Beyond BMD: Bone Quality and Bone Strength

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Structural failure of the skeleton
Design of a Structure

- Consider what loads it must sustain
- Design options
  - Overall geometry
  - Building materials
  - Architectural details

Evolving View of Osteoporosis

Skeletal disorder characterized by decreased bone mass and architectural deterioration leading to an increased risk of fracture.

NIH Consensus Conference, 1993

Skeletal disorder characterized by compromised bone strength leading to an increased risk of fracture.

NIH Consensus Conference, 2000

Outline

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

Determinants of Whole Bone Strength

Morphology:
- size (mass)
- shape (distribution of mass)
- porosity
- microarchitecture

Properties of Bone Matrix:
- mineralization
- collagen
- microdamage
- ...others...

Bouxsein, Osteop Int, 2003
Assessing Bone Biomechanical Properties

Structural Properties

Load vs. Displacement

Material Properties

Biomechanical Testing

Key Properties

Load vs. Displacement

Strength

Stiffness

Energy absorbed (toughness)

Mechanical Behavior of Common Materials

Glass (brittle)

Plastic (ductile)

Load (Stress)

Deformation (Strain)

Mechanical Behavior of Bone and Its Constituents

Mineral

Bone

Collagen

Stress

Strain
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

Does not distinguish several attributes of whole bone strength

– 3D geometry
– Microarchitecture
– Intrinsic properties of bone matrix

Fracture risk prediction:
Less than half of patients who fracture have osteoporosis by BMD testing
(ie t-scores > -2.5*)

• Only 34% of women and 21% of men suffering a non-vertebral frx had BMD in osteoporotic range
(Schuit et al, 2004; 2006)

• Only half of elderly women with incident hip frx had BMD in osteoporotic range at baseline
(Wainwright et al , JCEM 2005)

* Based on WHO guidelines for Osteoporosis Diagnosis
Outline

• Osteoporosis & Bone Strength

• Limitations of BMD

• Beyond BMD
Effect of cross-sectional geometry on long bone strength

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

Role of Geometry in the Prediction of Hip Fracture by QCT: MrOS

- MrOS - a prospective, observational study
- 5995 men > 65 yrs from six US sites
  - QCT subset, n=3358
- Used QCT to measure femoral neck vBMD & geometry
- Followed prospectively for fracture, mean 5 ± 1 yrs
- 40 hip fractures in QCT cohort
- Analyses adjusted for age, BMI, race, and clinic

Femoral neck measures and hip fracture risk: Multivariate analyses

<table>
<thead>
<tr>
<th>Measure</th>
<th>HR per SD</th>
<th>HR per SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>QCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% cortical volume</td>
<td>3.4 (2.3–4.9)</td>
<td>2.5 (1.6–3.9)</td>
</tr>
<tr>
<td>Min FNeck area (cm²)</td>
<td>1.6 (1.3–2.1)</td>
<td>1.5 (1.1–2.0)</td>
</tr>
<tr>
<td>Trab vBMD (g/cm³)</td>
<td>1.6 (1.1–2.3)</td>
<td>1.2 (0.8–1.9)</td>
</tr>
</tbody>
</table>

Fem Neck aBMD (g/cm²)

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<tr>
<td>QCT</td>
<td>2.1 (1.1–3.9)</td>
</tr>
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Black et al, JBMR 2008
Bone Strength

SIZNE & 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)

Effect of Increased Bone Resorption on Trabecular Architecture

Perforation of Trabecular Strut
Trabecular Microfracture

L. Mosekilde, Tech and Health Care, 1998
Effect of Resorption Cavities on Trabecular Bone Strength

van der Linden, et al, JBMR 2001

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

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

Silva and Gibson, Bone, 1997

Importance of Cross-struts

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
  - \((\text{Length of column})^2\)

Mosekilde, Bone, 1988
**Theoretical Effect of Cross-Struts on Buckling Strength**

*Buckling Strength proportional to (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>

**High Resolution pQCT**

(X-treme CT, Scanco Medical AG)

- ~ 82 µm$^3$ voxel size
- ~ 3 min scan time, < 4 µSv

Reproducibility:
- density: 0.7 to 1.5% *
- structure: 1.5 - 4.4 *

Peripheral skeleton only

Specialized equipment

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**HR-pQCT discriminates osteopenic women with and without history of fragility fracture**

(age = 69 yrs, n=35 with prev frx, n=78 without fracture)

* p < 0.05 vs fracture free controls

Boutroy et al, JCEM (2005)
Osteopenic by DXA BMD (70 yr old woman)

Dramatic Changes in Trabecular Architecture in Early Postmenopausal Women

Images courtesy of S. Boutroy & P. Delmas, Inserm U831, Lyon


Anti-Resorptive Tx Preserves Trabecular Architecture in Early Postmenopausal Women
(Placebo vs Risedronate, 5 mg/d, 1 yr)

Baselina

Bone Strength

Mechanisms that may lead to increased BMD

- Increase Trabecular Thickness
- Increase Trabecular Number
- Increase Mineralization

How is mineralization density influenced by rate of bone turnover?

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

How is mineralization density influenced by rate of bone turnover?

- Decreased bone turnover allows mineralization to proceed

Increased bone turnover with estrogen deficiency decreases mineralization density

- Meunier and Bovin, Bone, 1997

Relationship between mineralization and biomechanical properties

- Normal
  - Stiffness
  - Strength
- High (osteopetrosis)
  - Stiffness
  - Strength
- Low (osteomalacia)
  - Decrease in Toughness
  - Increase in Mineralization
What do these changes in mineralization mean in terms of the bone strength?

- Independent of the quantity of bone -

Strength of bone material is related to mineralization in a non-linear fashion.

Anti-resorptive therapies ↑ mineralization by 3 - 11%  

↑ strength of trabecular bone by 13 - 20%

Bone remodeling & microdamage

What is “damage”?

- Repetitive loading
- No repair process
- ↓ Mechanical properties

Microdamage in Bone

- Associated with decreased mechanical properties in vitro
- Observed in human cortical and trabecular bone, increases with age
- Signal for remodeling & repair
- No direct relationship to fracture risk

Age-Related Changes in Bone Properties Associated with Fracture Risk

- Decreased bone mass and BMD
- Altered geometry
- Altered architecture
  - Cortical thinning
  - Cortical porosity
  - Trabecular deterioration
- Altered matrix properties

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

Outline

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

Fracture Etiology

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

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 \( \uparrow \) by \( \uparrow \) body wt
- Force \( \downarrow \) by \( \uparrow \) thickness of trochanteric soft tissue

Human volunteers
Crash dummy
Mathematical models and simulations

Peak impact forces applied to hip:
2300 - 6200 N (600 - 1600 lbs)
(for 5th to 95th percentile woman)


Measuring femoral strength ...

Femoral Strength in Sideways Fall

Stance Sideways Fall

 failure Load (kN)

3.4-fold lower
P < 0.001

Keyak et al, J Biomechanics, 1998
Effect of Aging on the Load / Strength Ratio

Sideways Fall Configuration

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

Thus, \( \Phi \) is often > 1 for sideways fall in elderly persons.

Range of Loads during sideways fall

- Young (age = 33)
- Old (age = 74)

Courtney et al, J Bone Jt Surg 1995

Biomechanics of Vertebral Fractures

- Difficult to study
  - Definition is controversial
  - 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

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

Biomechanical model

- Simulate bending and lifting activities
- Height, weight, body position
- Determine compressive forces on vertebra for different activities
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 0.6 0.4 0.3 0.2 0.2</td>
</tr>
<tr>
<td>Lift 15 kg knees straight</td>
<td>2.6 1.1 0.7 0.5 0.4 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</td>
</tr>
<tr>
<td>Lift 20 kg knees straight</td>
<td>3.7 1.5 1.0 0.7 0.6 0.5</td>
</tr>
<tr>
<td>Lift 20 kg w/ deep knee bend</td>
<td>3.0 1.3 0.8 0.6 0.5 0.4</td>
</tr>
<tr>
<td>Open window w/ 6 kg of force</td>
<td>1.1 0.5 0.3 0.2 0.2 0.1</td>
</tr>
<tr>
<td>Open window w/ 10 kg of force</td>
<td>1.4 0.6 0.4 0.3 0.2 0.2</td>
</tr>
<tr>
<td>Tie shoes sitting down</td>
<td>1.4 0.6 0.4 0.3 0.2 0.2</td>
</tr>
</tbody>
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Adapted from Myers and Wilson, Spine, 1997

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

Summary: Factors Affecting Bone Strength and Fracture Risk

- **Material**
- **Micro architecture**
- **Macro architecture**
- **Loading**
Thank you for your attention