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The Effect Of Ovariectomy On Cholesterol And The Inflammatory-Associated Markers RANKL And TNF-α In The Rat Animal Model Of Postmenopausal Osteoporosis

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Objectives: The aim of the present study was to investigate the effect of ovariectomy in mature rats, a frequently used animal model in postmenopausal osteoporosis research, on plasma cholesterol and the inflammatory markers RANKL and TNF-α. RANKL is a cytokine necessary for osteoclast differentiation and activation. TNF-α is a cytokine involved in acute systemic inflammation.

Materials & Methods: Forty mature (10-month-old) female Wistar rats were separated into 2 groups: Group A (n=20) subjected to ovariectomy, while Group B (n=20) was used as a control age-matched group, not subjected to any intervention. Blood was collected six months after ovariectomy by retroorbital puncture and measurements were conducted by Enzyme-Linked-Immuno-Sorbent-Assay (ELISA) using rat-specific Millipore Milliplex Map kits.

Results: In Group A (ovariectomized rats) total plasma cholesterol values were 102±2.8 mg/ml (mean±SEM) and in Group B (non-ovariectomized rats) they were 82.2±4.1 mg/ml. Respective RANKL values were 9.28±1.2 pg/ml and 6.33±0.99 pg/ml. Respective TNF-α values were 0.89±0.28 pg/ml and 0.84±0.19 pg/ml. Comparison between groups was conducted with Mann-Whitney test and revealed significantly higher (p=0.01) cholesterol levels as well as significantly higher (p=0.006) values of RANKL in Group A, whereas comparison of TNF-α between groups showed no significant difference.

Discussion: Ovariectomy induced a significant increase in Group A rats' cholesterol and RANKL values, while no difference was observed in TNF-α values between groups six months after surgery. The relationship of cholesterol in inflammatory processes has been documented and is supported by the present results. RANKL is an inflammatory marker and is related to increased bone resorption, which is in agreement with its increased levels in the ovariectomized rats. The non-significant difference of TNF-α between groups is possibly due to its role in acute systemic inflammatory conditions. Since blood sampling was conducted six months after ovariectomy, it can be supported that the phase of acute inflammation due to surgery had passed.

Summary: Cholesterol and RANKL plasma levels increased significantly in ovariectomized rats, whereas there was no change in TNF-α. A future investigation from the acute to the late post-operative phase is necessary for further documentation of the consequences of rat ovariectomy on the temporal changes of these parameters.

Gravitational Loading Alone Is Insufficient To Maintain Bone Strength

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Objectives: Bone mineral content decreases as a consequence of microgravity and immobilization. Therefore, models like bed rest, cast immobilization, and lower limb suspension have been applied to study bone responses to unloading in humans. However, these models cannot distinguish between the relative roles of muscle contraction and gravitational loading for maintaining healthy bones. An alternative model is proposed to study the muscle-bone relationship.

Subjects & Methods: HEPHAISTOS is a newly developed orthotic device for the lower limb that allows normal ambulation while greatly reducing forces generated by the calf musculature. Eleven male subjects wore HEPHAISTOS unilaterally for eight weeks within the frame of an ambulant study. Functional and anatomical muscle data of the calf musculature were obtained periodically during the intervention as well as during a six months recovery period. Bone density was assessed via peripheral Quantitative Computed Tomography (XCT 3000, Stratec and Xtreme CT, Scanco). Muscle strength was assessed by means of dynamometry and muscle volume was estimated based on magnetic resonance imaging.

Results: As a result of the intervention, total bone mineral content dropped in the distal tibia by 1.8% (p=0.03), compact bone mineral content was reduced by 3.45% (p=0.03) whereas trabecular bone mineral content was only lowered by 0.71% (p=0.3). Maximal isokinetic plantarflexion torque decreased by 21.8% (p=0.002). Plantarflexor muscle volume decreased by 16.6% (p=0.02) for m.Gastrocnemius medialis, 20.0% (p=0.01) for m.Gastrocnemius lateralis, and 15.6% (p=0.007) for the group m. Soleusm.Flexor hallucis longus.

Discussion: The observed changes in muscle volume in the present study compare to the changes observed during bed rest of the same duration, whereas the loss in bone mineral content approximated to about 50% of that induced by bed rest.

Summary: To the knowledge of the authors, this study is the first to isolate the role of muscle contractions and gravitational loading in maintaining bone health. Our findings indicate that gravitational loading alone is insufficient to maintain bone strength. Interventions aiming at maintaining or improving bone heath should therefore integrate muscular activity.

Adaption Of Bone Shaft Geometry In Patients With Rheumatoid Arthritis And The Influence Of Bisphosphonate Use

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Background: The geometry of long bone shafts is adapted in response to prevailing loads by bone modeling and remodeling at the outer and inner en-

velopes of the cortical bone shaft (periosteal and endosteal surface, respectively). In healthy age-related bone endosteal resorption is compensated by periosteal apposition, with resulting maintenance of bone strength. In recent cross-sectional studies using peripheral quantitative computed tomography (pQCT) we have shown that the metacarpal bone shaft of RA patients has a thinner cortex but a greater outer circumference. In the last years, several case studies linked RA with increased risk of bone shaft fractures at metatarsal, tibial and femoral bone. A recent American Society for Bone and Mineral Research task force report related long bone shaft fractures of the femur to long-term use of bisphosphonates (BP), particularly in patients with rheumatoid arthritis (RA) and those treated with glucocorticoids (GC). The mechanisms causing these fractures are unknown, and the task force stressed the need for studies that elucidate the effect of BP on bone in patients with other morbidities such as RA and on other bone-affecting drugs such as GC. The aim of the present study was to compare longitudinal changes in cross-sectional areas (CSA) of the marrow cavity and total bone at the tibia and metacarpal bone shafts between a group of RA patients under BP therapy, a group of RA patients who are BP naïve, and a group of healthy controls.

Methods: Longitudinal study of consecutive RA patients with BP (RA-BP), and RA patients without bisphosphonate (RA) seen at the Department of Rheumatology of the Inselspital Bern. Additionally, a group of healthy controls was recruited from hospital staff and through locally distributed flyers. PQCT measurements were performed at the third metacarpal bone and the tibia. Scans were placed at 4% of the distal epiphyses, and at 50% of total bone length at the metacarpal bone and 66% at the tibia (measured from the distal bone end). From the epiphyseal scans total and trabecular BMD were calculated, and from the shaft scans total boneCSA(including medullary CSA), cortical CSA (excluding medullary CSA), medullary CSA and cortical wall thickness were determined.Linear regressions were performed between changes in medullary CSA and total bone CSA at the tibia and metacarpal bone shaft for each separate group (RA, RA-BP, Control). Changes in total and trabecular BMD were related to GC cumulative dose and DAS28 (score calculated from swelling and tenderness of joints as well as erythrocyte sedimentation rate)within the RA and RA-BP group.

Results: Our preliminary data on 32-month changes in female RA patients with (9) and without BP therapy (14) and 22 healthy female controls show that in healthy controls and RA patients without BP endosteal resorption at the tibia and metacarpal shaft is fully compensated by periosteal apposition. RA-BP marrow CSA also increased, however, there was hardly any compensation in total bone CSA. Linear regressions between changes in marrow CSA and changes in total CSA were significant for the control group and the RA group without BP ($r^2 \geq 0.6$, $p \leq 0.001$ at the tibia and $r^2 > 0.3$, $p < 0.03$ at the metacarpal bone), but not in the RA group with BP. Slope differences between RA and RA-BP were 0.46 at the tibia and 0.40 at the metacarpal shaft ($p < 0.05$).Interestingly, while at the tibial shaft the size of the compensatory mechanism at the tibia seems to be the same in RA patients without BP and healthy controls, at the metacarpal shaft periosteal apposition seems to overcompensate endosteal resorption in RA patients without BP. No difference in cortical BMD (porosity) between the RA-BP,RA and control group was found. Loss in trabecular and total BMD was also present in some RA-BP subjects.

Conclusion: Preliminary data from longitudinal measurements at the shaft of metacarpal bone and tibia confirm that the endosteal bone loss is fully compensated by periosteal apposition in RA patients without BP. However, our data of RA patients on BP therapy indicate that in some patients, BP fails to stop the endosteal bone loss but may in fact inhibit the compensatory periosteal bone apposition. The resulting bone loss leads to cortical thinning, which reduces bone strength and may predispose to fractures. Further, our preliminary data show that BP fails to stop epiphyseal trabecular bone loss in some RA patients.

Whole Body Vibration Exercise Improves Body Balance And Walking Velocity In Postmenopausal Osteoporotic Women Treated With Alendronate: Galileo And Alendronate Intervention Trail (GAIT)

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Objectives: Recently, whole-body vibration (WBV) exercise has been developed as a new modality in the field of physiotherapy and has been used to improve physical function in the elderly. However, the effect of WBV exercise on physical function in postmenopausal osteoporotic women has rarely been investigated using randomized controlled trials. A randomized controlled trial was conducted to determine the effect of 6 months of WBV exercise on physical function in postmenopausal osteoporotic women treated with alendronate.

Subjects & Methods: Fifty-two ambulatory postmenopausal women with osteoporosis (mean age: 74.2 years, range: 51-91 years) were randomly divided into two groups: an exercise group and a control group. A four-minute WBV exercise was performed two days per week only in the exercise group. No exercise was performed in the control group. All the women were treated with alendronate.

Results: There were no significant differences in baseline characteristics including age, height, body weight, body mass index, number of fallers in the past 3 months, number of subjects with history of clinical fracture, bone turnover markers including serum alkaline phosphatase (ALP) and urinary cross-linked N-terminal telopeptides of type I collagen (NTX), and physical function parameters in terms of the indices for flexibility, body balance, muscle power, and walking velocity. After 6 months of the WBV exercise, the indices for flexibility, body balance, and walking velocity were significantly improved in the exercise group compared with the control group. The exercise was safe and well tolerated. The reductions in serum ALP and urinary NTX during the 6-month period were comparable between the two groups.

Conclusions: The present study showed the benefit and safety of WBV exercise for improving physical function in postmenopausal osteoporotic women treated with alendronate.

Age And Ethnic Differences In Neuromuscular Function

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Objective: Ageing is associated with physiological changes to muscle mass, composition, and function. Poor muscle function is associated with increased risk of falls and fragility fracture. However, little is known about ethnic differences in muscle function with ageing. The aim of this cross-sectional study was to compare neuromuscular performance in an ethnically diverse group of middle aged and elderly men using jumping mechanography.

Subjects & Methods: 303 male participants aged 40-82 (mean 62 SD±11) years were recruited from the Greater Manchester area: 67% (n=203) European Caucasian, 14% (n=43) South-East Asian, and 19% (n=57) Afro-Caribbean. Jumping mechanography (Novotec Medical GmBH) was used to assess relative-muscle force (N/kg), relative-power (W/kg) and velocity (m/s) from a single 2 leg counter-movement jump for maximal height. ANOVA with Scheffé test for post-hoc analysis tested age and anthropometric differences between groups. Linear regression tested age-related differences in all output measurements. Age adjusted ANCOVA with post-hoc Scheffé analysis tested ethnic differences in neuromuscular performance. Results are presented as mean difference [SEM].

Results: Caucasians were 6.6 [1.6] years older than Asians ($p < 0.001$) and 4.9 [1.8] years older than Afro-Caribbeans ($p = 0.02$). There were no significant differences in age between Afro-Caribbeans and Asians or in height between Afro-Caribbeans and Caucasians. Caucasians were 0.04m [0.1] taller than Asians ($p < 0.001$). Body mass (mean 84.4kg SD±12.4) and BMI (mean 28.3 SD±3.7) did not significantly differ between groups. Relative-force ($R^2 = 0.05$, $p = 0.002$), relative-power ($R2 = 0.42$, $p < 0.001$) and velocity ($R^2 = 0.39$, $p < 0.001$) were negatively associated with age.

After correcting for age, Asians produced less relative-force compared to Afro-Carribeans (-9.1%[2.9], $p = 0.007$); relative-power than Caucasians (-14.2%

[3.0], p<0.001) and Afro-Caribbeans (-18.7%[3.9], p<0.001); velocity than Caucasians (-9.6%[2.2],p<0.001) and Afro-Caribbeans (-10.5%[2.9], p=0.002). There were no significant differences in relative-force between Caucasians and Asians or relative-force (-5.7%[2.4], p=0.06), relative-power and velocity between Caucasians and Afro-Caribbeans.

Discussion: Neuromuscular performance was negatively associated with age. Asians generated less relative-force than Afro-Caribbeans, and less relative-power and slower speed of movement compared to Afro-Caribbeans and Caucasians. There were no significant differences in relative-force between Caucasians and Asians or neuromuscular function between Afro-Caribbeans and Caucasians: force approached significance. Whether ethnic differences in muscle function correspond to differences in bone geometry and strength and can be explained by variances in muscle composition, nutrition or hormonal status remains to be determined.

Summary: Our data show age and ethnic related differences in neuromuscular performance. It remains to be determined whether neuromuscular differences relate to ethnic variation in fracture risk.

Falls, Physical Activities And Vitamin D3 Serum Concentration In Women With Primary And Secondary Osteoporosis: A Prospective Study – First BaseLine Results

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Objectives: Since March 2011, a prospective survey has been in progress on the multifactorial influences in the development of osteoporosis in women treated in the osteoporosis outpatient clinic at the Charité. The aim of this survey is the development and implementation of an assessment to be included in the framework for treatment of osteoporosis patients. This will then be used as a supplement to the current DVO guidelines for osteoporosis therapy. This analysis will evaluate the first data from the baseline survey in falls/fallers, physical activity and the vitamin D status in women with primary and secondary osteoporosis.

Subjects & Methods: In total, 150 patients were asked to participate in the baseline interview. Fifteen patients declined to participate and for 33 patients, data entry was not completed at the time of the analysis. Using a sample of 102 patients with primary and secondary osteoporosis, physical activity and falls were evaluated using questionnaires for this interim analysis.

In total, the following data was collected in the survey: sociodemographic status, duration of the disease, risk factors, osteoporosis medications, physical activity, number of falls and fractures, blood parameters (BAP, CTX, calcium, 25-OH-vitamin D3), bone density, QCT and standardised questionnaires to assess psychological factors (personality, depression, state anxiety, trait anxiety), pain assessment (pain medications, pain perception, intensity, chronicity) and information on activities of daily living (ADLs).

Results: The mean age of the patients was 73.6±6.9 years, where mean age of onset of osteoporosis was 63±9.2 years and mean duration of the disease was 10.6±7.7 years. From the 102 patients assessed, in the 12 months prior to the conduction of the baseline survey, 29 (28.4%) patients reported a fall. Overall, there were 43 reported falls, from which 48.8 % were of a locomotive nature, 23.3% were due to a syncopal episode, 11.6% were due to an accident and 16.3% could not be classified. 82.8% of the fallers were physically active and 17.2% reported no physical activity. In the group of physically active patients, the proportion of fallers was 29.3%, whereas in the physically inactive group, the proportion of fallers was 25%. The vitamin D serum levels of all patients were in the lower normal range. On average, the fallers demonstrated a lower but not significant vitamin D serum level as the non-fallers (72.86±28.4 nmol/l vs. 76.18±25.4 nmol/l). All physically inactive patients that reported a fall also reported at least one fracture after menopause. In comparison, 70.8% of the fallers that were physically active reported at least one fracture post menopause. The age of onset and duration of the disease did not differ between fallers and non-fallers.

Conclusions: It should be checked whether the vitamin D supplementation can be optimized. The rate of fallers in this study (about one third) corresponds to the faller's rate published in the literature. The number of patients which are physically active (group A) and sustained at least one fall was slightly higher (4%) in comparison to the number of physically inactive patients (group B) who sustained at least one fall. In group A, however, the rate of patients who experienced at least one fracture after menopause was lower compared to group B (30%).

Summary: A detailed evaluation of the complete baseline data will provide further information and insight into the specific factors associated with risk of falls.

A Study Examining The Effect Of Two-Year Physical Activity History On Current Bone Health Status And Body Composition Using pQCT In Pre-Pubertal South African Children

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Objectives: Although a paucity of data exists on SA children, what has been previously demonstrated is that Black children despite difficult living conditions, including poor nutrition and low physical activity levels, have greater hip BMD, greater bone strength and a decreased hip fracture incidence compared to White children. What is not known is whether a two year history of equal levels of PA could negate the ethnic differences observed between the two groups. In addition these differences have not been observed using the more novel technique of pQCT.

Subjects & Methods: Seventy six pre- to early pubertal children between the ages of 8 and 11 participated in the study. Children were classified as being at either Tanner pubertal stage 1, 2 or 3. Children reported on all their physical activities over the past 2 years in an interviewer administered physical activity questionnaire (PAQ). Children were divided into 3 groups (high, medium and low bone loading) based on the peak bone strain score (PBSS) obtained from the PAQ. All participants underwent a whole body and site specific bone density scan using DXA and pQCT. Comparisons were made between the PBSS and DXA and pQCT measures of bone density, strength and geometry. Serum IGF-1 levels (ng/mL) were also measured and correlated to measures of bone health. BMC was adjusted for height, weight and bone area.

Results: The high bone loading group had significantly greater lumbar vertebrae BMC compared to the medium bone loading group (p=0.007). The high bone loading group also had higher whole body BMC than both the low and medium groups (p=0.001). The high and medium bone loading groups had significantly higher radial strength strain indices compared to the low bone loading group (p=0.004 and p<0.0001 respectively). There was no difference between Black and White children in bone content and density measures in the high bone loading group. There was a significant relationship between IGF-1 concentration and proximal tibial strength strain index (p=0.03).

Discussion: South African children who in the past 2 years, regularly participated in weight-bearing physical activity, had more bone mineral content than those children who had lower peak bone strain scores in the 2 years preceding assessment, irrespective of race.

Summary: This study has examined physical activity levels in conjunction with pQCT scans for the first time in South African children. Our study suggests that the racial differences in bone health previously reported in Black and White South African children may be attenuated with equivalent levels of participation in weight-bearing physical activity.

Patients With Turner Syndrome And Isolated SHOX Deficiency Have Similar Bone Geometry But Different Trabecular Bone Mineral Density At The Radius

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Objectives: Girls with Turner syndrome (TS) have altered bone density and geometry at the radius. The exact etiology of their increased fracture risk remains unknown, but since short stature homeobox gene *(SHOX)* plays a major role in long bone growth, *SHOX* gene haploinsufficiency has been suggested as one of the possible causal factors. Our objective was to compare bone geometry and mineral density between girls with TS and patients with isolated SHOX deficiency in order to test the hypothesis that there is a similarity in skeletal features between these two conditions.

Subjects & Methods: Sixty-seven girls with TS (median age 14.3 yrs, range 6.0-19.4) were examined by peripheral quantitative CT (pQCT) at the non-dominant forearm. Results were expressed as Z-scores using published reference data and then compared to the results of seventeen patients with isolated SHOX deficiency (median age 12.3 yrs, range 6.7-37.2, 12 children and 5 adults). The differences from reference data were tested by one-sample T test and differences between TS and SHOX deficiency were tested by two-sample T test.

Results: There was no difference in anthropometry except BMI (mean Z-scores 0.7±1.0, $p<0.001$ and 1.3±1.0, $p<0.001$, for TS and SHOX deficiency, respectively, group difference $p=0.031$). Trabecular volumetric bone mineral density (vBMD) was decreased in TS (mean Z-score -0.7±1.3, $p<0.001$) but normal in isolated SHOX deficiency (Z-score 0.5±1.5, n.s., group difference $p=0.015$). Cortical vBMD was low in both groups (Z-scores -1.6±1.5, $p<0.001$ and -2.2±2.2, $p<0.001$, respectively) without significant group difference. After adjustment for height both groups had increased total bone cross-sectional area (CSA) at the diaphysis (Z-scores 0.5±1.5, $p<0.01$ and 1.5±1.3, $p<0.001$), but decreased relative cortical bone CSA (-0.3±1.3, $p<0.05$ and -1.5±1.6, $p<0.01$, for TS and SHOX deficiency, respectively). Patients with isolated SHOX deficiency had larger total CSA ($p=0.0152$) but smaller relative cortical CSA ($p=0.0079$) compared to TS.

Discussion and Summary: While the similarities in bone geometry at the diaphysis of the radius support the hypothesis that changes in bone structure in patients with TS are caused by SHOX haploinsufficiency, decreased trabecular vBMD in TS is probably a consequence of hypogonadism due to ovarian failure.

Keywords: Turner Syndrome, SHOX Deficiency, Bone Density, Bone Geometry, pQCT.

Effects Of 13-Week Exercise Program With Whole-Body Vibration On Muscle Hypertrophy, Muscle Strength, And Abdominal Fat Reduction In Untrained Adults

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Objectives: The effects of exercise (EX) combined with whole-body vibration (WBV) on muscle hypertrophy, muscle strength, and abdominal fat reduction are not well understood. We therefore investigated the effects of WBV in healthy, untrained participants after a 13-week EX course via magnetic resonance imaging (MRI) and a maximal isometric lumbar extension torque test.

Subjects & Methods: Thirty-two individuals (aged 22-49 years) were randomly assigned to EX groups with (EX-WBV, n=16) or without WBV (EX, n=16). A synchronous vibration device (Power Plate Next Generation; Power Plate International, Northbrook, IL, USA) was used at a frequency of 35 Hz and amplitude of 2 mm (peak-to-peak). Participants performed long-term slow velocity exercises (concentric, 4 sec; isometric, 2 sec, eccentric, 4 sec; 80 sec/set; two for the lower extremities and six for the trunk muscles) on the vibration platform twice weekly, either with (EX-WBV group) or without WBV (EX group). We progressively increased training intensity by adding external loads throughout the trial. Before and after the EX program, cross sectional area (CSA) of trunk muscle and abdominal fat at L4-5 level were assessed using MRI, and maximal isometric lumbar extension torque was measured.

Results: Increases in the CSA of the m. psoas major and erector spinae muscles were significantly ($P<0.05$) greater in the EX-WBV group (+10.7%; +8.7%) than in the EX group (+3.8%; 0.0%). Similarly, increases from baseline in maximal isometric lumbar extension torque were also significantly greater in the EX-WBV group (+51.5%) than in the EX group (+26.4%). No significant interactions were observed in the CSA of visceral and subcutaneous fat.

Discussion: In our previous study, we noted no significant effects of short-term (30 sec/set) body weight exercise with WBV on muscle strength or bone-free lean body mass were (Osawa, 2011). Similarly, training regimens used in other studies also demonstrated no additional effects of WBV on muscle strength or power, either with light exercise and low volume (5-8 min/session) or high-intensity training for a short duration (approximately 30 sec/set) (de Ruiter, 2003; Kvorning, 2006; Carson, 2010). Our present findings therefore suggest that additional effects of WBV may be dependent on the training regimen, particularly the duration of WBV exposure and the intensity of training.

Summary: The WBV-induced increases in muscle hypertrophy and muscle strength observed in the present study suggest potential benefit in incorporating WBV into slow-velocity EX programs involving long-duration exercise.

Abnormalities In Muscle Density And Muscle Function In Hypophosphatemic Rickets

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Objectives: Animal studies suggest that hypophosphatemic rickets (HPR) is associated with muscle function deficits, but it is unknown whether humans with HPR have a muscle disorder. In this study we therefore assessed calf muscle size and density (an indicator of muscle quality), and lower extremity muscle function in patients with HPR.

Subjects & Methods: 34 individuals with HPR (6 to 60 years; 9 males) and 34 age- and gender-matched controls participated in this matched case-control study. Calf muscle parameters (muscle cross-sectional area and density) were measured by peripheral quantitative computed tomography. Lower extremity muscle function (peak force per body weight and peak power per body mass) was measured by jumping mechanography through five tests with different levels of difficulty: multiple two-legged hopping, multiple one-legged hopping, single two-legged jump, chair-rise test and heel-rise test.

Results: Compared to age- and gender-matched controls, patients with HPR had normal muscle size ($P=0.08$) but lower muscle density ($P=0.03$) and lower peak muscle force and power ($P<0.001$ in each test). Muscle function tests were also lower in the subgroup of patients with straight legs (N=13) than in controls, even though patients with straight legs had higher muscle function test results than patients with severe leg deformities.

Conclusions: The present study suggests that lower extremity muscle weakness is a clinical feature of HPR. Lower muscle quality and limb deformities contribute to this functional deficit.

3D Imaging Methods In ;uantifying Rat Femoral Bone Changes With Prednisolone Administration: µCT, SEM And Confocal LM

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Objectives: 1) To study X-ray microtomography (µCT) in context of information gleaned from two SEM methods and confocal fluorescence LM for

mineralising front labels. 2) To develop new methods for utilising µCT data.

Subjects & Methods: Male Lewis rats (209 +/- 15g) were untreated or dosed with vehicle +/- prednisolone (30 or 100 mg/kg), intravenous calcein on day 20 and tetracycline day 32, termination day 35. Intact limbs were imaged using digital microradiography (26kV, Faxitron). Eight micron voxel µCT of distal femurs was conducted after mid-shaft section, before parasagittal bisection: medial half embedded in PMMA to produce polished blocks, lateral macerated, both imaged using 20 kV backscattered electron SEM. *Post hoc* µCT reconstructions corresponded to SEM. Usual analyses used BoneJ, but we also extracted spherical volumes of condylar trabecular bone to avoid any influence of anisotropy.

Results: Excellent matching between SEM and µCT shows that finer 2 µm to 7 µm trabeculae are routinely lost to µCT visualisation and analysis. SEM can determine surface activity state and show newer bone packets on cancellous surfaces.

We developed methods for mapping cortical position and dimensions from a central longitudinal axis with one degree angular resolution. For both outer and inner maps, the values can be averaged between bones within a group to produce an average bone. The group-averaged images can be subtracted to study average differences between groups. For individual bones or group-averaged images, the inner map can be subtracted from the outer to display the cortical thickness.

Discussion: In rodent bone "histomorphometry" in, much is made of studying apposition in metaphyseal trabeculae, though they do not persist in the mature animal, and cortical midshaft periosteum. Measuring cortical endosteal apposition might make more sense. Long bone diameters taper from the growth plate to the mid-diaphyseal region, achieved by expansion of the growth plate, resorption of periosteal surface, and endosteal formation. Study of calcein and tetracycline labels using intact PMMA supported tissue and confocal offers major advantages. However, whatsoever LM preparation is used, bone has to be cut with the loss of 3D context. We therefore investigated what could be done with µCT data.

Summary: 1) Treat µCT fine-trabecular connectivity data with caution. 2) Mapping the cortex with respect to a central longitudinal axis, rotation defined, and over a standard length of the bone within which maximal cortical tapering occurs is an informative approach to examining differences between animals, and between and within experimental groups.

Jumping Mechanography In Patients With Osteogenesis Imperfecta Type I

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Objectives: Osteogenesis imperfecta (OI) type I is a heritable bone fragility disorder that is caused by mutations affecting collagen type I. Studies using isometric force tests have observed muscle weakness in some patients with OI type I. However, there is little information on dynamic muscle function in OI type I. In this study we therefore aimed at quantifying dynamic muscle function in OI type I patients through jumping mechanography.

Subjects & Methods: 70 individuals with OI type I (Mean age [SD]: 15.4 years [9.4]) and 70 age- and gender-matched controls participated in this study. Lower extremity muscle function (peak force per body weight and peak power per body mass) was measured by jumping mechanography through five tests with different levels of difficulty: multiple two-legged hopping (M2LH), multiple one-legged hopping (M1LH), single two-legged jump (S2LJ), heel-rise test (HRT) and chair-rise test (CRT).

Results: The OI group produced significantly lower force per body weight (M2LH: -17%, p<0.001; M1LH: -13%, p<0.001) and power per body mass (S2LJ: -9%, p<0,001; HRT: -16%, p<0.001; CRT, -8%, p=0.002) than the age- and gender-matched controls. Nonetheless, not all individual with OI type I had low muscle function. Depending on the test, between 16 and 35% of OI patients had higher test results than their healthy counterparts.

Conclusions: These results demonstrate dynamic muscle function deficits in patients with OI type I. However, this deficit is not systematically observed in all OI individuals.

Osteocytes: Morphological Analysis Of Bone Biopsies Of The Jaw From Healthy And Osteoporotic Women Using Synchrotron Radiation Computed Tomography

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Objectives: Reduced number of osteocytes appears to be correlated with bone capacity to gain and maintain bone mass. To analyze osteocyte distribution and quantity a new method was developed.

Materials & Methods: From a group of 20 healthy (HB) and 20 osteoporotic (OB) bone biopsies of the jaw measured using computed tomography (CT, resolution: 20 µm) two biopsies from different groups but same region (R36) were selected for synchrotron radiation CT measurements (BESSY) for this pilot study. The criterion selection was to have differences in the bone volume to tissue volume ratios (BV/TV) between osteoporotic versus healthy >60%. Two stacks were required to measure each biopsy using 2.174 µm (L= 10 mm, Ø= 2.2 mm, approx. 5000 slices 50 GB). After filtering the projections were reconstructed and imported for image analyses in Amira (ZIB). Voxel based density distribution maps were used to differentiate old bone from new bone on the orthoslices. After segmentation osteocytes (lacunae) number and volume were quantified by adapting routines employed for skeletonization. To reduce computational costs, osteocytes morphological analyses were performed at selected volumes of interest located at the center of each biopsy. Additionally, finite element meshes were created for numerical analysis of osteocytes in their natural environment.

Results: BV/TV differences up to 0.346 for the HB and 0.1791 for the OB were found. Osteocytes number was clearly larger in the healthy bone biopsy as expected but interestingly minor in size. At regions near the bone surface (mainly low mineralization zones), osteocytes were aligned at the side directed towards the high mineralization region. These findings were confirmed after SR-CT measurements and analysis of two additional biopsies (R36). In all cases, osteocytes were mainly aligned along the cement lines. Differences of up to 64% in number and 55.3% in volume were determined. Osteocytes appear to be aligned following the principal load direction.

Discussion: SR-CT using at least 2.174 µm allows not only to quantify the number and volume of osteocytes at different aging states but also to visualize their distribution. Its characterization is fundamental to understand bone remodeling activities. The interdisciplinary work between Charité, BAM and ZIB allowed development of this reproducible and reliable method for osteocytes characterization, which can be used to analyze osteocytes morphological changes due to different bone diseases or pharmacological interventions.

Summary: Our findings suggest that with aging osteocytes number is reduced, they increase in size and are spaciously distributed at high mineralization regions compared with young healthy bone biopsies.

Does Subclinical Hiperthyroidism Affect Muscle Mass And Bone Mineral Density In The Postmenopause?

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Subclinical hyperthyroidism, a clinical condition characterized by a suppressed TSH and normal thyroid hormones blood levels, has been associated to BMD reduction/osteoporosis due to the both bone formation and resorption inhibition by the TSH independently of the thyroid hormones effects. Also, it is still unclear if the decrease in the lean mass described in overt hyperthyroidism is already present in subclinical hyperthyroidism, worsening the age related muscle mass decrease.

Objectives: To evaluate the effects of subclinical hyperthyroidism in the total lean body mass and as well as in the bone mineral density (BMD) of elderly women.

Materials & Methods: In a group of 39 postmenopausal women (15.3±11.4 years after menopause) with subclinical hyperthyroidism, the total body lean

mass (kg) as well as the BMD (g/cm²) at the lumbar spine (L_1-L_4), hip, distal radius (1/3 or 33%) and whole body were evaluated by dual X-ray absorptiometry, using the Hologic QDR Discovery W densitometer.

Fast blood collection was also performed to measure the TSH, FT4, FT3 and pituitary hormones levels.

No patient was previously treated for hyperthyroidism, osteoporosis or low bone mass.

The BMI (kg/m²) also was calculated.

Descriptive, Anova and regression analysis statistical tests were used.

Results: The mean age, height, weight, BMI and total lean body mass are described in Table 1.

Table 1. The mean (±SD) antropometric and TSH data, lean body mass and the BMD at several skeletal sites.

Variables	Postmenopausal women with subclinical hyperthyroidism *(n=39)*
Age years	**63.6** (9.8)
Height m	**1.55** (0.06)
BMI kg/m²	**28.9** (4.2)
TSH µUI/mL	**0.09** (0.1)
Total body lean mass kg	**39.1** (4.9)
Total body fat mass kg	**28.2** (6.7)
BMD L_1-L_4 g/cm²	**0.903** (0.1)
BMD hip g/cm²	**0.889** (0.1)
BMD distal radius g/cm²	**0.620** (0.1)
BMD whole body g/cm²	**1.056** (0.1)

Significant correlations were detected between the total lean body mass vs. the BMD at the lumbar spine, vs. the BMD at total hip and vs. the BMD at whole body.

Conclusions: The results of this study suggest that subclinical hyperthyroidism in the postmenopause, a frequently silent clinical condition, may be an additional risk factor to postmenopausal bone mass loss, which in association with the muscle mass changes may aggravate the lean mass of the aging, increasing the risks of falls and subsequently of osteoporotic fractures.

Adaptation Of The Muscle-Bone Unit In The Lower Leg Of Children And Adolescents Consequent To Exercise

E. Anliker

Objectives: To quantify the muscle-bone unit in the lower leg and to assess adaptations thereof following exercise. Based on the Mechanostat theory we hypothesized that maximum voluntary ground reaction force (F_{m1LH}) should predict volumetric bone mineral content (*vBMC*) better than muscle area, and that following long-term exercise, changes in F_{m1LH} and *vBMC* should occur in proportion to each other.

Methods: Multiple one-legged hopping (m1LH) and peripheral quantitative computed tomography (pQCT) were performed to assess F_{m1LH} and tibial bone strength/geometry at 4-, 14-, 38- and 66% of tibia length. (1) We used linear regression with site-specific *vBMCs* as dependent variables to compare F_{m1LH} and muscle area as possible predictors in 323 8-82 years old healthy adults (185 females and 138 males). (2) We performed a 9-month, randomized controlled jumping exercise study to determine ΔF_{m1LH} in relation to the change in bone strength/geometry (in particular $\Delta vBMC14\%$) in 45 8-12 years old boys and girls, and (3), we investigated side-to-side differences between the supporting and non-supporting leg for F_{m1LH} and bone strength/geometry in 66 elite male soccer players (12-18 years old).

Results: (1) The correlations between F_{m1LH} and *vBMC* at any site were stronger than those between muscle cross-sectional area and *vBMC*. The strongest correlation was found between F_{m1LH} and $vBMC_{14\%}$ (R^2=0.840). (2) Children undertaking jumping exercise tended to have greater gains in F_{m1LH} and bone strength/geometry (+1 to +3% points, P>0.05) relative to those who did not. At the distal tibia, the highest adaptations were found for the amount of bone, while in the proximal direction, children predominantly changed bone geometry. Critically, ΔF_{m1LH} was not related to $\Delta vBMC_{14\%}$ in either group. (3) Higher bone strength/geometry values were found for the supporting leg (P<0.05) of adolescent young elite soccer players, while no side-to-side differences were observed for F_{m1LH}.

Conclusion: Unlike proposed by the Mechanostat theory, ΔF_{m1LH} was not related to $\Delta vBMC_{14\%}$, neither after a 9-month jumping intervention period in children, nor when comparing the supporting and non-supporting leg of adolescent soccer players. However, F_{m1LH} and $vBMC_{14\%}$, were tightly linked (R^2≈0.8) at all times, suggesting that a common factor influences these parameters, yet this factor does not tightly couple the adaptive process that occurs during training in children. Nevertheless, the strong and robust relationship between the two parameters generally might be very useful for quantitatively assessing the muscle-bone status in health and disease.

Muscle Mass, Bone Quality And Testosterone Levels In A Group Of Normal Men

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The bone strength is dependent on the bone mineral density (BMD) and the quality. The measurement of BMD by DXA is the gold standard for the precocious diagnosis of osteoporosis. The trabecular bone score (TBS) is determined from gray-level variation analysis of the DXA images and uses the existing DXA images to assess and qualify the bone micro-architecture. In normal men there is a trend of the BMD to decline with aging, but the data about the bone micro-architecture are scarce.

Objectives: To study the TBS and the BMD at the spine and the muscle mass in a group of normal men.

Materials & Methods: In a group of 83 normal men the BMD (g/cm²) at the L_1-L_4, at the hip, at the distal radius (1/3 or 33%) and at the whole body were evaluated by DXA, using the QDR Discovery W densitometer (Hologic, Inc.). The lumbar spine TBS was derived for each spine DXA scan (Med-iMAPS). Fast blood collection was also performed to measure the LH, FSH, prolactin, and sex steroid hormones plasma levels. The BMI (kg/m²) was also calculated. Adequate statistical tests were used.

Results: The mean age, height, weight, BMI and total lean body mass in this normal men group are presented in Table 1.

Table 1. The mean (±SD) age, height, weight, BMI and total lean body masses in a normal men group.

Variables	Normal men (n=83)
Age years	**52,0** (16.8)
Height m	**1,719** (0.07)
Weight kg	**82.4** (14.2)
BMI kg/m²	**27.8** (4.4)
Total body lean mass kg	**59.2** (8.2)

The TBS at the L_1-L_4 was positively correlated with height and total testosterone, but the correlations with the age, the weight and the BMI were negative in these men (P<0.05).

Nevertheless, no correlation was detected between the TBS and the BMD at the spine and the total lean body mass.

Conclusions: The correlation between TBS and BMD at the spine confirms that TBS is measuring other bone properties than BMD. The results of this study may suggest that the quality of bone accessed by TBS is positively related with height, but the age, the weight, the BMI may affect negatively the bone quality in men; however the total lean body mass does not seem to influence the bone quality. Finally, the total testosterone levels are positively associated with the bone quality and the total lean body mass.

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Upper Limb Muscle-Bone Asymmetries In Elite Junior Tennis Players

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Studies in tennis players have shown large side differences in bone strength parameters in favour of the racquet arm, whereas these differences are smaller or not present in non-playing controls[1,2]. The role of internal forces (i.e. those produced by the muscles) on bone development remains a controversial topic, and study of muscle-bone relationships in the arms of elite tennis players would give useful information pertaining to this link.

Forty-one national-level tennis players (26m, 15f - mean age 13.4±1.7 yrs) were recruited. Bone strength parameters were examined in both arms from pQCT scans at 4% (R4) and 60% (R60) distal-proximal radial length and 35% (H35) distal-proximal humeral length. Muscle CSA (MuscA) was also examined at R60 and H35. Peak force and power during a press-up on a force platform and grip strength in both arms was also measured.

Large side differences in total BMCwere found at all sites in favour of the racquet arm - $P<0.001$ for all sites except distal radius ($P<0.01$) and distal ulna ($P<0.05$). These differences were due almost entirely to larger cortical area (Ar.ct) at R60 and H35 sites in racquet arm radius (18.9±8.1%), ulna (15.1±9.0%) and humerus (39.8±13.5%) - all $P<0.001$, with little or no difference in cortical BMD. In contrast, at R4 site differences in radius and ulna BMC (39.6±20.5% and 23.7±34.5%) were made up of both larger total bone area and higher BMD.Smaller side differences in MuscA at R60 and H35 meant that racquet arm muscle-bone ratio was lower in the ulna (3.2±9.0%, $P<0.01$), radius (5.6±9.6%, $P<0.001$) and humerus (20.2±7.5%, $P<0.001$), and side differences in power press-up maximal power, (13.0±11.4%) maximal force (4.9±7.1%) and grip strength (24.2±26.9%) were found (all $P<0.001$).

The results show large side differences in force production, muscle size and bone strength parameters in youth tennis players - attributable to their elite status and high training load. Whilst racquet arm muscle and bone were greater than age-matched reference data, values in the non-racquet arm were no bigger than average suggesting a localised effect of exercise. Examination of muscle:bone ratioshowed strong relationships between the two, but a significantly lower ratio at both mid-shaft sites in the racquet arm.

These results suggest a largeosteogenic potential of tennis, support a strong muscle-bone relationship but suggest other factors aside from muscle size dictate exercise-induced bone adaptation.

References

1. Haapasalo H, Kontulainen S, Sievänen H, Kannus P, Järvinen M, Vuori I. Exercise-induced bone gain is due to enlargement in bone size without a change in volumetric bone density: a peripheral quantitative computed tomography study of the upper arms of male tennis players. Bone 2000; 27:351-357.
2. Daly RM, Saxon L, Turner CH, Robling AG, Bass SL. The relationship between muscle size and bone geometry during growth and in response to exercise. Bone 2004;34:281-7.

Functional Activity And Quality Of Life In Patients With Vertebral Fractures

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The purpose of the study was to examine the functional activity and quality of life in patients with vertebral fractures.

Materials & Methods: We examined 153 women aged 60-89 years old in postmenopausal period (mean age 69.67±0.54 years). Patients were divided into two groups: the first (control group) - without osteoporotic fractures, and the second - with vertebral fractures.

Methods of research - questionnaires (to assess life style, Euro-Qul-5D, Roland-Morris, ECOS-16), functional tests (dynamometry, static balancing, 15-meter test), Thomayer's, Schober's, Ott's tests, orthopedic examination (range of movement assessment in the thoracic/lumbar spine, determination of the chest excursion and breath holding spell), dual- energy X-ray absorptiometry (DXA).

Results: Bone mineral density (BMD) of lumbar spine and femoral neck in patients with vertebral fractures was significantly lower than appropriate data in control group. Indexes of quality of life and daily activity in patients of the second group were considerably lower compared to the control group. It was found significant differences in Schober's test (p=0.04) and parameters of movement of the thoracic and lumbar spine (p=0.04). Others functional tests were without significant difference.

In patients without vertebral fractures it was found the significant positive correlation between BMD of the femoral neck and lumber spine and data of functional tests indexes such as dynamometry, Thomayer's, Schober's tests, maximum and average chest excursion. In contrast, patients with vertebral fractures didn't have significant correlation between BMD data and indexes of functional tests and orthopedic examination data.

In patients with vertebral fractures was determined significant correlation between ECOS-16 indexes and Schober's tests (p=0,006) and breath holding spell (p=0,03) in contrast to patients without vertebral fractures.

Conclusion: Our study found significant correlations between BMD and some functional tests in patients without vertebral fractures. Vertebral fractures leads to reducing of functional ability and decreasing of quality of life.

Vertebral Pain Syndome In Elderly Patients

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Aim of study was determining of peculiarities of vertebral pain syndrome in elderly patients with vertebral pain syndrome depending on sex.

Materials & Methods: 44 women (average age - 63,1±9,1 years, average height - 160,2±6,7 cm, average weight - 75,5±14,4 kg, BMI - 29,4±5,3) and 32 men (average age - 62,7±11,3 years, average height - 172,9±5,4 cm, average weight - 83,2±11,4 kg, BMI 27,8±3,4) were examined. The following methods of study were used: visual analogue scale (VAS), determination of life quality by Roland-Morris questionnaire, EuroQol 5D scale.

Results: The intensity of thoracic vertebral pain syndrome using VAS was not differ in women and men. In lumbar spine intensity of pain syndrome (VAS) was higher in women compared with men (women - 3,5±1,8; men - 2,6±1,5; F=1,422, p=0,03). The life quality, according to the EuroQol 5D scale, in women with was significantly increased in comparison with men (women - 4,5±1,5; men - 3,7±1,7; F=1,308, p=0,04). The daily activity using Roland-Morris questionnaire was not differ between women and men (women - 8,8±5,0; men - 6,6±5,2; F=1,079, p=0,07).

Conclusion: The intensity of vertebral pain syndrome in elderly patients depends on sex. The intensity of thoracic vertebral pain syndrome was not differ; the intensity of lumbar vertebral pain syndrome was significantly higher in elderly women compared with elderly men.

Effect Of Strontium Ranelate On Vertebral Pain Syndrome And Functional Abilities In Postmenopausal Women With Systemic Osteoporosis

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Aim: To evaluate the effect of strontium ranelate in treatment of systemic osteoporosis in postmenopausal women.

Matherials & Methods: There were examined 894 postmenopausal women with systemic osteoporosis (average age 59,97±10,57 years, average height 161,82±7,09 cm, average weight 71,32±13,44 kg). Evaluation of pain syndrome and level of physical activity was carried out with visual analogue scale (VAS). Examination was performed before onset of treatment and after a four, eight and twelve month treatment course. Strontium ranelate (Bivalos, "Servier") was taken in a dose of one 2 g sachet as a suspension in water once

a day and 1 tablet of Calcemin-advance (Calcium - 500 mg, Vit. D - 400 IU) 2 times a day during 12 months.

Results: The patients had the risk factors of osteoporosis: 28 % of patients had osteoporotic fractures in their anamnesis; 17% - hip fractures in mother or father of patients, 12% - smoking, y 8% - alcohol abuse, 27% of patients have taken corticosteroid tablets for more than 3 month. We observed a reliable decrease of vertebral pain syndrome (after treatment - 2.97±0.77, after four months - 2.24±0.85, after eight months - 1.61±0.94; after twelve months - 1.24±1.04; p<0.00001) and increase of functional abilities of patients (after treatment - 1.50±0.67, after four months - 2.08±0.52, after eight months - 2.67±0.53; after twelve months - 2.88±0.63; p<0.00001).

Conclusion: It has been demonstrated that strontium ranelate treatment significantly decreases pronounced vertebral pain syndrome and improves functional abilities of patients in the postmenopausal women.

Trabecular Bone Score In Normal Ukrainian Women Of Different Age

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The aim of this study is evaluating Trabecular Bone Score (TBS) in normal women of different age.

Materials & Methods: We' ve examined 176 normal women aged 40-79 years (mean age - 53,4±0,6 yrs; mean height - 163,5±0,5 cm; mean weight - 80,4±1,1 kg). The patients were divided into the following age-dependent groups: 40-49 yrs (n=53), 50-59 yrs (n=89), 60-69 yrs (n=17), 70-79 yrs (n=17). TBS (L1-L4), total body, lumbar spine, femoral neck bone mineral density (BMD), lean and fat masses were measured by DXA using a densitometer Prodigy, GE.

Results: We have determined the significant decrease of TBS (L1-L4) in women with age (40-49 yrs - 1,334±0,016 mm^{-1}; 50-59 yrs - 1,289±0,013 mm^{-1}; 60-69 yrs - 1,194±0,034 mm^{-1}; 70-79 yrs - 1,205±0,050 mm^{-1}; F=6,56; p=0,0003). BMD of spine is significantly increase with age (BMD of spine: 40-49 yrs - 1,126±0,015 g/cm^2; 50-59 yrs - 1,234±0,013 g/cm^2; 60-69 yrs - 1,343±0,053 g/cm^2; 70-79 yrs - 1,348±0,100 g/cm^2; F=4,04; p=0,008). BMD of femoral neck didn't show significant differences. The significant correlation was observed between TBS (L1-L4) and age, fat and lean masses:

- TBS = 1,64-0,007*Age; r=-0,34; t=4,41; p=0,00002.
- TBS = 1,47-0,000005*Total fat (g); r=-0,37; t=4,86; p=0,000003.
- TBS = 1,90-0,00001*Lean mass (g); r=-0,59; t=8,98; p<0,000.

We did not find significant correlation between TBS and BMD of spine and femoral neck:

- TBS = 1,36-0,05*BMD of spine; r=-0,05; t=0,66; p=0,5.
- TBS = 1,53-0,22*BMD of femoral neck; r=-0,16; t=1,94; p=0,05.

Conclusion: The significant correlation between TBS and lean mass indicates that bone quality can be associated with muscular system. TBS was significantly decreased with age. TBS is independent parameter which has potential diagnostic value without bone mineral density.

Quantitative Ultrasound Denditometry And Frax® In Evaluation Of Structural-Functional State Of Bone In Postmenopausal Women

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The aim of the study was to estimate the informative value of quantitative ultrasound and its combination with FRAX® in evaluation of structural-functional state of bone in Ukrainaian postmenopausal women.

Material & Methods: 363 postmenopausal women aged 45-87 years were examined, average age 65,1±0.5 years, duration of postmenopausal period 16,5±0.5 years. Bone mineral density (BMD) was measured by Dual-energy X-ray absorptiometer (DXA) "Prodigy" and calcaneus quantitative ultrasound (QUS) "Sahara". The ten years probability of major osteoporotic fracture calculated with FRAX® tool.

Results: There is difference in distribution of bone indexes in depending of used methods. Among women which had osteoporosis of femoral neck by DXA, 34% had osteoporosis, 57% - osteopenia, 9% - norma data by QUS. Sensitivity of QUS indexes ranging was from low to moderate, but specificity was low (with femoral neck - 38% and 39%, total hip - 63% and 34%, lumbar spine - 45% and 34%, total body - 56% and 34% accordingly). Such sensitivity and specificity increased when combining QUS with the ten years probability of major osteoporotic fracture without BMD (FRAX®) (with femoral neck - 71% and 87%, total hip - 90% and 100%, lumbar spine - 72% and 83%, total body - 79% and 91% accordingly).

Conclusions: QUS of is informative method in evaluation of structural-functional state of bone in postmenopausal women. Sensitivity and specificity increased when combining QUS with FRAX® from 38% and 34% up to 90% and 100% accordingly.

Vitamin D Deficiency And Bone Mineral Density

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Objective(s): To study determine the frequency of vitamin D deficiency and insufficiency and it influence to bone mineral density (BMD) in patients of different region of Ukraine.

Material & Methods: It was examined 1575 people aged 20-95 yrs. old who lived in different regions of Ukraine. 25-OH vitamin D and PTH level was evaluated by electrochemiluminescence method (Elecsys 2010, Roche). Vitamin D deficiency was diagnosed in level of 25-OH vitamin D below 49.5 nmol/l, vitamin D insufficiency - between 74.5 and 50.0 nmol/l. BMD was determined by ultrasound densitometry Sahara (Hologic) and DXA (Lunar).

Results: Vitamin D deficiency was registered in 81.8% persons, 13.6% examined had vitamin D insufficiency. It was determined negative significant correlation between PTH and 25OHD (r= -0.16, p<0.0000001). Secondary hyperparathyroidism was diagnosed in 11.9 % patients. The mean level of 25OHD was significantly higher in southern resident of the country (p<0.001) and during summer (p<0.05). No significant correlation between 25OHD and BMD was found. But, only patients with vitamin D deficiency had significant negative correlations between PTH level and BMD at the level of femur neck (r=-0.12, p<0.004), dual femur (r=-0.09, p<0.004), upper and lower extremities (r=-0.11, p<0.01 and r=-0.10, p<0.01 accordingly), forearm 33% (r= -0.20, p<0.001).

Conclusion(s): In Ukrainian population the frequency of vitamin D deficiency is 81.8%. Only patients with vitamin D deficiency have significant negative correlations between PTH level and BMD at the level of femur neck, dual femur, forearm 33%, upper and lower extremities.

The Effect Of Whole-Body Vibration (Wbv) And Igf-I On Clostridium Botulinum Toxin Typ A (Bta) Induced Bone Degradation

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Objectives: Muscle force is essential for bone development and homeostasis [Schönau, 2005]. This relationship was demonstrated in previous studies in which Botox-induced muscle paralysis resulted in bone degradation [Bouvard et al., 2011; Grimston et al., 2007; Warner, 2006]. Vibration exercise, however has an anabolic effect on bone [Rubin et al., 2004] and IGF-1 is essential for bone growth and formation [Baker, 1993]. The purpose of the present study was to analyze if WBV and IGF-1 could compensate bone degradation induced by muscle paralysis.

Subjects & Methods: Fifty female C57BL/6 mice (16 weeks of the age at the start of the study) were randomized into five groups (n=10 each): saline (CON), BTA (IM), BTA+WBV (IM+WBV), BTA+IGF-I (IM+IGF-1) and BTA+WBV+IGF-I (IM+WBV+IGF-I).

All mice received BTA (1.0 unit/0.1 ml) or saline (CON group, equal volume) in both, quadriceps and calf of the right leg. IGF-1 was applicated as daily injections (sc) in the neckfold (human IGF-I, 1.0 µg/day). WBV was performed for 30 min/day at 5 days/week (25 Hz, 2.1 g, 0.83 mm, NOVOTEC Medical). Mice were sacrificed after 28 days and both hindlimbs were analyzed by peripheral quantitative computer tomography (pQCT).

Results:

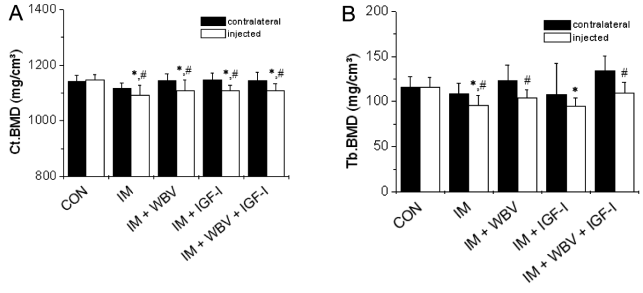

Figure 1. (A) Cortical bone mineral density (Ct.BMD) and **(B)** trabecular bone mineral density (Tb.BMD). Values presented as means ± SD, *different to CON ($p<0.05$), #different to contralateral side ($p<0.05$).

Muscle paralysis by BTA resulted in decreases of trabecular and cortical bone mineral density in the IM group. The IM+WBV and IM+WBV+IGF-I groups showed no difference in trabecular bone mineral density compared to the CON group.

Discussion: IM+WBV and IM+WBV+ IGF-I could compensate trabecular but not cortical bone loss. The results also provide further evidence that skeletal unloading induces resistance to IGF-I [Sakata, 2004].

Summary: WBV can compensate bone loss induced by muscle paralysis.

References

1. Schönau. J Musculoskelet Neuronal Interact 2005;5:232-238.
2. Bouvard et al. Bone 2012;50:858-860.
3. Grimston et al. Ann NY Aca Sci 2007;1116:444-460.
4. Warner et al. Bone 2006;38:257-264.
5. Rubin et al. Nature 2001;412:603-604.
6. Baker et al. Cell 1993;75:73-82.
7. Sakata et al. J Bone Miner Res 2004;19:436-4446.

Calf Musculature Atrophy During 60-Days Bed Rest And The Effect Of Two Different Countermeasure Exercises

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Objectives: Data from several studies have demonstrated that the gastrocnemius and soleus muscles are particularly susceptible to atrophy during prolonged bed-rest. However, limited information is available on the response of other calf muscles to bed-rest. Furthermore, our understanding of countermeasure exercise prescription against atrophy in these muscles needs to be improved.

Methods: 24 male subjects underwent 60-days of 6° head-down tilt bed-rest and performed high-load resistive vibration exercise (RVE; n=7), high-load resistive exercise alone (RE; n=8) or no exercise (CTR; n=9) as part of the 2nd Berlin BedRest Study (BBR2-2). Countermeasure exercises included double leg squats, double and single leg calf raises and back-lift exercise manoeuvres, performed 3-days a week, with 5 to 6 minutes of actual loading time each session. Muscle volumes of the calf musculature were measured using axial magnetic resonance images collected prior to bed-rest, mid-bed-rest (day-27/28), end-bed-rest (day-55/56), and 14-, 90 and 180-days after bed-rest.

Results: Both countermeasures had a significant (p all≤0.002) impact on reducing atrophy in the soleus (end bed-rest mean[SD] percentage change: CTR: -23.2[6.3]%, RE: -12.8[3.5]%, RVE: -14.8[5.1]%), medial gastrocnemius (CTR: -24.5[6.6]%, RE: -9.3[3.7]%, RVE: -8.4[4.5]%), lateral gastrocnemius (CTR: -20.4[8.4]%, RE: -4.5[5.7]%, RVE: 0.8[5.8]%), flexor digitorum longus, flexor hallucis longus, peroneal and tibialis posterior muscles. Reductions in tibialis anterior volume (~11%) and extensor digitorum longus volume (<6%) were seen in all groups. There were no significant differences between the RVE and RE groups for any of the muscles considered (p≥0.15).

In the CTR group only, significant volume loss persisted in the flexor hallucis longus and extensor digitorum longus muscles 90-days after bed-rest. In all remaining muscles, muscle volume recovery appeared complete by 90 days post bed-rest.

Discussion: A short duration (5-6 minutes) high-load resistive exercise countermeasure, with or without whole body vibration, performed 3-days a week was able to reduce, but not entirely prevent, muscle atrophy in the calf region during 60-days bed-rest. The results exemplify the importance of muscle specific high-load exercises: the tibialis anterior muscles were not targeted with resistive exercises and hence similar amounts of atrophy were seen in all subject-groups. Recovery of calf muscle volume requires greater than 2-weeks after 60-days bed-rest.

Reference

1. Belavý et al. J Musculoskelet Neuronal Interact 2010;10:207-219.

Traditional Versus Non-Traditional Measures Of Isometric Exercise Intensity: Relative Importance For Subsequent Cardiovascular Adaptation

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Objectives: To investigate the relative importance of both traditional markers of exercise intensity and less frequently used indicators of neuromuscular fatigue, for reductions in resting blood pressure following a period of isometric exercise training.

Subjects & Methods: Thirteen male participants performed a bilateral-leg maximum voluntary contraction (MVC) during which peak surface electromyographic activity (EMG_{peak}) was identifiedover the muscle site. They then performed a discontinuous incremental isometric exercise test to volitional exhaustion, before a 4-week crossover training study. The incremental test comprised 2 minute stages and commenced at 10% EMG_{peak}, increasing by 5%EMG_{peak} at each stage. At exhaustion, the mean torque for the final 2-minute stage (2 min-$torque_{peak}$) and heart rate peak (HR_{peak}) were identified. Training involved 3 sessions per week (4 x 2 min bilateral-leg isometric exercise) at 95%HR_{peak}. Heart rate (HR_{train}) and changes in EMG amplitude (ΔEMG_{amp}) and frequency (ΔEMG_{freq}) were monitored from the first to second minute of each 2-minute training exercise bout. As markers of training intensity the mean training torque was expressed relative to the 2min-$torque_{peak}$ (%2min-$torque_{peak}$) and to initial maximal voluntary contraction (%MVC).

Results: Training resulted in reductions in all blood pressure measures (-4.9±5.8; -2.8±3.2; -2.7±2.4 mmHg for SBP, DBP and MAP respectively). Systolic and MAP reductions correlated ($p<0.05$) with %2min-$torque_{peak}$, ΔEMG_{amp} and ΔEMG_{freq}, but did not relate to the traditionally used %MVC or HR_{train}. Regression analysis predictsa likely adaptation of 5 mmHg reduction in SBP in 4 weeks if overall training is performed at 105% initial 2min-$torque_{peak}$.

Discussion: The stimulus for the reduction in resting blood pressure seems to be more closely related to the action of sustaining torque, rather than the magnitude of torque relative to maximum voluntary contraction. These findings make it possible to set training intensity in such a way as to increase the likelihood of a significant reduction in resting blood pressure following isometric exercise training. The relationships between reductions in resting blood pressure and ΔEMG_{amp} and ΔEMG_{freq} suggests that it is important to induce neuromuscular fatigue during training, when reductions in resting blood pressure are required.

Summary: Sustaining torque might be a more important stimulus in the mechanism whereby resting blood pressure is reduced than previously thought. Markers that reflect the extent to which local muscle fatigue was inducedappear to have been of utmost importance in the reductions in resting blood pressure observed after isometric exercise training.

The Effects Of Idiopathic Hypercalciuria On Bone Mineral Mass And Bone Geometry In Post-Menopausal Women: A Tibia pQCT Study

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Aim: We assessed the effects of Idiopathic Hypercalciuria (IH) on bone mineral mass and bone geometry in different age groups using pQCT of the tibia.

Material & Methods: We reviewed medical records of 41 postmenopausal women with IH who presented as outpatients in our department. Inclusion criteria: 1) Recently (<6 months) diagnosed and untreated IH 2) postmenopausal status >2y 3) Normal renal function (normal serum Creatinine, eGFR) Exclusion criteria: 1) Diseases causing hypercalciuria other than IH (granulomatous and endocrine diseases, malignancies), 2) Bone metabolic disorders, 3) Drug-induced hypercalciouria, 4) use of any medication for osteoporosis during the last 12 months. The patients were assigned in 3 different age groups: 48-59y (N=15), 60-69y (N=21), 70-79y (N=5). All patients underwent pQCT of the tibia (XCT 2000 scanner, Stratec Medicintechnic, Germany) and 3 slices were obtained at the 4% (trabecular bone), 14% (subcortical and cortical) and 38% (cortical) of tibia length sites. For each site we estimated bone mineral content, bone areas, cortical thickness, periostal and endosteal circumference and we compared results with our published tibia pQCT database of 219 age-matched healthy postmenopausal women. We performed statistical analysis and data is expressed as mean±standard deviation (S.D.).

Results: There were no statistical differences between patients with IH and healthy subjects in all age-groups concerning variables of trabecular bone. Concerning cortical bone (38% slice) we found statistical differences only in the younger (48-59y) age group between patients with IH vs age-matched controls: patients with IH had lower cortical bone mineral mass (256.54±39.95 vs 282.63±38.63 mg/cm, p=0.019), cortical area (220.4±33.34 mm^2 vs 246.85±32.85, p=0.005) and cortical thickness (3.90±0.81 vs 4.53±0.57 mm, p=0.0005), while they had greater endosteal circumference (45.27±8.11 vs 40.34±4.51 mm, p=0.001).

Conclusions: Early (48-59y) postmenopausal women with IH have lower values of cortical bone mass, cortical area, cortical thickness and greater endosteal circumference vs age-matched controls. Older women with IH were not found to have statistical differences on bone measurements vs age-matched controls using pQCT of the tibia.

Countermeasures Of Muscle Wasting: Does Bone Reap Some Benefits?

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Statement of the Problem: It is now widely accepted that bones adapt to mechanical stimuli, and ample evidence suggests that the largest forces imposed upon bone are generated by skeletal muscle. The moderate to strong correlation between bone strength and surrogate measures of muscle strength suggests muscular force generation to be a key determinant for bone geometry and structure. However, there is still controversy as to whether muscle strength training is a viable means to safeguard bone, in particular in relation to age-related bone losses.

Available Evidence: Two strands of evidence are reviewed here. Firstly, data from studies with experimental bed rest are considered as one source of information. Bed rest is regarded as a ground-based model of spaceflight, in which muscle atrophy and bone loss are typically occurring along with deconditioning effects in other physiological systems. The available data suggest that resistive exercise can prevent bone loss when it is also maintaining muscle strength[1,2], but not when the regimen is in-effective for muscle[3].

The second line of evidence arises from studies into training effects upon bone. Cross-sectional studies suggest that sprint runners have greater tibial bone strength than medium and long distance runners and race walkers (in that order). However, these athletics-specific benefits seem to get lost with increasing age[4]. Moreover, side-to-side differences in the tibial bone strength of jumpers are surprisingly small, and longitudinal studies suggest that training interventions can increase bone strength by but very small amounts in the legs. Turning to the upper extremity, throwers fail to depict side-to-side differences in the forearm, but do have increased bone strength in the humerus on the throwing side.

Conclusion: Muscle strength training seems to be a very viable way - if not even a prerequisite - to prevent immobilization-induced bone losses in the legs. However, muscle strength training does not seem to affect the leg bones in ambulatory people. Taken together, this suggests that there is an effective upper limit for bone strength, and the jury is hung to explain the mechanism behind this limit[5]. In the arms, the available evidence suggests that muscle strength is an important factor, but that sport-specific mechanics may be even more relevant to bone.

References

1. Shackelford LC, LeBlanc AD, Driscoll TB, Evans HJ, Rianon NJ, Smith SM, Spector E, Feeback DL, Lai D. Resistance exercise as a countermeasure to disuse-induced bone loss. J Appl Physiol 2004;97(1):119-29.
2. Rittweger J, Beller G, Armbrecht G, Mulder E, Buehring B, Gast U, Dimeo F, Schubert H, de Haan A, Stegeman DF, Schiessl H, Felsenberg D. Prevention of bone loss during 56 days of strict bed rest by side-alternating resistive vibration exercise. Bone 2010;PMID: 19732856(46):137-47.
3. Rittweger J, Frost HM, Schiessl H, Ohshima H, Alkner B, Tesch P, Felsenberg D. Muscle atrophy and bone loss after 90 days of bed rest and the effects of flywheel resistive exercise and pamidronate: results from the LTBR study. Bone 2005;36(6):1019-29.
4. Wilks DC, Winwood K, Gilliver SF, Kwiet A, Chatfield M, Michaelis I, Sun LW, Ferretti JL, Sargeant AJ, Felsenberg D, Rittweger J. Bone mass and geometry of the tibia and the radius of master sprinters, middle and long distance runners, race-walkers and sedentary control participants: a pQCT study. Bone 2009;45(1):917.
5. Rittweger J, Reeves ND, Narici MV, Belavy DL, Maganaris CN, Maffulli N. Persisting side-to-side differences in bone mineral content, but not in muscle strength and tendon stiffness after anterior cruciate ligament reconstruction. Clin Physiol Funct Imaging 2011;31(1):73-9.

Muscle X-ray Attenuation During 90 Days Of Bed Rest With -6° Head-Down Tilt

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Introduction: Literature suggests that muscle x-ray attenuation (MXA) in Hounsfield units (HU) is decreased in dystrophy, ageing and reportedly in immobilization. It is commonly thought that the MXA-decrease in dystrophy in ageing and in dystrophy reflects the accumulation of intra-muscular fat. However, a study on the ultrastructure of the deltoid muscle indicated that the intramuscular lipid content is decreased as a result of bed rest, and one would expect an increase, rather than a decrease in MXA. The aim of the present study therefore was to assess the time-course of any MXA changes during 90 days of bed rest with -6° head down tilt.

Subjects & Methods: Data from the Long Term Bed Rest (LTBR) study, which was carried out in Toulouse in 2001 and 2002 were analyzed in retrospective. In that study, twenty-five healthy men performed BR for 90 days, eight of which performed flywheel exercise 2-3 times per week. Muscle cross sectional area (CSA) and MXA were assessed at the calf at 66% of the tibia's length by peripheral quantitative computed tomography with an XCT 2000 (Stratec, Pforzheim, Germany). Regions of interest (ROI) was placed just inside the calf muscle, just outside the tibia, and just outside the fibula. All segmentation thresholds were set to 0 mg/cm^3.

Results: Calf muscle CSA decreased during 89-day bed rest by 26.6 (SD 3.8) % in the control group. In the same group, MXA increased by 1.2 HU on day 28 of bed rest, but tended to approach baseline values on day 89. In the flywheel group, changes paralleled those in the control group, but were miti-

gated (P<0.001). In both groups, all changes were reversed within 90 days after reambulation.

Discussion: The obtained results indicate that MXA is not decreased as a result of bed rest in young healthy men. However, it is currently unclear what effects have caused the small but consistent increase during bed rest. As possible mechanisms, we suggest an increase in intramuscular blood content, interstitial fluid space shrinkage, or a reduction of intramuscular lipid stores.

What Do Bisphosphonate-Associated Osteonecrosis Of The Jaw And "Phossy Jaw" Have In Common?

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Objectives: Since 2003 bisphosphonate medication has been related to several cases of osteonecrosis of the jaws (ONJ). Some authors have pointed out parallels between ONJ and "phossy jaw" or phosphorus necrosis, a disease which was observed in the 19th century among workers in the matchmaking industry who were in regular contact with white phosphorus. The purpose of this work is to explore what the historical and the current disease have in common.

Subject & Methods: The Centre of Muscle and Bone Research at Charité University Medicine in Berlin collects data about bisphosphonate-associated cases of osteonecrosis of the jaw in Germany. By now 1195 cases have been reported, 163 of them are cases of patients having been treated at the Charité. A review of these bisphosphonate-associated ONJ cases in Germany and the existing medical history literature about "phossy jaw" will help to show the characteristics and similarities of both diseases.

Results: "Phossy jaw" was described as an inflammation of the periost of the jaw induced by direct contact with phosphorus vapours. The authors put emphasis on the fact that there had to be a trigger for the development of "phossy jaw", such as a carious tooth. The symptoms and clinical picture of "phossy jaw" and bisphosphonate-associated ONJ are similar, including toothache, swelling of the gum, tooth loosening, purulence, exposed bone etc. ONJ also seems to need a trigger. For example of the 626 reports which mentioned the dental record of the patient, only 11 were not related to factors such as parodontitis, tooth extraction and implants, osteotomies or prostheses. Another fact that "phossy jaw" and bisphosphonate-associated ONJ have in common is that there is very little known about their aetiology.

Discussion: "Phossy jaw" and bisphosphonate-associated ONJ seem to be the same disease, but although we do not know much about their aetiology, this seems to be the crucial point where they differ. "Phossy jaw" is merely the result of a toxic effect on the mucosa and the periost, whereas according to a current hypothesis ONJ is basically caused by the combination of an altered bone metabolism, immune modulation and an intervention/inflammation near the affected location of the jaw.

Conclusions: A literature review and comparison of cases of ONJ and "phossy jaw" lead to the conclusion that both diseases seem to be strikingly similar when it comes to the description of the symptoms and the clinical process, but there is little knowledge about their aetiology.

The Role of Muscles Contraction In Human Tibia Deformations During Different Locomotive Activities: An *In Vivo* Study

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Objectives: Evidence suggests that bone deformation plays a decisive role in bone adaptation to the environment. However, currently, the mechanisms are not completely clear yet. First, to date, assessing *in vivo* bone deformation is still a big challenge due to the technical difficulties. Traditional strain gauge methods are of limited value because of inherent limitations. Second, it is commonly thought that both ground reaction force and muscular contractions contribute to the loading of bone in human lower limb. Nevertheless, among these two forces, it is still controversial which one predominates, even if biomechanical analyses suggest that muscular contraction normally causes larger forces. Based on the above considerations, the main hypotheses of this study would be that there is a considerable amount of global bending and torsion deformation in human tibia during the locomotive activities. Second, we anticipate the tibia deformations are strongly correlated with the activities of the lower limb muscles.

Subjects & Methods: The experiments were performed at the Department of Orthopedic and Trauma Surgery of the University Hospital of Cologne. One subject will have participated in this study.

Novel optical approach for tibia deformation recording has been established and adopted in this study. Briefly, three marker clusters with three non-collinear retro-reflective markers (diameter Ø5 mm) on the cluster were affixed into the anterior-medial aspect of tibia by bone screws (Cannulated screws, Ø3 mm, Stryker Leibinger GmbH & Co. KG, Germany). The sites for installing bone screws with marker clusters were approximately 10 cm below the tibia plateau, mid-site of the tibia diaphysis and approximately 7 cm above the tibia medial malleolus, respectively. These three bone screws were inserted and penetrated into tibia approximately 4 mm to keep the screws in the cortical tibia. With the Vicon MX motion capture system (eight Vicon F40 cameras, Vicon Motion System Ltd., LA, USA), the trajectories of retro-reflective markers affixed on tibia were captured at 300 Hz during different locomotive activities. The best configuration of the optical system has been adopted in this study to fulfill the requirement of accuracy and precision for bone deformation recording. Tibia deformations (axial deformation, bending and torsion) were calculated based on the relative movement between the markers. Simultaneously, the activities of the lower limb muscles were evaluated with superficial electromyography during the locomotive activities.

Results: As soon as the data from this study is available, the results will be reported during the conference.

In Vitro Evaluation Of Commercially Available Scaffolds For Use In Musculoskeletal Regenerative Medicine

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Objectives: To seek biocompatible scaffolds for use in skeletal regeneration. Injuries to bone and tendons can cause major morbidity in healthy, active people. Providing a scaffold that encourages appropriate cell attachment, growth, and ultimately tissue regeneration, could improve the clinical outcomes from injuries such as rotator cuff tears and non-union fractures. Scaffold materials of both natural and synthetic origin have been tested in this study to evaluate their potential utility in musculoskeletal regenerative medicine.

Methods: Two scaffolds were evaluated as biomaterials: Spidrex® 543 (Oxford Biomaterials Ltd, UK), a spider-like silk fabric; and Endoform™ (Mesynthes, NZ), a decellularised ovine forestomach matrix then compared to three-dimensional (3D) collagen gels as a control and FiberWire® (Athrex. Inc, US) a polyethylene and polyester composite suture, which is currently utilised in orthopaedic surgery.

Primary human dendrocytic cells were exposed to scaffolds, with cell-surface activation markers analysed using FACS to determine scaffold immunogenicity. Attachment and growth of primary osteoblasts and tenocytes were analysed using live-dead staining and alamar Blue fluorescence. Phenotypic retention was assessed through morphological studies, while realtime PCR was employed to evaluate cell differentiation.

Results: FACS analysis determined that Spidrex® 543, invoked a high immune response in the primary human dendrocytes, while Endoform™ and the 3D collagen gels provided relatively low immunogenicity. FiberWire®, the synthetic suture material currently used in orthopaedic surgery produced relatively high immune activation within these cells.

Osteoblasts and tenocytes both successfully adhered to and grew on the Endoform™ , Spidrex® 543 and within the 3D collagen gels, whereas the orthopaedic suture material proved unsuitable for cell attachment/growth (Figure 1). Gene analysis and morphology in the three permissible scaffolds suggest cells retain their phenotype when cultured in them.

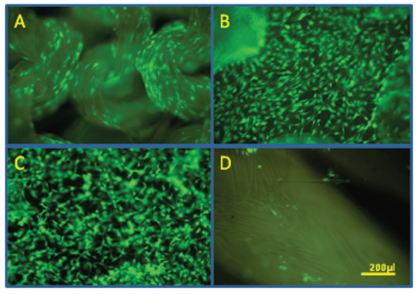

Figure 1. Calcien staining of tenocytes growing on **A:** Spidrex®, **B:** Endoform™ , **C:** within 3D collagen gels and **D:** on FiberWire®.

Discussion: 3D culture systems support and amplify proliferation and differentiation. Notably, the effect of key osteoblast-stimulating factors Lactoferrin, TGFβ and PDGF were significantly enhanced in osteoblasts within 3D gels (P≤0.05) compared to osteoblasts in 2D, while gene expression of key osteoblastic markers Alkaline Phosphatase, Osteocalcin and Bone Sialoprotein were increased 7-, 350- and 22-fold, respectively, in osteoblasts cultured within 3D collagen gels (P≤0.05).

Summary: We have developed an *in vitro* evaluation package to identify the biocompatibility of biomaterial scaffolds; whether the materials support and promote target cell growth and have potential for use in bone and tendon regeneration. Much time and expense can be saved by such *in vitro* evaluation of biomaterials prior to embarking on *in vivo* studies.

Short Duration Resistive Exercise Sustains Neuromuscular Function After Bed Rest

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Purpose: To assess the effectiveness of a short duration, three times weekly, high-load resistive exercise program on preventing deterioration in neuromuscular function after prolonged bed rest.

Methods: Twenty-four male subjects performed high-load resistive exercise (RE; n=8), high-load resistive exercise with whole-body vibration (RVE; n=9) or no exercise (control, n=9) during 60-day head-down tilt bed rest as part of the 2nd Berlin Bed Rest Study (BBR2-2). Peak countermovement jump power and height, sit-to-stand performance, sprint time over 15 m and 30 m and leg-press one repetition maximum were measured before and after bed rest.

Results: The exercise interventions as compared to controls without exercise were capable of ameliorating losses of peak countermovement jump power (p<0.001) and height (p<0.001), deterioration of sit-to-stand time from 45 cm (p=0.034) and 30 cm (p<0.001) sitting positions, increases of 15 m (p=0.037) and 30 m (p=0.005) sprint time and losses of one-repetition maximum leg-press (p<0.001).

Conclusion: The short duration (6 minutes time under tension per training session) exercise countermeasure program performed three times a week was capable of reducing the impact of prolonged bed rest on a number of neuromuscular function measures.

Effects Of Low Dose Calcium And Vitamin D Supplementation On Bone Density And Structure Measured *In Vivo* By µCT At The Distal Tibia In Postmenopausal Women With Low Bone Mass

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Objectives: To examine *in vivo* the effect of low dose supplementation of calcium 500 mg and vitamin D 400 IU daily on bone density and structure at distal tibia in postmenopausal women with osteopenia or mild osteoporosis.

Patients & Methods: 68 postmenopausal women with low bone mass and without prevalent vertebral fractures were equally randomized into a mono-centric, placebo-controlled, double-blind study of one year (SPIMOS-3D). All patients in the verum (oral ibandronate 150 mg once monthly) and placebo group received calcium 500 mg and vitamin D3 400 IU daily. Bone density and structure were measured *in vivo* by µCT (Xtreme-CT, Scanco Medicals) at the distal tibia (DT). These are the results of a post-hoc analysis of the placebo group (CaD; n=33; mean age 68.6±3.2 years; mean T-score of DXA-BMD at lumbar spine and total hip -2.47±0.47 and -0.86±0.75 SD, respectively) showing the effects of calcium and vitamin D alone on the above mentioned parameters.

Results: µCT values at baseline and after one year of treatment were available for 29 patients in the CaD group. Over the one year treatment period, there was a significant increase of BV/TV by 1.21% (p=0.002) and a reduction of Tb.Sp by 6.94% (p<0.001) in these patients. In addition, there was also a significant change in other parameters possibly relevant for bone strength at the distal tibia (Table).

Parameters of bone density and structure	Baseline (mean values)	12 months (mean values)	Changes (%)	*p* values
BVTV	0.115	0.117	1.21	**0.002**
TbSp (mm)	0.598	0.557	-6.94	**<0.001**
CortArea (mm²)	80.328	82.821	3.10	**<0.001**
TrabArea (mm²)	594.986	593.231	-0.30	**<0.001**
Dcomp (mgHA/cm³)	773.200	770.224	-0.39	0.220
Dtrab (mgHA/cm³)	138.255	140.055	1.30	**0.001**
CtTh (mm)	0.782	0.807	3.13	**<0.001**
CtPm (mm)	103.783	103.641	-0.14	0.104
TbN (1/mm)	1.518	1.635	7.73	**<0.001**
TbTh (mm)	0.076	0.071	-5.80	**<0.001**

There were no statistically significant differences in µCT parameters between the CaD group and the verum group receiving oral ibandronate in addition.

In the CaD group serum bone turnover markers as CTx and P1NP showed also significant changes in accordance to those of the µCT parameters. CTx decreased by 16.78% (p=0.006), P1NP increased by 8.68% (p=0.048). On the other hand, and as expected, no significant changes could be detected in DXA BMD measurements at lumbar spine and total hip (+0.16% and +0.24%; p=0.755 and 0.569, respectively).

Conclusions: After one year of low dose calcium and vitamin D supplementation, bone density and structure as measured by µCT at the distal tibia, but not DXA BMD at lumbar spine and total hip, show moderate, but statistically significant, changes in postmenopausal women with low bone mass. The results will be discussed from the clinical perspective as well as with respect to the methodological limitations of currently available *in vivo* µCT.

Atypical Subtrochanteric And Diaphyseal Femoral Fractures Associated With Long-Term Bisphosphonate Use In Postmenopausal Osteoporosis - A Case Study

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Objectives: The incidence of atypical (subtrochanteric and diaphyseal) femoral fractures (AFF) associated with the use of bisphosphonates (BP) for the treatment of patients with osteoporosis appears to be very low. Moreover, a causal association between BP and AFFs has not been clearly established. However, recent observations suggest that the risk rises with increasing BP exposure, and there is concern that lack of awareness and underreporting may mask the true incidence of the problem.

Despite their relative rarity, AFF, if occurring in individual patients, are of great challenge for further medical management. A few case reports and anecdotal findings, but a lot of preclinical data as well, suggest that osteoanabolic

treatment with teriparatide or parathyroid hormone (possibly also with strontium ranelate) could improve the outcome of these fractures. Nevertheless, it seems unlikely for several reasons that there will be a randomized, controlled trial of teriparatide or other osteoanabolics for AFF management.

Patients & Methods: We report here on five patients with altogether eight BP-associated AFF who were identified in or referred to our osteoporosis outpatient clinic since November 2009. This case study follows the recommendations given by the ASBMR for AFF reports and includes demographic data, key radiographic features of AFF, prior fracture history, bone mineral density (BMD) before fracture and at the time of fracture, osteoporosis treatment, concomitant medications, comorbid medical conditions, biochemistries incl. markers of bone turnover (BTM). We provide detailed information on individual risk patterns and treatment considerations as well as on different therapeutic outcomes.

Results: All five AFF patients in our case study were treated with BP for postmenopausal osteoporosis (including one case with primary hyperparathyroidism occurring later during BP treatment). Their mean age at the time of (first) AFF was 75 years (range: 66-86 years), the mean duration of BP treatment was 7 years (range: 3-11 years). Two patients suffered from bilateral, complete subtrochanteric AFF followed by delayed healing after osteosynthesis - both these patients had a medical history with long lasting rheumatoid arthritis, glucocorticoid and proton-pump inhibitor treatment. The other four AFF occurred in three patients without any additional clinical risk factors recently discussed in the pathogenesis of AFF and showed the radiological patterns of incomplete diaphyseal insufficiency fractures with involvement of the lateral cortex only. Otherwise, our patients with complete or incomplete AFF and with subtrochanteric or diaphyseal AFF, respectively, did not differ in prior fracture, BMD and BTM history.

As for the moment of abstract submission, one out of three patients treated with teriparatide showed after two years clinical and radiographic evidence for improved fracture healing. On the other hand, in a case with assumed contraindications for teriparatide one complete diaphyseal AFF developed from an originally incomplete insufficiency fracture.

The Early Onset And Severe Osteoarthropathy Of Alkaptonuria Has Major Lessons For The Pathogenesis Of Osteoarthritis

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Objectives: The biomedical literature contains many examples of how research on extreme phenotypes in monogenic diseases has helped elucidate the molecular pathogenesis of more common disorders. We have investigated how ochronosis, the deposition of pigmented polymers in cartilage in the ultra rare disease Alkaptonuria (AKU), leads to a severe and early onset osteoarthropathy. AKU is caused by a deficiency of HGD, an enzyme in the metabolism of tyrosine, leading to elevated circulating levels of homogentisic acid (HGA).

Subjects & Methods: We investigated ochronosis by a combination of biochemical, structural, and ultrastructural methods using an *in vitro* model in which chondrocytes were cultured in medium supplemented with HGA, *ex vivo* studies on ochronotic cartilage obtained at joint replacement surgery and *in vivo* studies on AKU mice genetically deficient in HGD.

Results: At the ultrastructural level, the earliest deposition of ochronotic pigment was found to be associated with the periodicity of collagen. Furthermore, disruption of the integrity of collagen fibrils appears to precede pigmentation. Ochronosis is initiated in the matrix associated with individual chondrocytes in calcified articular cartilage, then spreads to adjacent chondrocytes and eventually proliferates throughout the cartilage. Pigmentation makes hyaline cartilage stiff, brittle and resistant to turnover. The altered biomechanical loading on the underlying bone leads to defective remodelling, including complete resorption of the subchondral plate and the development of excrescences on the trabecular surface, some of which appear to be templated by adipocytes.

Discussion: Our results suggest that extracellular matrix is initially resistant to pigmentation but becomes susceptible following degenerative changes. Pigmentation appears to be a response to, rather than the cause of, initial degeneration. However, once the early pigment has been deposited, changes in the biochemical and/or biomechanical environment ensue leading to further degeneration and a downward spiral of pigmentation throughout the cartilage. These results highlight the role of calcified articular cartilage in the initiation of degenerative changes in cartilage and also demonstrate that interactions between bone and cartilage lead to focal aberration in normal "Frostian remodelling".

Summary: Our findings demonstrate that investigating severe phenotypes, such as ochronosis observed in AKU, will provide major insights into the pathogenesis of the more common forms of osteoarthritis.

Effects Of Strontium Ranelate Compared To Alendronate On Strength Parameters At The Tibia In Post Menopausal Osteoporotic Women After A Treatment Period Of 2-Years

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Objective: Comparison of the effects of strontium ranelate (SrRan) and alendronate (ALN) on bone strength parameters measured by peripheral Quantitative Computed Tomography (pQCT) in women suffering from postmenopausal osteoporosis.

Subjects & Methods: A randomized, double-blind and double-dummy multicenter international study. 189 women were randomized to SrRan 2 g/day or ALN 70 mg/week during 2 years. Bone strength parameters were assessed by pQCT at 14%, 38% and 66% of the tibia's length and at 66% of the radius' length, respectively.

Results: Baseline characteristics were similar between groups with a mean age (±SD) of 67.6±5.7 years; L1-L4 and total hip DXA T-scores of -3.1±0.6 and -2.0±0.8, respectively. No relevant between-group differences were seen for any pQCT parameters at baseline. After 24 months of treatment, a significant between-group difference in favor of SrRan was observed for polar moment of inertia (Ip) (p=0.017), density-weighted Ip (Ipw) (p=0.011), polar section modulus (Rp) (p=0.013) and density-weighted Rp (Strength Strain Index - SSI) (p=0.001) at the 14 % location of the distal tibia. Significant between-group difference in favor of SrRan was also observed for Ipw (p=0.011) at the 38% location and for Ipw (p<0.05) and SSI (p<0.001) at the 66% location (Table).

Table.

	Polar moment of inertia (Ip) Mean (SD)		Density-weighted Ipw Mean (SD)		Polar section modulus (Rp) Mean (SD)		Strength Strain Index-(SSI) Mean (SD)	
Tibial level	**SrRan**	**ALN**	**SrRan**	**ALN**	**SrRan**	**ALN**	**SrRan**	**ALN**
14%	**1.2(1.6)§**	**0.5(1.8)***	**1.7(2.1)§**	**0.9(2.4)***	**0.7(1.8)***	**-0.1(2.2)NS**	**1.3(2.4)§**	**0.1(2.3)NS**
38%	0.9(1.8)§	0.9(1.7)§	**2.2(2.3)§**	**1.5(2.0)§**	0.7(1.8)*	0.7(2.0)*	1.8(2.4)§	1.3(2.2)§
66%	1.2(1.7)§	1.1(2.8)**	**2.2(2.7)§**	**1.5(2.4)§**	0.9(1.9)§	0.6(2.2)*	**2.0(2.3)§**	**0.8(2.1)****

*Within group difference: *p<0.05; **p<0.001; §p<0.0001. Significant between group differences are marked in **bold** letters.*

At the 66% position of the radius, no between-group difference was observed regarding bone strength parameters with a significant Ipw and SSI increase in both groups. The two treatments were well tolerated.

Conclusion: Strontium ranelate demonstrates greater effects on strength parameters at the 14%, 38% and 66% location of the tibia, compared to alendronate, in women with postmenopausal osteoporosis after two years of treatment. These findings consolidate the results of previous studies supporting a beneficial effect of strontium ranelate on bone strength.

Transsexual Women Have Low Bone Mass Before Cross-Sex Hormonal Treatment And Gonadectomy

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Objectives: Sex steroids have an important impact on gender differences in bone geometry acquired during puberty. Male-to-female transsexual persons (transsexual women) undergo extreme hormonal changes due to orchidectomy (sex reassignment surgery, SRS) and estrogen substitution, which leads to altered body composition and may change bone mass and size. The objective of the present study was toexamine body composition, bone mass and geometry in transsexual women before cross-gender sex steroid exposure and SRS in comparison to age- and height-matched control men.

Subjects & Methods: A prospective intervention study with 42 transsexual women (median age 31 years) with age-and height-matched control men. Grip strength, using a hand dynamometer, physical activity, areal bone mineral density (aBMD), using DXA, bone geometry and volumetric bone mineral density (vBMD), using peripheral quantitative computed tomography, were measured, before the start of cross-sex hormonal therapy and SRS.

Results: No differences were observed in weight, height, BMI, smoking and physical activity scores or fracture prevalence between transsexual women and controls. Body composition was also similar without significant differences in lean and fat mass, muscle mass and strength and waist and hip circumference. Prevalence of osteoporosis was higher in transsexual women (21%) compared to control men (3.4%) ($p<0.05$). They had a lower aBMD at the lumbar spine, hip and femoral neck (all $p\leq0.01$) and lower trabecular and cortical vBMD at the radius and tibia (all $p<0.05$) compared to control men. A significantly thinner radial and tibial cortex (both $p\leq0.016$), possibly due to a smaller periosteal and larger endosteal circumference (n.s.), was also found in transsexual women compared to control men.

Positive associations were found between physical activity, in particular participation in sports, and aBMD at the lumbar spine, total hip and femoral neck in transsexual women (all $p<0.05$), but not in control men.

Conclusions: Transsexual women before the start of hormonal therapy appear to have a lower bone mineral density as well as a thinner bone cortex at the radius and the tibia compared to control men. The reasons for these differences are unclear.

Male Obese Adolescents Have Stronger And Bigger Bones Than Their Normal-Weighted Peers

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Background & Objectives: Recent studies have shown that obesity is associated with an increased risk of fracture. Whereas some studies report higher bone mineral density (BMD) (measured by DXA) in overweight children, other studies conclude that obesity is linked to a lower BMD. However, there are few data on bone geometry and true volumetric bone mineral density (vBMD) in obese adolescents. This study wants to determine bone strength, bone geometry and vBMD in obese male adolescents by peripheral quantitative computed tomography (pQCT) and the relationship between muscle force and bone characteristics at the tibia in adolescents.

Subjects & Methods: 51 male obese (mean BMI sds: 2.55) adolescents, aged 10-19 y, recruited at the start of a residential obesity treatment program in De Haan (Belgium), and 51 healthy male controls matched for age and height (mean BMI sds: -0.17) were included in this cross-sectional study. Trabecular (4% site from distal end) and mid shaft cortical (38 % site from distal end) vBMD and bone geometry were assessed at the non-dominant leg using the Stratec XCT 2000 device. Maximal muscle force (F max) was evaluated by two leg jumping mechanography using a ground force reaction plate (Leonardo, Novotec Medical GmbH).

Results: The trabecular vBMD and area measured at the distal end of the tibia (4%) were higher in the obese group. At mid shaft, tibial cortical area, periosteal circumference and endosteal circumference were larger in the obese group. There was no significant difference in cortical vBMD between the two groups. The stress-strain index (SSI) was significantly higher in the obese group. Obese adolescents developed a significantly higher maximal force (2.1 (range: 2.8) vs 1.2 (range: 1.3) kN; $p<0.001$) compared to the control group. In the merged study groups significant positive associations were observed between F max and cortical bone area (β: 0.60; $p<0.001$), periosteal circumference (β: 0.59; $p<0.001$), endosteal circumference (β: 0.41; $p<0.01$), trabecular bone area (β: 0.50; $p<0.001$), and trabecular vBMD (β: 0.34; $p=0.01$), but not cortical vBMD (β:0.13; p=NS) (Table).

Discussion & Summary: Obese adolescents have a bigger bone size and higher bone strength at the tibia compared to normal-weighted controls. They develop higher ground reaction forces and apply higher mechanical load to the skeleton.

Table.

	Obese boys (mean± SD)	Control boys (mean± SD)	Difference between groups (%)	Significance (p)
pQCT results T4				
Trabecular vBMD (mg/cm^3)	240±29	227±35	5%	<0.05
Trabecular area (mm^2)	545±111	452±97	20%	<0.001
pQCT results T38				
Cortical vBMD (mg/cm^3)	1079±37	1074±62	-	NS
Cortical area (mm^2)	307±69	257±51	19%	p<0.001
Periosteal circumference (mm)	80±10	74±8	8%	p<0.001
Endosteal circumference (mm)	52±8	46±10	13%	p<0.01
SSI (mm^3)	1817±468	1416±339	28%	p<0.001