Trabecular bone density was reduced by 85% with both doses of RANKL ($p<0.001$ vs. VEH). Cortical bone geometry and strength were also negatively influenced by RANKL. MicroCT analysis of an 8 mm section of the femoral diaphysis showed that both doses of RANKL significantly reduced cortical bone volume (10-13% vs VEH, $p<0.001$). Biomechanical testing confirmed that RANKL directly reduces bone strength. Three-point bending of the femoral diaphysis showed that both doses of RANKL caused significant reductions in maximum bending load (19-25% lower than VEH, $p<0.001$). These data demonstrate for the first time that soluble RANKL administration has direct catabolic effects on both trabecular and cortical bone. These catabolic effects included reductions in bone volume and mineral density, and a significant decrease in bone strength. Inhibition of RANKL is therefore a logical and promising approach for improving cortical and trabecular bone mass and strength.

Disclosures: ***Y.Y. Yuan****, Amgen Inc. 2.*

SA358

See Friday Plenary number F358.

SA359

Longitudinal Assessment of Bone Architecture in Women - Relation to Hormonal Status, Bone Turnover Markers (BTM) and Fracture Risk. The OFELY Study. P. Szulc, F. Duboeuf*, E. Sornay-Rendu*, F. Munoz*, P. D. Delmas. INSERM 403, Hopital E. Herriot, Lyon, France.

Longitudinal data on age-related changes in bone architecture in women and their relation to the fracture risk are scarce. We studied age-related changes of bone architecture at the third distal radius measured annually by QDR Hologic 2000 in 535 women aged 31-89 from the OFELY cohort. In 53 women, 71 incident fragility fractures occurred during the follow-up (7.1±2.5 years). Before the menopause, areal bone mineral density (aBMD) and cortical thickness decreased due to centrifugal displacement of the constant amount of bone mineral assessed by cross-sectional area (CSA). After the menopause, decrement in CSA and cortical thinning resulted in the decrease of estimated bending strength despite continuous periosteal expansion. In 72 women, these changes were significantly reduced by the hormone replacement therapy. In postmenopausal women, elevated serum levels of BTM (osteocalcin, ß-CTX-I) at baseline were associated with accelerated decrease in CSA and cortical thinning but not with periosteal expansion. Low values of external diameter, CSA, cortical thickness and section modulus were associated with increased risk of incident fracture (O.R. = 1.46 - 1.99 per 1 SD decrease, $p<0.01$-0.0001). Bone width and section modulus remained predictive of fractures after adjustment for aBMD (O.R. = 1.63 and 1.74 per 1 SD decrease, respectively, $p<0.0001$). In summary, our longitudinal data show age-related changes of bone architecture and estimated bending strength at the distal radius that vary according to the hormonal status. Elevated BTM are associated with accelerated bone mineral loss and cortical thinning. Low bone width and section modulus were predictive of incident fractures independently of aBMD.

Disclosures: ***P. Szulc****, None.*

SA360

See Friday Plenary number F360.

SA361

Latent Hypothyroidism Is Related to Lower Heel QUS in Postmenopausal Japanese Women. S. Sekiguchi, M. Nagata*, K. Nishiwaki-Yasuda, Y. Ono*, K. Inagaki*, T. Matsumoto*, S. Imamura*, H. Kakizawa*, N. Hayakawa*, N. Oda*, A. Suzuki, M. Itoh*. Division of Endocrinology, Fujita Health University, Toyoake Aichi, Japan.

In untreated hypothyroidism, histomorphometric studies have disclosed a decreased bone turnover in both trabecular and cortical bones with an increased cortical thickness. Recent findings suggest that thyroid stimulating hormone (TSH) is a negative regulator of skeletal remodeling by reducing both differentiation of osteoblasts and formation of osteoclasts. In addition, increased fracture risk in untreated hypothyroid patients has been reported to begin up to 8 years before diagnosis. The aim of the present study was to investigate the bone quality by using the heel QUS in the patients with latent hypothyroidism. Subjects were outpatients without any past or present history of thyroid disease. Among 210 postmenopausal women, 23 subjects of 33 patients (Hypo), who had elevated serum TSH level (TSH > 4 μU/ml) with normal serum free T4 (FT4) levels, agreed to join to this study. We also randomly selected 24 control subjects (Cont) from 176 postmenopausal patients with normal thyroid status. Calcaneus osteo sono assessment indeces (OSI) of right feet were measured using the ultrasound bone densitometry AOS-100 (Aloka Co., Japan). Serum TSH levels in Hypo patients (5.31 ± 1.3 μU/ml) were higher than those in Cont patients (2.05 ± 1.1 μU/ml), but there was no significant difference of FT4 levels (Cont 1.33 ± 0.15 ng/dl; Hypo 1.19 ± 0.17 ng/dl). OSI in Hypo subjects (Mean ± SD, 2.138 ± 0.152) were significantly lower than those in Cont subjects (Mean ± SD, 2.347 ± 0.243) (Student's *t*-test, $p < 0.001$). Simple regression statistical analysis showed that OSI decreased according to the increase of serum TSH level ($R = 0.415$, $n = 47$, $P<0.037$). In addition, multiple regression analysis showed that serum TSH level more than 4 μU/ml was associated with the decrease of OSI. These results suggest that latent hypothyroidism affects the structure of bone, resulting in the elevation of fracture risk.

Disclosures: ***S. Sekiguchi****, None.*

SA362

See Friday Plenary number F362.

SA363

Remodeling Cavities and Stress Risers: A Biomechanical Study on Cancellous Bone Strength. C. J. Hernandez, A. Gupta*, T. M. Keaveney. Orthopaedic Biomechanics Laboratory, Department of Mechanical Engineering, University of California, Berkeley, CA, USA.

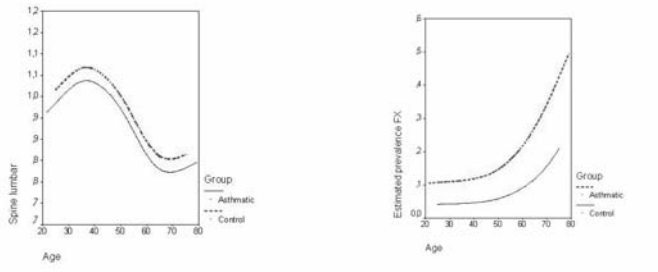
Bone turnover has been implicated as an aspect of bone quality. One proposed mechanism for this effect is the possibility that remodeling cavities can act as stress risers, substantially altering the strength of cancellous bone with only small changes in bone mass. This mechanism does not require disconnection of trabeculae and thus is independent of connectivity. In this study we tested this theory, namely, that geometric effects associated with remodeling cavities can alter cancellous bone strength more than would be expected from the associated loss of bone mass. Cubes of cancellous bone (5mm in each dimension) were derived from micro-computed tomography based images (22 m resolution) of vertebral bone from 10 female and 7 male donors (aged 54-90 years). Remodeling cavities (88 m in depth) were added at random to the cancellous bone surface using an algorithm that prevented trabeculae from being disconnected. Cavities were added until a total of 6% of the initial bone mass was removed. Each image was then converted into a high-resolution finite element model to compute elastic modulus (stiffness) and strength of the cube in compression. These models included both material and geometric non-linearities, and can be considered surrogates for actual biomechanical testing. Results indicated that addition of cavities reduced compressive elastic modulus in each sample by 18.4 ± 2.6% (mean ± SD) and strength by 22.2 ± 4.4%. After accounting for differences in bone volume fraction, elastic modulus and strength were typically 11% ($p = 0.10$) and 15% ($p=0.08$) lower when cavities were present, but these changes did not reach statistical significance Overall, the changes reported here represent an upper bound on expected effects since the assumed cavity depth was high. These results suggest two possibilities. First, that there is no appreciable stress riser effect - independent of bone mass. Or second, that stress riser effects are manifested either by cavities that occur exclusively in regions of high stress (van der Linden et al. 2001) (as opposed to random placement studied here), or, under more complex apparent loading conditions than studied here. Further study is therefore recommended to elucidate this potentially important aspect of bone quality.

Disclosures: ***C.J. Hernandez****, None.*

SA364

Inhaled Steroids Decrease Bone Mineral Density and Increase the Risk of Fractures: Data from the GIUMO Study Group. M. Sosa, P. Saavedra*, &. the GIUMO Study*. Medicine, University of Las Palmas de GC, Las Palmas de Gran Canaria, Spain.

Background: Although the negative effect of systemic steroids on bone is well documented, there is not clear evidence about the possible adverse effects of inhaled steroids on bone metabolism and fractures. **Design:** Cross-sectional study performed on 105 women suffering from bronchial asthma treated with inhaled steroids and 133 controls. Bone mineral density (BMD) was measured either by quantitative ultrasound (QUS) at the calcaneus or by dual x-ray absorptiometry (DXA) both at the lumbar spine and proximal femur. **Results:** Patients suffering from bronchial asthma showed no statistically significant changes in BMD measured by DXA or QUS compared to controls. However, the age-adjusted mean at the lumbar spine was of borderline significance ($p = 0.098$), being the 96%CI for the difference of means (-0.006 ; 0.067) and the upper bound for the percentage of diminution of 6.8%. A higher prevalence of fractures was found in the group of women with bronchial asthma, with an age-adjusted odds ratio of 2.79 (95% CI = 1.19 ; 6.54). **Conclusions:** Inhaled steroids do not seem to decrease BMD, but they are associated with an increased risk of fracture in women.



Disclosures: ***M. Sosa****, None.*

SA365

See Friday Plenary number F365.