Bone Pathologies

TOPICS
- Bone Fracture and Bone Repair
- Degenerative Changes Associated with Aging
  - Trabecular Resorption
  - Singh Index
- Rickets and Osteomalacia
- Osteopenia
- Osteosarcoma (Bone Cancer)
- Paget's Disease
- Overuse Damage (Stress Fractures)
- Considerations for Bioengineers

Bone Fracture and Bone Repair

A radiograph of a torsional bone fracture from a skiing accident.
Fracture Repair: Treatment Options

- Nothing
- Plaster
- Cast brace
- Internal
  - Plate
  - Intramedullary nail
- External fixator
- Mixture

Fixation of Fractures through Compression (Cont.)
Fixation of Fractures through Compression (Cont.)

Fixation of a patellar fracture using wires

Fig 1A  Fig 1B  Fig 1C  Fig 1D
Effects of Aging on Bone Quality

Vertebral cross-sections from autopsy specimens of young (A) and old (B) bone show a marked reduction in trabecular bone in the later. Bone reduction with aging (C) is schematically depicted.

Effects of Aging on Bone Density

<table>
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<th>Age</th>
<th>Average Woman</th>
<th>Average Man</th>
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<tr>
<td></td>
<td>mg/cm³</td>
<td>T-score</td>
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<td>750</td>
<td>2.15</td>
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<tr>
<td>30</td>
<td>641</td>
<td>2.35</td>
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<td>40</td>
<td>679</td>
<td>2.62</td>
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<td>725</td>
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<td>149</td>
<td>3.71</td>
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<tr>
<td>85</td>
<td>979</td>
<td>2.84</td>
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</table>

The T-score is the number of standard deviations from the value at peak bone density of a young (25-30 year old) adult.
Ethnic Differences in Rate of Bone Degradation with Age

Effects of Aging on Prevalence of Bone Pathologies

Effects of Aging on Bone Properties

Stress-strain curves for samples of adult human tibia of two widely differing ages tested in tension
Bony tissue is capable of self-repair. The repair and healing is managed routinely throughout life by delicate balance of osteoblast and osteoclast cell activity.

This animation loops perpetually, showing about 2 years of NORMAL bone turnover in one loop.

A micro-crack starts the process. The osteocytes (not shown here) sense damage and send signals into the marrow space. Pre-osteoclasts turn into multi-nucleated osteoclasts and start resorption, meanwhile pre-osteoblasts turn into osteoblasts and start forming osteoid (orange) which then mineralizes (green). The video lasts about 11 seconds and represents about 6 months of real time.

Bone Turnover

This animation shows a slice through a piece of bone about a millimeter long. It lasts 13 seconds and shows 30 months of "real time." The view is similar to the view seen under the microscope of a bone biopsy from a patient. The animation is derived from measurements of the bone surfaces and tetracycline labelling. The bone formation rate in this movie is a bit above average, but within the normal range. The shades of green represent the mineralization density: newly formed bone is not very dense (pale green) and older bone is denser (dark green). This is not seen well on standard biopsies but can be determined with backscattered electron micrography.
Deficient Balance Between Bone Remodeling and Modeling Processes

OSTEOPOROSIS

Osteopenia
Osteoporosis

Standardized femur hip BMD, young white women, mg/cm²
Here is what happens with estrogen deficiency. The resorption cavities go a little deeper and resorption lasts a little longer, and the bone formation increases but doesn’t quite match the higher resorption rate. Notice the trabecular fractures and callus formation.

This animation starts the same place as the one showing normal turnover. The initial bone volume is 25%. The movie then shows what happens with estrogen deficiency. The resorption cavities are deeper and they occur more frequently. With these small changes, the trabeculae become perforated. They lose strength and have microfractures with microcallus formation. By 30 months the bone volume has decreased to 22%. Note that the width of the individual trabeculae are normal.

This animation starts after the estrogen deficiency. The first 6 months show high turnover; then the little blue diamonds representing a bisphosphonate start to attach to the bone; resorption stops suddenly and formation stops after a few months. The bone continues to become more mineralized (darker). The very low bone formation and increased mineralization have been reported from studies in humans. The accumulation of micro-cracks is theoretical; it has not been demonstrated.
Effects of Osteoporosis (a)

Normal Trabecular Structure

Osteoporotic Trabecular Structure

Effects of Osteoporosis (b)

Effects of Osteoporosis (c)

Classic appearance of osteoporosis in a biopsy
Three-dimensional structure of trabecular bone. From Kaplan.

Pattern of trabecular resorption in the femur due to osteoporosis. From Singh.

Osteoporosis: Risk Factors

- Females
- Small skeletal frame
- Advanced age
- Family history
- Early menopause
- Diet low in calcium
- Steroids
- Anti-convulsants
- Cigarettes
- Low testosterone
- Inactive life style
- Excessive alcohol
- Caucasian or Asian
A Negative Bone Balance Leads to Osteoporosis

8 million women & 2 million men with Osteoporosis (US)
18 million with osteopenia (prelude to Osteoporosis)
1 of 2 women, 1 of 8 men over 50 will have Osteoporosis-related fracture

Osteoporosis is responsible for 1.5 million fractures per year in the US:
300,000 hip, 700,000 vertebral, 200,000 wrist and 300,000 other fractures
24% of hip fracture patients 50 and over die during the year following their fracture
Death rate for men within 1 year after hip fracture is 26% higher than in woman.

Osteoporosis is Costly

In the USA, costs related to osteoporosis and associated fractures are about $38 million dollars per day or $14 billion per year!

DEXA SCANS

DEXA=Dual Energy Xray Absorptiometry

Several methods are available to measure bone density, but currently the most widely used technique is DEXA

This is the method used to determine efficacy in the recent large clinical trials, and to characterize fracture risk in large epidemiological studies.
The DEXA technique analyzes the attenuation of x-rays as they pass through an area of the body. The method cannot detect the depth of the bone which is being measured, and thus is actually an "areal density in g/cm² rather than a "volumetric" or Archimedes density in g/cm³.

DEXA SCANS

The image shows the regions usually measured on the proximal femur: Neck, Trochanteric, and Intertrochanteric.

Note that the trochanteric region is less dense because it has more trabecular bone.

DEXA SCAN OF THE HIP

The first 4 lumbar vertebrae are measured. Many conditions or artifacts can make the spine data inaccurate, including:
- scoliosis
- degenerative arthritis
- compression fractures
- spondylitis
- aortic calcifications
- navel jewelry
- surgical changes

DEXA SCAN OF THE SPINE
**DEXA SCANS:**

Interpretation

The bone mineral density of the lumbar spine was XXX g/cm² which is XX standard deviations below the mean for age-matched persons.

The total hip BMD was XXX g/cm² which is XX standard deviations below expected for her age.

The T-score was XXX at the spine and XXX at the total hip which places her in the WHO category of _______

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**BONE ULTRASOUND:**

Emerging Technique for Diagnosis of Osteoporosis

Cost much less than DEXA

Reproducibility not quite as good as DEXA

Relative risk for hip fracture predicted as well by ultrasound of the calcaneus as by DEXA of the hip

Fracture prediction is independent of DEXA, but adding ultrasound to DEXA does not enhance prediction

In vitro studies show that ultrasound is mainly measuring the bone mass; DEXA better able to predict bone strength

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**SAMPLE REPORT**

The bone mineral density of the lumbar spine was XXX g/cm² which is XX standard deviations below the mean for age-matched persons.

The total hip BMD was XXX g/cm² which is XX standard deviations below expected for her age.

The T-score was XXX at the spine and XXX at the total hip which places her in the WHO category of _______
Osteoporosis: Basic Prevention

- Calcium
- Vitamin D
- Exercise
- Prevent falls
- Maintain weight
- Stop smoking

SCLEROSIS. This is the opposite of osteoporosis.

Rickets and Osteomalacia
Osteomalacia results when the osteoid does not have mineral. This can also happen quickly, depending on the severity of mineral deficiency.

Bony sample from a patient with rickets. Notice that the red osteoid is too thick and covers most of the surface of the bone.

OSTEOPETROSIS
A-traumatic fracture of the femur in osteopetrosis
From B nichou et al., Bone.

Thickening and sclerosis of the vertebral endplate in osteopetrosis.
From B nichou et al., Bone.

Bone-within-bone sign according to the skeletal site.
From B nichou et al., Bone.

Osteosarcoma
(Bone Cancer)
Scanning Electron Microscope Images of Human Osteosarcoma Cells

Osteosarcoma: Osteoblastic type showing mature trabeculae and large osteoblastic cells

The above image at a higher magnification

Osteosarcoma, upper tibia at knee joint, gross, X-ray

Osteosarcoma, upper tibia at knee joint, gross, post mortem.
An area of severe osteolytic activity, which is associated with a small degree of bony expansion, is visible in the distal region of the tibia.

Between 40% and 50% of patients with Paget's disease will have vertebral involvement. Vertebral compression fractures may be associated with both cord compression and radicular deficits. This CT of a vertebra demonstrates both sclerosis and osteolytic activity of Paget's disease.

Musculoskeletal Complications: Lower Extremities

The lower extremities of this patient with Paget's disease demonstrate the frequent asymmetry of the disease. Severe bowing of the right tibia in this patient resulted in knee pain and ankle pain. The left tibia also appears to be somewhat bowed, but x-ray films did not reveal Paget's disease.
Osteogenesis Imperfecta (OI) "brittle bone disease"

- Skull: Minimal mineralization at the skull base only.
- Long Bones: General demineralization; short, telescoped long bones secondary to in utero fractures. The provisional zones of calcification are preserved (ends of long bones are sharp).
- Ribs: Beaded appearance secondary to multiple fractures.

Plain radiographs (antero-posterior and lateral views) of the fetus indicate the following:

Typical sections of biopsies from a control subject (boy, 9 years), and OI patients.
Rauch et al., Bone.
New Treatment of Osteogenesis Imperfecta

Nails are inserted throughout the medullary canal to support and provide strength to the OI bone.

Overuse Damage

stress fractures

Symptoms:
- sharp pain
- swelling

Stress Fractures:
- breaks in bone caused by repetitive mechanical stress
- Sharp pain, swelling
Roles of Lower-limb Muscle Contraction During Walking

Normal contraction of the lower-limb muscles during the stance phase of walking/running not only generates propulsion, but also protects the body by absorbing some of the foot-ground impact energy:

The lower-limb muscles exert a protective effect on bone surfaces by contracting to reduce tension stresses and strains.

Distribution of Compressive and Tensile Stresses in a Tibia Subjected to Bending

Muscles are INACTIVE

Compression Only

Hypothesis: the process leading to stress fractures during intensive, long marches or athletic activity force output of the lower limb and foot muscles decreases due to fatigue

bones surfaces are no longer protected effectively

Crack initiation

Crack propagation

Fracture
### Objectives

Identify risk factors for stress fracture injury of the lower limb and foot. Suggest means for obviating them. In order to achieve the above goals, comprehensive experimental-computational analysis of the foot mechanics during walking is needed.

### The Integrative Experimental-Computational Analysis (a)

- **The DRF/CPD Gait Platform**

- **Computer Reconstruction of the 3D Foot Geometry**
  - Adapt 3D Model Geometry to Characteristic Positions of Stance as Measured by DRF
  - Solve Simulated Structural Stresses and Foot-Ground Contact Stresses Using the Computational Model

- **Validate the 3D Model by Comparing Measured with Simulated Foot-Ground Contact Stresses**

### Common Locations

- **Calcaneus** (heel bone)
- **Metatarsals**

### Diagnosis

- **X-ray**
- **Bone Scan**
- **MR (Magnetic Resonance)**

### Stress Fractures of the Foot
Muscle Exercise Protocols to Achieve Fatigue

Study the Stress State of the Foot in Conditions of Muscular Fatigue

Surface EMG

Alter Muscular Loading of the Model According to EMG Measurements

Compare Model Predictions of the Foot-Ground Pressure with Respective Measured CPD Data to Characterize Fatigue Effects

The Integrative Experimental-Computational Analysis (b)

Adaptation of the Model to the Stages of Walking

Stress Distributions in the Foot Model During Walking

Laboratory Simulations of Military Marching

Subjects were required to complete 2 km march, at 8 km/hr

- peroneus longus activity
- MF=103 Hz
- 0 min (10 meters)
- MF=140 Hz
- 10 min (1330 meters)
- MF=82 Hz

Muscles monitored:

- EMG 

Evaluation of Fatigue of Individual Lower-Limb Muscles

Muscular Fatigue is quantified by the shift of the Median Frequency (MF) of the EMG spectrum towards the lower band, this is correlated with alterations in propagation velocity along fibers, motor unit recruitment patterns, muscle activity level.

Computational Simulation of Marching

The foot model was utilized to study the effect of the muscular fatigue pattern of marching on skeletal stresses.

We define:
- moderate fatigue: 80% the normal force output
- severe fatigue: 60% the normal force output

We decrease force outputs of the peroneus longus, pre-tibial muscle group, triceps surae muscle group

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<td>2</td>
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<td>5</td>
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Ankle Joint Load: 1380 Nm

Med. Pulley Reaction: 865 N
Lat. Pulley Reaction: 716 N
Computational Results (a) Heel Strike

Effects of Muscle Fatigue on Formation of Elevated Stresses

- Normal
- Moderate fatigue
- Severe fatigue

Position S

Summary:
Development of Stress Fractures

Marching Exercise
Fatigued Muscles
Loss of Shock Absorbing Capacity
Altered Walking
Abnormal Loading
Abnormal Skeletal Stresses (cyclically developing) in the Calcaneus (heel) & Metatarsal Bones
Micro-Cracks
Accumulation of Damage to Stress (Osteone) Fracture