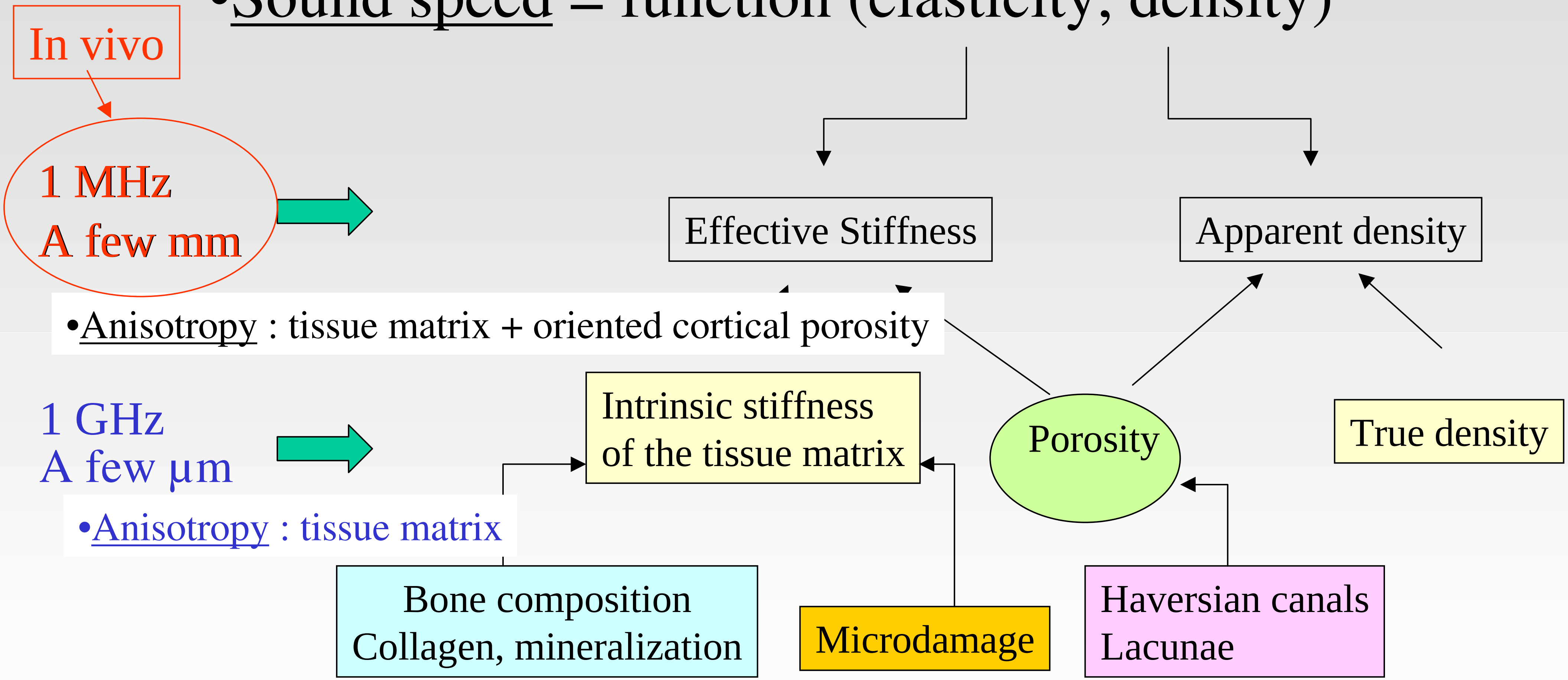






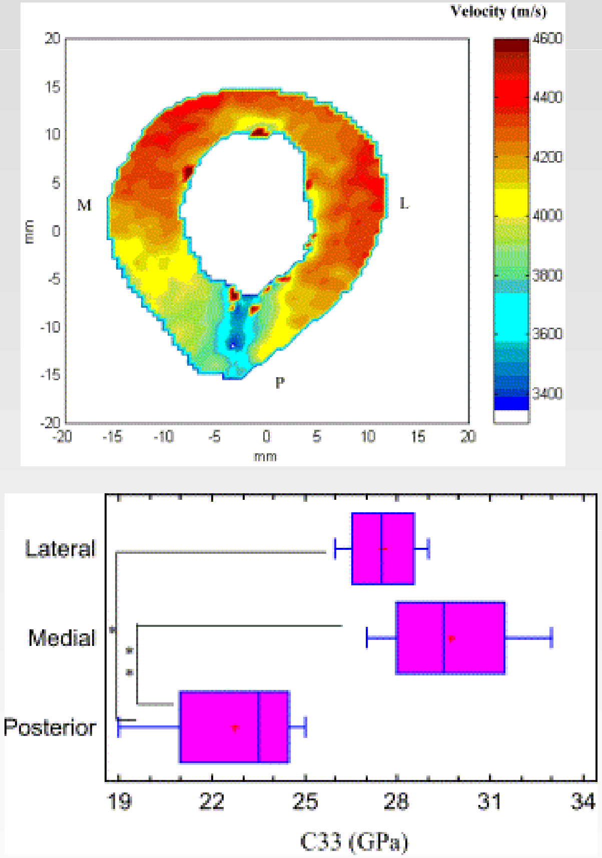
At any level of measurement (i.e., at the scale of the wavelength), we consider bone as a continuous homogeneous medium. At each level, there is a specific organization that is contributing to the properties of what we are measuring as a continuous medium.

•<u>Sound speed</u> = function (elasticity, density)



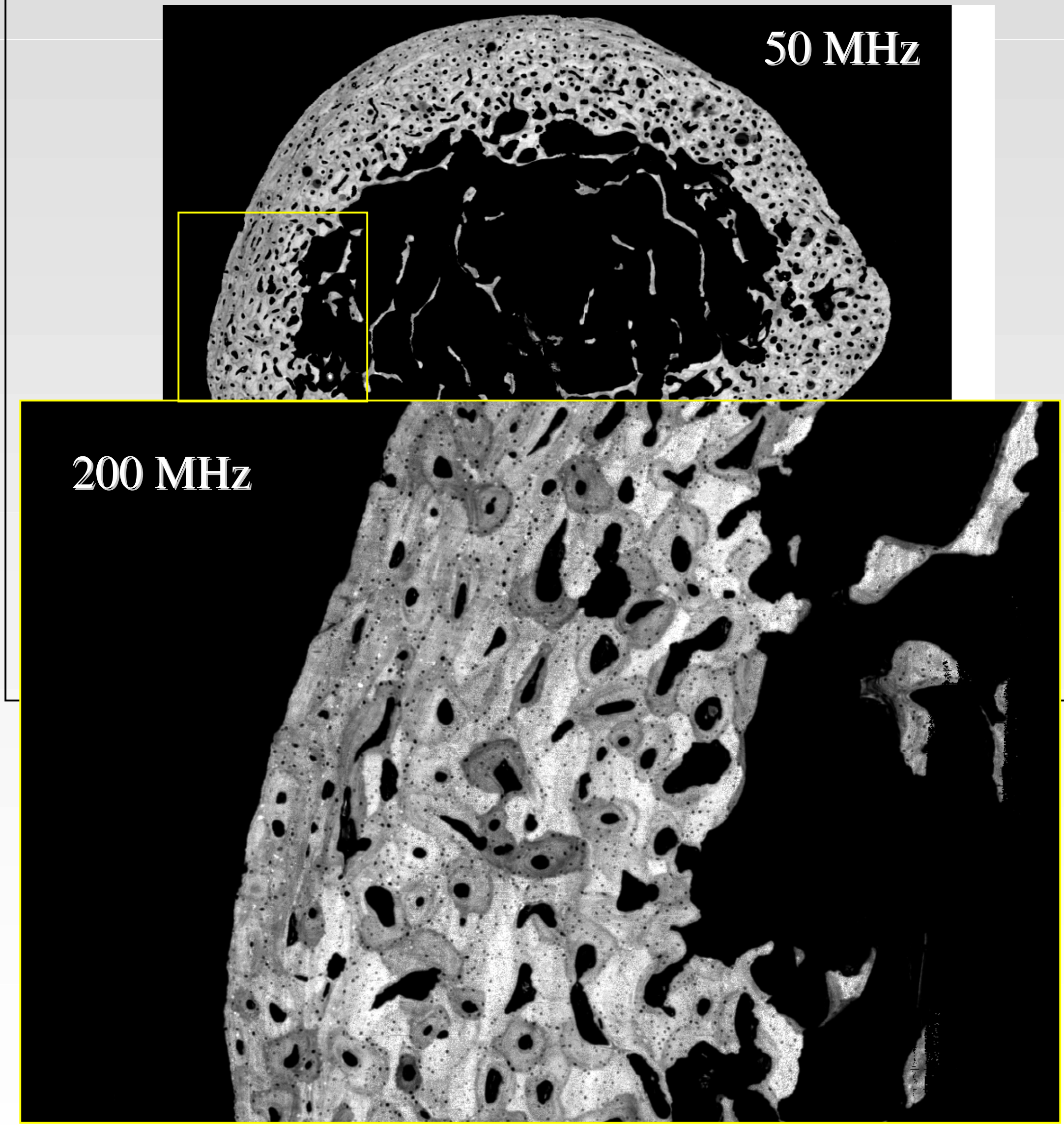
The frequency (wavelength) can be adapted to the required level of measurement.

Multi-scale characterization



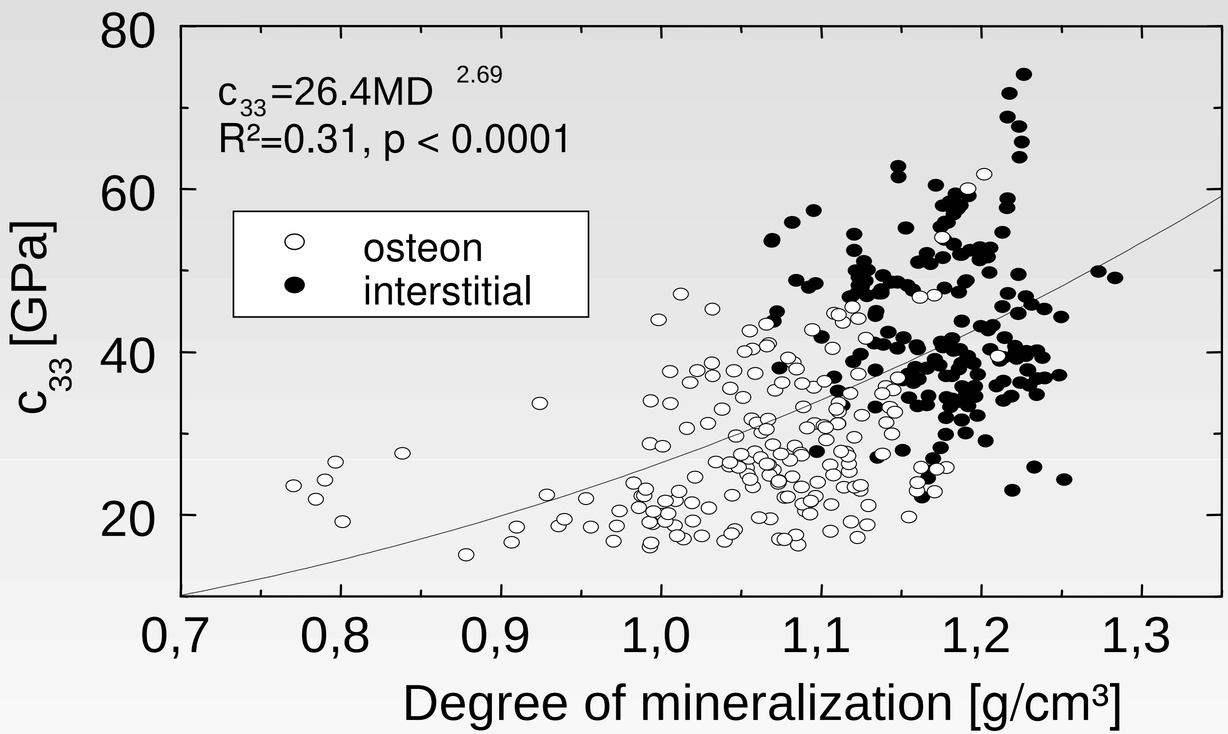
Velocities (Human femur) 5 MHz

Bensamoun et al., J Biomechanics 37: 503-510; 2004



Raum, Saied, Leguerney, 2004

Elasticity assessment (c_{33}): human radius (200 MHz)



The degree of mineralization cannot explain the variability of the stiffness, which is locally determined in addition to mineralization by HAP or collagen fibers orientation

Raum, Saied, Talmant, Peyrin et al., Phys Med Biol, 2006

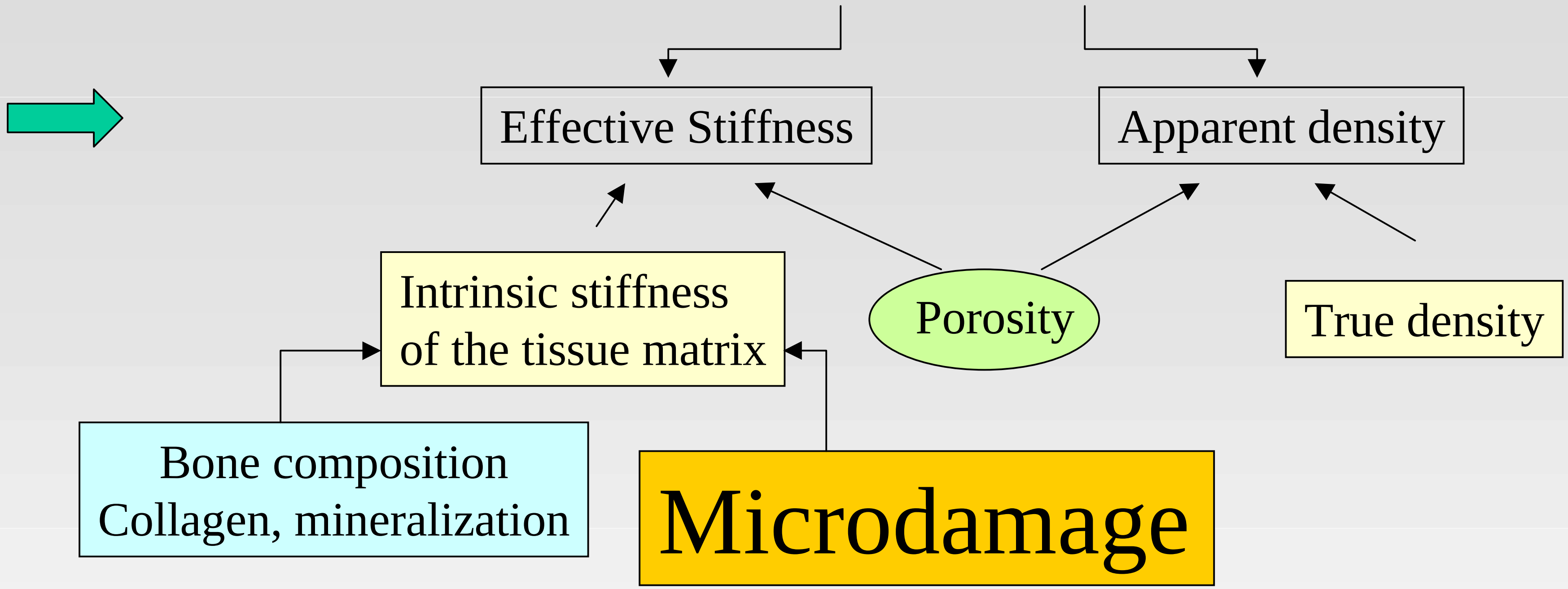
What is required to make progress ?

- Experimental models (e.g., genetically modified small animals) in which the organic and mineral phases can be controlled and assessed by independent means.
- *Expected results* :
  - multiscale QUS evaluation of bone stiffness (including SAM) to gain deep insight into the role of each bone property on the stiffness coefficients that governs sound speed values.
  - values of stiffness coefficients for computational models

• Sound speed = function (elasticity, density)

1 MHz

A few mm



Comment on microdamage

Microdamage produces a second order effect that cannot be measured with conventional sound speed measurements. It requires new concepts such as non linear acoustics to be measured.

In vivo Quantitative ultrasound

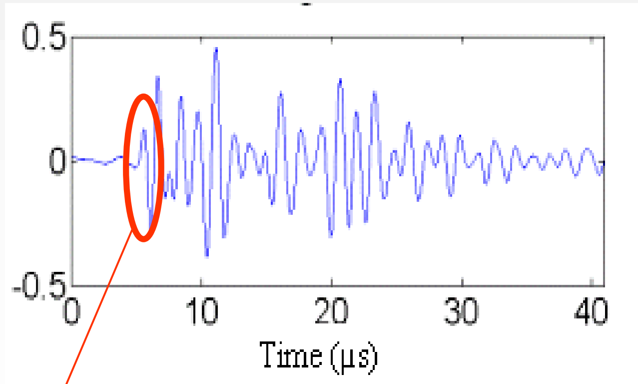
The situation is complex

- Much lower ultrasonic frequencies, typically in the range of 200 kHz to 2 MHz, must be used for *in vivo* assessment of cortical bone
- Whole bone is measured
- Irregularly shaped specimens
- Soft tissue

- *Requirements*
  - Interaction ultrasound/whole bone needs to be fully elucidated
  - To define measurements modes to probe independently relevant material and/or structural properties

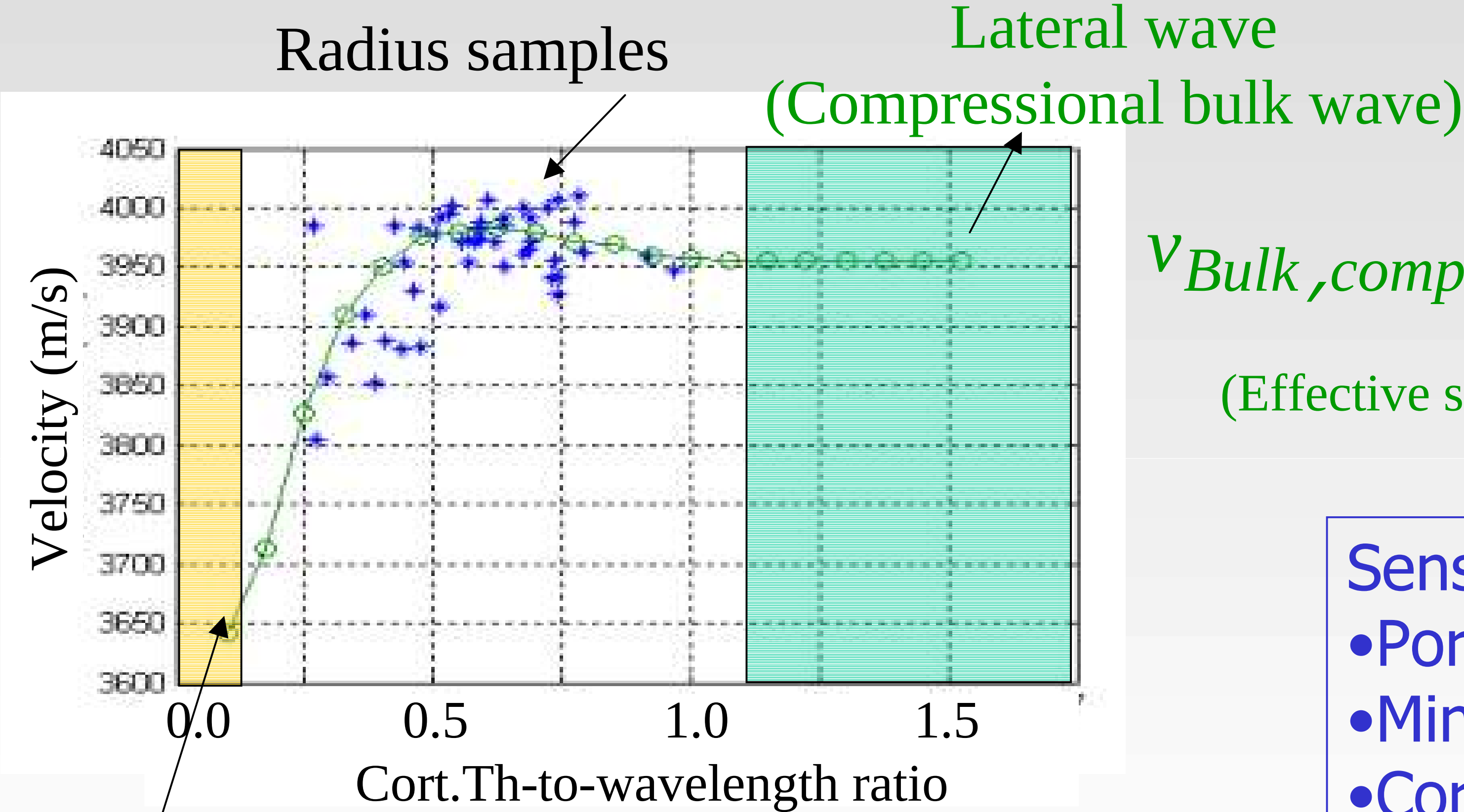
Axial transmission

- Generic term that designates a measurement configuration in which emitters and receivers are placed on the same side of the skeletal site, along the bone axis.
- Several modes can be excited
- The sound speed of each mode is governed by a specific combination of stiffness coefficients and sensitivity to cortical thickness



FAS velocity

First arriving signal (FAS)



« S_0 – like » guide wave

$$v_{S_0} = \sqrt{\frac{c_{33}}{\rho} \times \left(1 - \frac{c_{13}^{\,2}}{c_{11} \times c_{33}}\right)}$$

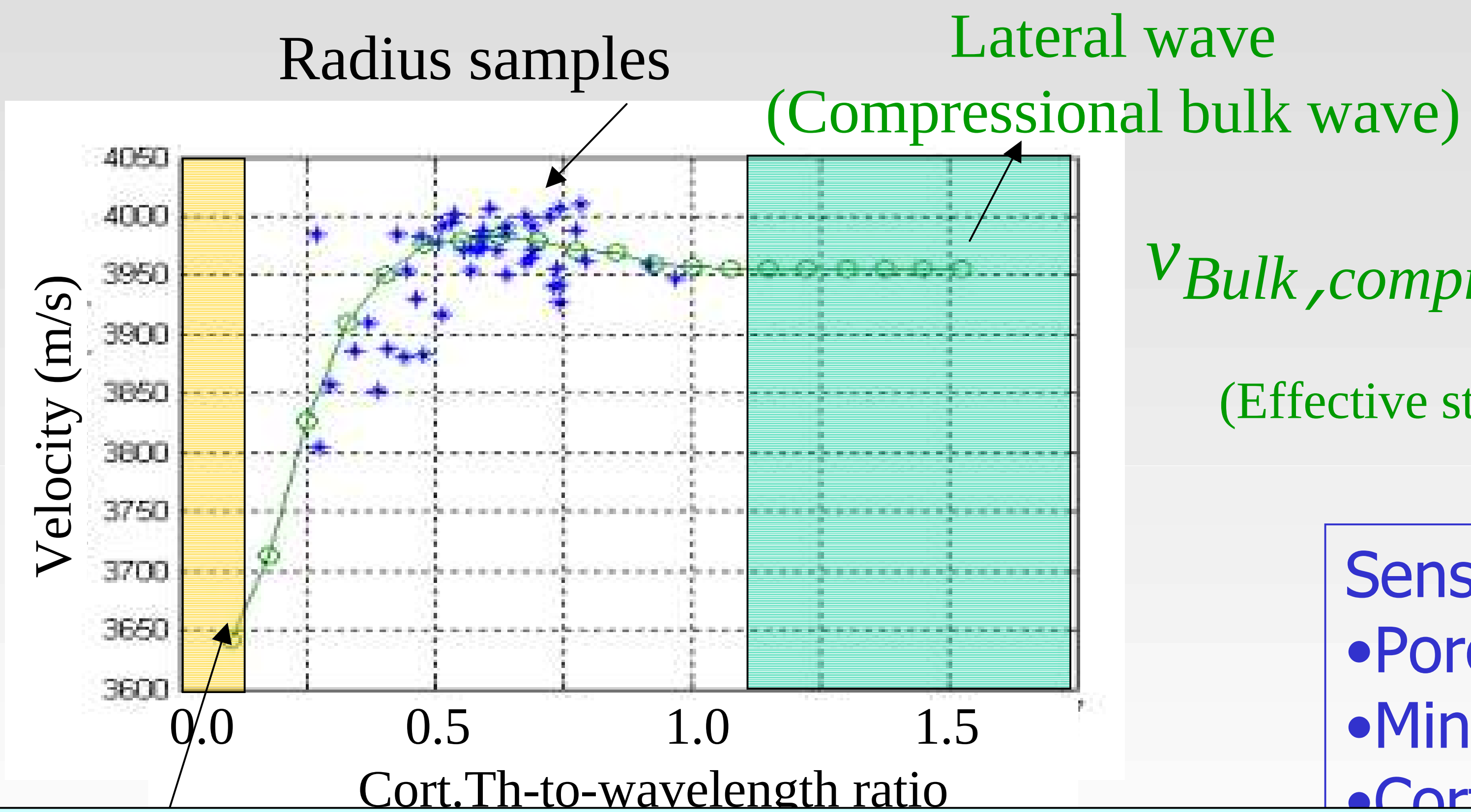
$$v_{Bulk,compr} = \sqrt{\frac{c_{33}}{\rho}}$$

(Effective stiffness)

Sensitivity to :
- Porosity
- Mineralization
- Cortical thickness
- Stiffness

Bossy & al. J Bone Miner Res, 2004
Bossy & al. JASA, 2004
Raum & al. Ultrasound Med biol 2006

First arriving signal (FAS)



$$v_{Bulk,compr} = \sqrt{\frac{c_{33}}{\rho}}$$

(Effective stiffness)

Sensitivity to :

- Porosity
- Mineralization
- Cortical thickness

Proposal

In the intermediate regime, the inverse problem cannot be easily solved.

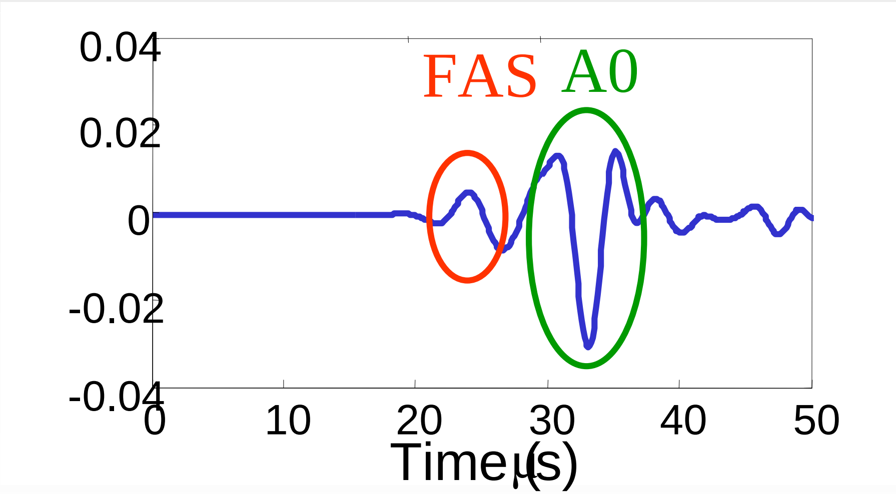
Instead, the frequency can be tuned to excite subsequently the well-defined lateral wave and "S0-like" guide wave mode

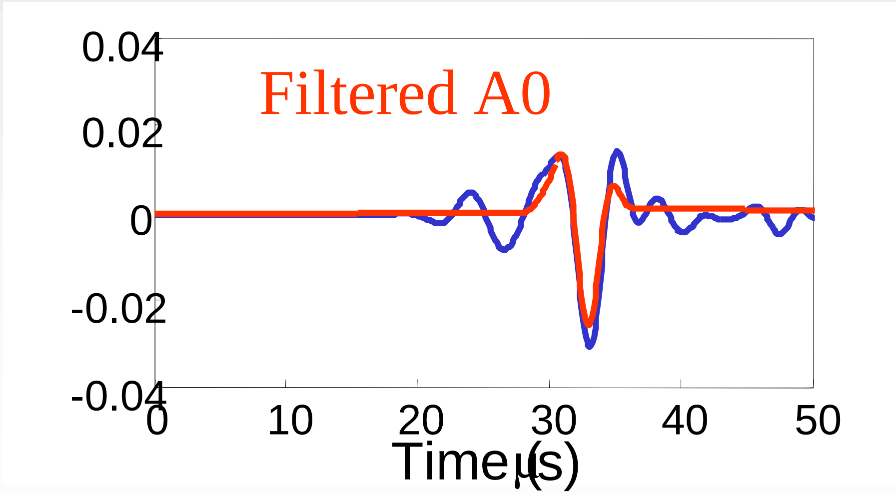
Slow A0 - Guided waves

P Moilanen, Ultrasound Med Biol 2006 May;32(5):709-19

- **LF** transmission **200 kHz – "A0 mode"** - whole cortical thickness
- Sensitivity to cortical thickness.

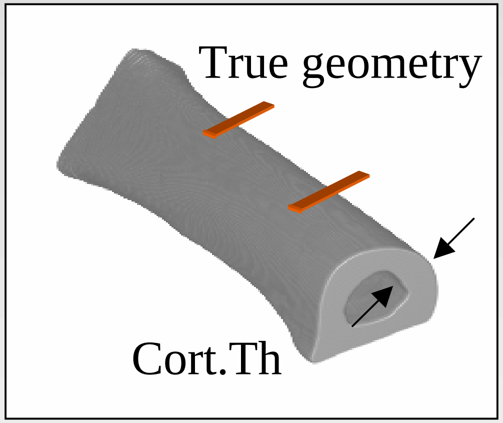
•Can be used to estimate cortical thickness

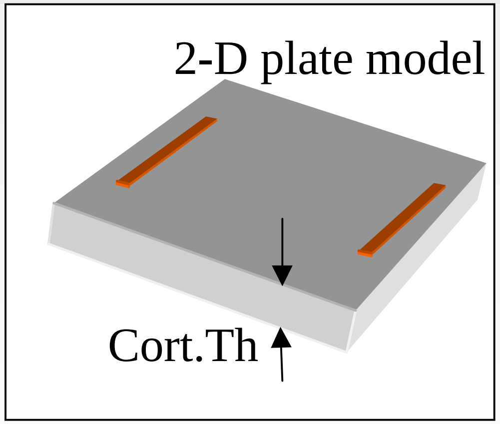




Slow A0 - Guided waves

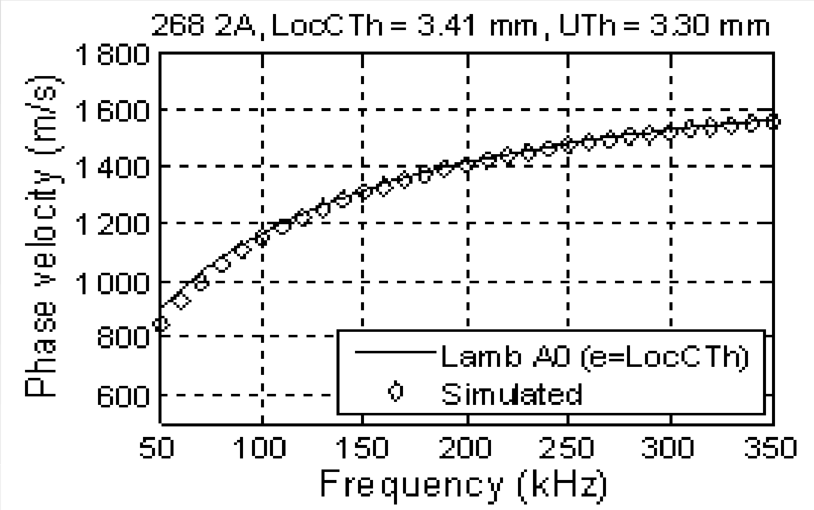
Inversion scheme – Ultrasonic estimation of cortical thickness

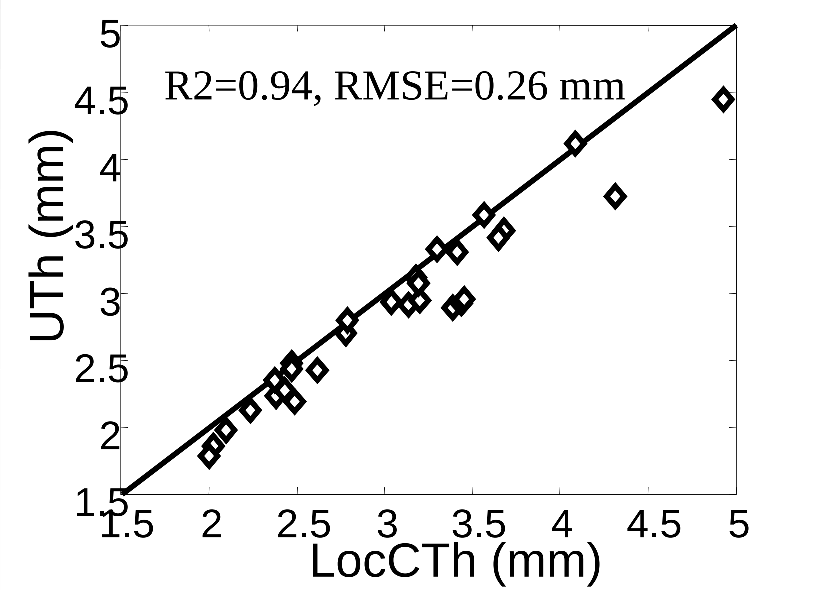




Comparison between experimental data and the analytical expression for a plate model

Minimization of a cost function
→ Estimate of Cort.Th





Computational bone model
Finite-Difference Time-Domain method (FDTD)

Step 1: the microscopic bone model

Input

- 3D μ-structure (SR-μCT)
- Material properties
  - – Density, Stiffness tensor
  - –Generic values (literature)
  - – Data from SAM (Heterogeneous medium)

Output

Effective stiffness coef.
function of porosity and intrinsic stiffness

Step 2: the macroscopic bone model

Input

- 3D structure (CT)
- effective properties
  - – Density, Stiffness tensor

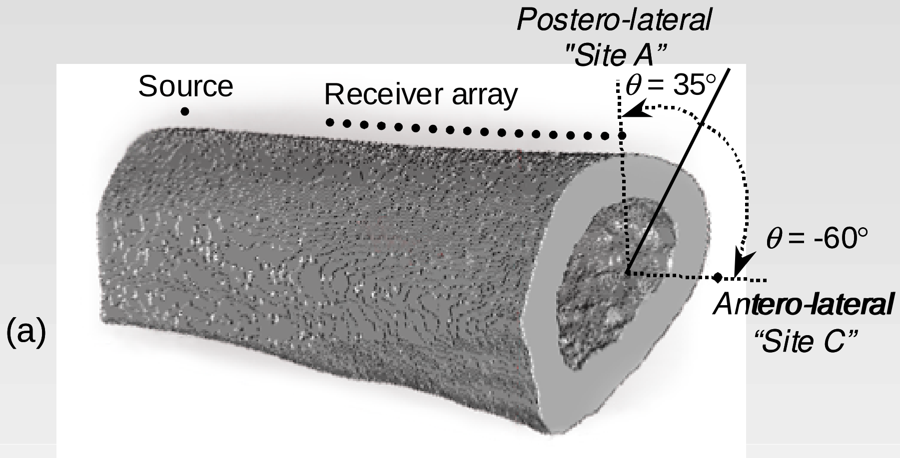
Soft tissue

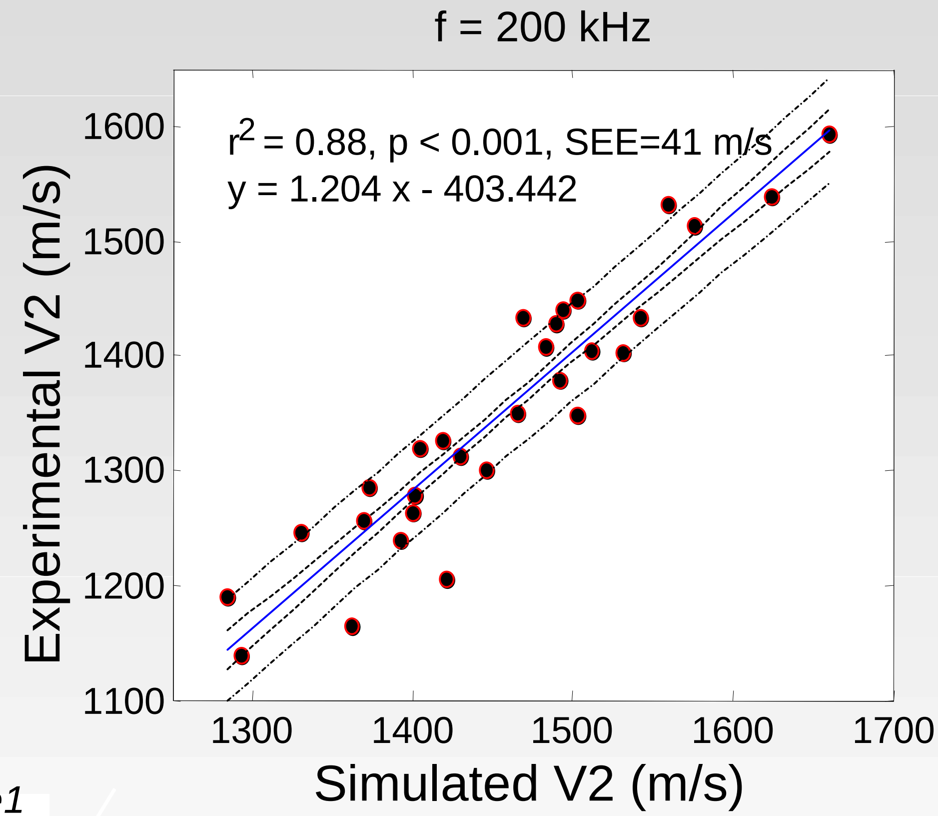
Output

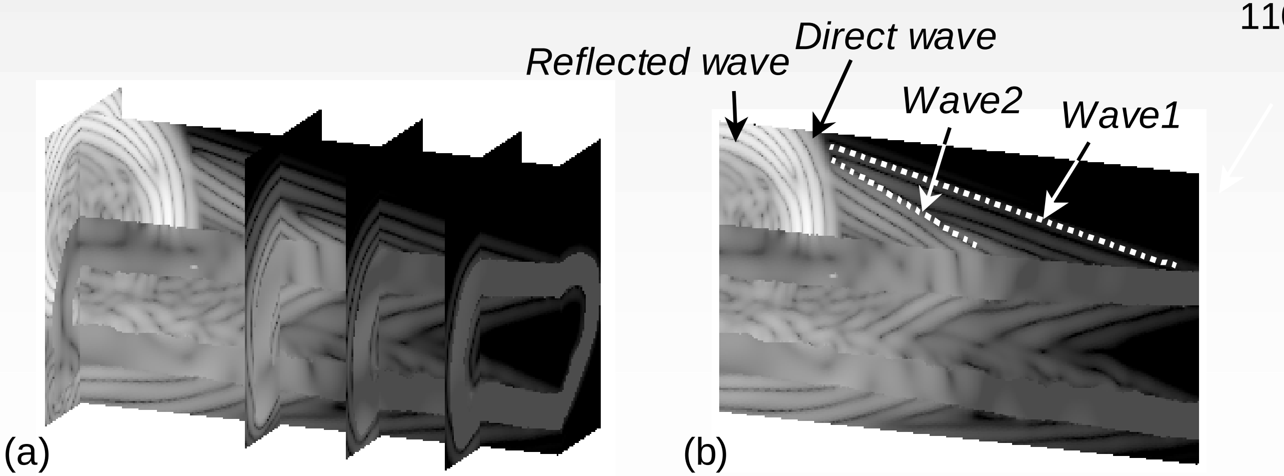
Sound speed (attenuation) of different wave types
Function of porosity and intrinsic stiffness

The whole process permits to study the sensitivity of a selected wave to multiscale bone material and structural properties and may be helpful as an aid to devise a technique specific for the assessment of a given bone property.

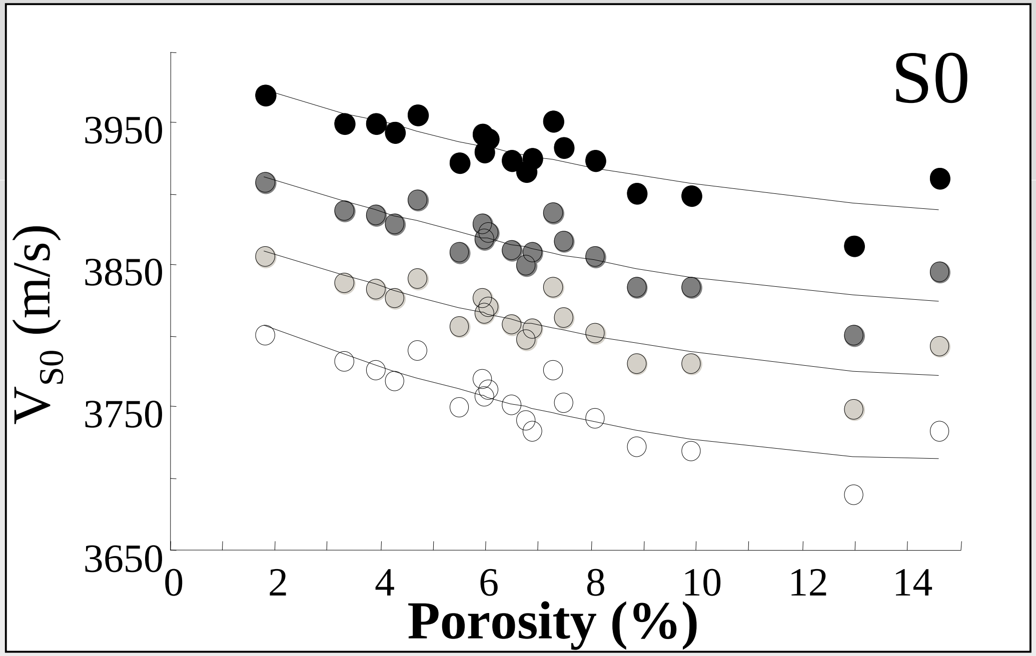
Computational bone model : validation





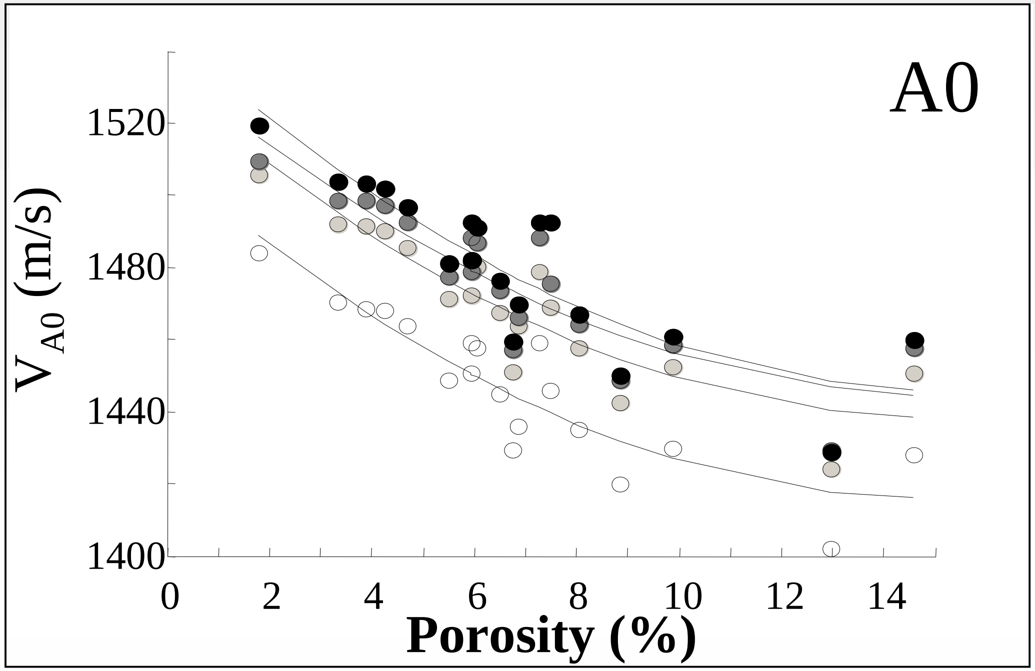


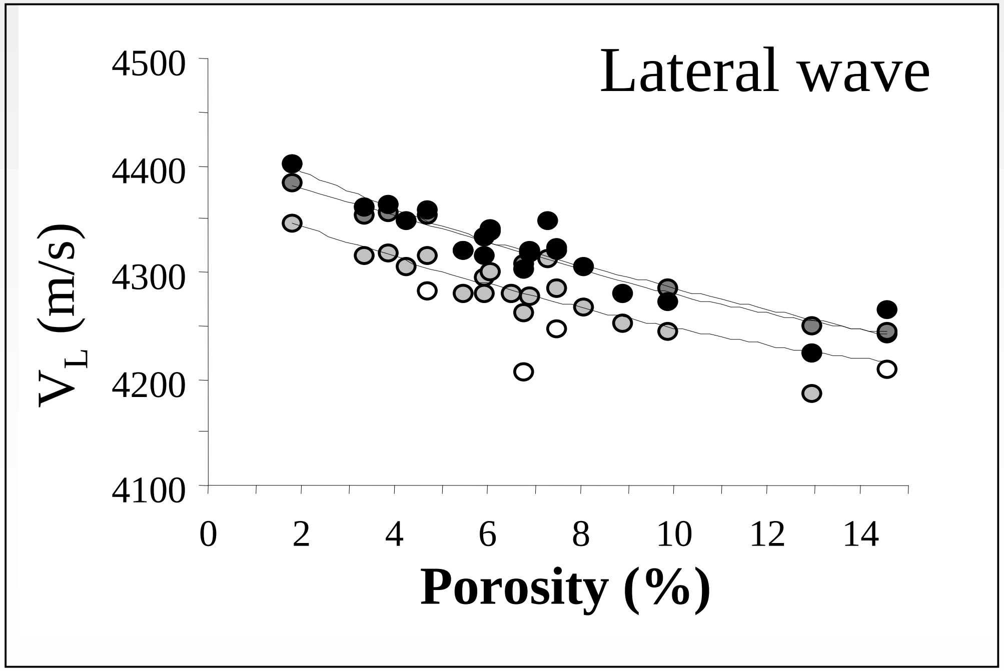
$$AR = \frac{c_{33}}{c_{11}}$$



Sensitivity of three modes to porosity and anisotropy ratio

Highest sensitivity to :
Porosity → Lateral wave
Anisotropy ratio → S0





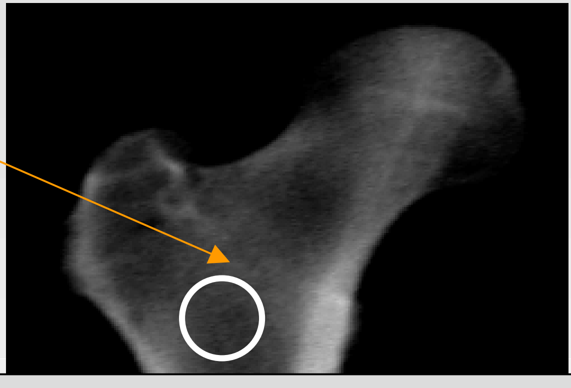
QUS : a look into the future

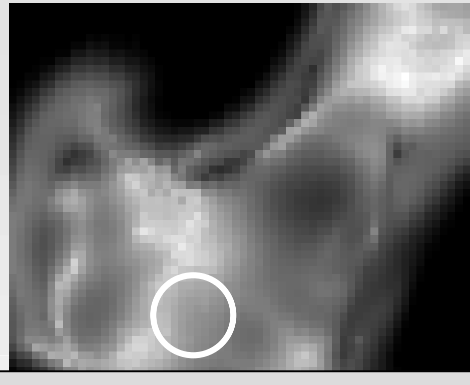
- Spine
  - – Non linear acoustics to detect microdamge at the spine
- Hip
  - – Combination of modes (transmission, backscatter, guided waves) for measuring several bone strength factors
    - cancellous bone compartment : prediction of BMD with transverse transmission, microstructure with scattering)
    - cortical bone : cortical thickness, material properties)

BMD (X-ray)

BUA

Cancellous bone

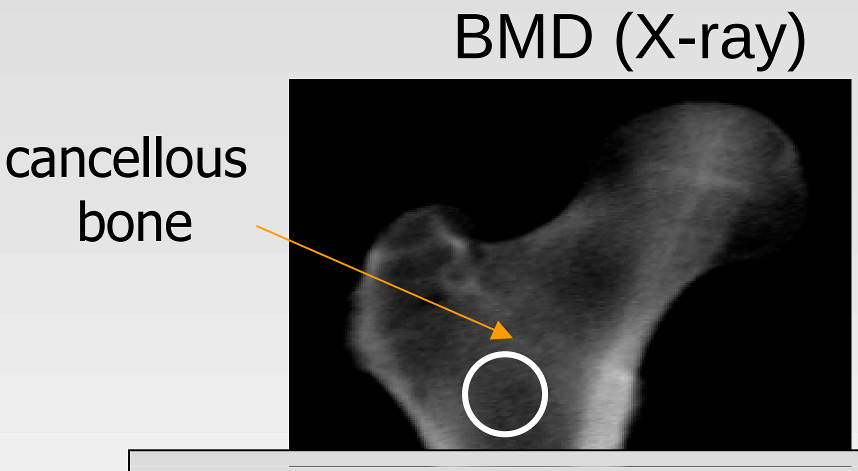


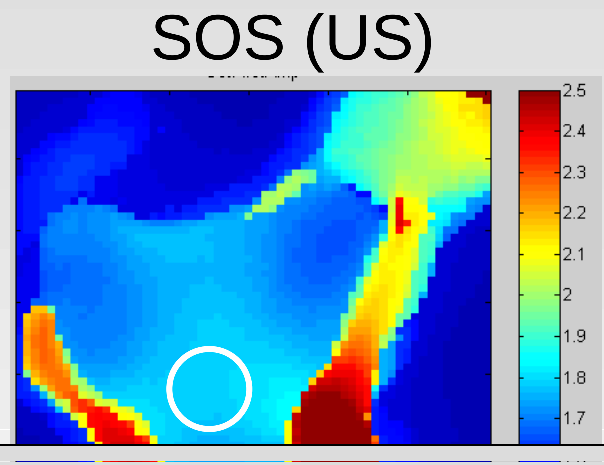


<u>Cancellous bone</u>

Excellent prediction of BMD with a linear combination of SOS and BUA : r^2=0.95, $p<10^{-4}$, RMSE = 0.045 g/cm²

Haiat, Padilla et al. Ultrasound Med Biol 2005
Calcif Tissue Int 2005





<u>Cortical bone</u>

Application of circumferential guided waves for the assessment of cortical bone at the femoral neck?

Conclusion

- **Ultrasound techniques** merged with with sophisticated theoretical or computational models **has the potential to unlock the gates of better in vivo bone strength assessment**
- On the bright side, the development of new ultrasound technologies could expand current boundaries
  - Microstructure, cortical thickness, stiffness, anisotropy ratio, microdamage

Conclusions

- There are caveats and challenges ahead for the technique, however.
- Researchers need to learn the bone properties that must be measured.

  They also must devise systems that provides measurements of these properties.
- One of the real challenges is going to be translating the successes obtained in the laboratory into clinical success.

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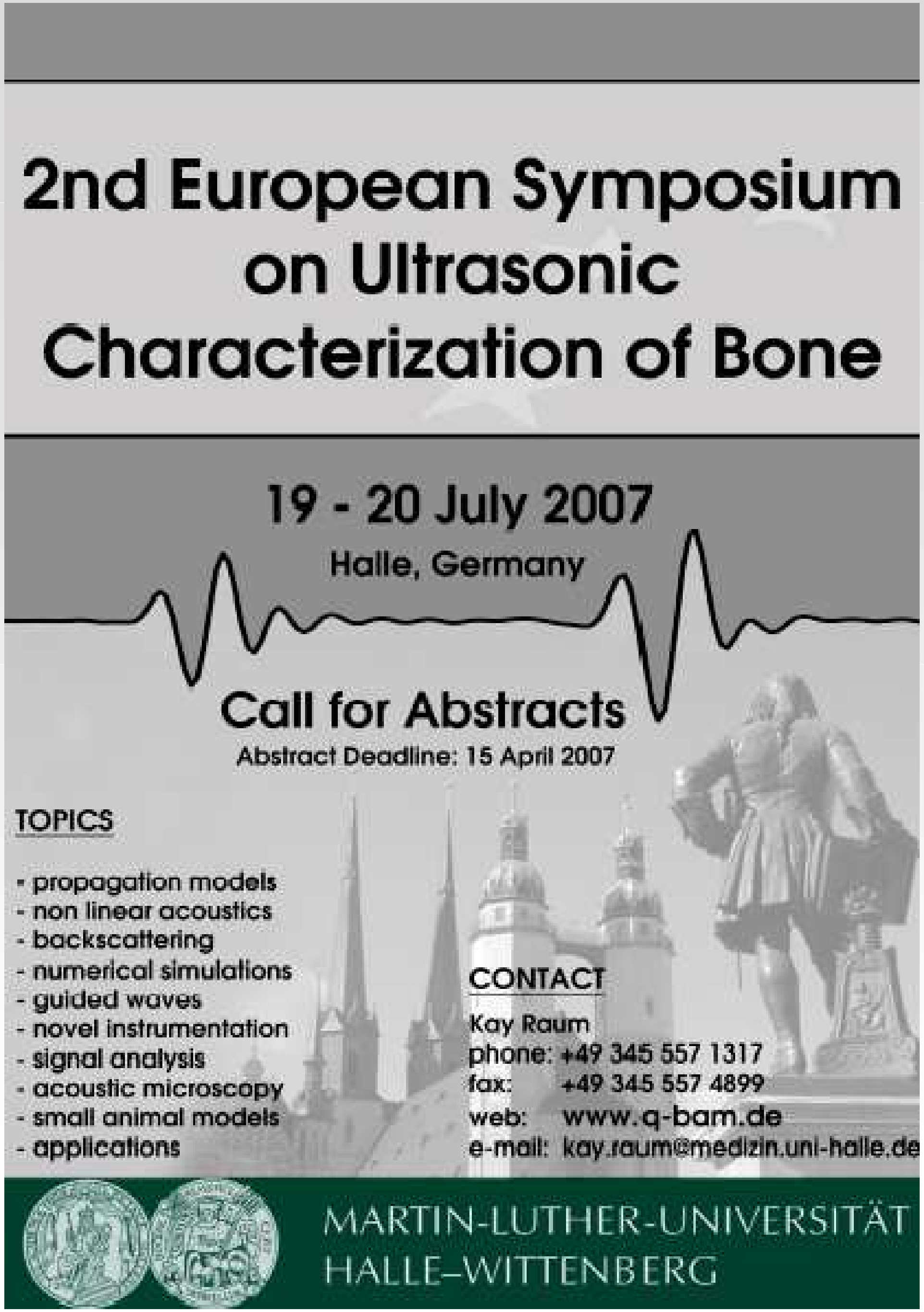
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TOPICS
- propagation models
- non linear acoustics
- backscattering
- numerical simulations
- guided waves
- novel instrumentation
- signal analysis
- acoustic microscopy
- small animal models
- applications
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