Age changes in the human femoral neck and progression to failure

- Functional Adaptation in the Femoral Neck
- Changes with Ageing
- Processes Associated with Structural Failure
From the macroscopic to the microscopic and back again

Courtesy of Emma Fallon, University of Cambridge
Normal Loading of the Proximal Femur
Bone strength is dependent on the amount of bone, its material properties and its distribution about the neutral axis

- **Elasticity**
  The ability of a material to return to its original shape following deformation. Influenced by mineralisation and porosity.

- **Plasticity**
  The phase between the elastic limit and failure during which a structure absorbs the load placed upon it. Influenced by presence of microcracks

- **Cross sectional moment of inertia (CSMI)**
  Estimate of the resistance to bending moments. Increased if bone is further from the neutral axis
Predicted Stress Patterns During Normal Gait

Lovejoy, Scientific American 295: 1988
All Cortical Bone is Not The Same

**Osteon Density**

<table>
<thead>
<tr>
<th>Compression</th>
<th>Tension</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>20</td>
</tr>
</tbody>
</table>

**% 2nd Remodelled**

<table>
<thead>
<tr>
<th>Compression</th>
<th>Tension</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>60</td>
</tr>
</tbody>
</table>

**% Porosity**

<table>
<thead>
<tr>
<th>Compression</th>
<th>Tension</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>7.5</td>
</tr>
</tbody>
</table>

Skedros et al 1994
Effect of Adaptation on Bone Strength

Ultimate Stress (MPa ± SD)

Loading Mode
- Light blue: Loaded in Tension
- Red: Loaded in Compression
- Green: Loaded in Bending

Habitual Loading Mode

Riggs et al Anat Embryol 1993
"Mechanically adaptive bone modeling and remodeling can be regarded as a homeostatic mechanism regulating functional bone strains at each location throughout the skeleton"*

*L.E. Lanyon, BONE: 18, 37S-43S.*
Cross Sectional Moment of Inertia (CSMI) and Section Modulus

\[ CSMI = \sum (A \times (x-x_1)^2) \]

Section Modulus = \( CSMI / d \)

Yoshikawa et al JBMR 9:1053, 1994
Remodelling and Strain

- High strains stimulate bone formation
- Low strains stimulate resorption

Formation favored

Resorption/turnover favored
Evidence of Subperiosteal Expansion in Aging Long Bones; Femoral Neck?

LONG BONES
Ruff and Hayes, 1982 Science 217:945-948; 6:886-896
Cummings et al., 1989 Arch Intern Med 149:2445-2448; 6:872-873
Heaney et al., 1997 Osteoporos Int 7:426-431

Femoral Neck
Martin and Atkinson, 1977 J Biomech
Ruff and Hayes, 1988 J Orthop Res
Jacobsen et al., 1990 Am J Publ

Power et al 2002
Sievanen et al., 1999 Osteoporos Int 10: 295-302
Femoral Neck Subperiosteal Width NHW
Adults

Source: NHANES III data, Beck et al, JBMR, 15, 2297
Neck BMD and Section Modulus – NHW Males*

Source: NHANES III data, Beck et al, JBMR, 15, 2297

*Adjusted for body weight
Neck BMD & Section Modulus - Females

Source: NHANES III data, Beck et al, JBMR, 15, 2297

*Adjusted for body weight
Homeostasis in Bending Strength

• With aging, normal turnover should cause:
  
  ↑ Bone diameter
  ↓ Bone mass and density
Progression to Fragility

Mid-Femoral Shaft

Cortical Width with Age

Left: proximal femur from in front to show position of blow during a sideways fall and location of pQCT cross-sectional images. Right Top – images of (right) an 80-year old and (left) a 20-year old female femoral neck. Pseudo-colours indicate grey levels relative to maximum (red, if colour printed) for the image. Bottom, the cortices shown segmented into 8 octants (S: Superior; S-A: Supero-anterior; A: Anterior; I-A: Infero-anterior; I: Inferior; I-P: Infero-posterior; P: Posterior; S-P: Super-posterior) and the position of the centroid calculated (white spot in marrow space).

From Mayhew et al 2005
Change in cortical width in women with age

From Mayhew et al Lancet 2005
Cortical Widths at Age 20 (red) and 80 (green)

From Mayhew et al 2005
Summary

• Bones become more “structurally efficient” with age – able to maintain Z with less bone
• Carried to extreme -- too little bone for stability
• Progression is unidirectional toward larger diameter and thinner cortices
• This is accompanied by an increasing difference between superior and inferior cortices leading to increased instability.
The Problem
National Service Framework 2001/NOS)

- Osteoporosis affects 1:3 women and 1:12 men aged >50y.
- An osteoporotic fracture occurs every 3 minutes.
- Costs £5million/day.
- 70,000 hip fractures every year (7x that in 1960). Accounts for 20% of orthopaedic bed occupancy.
- 14,000 deaths as a result of hip fracture:- more than for ovarian, uterine and cervical cancer.
The most important feature of osteoporosis:

Reduced Bone Strength*

*Less force required to cause failure (fracture) under a particular loading condition.
Stress (force concentration) is determined by:

- **Loading conditions**
  - Force directions and magnitudes

- **Geometry of CROSS-SECTIONS**
  - Surface area of bone
  - Distribution of surface area
Hip fracture & the sideways fall

- 90% of hip fractures result from a sideways fall onto the greater trochanter.
Predicted Strain Distribution Across The Femoral Neck

Normal Gait

Sideways Fall

Lotz et al. 1995 Osteop. Int.
Whole femoral neck biopsies taken at hemi-arthroplasty from cases of femoral neck fracture.

Similar biopsies removed at post-mortem from age and gender-matched subjects with no recent history of disease or treatment known to affect bone metabolism.

Biopsies analysed at a single plane and by pQCT at various planes between the cut face and the fracture site.
Is it Cortical or Cancellous Bone That is Important in Hip Fracture?

- **Area (mm²)**
  - Control: p=0.857
  - Case: p=0.0099

- **Density (g/cm³)**
  - Control: p=0.657
  - Case: p=0.0003

- **Mass (mg)**
  - Control: p=0.890
  - Case: p=0.0005

### Graphs
- **Control**
- **Case**
Regional Distribution of Bone

Cancellous Bone Area (%)

Cortical Bone Area (%)

* p < 0.05

Bell et al, JBMR, 14:112-120, 1999
Cortical Porosity in the Femoral Neck: Role of “Giant” Canals

Superior 14.28 v 15.33%
Anterior 16.84 v 12.12%
Posterior 13.06 v 11.47%
Inferior 9.8 v 7.5%

Total Canal Area/Biopsy (mm²)

Bell et al, Bone, 24: 57-64, 1999
Cortical BMUs

Quiescence
Formation
Mineralisation Lag Time
Resorption

Days

- Pre-menopausal
- Post-menopausal

Brockstedt et al Bone 14: 681 1993
Osteonal Structure

- Lamellae
- Osteocytes
- Haversian Canal
- Cement line
Mathematical Models of Giant Canal Formation

1) Random
2) Sequential
3) Return

Assumptions:
10% Osteons Active
10% Remodelling Deficit
Giant/Composite Canal
Osteon Clustering (Super-Osteons)
Regional Analysis

Superosteons/25mm²

5.3 vs 1.8
4.1 vs 1.7
3.2 vs 1.3
2.7 vs 1.8
2.4 vs 1.9
3.0 vs 1.9
2.3 vs 3.4
2.2 vs 1.4

\[ y = 1.894 \times 10^{0.02x} \quad r^2=0.746 \]

Jordan et al, Bone 26: 305, 2000
Disuse and Cortical Porosity

Rubin et al JBJS 78A:1523-1533, 1997
Material Properties (Mineralisation)

A

83 y

B

89 y
Mineralisation after accounting for remodelling

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>F Ratio</th>
<th>Prob&gt;F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Model</td>
<td>4</td>
<td>4.43</td>
<td>0.0003</td>
</tr>
<tr>
<td>Region</td>
<td>3</td>
<td>2.93</td>
<td>0.041</td>
</tr>
<tr>
<td>Case/Control</td>
<td>1</td>
<td>8.92</td>
<td>0.004</td>
</tr>
<tr>
<td>Error1</td>
<td>59</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Interaction</td>
<td>3</td>
<td>0.30</td>
<td>0.82</td>
</tr>
<tr>
<td>Error2</td>
<td>56</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>F Ratio</th>
<th>Prob&gt;F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Model</td>
<td>4</td>
<td>3.94</td>
<td>0.007</td>
</tr>
<tr>
<td>Region</td>
<td>3</td>
<td>1.32</td>
<td>0.28</td>
</tr>
<tr>
<td>Case/Control</td>
<td>1</td>
<td>11.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Error1</td>
<td>59</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>Interaction</td>
<td>3</td>
<td>0.45</td>
<td>0.72</td>
</tr>
<tr>
<td>Error2</td>
<td>56</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>
Micro-hardness

- There were significant differences between regions (p<0.0001)
- The controls were significantly harder than the cases (p=0.033)
- There was no interaction between region and case/control (p=0.92)
Crystallinity (FTIR)

Crystal size

1.15 1.2 1.25 1.3 1.35 1.4 1.45 1.5
antarior inferior posterior superior

1030/1020

case (p) mask
case (m) mask
control (p) mask
control (m) mask
Collagen Cross Linking (FTIR)

Collagen cross-linking

- anterior
- inferior
- posterior
- superior
Mineral/Matrix Ratio (FTIR)

Phosphate band area/amide I band area

- anterior
- inferior
- posterior
- superior

Case (pmask)
Case (mmask)
Control (pmask)
Control (mmask)
Cortical Changes in Femoral Neck Fractures

Infero-anterior cortex under subject to tensile stress

Supero-posterior cortex subject to compressive stress

Load
3D Biomechanical Properties (pQCT)

% Difference Between Fracture Cases & Controls

-40 -35 -30 -25 -20 -15 -10 -5 0

aBMD

CSMI

Section Modulus

-33

-30

-34

-29

-30 CSMI

-30 Section Modulus

-11
Progression Towards Fragility

- Cortical thinning induced by sterotypical walking
- Clustering of cortical remodelling (superosteons)
- Merging of canals during the resorptive phase of remodelling
- Cortical thinning, porosity and variation in mineralisation & crystallinity
- Region specific relative disuse
- Bone Geometry
  - Cross-Sectional Area
  - Principle Axes
  - Perimeter (including Isoperimetric Quotient)
- Cortical Bone Distribution
  - Cortical Cross-Sectional Area
  - Sector-Based Cortical Thickness Estimates
  - Sector-Based Curvature
  - Sector-Based Distance to Center-of-Mass

- Validity of Cortical Thickness Estimates
- Improved detection of those at risk of intracapsular hip fracture