



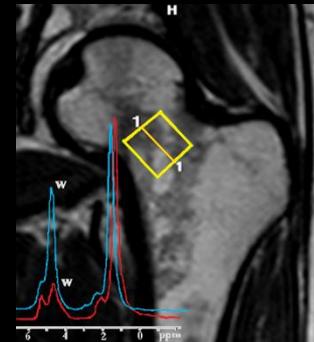
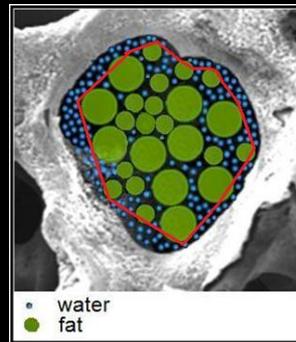
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# **La diffusione NMR per la diagnosi dell'osteoporosi.**

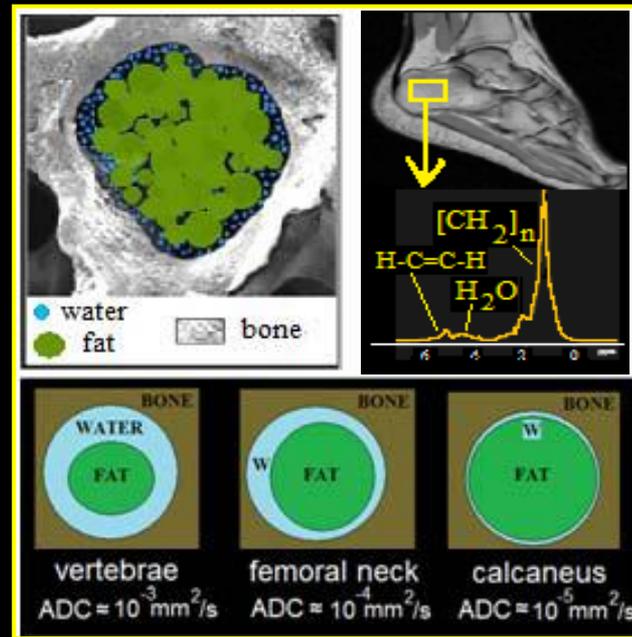
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# Highlights

Fundamental  
physics

NMR  
Diffusion in  
porous  
systems



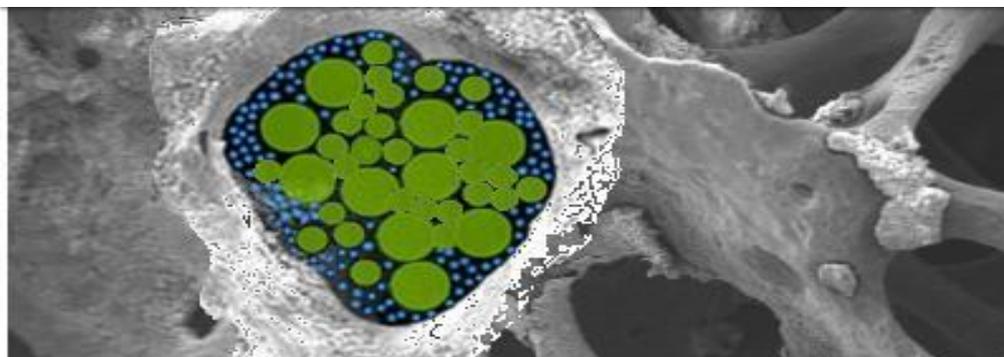
Biophysical  
applications

Translational  
longitudinal studies  
in Humans

Transfer of  
technology

Models

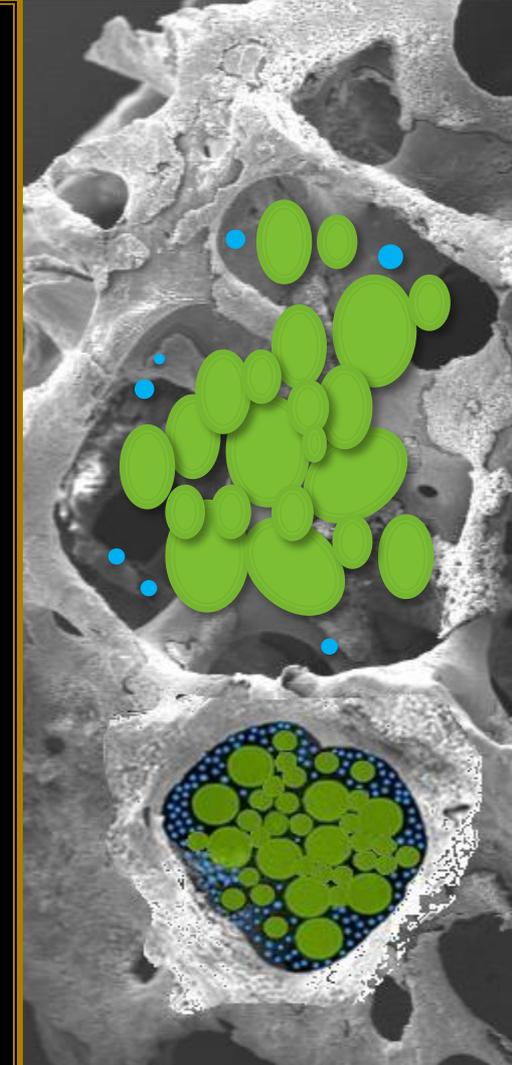
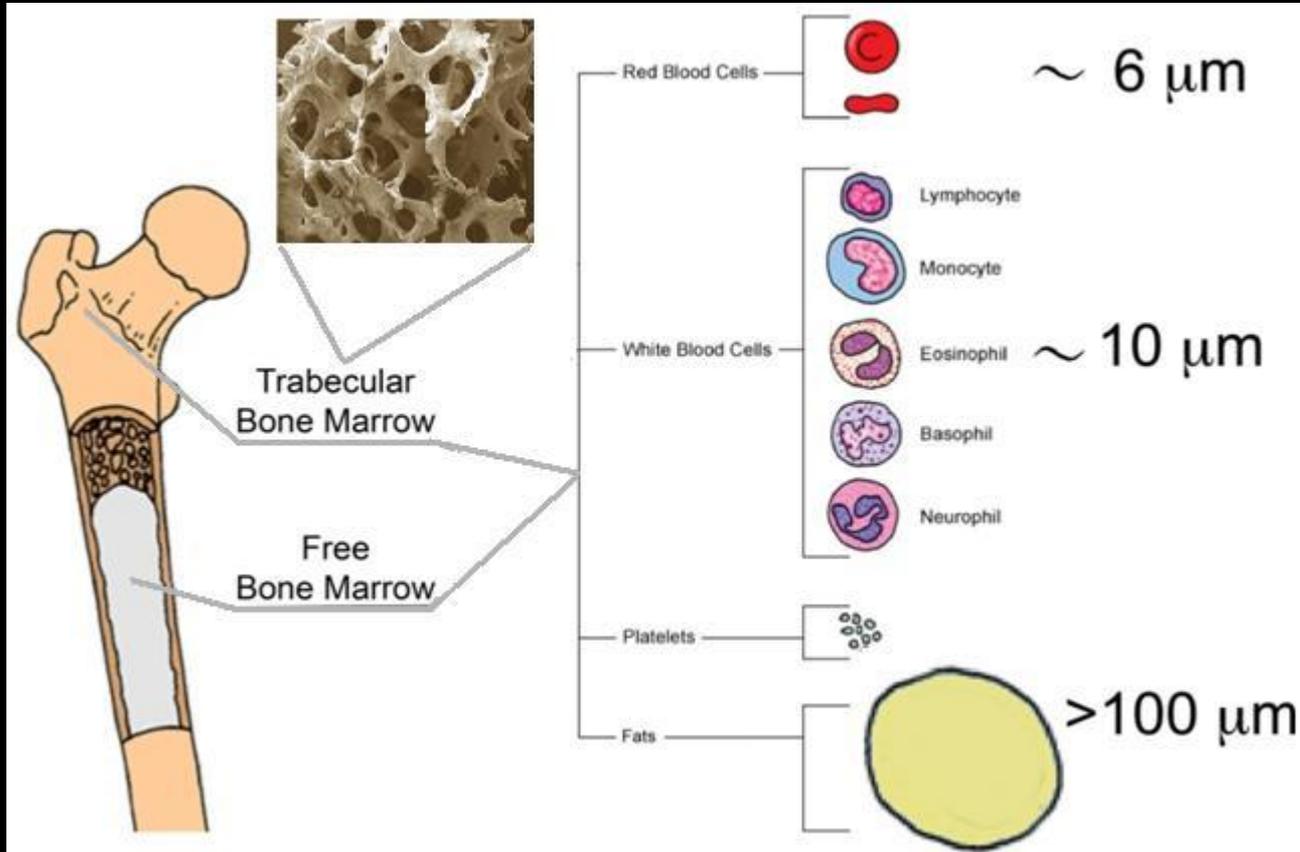
Clinical  
application



- S. Capuani, et al. Solid State NMR 2005;28:266-272
- C. Rossi, et al. Magn Reson Imag 2008;26:1250-1258
- S. De Santis, et al. Phys Med Biol 2010;55:5767-5785
- S. Capuani, Microp Mesop Mater 2013;178:34
- M. Rebuzzi et al. BONE 2013;57:155-163
- G. Manenti et al. BONE 2013;55:7-15
- M. Palombo et al. Appl Magn. Reson 2014; 45:771-784
- S. Capuani et al. BioMed Res Intl 2015; 948610
- G. Di Pietro et al. Acad. Radiology accepted 2015
- G. Di Pietro et al. NMR Biomed submitted

## ● Introduction

Human cancellous bone: components and porous structure



Osteoporosis = "porous bone"

**BMD is reduced**

**Trabecular bone network is rearranged or disrupted**

**Bone marrow quality is altered**

## Why would we want to evaluate the Diffusion Coefficient of water in cancellous bone tissue?

Clinical diagnosis of osteoporosis: is based on BMD quantification in skeletal sites with high trabecular content, such as spine, proximal femur calcaneus...

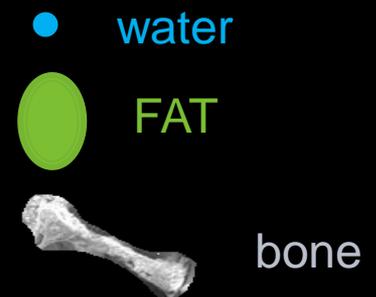
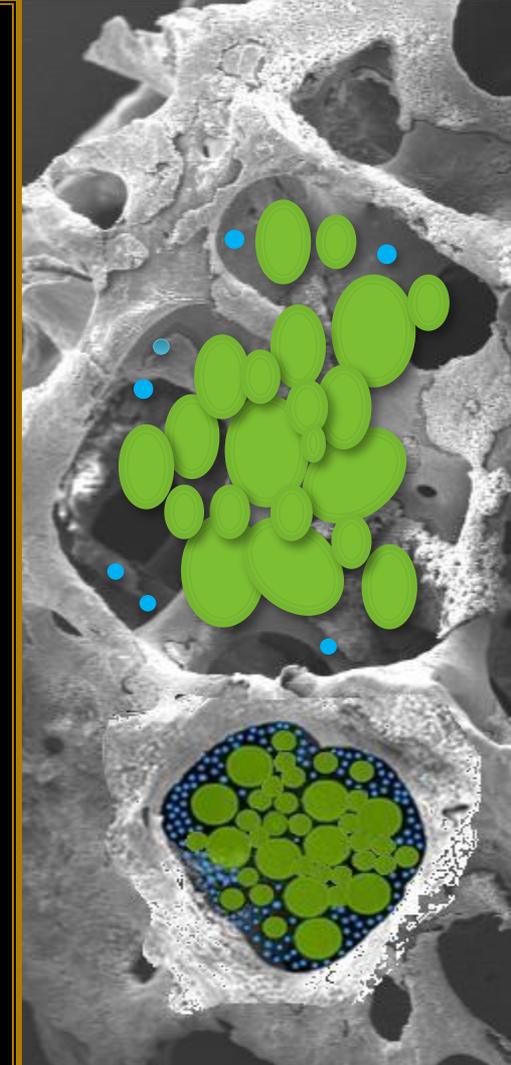
the poor correlation between fracture prevalence and BMD diagnosis suggests that other factors besides low BMD contribute to bone fragility

New potential surrogate markers for osteoporosis

$T_2^*$

Mfc

don't allow the definition of cut-off values of normality to be applied on a single subject level



## ● Purpose

Diffusion NMR methods allow to measure water displacements at the cellular level by probing motion on the micrometer length scale

$$S_{\text{NMR}}(D) \propto \text{FT (MP)}$$

$$\text{MSD} \propto 2nDt$$

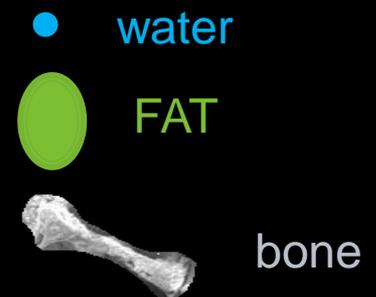
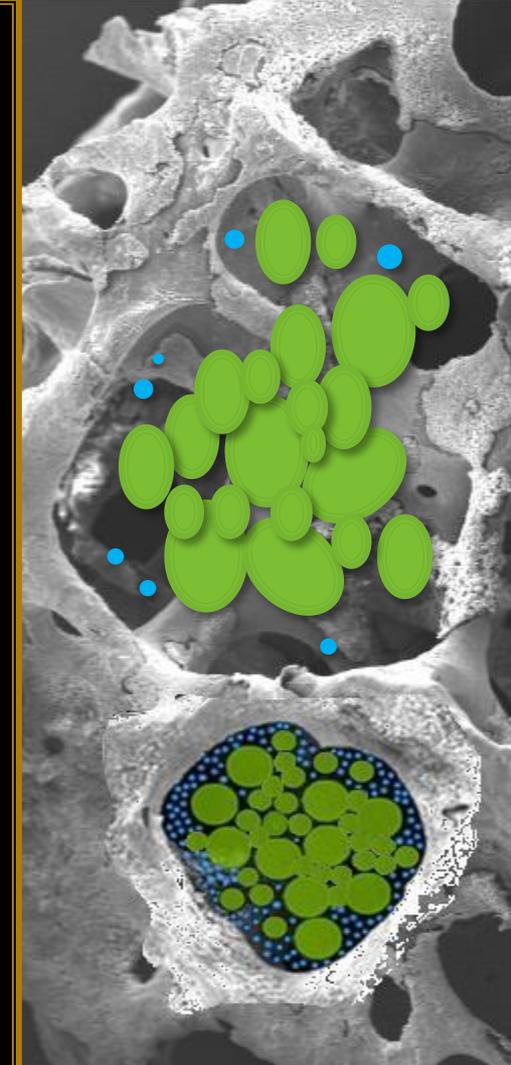
$$(\text{MSD})^{1/2} \ll \text{voxel resolution}$$

### Aims of the study were:

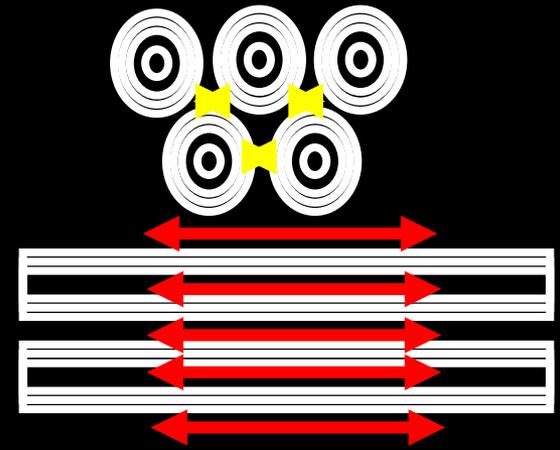
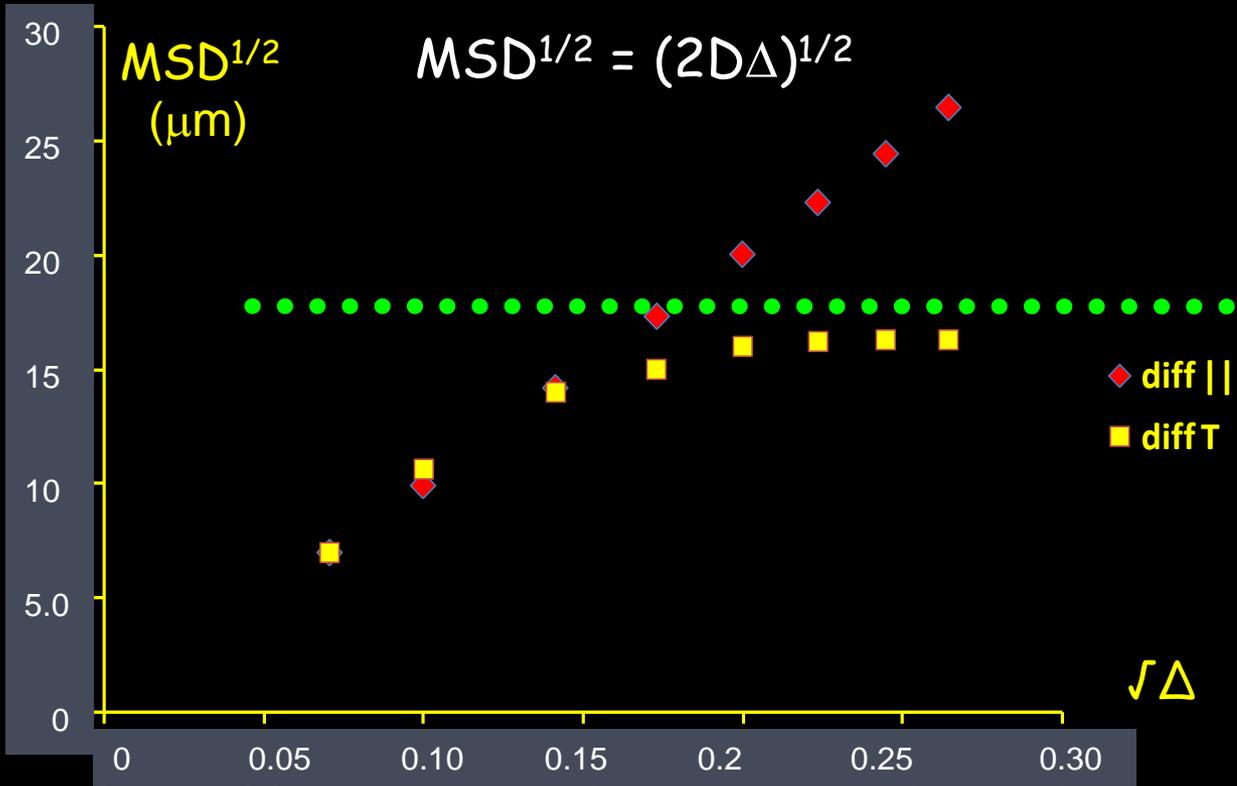
To describe and corroborate by means of in vivo experiments, the porous system model suitable to investigate the structural properties of the cancellous bone by using diffusion NMR techniques

### The final goal of the study was :

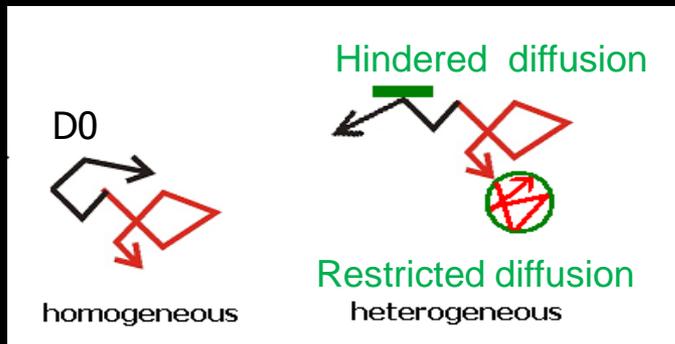
To evaluate the potential ability of diffusion techniques, in association with bone marrow NMR spectroscopy to discriminate among healthy, osteopenic and osteoporotic postmenopausal women



● Restricted diffusion, Apparent diffusion coefficient :ADC



D(parallel) about free diffusion coefficient, where D(perp.) is more defined by the geometric barrier, as  $t = \Delta$  becomes longer:



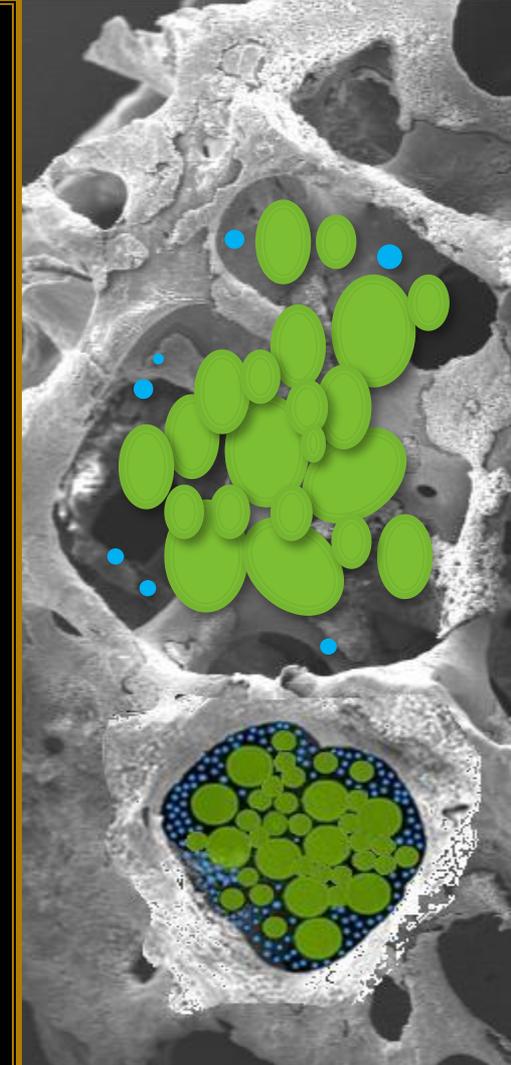
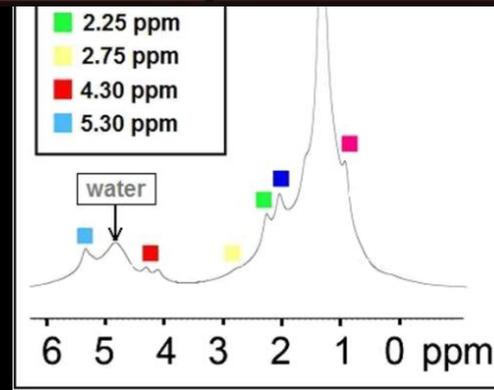
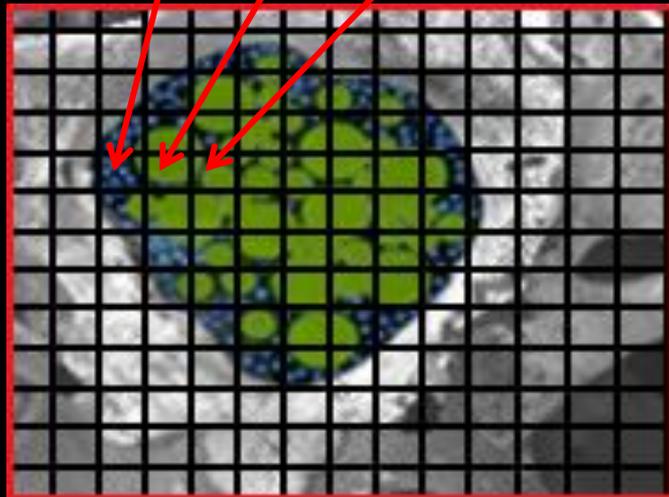
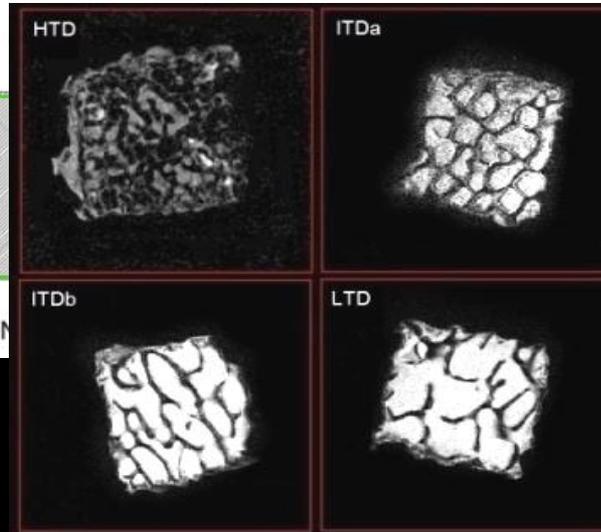
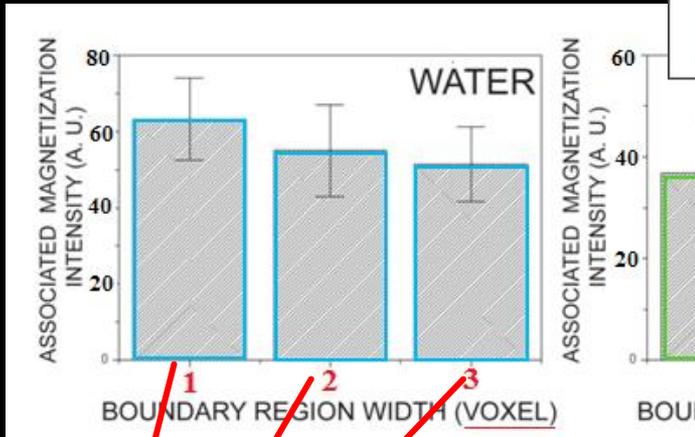
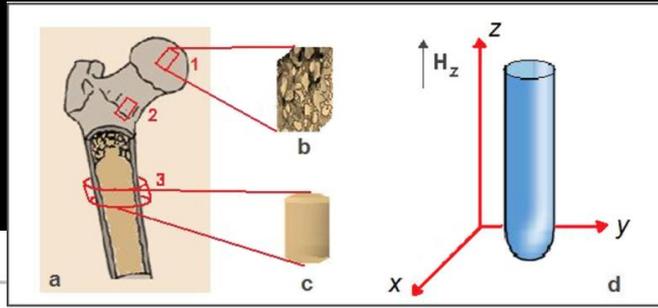
$D0 = 2.3 \cdot 10^{-9} \text{ m}^2/\text{s}$

$D1 = 2.0 \cdot 10^{-9} \text{ m}^2/\text{s}$

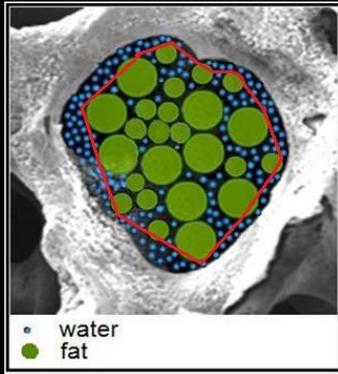
$D2 = 9 \cdot 10^{-11} \text{ m}^2/\text{s}$

● Water diffusion behavior in calf bone samples at 9.4T

In vitro experiments  
20x20  $\mu\text{m}^2$  resolution



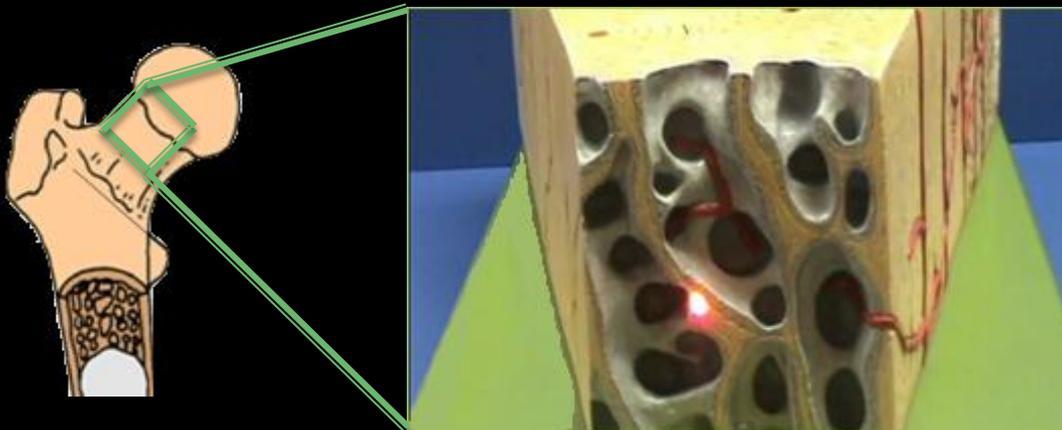
## ● The porous system model



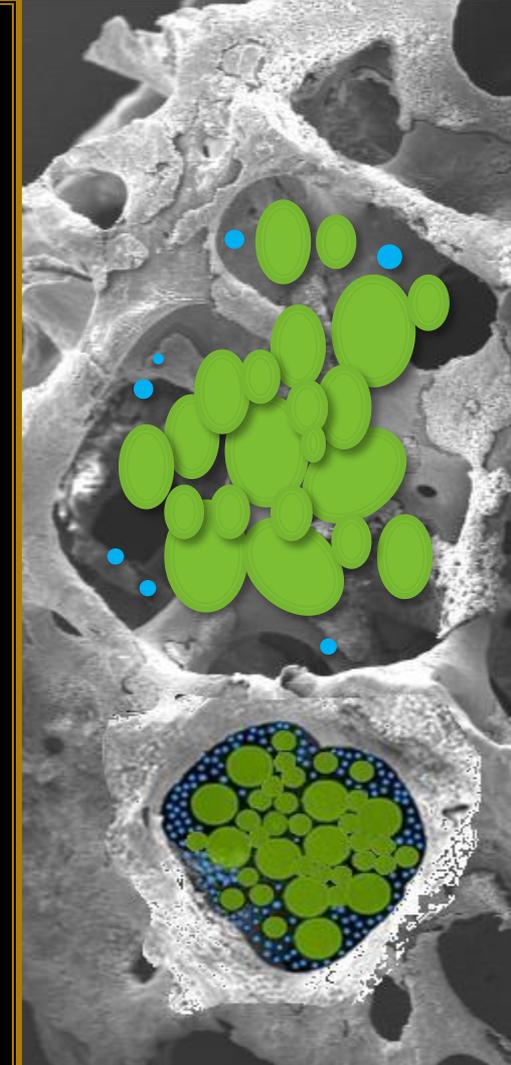
“Water is more prevalent in the boundary zone while fat occupies primarily the central zone of the pore”

De Santis S. et al. *Phys Med Biol* 2010;55:5767-5785.

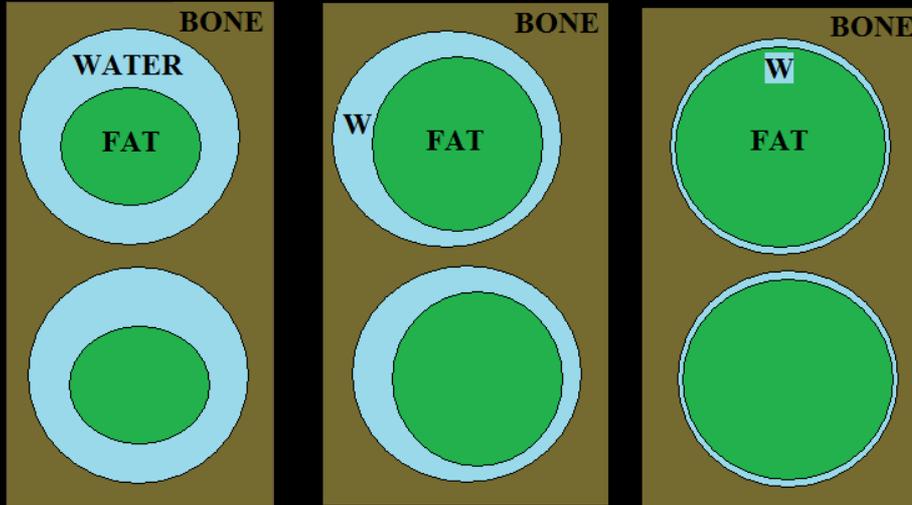
Justification: histology of bony surface



**Endosteum**, is a thin membrane ( $\approx 5-10\mu\text{m}$ ) of soft tissue that lines the medullary cavity. Moreover, due to a biological division of the bone-marrow compartment, granulocytes and other non-fat entities accumulate at the boundary of the bone-marrow compartment adjacent to the endosteum



● The porous system model: restricted diffusion



Vertebrae

ADC  $\approx 10^{-3}$  mm<sup>2</sup>/s

Femoral neck

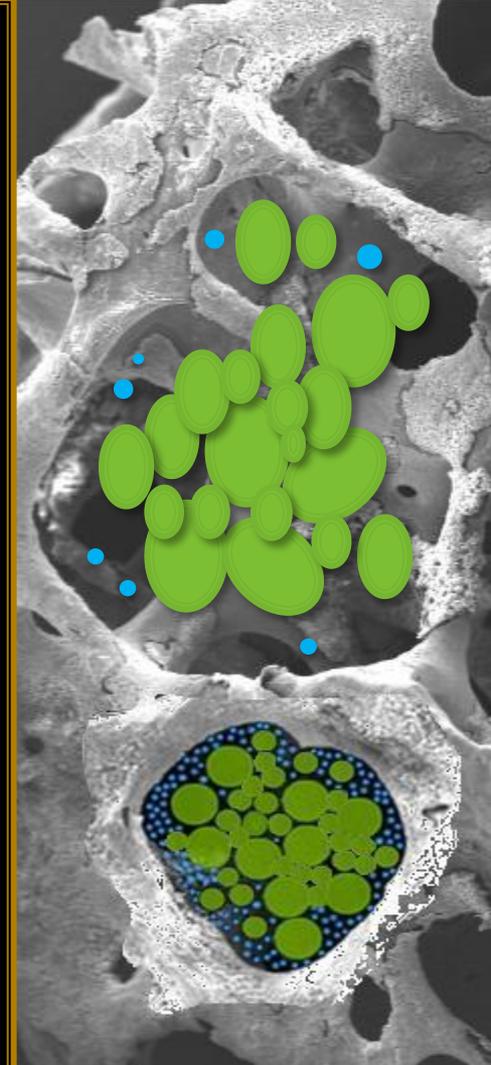
ADC  $\approx 10^{-4}$  mm<sup>2</sup>/s

Calcaneus

ADC  $\approx 10^{-5}$  mm<sup>2</sup>/s

S. Capuani,  
Microp Mesop Mater  
2013;178:34

Healthy



● water

● FAT



bone

## ● Methods: patients selection

### Group I: calcaneus

30 postmenopausal women  
mean age (64.5±6 years)

10 healthy,

10 osteopenic

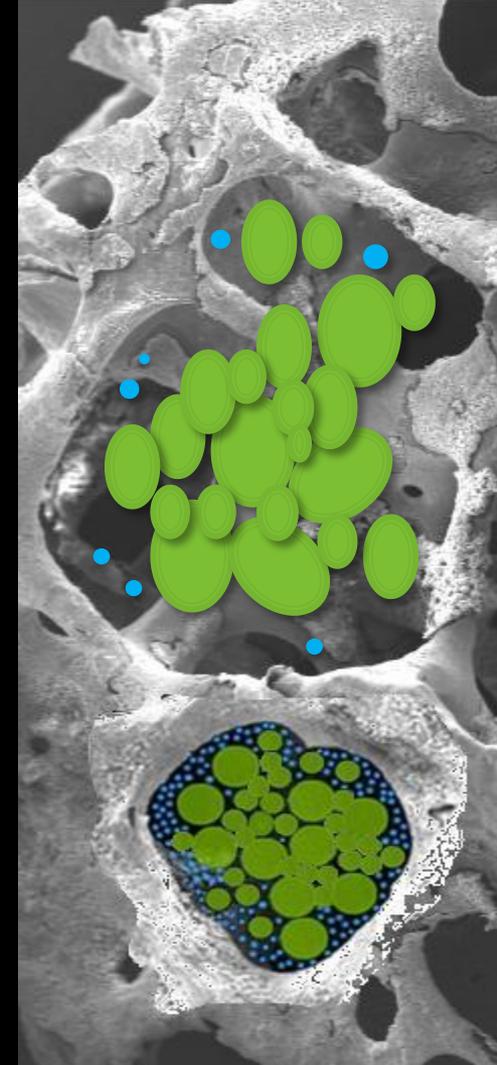
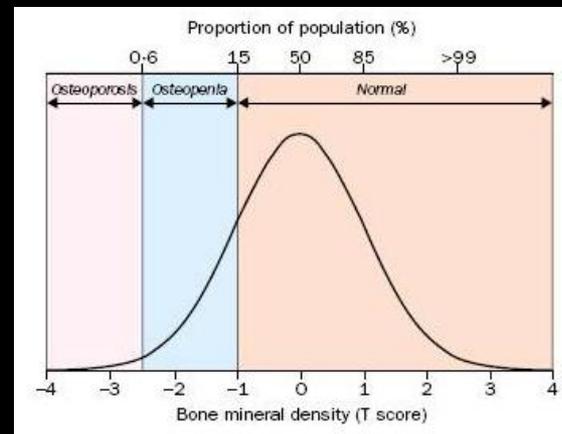
10 osteoporotic women,

The status of each subject was assessed with **QCT** BMD measurements in **lumbar vertebral** according to the following criteria\*:

T-score  $\geq -1.8$  :healthy

$-3.3 < \text{T-score} < -1.8$  :  
osteopenia

T-score  $\leq -3.3$  osteoporosis



● water

● FAT

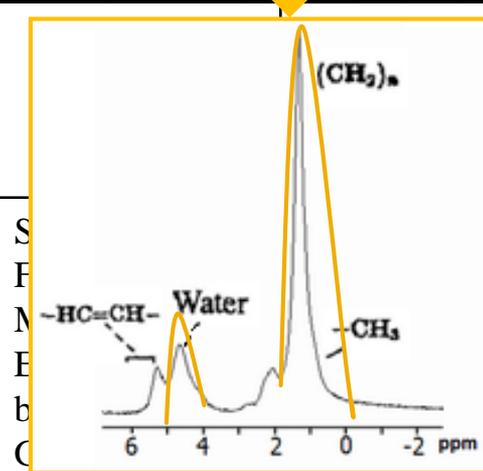
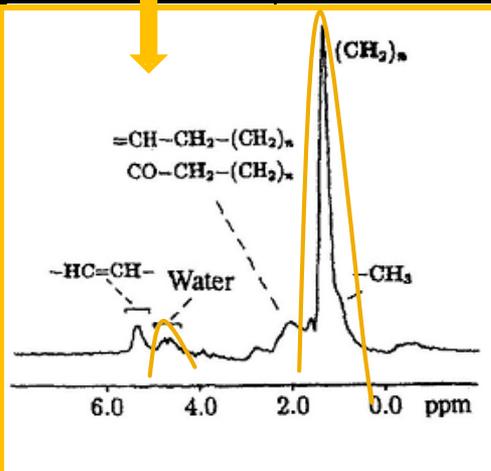
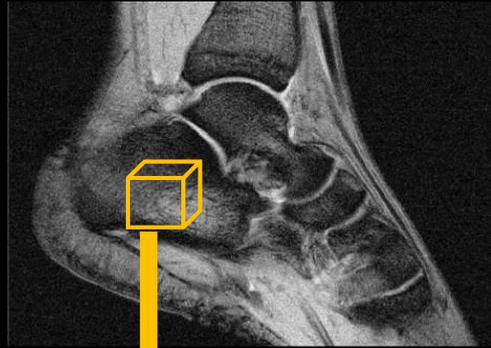


bone

\*ISCD Official Position, reported by K. Engelke, J.E. Adams et al., *Journal of Clinical Densitometry: Assessment of Skeletal Health*, 2008;11:123-162

● **Methods: MR at 3T**  
**ADC +MRS in calcaneus**

**ADC+MRS in femoral neck**



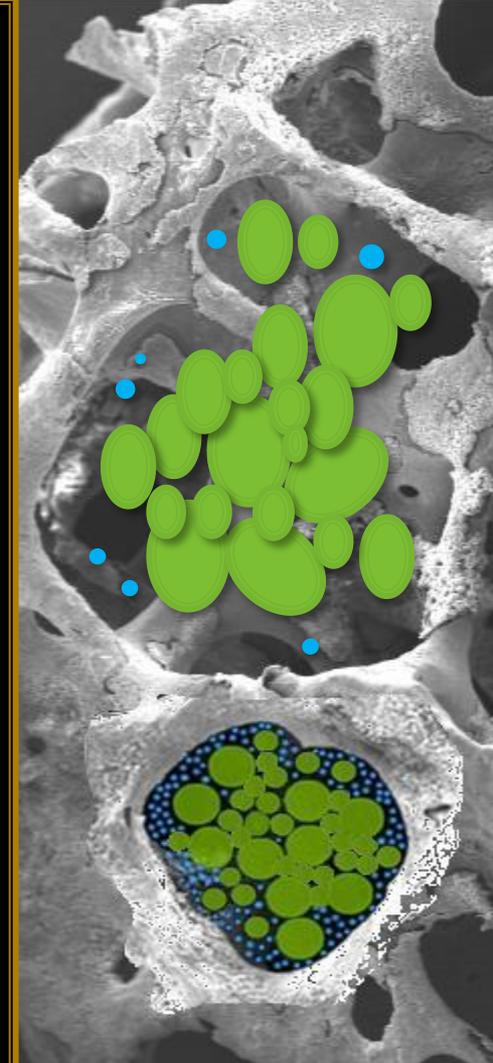
TE/TR 89/2500ms  
 NS 2

TE/TR 104/2500ms

**Fat fraction %**

$$FF = A^{fat} / (A^{fat} + A^w)$$

Parameter	Protocol: <b>SVS (PRESS)</b> to obtain bone marrow spectra
Voxel size	15x15x15 mm
TE/TR	22/5000 ms
NS	32



● water

**Mono-exponential decay**  
 $S(b) = S(0) \exp(-ADC * b)$



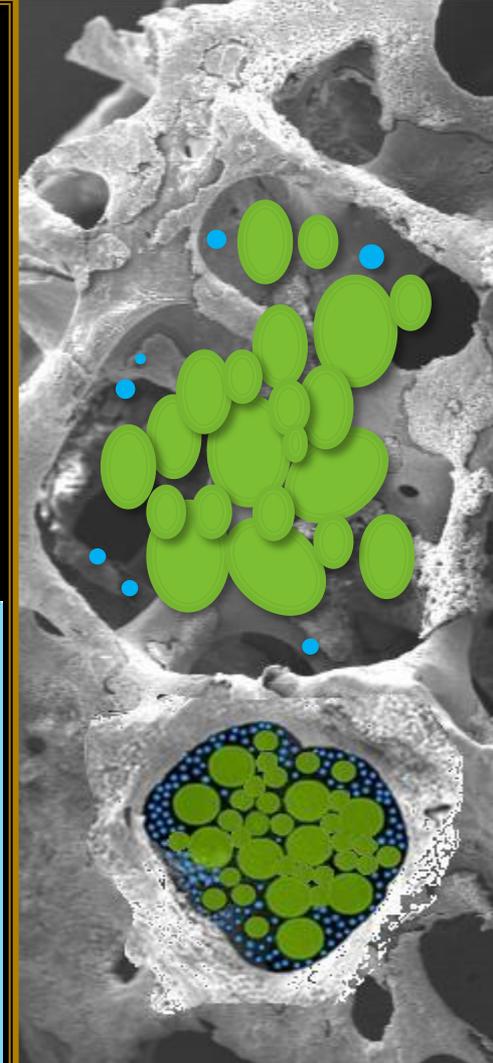
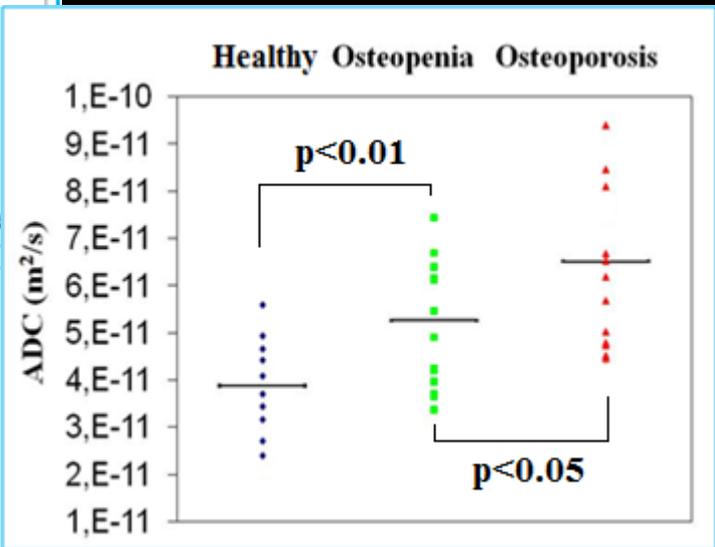
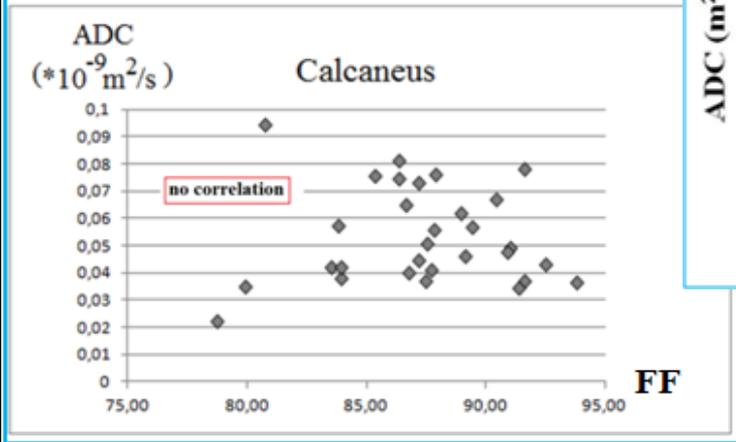
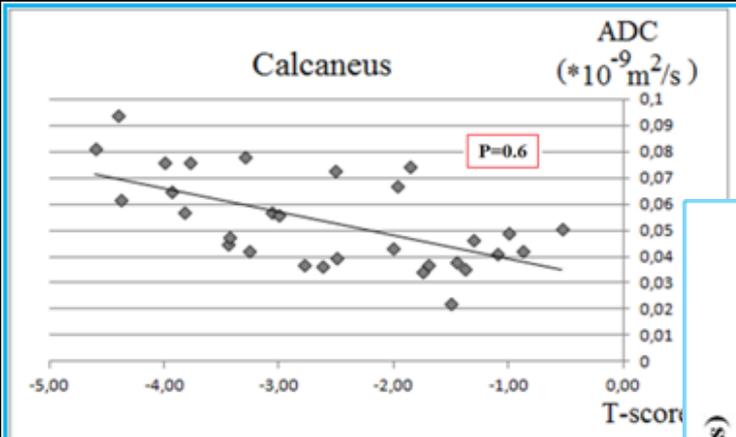
bone

● Results  
 ADC +MRS in human calcaneus

FF was not significantly different between BMD groups

$MSD = 6 D \Delta$

$MSD^{1/2} \approx 4 \mu m$   
 $D = 5 \cdot 10^{-5} \text{ mm}^2/\text{s}$     $\Delta = 70 \text{ ms}$



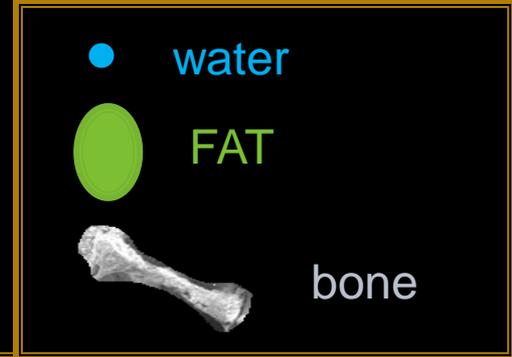
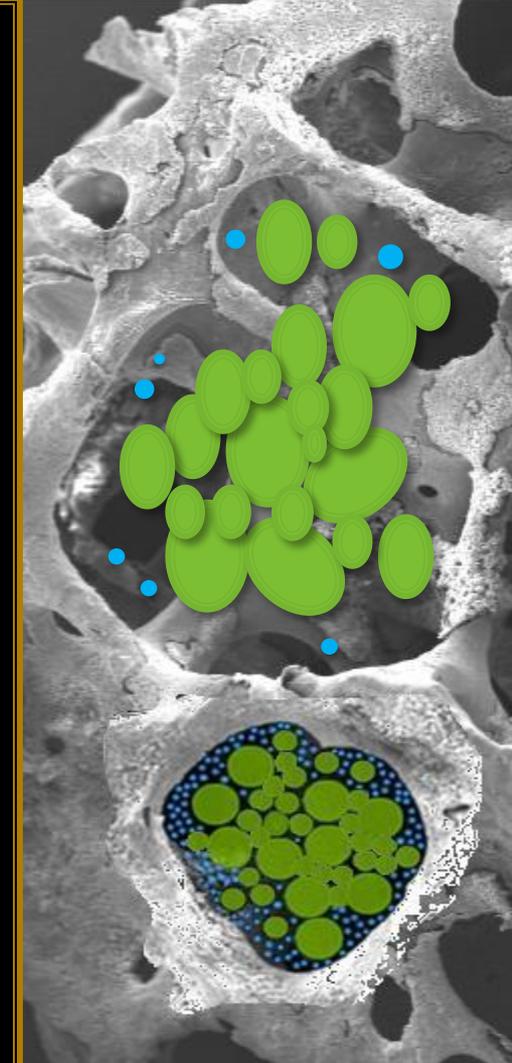
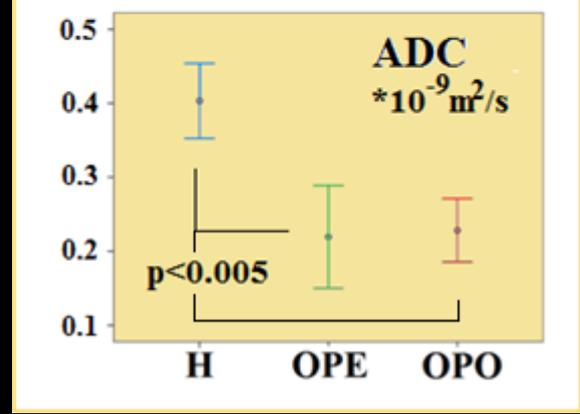
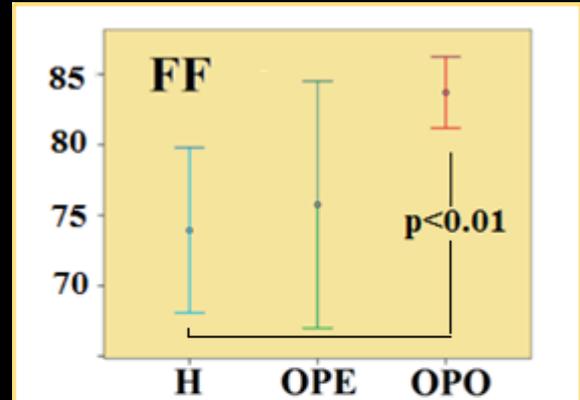
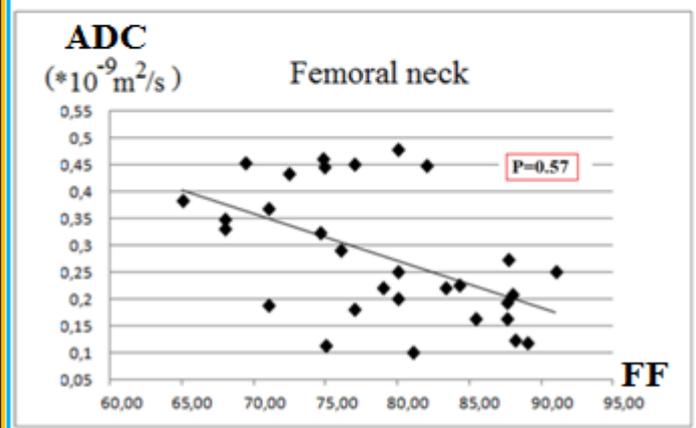
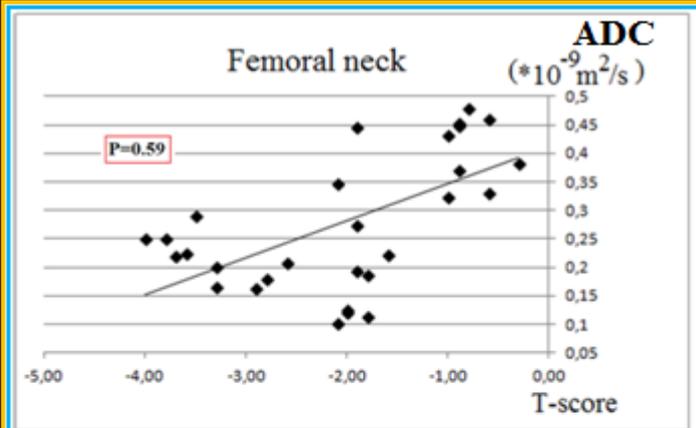
● **ADC+MRS results obtained in human femoral neck**

FF was significantly different between healthy (H) subjects and patients with osteopenia (OPE) and osteoporosis (OPO)

$MSD = 6 \Delta$

$MSD^{1/2} \approx 9 \mu m$

$D = 2 \cdot 10^{-4} \text{ mm}^2/\text{s} \quad \Delta = 8 \text{ oms}$



## ● Conclusions

Water is more prevalent in the endosteal boundary zone while fat primarily occupies the central zone of the intra-trabecular space. The work shows that water diffusion in this boundary zone provides new insight into cancellous bone microstructure.

### In calcaneus

FF was not significantly different between BMD groups  
Patients with osteoporosis compared to age-matched controls showed significantly higher ADC values.

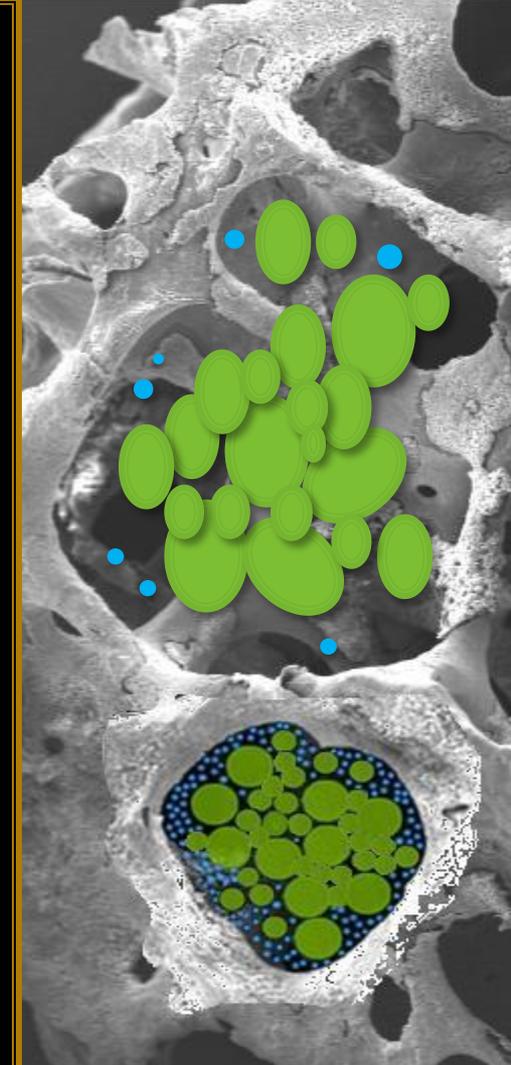
Findings may be a consequence of pore enlargement and increase in interconnections between adjacent pores in the trabecular bone network due to formation of perforations of trabecular plates.

### In femoral neck

FF was significantly different between healthy subjects and patients with osteopenia and osteoporosis

Patients with osteopenia and osteoporosis compared to age-matched controls showed significantly lower ADC values.

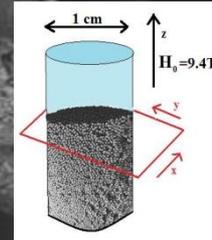
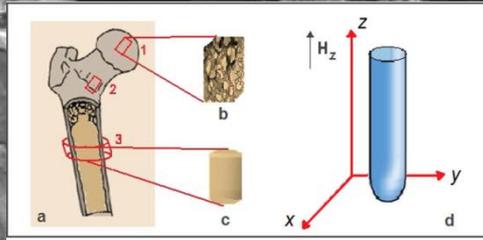
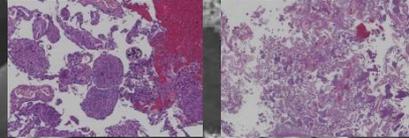
Findings may be a consequence of fat increase in each cancellous bone pore that causes a narrowing of the space between fat and bone where the water diffuses (more restricted water!)





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Thank you for your attention.

