La diffusione NMR per la diagnosi
dell'osteoporosi.

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Highlights

Fundamental physics

NMR Diffusion in porous systems

Models

Biophysical applications

Translational longitudinal studies in Humans

Transfer of technology

Clinical application

-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
-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

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

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

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

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

\[ \text{MSD}^{1/2} = (2D\Delta)^{1/2} \]

- **Hindered diffusion**
  - \(D_0 = 2.3 \cdot 10^{-9} \text{ m}^2/\text{s}\)
  - \(D_1 = 2.0 \cdot 10^{-9} \text{ m}^2/\text{s}\)
  - \(D_2 = 9 \cdot 10^{-11} \text{ m}^2/\text{s}\)

D(parallel) about free diffusion coefficient, where D(perp.) is more defined by the geometric barrier, as \(t=\Delta\) becomes longer.
Water diffusion behavior in calf bone samples at 9.4T

In vitro experiments
20x20 µm² resolution

Water diffusion behavior in calf bone samples at 9.4T
The porous system model

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


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-marrows compartment adjacent to the endosteum.
The porous system model: restricted diffusion

Vertebrae
ADC \approx 10^{-3} \text{ mm}^2/\text{s}

Femoral neck
10^{-4} \text{ mm}^2/\text{s}

Calcaneus
10^{-5} \text{ mm}^2/\text{s}

Healthy

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● 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

Methods: MR at 3T
ADC + MRS in calcaneus

ADC + MRS in femoral neck

Fat fraction %

\[ \text{FF} = \frac{A_{\text{fat}}}{(A_{\text{fat}} + A_{\text{w}})} \]

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

Mono-exponential decay

\[ S(b) = S(0) \exp(-\text{ADC} \times b) \]
Results

ADC + MRS in human calcaneus

FF was not significantly different between BMD groups

\[ \text{MSD} = 6 \Delta \]

\[ \text{MSD}^{1/2} \approx 4 \mu m \]

\[ D = 5 \times 10^{-5} \text{ mm}^2/\text{s} \quad \Delta = 70 \text{ms} \]

ADC+MRS results obtained in human femoral neck

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

\[ \text{MSD} = 6 D \Delta \]

\[ \text{MSD}^{1/2} \approx 9 \mu m \]

\[ D = 2 \times 10^{-4} \text{ mm}^2/\text{s} \quad \Delta = 80 \text{ms} \]

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!)
Thank you for your attention.