In vitro micro-imaging investigation of osteoporotic and osteoarthritis femoral specimens by means of internal magnetic field gradient (IMFG)

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Purpose. Osteoporosis (OP) and osteoarthritis (OA) are the most common diseases of musculoskeletal system. Osteoporosis is characterized by low bone mass and microarchitectural deterioration of bone tissue[1]. Osteoarthritis consists in a progressive articular cartilage loss with concomitant changes in the bone underneath the cartilage[2]. Recently has been highlighted that internal magnetic field gradient (IMFG) measured in calcaneus cancellous bone, is able to discriminate between healthy osteopenic and osteoporotic subjects better than other MR parameters such as T2* [3]. This is because IMFG depends on both magnetic susceptibility differences between bone-marrow water and bone and apparent diffusion coefficient (ADC) of water diffusing between fat and bone in each cancellous bone pore [4,5]. However calcaneus is not a typical site in which osteoporotic fractures occur. Therefore, aim of this study was to test the ability of IMFG, evaluated in femoral neck, to discriminate between OP and OA patient bone specimens. Toward this goal we examined in vitro, at 9.4T, cancellous bone samples extracted from femoral neck of OA and OP postmenopausal women. We assessed IMFG association with T-score (evaluated in femoral neck), menopausal age, Harris Hip Score (HH) and body mass index(BMI).

Methods. Femoral neck biopsy (**Fig.1**) was performed in 16 women with osteoporosis (mean age=84±9, mean T-score=-2.6±1.5) and 19 osteoarthritis women (mean age=75±9, mean T-score=-1.4±1.3) undergoing surgery for femoral head replacement. This study was approved by the local Ethics Committee and written informed consent was obtained in all cases before study initiation. A Magnetic Resonance (MR) system operating at 9.4T and equipped with a micro-imaging probe with a maximum gradient strength of 1200 mT/m (rise time of 100 μs) was used to investigate bone samples. Each bone sample was stored in a 4% paraformaldeyde and PBS immediately after being extracted from the patient and then placed in a 8mm NMR tube. MSME (Multi Slice Multi Echo) imaging sequences (TEs range =3-100 ms, TR=1500, matrix dimension = 128x128, Field of view (FOV)=0.8 cm, number of average (NS)=8) were used to assess SE decay. ADC was measured by means of Pulsed Field Gradient Stimulated Echo (PGSTE) imaging sequences (TE/TR=27/3000 ms, diffusion gradient pulse delay Δ=40 ms, diffusion gradient pulse duration δ=2 ms and ten b-values ($b=\gamma^2g^2(\Delta-\delta/3)$ ranging from 1000 to 20000 s/mm^2). IMFG can be extracted by a fitting procedure from SE decay and ADC measurement: $S(TE)=S_0\exp((-TE/T_{2,true})-(\gamma(IMFG)^2DTE^3/12))$ as previously reported[3,4]. Twelve axial slices (slice thickness ST=1mm) were acquired. We evaluated IMFG in each slice and this quantity was averaged over all slices within the bone. Moreover we evaluate mean IMFG values in subchondral and metaphysis section (**Fig.1C**) of each group. Relationship between pairs of variable were assess with linear correlation analysis (Pearson correlation coefficient). Between group comparison to asses group and cancellous bone section differences was performed. P values<0.05 were considered statistically significant.

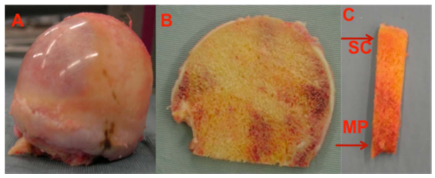

Fig.1 Material used for MR investigation: A)Bone sample extracted from femoral neck. B) femoral head of a subject after the surgical operation. C) bone sample ad hoc cut to fit NMR glass tube. Rows indicate the subchondral (SC) and the metaphysis (MP) section.

Results and discussion. All IMFG values evaluated in femoral neck are lower than those evaluated in calcaneal skeletal site. This is in agreement with the cancellous bone model[5] for which the interspace between fat and bone in femoral neck pores is higher than that in the calcaneus cancellous bone. As a consequence magnetic field inhomogeneities at the interface between water and bone are averaged out better, due to a faster water diffusion[3]. IMFG values were significantly lower in OP compared to OA bone samples (P=0,03)(**Fig.2A**). Moreover, IMFG values were significantly lower in in the metaphysis section compared to the subchondral one in both OP and OA samples (P=0,0009 **Fig.2B** P=0,01 **Fig.2C**). A significant correlation was found between IMFG and T-score in OP subjects only (r=0,0768, P=0,0049). Conversely no significant correlation was found, in OP and OA subject samples, between IMFG and HH, BMI and menopausal age.

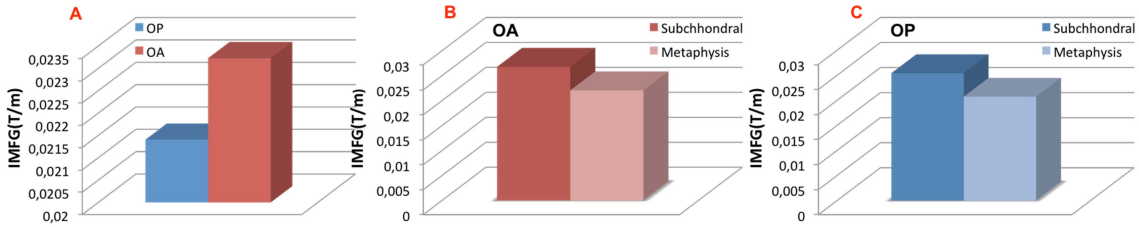

Fig 2. A) IMFG values were significantly lower in OP compared to OA bone samples (P=0,03). B, C) IMFG values were significantly lower in in the metaphysis section compared to the subchondral one in both OP and OA samples (P=0,0009, P=0,01, respectively)

As expected, IMFG is higher in OA compared to OP patients suggesting that OA samples are characterized by a higher trabecular density as compared to OP samples. Moreover we found that in OA specimens the subchondral region had a higher IMFG as compared to metaphysis region. These results are in agreement with the packing (i.e. the increased trabecular density with consequent reduction of pores diameter) of the subchondral bone that is a characteristic feature of the osteoarthritis. However, we also found a higher IMFG in subchondral as compared to metaphysis region in OP specimens. A possible explanation of the IMFG increase is the change of the marrow fat content that increases in OP patients[6]. As reported by Capuani et al[5] an increase of bone marrow fat causes a reduction of the space in which bone marrow water diffuses and a reduction of water ADC. This scenario causes an increase of IMFG[3].

Conclusions Our preliminary data better clarifies the potential applications of IMFG for the evaluation of cancellous bone microstructures. Moreover our data obtained in a larger number of OA and OP samples could add information about OP and OA cancellous bone microstructural changes.

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