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COMPARATIVE STUDY OF TWO TYPES OF BIOACTIVE EPIMEDIUM FOR OSTEOPOROSIS TREATMENT IN AN OVARIECTOMIZED RAT MODEL
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Background: Osteoporosis is a systemic metabolic disease causing a reduction of bone mass and strength, and an increase in fracture risk consequently. Traditional Chinese Herbs, e.g. Epimedium are often used as a major composition to formulate herbal formula for osteoporosis treatment. Different localities of herbs may cause different properties that would be a decision of herbal formula selection for R&D of anti-osteoporosis herbal drugs. This study aims to compare the efficacy of two Epimedium species, namely Epimedium koreanum Nakai (X1) and Epimedium pubescens Maxim (X2).

Methods: Ovariectomized (OVX) model was established in sixty female Sprague Dawley rats (220±20g). High (90 mg/kg/day) and low (45 mg/kg/day) dosages of X1 and X2 were designed for daily intragastric administration for 90 days post OVX, namely X1L, X1H, X2L and X2H groups, also sham-operated rats (sham group) and OVX rats (OVX group). After scarifying the animals, micro-CT scanning of the proximal tibia and the fourth lumbar vertebra was conducted for evaluations of bone mineral density (BMD), bone tissue volume fraction (BV/TV) and trabecular number (Tb. N). Biomechanical properties of the mid-shaft of tibia and the fourth lumbar vertebra were also obtained.

Results: Micro-CT results of proximal tibia showed that as compared to OVX group, significant higher BMD (28.41% and 25.35%) and BV/TV (33.01% and 38.33%) were found in X1H and X2L groups, respectively (p<0.05, n=6). For micro-CT results of vertebra, significant higher BMD (23.72% and 22.90%), BV/TV (31.70% and 30.96%) and Tb.N (26.85% and 18.27%) were pre-sented in X1H and X2L groups, respectively (p<0.05, n=6). Based on the results of 3-point bending test in tibia, there was no significant difference of the mechanical strength between OVX group and each Epimedium groups (p>0.05, n=6), however, the results of compression test indicated the significant higher E-Modulus (81.82%, 80.21% and 72.04%) and compressive strength (74.59%, 64.92% and 81.05%) in X1L, X1H and X2L groups, respectively (p<0.05, n=6).

Conclusion: The two species of Epimedium showed significant efficacy for slowing the loss of bone mass and strength in osteoporosis, which presented a potential dose effect for both of the two species. However, there was no significant difference found between the high dose of X1 and low dose of X2, which indicated that both two Epimedium species could be selected for R&D of herbal drug.

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POPULATION-BASED LOCAL MULTI-PARAMETRIC COMPARISONS OF HR-pQCT STUDIES
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Objective: Conventional HR-pQCT quantification approaches average bone features over large regions and ignore their spatial association within the structure, obscuring local information regarding their distribution and how they contribute to bone strength. Here, we present 3D image analysts techniques for population-scale multi-parametric spatial comparisons of bone quality features. Specifically, we present: 1) voxel-based morphometry (VBM), and 2) a surface-based framework to encode cortical bone features in a laminar-wise manner, which is then used to measure cortical bone thickness and perform statistical parametric mapping (SPM).

Methods: Imaging Scan-rescan HR-pQCT acquisitions with repositioning of the distal radius and tibia were acquired in 30 subjects. VBM
The radius and tibia of one subject were selected as references. Bone feature maps of the remaining subjects were homogenized and spatially normalized to the references based on affine and nonlinear registrations. Voxel-wise multi-parametric comparisons (vBMD and BV/TV) were then performed between “follow-up” and “baseline” scans, using Hotelling’s T2 tests for dependent samples and false discovery rate correction (FDR).

Surface-Based Cortical Bone Analysis
Bone segmentations, vBMD maps, non-local means, and fuzzy logic were used to generate soft cortical bone segmentations: {D=marrow, 1=bone}. A one-to-one matching between the periosteal surface and the endosteal boundary was established through streamlines computed with the Laplace’s equation, thus enabling a laminar analysis.

-Streamline Integral Thickness (SIT)
Integrals of the soft segmentation along the streamlines yielded a porosity-weighted cortical bone thickness measure. The streamline lengths provided an apparent measure of cortical thickness.

-SPM
VBM registrations were used to spatially normalize the periosteal surfaces. Analogous to VBM, multi-parametric vertex-wise comparisons of SIT and mean streamline vBMD were performed.

-Global Reproducibility
Rigid matching of individual “follow-up” and “baseline” surfaces was performed to assess global reproducibility of thickness and mean streamline vBMD using CVRMS (absolute errors).
Results: Figure-1 shows a spatial normalization example and a mean BV/TV map. Cortical thickness maps of a scan-rescan example, mean cortical thickness maps, and a laminar vBMD example are shown in Figure-2. No significantly different voxels or vertices were found after FDR correction, indicating no significant multi-parametric differences between "baseline" and "follow-up" scans. Global reproducibility yielded CVRMS of 1.6% (0.018mm) and 0.9% (0.013mm) for apparent thickness, 1.5% (0.014mm) and 0.8% (3.05mg/cm³) for vBMD, for the radius and tibia, respectively.

Conclusion: Advanced 3D image analysis techniques may be employed for population-based local multi-parametric comparisons of HR-pQCT studies with high reproducibility.

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HIGH RESOLUTION COMPUTED RADIOGRAPHY OF CORTICAL BONE POROSITY IN WEIGHT BEARING AND NON-WEIGHT BEARING LONG BONE SHAFT UNDER HABITUAL LOADING
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Objective: Differential mechanical loading in weight bearing and non-weight bearing long bone could result in adaptation of bone mineral density and microarchitecture. Understanding of the bone adaptation could shed light into the bone remodelling processes underpinning the adaptation. This study used high resolution computed radiography and post-image enhancement approach to quantify the intracortical porosity (ICP) of weight bearing and non-weight bearing long bone shafts under lifetime habitual loading at distal tibia and radius regions, respectively.

Methods: Cortical bone segments of 7.5 mm in length at distal tibia and radius were harvested from 20 Chinese cadavers aged 52 to 92. These were processed and embedded in methyl methacrylate (MMA) without decalcification. Bone slices of 500 μm were then cut from the MMA embedded bone specimens. Images of the bone slices were acquired using high resolution computed radiography with magnification technique. This rendered an in-plane resolution at 100 μm. Segmentation and quantification of cortical porosity from the mineralised tissues was achieved using Image J (National Institute of Health).

Results: The study demonstrated that tibial ICP (27.03 ± 2.93%) was 33% significantly higher than that of radius (20.37 ± 2.43%) (p < 0.001). The ICP correlated significantly with age, with radius showing strong correlation, r (17) = 0.75, p < 0.001, whereas tibia showing moderate correlation, r (18) = 0.44, p = 0.06. Two-way analysis of variance was carried out to study if there were any interaction effects of bone region (tibia and radius) and bone sector (anterior, posterior, medial, lateral cortices) on ICP. There was a marginally significant interaction between bone region and sector on ICP (p = 0.09). Follow-up test showed a marginally significant simple main effects for different sectors only in tibia (p = 0.03). The anterior cortex (28.26 ± 4.68 %) had 15% higher in ICP than the posterior cortex (24.55 ± 5.26 %) at the distal tibia (p = 0.003). No significant pairwise differences were found elsewhere.

Conclusion: It suggested that ICP increased with age because of unbalanced remodelling after mid-life. The high ICP in tibia may be a result of bone remodelling in response to dynamic loading so as to reduce the expenditure of mechanical energy for locomotion. Sectorial differences between the anterior and posterior cortex in distal tibia exemplified the bone adaptation to differential tension and compression strain mode, respectively.

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ADVANCED MUSCULOSKELETAL IMAGING SYSTEMS ADOPTED FOR STUDY A NOVEL BONE-TARGETING DELIVERY SYSTEM CARRYING OSTEOPROMOTIVE PHYTOMOLECULE(S) DEVELOPED FOR PREVENTION OF ESTROGEN DEPLETION INDUCED OSTEOPOROSIS
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Objectives: To evaluate the efficacy of icaritin with targeting liposome delivery system on prevention of estrogen depletion induced osteoporosis in vivo by analyzing the bone quality and microarchitecture by micro-Computed Tomography (micro-CT) and the distribution of the delivery system by using Xenogen IVIS spectrum system.

Figure 1. Cross-sections of voxel-wise analyses: A) Representative homogenized BV/TV map. B) Reference shape. C) Map in A after spatial normalization to B. D) Mean "baseline" BV/TV map.

Figure 2. Surface-based analysis: A) Representative "baseline" and "follow-up" apparent cortical bone thickness maps. B) Representative "baseline" and "follow-up" SIT maps. C) Mean apparent cortical bone thickness map. D) Mean SIT map. E) Representative laminar vBMD maps: periosteal layer, middle layer, and endosteal layer.