General Poster Abstracts

Abstracts of the General Posters attended by authors on TUESDAY (24 Oct 2006)

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ANIMAL MODELS OSTEOPOROSIS

P-TUE-02

Mechanisms of action of alendronate, droloxifene and calcium in preventing bone loss in the femoral epiphysis of the rat

A.J. Moore, A. Mulaibrahimovic, R.J. Moore* and H.A. Morris
*Hanson Institute, Frome Road, Adelaide, South Australia, *Adelaide Centre for Spinal Research, Frome Road, Adelaide, South Australia*

Antiresorptive treatment therapies demonstrate a marked efficacy for improving bone mineral volume. However, the precise mechanisms by which these effects are achieved are unclear. The effects of alendronate, high dietary calcium and the SERM, droloxifene, were assessed on bone remodelling in the epiphysis of the femur in the ovariectomised (OVX) rat. At 3 months of age, 42 female Sprague-Dawley rats were either OVX or sham-operated (SHAM). At 6 months, rats were assigned to alendronate treatment (0.25mg/kg/BW/FN), droloxifene (10mg/kg BW/day), high dietary calcium (1.6%), or one of three control groups and treated for a further 3 months. At 9 months, femora were removed and processed for histomorphometric analysis. The epiphysial bone mineral volume (BV/TV%) in both alendronate and droloxifene treated animals was 40% higher than untreated levels. In both treatment groups, the bone resorption surface levels (Oc. Sur%) were reduced by approximately 45%. In the alendronate treated animals, however, bone formation rate (BFR) was markedly suppressed and the period of formation (FP) was extended 3-fold over the levels in the droloxifene treated animals. Interestingly, high dietary calcium was also able to maintain BV/TV% to levels observed in the

alendronate and droloxifene groups. The FP was extended in these animals without suppressing BFR. Our results suggest that alendronate decreases bone turnover and extends the duration of bone formation, while droloxifene improves bone mineral volume largely through a reduction in resorption only. A diet high in calcium, however, maintains bone mineral volume by the reducing osteoclast numbers and prolonging osteoblastic bone formation.

P-TUE-04

The Influence of glucocorticoid administration exerts on bone volume in rats at different months of age.

T. Ogoshi, O. Toru., H. Hagino and R. Teshima
Department of Orthopaedic Surgery, Tottori University Hospital ,Tottori, Japan

Purpose: To elucidate the influence of glucocorticoid (GC) administration on rat bone of different age for making a similar glucocorticoid induced osteoporosis model to man from the rat.

Animals and Method: We divided 3, 6, 12 month-old female Wistar rats(32 rats of each age) into the following four groups: killed at the start for zero-time control (ZT), saline 2ml (CNT), prednisolone (PSL) 2 mg/kg group (P-L), PSL 20 mg/kg group (P-H). PSL was subcutaneously administered everyday for 4 weeks. BMD was measured by peripheral quantitative computed tomography (pQCT) at the tibia at baseline 2 weeks after and 4 weeks after.

[Results] Trabecular bone BMD: <3-month-old rats> At 2 weeks and 4 weeks, the BMD of P-L and P-H were significantly higher than that of CNT. <6-month-old> The trabecular bone BMD of P-L and P-H decreased significantly lower than that of CNT at 4weeks. <12-month-old> There was no significant change overtime and no difference among the three groups. Histomorphometry: <3-month-old> Tb.N were higher in P-H than CNT. MAR was significantly higher grouping P-H; however, Oc.S and BFR didn't show significant difference among groups. <6-month-old> Oc.S were lower in P-H than CNT. MAR was significantly lower in P-L than CNT and ZT and BFR was significantly lower in P-L than ZT.

Conclusion: Six-month-old rats treated with glucocorticoid at a dose of 20 mg/kg are suitable models of GC induced osteoporosis with dominant cancellous bone decrease.

NEURAL CONTROL

P-TUE-06

Bone mineral density accrues in growing spinal cord transected rats

C.G. Schultz[3], I.J. Llewellyn–Smith[2], D.M. Findlay[4] and J.M. Clark[1]
[1] *South Australian Spinal Cord Injury Research Centre, Hampstead Rehabilitation Centre*
[2] *Cardiovascular Medicine, Flinders University*
[3] *Nuclear Medicine, PET and Bone Densitometry, Royal Adelaide Hospital*
[4] *Department of Orthopaedics and Trauma, University of Adelaide*

This study aimed to document effects of spinal cord injury (SCI) upon bone homeostasis in rats.

Eight week old Male Sprague Dawley rats were spinal cord transected (T5) or sham-operated (T5 laminectomy). Rats were killed after 12 weeks, and bones dissected out for *ex vivo* analysis.

Limb and spine bone mineral density, and fat mass (FM) were measured on a Lunar Prodigy at pre-, two, six, ten and 12 weeks post injury (PI). Excised proximal tibial trabecular bone volume (TBV), thickness (TbTh), number (Tb.No) and space (Tb.Sp) were determined on a μCT (SKYSCAN 1072).

All rats accrued BMD (hindlimb: Sham 34.0% $\pm$1, Tx 29.2% $\pm$8.8; forelimb: Sham 56.7% $\pm$4.6, Tx 30.1% $\pm$3.2, all $p>0.05$). Hindlimb BMD differed at two weeks PI only ($p<0.05$). Scoliosis in treated rats limited meaningful *in vivo* estimates of spine BMD. FM showed co-linearity to fore- and hindlimb BMD in both groups. Proximal

tibia TBV and TbTh differed significantly at 12 weeks PI (TBV Sham: 39.43*mm* $^{-3}$, Tx 46.15*mm* $^{-3}$; TbTh: Sham 0.20mm, Tx 0.49mm).

SCI rats developed few of the characteristic bone abnormalities described in patients with SCI, such as accelerated bone resorption and altered trabecular architecture. Similar BMD in treated and control rat proximal tibias contrasts sharply with large losses of bone in the inactive limbs of patients.

Future studies will examine central nerve pathways to determine the relative significance of supraspinal versus spinal control of bone homeostasis.

This project was supported by the Christopher Reeve Paralysis Foundation (USA) and the NHMRC.

MINERAL METABOLISM

P-TUE-08

Administration of pravastatin ameliorates suppressed bone formation in uremic rats without hyperparathyroidism

Y. Iwasaki, H. Yamato and M. Fukagawa
Oita University of Nursing and Health Sciences, Oita, Japan,
Kureha Special Laboratory, Fukushima, Japan, Kobe University school of Medicine, Kobe, Japan

Adynamic bone disease (ABD) is emerging as a major type of renal osteodystrophy in chronic dialysis patients. ABD has the reduction of number of osteblasts and bone formation. On the other hands, HMG-CoA reductase inhibitors (statins) are widely used for treatment of hypercholesterolemia. Recent studies reveal that statins stimulate bone formation and suppress bone resorption. To evaluate the effect of pravastatin, which is a major statin, on bone formation in low-turnover bone disease with renal failure, we demonstrated bone histomorphometry on our model rats which simulated ABD. Male SD rats underwent thyroparathyroidectomy (TPTx). The TPTx rats underwent 5/6 nephrectomy (Nx) or sham operations. These rats were continuously infused with rat PTH and injected with L-thyroxin subcutaneously to maintain physiological levels. Six weeks after the second Nx, TPTx-Nx rats were assigned to receive pravastatin at a dosage of 3 or 30 mg/kg body weight per day or vehicle in the diet. By bone histomorphometry, bone formation rate in the TPTx-Nx with vehicle group was reduced to 8% of the TPTx-Sham group. The reduction of bone turnover was ameliorated by pravastatin administration in a dose dependent manner. In high dose group, osteoblast surface was recovered up to 40% of the TPTx-Sham group. The Serum biochemical parameters, including lipid metabolic parameters, did not change among all the groups. These results suggest that pravastatin ameliorates bone formation, at least in part, by improving osteoblasts function.

P-TUE-10

L-amino acid sensitivity is reduced in human adenomatous parathyroid disease

H. Mun*[1], L. Delbridge*[2], M. Wilkinson*[3], A. D. Conigrave[1]
[1]School of Molecular and Microbial Biosciences, University of Sydney, Sydney, NSW, Australia, [2]Department of Surgery, University of Sydney, Royal North Shore Hospital, St Leonards, NSW, Australia, [3]Department of Endocrinology, Royal North Shore Hospital, Sydney, NSW, Australia

The calcium-sensing receptor (CaR) is a G-protein coupled receptor that responds physiologically to fluctuations in the extracellular concentrations of Ca^{2+} and L-amino acids. Previously we demonstrated that, L-amino acids stimulate intracellular Ca^{2+} mobilization and inhibit PTH secretion from normal human parathyroid cells. In the current study, we have investigated whether amino acid sensitivity is reduced in cells prepared from parathyroid adenomas excised during surgery in patients with primary hyperparathyroidism. For comparison, normal parathyroid tissue was obtained from patients undergoing major thyroid surgery and parathyroid cells were prepared as previously described.

In normal parathyroid cells (eight preparations), PTH secretion was suppressed by extracellular Ca^{2+} with an IC_{50} of around 1.1 mM and CaR-active amino acids including L-Phe and L-Trp (0.1 – 5 mM) maximally suppressed PTH secretion by around 40 %. In adenomatous parathyroid cells (ten preparations), there was a

reduction in extracellular Ca^{2+} sensitivity. Typically, the IC_{50} value for Ca^{2+} increased to between 1.2-1.3 mM. Furthermore, none of the adenomatous cell preparations was sensitive to L-amino acids. The data suggest that loss of L-amino acid sensitivity may contribute to PTH hypersecretion in human parathyroid adenomatous disease.

P-TUE-12

Recovery pattern in Bone Mineral Density (BMD) after treatment in vitamin D deficiency patients

R. Khadgawat, K.S. Brar, N. Tandon and N. Gupta

Introduction: Vitamin D deficiency is very common in developing countries. Treatment with calcium and vitamin D gives excellent clinical improvement within few weeks. Decreased BMD has been clearly described in vitamin D deficiency. However, Changes in BMD after treatment have not been studied. We planned a study to see the recovery pattern of BMD after treatment in cases of vitamin D deficiency.

Material and methods: 15 patients (9 male, 6 female, mean ages 23.3 ± 10.7 yr.), who were diagnosed as vitamin D deficiency in last one year in our department, were studied. The diagnosis of vitamin D deficiency was considered when serum 25 vitamin D levels were below 20 ngm/ml (Serum 25 vitamin D estimation - Radioimmunoassay). These patients were treated with oral calcium (one gram elemental calcium per day) and vitamin D (60, 000 units of calcirol at the time of diagnosis, weekly for one month and then every monthly). BMD was measured before starting the treatment and 9 months after treatment with DXA (Hologic QDR 4500).

Results: Changes in BMD before and after treatment are shown in table 1.

Parameter	BMD before treatment Mean ± SD	BMD after treatment Mean ± SD	P
Spine BMD (Gm/sq. Cm)	0.788 ± 0.15	0.871 ± 0.12	0.009
Spine T score	-2.6 ± 1.5	1.7 ± 1.2	0.004
Spine Z score	-2.2 ± 1.2	-1.3 ± 0.95	0.005
Hip BMD (Gm/sq. cm)	0.766 ± 0.16	-0.845 ± 0.1	0.014
Hip T score	-1.6 ± 1.1	-0.98 ± 0.7	0.013
Hip z score	-1.7 ± 1.4	-0.9 ± 0.6	0.124

** p <0.05 significant*

Significant increase in BMD was seen at spine and hip while no significant changes were seen in forearm with treatment although improving trend was seen. No significant difference in BMD recovery was noticed in severe VDD (25 Vitamin D level less 5 ngm/ml) and mild to moderate vitamin D deficiency (5-20 ngm/ml). No relation of BMD recovery was seen with age and sex of patient.

Conclusion: BMD recovery in vitamin D deficiency is seen predominantly spinal region (trabecular bone) and to less extent, in hip region (combination trabecular and cortical bone). Forearm bone, predominantly cortical bone; do not show significant changes in first 9 month after treatment.

P-TUE-13

Primary hyperparathyroidism: effect of parathyroidectomy on regional bone mineral density in Chinese patients

C.K. Liu and I.T. Lau
Department of Medicine, Tseung Kwan O Hospital, Hong Kong

Objective: To investigate short-term bone mineral density (BMD) changes at both trabecular and cortical sites in Chinese patients with primary hyperparathyroidism (PHPT) after parathyroidectomy (PTX).

Methods: 44 patients who were diagnosed to have PHPT and who had undergone successful PTX during the period of July 1995 to April 2005 were recruited. BMD pre- and 1-year post PTX at the forearm, hip and lumbar spine were measured by dual-energy X-ray absorptiometry. Relevant biochemical parameters were measured.

Results: There were significant rise in BMD at lumbar spine and total hip but not the forearm from the preoperative value one year after PTX (4.60±0.8% for spine; $p<0.01$; 3.96±0.9% for hip; $p<0.01$). The 1-year percent changes in BMD at lumbar spine, total hip and forearm were significantly and negatively correlated with their respective baseline Z-score. There was no correlation between the 1-year percent change in BMD at any site and the baseline biochemical markers.

Conclusions: It suggests that there is a modest but significant rise in BMD mainly in cancellous bone even at one year after PTX in Chinese patients. The preoperative Z-score may be useful to predict the degree of BMD gain after PTX.

CYTOKINE, GROWTH FACTOR AND HORMONE MECHANISMS OF ACTION

P-TUE-15

Global knockdown of the Calcitonin Receptor results in a higher ratio of RANK to OPG mRNA expression in young female mice

C. Ma[1], M.W.S Chiu[1], E.A. Doust[1], D.M. Findlay[2], J.D. Zajac[1] and R.A. Davey[1]
[1]Department of Medicine, The University of Melbourne, Austin Health, Heidelberg, Victoria, Australia, [2]Orthopaedics and Trauma, University of Adelaide, Australia

The calcitonin receptor (CTR) has been implicated to play a role in coupling between osteoclasts and osteoblasts by modulating osteoclast activity. Our aim was to examine the relationship between the expression of receptor activator of nuclear factor-κB (RANK), corresponding ligand (RANKL) and decoy-receptor osteoprotegerin (OPG) in mice where the CTR is globally knocked-down by >95% (CTR-KD mice).

Bone mRNA levels of RANK, RANKL and OPG were determined in 6-week-old male and female control and CTR-KDs and normalised to 18s rRNA (ΔC_T) using real-time PCR. 8 mice/group will be analysed. To date, we have analysed 3-7 mice/group.

RANK, RANKL and OPG mRNA levels did not differ between controls and CTR-KDs in both sexes. However, in control mice OPG and RANKL mRNA expression were higher in females than in males ($P<0.05$), suggesting possible sex differences in OPG and RANKL mRNA expression.

RANKL and OPG mRNA levels were positively associated in female CTR-KDs (ΔC_T: $R_2=1.0$, p=0.01, n=3) but not in controls (ΔC_T: $R_2=0.4$, n=3). No relationship was observed in males. Furthermore, the RANK ΔC_T to OPG ΔC_T ratio was elevated in female CTR-KDs compared to controls ($2^{-\Delta\Delta CT}_{(CTR\text{-}KDs)}=6.0\pm1.2$ (n=3); $2^{-\Delta\Delta CT}_{(Controls)}=3.0\pm0.8$ (n=3); $P=0.08$). We are currently confirming this effect of CTR-KD in a larger sample size. In conclusion, our results suggest that mice with >95% global deletion of the CTR express a higher level of RANK for a given level of OPG, conditions which can support osteoclast formation. This is consistent with our previous observation of decreased trabecular volume and number in 6-week-old CTR-KD females.

P-TUE-17

Angiotensin II inhibition of mineralization by osteoblast cells in culture

C. Sernia and M. Chen
The University of Queensland, Department of Physiology and Pharmacology, Brisbane, Queensland 4072 Australia

The Renin-Angiotensin System (RAS), via its effector peptide hormone Angiotensin II (AngII), is best known for its role in cardiovascular functions. Clinical observations in hypertensive post-menopausal patients and experimental evidence from cultured primary osteoblasts suggest that Ang II decreases bone density, at least partly, by the inhibition of osteoblast function. The purpose of this study was to test the hypothesis that AngII inhibits the mineralization activity of osteoblasts. The rat osteoblast cell line UMR 106 was used in all experiments. Mineralization activity was measured as the cellular uptake over 4 days of the fluorescent dye, and by staining nodules with Alizarin Red. Collagen secretion was also measured by Picrosirius Red dye. Cells were incubated in the presence 0-0.1mM AngII or 100µM Dexamethasone (positive control). Specificity was shown by incubation with Losartan, an angiotensin receptor antagonist. Mineralization, measured by calcein, decreased in a dose-related manner to 65±1 % of control at 0.1mM AngII and by a similar extent (58±13%) when measured as nodule number ($p<0.01$). In contrast, dexamethasone increased calcein uptake to 138±5% of control ($p<0.01$). Type I collagen secretion decreased to 37±4% of control at 0.1mM AngII. Losartan reversed the effects of AngII on mineralization and on collagen secretion. These results show that AngII has a marked effect on the mineralization activity of osteoblasts. In conclusion, our study supports clinical and experimental observations suggesting an osteolytic role for AngII. Further studies are needed to determine the importance of this effect on bone density in hypertension, ageing and other conditions with overactive RAS activity.

P-TUE-19

TNFα potentiates bone remodelling via both the osteoblastic and osteoclastic compartments

C. Vincent[1], A.C.W. Zannettino[2], K.J. Welldon[1], D.M. Findlay[1] and G.J. Atkins[1]
Discipline of Orthopaedics and Trauma, University of Adelaide and the Hanson Institute, Adelaide, South Australia, Australia, (2) Division of Haematology, Institute of Medical and Veterinary Science and the Hanson Institute, Adelaide, South Australia, Australia

Bone remodelling involves a complex interplay between diverse cell types, including haemopoietic cells and cells of the osteoblast lineage. Proinflammatory cytokines, such as TNFα, are involved in fracture repair, and have been implicated in pathological conditions, such as RA. Their effects have been mostly studied with respect to osteoclast formation, however, effects on the osteoblast and cross-talk between these two compartments in response to these cytokines is less well characterised. In this study, we investigated the effect of TNFα on both osteoblasts and PBMC, which includes the pre-osteoclast (preOC). Human primary osteoblasts were treated with TNFα, under conditions permissive for mineralisation, for a period of 3 weeks. TNFα increased the percentage of immature osteoprogenitors, as defined by the expression of the cell surface marker, STRO-1, with a concomitant increase in surface RANKL expression. Timecourse experiments with continuous TNFα exposure, revealed a bi-phasic response, with early elevation of pro-osteoclastogenic genes, such as RANKL and M-CSF, and suppression of genes involved in osteoblast differentiation, such as OCN and BSP-1, followed by a subsequent increase in OPG and osteogenic gene expression. Consistent with this and with the increase in osteoprogenitor cell number, a corresponding increase in mineralisation was observed in the TNFα-treated osteoblasts. As expected, TNFα also had direct effects on RANKL-mediated OC formation, significantly increasing numbers of multinucleated, $TRAP^+$ cells and resorption. Taken together, these results suggest that proinflammatory cytokines influence bone remodelling via both cellular compartments. We are investigating the effects of TNFα on osteoblast-driven osteoclast formation to further elucidate this highly complex system.

P-TUE-21

Parathyroid hormone peptide (1-34) derived from the Japanese puffer fish is a proven anabolic agent in an osteopenic rat model

J.F. McManus[1], E.A. Doust[1], R.A. Davey[1], H.E. MacLean[1], C. Ma[1], N.A. Sims[2], M.L. Bouxsein[3], V. Glatt[3], J.D. Zajac[1,4] and J.A. Danks[2,4,5]
[1]Department of Medicine, University of Melbourne, Austin Health, Heidelberg, Victoria, Australia, [2]St Vincent's Institute of Medical Research, Fitzroy, Victoria, Australia, [3]Department of Orthopedics, Beth Israel Deaconess Medical Center, Boston, MA, USA, [4]Teeleostin Pty Ltd, [5]RMIT University, Australia

We have shown previously that a parathyroid hormone peptide derived from the Japanese puffer fish (fPth1[1-34]) has biological activity in UMR106.1 cells (1) and increases bone formation in young male rats. Here we describe the effects of fPth1(1-34) in osteopenic ovariectomised (OVX) rats.

Twelve week old female Sprague Dawley rats were either subjected to an ovariectomy or sham operation. Fifteen weeks post-ovariectomy rats were administered subcutaneously either 50ug of fPth1(1-34) per 100g body weight, 50ug of human parathyroid hormone (1-34), (hPTH[1-34]) per 100g body weight or vehicle (2% rat serum in normal saline) five days per week for 11 weeks. After 5.5 weeks due to increased morbidity and mortality, injections in rats receiving hPTH(1-34) were ceased.

fPth1 (1-34) increased trabecular bone volume (BV/TV) and thickness by 172% ($p=0.001$) and 103% ($p<0.05$) respectively in the proximal tibiae of OVX rats thus restoring BV/TV to sham levels. fPth1(1-34) also increased bone formation rate by 533% ($p<0.01$) and decreased osteoclast surface by 48% ($p<0.01$) in OVX rats compared with controls. Results of micro CT of lumbar vertebrae (L6) mirrored findings in the proximal tibiae. Furthermore the increase in bone volume translated into an increase in strength. The failure load and stiffness of vertebrae (L6) of OVX rats treated with fPth1(1-34) were significantly increased ($p<0.05$) relative to the OVX control group.

We have demonstrated unequivocally that in an osteopenic rat model, fPth1(1-34) can markedly increase bone formation and decrease resorption with the net effect of increased bone strength.

1. JA Hanks, PMW Ho, AJ Notini, F Katsis, Peter Hoffmann, BE Kemp, TJ Martin, JD Zajac 2003 Identification of a Parathyroid Hormone in the Fish *Fugu rubripes.* JBMR 18:1326.

P-TUE-23

Resistin, an adipocytokine, stimulates osteoblast and osteoclast proliferation

P.C. Tong, A. Zhu, K.E. Callon, M. Watson, J-M. Lin, I.R. Reid and J. Cornish
Department of Medicine, University of Auckland, New Zealand

Fat mass is one of the principal determinents of bone density but the mechanism of this remains controversial. Resistin or FIZZ3, is a member of a novel class of cysteine-rich secretory protein family, referred to as resistin-like molecules (RELM) or 'found in inflamatory zone' (FIZZ). Resistin is an adipocytokine that appears to be regulated by PPARγ and is down-regulated by agonists of PPARγ. These agonists are suggested to regulate bone turnover in diabetic patients. However, few studies have reported effects of resistin on bone metabolism, although recent work indicates that both osteoblasts and osteoclasts express it and an inverse correlation has been shown between serum resistin levels in humans and lumbar BMD. Resistin is highly expressed in bone marrow containing mesenchymal cells, precursors of both osteoblasts and adipocytes. Differentiation into the osteoblast lineage is inhibited by PPARγ, while adipocytes are stimulated.

In the present study we explored the activity of resistin in bone cell function in vitro. Resistin activated osteoblast proliferation at concentrations of 10^{-10}M and greater in primary cell cultures and in the calvarial organ culture model. In mouse bone marrow cultures, resistin (10^{-8}M) stimulated osteoclastogenesis and bone resorption was increased in the calvarial organ culture model (10^{-10}M and greater). These data suggest elevated levels of resistin may contribute to higher levels of bone turnover.

Further investigations are required to explore the potential role of PPARγ, and hormones like resistin that are likely regulated by the receptor, in bone metabolism in humans.

P-TUE-25

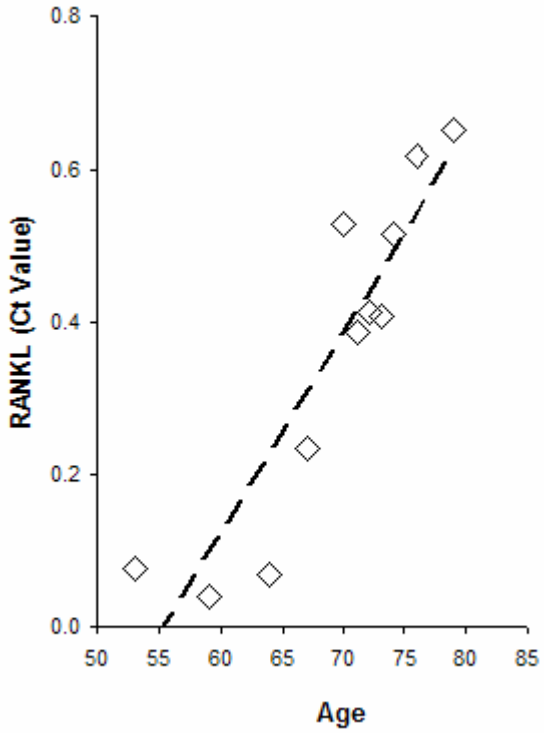
Circulating RANKL is inversely related to RANKL mRNA levels in bone

H. Tsangari[1], S. Neale[2], S. Hay[2], B. Hopwood[1], S. Pannach[2], M. Chehade[2,3], N. Fazzalari[1,3] and D. Findlay[2,3]
[1]Division of Tissue Pathology, Institute of Medical and Veterinary Science, and [2]Department of Orthopaedics and Trauma, Royal Adelaide Hospital and [3]University of Adelaide

Aim: Many reports describe the circulating levels of RANKL and OPG in health and disease. However, neither the significance of these parameters, nor their relationship to the expression of these molecules in bone, has been established. The aim of this study was to measure, in the same human subjects, the circulating levels of RANKL and OPG, and the corresponding levels of mRNA encoding these proteins, in trabecular bone.

Methods: Fasting blood samples, for measurement of serum OPG and total RANKL, were obtained on the day of surgery from patients presenting for hip replacement surgery for primary osteoarthritis. Intra-operatively, samples of intertrochanteric trabecular bone were collected for analysis of OPG and RANKL mRNA, using real time RT-PCR. Samples were obtained from 29 patients (11 males, age range 53-79; 18 females, age range 47-79).

Results: Serum OPG levels increased over the age range of these patients, in both males and females. In neither group did the levels of OPG mRNA in bone significantly relate to age. In the males, OPG serum levels and OPG mRNA levels were positively related (r = 0.74). RANKL mRNA levels were strongly positively related to age in the male group (r = 0.91; Figure) but not significant in the females. Serum RANKL levels related negatively (r = -0.70) to RANKL mRNA levels, in the males only.



Conclusions: This is the first report showing a relationship between serum RANKL and the expression of RANKL mRNA in the bone microenvironment. Ongoing work will investigate the intriguing negative relationship between these parameters.

P-TUE-27

Effects of Thrombin on Bone Resorption by Human Osteoclasts

S. Sivagurunathan[1], C.N. Pagel[1], R.N. Pike[2] and E.J. Mackie[1]
[1]School of Veterinary Science, University of Melbourne
[2]Department of Biochemistry and Molecular Biology, Monash University

The serine protease thrombin is well known to have a central function in blood coagulation, converting fibrinogen to fibrin, but it also exerts specific hormone-like effects on cells, including bone cells through cleavage of protease-activated receptors (PARs)-1, -3 and –4, of these PAR-1 and PAR-3 are expressed by human peripheral blood mononuclear cells (PBMC). Thrombin has been shown to stimulate osteoclastic bone resorption in rodent organ culture, however little is known about the mechanism of thrombin's effect. The aim of the current study was to investigate whether thrombin can regulate human osteoclast differentiation or activity in an *in vitro* system with an exogenous source of RANKL and human macrophage-colony stimulating factor (M-CSF). PBMC were cultured on whale dentine and induced to differentiate to osteoclasts by RANKL and M-CSF. Resorptive activity was assessed as resorption pit area by scanning electron microscopes. Thrombin markedly inhibited bone resorption over 21 days of culture. In order to determine whether this was due to cleavage of RANKL or M-CSF by thrombin, these factors were treated with thrombin for 0.5 hrs

at 37°C, and then the thrombin activity was inactivated by D-phenylalanyl-L-polyl-L-arginine-chloromethyl ketone (PPACK). This medium was unable to stimulate bone resorption. Thrombin did not affect the proliferation of PBMC as analysed by BrdU incorporation. The thrombin's inhibition of bone resorption may be due to thrombin cleavage of either RANKL or M-CSF, rather than to activation of one of its receptors.

CELL BIOLOGY

P-TUE-29

A Phytoestrogenic extraction derived from epimedium prevents steroid-associated osteonecrosis through inhibiting adipogenic differentiation and promoting angiogenesis of mesenchymal stem cells

Sheng H[1], Qin Ling[1], Zhang G[1], Cheung, W. H[1], Leung PC[2], Leung KS[1]
1. Department of Orthopaedics & Traumatology, The Chinese University of Hong Kong
2. Institute of Chinese Medicine, The Chinese University of Hong Kong

Objectives A phytoestrogenic extraction derived from Epimedium(I-Sb) has been proven to be effective in prevention of steroid-associated osteonecrosis(ON) in our previous study. This study was designed to explore its underlying mechanisms by studying the extravascular events including the adipogenic differentiaiton and angiogenesis of mesenchymal stem cells(MSCs).

Methods Twenty-four mature male rabbits were divided into three groups: normal control group, ON group, and ON + I-Sb group (I-Sb group). The phytoestrogenic extraction I-Sb was administrated orally for 4 weeks from the time when the rabbits were injected with steroid. Bone marrows were drawn from proximal femurs and cultured for colony-forming-unit fibroblasts(CFU-Fs). The CFU-Fs were stained with Giemsa and quantified; The adipogenic differentiation was evaluated by Oil Red O staining. The expression of osteogenic and adipogenic transcription factors core binding factor {alpha}1(Cbfa1) and peroxisome proliferator activated receptor {gamma} 2 (PPARγ2), and vascular endothelial growth factor (VEGF) were analyzed by RT-PCR.

Results The number of CFU-Fs in I-Sb group was 2.75 times higher than ON group, but accounted for 69.6% of control group; The adipocyte-like cells decreased from 3.2 times in ON/Control to 1.5 times in I-Sb/Control. RT-PCR results showed Cbfa1 gene expression increased from 65% in ON group to 87% in I-Sb group, compared with control group, while PPARγ2 decreased from 2.1 times in ON/Control group to 1.3 times in I-Sb/Control group. VEGF gene expression increased from 51% in ON/Control group to 89% in I-Sb/Control group.

Conclusions The herbal I-Sb could inhibit MSCs differentiation into adipocytes and enhance angiogenesis in steroid-associated ON.

P-TUE-31

Regulation of mouse BAMBI gene expression

T. Kondo, R. Kitazawa, and S. Kitazawa
Division of Molecular Pathology, Kobe University Graduate School of Medicine, Kobe, Japan

As a pseudoreceptor lacking an intracellular domain of type I receptor of the TGF-β family, BMP and activin membrane-bound inhibitor (BAMBI) is known to interact with many of the type I and II TGF-β receptors and to function as a negative regulator of TGF-β signaling. Here, we analyzed mouse BAMBI gene expression during osteoblastic differentiation. The steady-state transcription of the BAMBI gene in ST2 cells was twice that in MC3T3-E1 cells. BAMBI mRNA expression increased 95-fold in C2C12 cells induced into the osteoblastic lineage by rhBMP-2. Transient transfection studies showed that mouse BAMBI promoter activity increased 1.8-fold by TGF-β, 1.2-fold by rhBMP-2 and 1.9-fold by LiCl, an agonist of the β-catenin signaling. BAMBI is, therefore, speculated to be positively regulated by both TGF-β/BMP and Wnt/β-catenin signaling pathways. In the 5'-flanking region of the mouse BAMBI gene numerous CpG loci are clustered to form a typical CpG island. Southern blot analysis to screen the methylation status revealed the possible involvement

of the epigenetic mechanism in tissue-specific BAMBI gene expression. Since BAMBI plays an important role as part of the negative feedback loop system in TGF-β/BMP-2 signaling, we speculate that it is involved in preventing part of the precursor osteoblastic population from terminal differentiation into osteocytes. We are currently investigating the relation between mouse BAMBI gene inactivation by promoter hypermethylation and the terminal differentiation of osteoblasts into osteocytes.

P-TUE-33

PTHrP sensitises breast cancer cells to Apo2L/TRAIL-mediated cell death in a cell cycle dependent manner

S. Bouralexis, M. Vazquez, V. Cheung, T.J. Martin and M.T. Gillespie
Bone, Joint and Cancer unit, St. Vincent's Institute, 9 Princes St. Fitzroy, Victoria, 3065

Parathyroid hormone-related protein (PTHrP) is a multifunctional protein that is produced by approximately two-thirds of breast cancers. A clinical study associates breat cancer PTHrP expression with enhanced patient survival We investigated the interaction of PTHrP with molecules known to link into cell survival and cell death pathways namely Apo2L/TRAIL. Apo2L/TRAIL is a member of the tumour necrosis factor (TNF) family of cytokines and induces death of tumour cells, but not normal cells. Its potent apoptotic activity is mediated through cell surface death domain-containing receptors, DR4/TRAIL-R1 and DR5/TRAIL-R2. We over-expressed PTHrP in a number of breast cancer cell lines and assessed their DNA content and determined their responsiveness to Apo2L/TRAIL. Compared to parental and vector transfected cells, PTHrP over-expression in either MCF-7 or MDA-MB-231 enhanced cell cycle progression of synchronized. Proliferation assays on synchronized cells demonstrated that PTHrP over-expressing cells had an increased growth rate over parental and vector controls. mRNA and flow cytometric analysis of TRAIL receptors demonstrated an increase of the Death receptors DR4 and DR5 in cells over-expressing PTHrP. No increase in Decoy receptor was noted. Interestingly, this increase in death receptor expression appeared to be cell cycle dependent. Stimulation with Apo2L/TRAIL in PTHrP over-expressing cells resulted in a greater than 2 fold increase in apoptosis. This highlights a new action for PTHrP in breast cancer that could be related to cell survival control.

P-TUE-35

The bacterial gene *LFPA* influences the potent induction of calcitonin receptor and osteoclast-related genes in *Burkholderia pseudomallei*-induced TRAP-positive multinucleated giant cells

J.A. Boddey[1], C.J. Day[2], C.P. Flegg[1], R.L. Ulrich, S.R. Stephens[2], I.R. Beacham[1], N.A. Morrison[2] and I.R.A. Peak[1]
[1]Institute for Glycomics and [2]School of Medical Science, Griffith University, Gold Coast, Queensland, Australia. [3]United States Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, Maryland, USA

Osteoclasts are multinucleated cells that share many characteristics with macrophages. However, the extent to which other macrophage related giant cells have osteoclast features is not known. In addition, the extent to which so-called osteoclast related gene represent macrophage functions is still largely unknown. We used bacteria to explore this question. *Burkholderia pseudomallei* intracellular pathogen and the causative agent of melioidosis, a disease endemic in Northern Australia and south east Asia. *B. pseudomallei* rapidly modifies infected macrophage-like cells in a manner analogous to osteoclast differentiation: including multinucleation and expression of mRNA for chemokines MCP-1, MIP-1γ, and RANTES, and the transcription factor NFAT2. An increase in expression of these factors was also observed after infection with *B. thailandensis*. Gene-expression of osteoclast markers calcitonin receptor (CTR), cathepsin K (CTSK), and tartrate resistant acid phosphatase (TRAP), was also increased by *B. pseudomallei*-infected. *B. pseudomallei*-infected cells showed remarkably similar expression profiles to cells treated with RANKL. Analysis of dentine resorption by *B. pseudomallei*-induced osteoclast-like cells revealed that demineralisation may occur but that authentic excavation does not take place under the tested conditions. Furthermore, we identified and characterised *lfpA* (for lactonase family protein A) in *B. pseudomallei*, which shares significant sequence similarity with the eukaryotic protein 'regucalcin', also known as 'senescence marker protein 30' (SMP-30). Mutation of *lfpA* reduced expression of the tested host genes, relative to the response to wild-type *B. pseudomallei*. We show

that *lfpA* is required for optimal virulence *in vivo* and is necessary for the induction of osteoclast markers by *B. pseudomallei*.

P-TUE-37

Identification of genes cooperatively regulated by RUNX2 and BMP2

A.S.J. Stephens and N.A. Morrison
Genomics Research Centre, School of Medical Science, Griffith University Gold Coast Campus, PMB 50 Gold Coast Mail Centre, Queensland 9726 Australia

Skeletogenesis is a complex process characterized by the recruitment and differentiation of specific cell lineages in areas destined to become bone. Skeletal development and bone remodelling require the coordinated activity of a variety of transcription factors, co-factors and signalling molecules. RUNX2 plays an important role during bone formation by directing the differentiation and development of osteoblasts from mesenchymal progenitors. BMP2 is a powerful promoter of bone formation and belongs to the TGF-β superfamily. The coordinated activity of BMP2 and RUNX2 is necessary for successful bone development and remodelling. RUNX2 and BMP2 dependent gene expression was investigated through the creation of a series of stably transfected NIH3T3 cell lines. The mRNA expression profile of NIH3T3 cells was compared to the expression profile of NIH3T3 cells overexpressing both RUNX2 and BMP2 via cDNA microarray analysis. Eight differentially regulated genes, CCL9, CSF2, DPT, EHOX, LUM, MMP-13, OSF-1 and POSTN were subjected to quantitative RT-PCR using cDNA derived from NIH3T3 cells and NIH3T3 cells overexpressing RUNX2 (NIH3T3-RUNX2), BMP2 (NIH3T3-BMP2) and both BMP2 and RUNX2 (NIH3T3-BMP2-RUNX2). CSF2, EHOX and MMP-13 were determined to be synergistically induced by RUNX2 and BMP2. DPT, LUM, OSF-1 and POSTN were cooperatively repressed by RUNX2 and BMP2. CCL9 repression was dependent upon BMP2. We have established a tissue culture model enabling the identification of genes regulated by RUNX2 and also genes cooperatively regulated by BMP2 and RUNX2 providing an insight into the complex functions carried by RUNX2 in terms of its role as a master regulator of gene transcription.

P-TUE-39

Gene expression profiling of fragility fracture bone by microarray analysis

B. Hopwood[1,4], A. Tsykin[2,4], D.M. Findlay[3,4] and N.L. Fazzalari[1,4]
[1]Division of Tissue Pathology, Institute of Medical & Veterinary Science, South Australia
[2]School of Mathematics, University of Adelaide, South Australia
[3]Department of Orthopaedics & Trauma, University of Adelaide, South Australia
[4]Hanson Institute, Adelaide, South Australia, Australia

Osteoporosis (OP) is a common age related disease characterised by reduced bone mineral density, deterioration in skeletal microarchitecture and increased risk of fragility fracture. OP affects 1 in 3 women with family and twin studies demonstrating a strong genetic component to OP. In this study we used microarray analysis to identify differences in gene expression in bone from neck of femur fragility fracture (#NOF) and non-fracture control (CTL) individuals that may shed light on the underlying molecular mechanisms predisposing individuals to fragility fracture/OP. Trabecular bone was sourced from the intertrochanteric region of the proximal femur. #NOF samples were determined to have decreased bone tissue mineralisation compared to non-fracture CTL samples. Microarray analysis was performed using Compugen human 19K oligo microarrays on 20 pairs of female, age-matched, #NOF versus non-fracture CTL samples. All analyses were performed in R using *SPOT* for image processing and *limma* for normalization and linear models. The data were characterised by small expression ratios and duplicate scans, done at different PMT voltage, were used to improve identification of regulated genes. As little as 1.2 fold changes on arrays were reliably identified and confirmed by RT-PCR as 2 fold or more. Several groups of genes not previously associated with bone fragility/OP, involved in the TGFβ signalling pathway, adipogenesis, bone development and osteoclast differentiation and function, among others, were identified as differentially expressed in #NOF bone. This study indicates the potential of microarray analysis of trabecular bone samples to identify new candidate fragility fracture/OP disease genes.

P-TUE-41

Vitamin K analogues phytonadione (K1) and menatetrenone (K2) promote the differentiation of primary human osteoblasts

K.J. Welldon, D.M. Findlay, C. Vincent and G.J. Atkins
Department of Orthopaedics and Trauma, University of Adelaide and the Hanson Institute, Adelaide, Australia

The vitamin K family members, phylloquinones (vitamin K1) and the menaquinones (vitamin K2) are currently under study for their roles in bone metabolism and as potential therapeutics for skeletal diseases. Current data suggest that K2 in particular has a positive role in post-menopausal bone loss, both as a single agent or in combination with anti-resorptives. There is considerable evidence that high plasma vitamin K levels equate with healthier bone in population based studies, and that under conditions of bone loss in both humans and animal studies, vitamin K is protective. While there is evidence for direct effects of vitamin K on rodent osteoblasts, there are few reports of the action of vitamin K in human osteoblasts. In the present study, we have investigated the effects of phytonadione (K1) and menatetrenone (K2) on human primary osteoblasts (NHBC) derived from trabecular bone. Both analogues induced mineralisation in vitro, with K2 having the more consistent effect on all parameters. K2 (10 μM) reproducibly increased calcium apposition approximately two-fold that of controls. This effect corresponded with phenotypic maturation, as assessed by the expression of alkaline phosphatase (TNSAP) and the immature osteoblast marker, STRO-1. K2 induced maturation, indicated by eventual loss of TNSAP on mature osteoblasts. Only transient effects on STRO-1 expression were observed, indicating that the principal effect was on the mature osteoblast. Consistent with this, both K1 and K2 inhibited osteoblast proliferation. Both analogues also decreased collagen type 1-alpha1 mRNA expression, while K2 but not K1 increased markedly the expression of osteocalcin mRNA. Overall, the results are consistent with K2 in particular inducing a maturational effect on human osteoblasts, increasing the prevalence of a post-osteoblast, pre-osteocyte phenotype.

P-TUE-43

Osteoclasts are functionally redundant in initial endochondral fracture union but not hard callus remodeling: insights into optimal bisphosphonate dosing

M.M. McDonald, S.K. Dulai, C. Godfrey, T. Sztynda and D.G. Little
The Children's Hospital Westmead, NSW Australia
The University of Technology Sydney

Bisphosphonates (BP's) are being investigated to augment fracture healing. However, inhibition of osteoclast function during initial endochondral fracture union and hard callus remodeling has raised concerns.

Using the BP zoledronic acid (ZA) and the osteoclast mutant incisor absent *(ia/ia)* rat we investigated the role of the osteoclast during fracture healing.

Administration of a 0.1mg/kg bolus or 5 weekly 0.02mg/kg doses of ZA or Saline commenced 1 week post fracture. Analysis of initial union was performed at 2, 4 and 6 weeks, and hard callus remodeling at 12 and 26 weeks. Further, fractures were produced in *ia/ia* rats and initial healing analysed.

Neither ZA administration nor the absence of functional osteoclasts in the *ia/ia* rats slowed the rate of endochondral fracture union, with no difference in the percent of cartilaginous callus.

ZA increased callus BMC, volume and importantly strength. Bolus ZA showed hard callus remodeling at 4 weeks post fracture; this was delayed until 6 weeks with weekly ZA. By 12 and 26 weeks bolus ZA had equal callus content of remodeled neo-cortical bone to saline, weekly ZA had significantly less at these times ($p<0.01$).

In conclusion, both ZA treatment and reduced osteoclast function did not delay endochondral fracture union, suggesting the redundancy of osteoclasts during endochondral fracture repair. While ZA treatment delayed hard callus remodeling, bolus ZA was superior to weekly, with earlier and more complete remodeling. This study supports the use of less frequent ZA doses during fracture repair, providing a stronger callus whilst minimizing delays in hard callus remodeling.

P-TUE-45

Gene array analysis of actions of PTH(1-34) and PTHrP(1-141) on committed preosteoblasts

E.H. Allan[1], T. Wei[2], K. Hausler[1], P.W.M. Ho[1], M.T. Gillespie[1], J.E. Onyia[2] and T.J. Martin[1]
St Vincent's Institute of Medical Research, Melbourne, Australia[1] and Lilly Research Laboratories, Indianapolis, IN46285, USA[2]

Recent studies using mouse genetics reveal that PTHrP produced in cells of the osteoblast lineage act upon committed osteoblast precursors to enhance their differentiation, as well as reducing apoptosis of osteoblasts and osteocytes. The main implications of these results are that locally generated PTHrP is a crucial paracrine regulator of bone remodelling, and that the anabolic action of PTH in the treatment of bone loss might simply reflect this physiological function of paracrine PTHrP. Since this implies that that the normal ligand presented to the PTH1 receptor in bone would be PTHrP, we aimed to compare the actions of PTH(1-34) with those of PTH(1-141) on committed preosteoblasts.

After they had differentiated to the stage of developing functional PTH/PTHrP receptors, Kusa 4b10 cells were treated with maximum doses of PTH (1-34) or PTHrP (1-141) for 1, 6, 24 hours. RNA was prepared and used to interrogate whole mouse genome Affymetrix arrays. For array profiling and pathway mapping and annotation Spotfire Bioinfomatic Software was used. Several genes known to be regulated through PTH1R (e.g. RANKL, IL6, RGS-2) were used to validate responses on independent Kusa 4b10 RNA samples. In addition, RNA from rat UMR 106-01 cells was used in some validation studies. Bioinfomatic analysis revealed sets of genes that responded to both PTH and PTHrP and some that appear to respond uniquely to either PTH(1-34) or PTHrP(1-141).

P-TUE-47

Carotenoid β-cryptoxanthin stimulates apoptotic cell death and suppresses cell function in osteoclastic cells

S. Uchiyama and M. Yamaguchi
Laboratory of Endocrinology and Molecular Metabolism, Graduate School of Nutritional Sciences, University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka 422-8526, Japan

The effect of β-cryptoxanthin, a kind of carotenoid, on osteoclastic cells in mouse marrow culture system in vitro was investigated. The macrophage colony-stimulating factor (M-CSF)-dependent bone marrow macrophages were cultured in the presence of M-CSF and receptor activator of NF-κB ligand (RANKL) for 4 days. The osteoclastic cells formed were further cultured in medium containing either vehicle or β-cryptoxanthin (10^{-8} – 10^{-6} M) with or without M-CSF and RANKL for 24 to 72 h. Osteoclastic cells were significantly decreased with culture of β-cryptoxanthin (10^{-7} or 10^{-6} M) with or without M-CSF and RANKL for 72 h. β-Cryptoxanthin (10^{-8} M)-induced decrease in osteoclastic cells were significantly inhibited in the presence of caspase-3 inhibitor. Culture with β-cryptoxanthin induced DNA fragments of adherent cells for 24 or 48 h, indicating apoptotic cell death. Apoptosis-related gene expression was determined using RT-PCR. Culture with β-cryptoxanthin (10^{-7} or 10^{-6} M) caused a significant increase in caspase-3 mRNA expression in the presence or absence of M-CSF and RANKL, and it significantly increased Bcl-2 and Apaf-2 mRNA expressions without M-CSF and RANKL. Akt-1 mRNA expression was not significantly changed with culture of the carotenoid. Moreover, TRACP activity, or TRACP and cathepsin K mRNA expressions were significantly decreased with culture of β-cryptoxanthin in the presence or absence of M-CSF and RANKL. This study demonstrates that β-cryptoxanthin has stimulatory effects on apoptotic cell death and suppressive effects on osteoclastic cell function.

P-TUE-49

Role of mathematical modeling in bone biology: from intracellular signaling to tissue level

P. Pivonka[1], D. Smith[1], B. Gardiner[1] and C. Dunstan[2]
[1]Biomedical Engineering Group, The University of Melbourne, Melbourne, VIC, [2]Bone Biology Laboratory, ANZAC Research Institute, Sydney, NSW, Australia

With the rapid growth of knowledge in bone biology and the rapid development of mathematical modeling tools, it is challenging to be on top of all the new developments. This presentation aims to highlight recent developments in mathematical modeling and how these techniques can be applied to advance our current knowledge on bone biology over various scales of observation. The choice of examples is primarily based on our current research projects. The first example deals with modeling of the Wnt signalling pathway. This pathway plays a critical role in organism development including bone formation and in directing cell attachments and proliferation. In the adult, it is this same signaling pathway that is believed to be reactivated for many cancers. The hallmarks of malignant cancer are inappropriate proliferation, invasion and metastasis. The model development in Lee *et al*. (2003) benefited from the choice of a simplified experimental system. The experimental component of their research involved extracting the complete cytoplasm from a Xenopus egg and homogenising the contents. This provide an experimental model system without the complexity introduced by spatial distribution of molecules involved in the signaling pathway and without the added complexity of the cell membrane receptor signaling. The concentrations of key molecules (e.g. β-catenin) were then tracked after the addition of other components of the signaling pathway (e.g. Axin). This then provided an experimental system accessible to model formulation and experimental manipulation.

The second example deals with modeling of the interactions of cells of osteoblastic and osteoclastic origin. Discovery of the RANK-RANKL-OPG pathway in the end 90s revealed that osteoclast formation was tightly regulated by osteoblast/stromal cells. Factors exhibiting strong effects on resorption (such as PTH, prostaglandins, interleukins, vitamin D3, corticosteroids) all signal to the osteoblast/stromal cells. Several attempts have been made to model parts of this system. Recently however, an integrated model including various cell lines of the osteoblastic and osteoclastic lineage, and including the RANK-RANKL-OPG pathway was proposed (Lemaire *et al*. 2004). It has been demonstrated that many of current bone diseases can be qualitatively reproduced by this model. Further, possible therapeutic strategies can be studied with such a model, as well as in vivo and in vitro (i.e. cell culture) experiments.

P-TUE-51

A study of osteoclast effects on osteoblast

Y-M. Li, F-J. Yang, Y-M. Sun and X-J. Zeng
Institute of Radiation Medicine, Chinese Academy of Medical Sciences, Tianjin, PR China 300192

Aims: This study tried to probe into the effects of osteoclast (OC) and its sub-cellular structures on osteoblast(OB) growth, OB differentiation and its function.

Method: Spleen cells from C57 mice administrated 5-FU were induced by IL-3, 6 and GM-CSF, 1α, 25-$(OH)_2D_3$ to obtain sufficient OCs. Mouse OB cell line MC3T3-E1 were co-cultured several days with OC, the supernatant of OC culture media, and OC's sub- cellular structures, in which the OCs' either taken from culture plate or from bone slices where OCs were cultured on, viz post-bone-resorption OCs'. Then the osteoblast cell proliferation rates, alkaline phosphates activities (ALP), Osteocalcin, and the expression of Core binding factorα1(Cbfα1) were measured.

Results: OC and the supernatant of OC culture media made the proliferation rate of osteoblast increased, OC and its nuclear, and the supernatant of OC culture media could promote the activity of ALP, Osteocalcin and the expression of Cbfα1 up regulation.

Conclusion: The pre-osteoclast and osteoclast and their function may have the biological effects on the following osteoblast/pre-osteoblast. Therefore, it is necessary to unfold and study the effects of osteoclast on osteoblast/pre-osteoblast and its mechanisms under normal and pathological condition.

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P-TUE-53

Establishment of an in vitro model for studying physiological death of chondrocytes

Y. Ahmed, L. Tatarczuch, K-S. Chen, C.N. Pagel, H.M. Davies, M. Mirams and E.J. Mackie
School of Veterinary Science, University of Melbourne, Parkville, Australia

Death of hypertrophic chondrocytes is an obligatory step in the endochondral ossification pathway. It has recently been reported that hypertrophic chondrocytes die by non-apoptotic forms of physiological cell death (PCD). The aim of the current study was to establish a culture system for studying hypertrophic chondrocyte PCD *in vitro*. Chondrocytes isolated from prenatal, neonatal and older (growing and adult) horses were cultured as pellets in 10% foetal calf serum (FCS) or 10% horse serum (HS). After different time points, the pellets were collected and examined histologically, and RT-PCR to detect collagen type II and Sox9 expression was carried out. Chondrocytes isolated from prenatal foals formed a cartilage-like tissue grossly and histologically, and expressed collagen type II and Sox9 mRNA. Some cells expressed alkaline phosphatase, and extracellular matrix calcification increased from 7 to 28 days. The pellets showed two types of hypertrophic chondrocytes (dark and light cells) dying by the same modes of PCD seen *in vivo*. Cells isolated from older horses did not undergo hypertrophy. They formed intramembranous inclusion bodies, and included cells of osteoblastic appearance. Pellets from neonatal foals cultured in FCS resembled the pellets from older horses, however, those grown in HS underwent hypertrophy and showed dark and light cells but also contained inclusion bodies. This culture system will greatly assist in studying the molecular mechanisms of chondrocyte PCD.

P-TUE-55

A proteomics study on circulating monocytes (precursors of osteoclasts) identified functional proteins for osteoporosis

F-Y. Deng[1], C. Jiang[1], L-M. Li[1], S. Wu[1], Y. Chen[1], H. Jiang[1], F. Yang[1], S-F. Lei[1], X-D. Chen[1], P. Xiao[2] and H-W. Deng[1, 2]
1. Laboratory of Molecular and Statistical Genetics and the Key Laboratory of Protein Chemistry and Developmental Biology of Ministry of Education, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, P. R. China
2. Departments of Orthopedic Surgery and Basic Medical Sciences, University of Missouri - Kansas City, Kansas City, Missouri, 64108-2792, USA

Circulating monocytes may serve as the progenitors of osteoclasts and/or produce cytokines important to osteoclast differentiation, activation, and apoptosis. Protein expression studies of circulating monocytes between human subjects with high vs. low peak bone mass (PBM) may identify proteins functionally relevant to osteoclastogenesis and osteoporosis.

A population database, composed of up to 1000 Chinese adult females, was archived for extreme sampling in the present study. All the females belong to Chinese Han ethnicity, aged 20-45 yrs, and excluded from chronic diseases and conditions, which might potentially affect bone mass or metabolism. A total of 42 unrelated females were recruited: 21 individuals from the high extreme and 21 from the low extreme of the hip PBM distribution (Z score, 1.63 ± 0.16 vs. -1.67 ± 0.15, mean ± SE). Peripheral blood monocytes were freshly isolated using a negative isolation technique. Proteomics approaches including protein extraction and quantification, 2D-PAGE, gel spots quantification, in-gel digestion, and mass spectrometry (MS) or MS/MS, were used to identify proteins differentially expressed between the two subgroups.

With the help of statistical analyses, a total of 96 proteins were selected and identified. Among them, 78 were averagely up-regulated and 12 were averagely down-regulated in high BMD subgroup. Gene ontology (GO) classification indicated that most of these proteins are involved in cellular physiological process or metabolism (Table 1A), and 16 proteins are involved in regulation of physiological process. Among the identified proteins, RSU1, GSN, K-ALPHA-1, GPX1, PRDX3, PSMA5, and P4HB have been validated by western blotting for their differential expression (Table 1B, ↑ and ↓ indicate up- or down- regulation in high vs. low BMD subgroup). Previous evidences supported that some of them are associated with osteoclastgenesis and osteoporosis. To take gelsolin (GSN) for example, consistent with its down- regulation in high BMD group in this study,

previous study showed that its deficiency may block the osteoclasts' podosome assembly and produce increased bone mass and strength. Additionally, peroxiredoxin 3 (PRDX3), up-regulated in high BMD group in this study, possesses the function to suppress osteoclastic differentiation.

In conclusion, the present study represents our pioneer effort to utilize the strategy of in vivo proteomic analysis for gene identification of osteoporosis in humans. Proteomics strategy, combined with extreme sampling scheme, was proved promising for research of complex disease including osteoporosis. Continuous effort will explore the function of the disclosed factors in Chinese population.

Table 1A. Classification of the Identified Proteins According to GO Biological Process

Category	Numbers of proteins
Cellular physiological process	60
Metabolism	51
Regulation of cellular process	17
Regulation of physiological process	16
Cell Communication	15
Response to stimulus	15
Organismal physiological process	12
Localization	11
Morphogenesis	8
Organ development	7
Positive regulation of biological process	7
Negative regulation of biological process	5
Growth, cell differentiation or death	4
Locomotary behaviour	3
Other functions	7
Unknown	11

Table 1B. Differentially Expressed Proteins Validated by Western Blotting

Proteins identified by MS or MS/MS	Expression (high vs. low BMD)
gelsolin	↓
K-ALPHA-1 tubulin	↑
ras suppressor protein 1	↓
glutathione peroxidase 1	↑
peroxiredoxin 3	↑
prolyl 4-hydroxylase, beta subunit	↑
proteasome subunit, alpha type, 5	↑

P-TUE-57

Isoprenoid-independent pathway is involved in apoptosis induced by risedronate, a bisphosphonate (BP), in which Bim plays a critical role in breast cancer cell line MCF-7

K. Suyama, Y. Noguchi, A. Nagata, T. Yoshida, N. Koide, T. Tanaka, Y, Saito and I.Tatsuno
Department of Clinical Cell Biology, Graduate School of Medicine, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba-shi, Chiba 260-8670, Japan

Aims: Bisphosphonate (BP) has been demonstrated to prevent the bone metastasis of breast cancer and improve its prognosis. BP's effects are not only come from local bone effects but also come from direct effect to cancer cells that cause apoptosis. Although BP and HMG CoA reductase inhibitors were reported to induce apoptosis through inhibiting production of isoprenoids, the details of mechanism in the BP-induced apoptosis have been still obscure. In the present study, we examined risedronate (Rise)-induced apoptosis in the comparison with cerivastatin (Ceriva)-induced apoptosis in human breast cancer cell line MCF-7 cells.

Methods: 1) MCF-7 cells were treated by various concentrations of Rise and Ceriva with/without geranylgeranyol (GGOH) and farnesol (FOH) and cell growth and apoptosis was checked. 2) Expression of activated caspases and Bim were checked by western blot. 3) The effect of Inhibition of Bim induction by siRNA to the apoptosis caused by Rise was checked.

Results: 1) Rise and Ceriva inhibited proliferation at low concentrations, Ceriva induced cell cycle arrest at G1 phase but Rise induced G2 arrest. On the other hand, both rise and Ceriva induced apoptosis at high concentrations with activation of caspases. The apoptosis induced by Ceriva was restored by GGOH. The apoptosis induced by Rise was recovered by GGOH partially. 2) Bim expression is increased by Rise, not Ceriva, in time and dose dependent manner. 3) Inhibition of Bim induction by siRNA resulted in decrease of apoptosis by Rise.

Conclusion: These results showed that Rise induces the apoptosis both isoprenoid-dependent and -independent pathway. And Bim plays a critical role in isoprenoid independent pathway in MCF-7.

ORTHOPAEDICS, RHEUMATOLOGY AND TISSUE BIOLOGY

P-TUE-60

Does S100A8 protein play a role in articular cartilage degeneration?

*H. Zreiqat, #M. Smith, $C.L. Geczy and #C.B. Little
**Biomaterials and Tissue Engineering Research Unit, Biomedical Engineering, School of AMME, #Raymond Purves Laboratory, Institute of Bone and Joint Research, The University of Sydney, Sydney 2006, $School of medical Sciences, University of New South Wales, Sydney 2052 NSW, Australia*

Introduction*:* S100A8, a calcium binding protein, is upregulated in autoimmune diseases and rheumatoid arthritis (RA). Recent work has shown that S100A8 is expressed by chondrocytes and is upregulated by inflammatory cytokines. The effect of S100A8 on chondrocytes and its role in osteoarthritis (OA) has not yet been elucidated. This study aims to determine the role of S100A8 in cartilage degradation *in vivo* and *in vitro*. Specifically, we evaluated (1) whether S100A8 expression is modulated in articular cartilage chondrocytes in OA and (2) the effect S100A8 exerts on anabolic or catabolic factors in cultured chondrocytes.

Materials & Methods: OA was induced in wild type C57BL6 mice by destablilization of the medial meniscus. *In vitro* mRNA expression of aggrecan, MMP-13, type I and II collagens, ADAMTS-1, -4 & -5, were analysed using cultured adult ovine articular chondrocytes±10^{-7}M S100A8.

Results: In normal joints, positive immunostaining was observed in chondrocytes in the non-calcified cartilage and in osteocytes and occasional osteoblasts. There was progressive loss of S100A8 immunostaining in chondrocytes from 2-8 weeks following induction of OA, in association with increasing cartilage degradation. In contrast, there was no change in the S100A8 localization in bone. qRT-PCR revealed significant downregulation of MMP-13 in chondrocytes stimulated with S100A8 *in vitro*. There was no effect of S100A8 on the expression of the other genes examined.

Conclusion: Increased MMP-13 expression is associated with progressive cartilage degeneration in OA. Our data indicated that S100A8 down regulates MMP-13 expression by chondrocytes. Loss of S100A8 in non-calcified cartilage in OA may therefore play a role in the pathogenesis of cartilage breakdown.

P-TUE-62

Altered gene expression in early lesions of osteochondrosis

M. Mirams, L. Tatarczuch, Y.A. Ahmed, H.M.S. Davies and E.J. Mackie
School of Veterinary Science, University of Melbourne, Parkville, Australia

Osteochondrosis is a developmental disorder of bone which has been described in a number of domestic animal species as well as in humans. In the process of endochondral ossification, chondrocytes in growth cartilage undergo proliferation, hypertrophy and physiological death. In osteochondrosis, failure of endochondral ossification in articular-epiphyseal growth cartilage leads to the retention of cartilage foci in the subchondral bone. An equine model of the disorder was used in which osteochondrotic lesions were generated by feeding growing animals a high energy diet. Lesions were collected at an early stage of the disorder. Expression of mRNA of a number of genes involved in endochondral ossification was examined in chondrocytes from lesions by real time RT-PCR. Histological examination showed that, adjacent to the bone, chondrocytes in lesions were arranged in clusters similar in appearance to proliferating chondrocytes in the growth plate, while chondrocytes in normal articular cartilage were arranged mostly in pairs. Expression of matrix metalloproteinase-13, Runx2, and vascular endothelial growth factor mRNA was elevated in the lesions when compared to controls consisting of cartilage pooled from normal joints, as measured by real-time RT-PCR, while expression of connective tissue growth factor mRNA was decreased. These results suggest that osteochondrosis results from a focal increase in chondrocyte proliferation, rather than a loss of the ability to remodel cartilage matrix or attract vascular invasion.

P-TUE-64

The use of heparan sulfate to augment fracture repair in a rat fracture model

R.A. Jackson[1,2], M.M. McDonald[3], V. Nurcombe[2,4], D.G. Little[3] and S.M. Cool[2,4]
[1]School of Biomedical Sciences, University of Queensland, 4072 Australia. [2]Laboratory of Stem Cells and Tissue Repair, Institute of Molecular and Cell Biology, Proteos, 61 Biopolis Drive, 138673 Singapore. [3]Orthopaedic Research and Biotechnology, The Children's Hospital, Westmead, NSW 2145, Australia. [4]Department of Orthopaedic Surgery, Yong Loo Lin School of Medicine, National University of Singapore, 119074 Singapore

Fracture healing is a complex process regulated by numerous growth and adhesive factors expressed at specific stages during healing. The naturally occurring, cell surface-expressed sugar, heparan sulfate (HS), is known to bind to and potentiate the effects of many classes of growth factors, and as such, may be a potential candidate therapy for enhancing bone repair. This study investigated the local application of bone-derived HS in the repair of rat femoral fractures. After 2 weeks, there was a significant increase in the callus size of rats administered with 5 µg HS compared to the control and 50 µg HS groups, presumably due to increased trabecular bone volume rather than increased cartilage production. In addition, 5 µg HS increased the expression of ALP, Runx2, FGF-1, IGF-II, TGF-β1 and VEGF. It is hypothesized these increases resulted from changes in HS-mediated receptor/ligand interactions that increase local growth factor production to augment bone formation. The findings of this study demonstrate the anabolic potential of HS in bone repair by recruiting and enhancing the production of endogenous growth factors at the site of injury.

P-TUE-66

Vertebral fractures affect paraspinal muscle control

A. Briggs[1,2], A. Greig[1,2], K. Bennell[1] and P. Hodges[3]
[1] Centre for Health, Exercise and Sports Medicine, School of Physiotherapy; and
[2] Department of Medicine, Royal Melbourne Hospital, University of Melbourne, Victoria.
[3] Division of Physiotherapy, University of Queensland, Queensland

The vertebral fracture cascade cannot be explained solely by low bone mass. Neuromuscular control of the trunk is important for postural control, balance and influences spinal loading. This study aimed to explore any differences in neuromuscular control of the paraspinal muscles in women with and without osteoporotic vertebral fractures. Elderly women with (n=11) and without (n=14) fractures performed rapid arm movements while standing on a flat and short base. Neuromuscular postural responses of the paraspinal muscles at T6 and T12, and deep lumbar multifidus at L4 were recorded using intra-muscular electromyography (EMG). Both groups demonstrated bursts of EMG that were significantly greater than baseline EMG before and after shoulder flexion ($p<0.05$). Paraspinal and multifidus onset occurred earlier in the non-fracture group (50-0 ms before deltoid onset) compared to the fracture group (25 ms before – 25 ms after deltoid onset) in the flat base condition. In the short base condition, EMG amplitude increased significantly above baseline earlier in the non-fracture group (75-25 ms before deltoid onset) compared to the fracture group (25-0 ms before deltoid onset) at T6 and T12; yet multifidus EMG increased above baseline earlier in the fracture group (50-25 ms before deltoid) compared to the non-fracture group (25-0 ms before deltoid). Time to reach maximum amplitude was shorter in the fracture group. Longer time to initiate a postural response and shorter time to reach maximum amplitude in the fracture group may increase vertebral strains and point to a mechanism underlying subsequent fracture aetiology. This response may also be an adaptive characteristic of the central nervous system to minimise vertebral loading time.

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P-TUE-68

Epimedium-derived phytoestrogen fractions prevent steroid-associated osteonecrosis in rabbits through inhibition of both thrombosis and lipid deposition

L. Qin[1], G. Zhang[1], H. Sheng[1], K.W. Yeung[2], H.Y. Yeung[1], W.H. Cheung[1], J. Griffith[2], C.W. Chan[3], K.M. Lee[3] and K.S. Leung[1]
1. Musculoskeletal Research Laboratory, Department of Orthopaedics & Traumatology, The Chinese University of Hong Kong, Hong Kong SAR, PR China
2. Department of Organ & Imaging, The Chinese University of Hong Kong, Hong Kong SAR, PR China
3. Lee Hysan Clinical Laboratory, The Chinese University of Hong Kong, Hong Kong SAR, PR China

Objective: This study tested the hypothesis Epimedium-derived phytoestrogen fractions (PE) might prevent steroid-associated osteonecrosis (ON) in rabbits through a unique mechanism associated with inhibition of both thrombosis and lipid-deposition.

Methods: Thirty 28-week-old male New-Zealand white rabbits were divided into control group (CON; n=14) and PE group (PE; n=16; 5mg/kg body weight / day) after receiving an established inductive protocol for inducing steroid-associated ON. Before and after inductive protocol, Dynamic-MRI was employed on bilateral femora for local intra-osseous perfusion, blood samples were examined for coagulation, fibrinolysis and lipid-transportation, and marrow samples were quantified for adipogenesis-gene mRNA expression. Six weeks later, bilateral femora were dissected for Micro-CT-based micro-angiography, and then ON lesion, intravascular thrombosis and extravascular fat-cell-size were examined histopathologically.

Results: The incidence of ON in the PE group (31%) was significantly lower than that in the CON group (93%). Compared to the CON group, local intra-osseous perfusion was maintained in the PE group. Blocked stem vessels were seldom found in micro-angiography of the PE-treated rabbits. Thrombosis incidence and fat-cell-size were both significantly lower in the PE group than those in the CON group. In the early period after induction, indicator of coagulation, fibrinolysis, lipid-transportation and adipogenesis-gene expression were found with significantly changing pattern in the PE group compared to the CON group.

Conclusion: PE was able to prevent steroid-associated ON in rabbits through inhibition of both thrombosis and lipid deposition.

Acknowledgement: This study was supported by A Research Grant of the Chinese University of Hong Kong (Project ID Ref. 6901559), Hong Kong RGC (CUHK4503/06M) and Hong Kong ITF (ITS/012/06).

Reference: Qin L, Zhang G, Sheng H, et al. Multiple bioimaging modalities in evaluation of an experimental osteonecrosis induced by a combination of lipopolysaccharide and methylprednisolone. Bone. 2006 Jun 8; [Epub ahead of print]

P-TUE-70

Insufficient repair associated with reparative neo-vasculature characterized as abnormalities in both function-structure and VEGF-VEGFR expression: A steroid-associated osteonecrosis rabbit model

G. Zhang[1], L. Qin[1]*, H. Sheng[1], K.W. Yeung [2], Y.H. Yeung[1], Chan CY[3], Cheung WH[1], J Griffith[2] and K.S. Leung [1]

1. Musculoskeletal Research Center, The Chinese University of Hong Kong, Hong Kong SAR, PR China
2. Department of Organ & Imaging, The Chinese University of Hong Kong, Hong Kong SAR, PR China
3. Lee Hysan Clinical Laboratory, The Chinese University of Hong Kong, Hong Kong SAR, PR China
** Corresponding Author: lingqin@cuhk.edu.hk*

Aim: It was to investigate reparative neo-vasculature in function, structure and VEGF-VEGFR expression in our established steroid-associated osteonecrosis rabbit model with insufficient repair.

Methods: Twenty-two 28-week old male New-Zealand white rabbits received injection protocol for establishment of steroid-associated osteonecrosis[1]. Dynamic-MRI was performed for local perfusion function on bilateral proximal femur at 0, 2, 4 and 6 weeks after injection. At each time-point in early-stage (0~2 weeks), three rabbits were sacrificed. At each time-point in late-stage (4~6 weeks), eight rabbits were sacrificed. Before sacrifice, bone marrow from left proximal femur was obtained for mRNA-expression of VEGF-VEGFR by RT-PCR. After sacrifice, right proximal femur was dissected for imaging 3-D-structure of vessel network by Micro-CT-based micro-angiography and showing 2-D-structure of vessel wall by CD31 (endothelia-cell-surface-marker) immunohistochemistry staining. VEGF-VEGFR expression was quantified by immunohistochemistry staining. Osteonecrotic lesion and lesion repair was histopathologically examined.

Results: Histopathology: Osteonecrotic lesion formation was found at 2 weeks, insufficient lesion repair was found from 4 weeks. Perfusion function: 'Maximum Enhancement' showed a significant decrease from baseline at 2 weeks and increased moderately thereafter (Fig1). Structure of vessel: A blocked stem vasculature was found in early stage. In late stage, many small disconnected neovasculature and disseminated leakage of perfused substance was found around a blocked stem vasculature (Fig2), which was accompanied by loose endothelia-cell junction. Molecular pathway: An increasing over-expression of mRNA/protein of VEGF-VEGFR was found from 2 weeks (Fig3).

Conclusion: Insufficient repair for necrotic lesion was associated with neovasculature characterized as abnormalities in function, structure and VEGF-VEGFR signaling pathway.

Acknowledgement: This study was supported by A Research Grant of the Chinese University of Hong Kong (Project ID Ref. 6901559), Hong Kong RGC (CUHK4503/06M) and Hong Kong ITF (ITS/012/06).

Reference: 1. Qin L, Zhang G, Sheng H, et al. Multiple bioimaging modalities in evaluation of an experimental osteonecrosis induced by a combination of lipopolysaccharide and methylprednisolone. Bone. 2006 Jun 8; [Epub ahead of print]

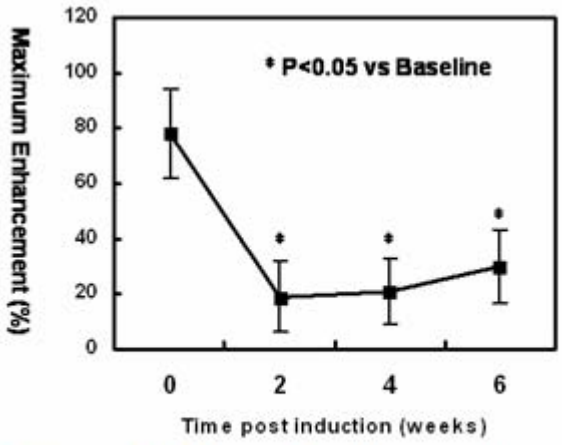

Figure 1. Perfusion function over time assessed by Dynamic MRI

P-TUE-72

Evidence for important role of osteocyte in mechanostat: steroid-associated osteonecrosis rabbits with both ineffective and catabolic shift of mechanostat

G. Zhang, L. Qin*, H. Sheng .H, W.Y. Hung, W.H. Cheung and K.S. Leung
Musculoskeletal Research Laboratory, Department of Orthopedics & Traumatology, The Chinese University of Hong Kong, Hong Kong SAR Corresponding Author: linggin@cuhk.edu.hk

Aims: Osteocytes play an important role in the proposed 'Mechanostat' for bone physiology. Osteonecrosis is characterized histopathologically as disappearance of a lot of osteocytes. We accordingly hypothesized that there might be a shift of 'Mechanostat' in our recently established steroid-associated osteonecrosis rabbit model[1], which has not been so far examined.

Methods: Twenty-four 28-week old male New-Zealand white rabbits were randomized into two groups: treatment group (n=14) receiving injection for establishment of steroid-associated osteonecrosis and control group (n=10) receiving injection with 0.9% normal saline. 6 weeks after injection, bilateral humeri were dissected for scanning the mid-diaphysis with a high resolution pQCT. PQCT-defined parameters include volumetric bone mineral density of cortical bone (DenC) as 'Material Quality', cross-sectional area of cortical bone (AreaC) as 'Bone Mass' and cross-sectional moment of inertia (CSMI) as 'Tissue Distribution'. Both 'Distribution-Mass curve' and 'Distribution-Quality curve' were used for describing 'Mechanostat' by 'linear curve estimation'[2]. Statistic difference between them was analyzed by linear regression.

Results: Numerous empty lacunae presented in cortical bone of treatment samples compared to control samples (Figure 1). A significantly higher slope of 'Distribution-Mass curve' was found in the control samples than that in the treatment samples ($P<0.05$). Estimated 'Distribution-Quality curve' in respective group showed the treatment data points shifted to the lower of

the control data points, which was defined as significant shift ($P<0.05$) (Figure 2).

Conclusion: There is both ineffective and catabolic shift of Mechanostat' in the steroid-dependent osteonecrosis rabbits. It gives strong evidence showing important role of osteocytes in Mechanostat.

Acknowledgement: This study was supported by Hong Kong RGC (CUHK4503/06M).

References:

1. Qin L, **Zhang G**, Sheng H, et al. Multiple bioimaging modalities in evaluation of an experimental osteonecrosis induced by a combination of lipopolysaccharide and methylprednisolone. Bone. 2006 Jun 8; [Epub ahead of print]

2. Ferretti JL, Cointry GR, Capozza RF, et al. Analysis of biomechanical effects on bone and on the muscle-bone interactions in small animal models. J Musculoskelet Neuronal Interact. 2001; 1:263-274.

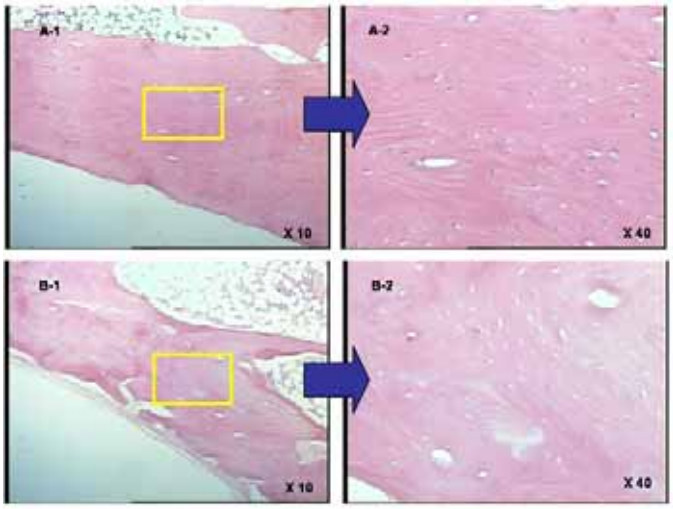

Figure 1. Numerous empty lacunae presented in cortical bone of treatment samples (B-1 and B-2) compared to control samples (A-1 and A-2).

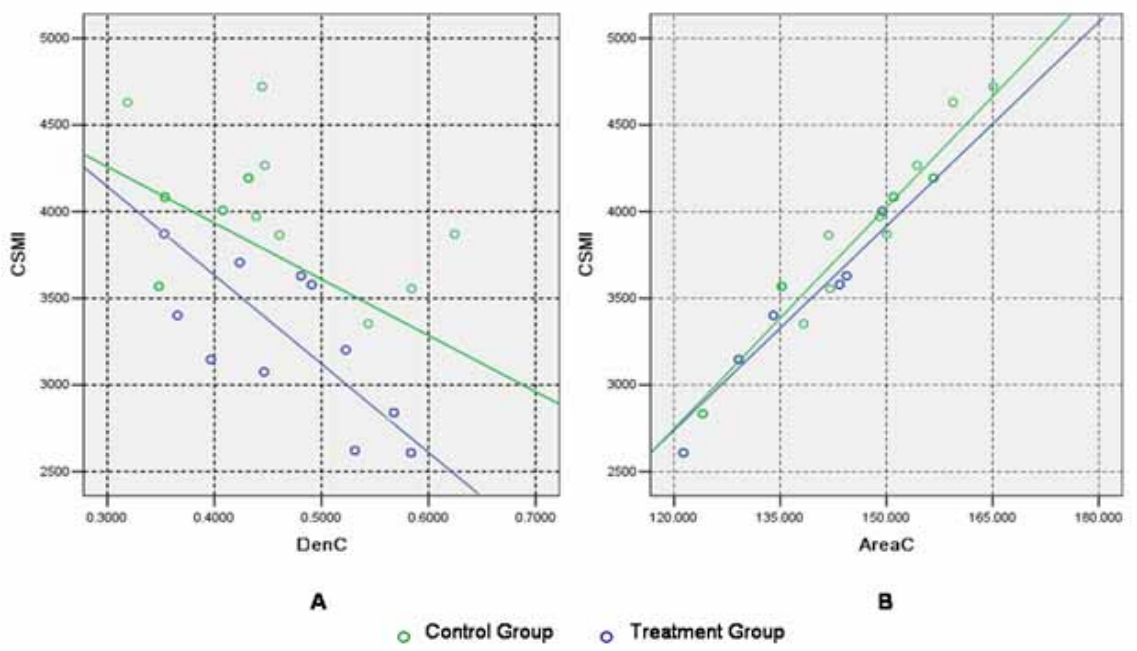

Figure 2. A significantly different pattern in 'Distribution/Quality' curve and 'Distribution/Mass' curve between treatment group and control group. **A:** The linear equeation of 'Distribution/Quality' curve was CSMI=1024.827-606.606DenC for the control samples (R^2=0.46, P<0.05), and CSMI=1386.130-938.992DenC for the treatment samples (R^2=0.52, P<0.05). **B:** The linear equation of 'Distribution/Mass' curve was CSMI=611.857+31.574AreaC for the control samples (R^2=0.92, P<0.05), and CSMI=531.508+27.539AreaC for the treatment samples (R^2=0.96, P<0.05).

CLINICAL METABOLIC BONE DISEASES

P-TUE-74

Intestinal radiocalcium absorption is related to 1,25-dihydroxyvitamin D levels but not estradiol in untreated women with postmenopausal osteoporosis

H.Wilson[1], H.Q.Zhou[1], R. Yao[1], S. Vasikaran[2], G.N. Kent[3] and R.K. Will[1]
[1]Metabolic Bone and Musculoskeletal Diseases Research Unit, and; [2]Clinical Biochemistry Royal Perth Hospital, & [3]PathWest Perth, WA.

Aims: Intestinal calcium absorption is important for maintaining calcium homoeostasis. Considerable inter-individual variability in calcium absorption exists, however the factors influencing this variation remain unclear. Vitamin D metabolites, particularly 1,25-dihydroxyvitamin D (1,25D), and estrogen have been implicated in regulation of calcium absorption in the intestine. The aim of this study was to investigate relationships between calcium absorption, 1,25D, estradiol (E_2) and various biochemical factors of bone turnover and in women with postmenopausal osteoporosis.

Method: Calcium and vitamin D replete postmenopausal women with osteoporosis (n=169), at least 6 months postmenopausal with a history of at least one past minimally traumatic fracture were studied. Parathyroid hormone (PTH) and biochemical markers of bone turnover osteocalcin, N-telopeptide (NTx) and alkaline phosphatase were measured as well as serum E_2, 1,25D, 25 hydroxyvitamin D (25D), calcium, phosphate, creatinine, albumin, urinary calcium/creatinine ratio and phosphate. Intestinal ^{45}Ca absorption was measured[1].

Results: Intestinal ^{45}Ca absorption correlated significantly to 1,25D ($r=0.287, p=0.002$) as well as urinary calcium/creatinine ($r=0.353$, $p=0.000$). Multiple linear regression confirmed that both 1,25D and calcium/creatinine were related to ^{45}Ca absorption in an enter model including age and urinary NTx (adjusted $R^2=0.227$, $p=0.031$ & 0.000, 95%CI=0.000-0.002 & 0.235-0.569, respectively).

Conclusion: Lower intestinal calcium absorption was associated with a lower serum 1,25D but not 25D, confirming that it is this metabolite that affects absorption in our population. Our results did not show a relationship between E_2 levels and calcium absorption.

1. Nordin BEC, *et al.* 1998. J Nucl Med. 39:108-13.

CLINICAL OSTEOPOROSIS

P-TUE-76

Impact of a hospital-based intervention on the outcome following minimal trauma fracture

D. Renouf, K. Quick and C. Gilfillan
Frankston Hospital, Peninsula Health Care Network, Victoria, Australia

A minimal-trauma fracture is a major risk factor for subsequent fracture with associated morbidity and mortality. Despite the availability of effective treatment, most minimal-trauma fracture patients are discharged from hospital without the initiation of medical therapy to prevent recurrent fractures.

This study was a prospective randomised evaluation of the efficacy of a hospital-based intervention versus conventional therapy on all patients with minimal trauma fracture presenting to Frankston hospital from October 2004 to August 2005.

The intervention group received clinical review during the hospital admission, outpatient DEXA scan, biochemical investigation for secondary causes of osteoporosis, a follow-up review in the endocrine outpatients clinic with treatment recommended as appropriate and a letter outlining results and treatment sent to the LMO. The conventional treatment group had no intervention except those offered by their usual practitioners. Patients were followed up by telephone interview at one year. The primary outcome measure was the proportion of patients who were initiated and remained on effective anti-fracture therapy at 1 year.

Results: A total of 169 patients were randomised, 84 in the intervention arm and 85 in the conventional arm. Investigation and treatment initiation has been completed in 50 patients in the intervention arm. A total of 55 patients have been reviewed at one year. Treatment initiation and persistence at one year is indicated in the table.

	Convention Initial therapy n = 44	**Intervention Initial therapy n = 50**	**Convention group Remain on therapy at 12 months n = 44**	**Intervention group Remain on therapy at 12 months n = 11**
Calcium	14	28	13 of 14 (93%)	4 of 5 (80%)
Vitamin D	6	26	5 of 6 (83%)	1 of 2 (50%)
Bisphosphonates	8	21	5 of 8 (62.5%)	3 of 3 (100%)
No treatment	24	17		

These preliminary results show a hospital-based intervention can increase the initiation of treatment with anti-fracture therapy after minimal-trauma fracture and improve persistence on bisphosphonate therapy.
This data will be updated prior to presentation with 12 month follow-up ongoing.

P-TUE-78

Static balance is affected by vertebral fracture but not thoracic kyphosis in individuals with osteoporosis

A.M. Greig[1,2], K.L. Bennell[1], A.M. Briggs[1,2], J.D. Wark[2] and P.W. Hodges[3]
[1]Centre for Health, Exercise and Sports Medicine, School of Physiotherapy
[2]Department of Medicine, Royal Melbourne Hospital, University of Melbourne, Victoria, Australia
[3]Division of Physiotherapy, University of Queensland, Australia

Aims: Balance impairment has been identified in people with osteoporosis, however, the relationship between osteoporosis sequelae (vertebral fracture and thoracic kyphosis) and balance is poorly understood. Altered balance strategies may contribute to fracture risk through changes in spinal loading and impact from falls. This study aimed to investigate the independent effects of vertebral fracture and thoracic kyphosis on balance characteristics.

Methods: Twenty-two postmenopausal women with osteoporosis participated in this study: 10 with and 12 without vertebral fracture. Participants were also dichotomised into low and high thoracic kyphosis groups. Force plate-derived measures were collected while participants performed three quiet standing tasks: flat surface, eyes open; flat surface, eyes closed; and short base, eyes open.

Results: All individuals reported less than 2/10 for pain on a numerical rating scale. Individuals with fracture had higher range in anteroposterior centre of pressure (COP) displacement (p = 0.049), and higher range and root mean square in AP shear forces (p = 0.048 and p = 0.032 respectively). When grouped into low and high kyphosis, there were no differences in balance parameters between groups.

Conclusions: The results indicate that individuals with vertebral fracture have altered balance characteristics compared with individuals without fracture, including greater AP COP displacement and increased use of hip strategy. Magnitude of thoracic kyphosis does not appear to affect quiet standing balance. Although the basis for the association between prevalent fracture and altered balance remains to be defined, these findings have important implications for fracture prevention and design of treatment programmes.

P-TUE-80

Clinic Based intervention of osteoporosis in patients with minimal trauma fractures. A prospective study.

I. Kuo[1,2], C. Ong[1], L. Simmons[1], J. Eisman[1,2,3], J. Center[1,2]
[1]Bone and Mineral Research Program, Garvan Institute of Medical Research [2]St Vincent's Hospital, Sydney, NSW [3]University of New South Wales, Sydney, NSW

Despite availability of effective therapy, osteoporosis remains under-treated, with <20% of postmenopausal women with prior fractures on anti-resorptive therapy[1]. The aim of this study was to determine whether individualized doctor-patient consultations would improve osteoporosis management of minimal trauma fracture subjects.

Over 2 years, 155 consecutive patients with minimal trauma fracture attending outpatient fracture clinic at St Vincent's Hospital, Sydney, underwent a registrar consultation, and were offered investigations. Results and therapeutic recommendations were given to the patient by telephone with follow-up at the Bone and Calcium clinic as required.

At baseline, 73 patients (47%) had had previous fractures, 40 (26%) had BMD testing, and only 29 (19%) were on anti-resorptive therapy. Twenty-three (15%) were on calcium and/or vitamin D.

After intervention, an additional 95 patients (83%) received BMD testing, of whom 68% were either osteopenic or osteoporotic. Age <50 but not gender predicted lower BMD uptake (p=0.04), but even in those <50, 70% had a BMD.

Of those not already on anti-resorptive therapies who undertook BMD measurement, an additional 45 patients (44%) were recommended therapy with a 78% compliance rate after 6 months. Female gender (p=0.01) and lower T-score (p=0.06) predicted compliance. Seventy-seven patients (56%) were recommended calcium and/or vitamin D supplementation, with 71% being compliant after 6 months. Female gender (p=0.002) and younger age (p=0.06) increased compliance.

Compared with previous information-based intervention in the same populatrion[2], our direct assessment-based intervention achieved a 2-fold increase in investigation and a 3-fold increase in treatment to almost 69% of those with low BMD.

[1] Eisman J, Clapham S, Kehoe L; Osteoporosis Prevalence and Levels of Treatment in Primary Care: The Australian BoneCare Study; JBMR; 19 (12), 1969-75.
[2] Biluc D, Eisman J, Center R; A randomized study of two different information-based interventions on the management of osteoporosis in minimal and moderate trauma fractures; Osteo Int; accepted 2006.

P-TUE-82

Falls and fracture risk in elderly aged care residents

S. Iuliano-Burns, X-F. Wang, J. Woods* and E. Seeman
*Endocrine Centre of Excellence, Austin Health / University of Melbourne, Heidelberg, Australia *Dept, of Medicine, Monash University, Clayton, Australia*

Falls and resulting injuries such as fractures are common in aged-care residents, and are a costly health burden.

Aim: To determine the number of falls, and fall-related injuries in elderly aged-care residents.

Methods: Prospective falls data was collected on 960 residents (mean age 83.5 years) from 17 hostels in Melbourne, Australia. Data was collected using a falls record sheet. Outcomes were verified using medical records and incident reports. Fracture history was determined from medical records. Lumbar spine and femoral neck BMD, and further health related data was ascertained on 10% of residents. Data from the first 6 months is presented below.

Results: A third of all residents fell, with a total of 747 falls recorded. Over 50% of fallers reported more than one fall. Over 40% of falls resulted in an injury, the most common of which was bruising, cuts and abrasions. Hospitalization after a fall occurred in over 10% of fallers. 12 hip fractures were reported. The risk

of fragility fractures is high with 52% of the sample tested being osteoporotic and 33% of residents having a history of fractures. Fall-related deaths, fractures and moves to high care were observed.

	All	Females	Males
Resident (#)	960	757	203
Fallers (#)	313	254	59
Fallers injured (%)	57.8	62.3	45.5
Fallers hospitalized (%)	10.1	8.6	1.5

Conclusion: The rate of falls in aged-care residents is high therefore, determining risk factors for falls and implementing falls prevention strategies is vital to minimize the cost of falls and fractures in this group.

P-TUE-84

Hypovitaminosis D and hyperparathyroidism counteract higher bone mineral density in obese women with minimal trauma fractures. A prospective study.

P, Lee, C. Yap, A. Lih, C. Nickolls and M.J. Seibel
Department of Endocrinology and Metabolism, Concord Repatriation General Hospital, NSW 2139, Australia

The association between BMI and BMD is well established in postmenopausal women. Serum 25-hydroxy vitamin D (25D) concentrations are however lower in obese than non-obese postmenopausal women. The impact of low 25D on fracture risk in obese women with high BMD is not known. We determined the relationship between BMI, BMD and 25D in postmenopausal women with a history of minimal trauma fracture (MTF).

METHODS: Anthropometric data, dietary calcium intake and physical activity were assessed in 95 women (68 ± 10 years) presenting with a MTF. BMD was measured by DXA. Serum 25D levels were measured by radioimmunoassay (Diasorin), parathyroid hormone (PTH) by automated immunoassay (Roche E170).

RESULTS: Of the women diagnosed with osteopaenia (T< 1.0SD) or osteoporosis (T< 2.5SD), 78% and 65% were overweight (BMI >25.0 kg/m^2), respectively. BMI correlated negatively with 25D (p=0.01) and dietary calcium intake (p=0.05); and positively with serum PTH concentrations (p=0.01), lumbar (p=0.01) and neck of femur BMD (p=0.01). Physical activity correlated positively with 25D (p=0.03). BMI predicted 25D and PTH independent of dietary calcium and physical activity. The association between BMI and PTH was independent of 25D.

CONCLUSIONS: While obesity is associated with higher BMD, hypovitaminosis D and hyperparathyroidism are more frequent in obese women with MTF, independent of physical activity and calcium intake. Hence, the beneficial effects of obesity may be counteracted by changes in vitamin D and mineral metabolism.

P-TUE-86

A case report: Remarkable recovery of bone density in secondary osteoporosis in a postmenopausal hyperthyroid woman

Y. Takahashi, T. Hirohashi, IK. Nakano and Y. Arii
Department of Orthopaedic Surgery, Kaetsu Hospital, Nigata, Japan
Ryouichi Yamakawa, Satoshi Ogawa and Hideo Okajima
Department of Internal Medicine, Kaetsu Hospital, Nigata, Japan

A 59-year-old woman consulted our hospital because of severe diarrhea and loss of appetite with marked weight loss from about one month previously. Some examinations were performed, from which we could detect increased levels of serum thyroid hormone (free-T3,T4), decreased levels of serum thyrotropin , goiter was revealed by ultrasound of the neck, and serum thyrotropin-receptor antibodies could be defined. Taking the above into account, the patient was diagnosed as having hyperthyroidism and was treated with thiamazole. The serum concentration of thyroid hormone declined and her complaints were reduced. Shortly thereafter

she had a sudden onset of severe pain in both ankle joints and was unable to walk. Imaging tests (X-ray exam and MRI scan) showed bone atrophy in her legs and insufficient fractures of the lower end of the both tibias.

She was found to have low bone mineral density (BMD) (FNBMD 0.506 g/㎠, 55% of YAM), and high urinary NTx (Urinary NTx/Cre 939). We treated her with bisphosphonate (alendronate) in addition to an antithyroid drug, which restored her bone density remarkably in a short period of time (after 5 months; FNBMD 0.635 g/cm^2, 69% of YAM; urinary NTx/Cre 57.4. After 10 months ; FNBMD 0.647 g/cm^2, 71% of YAM; urinary NTx/Cre 44.5 After 17 months ; FNBMD 0.737 g/cm^2, 81% of YAM.).

P-TUE-88

Fractured neck of femur pathway project: twelve month prospective observation study of clinical practice and outcomes

N.Gilchrist[1], K. Wilson[1], K. Hall[1], C. Frampton[2], J. McKie[1], K. Downes[1]
Department of Orthopaedic Surgery and Orthopaedic Medicine, Christchurch Hospital, New Zealand[1], Biostatistician, Christchurch School of Medicine, New Zealand[2]

The management of the elderly fractured neck of femur patient poses a challenge. We have developed a shared care model between orthopaedic surgeons and orthopaedic physicians. As a result of this shared care model we have introduced a clinical treatment process from presentation at accident and emergency to discharge from either the orthopaedic ward or the rehabilitation ward. Data was collected prospectively at all points during the patient journey (accident and emergency, acute ward, theatre, recovery, and orthopaedic ward and rehabilitation wards). Of the 492 fractured neck of femur patients, 420; 76% female and 23.3% male with an average age of 84.3 years, were deemed suitable for analysis. The average length of stay was 10 days in the acute setting and 22 days if patients needed rehabilitation. The overall mortality rate was 7.8%. The infection rate was low at 3.8%. The rate of deep venous thrombus was 0.4% and pulmonary embolus 1.1%. Very early effective management of pain was identified along with the treatments of delirium and dementia. Sixty one percent of patients returned to their original place of domicile. Delay to theatre for operation remains a continuing challenge. Over 50% of patients are receiving appropriate treatment for osteoporosis on discharge. Dietary supplements are now routine for pre and post operative patients. The introduction of a plan of care from presentation to hospital to discharge has significantly improved morbidity outcomes and mortality in this frail group of patients.

P-TUE-90

Structural effect and reproductive safety of epimedium-derived phytoestrogen fraction on osteopenic hip in postmenopausal women: a two-year randomized placebo controlled clinical trial

G. Zhang[1, 2], L. Qin[1]* and Y. Shi[2]
1. Musculoskeletal Research Center, Department of Orthopaedics & Traumatology, The Chinese University of Hong Kong, Hong Kong SAR, PR China
2. Department of Orthopaedics & Traumatology, Shanghai University of Chinese Medicine, Shanghai, PR China
* *Corresponding Author:* lingqin@cuhk.edu.hk

Objective: The objective of the study was to examine structural effect and reproductive safety of Epimedium-Derived Phytoestrogen-Fraction (PF)[1] on osteopenic hip in postmenopausal women.

Design: It was a two-year, randomized, double-blind, placebo-controlled clinical trial.

Setting: The study was performed at a hospital.

Patients: Participants were 85 patients who were postmenopausal for 8~12 years with osteopenic femoral neck.

Intervention: Daily oral PF (60000 μg Icariin, 3000 μg Genistein and 15000 μg Daidzein) or Placebo was given to patients.

Main Outcome Measure: The main outcome measure was the change from baseline in Hip-Structure-Analysis-derived envelope-geometry parameters and abnormal incidence of reproductive organs[2-3].

Results: For bone envelope, a significant increase from baseline in periosteal diameter was found in PF Group (1.11%, P=0.098), whereas a mild increase was found in Placebo Group. Endosteal diameter increased significantly from baseline in Placebo Group (1.30%, P=0.098), whereas there was no change in PF Group. For bone geometry, a significant increase from baseline in cross-sectional area, section modulus and cortical thickness and a significant decrease from baseline in buckling ratio were found in PF Group (P=0.050~0.100), which showed significantly different changing pattern over time from Placebo Group (P=0.000~0.050). For reproductive safety, there is no significant difference in abnormal incidence of either breast or uterine between PF Group and Placebo Group (Table-1 and Figure-1).

Conclusions: PF was able to exert beneficial effect with reproductive organ safety on both promotion of periosteal apposition and inhibition of endocortical resorption for improving mechanically structural geometry of osteopenic femoral neck in postmenopausal women.

Acknowledgement: This clinical trial (Registration Date:1998; Trial Number: SHUTCM-QN67) was supported by Young Investigator Research Grant of Shanghai Municipal Education Commission (1998-SHUTCM-QN67), Direct Grant of Shanghai University of Chinese Medicine (1998-SPZ), Young Investigator Research Grant of Shanghai Municipal Health Bureau (2000-SHUTCM-ZG), and Hong Kong RGC (CUHK/4097M).

P-TUE-92

The potential clinical role of NAC in slowing bone resorption in early post-menopausal women: a pilot study

K.M. Sanders, M.A. Kotowicz, M.J. Henry and G.C. Nicholson
Dept Clinical and Biomedical Sciences: Barwon Health, The University of Melbourne, Geelong, Victoria, Australia

There is compelling evidence from pre-clinical research that oxidative stress regulates bone cells. Our group and others have reported that antioxidants such as N-acetylcysteine (NAC) inhibit osteoclastogenesis and bone resorption. In a randomised, double-blind, placebo-controlled pilot study, we compared the change in the bone resorption marker, serum C-telopeptide (CTx) between NAC-treated and placebo in 22 early post-menopausal women (last menstrual period (LMP) >6months and <5years). Serum CTx was measured (ECLIA) monthly during a 3-month intervention. All participants were supplemented with 500 IU cholecalciferol and 600mg calcium daily (Ostelin™) and randomly assigned to either NAC (2g/day) or placebo.

There was no difference in (mean±SD) age (52.5±3.9 vs 53.5±2.6 yrs), weight (66.5±15.1 vs 68.1±13.2 kg), BMI (25.4±5.1 vs 24.8±4.3 Kg/m^2); months since LMP (32±16 vs 28±14 months) or baseline CTx (397±126 vs 465±154 pg/ml), NAC vs placebo, respectively, all p>0.05). Compliance was 91% (20/22 took >80% study medication). At 3 months CTx levels decreased by 15% in the NAC group compared with 6% in the placebo group to mean± SE of 412 ± 46 pg/ml vs 315 ± 38 pg/ml. However, change in serum CTx levels was not different between the groups (p=0.58, Two-way ANOVA).

These preliminary results do not refute findings from *in vivo* experiments. However, the wide variation in CTX levels suggests a greater number of participants or measurement of a more reliable bone marker is needed to determine the potential role of NAC in reducing accelerated bone resorption during the menopausal years.

P-TUE-94

MRI-based measurement of vertebral shape in Japanese women

T. Nakano[1] and A. Harada[2]
1) Tamana Central Hospital, Kumamoto, Japan
2) National Chubu Hospital, Aichi, Japan

We propose the cutoff values for diagnosing a previous vertebral fracture by determining the dimensions of the normal vertebral body, as expressed by the anterior-posterior (A/P) ratio, central-posterior (C/P) ratio, and other indices. The subjects were 56 female volunteers, and their age distribution was as follows: 20-29

years (n=13), 30-39 years (n=14), 40-49 years (n=15), and 50-59 years (n=14). T1-weighted magnetic resonance imaging (MRI) scan of 14 vertebral bodies from T4 to L5 revealed that measured values of L4 and L5 were remarkably different from those of the remaining vertebral bodies. No age-related tendency was observed. The A/P ratios obtained from images of the thoracic and upper lumbar spine were below 1.00, showing a slight wedge or rectangular deformity. The A/P ratios obtained from images of the lower lumbar spine exceed 1.0 with an inverse wedge deformity. Few differences were found in C/P ratios obtained from images of the parts from the upper thoracic spine to the upper lumbar spine. The levels of −3.0 SD of the A/P and C/P ratios of the parts from T4 to L3 were 0.82 and 0.79, respectively, therefore it is reasonable that the A/P ratio below 80% and the C/P ratio below 75% are considered as the cutoff values for diagnosing a vertebral fracture based on vertebral body measurement from T4 to L3.

P-TUE-95

Osteoporosis - a generalists perspective

R. Biswas
Associate professor, Department of Medicine, Melaka-Manipal Medical College, Jalan Batu Hampar, Bukit Baru, 75150 Melaka, Malaysia

Aim: This is a power point presentation of a generalists personal viewpoint on his tryst with osteoporosis in his day to day practice.

Methods: It begins with a case description of a lady who presents with chest pain and after a brief period of diagnostic uncertainty is finally found to have a wedge shaped osteoporotic fracture of a dorsal vertebra. The author discusses various issues in management of osteoporosis from a generalists perspective.

Conclusion: A few slides projected as a twister to provoke a discussion on osteoporosis from an evolutionary perspective.

PAEDIATRICS

P-TUE-97

Peripheral bone mineral density and its predictors in healthy school girls from two different socioeconomic groups in Delhi

N. Tandon, R.K. Marwaha*, D.H.K. Reddy, K. Mani**, S. Puri$, N. Aggarwal$, K. Grewal* and S. Singh*
Department of Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India
**Department of Endocrinology and Thyroid Research, Institute of Nuclear Medicine and Allied Sciences, Delhi, India*
***Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India.*
$ Institute of Home Economics, New Delhi, India

Factors that lead to the attainment of peak bone mass at peripheral sites, during period of growth are not clearly known.

Six hundred and sixty four randomly selected 7-17 year old girls from upper and lower socioeconomic status schools (USES; LSES) were subjected to anthropometric assessment. Serum calcium, phosphorus, total alkaline phosphatase (ALP), 25-hydroxyvitamin D [25-OHD_3] and parathyroid hormone (PTH) were measured in all of them. Bone mineral density (BMD) was measured at distal forearm (BMDdf) and calcaneum (BMDca) by peripheral dual energy X-ray absorptiometry (pDXA).

There was a significant difference in anthropometry between the groups. USES subjects had higher BMD at both sites than LSES subjects. BMDdf and BMDca increased with age and tended to plateau by 16 years and 12 years of age respectively in both the groups. Anthropometry and biochemical parameters explained approximately 50% and 30% of variability respectively at both the sites. The only biochemical parameter, which had a significant effect on BMD, was ALP at the distal forearm.

In conclusion, age, nutrition and anthropometry have a significant effect on BMD at peripheral sites.

P-TUE-99

Sex-specific differences in bone structural parameters are apparent before puberty

R. English, P. Eser, A. Patchett, R.M. Daly, G. Naughton, M. Seibel, R. Telford and S.L. Bass
Centre for Physical Activity and Nutriton Research, Deakin University, Victoria, Australia

Little is known about sexual dimorphism in bone parameters before puberty. In boys and girls we asked whether there are sex specific differences: (i) in bone structural parameters, and (ii) between the weight-bearing and non weight-bearing bones, and diaphyseal versus metaphyseal compartments. In 272 children (n=134 girls and 138 boys) aged 8 to 9 years, we used pQCT to assess non-dominant tibia and radius (distal 4% and mid-shaft 66% sites) BMC, total, cortical and trabecular vBMD and cross-sectional area (CSA), and muscle and fat CSA. There were no gender differences detected in age, height, weight and BMI. Muscle CSA was 6% greater at the arm in boys but was similar to girls at the calf. In contrast, fat CSA was greater in girls at the calf (10%) and arm (15%). At the metaphyses boys had greater BMC and total CSA at both the distal tibia (11% and 8% respectively) and radius (8% and 7% respectively). Total and trabecular vBMD were greater in boys at the distal tibia (4% and 3% respectively) but not at the distal radius. All significant differences remained after correcting for height, age, or muscle CSA. At the diaphysis none of the measured bone parameters differed significantly between boys and girls. In conclusion, we report sexual dimorphism in bone structural parameters in children before puberty to be present only at the metaphyses, where boys had larger bone CSA and concomitantly higher BMC than girls, with differences in vBMD only at the tibia.

EPIDEMIOLOGY, PUBLIC HEALTH AND GENETICS

P-TUE-101

Incremental prognostic values of non-BMD factors for the assessment of fracture risk

N.D. Nguyen, J.A. Eisman, J.R. Center and T.V. Nguyen.
Bone and Mineral Research Program, Garvan Institute of Medical Research, Sydney, Australia

The present study sought to assess the incremental prognostic values of clinical factors-based models in the prediction of fracture risk in women and men.

Participants in the Dubbo Osteoporosis Epidemiology Study were randomly divided into two groups: a development cohort (405 men, 632 women) and a validate cohort (418 men, 667 women), all aged 60+ years as at 1989. Femoral neck BMD (GE LUNAR, WI), body weight, and clinical history were assessed at baseline. Fracture was ascertained by X-ray between 1989 and 2004. In the development cohort, three models for predicting fracture were developed: model I included only FNBMD; model II, age and weight; and model III, age, weight, fall and prior fracture as predictors. These models were applied in the validation cohort.

In the validation cohort, 209 women and 71 men had sustained a fracture during the follow-up period. Model I correctly identified 52% and 45% fractures in women and men, respectively. Models II and III had a slightly higher predictive values than model I (62% and 68%). However, the concordance between model I and model II (or model III) was between 50% and 66%. Thus, when risk derived from model II was combined with model I, the predictive value increased to 77% in women and 70% in men, representing an absolute increase of 25% in both sexes.

These data indicate that the predicted value of non-BMD-based models were slightly higher than that of BMD-based model alone, and that the incorporation of clinical risk factors significantly increased the prognostic value of fracture prediction over and above BMD.

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P-TUE-103

The impact of an osteoporosis education intervention on knowledge in Australians aged over 40

K.L. Francis[1], B.L. Matthews[1], K.L. Bennell[1], R. Osborne[2] and W. Van Mechelen[3]
1. Centre for Health, Exercise and Sports Medicine, University of Melbourne, Parkville, Australia, 2. Centre for Rheumatic Diseases, Department of Medicine, University of Melbourne, Parkville, Australia, 3. Department of Public and Occupational Health, VU University Medical Centre, Amsterdam

The ever increasing health burden of osteoporosis is of major concern worldwide. In combating the progression of osteoporosis, both medication and behaviour change can play an important role. Behaviour is often influenced by knowledge; with a correct understanding of osteoporosis, appropriate behaviours are more likely. It is preferable that patients with chronic disease have sufficient understanding of their condition to carry out their own self-care and to communicate effectively with healthcare professionals. The Osteoporosis Prevention and Self Management Course (OPSMC) is an established Australian program to promote education and management skills for osteoporosis. This project aimed to assess change in osteoporosis knowledge associated with completion of the OPSMC.

In this wait listed randomised controlled trial, 187 people (91%female) aged over 40 (mean years = 62) were randomised into control (n=102) and intervention (n=85) groups. Osteoporosis knowledge was assessed by the Osteoporosis Knowledge Assessment Test. There was no significant difference between intervention or control groups in age, gender or disease status. At baseline the control group had a mean knowledge score of 9.85 (20 possible) and the intervention group had a mean score of 9.66 ($p>0.05$). At the six-week follow-up the intervention group showed a greater increase in level of osteoporosis knowledge compared with controls (13.36 vs 9.77 respectively, $p<0.001$). Those questions which showed substantial change related to understanding lifestyle factors (smoking, alcohol consumption), genetic factors (race, peak bone mass) and medication (hormone replacement therapy).These findings support the role of the OPSMC as an effective, intervention for improving patient understanding of osteoporosis.

P-TUE-105

Angiotensin converting enzyme gene polymorphism is associated with bone mineral density in older Chinese hypertensive men

T. Kwok[1], N. Tang[2], J. Woo[3], B. Tomlinson[1] and L.P. Sing[4]
[1]Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China.
[2]Department of Chemical Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China.
[3]Department of Community and Family Medicine, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China.
[4]Department of Physiology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China.

Background: There is an association between intake of angiotensin converting enzyme (ACE) inhibitors and greater bone mineral density (BMD) in older Chinese people. ACE I/D gene polymorphism, which has a significant influence on ACE activities, may therefore be associated with BMD in older Chinese hypertensive men.

Aim: To examine the association between ACE I/D gene polymorphism and BMD in older Chinese men. Sub group analysis on hypertensive subjects was performed.

Methods: Community-dwelling Chinese men aged 65 years and above were recruited in Hong Kong. A standardized and structured interview was performed to obtain demographic information, smoking, alcohol intake, physical activity, and medical and medication history. Body weight, height, sitting blood pressure, ankle brachial index and hand grip strength were measured. BMD at lumbar spine and total hip were estimated by Hologic QDR 4500 bone densitometer. Blood was taken, from which DNA was analyzed for ACE I/D polymorphism.

Results: Out of the 1747 eligible subjects, 166 subjects (9.5%) had DD genotype and 779 subjects (44.6%) had II genotype. There was no significant difference in BMD among the three ACE genotype groups. 885 subjects

(50.7%) reported to have hypertension or were taking antihypertensive medications. Among these subjects, there was a significant trend of greater BMD at total hip in subjects with ACE II genotype, with and without adjustment for various factors related to BMD (mean beta 0.018, p = 0.015 with adjustment).

Conclusion: ACE II genotype is associated with greater BMD at the hip in apparently healthy older Chinese hypertensive men.

P-TUE-107

A nomogram for predicting osteoporosis risk based on age, weight and quantitative ultrasound measurement

C. Pongchaiyakul, S. Panichkul, T. Songpattanasilp and T.V. Nguyen
Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; Department of Military Community Medicine and Department of Orthopedic, Phramongkutklao College of Medicine Phramongkutklao Hospital, Bangkok, Thailand; Garvan Institute of Medical Research, University of New South Wales, Sydney, Australia

Quantitative ultrasound measurement (QUS) or clinical risk index alone is not a reliable tool for the identification of women with osteoporosis. This study examined the prognostic value of combined QUS and clinical risk index for predicting osteoporosis risk in Thai women. The study was designed as a cross-sectional investigation with 300 women of Thai background, aged between 38 and 85 years (mean age: 58). Femoral neck bone mineral density (BMD) was measured by DXA (Hologic QDR-4500; Hologic, Waltham, MA, USA). A BMD T-scores ≤ -2.5 was defined as "osteoporosis"; otherwise, "non-osteoporosis". QUS was measured by Achilles+ (GE Lunar, Madison, WI, USA) and converted to T-score. Three models for predicting osteoporosis were considered: Model 1 included age, weight and QUS; model 2 included age and weight; and model 3 included only QUS. The prognostic performance among the models was assessed by the area under the receiver operating characteric curve (AUC).

The prevalence of osteoporosis was 36% (n = 107) by femoral neck BMD. Age, weight and QUS were each significantly associated with osteoporosis risk. The AUC±SE value for model I was 0.80±0.02, which was significantly higher (p = 0.002) than model II (AUC = 0.74±0.03) or model III (AUC = 0.74± 0.03). Based on the estimated parameters of model I, a nomogram was constructed for predicting osteoporosis for any given age, weight and QUS score. These data suggest that the combination of QUS and clinical risk index could significantly improve the prognosis of osteoporosis in Asian women.

P-TUE-109

The impact of osteoarthtitis on knee pain in urban and rural communities: the Research on Osteoarthritis Against Disability (ROAD) Study

S. Muraki, H. Oka, A. Mabuchi, Y. En-yo, M. Yoshida, A. Saiga, T. Suzuki, H. Yoshida, H. Ishibashi, S. Yamamoto, H. Kawaguchi, K. Nakamura and N. Yoshimura
22nd Century Medical Ctr., Univ. of Tokyo, Tokyo, Japan, Wakayama Medical Univ., Wakayama, Japan, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan

Background: Although knee osteoarthritis (OA) is an increasingly important cause of disability in the elderly, suggesting that strategies for preventing knee OA are urgently required in an aging society, few epidemiological data such as prevalence or impact on knee pain are available. To address this issue, a large-scale nationwide clinical study called Research on Osteoarthritis Against Disability (ROAD) was established in 2005. In this paper, the impact of knee OA to pain was determined in cohorts consists of an urban and a rural areas.

Methods: This study included 1752 subjects ≥60-years-old (539 men, 1213 women; mean age, 76.9 years) in urban and rural areas. Subjects underwent anteroposterior radiography of the knee, and severity of OA was determined according to the Kellgren-Lawrence method.

Results: Regarding the right knee, more subjects with grade 2 and grade 3/4 had knee pain than those with grade 0/1 significantly (men: OR 2.1, 12.7, women: OR 2.1, 7.5, respectively). These results also held true among rural subjects alone, but no significant differences were seen in knee pain between urban subjects with grade 2 and grade 0/1. These results also held true for the left knee.

Conclusions: This study is the first to identify a correlation between knee OA and pain. Until now, knee OA was defined as KL grade 2 or above, but these results indicate that knee OA differs between grade 2 and grade 3/4.

P-TUE-111

Establishment of peak bone mineral density in southern Chinese males and its comparisons with other males from different regions of China

L-J. Tan[1], S-F. Lei[1], X-D. Chen[1], M-Y. Liu[1], Y-F. Guo[1], H. Xu[1], X. Sun[1], C. Jiang[1], S-M. Xiao[1], J-J. Guo[1], Y-J. Yang[1], F-Y. Deng[1], Y-B. Wang[1], Y-N. Li[1], X-Z. Zhu[1] and H-W. Deng[1,2]
1.Laboratory of Molecular and Statistical Genetics and the Key Laboratory of Protein Chemistry and Developmental Biology of Ministry of Education, College of Life Sciences, Hunan Normal University, Changsha, Hunan 410081, P. R. China 2.Department of Orthopedic Surgery, School of Medicine, University of Missouri-Kansas City, 2411 Holmes Street, Kansas City, MO 64108, USA

Peak bone mineral density (PBMD) is an important determinant of osteoporotic fracture and a precondition for correct diagnosis of osteoporosis. The objective of this study was to establish the reference data of PBMD at the lumber spine and hip in Southern Chinese males. Bone mineral density (BMD) was measured at the lumbar spine and hip (femoral neck, trochanter, intertrochanter and total) in 1155 Chinese men aged 15-39 years, using dual-energy X-ray absorptiometry (DXA). We utilized a fit curve method to determine the best age range over which to calculate PBMD. Data were analyzed according to age using eight regression models and the cubic regression model was superior to the quadratic, linear, logarithmic, and exponential regression models. Our results indicated that the PBMD was observed at the age range of 18-22, 20-24, 19-23, 19-23, and 21-25 years, with the mean value and standard deviation of PBMD of 0.753±0.117, 1.156±0.148, 0.896±0.120, 0.989±0.122, 0.980±0.116 g/cm^{2}at the trochanter, intertrochanter, femoral neck, total hip and spine, respectively. When compared with the documented PBMD reference of males from other regions of China, our standardized PBMDs were great different from those from other regions of China. Our PBMDs at the various sites were 3.19%-11.33% lower than those for American Caucasian males. In conclusion, the PBMD at the spine and hip may be used as normal reference data for Southern Chinese males especially in Changsha city, instead of documented PBMD from other regions of China and the manufacture's reference data.

P-TUE-114

Sex-difference in the deficit of lean mass and fat mass in deltoid fibrosis patients

T.A. Le and V.V. Truong
Cho Ray Hospital, Ho Chi Minh City, Vietnam

This study sought to assess the body composition in patients with deltoid fibrosis (DF), which is a muscle disorder characterized by intramuscular fibrous bands.

There was a recent outbreak of deltoid fibrosis in Vietnam, in which 67 patients were admitted to Cho Ray Hospital for surgical treatment, among whom 30 males and 13 females were randomly invited and agreed to participate in the study. The patients aged between 11 and 28 years who have had DF for median 8 years. A separate group of 24 male and 14 female controls of similar age were also studied. Whole body BMD and body composition were measured by DXA (Hologic QDR 4500).

Compared to the controls, DF patients had significantly shorter height (6.3cm in males and 3.5cm in males) and lower weight (10.5kg in males and 5.6kg in females). The reduced weight in DF patients was mainly due to lower lean mass (LM) in males and lower fat mass (FM) in females. In multiple logistic regression analysis, the risk of having DF was significantly associated with lower LM (OR: 1.6; 95%CI: 1.2-2.0)) in males and with lower FM in females (1.4; 1.1-2.0). No difference in BMD between DF patients and the controls was observed.

These data for the first time suggested that DF was associated with impaired physical growth and deficit in LM among males and FM among females.

P-TUE-116

Estimation of female adolescents osteoporosis prevention behavior

Z. Moinfar, M. Karimi Khezri, F. Mirzaaghaee, S, Eftekhari, M and Sedaghat
Tehran University of Medical Sciences, Iran

Aim: Osteoporosis is a metabolic disease and a health problem that primarily affects women and result in fractures. Approximately 32.4% of 20 to 29 years Iranian females suffer from osteoporosis. The purpose of this study is to determine high school female students' osteoporosis prevention behavior.

Method: This study included a randomized sample of 1000 adolescent girls from 6 public high schools in Tehran. A questionnaire containing 27 questions was designed and filled out by the students. Students' prevention behavior scores were calculated by summing obtained score from questions. Scores more than 75th percentile were defined as optimal prevention behavior.

Results: Among the entire students, 14.9% had never consumed milk per week, compared to 10.6% for cheese, and 10.5% for soft drinks. Unfortunately, 3.8% of the students never used to exercise. A significant relationship between mothers' education and family income and students' behavior was observed ($p = 0.002$, $p = 0.008$)

Conclusion: Because the school girls are at a high risk of osteoporosis affection government should pay more attention to this group. This study showed that consumption of dairy products is more favorable than milk and fish for Iranian adolescents. Increasing mothers' knowledge levels and family income will promote students' behaviors.

DENSITOMETRY, IN VIVO ANALYSIS

P-TUE-122

Discordance of longitudinal changes in bone mineral density between DPX-L and prodigy densitometers

S.A. Frost, N.D. Nguyen, J.A. Eisman, J.R. Center and T.V. Nguyen
Bone and Mineral Research Program, Garvan Institute of Medical Research, Sydney, Australia

The DXA technology is continually evolved, and the concordance between old and new densitometers is a crucial issue. The present study examined the concordance in BMD measurement and longitudinal change in BMD between GE-Lunar Prodigy and DPX from the same manufacturer.

BMD at the lumbar spine and femoral neck was measured in 135 individuals (47 men) aged 60+ using both Lunar GE DPX and Prodigy densitometers at baseline. In this group, 56 individuals (21 men) had repeated dual BMD measurements on follow up (interval 2.2 years). The concordance between two densitometers was assessed by the coefficient of concordance (COC) and Bland-Altman's limits of agreement method.

For a single BMD measurement, the COC between the Prodigy and DPX was greater than 0.95. BMD measurements by Prodigy were within 1% of DPX measurements. The longitudinal rate of change in lumbar spine BMD measured by Prodigy was 0.0 ± 2.0% (mean ± SD), significantly lower ($p<0.01$) than that measured by DPX (-0.5% ± 1.8). Similar trend was also observed for femoral neck BMD (-1.0% ± 1.8 by Prodigy and -1.6% ± 2.9 by DPX; $p=0.10$). The correlation of rates of BMD change between Prodigy and DPX was 0.52.

These results indicate that there was a poor concordance in the assessment of BMD changes between the Prodigy and DPX-L densitometers, despite both densitometers were highly concordant in a single BMD measurement. These findings have implications regarding the assessment of response to therapy in multicenter setting when different densitometers are used.

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P-TUE-124

Timing and anthropometric correlates of peak bone mineral density in Vietnamese women

N.T.T. Huong[1], B. Schoultz[2], P.T.M. Duc[1] and T.V. Nguyen[3]
[1]Department of Physiology, Hanoi Medical University, Vietnam; [2]Department of Woman and Child Health, Karolinska Institute, Sweden; [3]Bone and Mineral Research Program, Garvan Institute of Medical Research, Australia

While peak bone mass and its determinants have been well documented in Caucasian populations, little has been studied in Asian populations. The present study was designed to estimate the peak bone mineral density and its association with anthropometric factors, and to examine the prevalence of osteoporosis in post-menopausal Vietnamese women.

The study was designed as a cross-sectional study with 328 women aged between 10 and 65 years (average age: 41) who were randomly selected from two districts around Hanoi city according to a stratified sampling scheme. BMD at the lumbar spine, femoral neck and total hip was measured by the GE Lunar Prodigy densitometer. Anthropometric parameters included sitting height, leg length, chest, waist, and hip circumferences were measured.

Peak BMD was estimated at 1.16 g/cm^2 (standard deviation [SD]: 0.15 g/cm^2) at the lumbar spine, 1.02 g/cm^2 (SD 0.12) at the total hip, and 1.00 g/cm^2 (SD 0.12) at the femoral neck. In cubic polynomial model, the age of attainment of peak BMD was estimated to range between 27 and 29 years. Among anthropometric measures, only hip circumference was consistently found to be an independent determinant of BMD in Bayesian average model. Collectively, age and hip circumference accounted for between 42% and 57% of the variation in BMD. At any skeletal site, the prevalence of osteoporosis was 46% among those aged 50 years or above.

These data suggest that although the peak BMD in Vietnamese women is comparable to, the prevalence of osteoporosis is much higher, that in Caucasian women.

P-TUE-126

Operator radiation exposure from the GE-lunar prodigy

T. Zammit[1], C. Schultz[2], R, Gaffney[2] and N. Pocock[1]
1. Dept of Nuclear Medicine and Bone Densitometry, St Vincent's Hospital, Sydney
2. Dept of Nuclear Medicine, PET and Bone Densitometry, Royal Adelaide Hospital, Adelaide

Introduction: Radiation doses to technologists performing DXA scanning is considered to be low, and well within the limits defined by the ICRP. However, a previous article (Yu 2001) based on theoretical modelling suggested that a technologist's radiation dose could exceed 2mSv per year.

Method: To test the predictions from the modelling study we examined 'real world' dosimetry data from technologists using GE-Lunar Prodigy scanners. We compiled radiation doses obtained from Personal Radiation Monitoring devices from nine DXA technologists operating GE-Lunar Prodigy scanners at various sites in Australia, as well as the number of patients scanned per day, and days spent scanning per week. We also examined radiation scatter adjacent to the scanner, from two centres.

Results: Technologist dose measurements were consistently well below the maximum permissible annual dose of 20mSv, at an average reported operator distance of 1.5m from the scanner. The annual dose ranged from 0.03mSv, to 0.55mSv, scanning 6 to 20 patients/day. From these data, if 32 patients are scanned daily (4 per hour, 8 hour day) by one technologist for 220 working days per year, the radiation dose would average 0.33mSv (range 0.07mSv – 0.88mSv). The scatter measurements indicated a technologist situated 1.75m from the scanner and performing 32 scans per day, could receive approximately 0.64µSv/day (or 1.41mSv/year).

Conclusion: A GE-Lunar Prodigy in heavy use will result in an average annual radiation dose to a technologist of 0.33mSv. This compares to the average annual background dose of 1.5-3.5mSv. The model of Yu (2001) significantly overestimates DXA radiation dose to the technologist.

P-TUE-127

The impact of scan speed and voxel size on peripheral QCT results

J.N. Briody[1] and C. Munns[2]
Departments of Nuclear Medicine[1] and Endocrinology[2], The Children's Hospital at Westmead, NSW, Australia

Paediatric peripheral QCT (pQCT) reference data has been acquired using various scan settings. Tibial scans were acquired using different voxel settings at the 4% and 66% site which complicates acquisition. Radial scans use slow CT speeds.

Prior to commencing paediatric studies at our centre, the impact of scan acquisition settings on pQCT results was investigated. A selection of lamb (in situ), turkey (in situ) and human bones (excised) were scanned using a variety of CT speeds (10-30mm/sec) and voxel sizes (0.3-0.6mm). Both trabecular and cortical bone sites were measured.

All scans were analysed using paediatric radius analysis parameters. Results were compared to those obtained with a CT speed of 0.6mm and voxel size of 30mm/sec (paired t-test). Mean differences (±SD) are tabulated below.

		Total		Cortical	
Voxel	**N**	**BMD (mg/cm^3)**	**BMC (mg)**	**BMD (mg/cm^3)**	**BMD (mg)**
0.5	108	-5..2±6.9*	-0.5±4.0	-24.7±16.8	-3.5±2.9*
0.4	122	-8.1±17..2*	1.2±26.7	-44.0±28.2*	-7.3±7.5*
0.3	67	3.6±52	-3.2±10.5*	-86.8±43.1*	-9.8±5.7*
CT					
25	52	5.1±17.2*	-6.6±52.9	0.8±13.4	2.4±11.0
20	105	-4.3±27.4	2.4±41.9	2.7±15.7	1.3±10.9
15	114	-3.5±15.5*	0.7±35.5	-4.5±24.1*	0.6±7.1

*p<0.05

Voxel size had a small impact on Total BMD and BMC (~1%), but a larger effect on Cortical BMD and BMC (2.5-8% and 5-20%, respectively). This may be explained by the "partial volume effect", and the different analysis parameters used to obtain the cortical values. More specific analysis parameters may lessen these differences.

CT speeds impacted on Total and Cortical BMD, however these represented variations of less than 1% indicating a faster speed may be used.

P-TUE-129

Investigating the effect of soft tissue on BMD results using DXA method employing a spine phantom

A Ghasemzadeh[1], B. Larijani [2], S.Sarkar[3], A.Bajoor[4] and A.Salimzadeh[5]
1- Department of Endocrinology, Austine Health, The University of Melbourne ,Heidelberg, Victoria 3084,Australia
2- Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran
3- Research Center of Science and Technology in Medicine (RCSTIM). Tehran University of Medical Sciences, Tehran, Iran
4- Dept. of Medical Radiation, Islamic Azad University, Tehran, Iran
5- Dept of Rheumatology, Sina Hospital , Tehran University of Medical Sciences, Tehran ,Iran

Background: The effect of tissue depth on results of bone mineral content (BMC) and bone mineral density (BMD) measurements could be important for the interpretation of any study examining the effect of weight change.

The decrease in body weight has been reported to lead to an underestimation in bone mineral density, a variety of scan modes has been introduced to overcome the technical problems in scanning people having

small or large tissue thickness, but an inappropriate choice of scan mode affects the validity of the DXA measurement.

Aim: The aim of this study was to measure BMD, BMC and bone area (BA) due to influences of tissue depth for Lunar DPX-MD bone densitometer system using spine phantom.

Material and Methods: A spine phantom was made by cooperation of Research Center for Science and Technology in Medicine (RCSTIM) and Endocrinology and Metabolism Research Center (EMRC). This phantom consists of 1300mg, 1550mg and 2000mg K2HPO4 powder to simulate osteoporosis, osteopenia and normal status respectively. We applied 10, 15 and 20 layers of Perspex with 3 mm thickness each layer for simulation of increasing depth of soft tissue in spine phantom. 10 scans were performed phantom to obtain L2-L4 BMD, BMC and BA, without repositioning between scans and medium scan mode was applied for Lunar DPX- MD. Acquisition and analyses of scans were performed by a trained technologist.

Results: Mean BA, BMC and BMD measured by the lunar DPX-MD system at various tissue depths. The BA results for this study were dependent on tissue depth. There was a significant decrease in BMC and BMD, for three phantoms as tissue depth decreased from 20 to 10 layers. The present study demonstrates that BA measurement depends on bone mass and is most highly underestimation when the bone mass is very low.

Conclusion: In following up studies, the effect of body weight and changes in soft tissue depth especially in lumbar spine, are considerable and must be taken in to account. The variation of BMD in serial BMD tests must be ruled out due to the weigh and soft tissue thickness fluctuations.

P-TUE-131

Possibility of performing BMD of radius-ulna using by conventional CT Scanners

A Ghasemzadeh[1], S. Sarkar [2] and Sh. Akhlaghpour[3]

1- Department of Endocrinology, Austine Health, The University of Melbourne ,Heidelberg, Victoria 3084,Australia

2- Research Center of Science and Technology in Medicine (RCSTIM), Tehran University of Medical Sciences, Tehran, Iran

3-Dept. of Radiology, Tehran University of Medical Sciences. Tehran ,Iran

Objective: Importance of the early diagnosis of osteoporosis leads to the establishment of several methods in this field. One of the recent methods is peripheral Quantitative Computed Tomography (pQCT), in which, axial images of radius and ulna are used for quantitative determination of bone density. In contrast with Dual Energy X-Ray Absorptiometry (DEXA), in this method trabecular and cortical bone can be evaluated separately. The advantage of this method is the possibility to show early stages of metabolic change in bone. Since pQCT scanners are not available in most undeveloped countries, the most available system is DEXA. QCT can be used for lumbar spine Bone Mineral Densitometry (BMD), in which a high radiation effective dose (250 µSV) is delivered to patient.

The aim of this work was to study the possibility of doing pQCT method using by conventional CT Scanner for bone densitometry of radius and ulna .

Materials & Methods: A radius-ulna phantom was constructed using Plexiglas, Aluminum and K_2HPO_4 solution, cortex and trabecular section of radius and ulna were contracted using 0.5 mm thick aluminum plate and 100 mg/cc K2HPO4 solution respectively, on which according QCT method, 43 axial computed tomography were performed by a GE 9800HR CT scanner.

Result: Our results showed that the coefficient variation (CV) and the accuracy of the technique were 1.5% and 1.2% respectively. The slope of scanner at 80kVp, 20mA and scan time of 3 seconds was to be within the concentration range of 10 to 400 mg/cc was obtained to be 2.01 for the K2HPO4 solution.

Discussion: Our experimental study showed that conventional CT Scanners are potentially suitable for doing pQCT. However further in vivo study is needed for clinical approval.

P-TUE-133

Effects of rotation on DXA lumbar spine BMD measurements

C. Barber C[1, 2], C.G. Schultz[3], A. Badiei[1, 2] and N.L. Fazzalari[1, 2]
1. Bone & Joint Research Laboratory, Division of Tissue Pathology,
2. Institute of Medical & Veterinary Science, Adelaide, South Australia
3. *Discipline of Pathology, School of Medical Sciences, University of Adelaide, South Australia*
4. Department of Nuclear Medicine, PET and Bone Densitometry, Royal Adelaide Hospital, South Australia

DXA measurement determines BMD by projecting three-dimensional information into two-dimensions. BMD is compared to a reference range to determine further action, relying on standardised bone orientation. Potential misdiagnosis may result from bones exhibiting axial rotation deviating from the ideal. The aim of the study was to assess the degree to which axial rotation of scanned objects could affect BMD measurements.

A GE-Lunar Aluminium spine phantom fixed to a custom made rotation cradle was measured 5 times each, on a GE-LUNAR Prodigy, at 0º, 5º, 10º, 20º and 30º from horizontal in a 15cm water bath. BMD of L1-L4 was determined. Exact projected areal dimensions of the phantom were measured using digital callipers. Theoretical projected areas and BMD for each angle were calculated by applying trigonometric principles and using the observed BMC at 0º.

Angle	Theoretical BMD (g/cm^2)	Observed BMD (g/cm^2)	T- score change
0º	1.125	1.115±0.007	0
5º	1.129	1.116±0.002	0.01
10º	1.155	1.129±0.002 *	0.12
20º	1.211	1.199±0.003 *	0.71
30º	1.306	1.229±0.005 *	0.95

Summary of results for L1-L4 (* = $p<0.0001$)

Theoretical and observed projected area and BMD showed strong correlations with observed DXA values ($R^2=0.938$, $p<0.01$; $R^2=0.931$, $p<0.01$ respectively).

This study demonstrates that changes due to axial rotation may significantly alter BMD measurement. Examination of the change on T score indicates that a 16º or greater change in axial rotation may account for an apparent 0.5 SD increase in BMD, even though the amount of bone is unchanged and may lead to under-treatment in some cases.

BONE QUALITY AND MECHANICAL PROPERTIES

P-TUE-135

Interaction between trabecular and cortical compartment - relationship with bone geometry

R.M.D. Zebaze[2], A.C. Jones[1], E. Seeman[2] and M.A. Knackstedt[1]
[1]Department of Applied Mathematics, RSPhysse, Australian National University, Canberra 0200, Australia
[2]Austin Hospital, University of Melbourne, Heidelberg 3084, Melbourne, Australia

The importance of the interaction between cortical and trabecular compartments in the pathogenesis of bone fragility is unstudied. We examined (i.) the relationship between the thicknesses (sizes) of trabeculae and cortices (ii.) The relationship between the thicknesses of trabeculae and cortices, and external bone geometry (FN volume, FNAL, and NSA) at the FN in13 proximal femurs specimens aged 29 to 85 using high-resolution (=2 µm) µ-CT. In each specimen, the thicknesses of bone elements were measured in 3D using the maximal covering sphere approach. In brief, all bone elements are fitted with virtual spheres. The thickness of a bone element is the diameter of the largest sphere that can be fitted (~ 1 million sphere / FN).

The thicker the cortices the thicker the adjacent trabeculae ($r=0.76$; $p<0.01$). There was no relationship between the cortical thicknesses on various aspects of the FN. There was no association between FN volume, FNAL and the thicknesses of bone elements (cortices and trabeculae). The NSA was the sole parameter associated with the size of bone elements - this was observed with the size of elements on the inferior aspect

only. The larger NSA, the thinner the cortices and the trabeculae inferiorly; respectively r= -0.65 and -0.67; both p<0.01.

We inferred that (i.) Strength in bones of different sizes is achieved by spatial re-organization of cortices and trabeculae of similar sizes. (ii.) The NSA is an evolutionary adaptation to reduce the stress on the inferior of aspect of the FN during bipedal gait.

P-TUE-137

Automatic detection of bone quality for adaptive screw tightening

T.C. Hearn, K.J. Reynolds and T.M. Cleek
Flinders University of South Australia

Internal fixation of fractures often requires the tightening of bone screws to stabilise fragments. Inadequate torque can leave the fracture unstable, while over-tightening results in thread stripping and loss of fixation. The optimal amount of screw torque is specific to each application and is difficult to attain in practice due to the wide variability in bone properties. The aim of this project was to develop an automated system for sensing the properties of a material through its interaction with a bone screw, and to use this data to determine an appropriate level of tightening. A custom test rig was designed and built for bone screw experiments. We established that differences in synthetic bone material density of 0.1 gm/cc in range corresponding to osteoporotic bone could be automatically detected through effects on the rotational characteristics of a cancellous bone screw. Based on this detection, an electric motor controller was demonstrated to change driver speed and stop implant tightening at a variable level corresponding to material density. Ovine cancellous bone specimens were then tested to evaluate the method given the continuously variable density and interface characteristics of bone. Results indicated that plateau current measured during screw insertion is directly related to bone density and is a strong predictor of peak current. Based on these relationships, a control system was programmed and subsequent shutoff tests results were encouraging. We have demonstrated that bone density can be automatically detected through screw rotational characteristics, establishing the basis for adaptive surgical control of screw tightening.

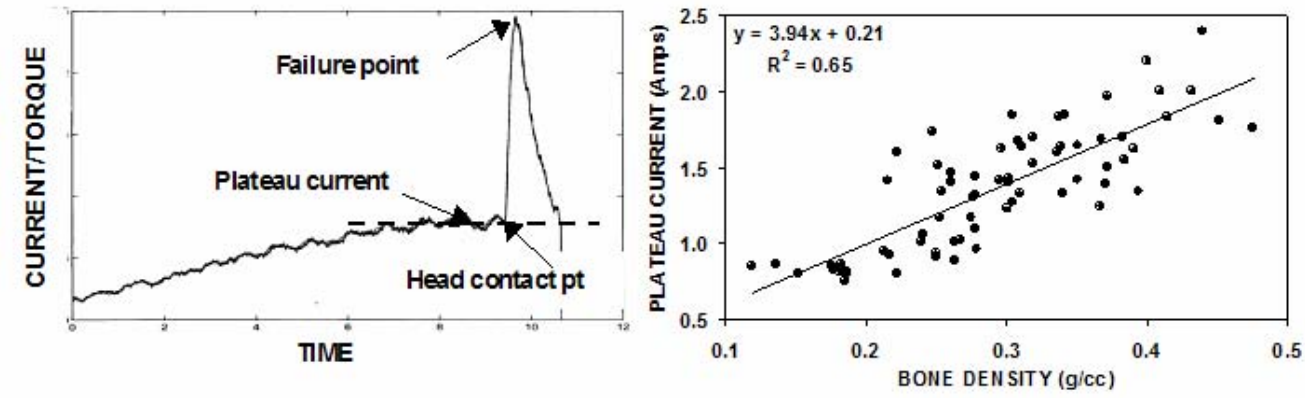

Figure 1. a) Sample motor current and torque profiles **b)** Plateau current versus specimen bone density

P-TUE-139

Peripheral quantitative computerised tomography of the tibia of the young pig

E.C. Firth, C.W. Rogers, *M. Kruger, D O'Brien and A. Darragh
*Institute of Veterinary Animal and Biomedical Sciences; *Institute of Food, Nutrition and Human Health, Massey University, Palmerston North, New Zealand*

The purpose was to define a suitable method for determining volumetric bone density (BMD_v) of the tibia in piglets, ten of which were housed indoors, fed on full cream milk with added vitamins and minerals according to NRC requirements, and euthanised at 6 weeks (bodyweight 13.85±0.6 kg). The tibia was scanned using

peripheral quantitative computerised tomography (XCT2000, Stratec Medical; slice thickness 2mm, voxel size 0.4mm, CV < 1.2% for any parameter) at consistent sites related to the externally measured bone length.

In the epiphysis and metaphyses, BMD_v of trabecular (45% of the core area of the bone) and cortical-subcortical (outer 55%) regions were determined (200mg/cm^{3}outer contour threshold). In the diaphysis bone mineral content (BMC), area and BMD_v (threshold 280mg/cm^3) were determined.

Trabecular BMD_v in the proximal epiphysis was 219.5± 6.8 mg/cm^3. In the proximal metaphysis trabecular BMD_v progressively decreased from 5mm (230.7±12.8mg/cm^3) to 15mm (173.1±12.4mg/cm^3) distal to the proximal physis, but total density increased (5mm 290.8±10.6mg/cm^3, 15mm 337.7±10.4mg/cm^3). There was no significant difference between the 5 contiguous diaphyseal sites in area, BMC, or BMD_v (709± 6.7mg/cm^3).

We conclude that in young pigs, bone size and density can be determined from one mid-diaphyseal site, and trabecular BMD_v at 10mm from the proximal and distal physes. The technique is simple, and allows the separation and relative change in the size and density of trabecular and cortical fractions to be assessed as they respond to nutritional, hormonal, pharmacological or exercise interventions.

P-TUE-141

Facilitating access to alendronate for elderly patients with osteoporotic fractures presenting to orthopaedic wards through a new initiative

S. Paul
Geriatrician, Middlemore Hospital, South Auckland Health, New Zealand

Osteoporosis is common and preventable disorder of the older adult skeleton. Bisphosphonates (eg Alendronate) are potent anti-resorptive agents effective in the prevention of both vertebral and non-vertebral fractures. On October 1, 2005, PHARMAC relaxed the criteria for subsidised access to fosamax.

Aim: This initiative was started by the Ortho-Geriatric team to address a gap in optimal managementt of osteoporosis in pateints with osteoporotic fractures admitted to the orthopedic acute services-an earlier audit of pateints witrh fracture Neck of femur had revealed that up to 50% of these pateints were returning home directly from the ortho wards hence potentially missing out on osteoporosis treatment

Method: During daily Othogeriatric Preop round by the team including Orthogeriatrician, Pharmacist, and Fracture Coordinator patients with osteoporotic fractures were identified, assessed and following the screening

- Fosamax was started for the patient while he/she was in the hospital.
- Special authority was applied for the respective patients, so that they get the approval before they leave the hospital and have no problems getting the medicine in the community, post discharge.
- Counselling regarding the osteoporosis medications provided, pre-discharge. Patients provided with printed, personalised medication cards detailing their medications for bone protection.

A survey was conducted starting October 1, 2005 (when PHARMAC relaxed the funding criteria)for 4 months.

Result and Conclusion: More than 125 patients were started on bone protection (Fosamax, calciferol and calcium carbonate) during the study period(details will be presented),the initiative has now been adopted as routine practice.