Beyond BMD: Bone Quality and Bone Strength

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Outline

• Determinants of Bone Strength
• Limitations of BMD
• Beyond BMD
• Biomechanics of Fractures:
  Comparing applied loads to strength

Disclosures

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Amgen, Eli Lilly, Merck

Research funding:
Amgen, Merck

Structural failure of the skeleton
**Design of a Structure**
- Consider what loads it must sustain
- Design options
  - Overall geometry
  - Building materials
  - Architectural details

**Determinants of Whole Bone Strength**
- Morphology
  - size (mass)
  - shape (distribution of mass)
  - porosity
  - microarchitecture
- Properties of Bone Matrix
  - mineralization
  - collagen
  - microdamage
  - ...others...

**Hierarchical Structure of Bone**
- Cell
- Matrix
- Lamellar Osteonal
- μ-architecture
- Whole Bone

**Assessing Bone Biomechanical Properties**
- Structural Properties
- Material Properties

Bouxsein, Osteop Int, 2003
Biomechanical Testing

Key Properties

Mechanical Behavior of Common Materials

Glass (brittle)
Load (Stress)
Deformation (Strain)

Plastic (ductile)

Mechanical Behavior of Bone and Its Constituents

Outline

- Osteoporosis & Bone Strength
- Limitations of BMD
Clinical Assessment of Bone Strength

Areal BMD by DXA
- Bone mineral / projected area (g/cm²)
- Reflects (indirectly)
  - Bone size
  - Mineralization
- Moderate to strong correlation with whole bone strength ($r^2 = 50 - 90\%$)

Age and BMD Are Independent Risk Factors for Hip Fracture

Age (yrs) 80
> 5-fold increase in fracture probability from age 50 to 80

Hip BMD T-score (SD)

Fracture risk prediction:
Less than half of patients who fracture have osteoporosis by BMD testing (i.e. t-scores $> -2.5\%$)

- Only 34% of women and 21% of men suffering a non-vertebral frx had BMD in osteoporotic range (Schul et al, 2004; 2006)
- Only half of elderly women with incident hip frx had BMD in osteoporotic range at baseline (Wainwright et al, JCEM 2006)

* Based on WHO guidelines for Osteoporosis Diagnosis
Outline

• Osteoporosis & Bone Strength

• Limitations of BMD

• Beyond BMD

Bone Strength

MORPHOLOGY
size & shape
microarchitecture

MATRIX PROPERTIES
tissue composition
matrix properties

BONE REMODELING
formation / resorption

OSTEOPOROSIS DRUGS

Distribution of Mass Affects Mechanical Behavior

Moment of Inertia proportional to \( d^4 \)
Effect of cross-sectional geometry on long bone strength

- aBMD (by DXA) = = =
- Compressive Strength = ↑ ↑
- Bending Strength = ↑↑ ↑↑

Bone Strength

- SIZE & SHAPE
  - macroarchitecture
  - microarchitecture
- MATRIX PROPERTIES
  - tissue composition
  - matrix properties
- BONE REMODELING
  - formation / resorption

Age-Related Changes in Trabecular Microarchitecture

Decline in bone mass and deterioration of trabecular bone structure both contribute to decreased bone strength.

Excessive Bone Resorption Weakens Trabecular Architecture

- Stress concentration (focal weakness)
- Perforation
Effect of Resorption Cavities on Trabecular Bone Strength

- 20% decrease in bone mass
  1) trabecular thinning
  30% decrease in strength
  2) add resorption cavities
  50% decrease in strength

van der Linden, et al, JBMR 2001

Effect of Density Reduction on Strength: Change in Trabecular Thickness vs. Number

<table>
<thead>
<tr>
<th>Density Reduction (%)</th>
<th>Residual Strength (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>75</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>15</td>
<td>25</td>
</tr>
</tbody>
</table>

Silva and Gibson, Bone, 1997

Microarchitectural changes that influence bone strength

Force required to cause a slender column to buckle:

- Directly proportional to:
  - Column material
  - Cross-sectional geometry

- Inversely proportional to:
  - (Length of column)$^2$

Moselioide, Bone, 1988

Theoretical effect of cross-struts on buckling strength

$\text{Buckling Strength proportional to } (\text{Strut Length})^2$

<table>
<thead>
<tr>
<th># Horizontal Trabeculae</th>
<th>Effective Length</th>
<th>Buckling Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>L</td>
<td>S</td>
</tr>
<tr>
<td>1</td>
<td>1/2 L</td>
<td>4 x S</td>
</tr>
</tbody>
</table>

Mosekilde, Bone, 1988
Dramatic Changes in Trabecular Architecture in Early Postmenopausal Women

(52 yr old woman, 3 yrs post-menopause)


Anti-Resorptive Tx Preserves Trabecular Architecture in Early Postmenopausal Women

(Placebo vs Risedronate, 5 mg/d, 1 yr)

*P < 0.05 vs baseline.
†P < 0.05 vs PBO.

Spine BMD

Trabecular bone volume

Trabecular number

Trabecular separation

PBO (n=12)
RIS (n=14)


Age-related changes in femoral neck cortex and association with hip fracture

Those with hip fractures have:

- Preferential thinning of the inferior anterior cortex
- Increased cortical porosity


Porosity is profound in the aging femoral neck

19 elderly female cadavers (87 ± 8 yrs)
Intracortical porosity ranged from 5% to 39%

Bousson et al. JBMR, 2004
Cortical porosity and trabecularization of the endocortical surface with age.

Cortical bone loss increases with age. Prior studies have likely underestimated cortical bone loss.

Prior studies have likely underestimated cortical bone loss.

Bone Strength

GEOMETRY
macroarchitecture
microarchitecture

MATERIAL
tissue composition
matrix properties

BONE REMODELING
formation / resorption

How is mineralization density influenced by rate of bone turnover?

- Slow process of 2nd mineralization
- Decreased bone turnover allows mineralization to proceed

Increased bone turnover with estrogen deficiency decreases mineralization density.
Relationship between mineralization and biomechanical properties

![Diagram showing the relationship between mineralization and biomechanical properties.]

Bone remodeling & microdamage

What is "damage"?

- Repetitive loading
- No repair process
- ↓ Mechanical properties

Microdamage in Bone

- Associated with decreased cortical bone strength
- Microcracks seen in human femur & vertebra, increase with age
- Signal for remodeling & repair
  - in animals, microdamage increases when remodeling is suppressed
- No demonstrated relationship with fracture risk

Images from L. Mosekilde, Technology and Health Care. 1998

Age-related changes in bone properties that lead to decreased bone strength

- Decreased bone mass and BMD
- Altered geometry
- Altered architecture
  - Cortical thinning
  - Cortical porosity
  - Trabecular deterioration
- Altered matrix properties
Whole bone strength declines dramatically with age.

Outline

- Determinants of Bone Strength
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- Beyond BMD
- Biomechanics of Fractures: Comparing applied loads to strength

Fracture Etiology

 Loads applied to the bone  

\[ \Phi = \frac{\text{Applied Load}}{\text{Failure Load}} \]

Fracture? 

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Fracture? 

Loads applied to the bone 

\[ \text{Bone strength} \]

Bending, lifting activity 

Propensity to fall 

Spine curvature 

Muscle strength 

Disc degeneration 

Fall traits 

Protective responses 

Soft-tissue padding 

Impact surface 

Geometry 

Microstructure 

Material Properties 

Bone strength
Biomechanics of Hip Fracture

- Over 90% of hip fx’s associated with a fall
- Less than 2% of falls result in hip fracture
- Fall is necessary but not sufficient
- What is a high risk fall?

Independent Risk Factors for Hip Fx

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall to side</td>
<td>5.7 (2.3 - 14)</td>
</tr>
<tr>
<td>↓ Femoral BMD</td>
<td>2.7 (1.6 - 4.6)*</td>
</tr>
<tr>
<td>↑ Fall energy</td>
<td>2.8 (1.5 - 5.2)**</td>
</tr>
<tr>
<td>↓ Body mass index</td>
<td>2.2 (1.2 - 3.8)*</td>
</tr>
</tbody>
</table>

* calculated for a decrease of 1 SD
** calculated for an increase of 1 SD

Greenspan et al, JAMA, 1994

Estimating Loads Applied to the Hip

- In young volunteers, only 2/6 were able to break the fall
- 85% of impact force delivered directly to femur
- Force ↑ by ↑ body wt
- Force ↓ by ↑ thickness of trochanteric soft tissue

Peak impact forces applied to greater trochanter:
270 - 730 kg (600 - 1600 lbs)
(for 5th to 95th percentile woman)


Very high forces applied to the hip during a sideways fall

- Human cadavers
- Human volunteers
- Crash dummy
- Mathematical models and simulations

Peak impact forces applied to greater trochanter:
270 - 730 kg (600 - 1600 lbs)
(for 5th to 95th percentile woman)

Femoral ‘strength’ depends on loading direction

Femur is weak in atypical loading conditions

Femoral strength in sideways fall declines markedly with age

Biomechanics of Vertebral Fractures

- Difficult to study
  - Many do not come to clinical attention
  - Slow vs. acute onset
  - The event that causes the fracture is often unknown

- Poor understanding of the relationship between spinal loading and vertebral fragility

Estimating Loads on the Spine

\[ \frac{\text{Applied Load}}{\text{Failure Load}} \]

Biomechanical model
- Simulate bending and lifting activities
- Height, weight, body position
- Determine compressive forces on vertebra for different activities

Predicted Loads on Lumbar Spine for Activities of Daily Living

<table>
<thead>
<tr>
<th>Activity</th>
<th>Load (% BW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td>51</td>
</tr>
<tr>
<td>Rise from chair</td>
<td>173</td>
</tr>
<tr>
<td>Stand, hold 8 kg, arms extended</td>
<td>230</td>
</tr>
<tr>
<td>Stand, flex trunk 30°, arms extended</td>
<td>146</td>
</tr>
<tr>
<td>Lift 15 kg from floor</td>
<td>319</td>
</tr>
</tbody>
</table>

for a 162 cm, 57 kg woman

Ratio of load to strength for L3 during activities of daily living

<table>
<thead>
<tr>
<th>Activity</th>
<th>Lateral Spine BMD t-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Get up from sitting</td>
<td>-3.5 -2.6 -2.2 -1.5 -0.8 0</td>
</tr>
<tr>
<td>Lift 15 kg knees straight</td>
<td>2.6 1.1 0.7 0.5 0.4 0.3 0.3</td>
</tr>
<tr>
<td>Lift 15 kg w/ deep knee bend</td>
<td>2.1 0.9 0.6 0.4 0.3 0.3 0.3</td>
</tr>
<tr>
<td>Lift 30 kg knees straight</td>
<td>3.7 1.5 1.0 0.7 0.6 0.5 0.5</td>
</tr>
<tr>
<td>Lift 30 kg w/ deep knee bend</td>
<td>3.0 1.3 0.8 0.6 0.5 0.4 0.4</td>
</tr>
<tr>
<td>Open window w/ 6 kg of force</td>
<td>1.1 0.9 0.3 0.2 0.2 0.1 0.1</td>
</tr>
<tr>
<td>Open window w/ 10 kg of force</td>
<td>1.4 0.8 0.4 0.3 0.2 0.2 0.2</td>
</tr>
<tr>
<td>Tie shoes sitting down</td>
<td>1.4 0.8 0.4 0.3 0.2 0.2 0.2</td>
</tr>
</tbody>
</table>

Fracture Prevention Strategies

- Reduce the Loads Applied to Bone
  - Decrease fall frequency / severity
  - Safe-landing strategies
  - Trochanteric padding
  - Avoid high risk lifting / bending activities

- Maintain or Increase Bone Strength
  - Exercise, diet (Ca, Vit D), pharmacologic treatment

Adapted from Myers and Wilson, Spine, 1997
Summary: Factors Affecting Bone Strength and Fracture Risk

<table>
<thead>
<tr>
<th>Material</th>
<th>Micro architecture</th>
<th>Size &amp; Shape</th>
<th>Loading</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Material Image" /></td>
<td><img src="image2.png" alt="Micro architecture Image" /></td>
<td><img src="image3.png" alt="Size &amp; Shape Image" /></td>
<td><img src="image4.png" alt="Loading Image" /></td>
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