The Best Bone Papers of 2013

So many; so...

I have chosen, what “I” think are the some of the most vital over a few years.

e.g. the opinions of P. Miller
• Why do people fracture who do not have “osteooporosis”? Or,....... 

what is osteoporosis?
NOT ALL PATIENTS WITH FRACTURES HAVE “OSTEOPOROSIS”

Women
Non-vertebral fractures

- 44% Osteoporosis
- 43% Low BMD
- 13% Normal BMD

Hip fractures

- 64% Osteoporosis
- 31% Low BMD
- 5% Normal BMD

Men
Non-vertebral fractures

- 21% Osteoporosis
- 61% Low BMD
- 18% Normal BMD

Hip fractures

- 39% Osteoporosis
- 58% Low BMD
- 3% Normal BMD

Osteoporosis: Identifying the Problem

“A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture.” “Bone strength is a composite of bone density and bone quality”

The Clinical Diagnosis of Osteoporosis

1. A low trauma fracture after age 50 independent of any BMD or T-score level.

2. The World Health Organization (WHO) BMD criteria: a T-score of -2.5 or lower in postmenopausal women or men 50 and older who have not suffered a fracture (an epidemiological enterprise).
Is The T-score

A good thing or, not?
Bone Strength

- Bone Density
- Bone Quality
The Search for The Holy Grail
Dr. P. Miller’s Patented Bone Quality Meter
Resolution of HRCT vs HRpQCT vs Bone Bx

HRCT
- 160-200 microns

HRpQCT
- 82 microns

MicroCT
- 28-30 microns
TBS

An office-based bone quality tool?
Trabecular Bone Score: A Noninvasive Analytical Method Based Upon the DXA Image

Barbara C Silva, William D Leslie, Heinrich Resch, Olivier Lamy, Olga Lesnyak, Neil Binkley, Eugene V McCloskey, John A Kanis, and John P Bilezikian

JBMR 2014
The Osteocyte: “The Boss”

Mechanostat
FGF-23
Sclerostin
PGE, NO, Rank-Ligand

Boneywald L-personal communication
Dallas SL, Prideaux M, Bonewald LF.

The Osteocyte, an Endocrine Cell, and More.

Endocrine Reviews 2013; 34(5): 658-690
Osteoclasts

RANKL, OPG, MCSF

FGF23

Osteocytes

Wnts, PGE$_2$

Sclerostin, PGE$_2$

A. Boyde, S. Jones

P. Nijweide

Osteoclasts

Bownwald L -PC

Osteoblasts
Sclerostin

- Serum levels go **higher** at each stage of chronic kidney disease (CKD)-could explain the adynamic bone disease in CKD.
- Serum levels are **higher** in diabetics - could explain the low bone formation seen in diabetics.
- Serum levels **higher** in younger patients with fragility fractures (pre-menopausal and visceral fat).
- GLP 1 agonists **reduce** serum sclerostin levels - might explain a bone potential anabolic effect of GLP 1 agonists on bone.
- Mono-clonal antibody to sclerostin may offer a novel anabolic therapy for osteoporosis (and other bone diseases associated with low bone formation)
Serum sclerostin as a function of CKD stage based on GFR measured by inulin clearance

Pellettier S et al. CJSAN May 2013

*
Diabetes and Sclerostin

• 1. Clarke B and Drake MT. Bone Key 2013
• 2. Yamamoto M et al JCEM 2013
• 3. Ardawi MS et al Bone 2013
• 4. Gennari L et al JCEM 2012
In vivo assessment of bone quality in postmenopausal women with type 2 diabetes.

Farr JN, Drake MT, Amin S, Melton LJ 3rd, McCready LK, Khosla S.

J Bone Miner Res. 2014
A Review of Rodent Models of Type 2 Diabetic Skeletal Fragility

Roberto J Fajardo, Lamya Karim, Virginia I Calley, and Mary L Bouxsein

Beyond glycemic control in diabetes mellitus: effects of incretin-based therapies on bone metabolism.

Ceccarelli E, Guarino EG, Merlotti D, Patti A, Gennari L, Nuti R, Dotta F.

Do GLP 1 agonists inhibit sclerostin ??

Could a diabetes drug be a bone drug ?

Front Endocrinol (Lausanne). 2013
FGF 23

Broad Clinical Implications
The Interactions Between the Parathyroid Glands, Kidneys, Bone and Systemic Vasculature: The Bond Between Bone and Body

Miller PD, Sprague S, Shane E

Ca Absorption
P Absorption

1,25 D

PTH

Ca Absorption
P Absorption

FGF 23

Serum P

GFR ↓

FGF 23 ↓ 1,25 D

FGF 23 ↓ P Reabsorption

FGF 23 ↓ PTH

1,25 D

↑ Ca and P

SCLEROSTIN

Osteoclast

Osteocytes

Osteoblast
Perspective

FGF23
more than a regulator of renal phosphate handling?

Harald Jüppner, Myles Wolf, and Isidro B. Salusky JBMR 2010
KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

Kidney Internat 2013; 3(1); 1-163
Elevated FGF 23 in CKD

1. Strong risk factor for CV mortality
2. Highly associated with LVH
3. Mono-clonal antibody to FGF-23 —results in hyperphosphatemia
When Should Clinician's Order a FGF-23

• 1. CKD ??
• 2. Unexplained osteomalacia
• 3. Unexplained persistent hypophosphatemia
• 4. Unexplained elevated BSAP
• 5. Normal 25 OH (D ) with low 1,25 OH (D )
• 6. Renal tubular acidosis
The Obesity Epidemic
What in vivo evidence is there that adipose depots can regulate skeletal turnover?

Rosen C (Personal communication)
The Bone Fat Interface: Basic and Clinical Implications of Marrow Adiposity

Maureen Devlin PhD and Clifford J Rosen MD

Lancet Diabetes Endocrinol 2014
Function of Marrow Fat; Physiologic vs Pathologic

Physiological
- Positive association with bone mass
- Puberty
- Fracture repair etc.
- Metabolic characteristics:
  - Responsiveness to external stimuli
  - Brown adipocyte-like phenotype
  - Expression of Ucp1
- Positive secretory factors: IGF-1, Leptin etc.

Pathological
- Negative association with bone mass
- Calorie restriction
- Anorexia nervosa
- Lipodystrophy
- GH deficiency
- Aging, Diabetes etc.
- Negative secretory factors:
  - Inflammatory cytokines
  - Free fatty acids etc.

Kawai M et al J Int Med 2013

Abdominal fat is associated with lower bone formation and inferior bone quality in healthy premenopausal women: a transiliac bone biopsy study.

Both relationships remained significant after adjustment for age. Similar relationships were seen with CT measured VAT (obtained in a subset).

Cohen et al., JCEM 2013
Bone Remodeling in Trunk Fat Tertiles

**Bone Formation Rate**

- **mm²/mm/yr**

**Activation Frequency**

- **cycle/yr**

**BIOPSIES**

- Low Trunk Fat
- Middle
- High Trunk Fat

**Serum Osteocalcin ng/mL**

- p<0.01

**Serum PINP mcg/L**

- p<0.01

**Serum CTX ng/mL**

- p=0.03

Cohen et al., JCEM 2013
Potential Mechanisms:
Physical Activity and Sclerostin

Low Reported Exercise / Mechanical Loading
↓
High sclerostin
Low IGF-1
↓
Low Bone Formation and Low Bone Volume

Cohen et al, ASBMR meeting 2014

<table>
<thead>
<tr>
<th></th>
<th>Low Trunk Fat N=13</th>
<th>High Trunk Fat N=13</th>
<th>P Low vs High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise Min/wk</td>
<td>150 ± 46</td>
<td>98 ± 46</td>
<td>0.01</td>
</tr>
<tr>
<td>Sclerostin Ng/mL</td>
<td>0.64 ± 0.18</td>
<td>1.14 ± 0.56</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Correlation with Serum Sclerostin R,p

<table>
<thead>
<tr>
<th></th>
<th>Correlation with Serum Sclerostin R,p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>-0.45, 0.005</td>
</tr>
<tr>
<td>Bone Formation</td>
<td>-0.34, 0.04</td>
</tr>
<tr>
<td>Bone Volume</td>
<td>-0.32, 0.046</td>
</tr>
<tr>
<td>IGF-1</td>
<td>-0.41, 0.008</td>
</tr>
</tbody>
</table>
TERTILES based on %Trunk Fat

<table>
<thead>
<tr>
<th></th>
<th>Low Trunk Fat N=13</th>
<th>Middle Trunk Fat N=14</th>
<th>High Trunk Fat N=13</th>
<th>Low vs High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin (ng/mL)</td>
<td>7.6 ± 3.6</td>
<td>16.4 ± 7.6</td>
<td>27.5 ± 12.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adiponectin (mcg/L)</td>
<td>16272 ± 5506</td>
<td>8782 ± 3156</td>
<td>7085 ± 4048</td>
<td>0.0001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.53 ± 0.16</td>
<td>0.92 ± 1.11</td>
<td>1.54 ± 1.08</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HDL</td>
<td>60 ± 10</td>
<td>47 ± 9</td>
<td>42 ± 17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TG</td>
<td>77 ± 47</td>
<td>65 ± 25</td>
<td>119 ± 68</td>
<td>0.08</td>
</tr>
<tr>
<td>IGF-1 (ng/mL)</td>
<td>203 ± 74</td>
<td>187 ± 46</td>
<td>163 ± 34</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Free estradiol, calcium, PTH, and vitamin D did not differ

Cohen et al., JCEM 2013
Leptin-Adiponectin: A Push-Pull System

1. Both secreted by fat cells
2. Both may have local bone cellular effects: leptin stimulates while adiponectin inhibits osteoblast differentiation.
3. Major effect: both go to the brain. Leptin stimulates the sympathetic nervous system resulting in inhibition of bone formation and increase in bone resorption (and regulates appetite). Adiponectin inhibits the sympathetic nervous system resulting in activation of osteoblasts (and increases insulin sensitivity)

Devlin MJ and Rosen CL. Lancet 2014
Leptin controls bone mass and energy metabolism through the CNS increasing SNS activity.
Adiponectin Has a Dual Action on Bone: Direct Inhibition of OBs And Indirect Stimulation of OBs via Inhibition of Sympathetic Tone

Kartensky G et al Cell Metabolism 2013

Adiponectin

Adipocytes  osteoblast progenitors

Kartensky G et al Cell Metabolism 2013
Osteocytes as Regulators of Muscle Mass and Function
Forum on Bone and Skeletal Muscle Interactions: Summary of the Proceedings of an ASBMR Workshop


Journal of Bone and Mineral Research 2013
What’s in a name revisited: should osteoporosis and sarcopenia be considered components of “dysmobility syndrome?”

N. Binkley & D. Krueger & B. Buehring

Osteoporos Int 2013
Muscle Regulation of Osteocyte Viability and Function
Muscle as an Endocrine Tissue

1. Muscle secreted cytokines known as ‘myokines’, appear to have systemic effects that create an anti-inflammatory environment, leading to the hypothesis that muscles are also endocrine organs (Pedersen 2008, 2009; Scheele et al 2009).

2. These myokines include factors such as insulin-like growth hormone, Interleukins 6, 8, 15, Leukemia Inhibitory Factor, FGF21, and Follistatin-like 1 (Broholm 2011).

3. Exercise increase myokine production reduces the risk of “diseasome” of physical inactivity (Pedersen 2011)
The 5th ISCD Position Development Conference was held March 21 & 22, 2013 in conjunction with the ISCD Annual Meeting in Tampa, Florida, USA and covered the following topics:

- Body Composition using DXA
- Use of Updated NHANES Reference Databases for Both Spine and Hip DXA
- Indications of DXA in Women Younger Than 65 and Men Younger Than 70
- Indications for VFA
2013

CLINICIAN’S GUIDE TO PREVENTION AND TREATMENT OF OSTEOPOROSIS

NATIONAL OSTEOPOROSIS FOUNDATION
Identification of Incident Fractures at One Year: By DXA

One year  
Baseline

Incident fracture  
Prevalent fractures

ISCD Certification
Systematic vertebral fracture assessment in asymptomatic postmenopausal women

A. El Maghraoui *, A. Rezqi, A. Mounach, L. Achemlal, A. Bezza, I. Ghozlani

Rheumatology Department, Military Hospital Mohammed V, Rabat, Morocco

ABSTRACT

Introduction: Recognition of vertebral fractures (VFs) changes the patient’s diagnostic classification, estimation of fracture risk, and threshold for pharmacological intervention. Vertebral fracture assessment (VFA) enables the detection of VFs in the same session as bone mineral density (BMD) testing.

Objective: To study prevalence and risk factors of VFs using VFA in asymptomatic women and measure its effect on treatment recommendations.

Methods: We enrolled 908 postmenopausal women (mean age, weight and BMI of 60.9 ± 7.7 (50–91) years, 73.2 ± 13.2 (35–150) kg and 29.8 ± 5.3 (14.5–50.8) kg/m², respectively. Lateral VFA images and scans of the lumbar spine and proximal femur were obtained using a GE Healthcare Lunar Prodigy densitometry. VFs were defined using a combination of Genant semiquantitative (SQ) approach and morphometry.

Results: VFs were identified in 382 patients (42.0%): 203 (22.3%) had grade 1 and 179 (19.7%) had grade 2 or 3. The prevalence of VFA detected fractures globally increased significantly with age and BMI and BMD declined. A fracture was identified on VFA in 63 (28.3%) women with normal BMD (8.5% had grade 2/3 VFs) and in 145 (38.5%) with osteopenia (15.7% had grade 2/3 VFs). Stepwise regression analysis showed that presence of VFs was independently related to age, BMI, number of parity, history of peripheral fracture and lumbar spine BMD.

Conclusion: A high proportion of women with asymptomatic VFs would not receive treatment if screening were based only on BMD evaluation. Our results support the recommendation to enlarge the indications of VFA in the presence of risk factors such as age over 60, multiparity, history of peripheral traumatic fractures and low BMI.
Fractures

• 1. Fractures beget fractures
• 2. Fractures rates increase with age
• 3. Fractures (all types) are associated with high mortality
Progressively Increasing Fracture Risk With Advancing Age After Initial Incident Fragility Fracture: The Tromsø Study

Luai Awad Ahmed,1 Jacqueline R Center,2 Åshild Bjørnerem,3,4 Dana Bluic,2 Ragnar M Joakimsen,3,5 Lone Jørgensen,1 Haakon E Meyer,6,7 Nguyen D Nguyen,3 Tuan V Nguyen,3 Tone K Omsland,5,8 Jan Størmer,9 Grethe S Tell,7 Tineke ACM van Geel,10 John A Eiseman,2,11,12,13 and Nina Emaus1

1Department of Health and Care Sciences, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway
2Osteoporosis & Bone Biology Program, Garvan Institute of Medical Research, Sydney, Australia
3Department of Clinical Medicine, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway
4Department of Obstetric and Gynecology, University Hospital of North Norway, Tromsø, Norway
5Medical Clinic, University Hospital of North Norway, Tromsø, Norway
6Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway
7Department of Community Medicine, Institute of Health and Society, University of Oslo, Norway
8Department of Public Health and Primary Health Care, University of Bergen, Norway
9Department of Radiology, University Hospital of North Norway, Tromsø, Norway
10Department of General Practice, Maastricht University, Maastricht, The Netherlands
11Department of Endocrinology, St Vincent’s Hospital, Sydney, Australia
12St. Vincent’s Clinical School, University of New South Wales, Sydney, Australia
13School of Medicine, University of Notre Dame, Sydney, Australia

Fig. 1. Incidence rates of initial and subsequent fractures by type and age at initial fracture in women and men.
Compound Risk of High Mortality Following Osteoporotic Fracture and Refracture in Elderly Women and Men

Dana Bluc,1 Nguyen D Nguyen,1 Tuan V Nguyen,1,3 John A Eisman,1,2,3,4 and Jacqueline R Center1,2,3

1Osteoporosis and Bone Biology, Garvan Institute of Medical Research, Clinical Excellence and Research, School of Medicine, University of Notre Dame Medical School, Sydney, Australia
2Clinical School, St Vincent’s Hospital, Sydney, Australia
3Faculty of Medicine, University of New South Wales, Sydney, Australia
4Clinical Translation and Advanced Education, Garvan Institute of Medical Research, Clinical Excellence and Research, School of Medicine, University of Notre Dame Medical School, Sydney, Australia

ABSTRACT
After fracture there is increased risk of refracture and premature mortality. These outcomes, particularly premature mortality following refracture, have not previously been studied together to understand overall mortality risk. This study examined the long-term cumulative incidence of subsequent fracture and total mortality with mortality calculated as a compound risk and separated according to initial and refracture. Community-dwelling participants aged 60+ years from Dubbo Osteoporosis Epidemiology Study with incident fractures, followed prospectively for further fractures and deaths from 1989 to 2010. Subsequent fracture and mortality ascertained using cumulative incidence competing risk models allowing four possible outcomes: death without refracture; death following refracture; refracture but alive, and event-free. There were 952 women and 343 men with incident fracture. Within 5 years following initial fracture, 24% women and 20% men refractured; and 26% women and 37% men died without refracture. Of those who refractured, a further 50% of women and 75% of men died, so that total 5-year mortality was 39% in women and 51% in men. Excess mortality was 24% in women and 27% in men. Although mortality following refracture occurred predominantly in the first 5 years post-initial fracture, total mortality (post-initial and refracture) was elevated for 10 years. Most of the 5-year to 10-year excess mortality was associated with refracture. The long-term (>10 years) refracture rate was reduced, particularly in the elderly as a result of their high mortality rate. The 30% alive beyond 10 years postfracture were at low risk of further adverse outcomes. Refractures contribute substantially to overall mortality associated with fracture. The majority of the mortality and refractures occurred in the first 5 years following the initial fracture. However, excess mortality was observed for up to 10 years postfracture, predominantly related to that after refracture. © 2013 American Society for Bone and Mineral Research.
After a fragility fracture, only 23% of patients receive screening/treatment for osteoporosis

- Nearly an 80% care gap

NCQA HEDIS Fragility Fracture National Average, 2011.
Osteoporosis Medication Use after Hip Fractures in U.S. Patients Between 2002-2011

Solomon DH, Johnston SS, Boystov NN, McMorrow D, Lane JM and Krohn KD

JBMR 2014
WHY ?
Proportion of Elderly Women in Fee-for Service Medicare who Received a DXA Scan, 2002-2012

% with any scan

2002: 10.3%
2003: 11.0%
2004: 11.4%
2005: 11.8%
2006: 12.4%
2007: 12.7%
2008: 13.1%
2009: 13.1%
2010: 12.6%
2011: 12.7%
2012: 11.7%

8% Decline
More Bone Density Testing Is Needed, Not Less

E. Michael Lewiecki, Andrew J. Laster, Paul D. Miller, and John P. Bilezikian

JBMR 2012
1. Kaiser Permanente
   - Reduced the hip fracture rate expected by 38% (since 1998)
   - If implemented nationally, a similar effort could reduce the number of hip fractures by over 100,000 (saving over $5 billion/year)

2. Geisinger Health System
   - Achieved $7.8 million in cost savings from 1996-2000

3. American Orthopaedic Association Own the Bone® Program
   - Achieved statistically significant changes in health professional behavior/referral (calcium and vitamin D, exercise, fall prevention, etc.)
   - Over 110 sites and 7,000 patients involved from 31 states
Major Therapeutic Advances in Pharmacological Treatment of Osteoporosis

1. Long-term denosumab data. (Amgen)
2. Mono-clonal antibody to sclerostin (Amgen, Lilly).
3. Parathyroid hormone related peptide agonist (abaloteraparatide) (Radius Research)
4. Cathepsin K inhibitor (odanacatib) (Merck)
Effect of denosumab on bone mineral density and biochemical markers of bone turnover: 8-year results of a phase 2 clinical trial

M. R. McClung · E. M. Lewiecki · M. L. Geller
M. A. Bolognese · M. Peacock · R. L. Weinstein
B. Ding · E. Rockabrand · R. B. Wagman · P. D. Miller
Nonvertebral Fracture Rate Ratios: Long-term DMAAb Subjects

Rate Ratio (95% CI) = 0.74 (0.59–0.95)  
P = 0.016

Rate Ratio (95% CI) = 0.73 (0.50–1.06)  
P = 0.096

Fracture Rate per 100 Subject-years (95% CI)

First 3 Years: 1.98
4th Year: 1.43
Years 4-7: 1.45

Fractures n = 140
DMAAb Treatment

N = number of subjects who did not miss > 1 dose of DMAab during FREEDOM and enrolled into the extension.

Ferrari S et al ASBMR 2014
Romosozumab in Postmenopausal Women with Low Bone Mineral Density

Michael R. McClung, M.D., Andreas Grauer, M.D., Steven Boonen, M.D., Ph.D., Michael A. Bolognese, M.D., Jacques P. Brown, M.D., Adolfo Diez-Perez M.D., Ph.D., Bente L. Langdahl, Ph.D., D.M.Sc., Jean-Yves Reginster, M.D., Ph.D., Jose R. Zanchetta, M.D., Scott M. Wasserman, M.D., Leonid Katz, M.D., Judy Maddox, D.O., Yu-Ching Yang, Ph.D., Cesar Libanati, M.D., and Henry G. Bone, M.D.

McClung M et al NEJM 2014
AMG 785 Phase 2 Trial

- 419 postmenopausal women with low BMD
- AMG 785 Increased BMD superior to TPTD and ALN
- Increase in bone formation markers
- Decrease in bone resorption markers
- AEs similar to PBO except for injection site reactions (4% PBO, 12% AMG 785)
- Phase 3 trial currently underway

Abaloparatide (PTHrp analogue): LS BMD at 48 Weeks

Hattersley G et al. ENDO. 2012. OR08-1.
THE OSTEOCLAST!

Odanacatib Effect on Biomarkers of Bone Resorption and Formation Geometric Mean Percent Change from Baseline at Year 8

**Urine N-Telopeptide/Creatinine Ratio (nmol/mmol)**

- ODN for 8 yrs
- ODN for 6 yrs
- ODN for 5 yrs
- ODN for 3 yrs

**Serum Bone Specific Alkaline Phosphatase (ng/mL)**

- ODN for 8 yrs
- ODN for 6 yrs
- ODN for 5 yrs
- ODN for 3 yrs

ODN, Odanacatib 25 or 50 mg once weekly
Bone Density, Turnover, and Estimated Strength in Postmenopausal Women Treated With Odanacatib: A Randomized Trial

Kim Brixen, Roland Chapurlat, Angela M. Cheung, Tony M. Keaveny, Thomas Fuerst, Klaus Engelke, Robert Recker, Bernard Dardzinski, Nadia Verbruggen, Shabana Ather, Elizabeth Rosenberg, and Anne E. de Papp

Context: Odanacatib, a cathepsin K inhibitor, increases spine and hip areal bone mineral density (BMD) in postmenopausal women with low BMD and cortical thickness in ovariectomized monkeys.

Objective: The objective of the study was to examine the impact of odanacatib on the trabecular and cortical bone compartments and estimated strength at the hip and spine.

Design: This was a randomized, double-blind, 2-year trial.

Setting: The study was conducted at a private or institutional practice.

Participants: Participants included 214 postmenopausal women with low areal BMD.

Intervention: The intervention included odanacatib 50 mg or placebo weekly.

Elizabeth Shane,* David Burr,* Bo Abrahamsen, Robert A Adler, Thomas D Brown, Angela M Cheung, Felicia Cosman, Jeffrey R Curtis, Richard Dell, David W Dempster, Peter R Ebeling, Thomas A Einhorn, Harry K Genant, Piet Geusens, Klaus Klaushofer, Joseph M Lane, Fergus McKiernan, Ross McKinney, Alvin Ng, Jeri Nieves, Regis O’Keefe, Socrates Papapoulos, Tet Sen Howe, Marjolein CH van der Meulen, Robert S Weinstein, and Michael P Whyte
ISCD Annual Meeting 1990------
Thank You Mike and All of You Who Support The Santa Fe Bone Symposium

Congeniality is Special and Unique in

2014