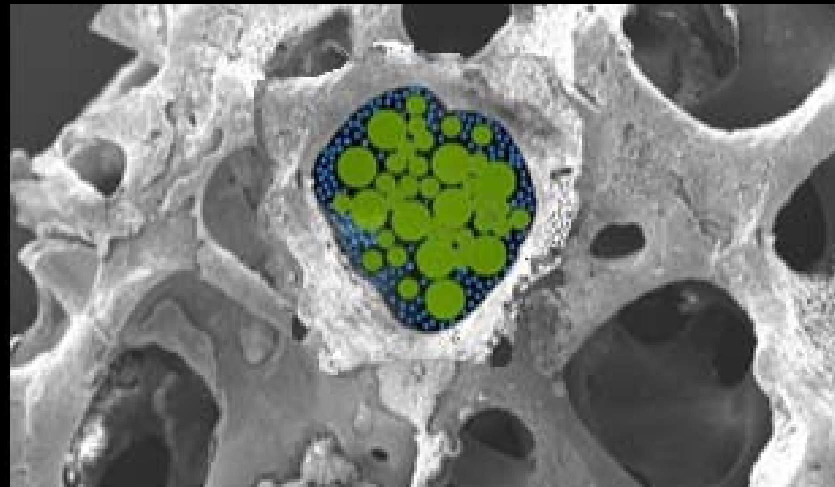
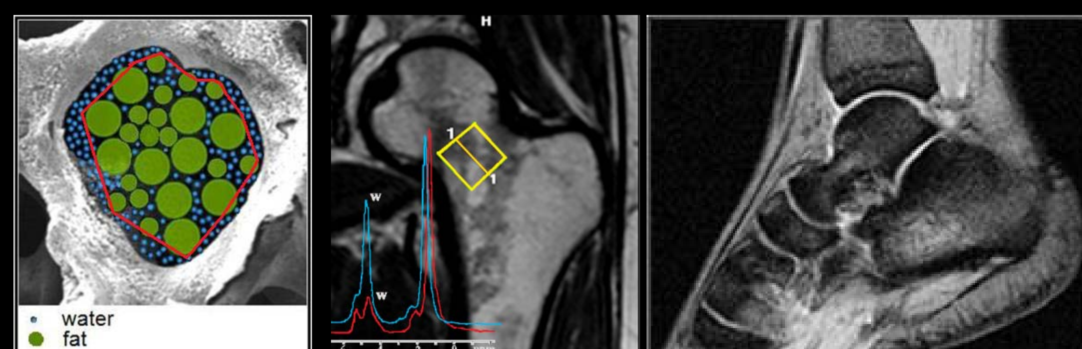


Silvia Capuani,*
Giulia Di Pietro,*
Guglielmo Manenti°,
*Umberto Tarantino^*

*CNR ISC, Physics Department Sapienza University, Rome, Italy
°Department of Diagnostic Imaging and Interventional Radiology, Molecular Imaging and Radiotherapy, PTV Foundation "Tor Vergata" University of Rome, Italy
^Department of Orthopedics and Traumatology, PTV Foundation, "Tor Vergata" University of Rome, Italy

La diffusione NMR per la diagnosi dell'osteoporosi.

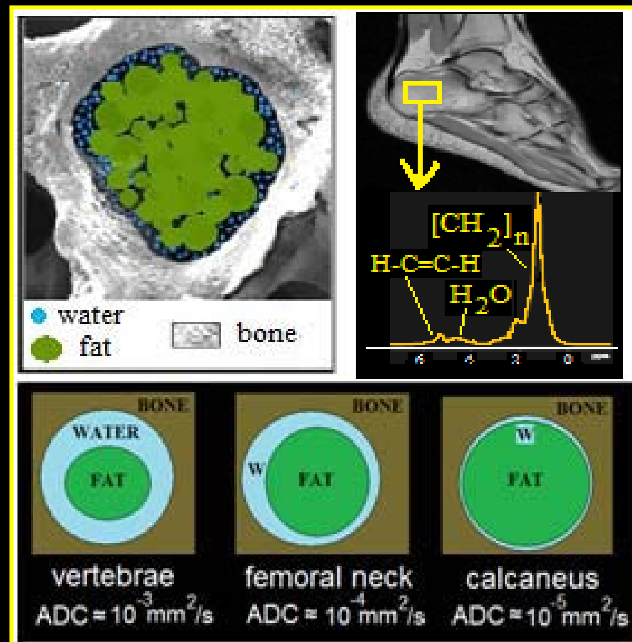
silvia.capuani@roma1.infn.it



Highlights

Fundamental physics

NMR Diffusion in porous systems



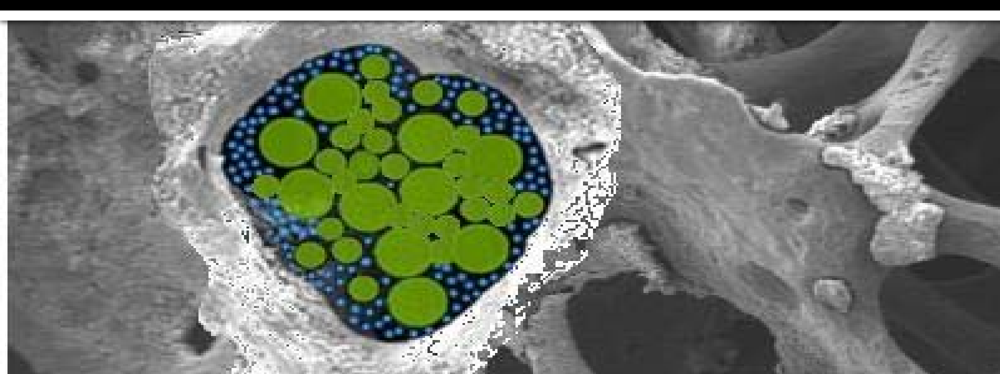
Models

Biophysical applications

Translational longitudinal studies in Humans

Transfer of technology

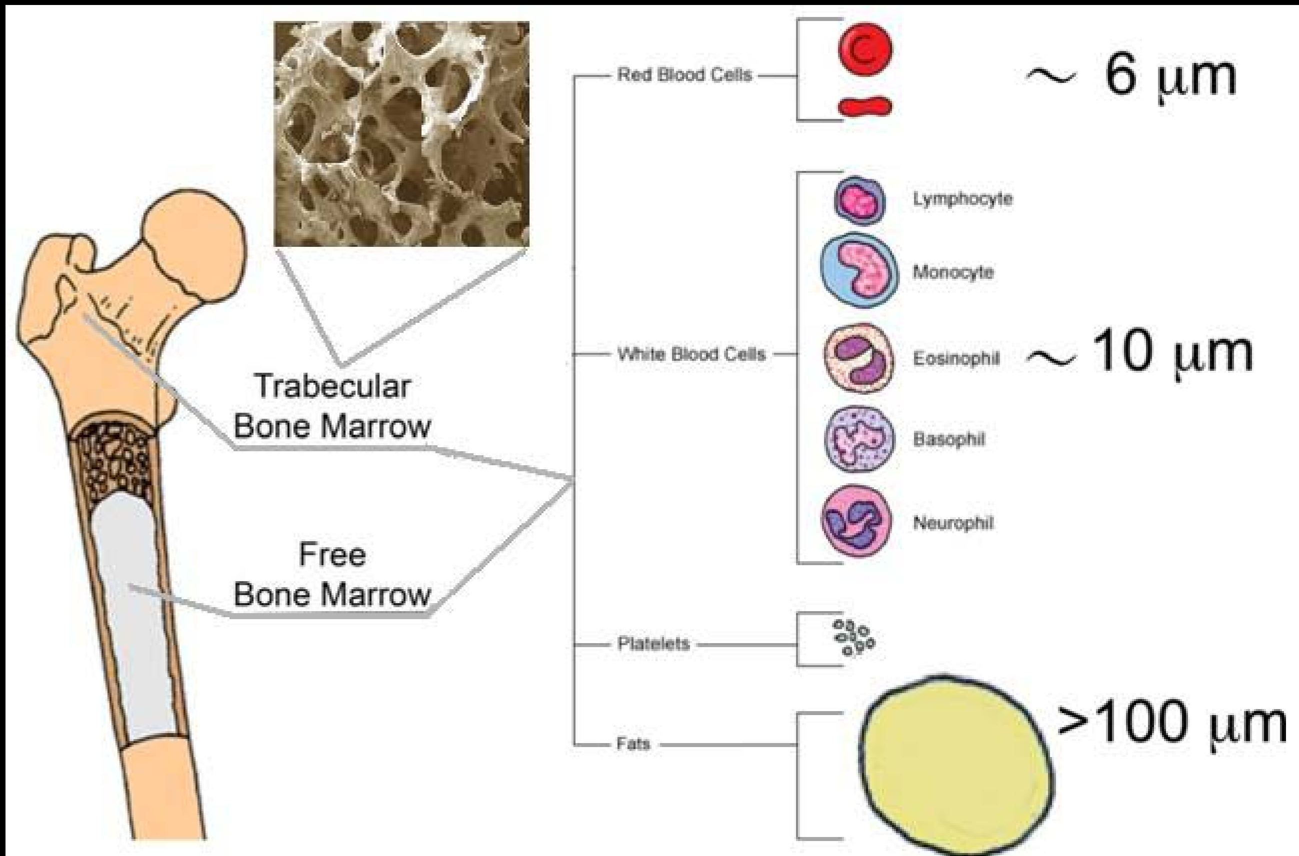
Clinical application

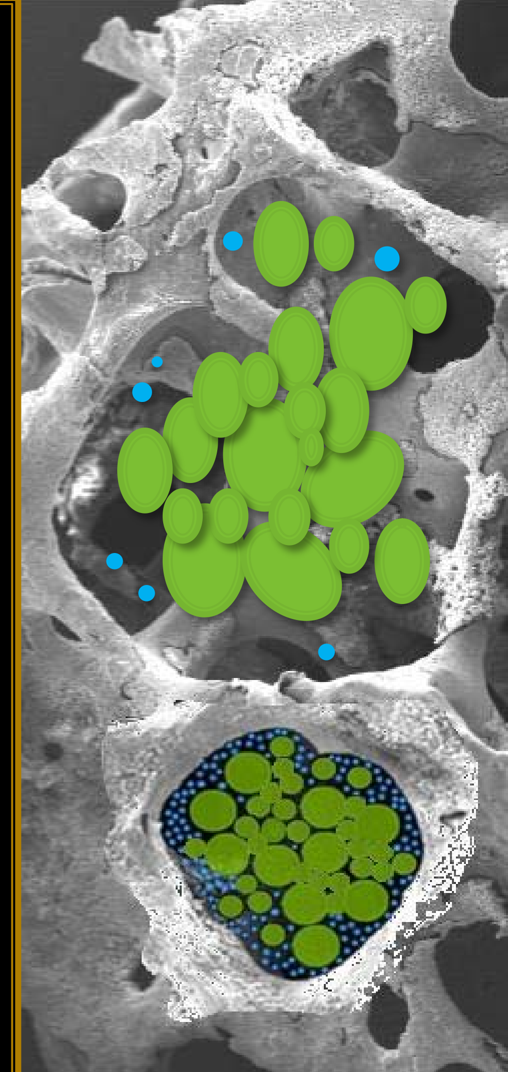


-S. Capuani, et al. Solid State NMR 2005;28:266-272
-C. Rossi, et al. Magn Reson Imag 2008;26:1250-1258
-S. De Santis, et al. Phys Med Biol 2010;55:5767-5785
-S. Capuani, Microp Mesop Mater 2013;178:34
-M. Rebuzzi et al. BONE 2013;57:155-163
-G. Manenti et al. BONE 2013;55:7-15
-M. Palombo et al. Appl 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...

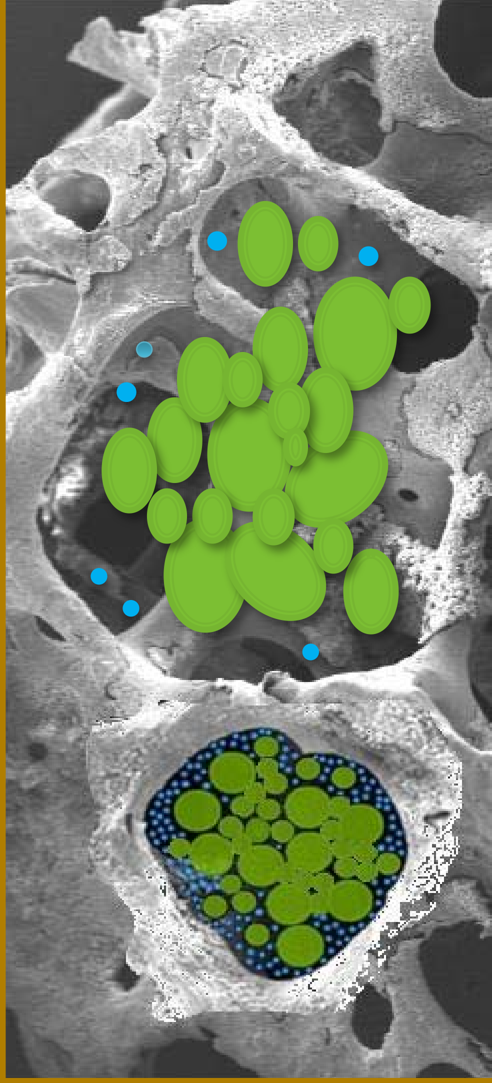
the poor correlation between fracture prevalence and BMD diagnosis suggests that other factors besides low BMD contribute to bone fragility

New potential surrogate markers for osteoporosis

$T2^*$

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

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

$$MSD \propto 2nDt$$

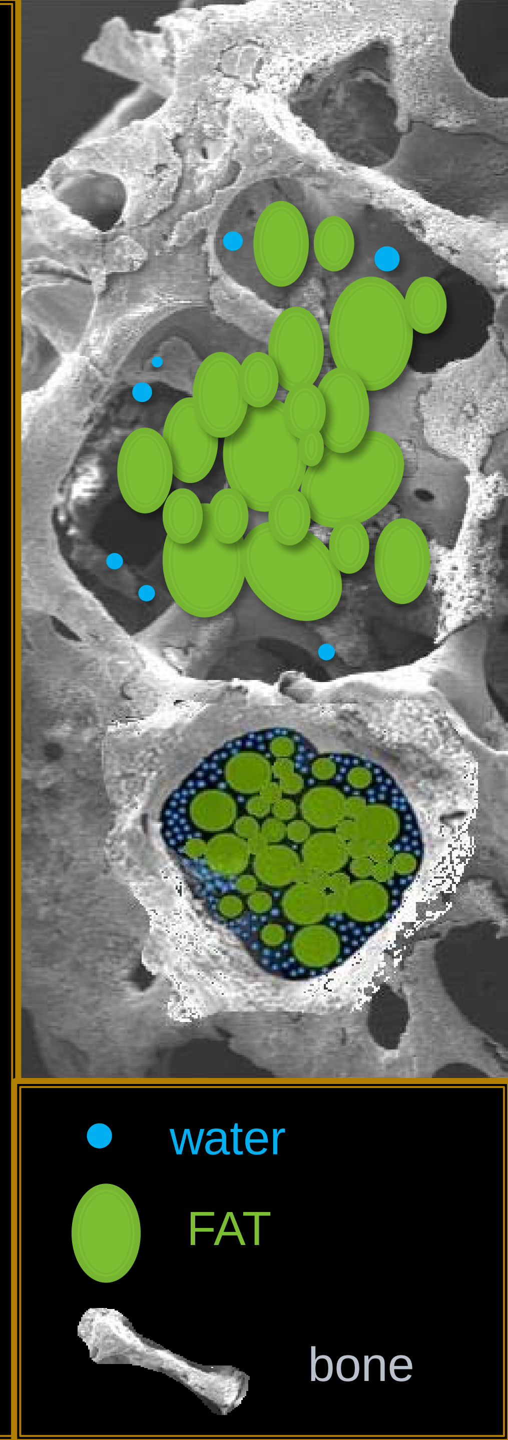
$$(MSD)^{1/2} \ll \text{voxel resolution}$$

Aims of the study were:

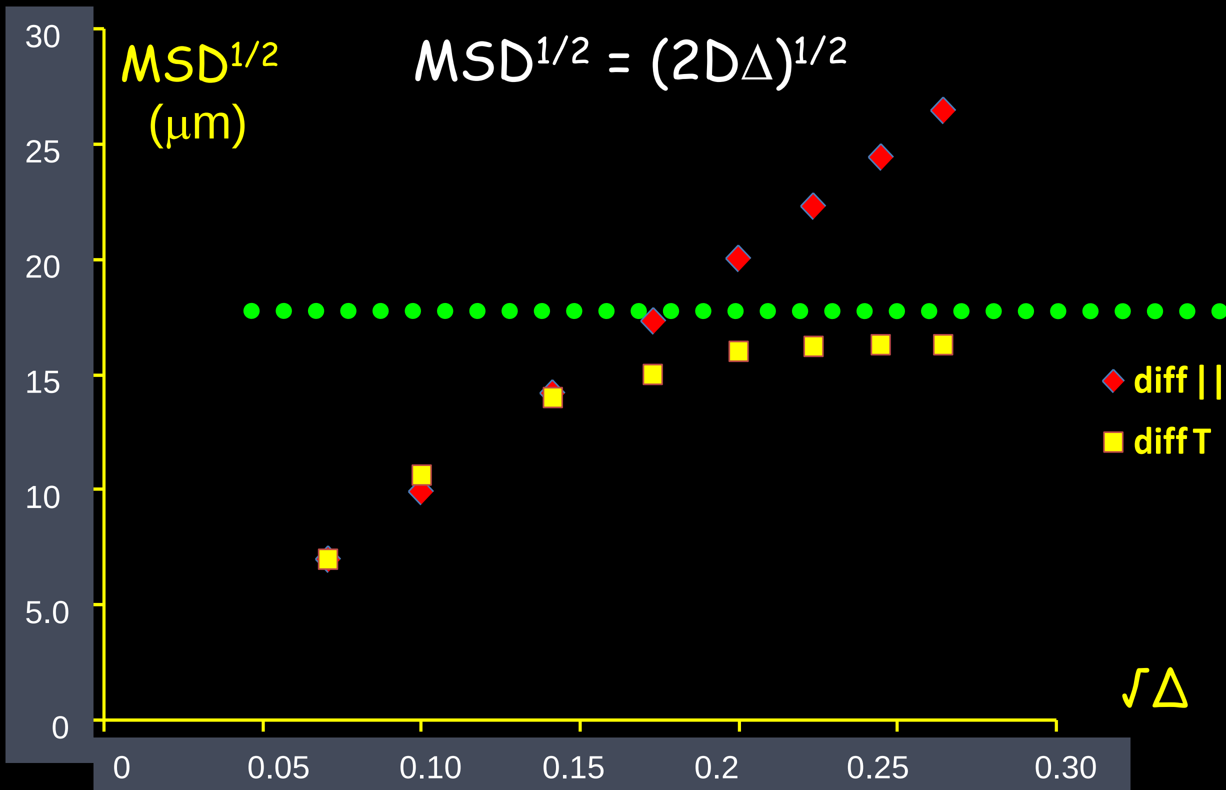
To describe and corroborate by means of in vivo experiments, the porous system model suitable to investigate the structural properties of the cancellous bone by using diffusion NMR techniques

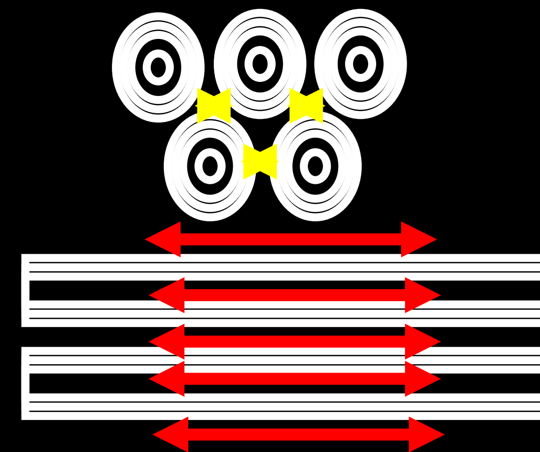
The final goal of the study was :

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

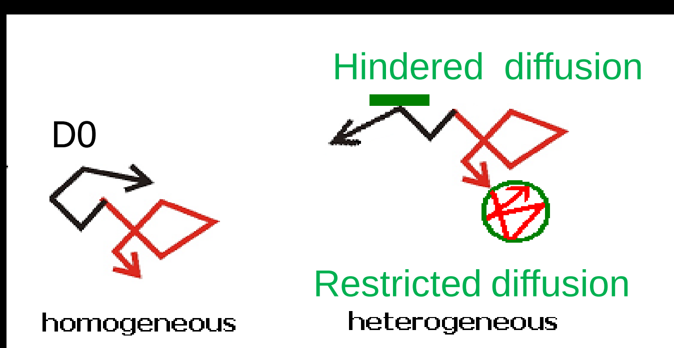


- Restricted diffusion, Apparent diffusion coefficient :ADC





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



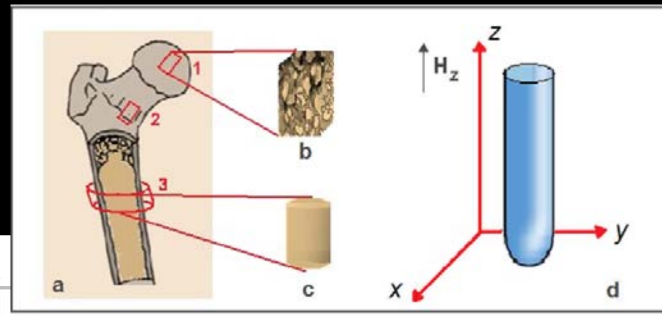
$D0=2.3\cdot10^{-9}\ m^2/s$

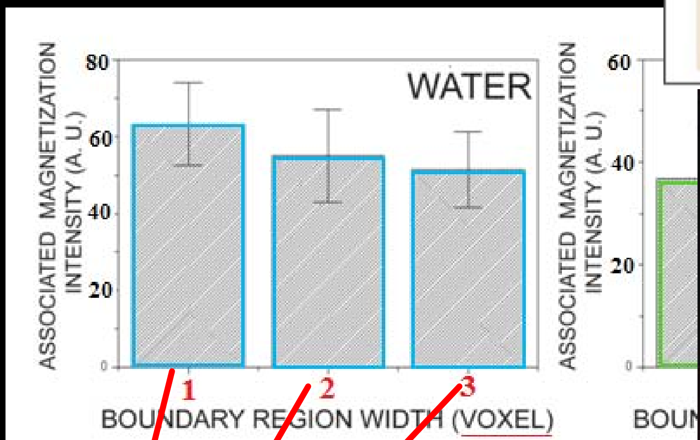
$D1=2.0\cdot10^{-9}\ m^2/s$

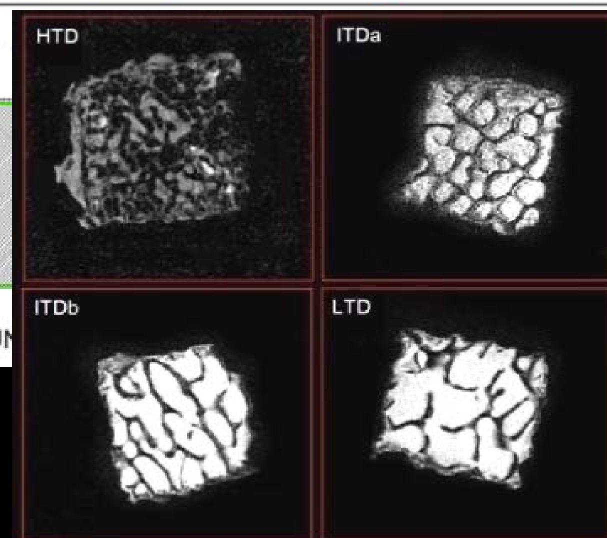
$D2=9\cdot10^{-11}\ m^2/s$

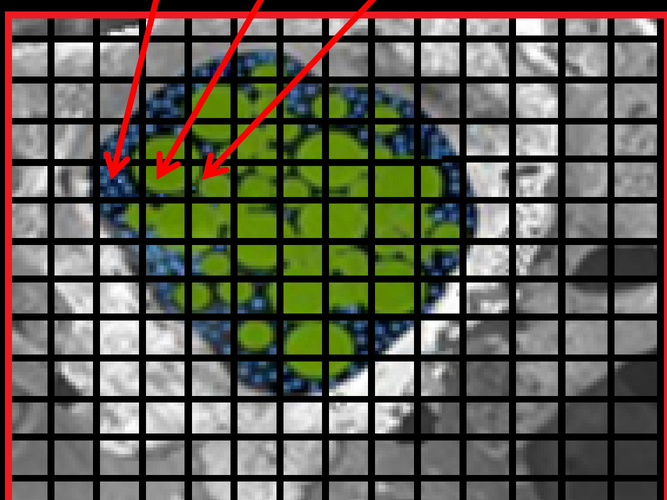
- Water diffusion behavior in calf bone samples at 9.4T

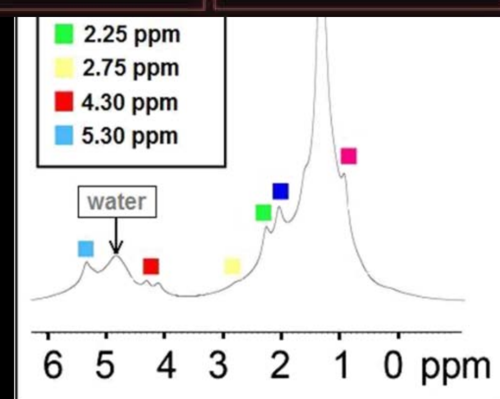
In vitro experiments
20x20 μm^2 resolution

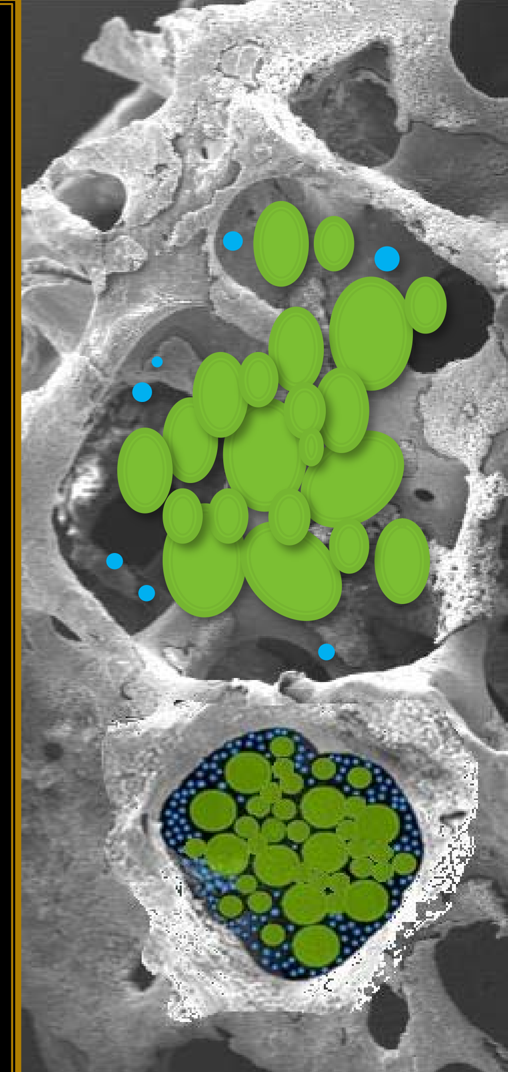


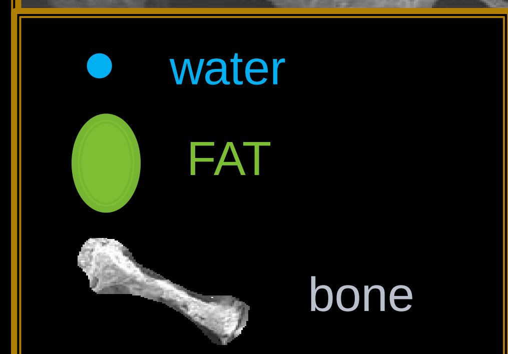




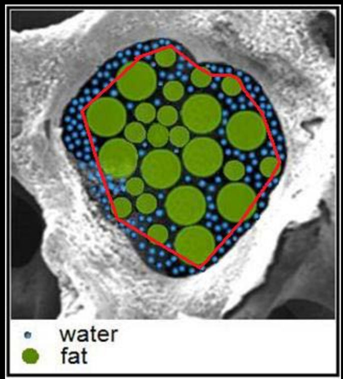








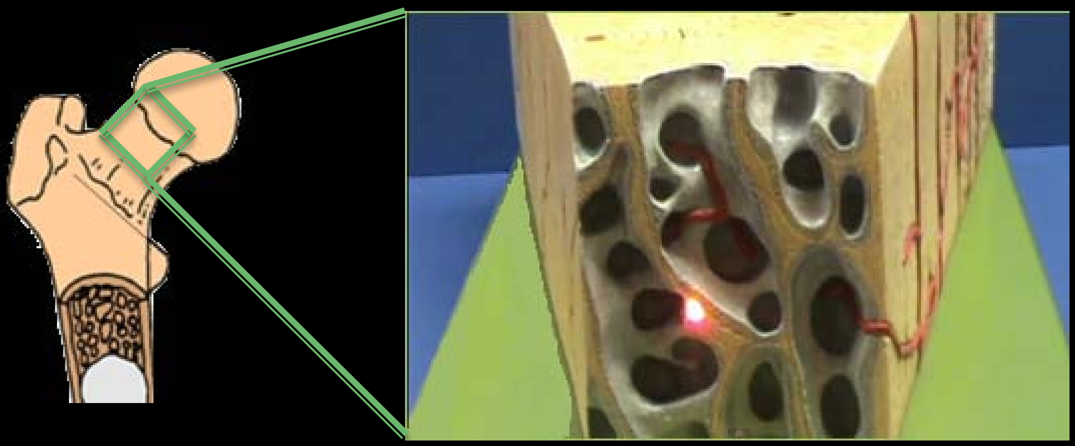
The porous system model



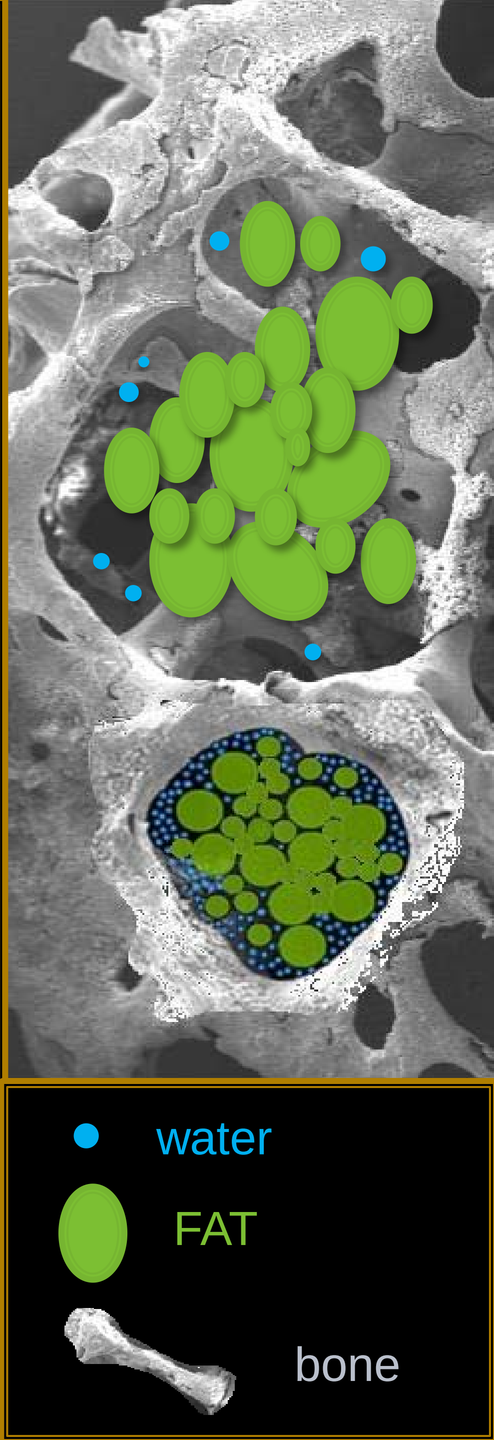
"Water is more prevalent in the boundary zone while fat occupies primarily the central zone of the pore"

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

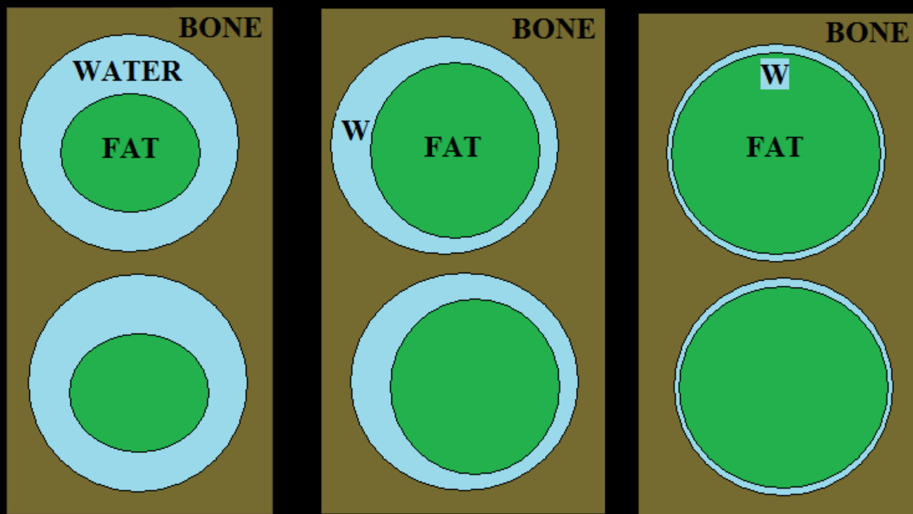
Justification: histology of bony surface



Endosteum, is a thin membrane (≈5-10μm) 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



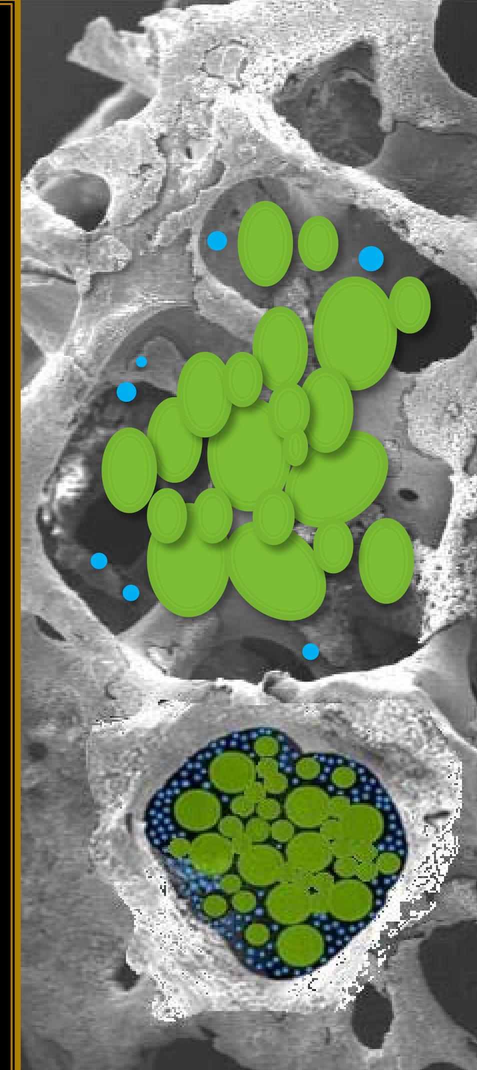
The porous system model: restricted diffusion



Vertebrae	Femoral neck	Calcaneus
ADC ≈ 10^{-3} mm²/s	10^{-4} mm²/s	10^{-5} mm²/s

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

Healthy



Methods: patients selection

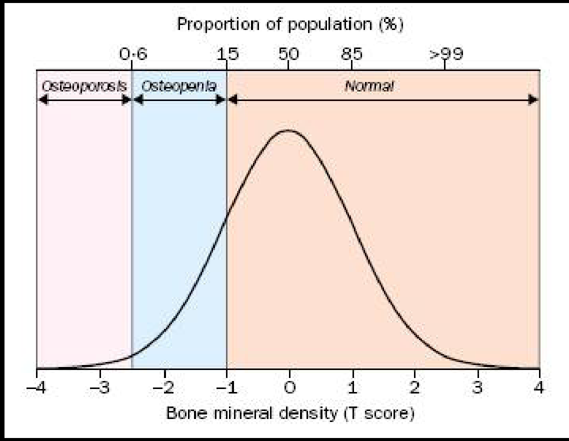
Group I: calcaneus
30 postmenopausal women
mean age (64.5±6 years)
10 healthy,
10 osteopenic
10 osteoporotic women,

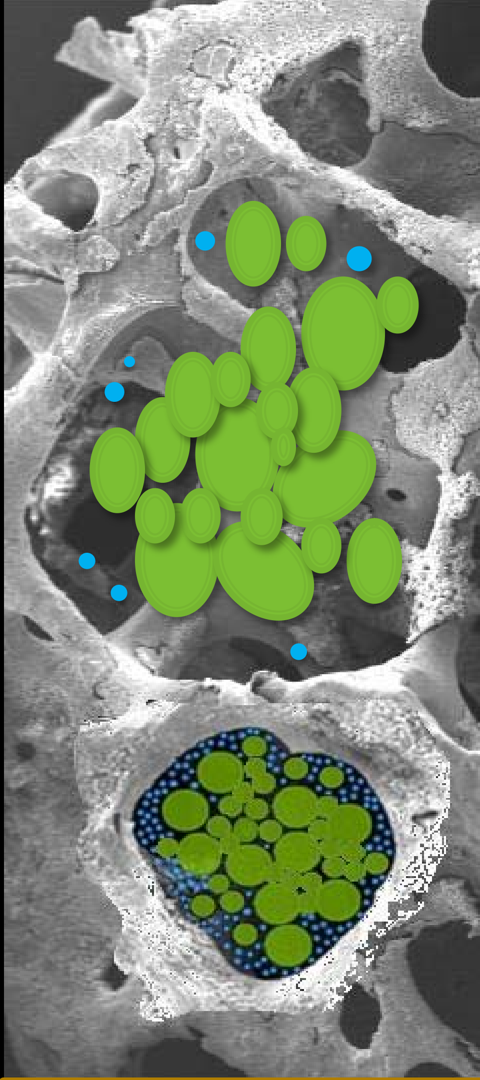
The status of each subject was assessed with **QCT** BMD measurements in **lumbar vertebral** according to the following criteria*:

T-score ≥ -1.8 :healthy

-3.3 < T-score < -1.8 : osteopenia

T-score ≤ -3.3 osteoporosis

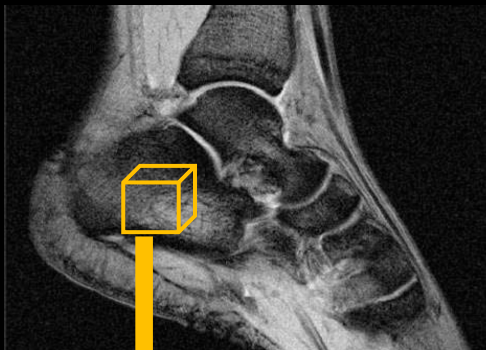


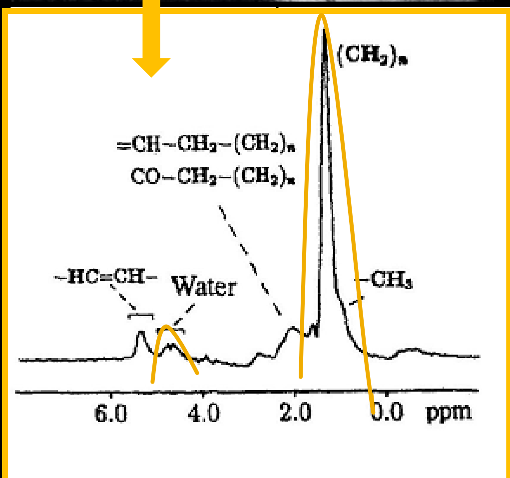


*ISCD Official Position, reported by K. Engelke, J.E. Adams et al., Journal of Clinical Densitometry: Assessment of Skeletal Health, 2008;11:123-162

Methods: MR at 3T

ADC +MRS in calcaneus



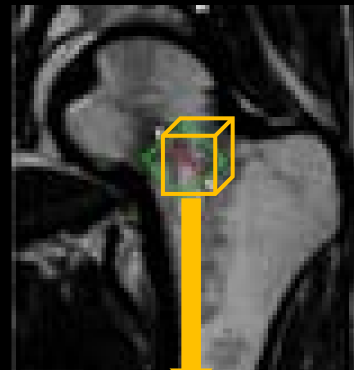


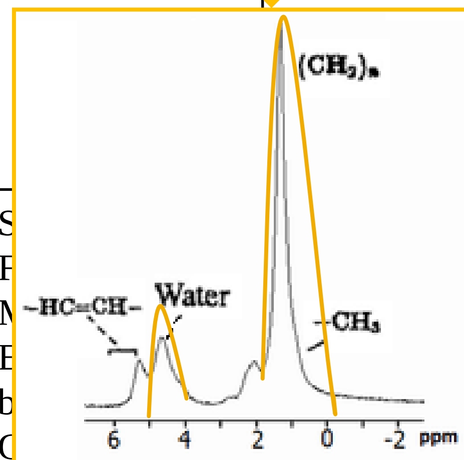
	fusion mented te ADC eus
	rior
TE/TR	89/2500ms
NS	2

Fat fraction %

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

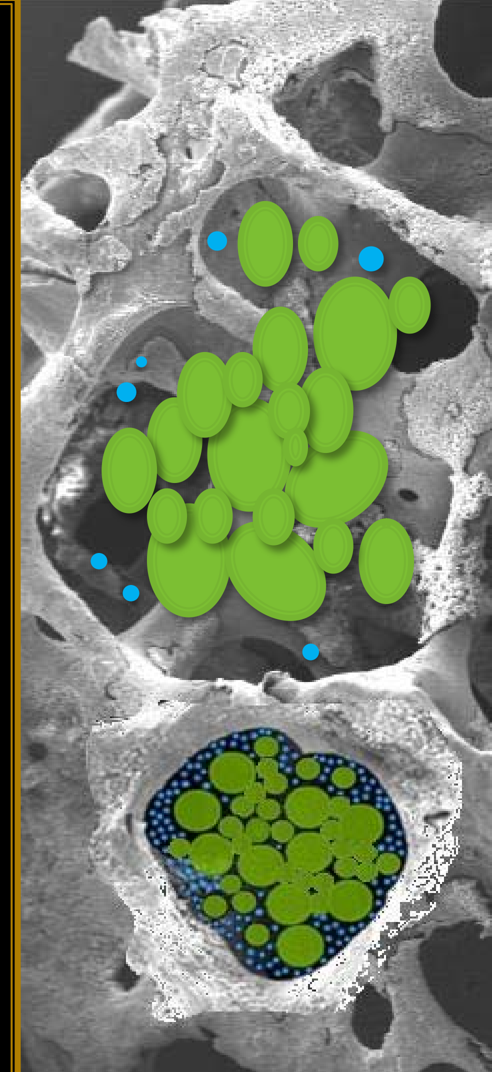
ADC+MRS in femoral neck





	iffusion gmented ate ADC l neck
S	
F	2mm
N	
E	
b	n^2
C	
TE/TR	104/2500ms

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



water

Mono-exponential decay

$S(b)=S(o)\exp(-ADC*b)$

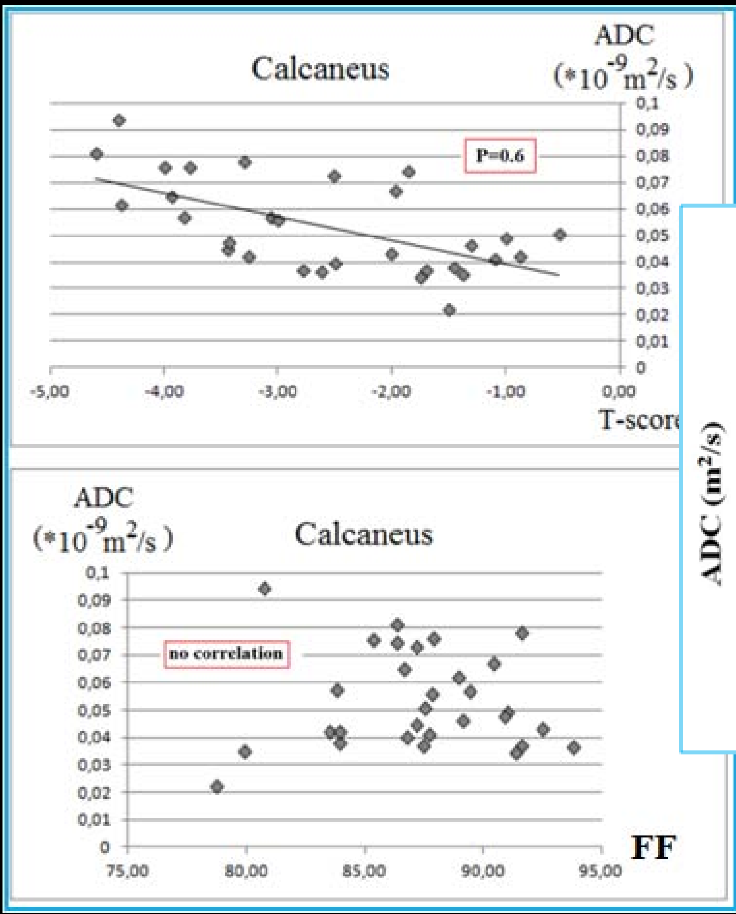
bone

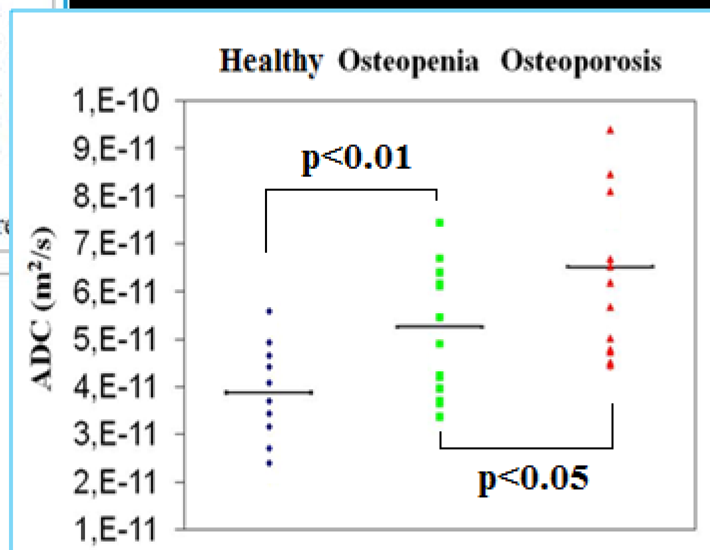
Results
ADC +MRS in human calcaneus

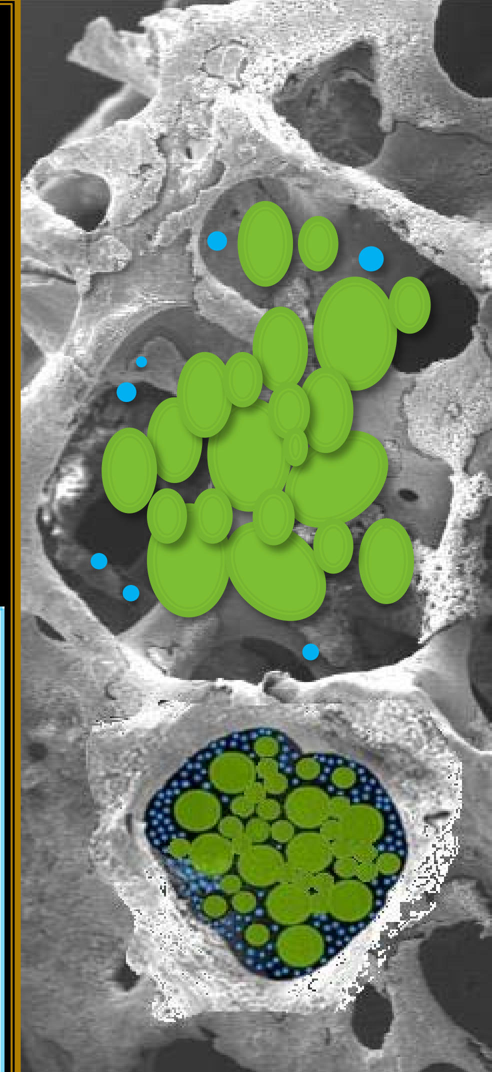
FF was not significantly different between BMD groups

MSD = 6 DΔ

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







water

FAT

bone

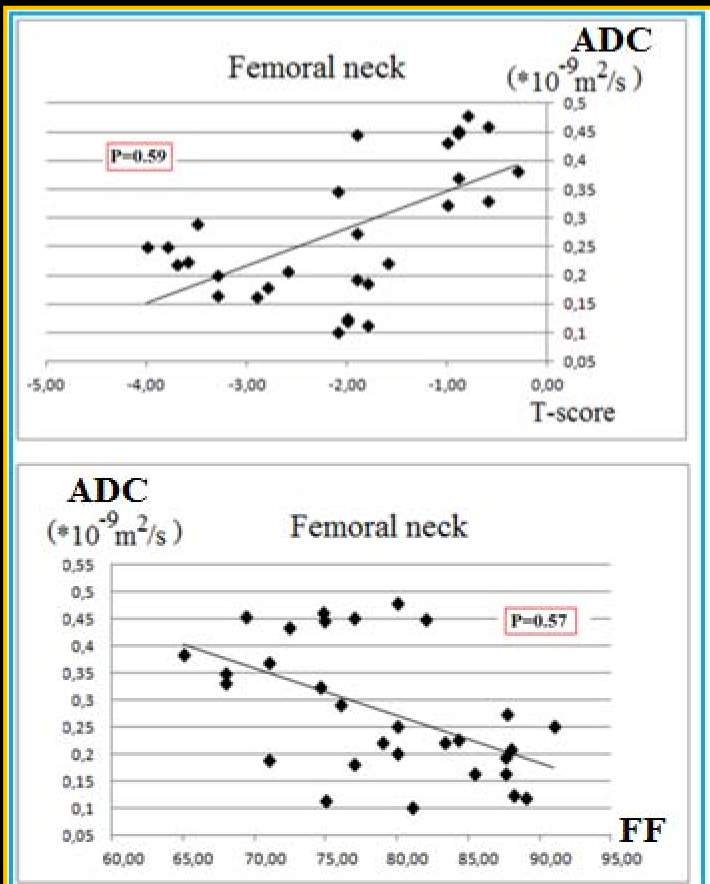
M. Rebuzzi ,et al. BONE 2013;57:155-163

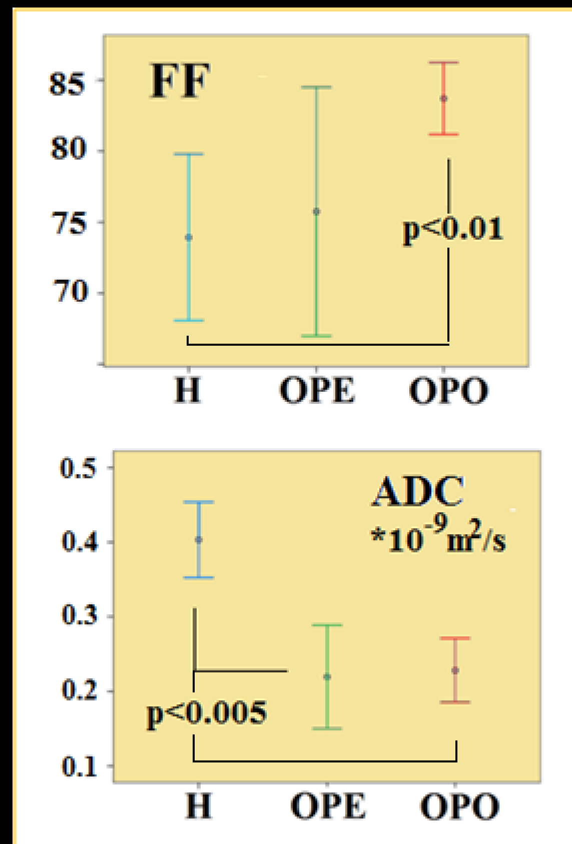
ADC+MRS results obtained in human femoral neck

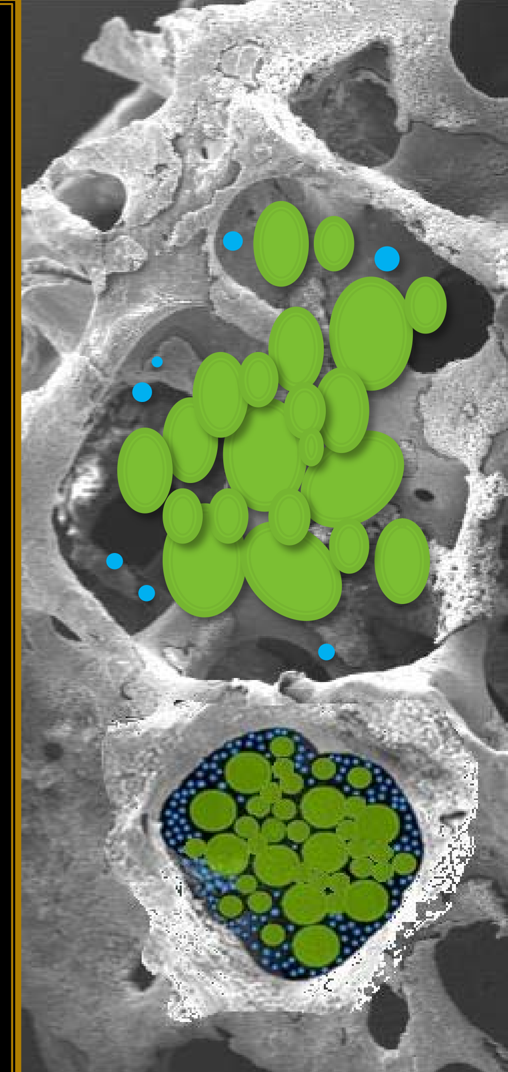
FF was significantly different between healthy (H) subjects and patients with osteopenia (OPE) and osteoporosis (OPO)

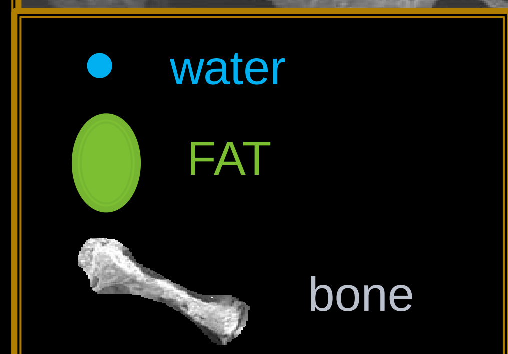
MSD = 6 DΔ

$MSD^{1/2} \approx 9\ \mu m$
$D = 2 \cdot 10^{-4}\ mm^2/s \quad \Delta = 80 ms$









G. Manenti, S. Capuani et al. BONE 2013;55:7-15.

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.

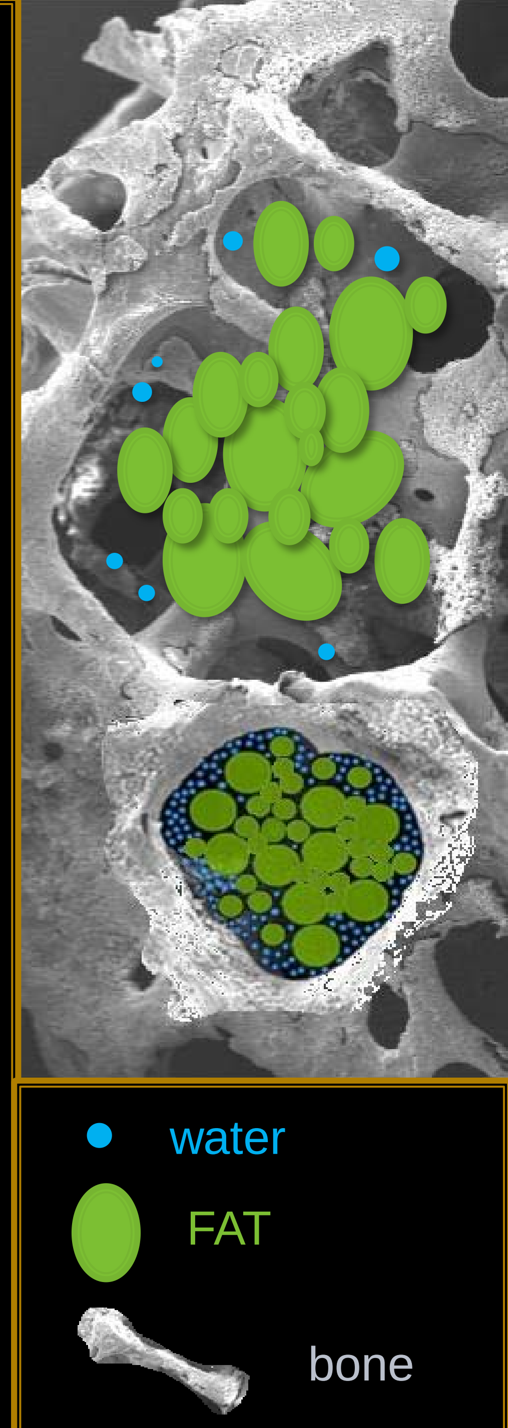
In femoral neck

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

Patients with osteopenia and osteoporosis compared to age-matched controls

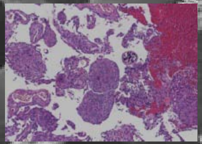
showed significantly lower ADC values.

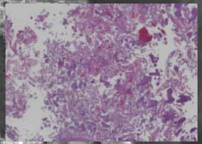
Findings may be a consequence of fat increase in each cancellous bone pore that causes a narrowing of the space between fat and bone where the water diffuses (more restricted water!)

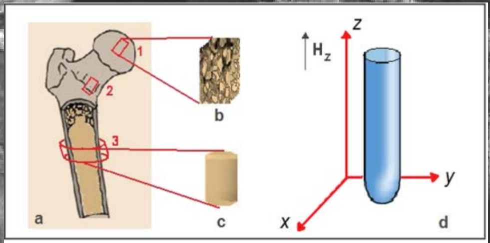


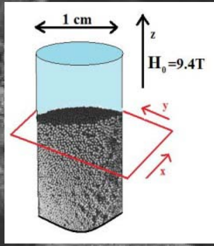
NMR Laboratory
Physics Dpt.
Fermi Building
Sapienza Univ.

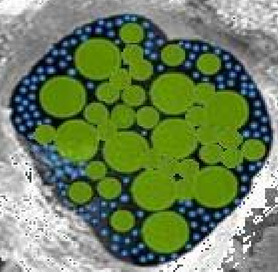
silvia.capuani@roma1.infn.it











Thank you for your attention.