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Purpose: Subjects with acromegaly (AG) suffers of increased bone fragility and, as reported in literature, have a higher prevalence for vertebral fracture even in subjects with normal BMD. Sparse information exists on the effect of AG on bone microarchitecture and no at axial sites. The aim of our study was to examine bone quality and quantity assessed by TBS and BMD in subjects with AG at lumbar spine.
Methods: In this longitudinal study 46 subjects with AG have been recruited (26 women and 20 men, mean age of 54.9±11.5 years, BMI of 29.3±4.2 Kg/m^2). BMD and TBS were evaluated at lumbar spine (LS) using an iDxa DXA device (GE-Lunar) and TBS iNsight® (v2.1, Med-Imaps, France). Presence of vertebral fracture has been confirmed by Vertebral Fracture Assessment by DXA (VFA).
Results: Among all AG subjects, 41% were in active phase of the disease, 74% suffered from hypogonadism (Hy) and 22% sustained at least a fracture (Fx). BMD and TBS showed high correlation ($p<0.0001$), with 49% of TBS explained by spine BMD. Subjects with Hy have a significant lower BMD and TBS ($p<0,002$). Those with fracture have a lower TBS ($p=0.02$) whereas no difference has been observed on spine BMD ($p>0.5$). TBS and fracture were associated with an odd-ratio per one SD decrease of 2.64 [1.1-6.3] and an area under the ROC curve of 0,71 [0.56-0,84]. BMD, Age, presence of Hy, or duration of Hy were not associated with the presence of the fracture. Compared to normative TBS value, AG subjects have a significant TBS impairment (-6%, $p<0,001$). Those with Hy or fracture have a lower TBS values when compared to normative values: -8% ($p<0,001$) and -13% ($p<0,02$) respectively.
Conclusion: This is the first study reporting changes in BMD and TBS at lumbar spine in subjects with acromegaly. AG induces bone microarchitectural texture impairment at lumbar spine. Presence of hypogonadism or fracture worsens this impairment. As previously obtained, TBS seems to be more sensitive to assess bone architecture impairment than BMD.

IBDW2014-00079-F0011
TRABECULAR BONE SCORE IN HEALTHY AGEING

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Objective: To report values of Trabecular Bone Score (TBS) of healthy subjects and to highlight the link between TBS and conventional parameters of bone and body composition by dual-energy x-ray absorptiometry (DXA).
Methods: Two hundred and fifty patients of five age decades (from 20s to 70s, equally distributed for both age and sex) were prospectively recruited. Whole-body and regional densitometric body composition parameters (iDXA, GE Healthcare, USA), including estimate of visceral fat (VAT) assessed by a new software, lumbar DXA and TBS by iNsight (version 2.1) were considered.
Results: A significant decrease of TBS was observed with ageing only in females, while BMD significantly decreased both in males and females. TBS values were slightly correlated with BMI ($r=0.133$, $p<0.01$), total lean mass in males ($r=0.187$, $p<0.05$) and total\regional fat mass in females ($r=0.197$-0.223, $p<0.05$). However lumbar spine BMD ($r=0.870$, $p<0.0001$) predominantly influences TBS values.
Conclusions: This report revealed more influence on TBS by bone "quantity" compared to body composition parameters. Moreover the age and sex-specific reference curves for TBS could help clinicians to improve patient management in the detection of impaired bone mineral status and to monitor microarchitectural changes.

IBDW2014-00080-F0012
MORPHOLOGICAL AND BONE STRENGTH INDICES IN GIRLS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS AND THEIR CORRELATIONS WITH LEPTIN AND SOLUBLE LEPTIN RECEPTOR

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Objective: Previous studies suggested that leptin has profound effects on bone metabolism and growth. Abnormal leptin and soluble leptin receptor (sOB-R) levels and their correlation patterns with bone mineral density and trabecular bone micro-architecture were recently found to be distinct in girls with adolescent idiopathic scoliosis (AIS). Structural Model Index (SMI) and data derived from Finite Element Analysis (FEA) are important HR-pQCT parameters that can provide important information on the rod/plate-like configurations in the trabecular bone and bone strength respectively. This study aimed to compare the differences and correlations between SMI, bone strength indices and leptin and sOB-R between AIS and controls.
Material and Methods: 104 AIS girls aged 12 to 14 (Cobb angle 22.7°±6.4°) and 82 age and gender-matched healthy controls were recruited. Subjects with BMI>23.0 kg/m2 were excluded. Anthropometric measurements including body height, body weight, sitting height and arm span were recorded. Sexual maturation was assessed with Tanner stages. SMI and bone strength parameters from FEA were determined at the non-dominant distal radius using HR-pQCT. Serum total leptin and sOB-R levels were measured with ELISA.
Results: Compared with controls, AIS subjects had higher sOB-R level ($p=0.006$), higher SMI value ($p=0.020$) reflecting more rod-like structures within the trabecular compartment, and numerically lower stiffness (-2.03%) and estimated failure load (-3.07%). Significant negative correlation was found between SMI and serum total leptin level in AIS ($r=-0.325$; $p=0.003$) but not in controls ($p=0.533$). Significant positive correlations were found between stiffness, estimated failure load, and serum total leptin in both AIS ($r=0.278$, $p=0.003$; $r=0.268$, $p=0.004$ respectively) and controls ($r=0.462$, $p<0.001$; $r=0.468$, $p<0.001$ respectively).
Conclusion: The higher SMI and numerically lower FEA derived bone strength parameters both reflecting decreased bone strength in AIS. The negative correlation between SMI and serum total leptin level was distinctly only detected in AIS, which indicated possible disturbance in leptin signaling affecting the trabecular bone of AIS. The results of this and previous studies provided strong evidences of deranged bone quality and bone strength and its association with abnormal leptin bioavailability and signaling in AIS.

IBDW2014-00081-F0013
CORTICAL MEASUREMENTS OF THE TIBIA FROM HIGH RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY IMAGES: A COMPARISON WITH MICRO-COMPUTED TOMOGRAPHY

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Objective: High Resolution-peripheral Quantitative Computed Tomography (HR-pQCT) measurements are carried out in clinical research protocols to analyze separately cortical bone and trabecular bone. Micro-computed tomography (micro-CT) is a standard tool for ex vivo examination of bone in 3D. The aim of this work was to evaluate cortical measurements derived from HR-pQCT images compared to micro-CT in a distal position with a sufficient amount of cortical bone (4.2 cm from the distal pilon).
Methods: Twelve tibia specimens were scanned with HR-pQCT using protocols provided by the manufacturer. The standard measured outcomes included volumetric bone density (mgHA/cm^3) of the cortical region

(Dcomp), and the cortical thickness (Ct.Th,mm). New features, such as cortical porosity (Ct.Po,%), pore volume (Ct.PoV,mm3) and mean pore diameter (Ct.Po.Dm,mm^2) were measured by an auto-contouring process. The cortical thickness derived from the auto-contour (Ct.ThautoC) was also obtained. All tibia were harvested in four quadrants at the same position of HR-pQCT measurements (9 mm height) for the conventional micro-CT analyses performed with a Skyscan 1172 ® device (voxel size=7.5μm). The posterior quadrant was also imaged by synchrotron radiation (SR) micro-CT at the ESRF Beam line ID 19 (voxel size=7.5μm).

First, site matched analyzes were performed to compare SR with conventional X-rays micro-CT results. Pore volume, (PoV), porosity (PoV/TV), pore size (Po.Si), pore spacing (Po.Sp), pore number (Po.N) and the degree of anisotropy (DA) were measured in site matched areas with micro-CT comparatively to HR-pQCT images. The cortical thickness (Ct.Thmicro-CT) was manually measured. Secondly, from conventional micro-CT images, the parameters of the cortical bone were averaged from the 4 quadrants and were compared to those from HR-pQCT images.

Results: The correlation coefficients between parameters from SR and conventional micro-CT were ($r=0.95$, $p<10\text{-}4$) for PoV, ($r=0.98$, $p<10\text{-}4$) for Po/TV, ($r=0.86$, $p<10\text{-}4$) for Po.Sp, ($r=0.76$, $p<10\text{-}4$) for CtThmicro-CT, ($\rho=0.71$, $p<0.001$) for Po.Si, and the coefficients were not significant for Po.N and DA.

The correlation coefficients of Ct.Thmicro-CT versus Ct.Th or Ct.ThautoC were high: $r=0.88$ $p<0.001$ and $r=0.84$, $p<0.001$, respectively. Dcomp were highly correlated to PoV/TV ($r=-0.83$, $p<10\text{-}4$). The Ct.Po versus PoV/TV($r=0.62$, $p<0.04$), Ct.PoDm versus Po.Si were not correlated ($r=0.47$, $p=0.14$), and CtPoV ($r=0.54$, $p<0.08$) was marginally correlated to PoV.

Conclusion: Distal tibia is a reliable region to study cortical bone with HR-pQCT measurements with Dcomp as the best parameter because it reflects both the micro-porosity (Havers canals) and macro-porosity (resorption lacunae) of the cortical bone.

IBDW2014-00082-F0014

VEGF-SRC SIGNALING IS ESSENTIAL FOR VASCULAR ENDOTHELIAL PERMEABILITY AND OSTEOCLASTS ACTIVITY

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Objectives: To delineate the role of VEGF and c-Src signals in triggering destructive repair of osteonecrosis in vitro.

Materials and methods: The primary endothelial cells and osteoclasts were adopted in this study. Pharmacological VEGF and Src specific pp60c-srcsiRNA were used to determine the contribution of VEGF-Src signaling to vascular permeability and osteoclasts activity. Cells were treated with 50 ng/ml VEGF and/or transfected with the pp60c-srcsiRNA every other day. In parallel, equivalent PBS and non-targeting siRNA were treated in the control groups. We analyzed the endothelial permeability associated structural elements and the osteoclast formation and function.

Results: Results showed that the appropriate pp60c-srcsiRNA significantly reduced Src expression both in the endothelial cells and osteoclasts. For decreasing VEGF-mediating higher vascular permeability, Src blockade significantly relieved actin stress and the formation of caveolae and vesiculo-vacuolar organelles (VVOs), as well as stabilized the complex beta-catenin/VE-cadherin/Flk-1 through decreasing phosphorylation of VE-cadherin, to keep endothelial junction integrity. In addition, VEGF promoted osteoclasts formation and function, while the adhesion activity and cytoskeleton were not obviously affected by VEGF. However, Src blockade significantly destroyed the cytoskeleton resulting in a lower adhesion activity and inhibited the osteoclasts differentiation and function through decreasing the phosphorylation of Src, Pyk2 and Cbl. These findings indicated that Src blockade not only reduced the VEGF mediating vascular permeability, but also reduced osteoclasts activity.

Conclusion: VEGF-Src signaling is essential for vascular endothelial permeability and osteoclasts activity. Thus, blockade of VEGF-Src signaling may provide us a new view to develop novel strategies for preventing and treatment of destructive repair in osteonecrosis.

Acknowledgements

This work was supported by NSFC (81171771) and HKGRF (473011).

IBDW2014-00083-F0015

EFFECT OF PSORALIDIN ON INHIBITING ADIPOGENESIS—AN *IN VITRO* EFFICACY AND MECHANISTIC STUDY

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Objective: Psoralidin, an coumarins extracted from the seed of Psoralea corylifolia L., and found it has estrogen-like activity that is mediated through estrogen receptors. In this study, we aimed to investigate the effects and molecular mechanism of psoralidin on adipogenesis dependent of ER signaling in vitro.

Methods: The cytotoxicity of psoralidin on 3T3-L1 preadipocytes and MCF-7 cell line was investigated by CCK-8 kit. Oil Red O staining in 3T3-L1 cells were used to demonstrate the effects of psoralidin on adipogenesis. The real time PCR was used to detect the mRNA expressions of the adipocyte-related genes, such as CCAAT/enhancer binding protein α (Cebpα), peroxisome proliferator-activated receptor γ (Pparγ), adipocyte lipid-binding protein (Fabp4) and lipoprotein lipase (Lpl). In addition, the protein expression of PPAR-γ, C/EBP α, Fabp4, LPL, phosph-GSK-3β-Ser9 and phosph-AKT-Ser473 were detected by western blot assay. All quantitative data were presented as means ± SD of three experiments.

Results: Psoralidin had no cytotoxicity effect on 3T3-L1 cell line, but it could significantly promote MCF-7 cells proliferation on selected dosage at 48 hours treatment. Psoralidin decreased the adipocytes in a dose dependent manner, as well as down-regulated the mRNA and protein levels of Cebpa, Pparg, Fabp4 and Lpl, but these effect would be weaken, even disappeared when co-treated with ICI182,780. The protein expression of phosph-GSK-3β-Ser9 and phosph-AKT-Ser473 on 3T3-L1 should be further proceed. These results suggested that psoralidin could inhibit adipogenesis, which might be through ER signaling pathway.

Conclusions: Psoralidin can inhibit adipogenesis in vitro. The underlying mechanism might be through ER signaling pathway.

Acknowlegement

This project was granted by Eu-NSFC grant (51361130034, FP7-604517), NSFC grant (81302782) and HKGRF grant (d00574).

IBDW2014-00084-F0016

A NOVEL MAGNESIUM COMPOSED PLGA/TCP POROUS SCAFFOLD FABRICATED BY 3D PRINTING FOR BONE REGENERATION

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Introduction: Bone regeneration is a crucial event in bone tissue engineering, and bioactive scaffold has become a focused strategy. Magnesium is a biodegradable and bioactive metal with needed mechanical strength for bone healing. An innovative Mg associated bioactive porous scaffold composed of poly (lactide-co-glycolide, PLGA), β-tricalcium phosphate (TCP) and magnesium (Mg) with well-defined biomimic microstructure for bone regeneration was designed and fabricated by low-temperature 3D printing technology. This PLGA/TCP/Mg scaffold has good biocompatibility and needed mechanical strength close to human trabecular bone and suitable for bone reconstruction. This study presented the enhancement of magnesium in mechanical properties and biocompatibility of the composite scaffold. The structure and mechanical properties and in vitro biocompatibility of this scaffold were investigated.

Results: The PLGA/TCP/Mg scaffold fabricated by low-temperature rapid-prototyping(LT-RP) with well-defined structure had high porosity with regular macropores (around 450 μm) and numerous micropores ranging from 2.5 μm to 90 μm distributed on the pore wall of the scaffold (see Fig.1). The high-resolution micro-computed tomography (micro-CT) results showed that the scaffold porosity was above 85% and the connectivity was almost 100%. The mechanical strength of the PLGA/TCP/Mg scaffolds was enhanced