Bone Biology and Bone Biomechanics
Mark F. Reinking, PT, PhD, SCS, ATC

1) Bone Introduction
   a) Metabolically active tissue
   b) Functions
      i) Structural support
      ii) Provision of levers for movement
      iii) Protection of vital organs/tissues
      iv) Mineral reservoir: 99% calcium stored in bone
      v) Hematopoiesis
      vi) Endocrine function: osteocalcin
   c) Bone types
      i) Cortical bone
         (1) Dense (compact) bone
         (2) 80% human skeleton
         (3) 5-10% porosity
         (4) Lower metabolic activity
         (5) Lower surface area/volume ratio
      ii) Cancellous bone
         (1) Spongy (trabecular) bone
         (2) 20% human skeleton
         (3) 50-90% porosity
         (4) Higher metabolic activity
         (5) Higher surface area/volume ratio
   d) Bone composition
      i) Bone cells: 10%
         (1) Osteoprogenitor cells: mesenchymal stem cells
            (a) Osteocytes (90% of all bone cells): secrete collagen
            (b) Osteoblasts: bone forming
         (2) Osteoclasts: hematopoietic origin. Bone resorbing
      ii) Bone matrix: 90%
         (1) Organic (20%)
            (a) Primarily Type I collagen protein
            (b) Noncollagenaceous proteins – proteoglycans, glycoproteins, growth factors
         (2) Mineral matrix (65%)
            (a) Primarily hydroxyapatite [Ca$_{10}$(PO$_4$)$_6$(OH)$_$_2$]
            (b) Small presence of carbonate, magnesium, fluoride
         (3) Lipids (5%)
         (4) Water (10%)
2) Bone Anatomy
   a) Periosteum
      i) Covers external surface of bone
      ii) Attached to outer cortex – Sharpey’s fibers
      iii) Blood supply to our third of bony cortex
      iv) Innervation to bone
      v) Osteoprogenitor cells in inner layer
      vi) Volkman’s canals – connection with endosteum
   b) Endosteum
      i) Membrane covering marrow cavity, Haversian canals, Volkman’s canals, and trabeculae
      ii) Vascularized
      iii) Cellular – osteoblasts & osteoclasts
   c) Structural unit: osteon
      i) Cortical osteon: Haversian system
         1) Central Haversian canal
         2) Lamellae (4-20/osteon): layers of collagen fibrils in alternating orientation
         3) Osteocytes within lacunae – canaliculi radiate out connecting to central canal
         4) Cement lines – boundaries between osteons
         5) Hydroxyapatite interposed linearly between collagen fibrils
      ii) Cancellous osteon: packets
         1) Plates and rods – contain lamellar bone
         2) Osteocytes within lacunae – canaliculi present
         3) Surrounded by red marrow
         4) Endosteal layer around trabeculae – osteoblasts and osteoclasts

3) Bone growth
   a) Longitudinal growth
      i) Occurs at growth plates: endochondral ossification
      ii) Epiphyseal growth – lengthens metaphysis
   b) Circumferential growth
      i) Response to mechanical loading of bone – mechanotransduction
      ii) Periosteal apposition of new bone (widening)
      iii) Endosteal resorption of old bone

4) Mechanotransduction in bone
   a) Julius Wolff (1892) – German anatomist and surgeon. Based on his observations of bone as a
      surgeon, proposed that bone will adapt to the loads imposed on it (Wolff’s law)
   b) Mechanotransduction – conversion of mechanical energy into biomedical signals
   c) Mechanical loading of bone creates fluid flow in lacunocanalicular system
   d) Osteocytes respond to fluid flow through cell membrane structures including integrins, cilia,
      gap-junctions, and other membrane structures
   e) Osteocyte-induced signaling to osteoblasts and osteoclasts for bone deposition and/or
      resorption
   f) Loading magnitude, frequency, and rate all influence cell signaling
5) Calcium homeostasis\textsuperscript{2-4,9}

a) Parathyroid gland
   i) Cells sensitive to level of calcium in bloodstream
   ii) Secretion of parathyroid hormone (PTH)
   iii) If calcium concentration decreased in plasma, PTH upregulated
   iv) If calcium concentration increased in plasma, PTH downregulated, calcitonin signaling
   v) Directly acts on bone to increase calcium release

b) PTH function
   i) Increases kidney resorption of calcium
   ii) Stimulates calcitrol production from Vit D precursor in liver and kidney
   iii) Binds to osteoblast membrane, upregulate RANKL, RANKL binds to RANK on osteoblast precursor cells, signals differentiation into osteoclasts

c) Calcitriol function
   i) Increased calcium absorption in gut
   ii) Increased renal tubular resorption of calcium

d) Calcitonin
   i) Secreted by thyroid gland
   ii) Functions
      (1) Inhibits activity of osteoclasts
      (2) Decreases resorption of calcium in the kidneys

e) Estrogen
   i) Closure of epiphyseal plates
   ii) Increases resorption of calcium from intestines
   iii) Prolongs osteoblasts lifespan and inhibits osteoclastic activity

f) Testosterone
   i) Androgen receptors on osteoblasts: increase matrix secretion and mineralization
   ii) Conversion of testosterone to estrogen

g) Growth hormones
   i) Secreted by pituitary gland
   ii) Stimulates production of growth factor-1 (IGF-1)
   iii) Growth hormone/IGF-1 system stimulates both osteoclasts and osteoblasts but dominant effect is on osteoblasts

h) Osteocalcin
   i) Secreted by osteoblasts
   ii) Target cells
      (1) Beta cells in the pancreas: insulin release
      iii) Fat cells: release of adiponectin, which increases sensitivity to insulin
      iv) Leydig cells of the testis: testosterone biosynthesis
      v) Myocytes to promote energy availability and utilization
6) Bone biomechanics\textsuperscript{7,10}

a) Determinants of bone strength
   i) Bone mass: 50-70\% of bone strength
      (1) More mass = stronger bone
      (2) More mass = increased metabolic cost and limits mobility
   ii) Bone geometry
      (1) As bone diameter increases radially, strength of bone increases
      (2) Bulk is avoided by endosteal resorption

b) Bone – anisotropic material
   i) Cortical bone
      (1) Compression (highest stress \textasciitilde 193 MPa)
      (2) Tension (130 MPa)
      (3) Shear (68 MP)
   ii) Trabecular bone
      (1) Compression (50 MPa)
      (2) Tension (8 MPa)
   iii) Clinical example – tibial bending in running (Yange 2014)

c) Bone geometry and strength
   i) Tension and compression – load to failure and stiffness – proportional to x-sectional area
   ii) Moment of inertia: bending resistance
   iii) Men – wider bones than women with increase cortical thickness
   iv) Women – less periosteal bone formation during growth; post-menopausal – more endosteal remodeling (N&F, p. 49)
   v) Bone health examples
      (1) Schilipow (2013) QCT\textsuperscript{11}
         (a) Skiers and soccer players had greater BMD and cortical thickness
         (b) Swimmers – lower BMD and cortical thickness
      (2) Ferry (2013) HAS\textsuperscript{12}
         (a) Soccer players and swimmers – pre and post bone measurements
         (b) 8-months training
         (c) Soccer – increased cortical bone width
         (d) Swimmers – no change
      (3) Milgrom (2012) QCT\textsuperscript{13}
         (a) Compared infantry recruits and religious scholars – 25 year follow-up
         (b) High musculoskeletal loading in early age = increased bone strength
         (c) Increased bone strength result of increased geometric strength, not increased BMD
      (4) Popp (2009) QCT\textsuperscript{14}
         (a) Lower bone strength in runners with history of stress fracture
         (b) Lower bone strength a result of poorer bone geometry, not BMD
      (5) Ackerman (2011) QCT & DEXA\textsuperscript{15}
         (a) Compared eumenorrhoeic athletes, non-athlete controls, and amenorrhoeic athletes
         (b) AA had lower BMD and poorer tibia bone geometry
Assessment of Bone Health
Jason E. Bennett, PT, PhD, SCS, ATC

1) Bone Densitometry
   a) Quantitative Ultrasound (QUS)
      i) Densitometer Characteristics
         (1) Non-ionizing
         (2) Sound waves at various frequencies
         (3) Portable
         (4) Inexpensive ($)
      ii) Measures
          (1) Speed of sound (SOS; m/s) – quantity (cortical)
          (2) Bone ultrasound attenuation (BUA; dB/MHz) – quality (trabecular)
          (3) Stiffness Index (SI) – linear combination of SOS & BUA
          (4) SI rescaled for estimated BMD (g/cm^2)
   b) Quantitative Computed Tomography (QCT)\(^2,3\)
      i) Densitometer properties\(^4,5\)
         (1) Ionizing – Higher than DXA
            (a) Low-energy protocols < 200 µSv
            (b) Low-energy, low dose protocols 50-60 µSv
         (2) Standard CT with phantom & software
         (3) Less precise than DXA (1.5%-4% vs 1%)
         (4) Allows for separate cortical and trabecular BMD measures
         (5) More sensitive to changes in BMD
         (6) Less susceptible to degenerative change
      ii) Measures
          (1) Attenuation (Hounsfield units) converted to BMD (mg/mL)
          (2) Volumetric (vBMD) measures of BMD (mg/cm\(^3\))
   c) Dual-Energy X-ray Absorptiometry (DXA)\(^6,7\)
      i) Densitometer properties\(^1\)
         (1) Ionizing – Lower than QCT
            (a) Hip = 9 µSv; spine = 13 µSv
         (2) Most Common
      ii) Measures
          (1) Areal density (g/cm\(^2\))
          (2) Decomposition of 2 different photon energies
          (3) Precision affected by adipose

2) Comparison of Bone Densitometers
   a) cQUS a good screening tool for low BMD\(^8\)
      i) 453 community dwelling subjects and 30 with LE fracture
   b) cQUS measures similar to those in proximal femur (trochanteric)\(^9\)
      i) DXA and Hip structural analysis (HAS)
      ii) 53 osteoporotic females
   c) cQUS can discriminate between women w/ and w/out fracture hx as well as axial DXA\(^10\)
      i) 342 postmenopausal women
ii) 1) no fracture, 2) fracture of wrist, 3) other fracture, not spine, hip, wrist
d) Combination of cQUS and DXA not better than either alone\textsuperscript{11}
i) 154 postmenopausal women w/ history of fracture, 221 healthy, postmenopausal women w/ no risk factors for osteoporosis
e) Clinical risk factors for osteoporosis affect cQUS and DXA z-score measures equally\textsuperscript{12}
i) Adopting WHO criteria, cQUS and DXA identify similar proportions of postmenopausal women as osteopenic or osteoporotic
f) No statistical difference in t-scores between cQUS and DXA\textsuperscript{13}
g) DXA BMD and cQUS bone strength significantly correlated\textsuperscript{14}
i) can be used as a screening tool for osteoporosis

3) Classification Guidelines
a) WHO Guidelines\textsuperscript{15}
i) DXA\textsuperscript{16} 
(1) t-score < 1.0 osteopenia or “low bone mass”
(2) t-score < 2.5 osteoporosis 
ii) T-score criteria for osteoporosis needs adjustment for QUS\textsuperscript{17,18}
(1) cQUS: osteoporosis = t-score -1.8
iii) Z-scores preferred in pre-menopausal women and men < 50 yrs\textsuperscript{16,19}
b) ACR Guidelines for QCT\textsuperscript{5,20}
i) 120-80 mg/mL = osteopenia ii) <80 mg/mL = osteoporosis 
c) Measurement reference data 
  i) Reference data in Caucasian children & adolescence 6-18 yrs\textsuperscript{21} 
  ii) Reference data in Chinese children & adolescence 10-21 yrs\textsuperscript{22} 
  iii) Age-related changes in cQUS measures in 6-20 y/o subjects\textsuperscript{23}

QUS/DEXA findings in collegiate and high school athletes, and similar physical active populations and their relationship with injury risk – Not for female athletes only!

Mitchell J. Rauh, PT, PhD, MPH, FACSM

1) Sport-specific BMD and Related Bone Factors  
a) College 
b) Other adult/Similar physical active populations 
c) High school

2) Stress fracture and Related Overuse injury Studies  
a) Collegiate 
b) Other adult/Similar physical active populations 
c) High school

3) Risk Factors for Low Bone Mineral Density and Related Bone Factors  
a) Bone-loading vs. Non-bone-loading Sports 
b) Sport Specialization 
c) Female Athlete Triad 
  i) Understanding of original vs. current triad spectrum
d) Male Athlete Triad – growing evidence
e) Anemia
f) Other factors

4) Relationships between Low Bone Mineral Density/Related Bone Factors and Stress Fracture and Other important Overuse-related musculoskeletal injuries
a) Collegiate
b) Other adult/Similar physical active populations
c) High school

The Female Athlete and Bone Health Considerations
Tricia Austin, PT, PhD, ATC

1) The Female Athlete Triad and bone health considerations¹
   a) Low energy availability
      a. Dietary energy intake – exercise energy expenditure = energy availability
      b. Potential impact on physiological mechanisms
   b) Menstrual dysfunction
      a. Considerations related to menstrual dysfunction
         1. Onset of menarche in athletes and non-athletes
         2. Potential impact of energy deficiency on menstrual function
         3. Menstrual function spectrum
         4. Menstrual function subclinical disorders²
   c) Low bone mineral density
      a. Loss versus failure to achieve optimal bone mineral density in childhood, adolescence, and early adulthood
      b. Fracture risk and bone mineral density
   d) Inter-related spectrum
      a. Energy availability promotes bone health and development
         1. Indirectly: preserving eumenorrhea and estrogen that restrains bone resorption
         2. Directly: stimulating production of hormones that promote bone formation
      b. Energy availability impairs bone health and development
         1. Indirectly: inducing amenorrhea and removing estrogen’s restrain on bone resorption
         2. Directly: suppressing hormones that promote bone formation
   c. Evidence that energy balance is the key
      1. Human and animal studies
   d. Causes of negative energy balance
   e) Role of estrogen in bone
   f) Cumulative history of energy availability, menstrual status, genetics, exposure to other nutritional, behavioral, and environmental factors
   g) Nonpharmacological management and potential impact on bone
   h) Pharmacological therapy and potential impact on bone

2) Relative Energy Deficiency in Sport (RED-S)³⁴

3) Clinical considerations as a physical therapist⁵⁶
Mechanobiological Considerations for Improving Bone Health

Jason E. Bennett, PT, PhD, SCS, ATC

1) Exercise Effects on Bone Health$^{24-29}$
   a) Exercise positively related to BMD$^{30}$
   b) No change in BMD over course of triathlete season$^{31}$
   c) Decreased strength in female athletes w/ stress fracture (QCT)$^2$
   d) BMD across a range of physical activity levels$^{32}$
   e) Exercise maintains cortical and trabecular BMD$^{33}$

2) Loading Considerations$^{34,35}$
   a) Mode
      i) Jump training
         (1) Improving BMD in premenopausal women$^{36}$
      ii) Resistance training$^{37,38}$
         (1) No benefit to adding UE resistance training to loading program$^{39}$
         (2) High intensity resistance training effective for increasing lumbar BMD$^{40}$
      iii) Aerobic training
         (1) Walking no effect on BMD except femoral neck when $> 6$ mths$^{41}$
         (2) Walking improves BMD femoral neck$^{42}$
      iv) Mixed-component
         (1) PRE + Core Stab + WB impact$^{43}$
   b) Intensity
      i) High/Moderate/Low impact
         (1) High Intensity better (80 jumps/session) vs. Mod. Intensity (40 jumps/session) in preventing decreased BMD$^{39}$
         (2) Mod intensity exercise (16-45 min TM/bike, 5 dxwk-1; HR 40-75%) no effect on BMD versus control in postmenopausal women
         (3) Decreased BMD in high intensity cycle training$^{44,45}$
      ii) Odd impact
   c) Duration$^{41}$
   d) Frequency
   e) Progression

3) Demographic Considerations
   a) Age
   b) Gender
   c) Menstrual Function
d) Medical history
   i) BSI history
   ii) BMD
   iii) Lactose intolerance

e) Supplementation
   i) Ca+ + Vit D

f) Contraception

**Bone Biology and Bone Biomechanics**

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6) Bonnett N, Ferrari SL. Exercise and the skeleton: how it works and what it really does. IBMS BoneKEy. 2010;7(7).
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