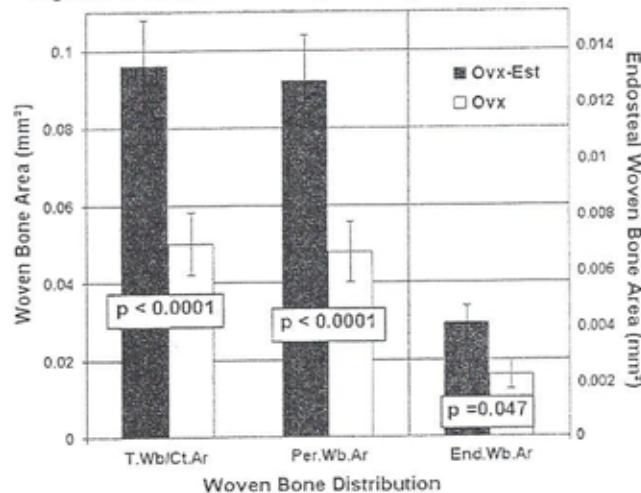


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73. The Periosteal and Endosteal Modeling Process Is Affected by Estrogen Differently in Response to Fatigue Loading Than During Development. S. D. Mendenhall*, J. B. Jones*, R. T. Kitterman*, J. G. Skedros. Dept. of Orthop. Surgery, Univ. of Utah, SLC, UT, USA.

Females are "set up" during skeletal development to have fragile bones later in life. This results primarily from the inhibitory effect of estrogen on periosteal modeling during bone mass acquisition, causing women's bones to be less robust than men's. Delayed pubertal development in female rats increases periosteal bone growth, but results in a minor decline in endosteal modeling [Yingling: Tran Orthop Res Soc 2007]. However, little is known about the effects of estrogen on periosteal/endosteal modeling responses to fatigue loading in rats. Using the rat ovariectomy (Ovx) model, we tested the hypothesis that estrogen-deficient rats would exhibit less endosteal modeling and more periosteal modeling following fatigue loading than Ovx rats that were estrogen-repleted (Ovx-Est). With IACUC approval, 36 five-month-old female F344 rats were obtained—6 for load/strain calibration and 15 for each of the experimental groups. Following Ovx, right forearms were cyclically loaded [Uthgenannt & Silva, J Biomech, 2006] and the contralateral ulnae served as controls. The Ovx Est group received daily β -Estradiol (0.05 mg/kg) injections. All animals received tetracycline injections 13 and 3 days prior to sacrifice at 18 days post-loading. Ten transverse sections were cut from mid-third ulnar diaphyses and mounted on slides. Endosteal woven bone area (End.Wb.Ar), periosteal woven bone area (Per.Wb.Ar), and total woven bone area (T.Wb.Ar) were then quantified. Kruskal-Wallis ANOVA was used with significance at $p < 0.05$. As expected, the Ovx rats had less endosteal bone growth when compared to Ovx-Est rats. Surprisingly, the Ovx-Est rats produced nearly twice as much periosteal woven bone than did Ovx rats (see Figure). These results show an interesting interaction between hormone status and fatigue-induced modeling responses in the rat. Although estrogen inhibits periosteal bone growth during development, heavy mechanical stimuli seem to reverse this role, thereby maximizing the amount of new bone growth on periosteal and endosteal surfaces. Similar anabolic effects of estrogen have been reported in women on estrogen replacement therapy [Vedi et al.: Osteoporos Int 1999]. Further work is needed to validate the rat Ovx model for evaluating novel therapeutic agents that target estrogen's actions on bone.

Figure: Woven Bone Response by Estrogen Status



Disclosures: S.D. Mendenhall, None.

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An Acute 7 Gray Dose of Gamma-Radiation Induces a Profound and Rapid Loss of Trabecular Bone in Mice. J. S. Willey*, D. S. Gridley*, M. J. Pecaut*, R. W. Norrdin*, T. A. Bateman*. ¹Bioengineering Department, Clemson University, Clemson, SC, USA. ²Department of Radiation Medicine, Loma Linda University, Loma Linda, CA, USA. ³College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO, USA.

Fracture rates of irradiated bones are elevated in patients receiving radiation therapy for a primary tumor as well as palliative care treatment. The mechanism for the elevated risk of fracture is unclear. Osteoblast death and damaged vascularity have been documented in patients as well as animal models, and contribute to atrophy after irradiation. But the effects of radiation on osteoclast number and function are not well defined. We investigated the effects of acute, high-dose radiation exposure on trabecular and cortical bone to document bone quantity and structural properties at an early time-point post-irradiation. Nine-week old C57BL/6 mice (n=6) received 7 Gray (Gy) gamma-radiation, with nonirradiated controls (n=6). Fourteen days after exposure the animals were euthanized, hind limbs removed, and tibiae analyzed via microCT and histomorphometry. Statistical analyses were performed using t-tests to compare the groups. Profound loss of trabecular bone within the metaphysis was observed. Significant reduction in BV/TV (-

54%), Conn.Dens (-69%), and Tb.N (-26%) were observed in irradiated animals compared with control. No differences were observed in cortical parameters. Decreased growth plate cellularity, disorganized chondrocyte arrangement, and a terminal bar of bone along the distal physal border indicated slow growth among all animals. Oc.S/BS and ES/BS were similar between both groups, with TRAP staining confirming presence of multinucleated osteoclasts. The large difference in the amount of bone between groups and evidence together with evidence of slow growth suggests bone loss as opposed to reduced bone growth. Evidence of stabilized resorption at sacrifice indicates that large declines in bone quantity occurred via increased resorption very early after exposure. Radiation-induced reduction in bone quantity and microarchitecture via elevated resorption could reduce bone quality and may provide insight into the nature of increased fracture rates among radiation therapy recipients.

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Reduced Levels of Serum Insulin Like Growth Factor 1 in Male with Idiopathic Osteoporosis. J. Dewailly*, L. Legroux-Gerrot*, M. D'Herbomez*, X. Marchandise*, D. Dewailly*, B. Duquesnoy*, B. Cortet*. ¹Rheumatology, CHRU Hopital Salengro, Lille, France. ²Service de Médecine nucléaire, CHRU Hopital Salengro, Lille, France. ³Endocrinology, CHRU, Lille, France.

Objective: The pathophysiology of idiopathic male osteoporosis remains unknown. The histomorphometric studies suggest reduction of bone formation. A disturbed secretion of IGF-1 could be involved in male idiopathic osteoporosis since IGF-1 has a stimulative effect on the osteoblastic proliferation and on the bone tissue synthesis. Few studies have evaluated the relationship between the circulating concentrations of IGF-1 and bone mineral density, particularly in osteoporotic men, and the results are controversial. The aim of our study was to evaluate the involvement of IGF-1 in idiopathic male osteoporosis and the relationships between bone density and the serum levels of IGF-1 and sex hormones. Materials and methods: Serum levels of IGF-1, estradiol, testosterone, SHBG and bone mineral density at lumbar spine, femoral neck and total hip were compared between 79 men with idiopathic osteoporosis and 26 healthy subjects. Inclusion criteria were a densitometric osteoporosis defined by a T-score ≤ -2.5 SD and/or an osteoporotic fracture. The osteoporotic patients were included after exhaustive work-up excluding the principal causes of secondary osteoporosis.

Results: A significant reduction in the mean serum IGF-1 levels was found in osteoporosis patients ($p = 0.02$) that persisted after adjustment for BMI. However, no correlation was found between bone density and the serum IGF-1 levels. The mean SHBG level was higher in osteoporotic patients ($p = 0.001$) thus yielding a reduction in the mean Free Testosterone Index (FTI, total testosterone / SHBG) ($p = 0.002$). These differences remained significant after adjustment for BMI. After adjustment for the FTI, the mean IGF-1 levels between patients and controls were not significantly different. However, after adjustment for the FTI and the BMI in patients, the IGF-1 level was significantly related to the presence of an osteoporotic fracture, thus indicating an independent effect of the IGF-1 level on fracture risk.

Conclusion: Our study confirms the presence of reduced serum IGF-1 levels in male idiopathic osteoporosis. This could be the cause or the consequence of a disturbance in sex hormones with increased SHBG serum level. This confirms the important role of SHBG in the pathophysiology of male osteoporosis.

Disclosures: J. Dewailly, None.

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See Sunday Plenary Number S466

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Birth Weight Predicts Lean Body Mass and Thus BMC in Healthy Men at Peak Bone Mass - Results from the Odense Androgen Study. L. Frederiksen*, T. L. Nielsen*, K. Wraae*, H. Claus*, M. Andersen*, K. Brixen*. Endocrinology, Odense University Hospital, Odense, Denmark.

Birth weight has been associated with low bone mass in later life. Previous studies, however, have relied on self-reported data on birth weight, included select populations, or been of a limited size. Moreover, it is unclear if the association between birth weight and bone mass is mediated by body weight, lean body mass, or fat mass.

We hypothesize that birth weight is associated with peak bone mass in men independent of current lean body mass and body weight.

The Odense Androgen Study is a population-based, prospective, observational study on the inter-relationship between endocrine status, body composition, muscle function, and bone metabolism in young men. In brief, 3000 males aged 20-30 years were randomly selected from the civil registration database in Funen County, Denmark, and invited by mail to participate in the study. A total of 2042 men returned the questionnaire, 783 gave written informed consent to participate in the study and the data are presented here. Bone mass measurements (spine, hip, and whole body) were performed using a hologic-4500a densitometer. Data on birth weight, length at birth, and gestational age was retrieved in a national database covering all birth clinics in Denmark in the current period. The relationship between Birth weight, BMC, Lean body mass and fat mass as tested using multiple regression analysis is shown in the table as partial correlation coefficients. Data on birth weight and birth length were available on 754 participants while gestational