Certified Clinical Densitometrist (CCD™®)

DXA Resource Materials
International Society for Clinical Densitometry

CCD™® DXA Resource Materials

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Section I  OVERVIEW OF OSTEOPOROSIS

A. Learning Objectives

1. State definitions and classification of osteoporosis
2. Summarize the pathophysiology of osteoporosis
3. Explain the prevalence and incidence of osteoporosis and fractures
4. Describe types of fracture and the morbidity and mortality related to osteoporotic fractures
5. List the economic costs of osteoporosis
6. Compare the incidence, prevalence, morbidity, mortality, and cost of osteoporosis with other chronic diseases
7. Explain the value of bone densitometry for diagnosis of osteoporosis, fracture risk estimation and monitoring

B. Definitions of Osteoporosis

1. Old definition[1]:
   To distinguish osteoporosis from osteomalacia
   • A reduced amount of bone that is qualitatively normal
   • Osteomalacia = normal amount of bone that is inadequately mineralized
   Introduces the concept of bone quality
   • A systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. [2]
3. Newest Definition of Osteoporosis
   NIH Consensus Conference [3]
   • Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture
   • Bone strength reflects the integration of two main features:
     - Bone density
     - Bone quality
   • There are no symptoms from low bone mass unless fracture occurs
4. See figure 1.1 for bone structure: normal and osteoporosis

C. Osteoporosis Can be Defined by the Presence or History of a Fragility Fracture

D. Many Are Suggesting that “Osteoporosis” be Diagnosed by Elevated Fracture Risk [4, 5]

1. Osteoporosis can be diagnosed by:
   • Occurrence of a low trauma spine or hip fracture
   • BMD T-score ≤ -2.5
   • Elevated fracture risk, e.g., by FRAX
     - This approach is being applied in many countries where the osteoporosis intervention threshold is based on fracture risk

E. Functions of the Skeleton

1. Supports the body
2. Protects internal organs
3. Muscles attached for movement
4. Cavities for blood formation
5. Reservoir for minerals
F. DXA Terminology: The Skeleton Has Different Regions
   1. **Central skeleton** (axial skeleton plus hips and shoulders):
      • Spine, ribs, pelvis, hips, shoulders
   2. **Peripheral skeleton** (appendicular skeleton minus hips and shoulders):
      • Extremities (arms and legs)

G. Different Skeletal Regions Have Different Type of Bone
   1. **Cortical** or **compact** bone makes up the outer envelope of all bones and the shafts of the long bones (appendicular skeleton)
   2. **Cancellous** or **trabecular** bone makes up the inner parts of the bones, particularly bones of the axial skeleton

H. Cancellous and Cortical Bone Differences in Mass, Surface Area and Turnover [6]
   1. Up to 10% of the adult skeleton is being remodeled at any one time (remodeling rates can be affected by age and diseases)
      • Cancellous bone makes up 20% of bone mass, 80% surface area and 25% of bone turn-over
      • Cortical bone makes up 80% of bone mass, 30% surface area and 3% of bone turn-over
      • Overall, up to 10% of the adult skeleton is being remodeled at any one time

I. Bone Modeling and Remodeling
   1. **Modeling**: Change in size and shape of bone during growth
   2. **Remodeling**: Mature bone is renewed through a process called remodeling
      • Involves replacement of old bone with new bone
      • Occurs in response to fatigue damage, micro-fractures, and other factors

J. Bone Remodeling Cycle [7]
   1. Cycle phases are: resting, activation, resorption, and formation
   2. A deficit occurs after about age 35 and especially in menopause resulting in net bone loss with each remodeling cycle

K. Bone Remodeling is Coupled and Regulated by Many Factors Including Estrogen and Cytokines [8]
   1. Osteoblast precursors and osteoclast precursors are closely regulated by cytokines, estrogen, RANK-L, OPG, and other factors
   2. Certain disorders and medications may result in changes in this regulation and some processes may result in uncoupling of formation and resorption

L. Peak Bone Mass [9]
   1. Peak bone mass is the maximum bone mass or density achieved during a lifetime
   2. It is reached when the growth in the size of bones and accumulation of bone mineral has stabilized (consolidation)
   3. Different skeletal sites peak at different times
      • Trochanter BMD: Mid-teens ($14.2 \pm 2.0$)
      • Femoral neck BMD: Late teens ($18.5 \pm 1.6$)
      • Spine BMD: Early 20s ($23.0 \pm 1.4$)

M. Factors Influencing Peak Bone Mass [10, 11]
   1. Heredity/Genetics (~60-80%)
   2. Gender
   3. Nutrition
      • Energy intake
   4. Endocrine factors
      • Protein intake
      • Calcium intake
      • Vitamin D
• Sex steroids
• Calcitriol
• GH–IGF-1 axis
5. Mechanical factors
• Physical activity

6. Smoking
7. Alcohol
8. Other factors

N. Changes in Bone Density with Age
1. Bone mass increases through adolescence with peak in the mid-20s
2. Bone mass plateaus until the late 30s
3. Age related bone loss is about 0.5-1% per year after late 30s.
4. Menopause may accelerate bone loss for a few years to about 1-2% per year

O. Influence of Gender on BMD [12]
1. On average, men have a higher BMD as measured by DXA as compared with women (about 10% higher)

P. Influence of Race on BMD [12]
1. On average, blacks have higher BMD (about 10% higher) as measured by DXA than whites

Q. Influence of Gender & Race on BMD
1. There is considerable overlap
2. You cannot predict BMD on the basis of sex or race

R. Cancellous and Cortical Bone Loss Occurs at Different Times and Different Rates [13]
1. Cancellous bone loss is greater than cortical bone loss
2. This may account for the higher risk of wrist and spine fractures earlier in life (Cancellous bone predominates) and the later occurrence of hip fractures

S. Trabecular Bone – Age Related Loss Differs Between Men and Women [14]
1. In women, resorption exceeds formation to a greater extent than in men
2. Men tend to have thinning of the trabecular bone and women have a higher risk of perforation

T. Summary: Bone Mass and Bone Loss
1. Women have lower peak bone mass than men
2. Whites have lower peak bone mass than blacks
3. Bone loss occurs
   • With advancing age
   • Because resorption is greater than formation
4. As bone loss occurs, there is loss of quality as well as quantity

U. Prevalence
1. Frequency of disease at a specific point in time
2. Number with disease ÷ number at risk
3. Often expressed as percent, or number per 1,000 people
4. Example: 30% of women over age 50 have osteoporosis

V. Prevalence of Osteoporosis Depends on:
1. Definition of low bone mass (WHO)
2. Densitometry technique (DXA)
3. Skeletal site selection
4. Number of skeletal sites measured
5. Study population
W. Osteoporosis Prevalence Increases With Age and Varies by Site [15]
   1. At younger ages, prevalence based on spine is higher than based on hip
   2. Prevalence increases with age
   3. In older age, prevalence based on hip is higher than based on spine
   4. Overall, prevalence at the spine and hip are similar

X. Osteoporosis Prevalence Differs by Race: USA Data (Caucasian reference data) [16]
   1. Osteoporosis: about 20% in whites, 5% in blacks, 10% in Mexican and 18% for all races
   2. Low bone density (osteopenia): about 52% in white, 35% in black, 49% in Mexican and 50% for all races

Y. Incidence
   1. New cases of disease over a specific period of time (rate)
   2. New cases within the period of time ÷ number at risk
   3. Often expressed as number of cases per person-years
   4. Example: the incidence of hip fractures in an elderly population is 12 per 1000 person-years

Z. Incidence of Radiographic Vertebral Fractures [17]
   1. European Prospective Osteoporosis Study: women with steeper slope than men with respect to age related vertebral fractures
      • Women – about 5 vertebral fractures per 1000 patient years at age 50-54; about 25 per 1000 at age 77-79
      • Men – about 3 per 1000 at age 50-54; about 15 per 1000 at age 75-79

AA. Incidence of Hip Fracture VARIES Worldwide [18]
   1. Highest risk in Sweden
   2. Medium to high risk in Argentina, USA, Germany, Australia
   3. Lower risk in Chile, Korea, China and France

BB. Osteoporosis Prevalence and Incidence Worldwide [19]
   1. Prevalence: Over 200 million people worldwide have osteoporosis
   2. Incidence: Hip fractures projected to increase substantially by 2050:
      • 240% in women
      • 320% in men
   3. Even if no increase in the age-adjusted hip fracture rate, the number of hip fractures will increase from 1.7 million in 1990 to 6.3 million in 2050

CC. Projected Worldwide Increase in Hip Fracture Number (1990 – 2050) [20]
   1. Most significant increases projected for Asia and South America
   2. Moderate increases projected for North America and Europe

DD. Types of Fracture
   1. Traumatic fracture
   2. Pathological fracture
      • Disease or disorders such as cancer, infection, and bone cysts
   3. Stress fracture
      • Injury to bone caused by repeated (rather than sudden) mechanical stress
   4. Osteoporotic fracture (sometimes called fragility fracture or low-trauma fracture)
      • Fracture Occurring with minimal trauma, such as force equal to or less than falling from standing height
EE. Bimodal Distribution Of Fractures [21]
1. Peak in adolescence (teenage years up to mid 20s) – males much more than females
2. Second peak in older age (over 65) – females much more than males

FF. Pathogenesis of Osteoporotic Fracture [22]
1. Low bone mass
   • Low peak bone mass
   • Postmenopausal bone loss
   • Age related bone loss
   • Other risk factors
2. Poor bone quality (architecture)
3. Non-skeletal factors (propensity to fall)

GG. Type of Fall Affects Fracture Site [23]
1. Younger
   • Intact protective mechanisms
   • Fall on hand
   • Forearm fracture
2. Older
   • Compromised protective mechanisms
   • Fall on side
   • Hip fracture

HH. Distal Forearm Fractures [24]
1. Third most common osteoporotic fracture (~250,000/year)
2. Prior forearm fracture is a marker for future fracture [25]
3. Most are caused by fall on outstretched hand
4. Most are diagnosed clinically and usually confirmed with radiography
5. Complications
   • Pain
   • Temporary disability; difficulty dressing, toileting, meal preparation
   • Degenerative arthritis
   • Complex regional pain syndrome (reflex sympathetic dystrophy syndrome)
   • Six months after fracture, 23% report fair to poor recovery in functional outcome [26]

II. Vertebral Fractures [13, 24]
1. Most common osteoporotic fracture (~550,000 per year)
2. Vertebral fracture is a marker for future fracture risk [25]
3. Many occur with every-day activities (lifting, pushing, pulling, etc)
4. Only 25% to 30% of vertebral fractures seen on x-ray are diagnosed clinically
5. Patients with clinical vertebral fractures may have severe pain and are confirmed with x-ray

JJ. Consequences of Vertebral Fractures
1. Back pain
2. Loss of height
3. Deformity (kyphosis, protuberant abdomen)
4. Reduced pulmonary function [27]
5. Diminished quality of life (loss of self-esteem, distorted body image, dependence on narcotic analgesics, sleep disorder, depression, loss of independence) [28]
6. Increased mortality
KK. Hip Fractures [24, 29]
1. 2nd most common osteoporotic fracture
   • Approximately 1.6 million per year worldwide (2000)
   • Estimated to increase to 6.3 million annually by 2050
2. Hip fracture is a marker for future fracture risk [25]
3. Most are caused by fall from standing height
   • Only about 5% are “spontaneous”
   • Only 1% of falls lead to hip fracture
4. Diagnosis
   • Most are diagnosed clinically
   • Often confirmed with radiography
   • Most are hospitalized and require surgery

LL. Complications of Hip Fracture
1. Up to 24-30% excess mortality within 1 year [30, 31]
2. Nearly 65,000 American women die from complications of hip fracture each year [32]
3. ~50% of hip fracture survivors are permanently incapacitated [33]
4. ~20% of hip fracture survivors require long-term nursing home care [34]

MM. Patients With Prior Fracture Are at High Risk for Future Fragility Fractures [25]
1. Wrist fracture: 3.3 fold risk for future wrist fracture, 1.7 for vertebral fracture and 1.9 for hip fracture
2. Vertebral fracture: 1.4 fold increase for wrist fracture, 4.4 for vertebral fracture and 2.5 for hip fracture
3. Hip fracture: 2.5 fold risk increase for vertebral fracture and 2.3 for hip fracture

NN. Survival Rates After Fractures [35]
1. Hip fracture relative survival 0.82 at 5 years with most of mortality in first year after fracture
2. Vertebral fracture relative survival of 0.81 at 5 years with gradual increase over time.
   Vital capacity decreases about 9% with each vertebral fracture contributing to morbidity and mortality

OO. Cost of Osteoporosis in USA (US Dollars) [36]
1. Total annual cost about 16.9 billion dollars
2. About 57% of cost is inpatient, 30% long term care and 13% outpatient

PP. Monetary Burden of Fractures 2010 in EUS + Sweden (million €) [37]

QQ. The Economic Burden of Osteoporosis Will Rise for All Races in the US [36]
1. By 2025, fracture costs are projected to grow to 25 billion annually
2. Increases projected for blacks (79% projected) and Hispanics (175% projected)

RR. Prevalence of Common Chronic Diseases: USA [38-40]
1. Osteoporosis and osteopenia prevalence about 45 million, hypercholesterolemia about 100 million, hypertension about 75 million and diabetes about 23 million

SS. Fracture Incidence Compared With Other Common Diseases [41]
1. Predicted incidence per year in white women per 10,000
   • Fracture – about 230
   • Breast cancer – about 50
   • MI/CVD – about 25
TT. Prevalence and Economic Impact of Osteoporosis
1. Annual economic cost of treating osteoporosis in the USA is similar to that of treating cardiovascular disease and asthma

UU. Clinical Utility of Bone Densitometry (DXA)
1. Diagnosis
   • WHO T-score classification
2. Prognosis
   • Facilitates fracture risk assessment
3. Monitoring
   • Requires knowledge of precision and least significant change (LSC)

VV. WHO Classification for Postmenopausal Osteoporosis [42, 43]
1. Normal: T-score -1.0 or higher
2. Low bone mass (ostopenia): T-score between -1.0 and -2.5
3. Osteoporosis: T-score -2.5 or lower
4. Severe (established) osteoporosis: T-score -2.5 or lower WITH low trauma fracture

WW. Caveats of Diagnosis Based on BMD
1. Diagnosis of osteoporosis by DXA is based on the WHO classification as a T-score of -2.5 or below
   • Some patients with T-score –2.5 or below do not have osteoporosis
   • Some patients with T-score above –2.5 may be diagnosed with osteoporosis
2. T-scores may differ at different skeletal sites
3. Patients with a diagnosis of osteoporosis may have substantially different fracture risk
4. Diagnosis of osteoporosis does not explain etiology

Section II  BONE MEASUREMENT DEVICE OPERATING PRINCIPLES

A. Learning Objectives
1. Describe basic DXA anatomy
2. Explain the basic principles of operation for:
   • DXA
     - Central skeletal DXA
     - Peripheral DXA
   • QCT and pQCT
   • High-resolution CT
   • Quantitative ultrasound (QUS)
3. Compare and contrast the accuracy of the available devices

B. Central Skeleton
1. Dual energy X-ray absorptiometry (DXA)
2. Quantitative computed tomography (QCT)

C. Peripheral Skeleton
1. Radiographic absorptiometry (RA)
2. Digital X-ray radiogrammetry (DXR)
3. Single X-ray absorptiometry (SXA)
4. Peripheral DXA (pDXA)
5. Peripheral QCT (pQCT)
D. Basic DXA Anatomy: Lumbar Spine
   1. Analysis includes L1-L4
   2. Iliac crest between L4 and L5
   3. Ribs usually on T12

E. Vertebral Shape May Help With Correct Labeling (See Figure 2.1)
   1. L5 often looks like a bow-tie or dog bone because of typical lumbar lordosis
   2. L4 box or X-shaped
   3. L1-L3 U-shaped
   4. Be consistent with labeling when anatomic variants are present

F. Human Spine Anatomy is Variable [44]
   1. Spine Segmentation Study
      • 375 women, age 50-85
      • 83.5%
         - 5 lumbar vertebrae
         - Lowest ribs on T12
      • 7.5%
         - 4 lumbar vertebrae
         - Lowest ribs on T11 or T12
      • 1.9%
         - 6 lumbar vertebrae
         - Lowest ribs T12 or L1
      • 7.2%
         - 5 lumbar vertebrae
         - Lowest ribs on T11

G. Basic DXA Anatomy: Proximal Femur
   1. Regions of interest:
      • Femoral neck
      • Total proximal femur
      • Greater trochanter
      • Ward’s area (not clinically useful)
   2. Points of interest
      • Ischium
      • Lesser trochanter

H. Basic DXA Anatomy: Forearm
   1. Diagnostic region of interest
      • 1/3rd Radius
   2. Research regions of interest
      • Ultradistal Radius
      • Mid Radius
   3. Points of interest
      • Ulnar styloid
      • Radius/Ulna point of overlap

I. Central vs. Peripheral Devices
   1. Central devices
      • Two x-ray based technologies: DXA and QCT
      • Measure hip and spine
      • DXA systems may also measure forearm and total body
   2. Peripheral devices
      • Two primary technologies: x-ray and ultrasound
- Measures phalanges, metacarpals, forearm or calcaneus

**J. Central Techniques**
1. Dual energy X-ray absorptiometry (DXA)
2. Quantitative computed tomography (QCT)

**K. Peripheral Densitometry Devices**
1. Peripheral DXA (pDXA)
2. Single x-ray absorptiometry (SXA)
3. Quantitative ultrasound (QUS)
4. Radiographic absorptiometry (RA)
5. Peripheral QCT (pQCT)

**L. Principle Behind DXA: Absorptiometry**
1. Attenuation refers to a reduction in the number and energy of photons in an x-ray beam (i.e., its intensity)
2. Attenuation is determined largely by tissue density and thickness
3. The denser the tissue, the more electrons it contains, e.g., hydrogen = 1, calcium = 20
4. The number of electrons in a given volume determines the ability of the tissue to attenuate photons in the x-ray beam
5. If the degree of attenuation could be measured, then it would be possible to quantitatively assess the tissue density as well

**M. Attenuation of X-rays**
1. Differential attenuation by bone and soft tissue
2. Incident beam \( I_0 \)
   - X-rays which enter
3. Transmitted beam (I)
   - X-rays which exit
4. Attenuation
   - \( I_0 - I \)
   - Depends on x-ray energy

**N. Why Dual Energies?**
1. Low energy (30-50 keV)
   - Bone attenuation greater than soft tissue attenuation
2. High energy (greater than 70 keV)
   - Bone attenuation similar to soft tissue attenuation

**O. DXA: Why Dual Energy X-rays?**
1. Differential absorption by bone and soft tissue
2. Low energy (30-50 keV): Bone mineral attenuation >> soft tissue
   - High energy (>70 keV): Bone mineral attenuation ≈ Soft tissue
   - Allows to suppress impact of overlying soft tissue
3. Eliminates the need for uniform object thickness
4. Partially corrects for presence of varying amount of fat

**P. Two Approaches to Producing Dual-Energies**
1. K-edge filtering (filtered x-ray)
   - GE
   - Norland
2. Voltage switching (switched x-ray)
   - Hologic
3. 2 distinct photo-electric peaks necessary to separate bone from soft tissue
4. The peaks are similar (K-edge versus voltage switching) but NOT identical - explaining in part why BMD results from different manufacturers are not comparable.

Q. Components of Central DXA Scanners
1. Below table: X-ray source, shutter, source collimator (pencil beam, wide fan, narrow fan)
2. Table with patient
3. Above table: detector collimator, photon detector on arm (rotatable C-arm or fixed)

R. DXA Acquisition Techniques [45]
1. Pencil Beam (DPX, QDR1000, QDR2000, XR)
2. Wide Fan Beam (QDR4500, Delphi, Discovery, Horizon)
3. Narrow Angle Fan Beam (Prodigy, iDXA, Stratos)

S. Different dual energy methods
1. Different calibration
2. Different detectors
3. Different edge detection software
4. Different regions of interest

T. Peripheral DXA (pDXA)
1. Smaller devices
2. More portable
3. Less radiation
4. Shorter scan times
5. Easier to operate
6. Less expensive

U. Differences Among Peripheral DXA Devices
1. Measurement sites
   • Finger
   • Forearm
   • Heel
2. Scan acquisition
   • Pencil-beam
   • Cone-beam
3. Region of interest may be different at the same skeletal site (e.g., heel)
4. Explains in part why results from different devices are not comparable

CT Based Absorptiometry – QCT

V. QCT
1. Originally developed in 1970's
2. Any commercial CT scanner
3. External calibration phantom or internal fat/lean reference
   • Convert HU to BMD values
   • Scan with patient/separate
4. Dedicated analysis software
5. Early 2D systems: spine only
   • Several thick image slices
   • L1-L4 analyzed
   • Required CT gantry tilt
**W. 3D Volumetric Spine QCT**

1. Vertebrae: 2-3 levels from T12-L4
   - Usually L1, L2 unless deformed
2. Reference phantom
3. Semi-automatic analysis
4. Can rotate image (e.g. for scoliosis)
5. Trabecular ROI
6. Volumetric BMD (mg/cm\(^3\))
7. High sensitivity (trabecular bone)
8. Precision error: <1%
   - For external phantom system
9. Radiation dose: 150 - 300 \(\mu\text{Sv}\)
   - Less than a mammogram

**X. QCT Spine Reporting & Interpretation [46]**

1. Should not be interpreted using WHO T-Score guidelines for fracture-risk categorization
2. American College of Radiology 2008 practice guidelines for the performance of QCT bone densitometry provide the following diagnostic categories for phantom calibrated QCT at the spine:
   - BMD > 120 mg/cm\(^3\) \(\Rightarrow\) “Normal”
   - 80 mg/cm\(^3\) \(\leq\) BMD \(\leq\) 120 mg/cm\(^3\) \(\Rightarrow\) “Osteopenia”
   - BMD < 80 mg/cm\(^3\) \(\Rightarrow\) “Osteoporosis”

**Y. Areal BMD Hip QCT**

1. Proximal femur (neck and total)
2. Reference phantom
3. Semi-automatic analysis
4. Rotate anatomy in software
5. Hologic-style ROI
6. Areal BMD (mg/cm\(^2\))
7. DXA-equivalent measurements
8. Use WHO T-Score categories
9. Precision error: 1-1.5%
10. Radiation dose: 300 – 500 \(\mu\text{Sv}\)
    - About the same as a mammogram

**Z. QCT Femoral Neck Data Can be Used in FRAX®**

**AA. QCT vs DXA**

1. **Central QCT**
   - 3D volume image
   - True volumetric BMD at spine and calculated areal BMD at hip
   - Trabecular bone at spine, integral bone at hip
   - Error sources – osseous fat
   - Spine plus hip dose around 500-800 \(\mu\text{Sv}\)
2. **Central DXA**
   - 2D projection
   - Areal BMD at all sites
   - Spine, hip, forearm and total body
   - Integral bone at all sites
   - Error sources: osseous fat, spine degenerative changes, soft tissue background
   - Spine plus hip dose around 1-10 \(\mu\text{Sv}\)

**BB. BMD Measurement**

**QCT (Volumetric: g/cm\(^3\)) vs. DXA (Areal: g/cm\(^2\))**

1. DXA is a good tool for fracture risk prediction as it incorporates bone density and bone size: Both are important contributors to bone strength

**CC. High-Res CT: 3D Structures**

1. Xtreme CT technology
2. Resolution 82 \(\text{um}\)
3. Virtual bone biopsy: BV/TV, trabecular number, thickness, separation
DD. Peripheral QCT (pQCT)
1. Dedicated CT scanner
   • Radius, Tibia (Stratec XCT 2000)
   • Femur, Radius, Tibia (Stratec XCT 3000)
2. Volumetric BMD (mg/cm³)
3. Measures bio-mechanical parameters
4. ROI: cortical or trabecular or both
5. Low radiation dose (< 1 µSv)
6. Minimum impact of degenerative changes

Quantitative Ultrasound - QUS

EE. QUS
1. No radiation
2. Does not measure BMD
3. Skeletal sites
   • Heel, finger, tibia, multiple sites
4. Transmission
   • Axial vs transverse
5. Transducer coupling
   • Gel (dry) vs water based
6. Data acquisition
   • Fixed single point vs imaging
7. Different output variables
8. Different calibration methods

FF. The Physical and Mechanical Properties of the Bone Progressively Alter the Shape, Intensity and Speed of the Propagating Wave
1. The bone tissue may be characterized in terms of ultrasound velocity (SOS) and broadband ultrasound attenuation (BUA)

GG. Transverse Transmission Technique Diversity of Approaches
1. Coupling between transducers and heel
   • Water-bath
   • Gel
2. Assessment of region of interest (ROI)
   • Fixed ROI
   • Scanning, ROI-definition from ultrasound image
3. Combined parameters
   • Stiffness, QUI etc.
4. Not all ultrasound approaches can be expected to work equally well!

HH. Ultrasound Measured Parameters
1. Propagation velocity (SOS)
   • Units: meters/second
   • Depends on density and elasticity
2. Broadband ultrasound attenuation (BUA)
   • Units: dB/MHz (dB/MHz/cm)
   • Depends on density and scattering architecture (structure)

II. Schematic View of QUS
1. Transverse Transmission
2. Components: Transmitter – gel or water bath - Receiver
3. Outputs: Speed of sound (SOS) and signal attenuation (BUA)

JJ. Examples of Ultrasound Calculated Parameters
1. Stiffness (GE)
2. Quantitative Ultrasound Index (QUI; Hologic)
3. Estimated BMD (Hologic)
4. Many other device specific parameters

Note: Stiffness, QUI and estimated BMD are proprietary terms. Stiffness as used here is not the same as the biomechanical measure of bone structural properties known as stiffness.

KK. Association of QUS and Density
1. BUA, SOS, and BMD are affected by different physical properties
2. Clinically, all three variables are correlated if measured at the same site
3. Correlation of QUS at peripheral sites and BMD at central sites is modest ($r^2 = 0.2$ to 0.3)
4. Therefore, QUS cannot be used to estimate density at main fracture sites

LL. QUS Does Not Match BMD
1. Modest correlation between BMD and BUA at same site
2. No correlation if not same site

MM. Accuracy [47]
1. The ability of a measurement to match the accepted reference value
2. Defined by the International Standards Organization (ISO) and is affected by both systematic (trueness) and random (precision) errors

NN. Trueness [47]
1. Ability to measure true value
2. No perfect way to measure the “true value” of bone mineral content in a bone specimen
3. Often expressed as a systematic difference
   • % error between true and measured value
4. All techniques have associated measurement error
   • FDA 510K requires of BMD devices <10% error

OO. Determining Trueness: Bone Ash Method
1. Laboratory method to estimate the “true value” of mineral content in a bone
   • Clean specimen of soft tissue and dry
   • Place in titanium crucible and carefully weigh
   • Incinerate in a furnace and weigh remaining bone ash
2. The ash is ONLY mineral because all else (e.g., collagen) is incinerated
3. Systematic accuracy error is determined by comparing grams of ash to previously measured bone mineral content (grams) using DXA
4. If DXA-measured BMC = 0.95 g and bone ash = 1.0 g, accuracy error = 5%

PP. QUS: Trueness
1. More difficult to determine than for DXA
2. QUS parameters affected by bone structure as well as BMC

QQ. Precision [48]
1. Comparison between serial measurements of the same object or person
2. Error is random in nature
3. Often expressed as precision error
   • % error between measurements
4. In vivo or in vitro
5. Essential for distinguishing random error from true biologic change when monitoring patients

**RR. Systematic (Trueness) vs. Random (Precision). Example with dart board**
1. Targets: darts all in center – good precision and good trueness
2. Targets: darts scattered about the center – poor precision, good trueness
3. Targets: darts all in one spot away from center – good precision, poor trueness

**SS. Central DXA [49]**
1. PA spine precision error 1-2%, trueness error 4-10%
2. Femur precision error 1.5-3%, trueness error 6%
3. Total body precision error 1%, trueness error 3%

**TT. Peripheral DXA [49]**
1. Forearm precision error 1-2%, trueness error 4-6%
2. Calcaneus precision 1-2%, trueness error 5%

**UU. Comparison of Techniques [49-51] Accuracy error, longitudinal sensitivity**
1. QCT spine error 5-15%; precision error 2-4%
2. pQCT forearm error 14%; precision error 1-2%
3. DXA spine error 4-10%; precision error 1-1.5%
4. DXA hip error 6%; precision error 1.5-3%
5. DXA forearm error 5%; precision error 1%

**VV. Coefficient of Variation (CV) or Precision Does Not Allow Comparison Among Different Devices**
1. Precision (CV) can be compared directly amongst the same technology/methodology/parameters but not between technologies.
2. Without taking into account biological range or responsiveness the ability to determine change may be over-estimated

**WW. QUS Precision Varies Amongst Devices**
1. CV% varies between 0.7% and 3.4%

**Section III  X-RAY SCIENCE, RADIATION SAFETY AND QUALITY ASSURANCE**

**A. Learning Objectives**
1. List the properties of x-rays
2. State and define the units for expressing radiation dose
3. State the typical dose for densitometric examinations
4. Describe biologic effects of radiation
5. Discuss radiation safety and protection
6. State influences on quality originating with the equipment, the patient and the operator
7. Describe instrument quality control procedures for bone densitometers
8. Discuss the considerations and cautions when comparing systems or upgrading equipment hardware and software

**B. What is Radiation?**
1. Radiation: The flow of energy through space and matter
   • Examples: Visible light, radio waves, X-rays
2. Radiation can be in the form of particles or waves
• Examples:
  - Electromagnetic waves such as X-rays and gamma rays
  - Particles such as neutrons, electrons, alpha particles

3. Radiation can penetrate matter to varying degrees (depends on type of radiation)
4. Ionizing radiation
   • Produces ions (charged atomic particles) after penetrating matter
   • Can damage cells by breaking chemical bonds, etc
5. X-rays are a subset of ionizing radiation
   • Waves of energy (electromagnetic radiation)
   • Short wavelength
   • Multiple energy levels (polyenergetic)
   • Emitted by electrical devices
   • Activates DXA scanner detector(s)
   • Can penetrate tissues and cause ionization

C. Electromagnetic Spectrum
   1. Photon energy – higher the frequency, higher the energy
   2. Upper end of spectrum – ionizing radiation capable of tissue damage

D. Radiation Units
   1. X-ray exposure
      • Measurement of number of ionizations of x-rays in air
      • Expressed in coulombs/kg
   2. Entrance skin dose
      • Measurement of the total amount of energy absorbed by the skin
      • Often reported by manufacturers
      • Entrance skin dose does not consider size of beam and organs exposed
      • Expressed as gray (Gy)
   3. Radiation absorbed dose (Rad/Gy)
      • The amount of energy absorbed per gram of tissue
   4. Equivalent dose
      • Takes into account differences between different types of ionizing radiation (x-rays/gamma rays, beta, alpha particles)
      • Expressed as micro-Sievert (uSv)
   5. Effective dose
      • Takes into account the organ/tissue being exposed
      • Is used to calculate the overall increased risk incurred as result of the radiation exposure
      • Expressed as micro-Sievert (uSv)
   6. Exposure : coulombs/kg or roentgens
      • Absorbed dose: gray (Gy) or rad
      • Equivalent dose and effective dose: sievert (Sv) or rem
   7. Conversions:
      • 1 gray (Gy) = 10 rad
      • 1 sievert (Sv) = 100 rem
      • $10^{-3} \mu \text{Sv} = 1 \text{mrem}$
      • $10^{-6} = \text{milli}$
      • $10^{-6} = \text{micro}$

Radiation Exposure to the Patient

E. Effective Dose
   1. Effective dose = $\sum T D_j W_R W_T$
   2. $D_T =$ absorbed dose in tissue T
3. \( W_R = \) radiation weighting factor (depends on type of radiation
   - X-ray, gamma ray, beta radiation; \( W_R = 1 \)
   - Alpha particles; \( W_R = 20 \)
4. \( W_T = \) tissue weighting factor
   - Reflects the volume of tissue irradiated and the radiation sensitivity of the tissues

F. Tissue Weighting Factors [52]
   1. A measure of relative radiosensitivity of different tissues

G. Determinants of Radiation Dose
   1. Equipment
      - Fan beam vs. pencil beam
      - Scan mode
   2. Patient
      - Body part scanned
      - Patient size

H. Effective Radiation Doses for Bone Mass Measurement Technologies [53]
   - DXA \( 1-10 \) uSv
   - pDXA \( <0.1 \) uSv
   - VFA \( <5 \) uSv
   - Single slice QCT \( 50-200 \) uSv
   - 3D QCT spine \( 1-2 \) mSv
   - 3D HRQCT T12 \( 3 \) mSv
   - 3D QCT femur \( 2.5-3 \) mSv
   - 3D HRpQCT \( 3 \) uSv
   - pQCT \( 1 \) uSv
   - QUS none

I. Effective Radiation Doses (uSv) for DXA Systems at Different Skeletal Sites [54]
   1. L1-L4: 0.5 to 2.0 uSv
   2. Proximal femur: 0.15 to 5.4 uSv
   3. Total body excluding ovaries: 0.5 to 3.6 uSv
   4. Total body with ovaries: 0.6 to 4.6 uSv
   5. Forearm: 0.01 to 0.07 uSv

J. Effective Doses for Common Radiographic Procedures [53]
   - Background \( 5-8 \) uSv per day
   - Mammography \( 450 \) uSv
   - Chest x-ray \( 50-150 \) uSv
   - L-spine x-ray \( 700 \) uSv
   - L-spine + T-spine x-ray \( 1800-2000 \) uSv
   - VFA \( <5 \) uSv

K. Biologic Effects of Radiation
   1. Carcinogenesis
   2. Mutagenesis
   3. Teratogenesis
      - These biologic effects are categorized as either stochastic or deterministic

L. Stochastic Effects [55]
   1. Can occur at any dose
   2. Probability of occurrence is a function of dose
3. Increased frequency of naturally occurring cancer and mutation
4. Small risk, no threshold dose
5. Example: skin cancer from sun exposure

M. Deterministic Effects [55]
1. Only occur at a very high dose
2. Occur in each individual receiving sufficient dose
3. Acute radiation sickness and cataracts
4. Total body threshold dose 1.2-3.0 Sv (120-300 rads) below which effects are stochastic
5. Example: Tumor cell death as result of radiation therapy

N. Radiation Dose in DXA
1. Dose to patient
   • Very small compared to other radiological exams
2. Dose to operator (technologist)
   • Even smaller
   • May be difficult to detect

O. Effective Radiation Doses for DXA Compared to Other Common Sources
1. DXA
   • 0.1-5 uSv per exam (varies by type of instrument and skeletal site)
2. Background
   • 5-8 uSv per day
   • Personal radiation exposure can be calculated at the following website: www.epa.gov/radiation/understand/calculate.html
3. Transatlantic roundtrip flight
   • 60 uSv

P. Radiation Dose Put In Perspective [56]
1. A DXA exam with a radiation exposure of ~5 uSv carries the same infinitesimally small risk of death comparable to:
   • Natural background radiation for 4 hours
   • Traveling 25 km by plane
   • Canoeing for 20 seconds
2. A QCT exam with a radiation exposure of 60 uSv carries a risk of death comparable to:
   • Traveling 300 km by car
   • Smoking 6 cigarettes

Q. Average Annual Effective Radiation Doses in the USA (uSv) [57]
1. Background about 2950 uSv
   • radon 1980, cosmic 290, terrestrial 290, internal 390
2. Man-made about 650 uSv
   • medical x-rays 390, nuclear medicine 140, nuclear industry 20, consumer products 100

R. Average Annual Effective Radiation Doses in Belgium
1. Medical – 48% (1.92 mSv)

S. Maximal Permissible Dose [58]
1. USA
   • General public
     - Excluding necessary medical or dental exposure
     - 5,000 uSv per year
   2. Occupational exposure
• Technologist
• 50,000 uSv per year

3. Europe
• General Public
  - 1,000 uSv per year
• Occupational Exposure
  - 20,000 uSv per year

4. International Standard for general public: 1,000 uSv per year [59]

T. Why Teach Radiation Safety?
1. Patient education
   • People fear what they do not understand
   • Patients deserve and require care from those properly trained and educated
2. Protection of patients and technologists
   • Protection requires understanding of radiation safety
3. Facilitates communication with:
   • Patients, technologists, and regulatory agencies

U. Elements of Radiation Safety
1. Justification
   • The procedure is necessary and will influence medical care
   • Can the information be obtained using other means?
2. Regulation
   • Practice must comply with local, state (provincial), and national regulations
3. Optimization
   • ALARA

V. Principles of Radiation Safety
1. Medical necessity
   • Is the information obtained from the test essential for patient care?
   • Can the information be obtained using other means?
2. ALARA:
   As
   Low
   As
   Reasonably
   Achievable

W. Radiation Safety: General Radiography
1. Time
   • Minimize exposure
2. Distance
   • Maintain safe distance
   • Intensity decreases as the square of distance away from source
3. Shielding
   • Use appropriate shielding when necessary

X. Radiation Safety: Bone Densitometry
1. Technologist
   • DXA
     - Stay at least 1 meter from table edge when scanning
   • pDXA
     - 1 m distance, 5 scans per hour: <0.1 uSv per hour
   • QCT
2. Public
   • Post room “Caution Radiation”
   • Room shielding not needed
3. Check national, state and local regulations

Y. Radiation Dose in Densitometry
1. Dose to be measured as effective dose (uSv)
2. Dose to patient
   • Small compared to other radiological exams
3. Dose to operator (technologist)
   • Small, may be difficult to detect
   • Still, for some equipment (fan beam DXA) and in units with many exams per day
cumulative dose levels need to be considered

Z. Precautions Regarding Pregnancy
1. Patient
   • Ask all premenopausal or perimenopausal women if there is a possibility of pregnancy
   • If patient may be pregnant, postpone DXA
2. Technologist
   • Should be encouraged to notify employer in writing of possibility of pregnancy
   • Pregnant technologist may be offered reassignment to other duties or shielding
   with lead apron to reduce concerns

AA. Factors Influencing DXA Quality
1. Scanner related
   • Accuracy and precision
   • Calibration
2. Patient related
   • Artifacts
   • Deformities
   • Cooperation (motion)
3. Operator related
   • Acquisition (positioning)
   • Analysis

BB. Quality Assurance Measures [45, 60]
1. Training of operators and physicians
2. Definition of Standard Operating Procedures (SOP’s)
3. Comprehensive documentation
4. Implementation of Quality Control Procedures
   • Checking device performance
   • Review procedures for patient results

CC. Quality Assurance in Bone Densitometry [45, 60]
1. Quality Assurance (QA)
   • A framework of guidelines, performance goals, quality control tests and
   preventive measures to assure adequate instrument performance and correct
diagnostic assessments
2. Quality Control (QC)
   • Tests to verify adequate diagnostic quality, e.g.
     - Proper instrument performance
- Correct analysis of patient results

**DD. Quality Assurance Is Important**

1. For the benefit of the patient
   - To avoid misguided clinical judgments based on suboptimal bone densitometry results
     - Making healthy people osteoporotic and vice versa
     - Selecting the wrong patients for treatment
   - To optimize device performance to allow to assess disease progression and treatment efficacy faster

2. For the benefit of the physician
   - To document good clinical practice and avoid legal problems (malpractice)

**EE. Instrument Quality Assurance and Quality Control**

1. QA
   - Performed daily prior to any patient scans
   - According to manufacturer's specification
   - Allows machine to calibrate and to check that x-ray source, detector and mechanical specification are operating correctly

2. QC
   - Scanning of a phantom with known BMD and BMC
   - Provides information on long-term variability and stability of the system
   - Should be performed regularly

**FF. Calibration Methods**

1. Continuous (internal)
   - Required with oscillating supply
   - Operates with patient in the beam path

2. Periodic (external)
   - Utilizes a calibration standard
   - Incorporated in daily quality assurance (QA) procedure

**GG. Device Calibration**

1. Calibration Methods
   - Continuous (Internal): During scan acquisition
   - Periodic (External): Quality control phantom
     - Manufacturer provided
     - Independent procedures in addition to those provided by the manufacturer are needed such as daily spine phantom scanning

**HH. Internal Calibration**

1. X-ray beam passed through calibration filters
   - Bone equivalent
   - Tissue equivalent
   - Air equivalent

2. Point-by-point calibration

3. Hologic DXA

**II. External Calibration**

1. Daily scanning of known bone and tissue standards
2. Adjustment of calibration factors as necessary
3. Used in
   - Lunar and Norland DXA systems
   - Peripheral X-ray based and ultrasound densitometers
JJ. Phantoms

- Monitor performance of your scanner: phantom BMD value should remain stable over time

1. Phantom Scanning and Calibration [61]
   - The Quality Control (QC) program should include adherence to manufacturer guidelines for system maintenance
   - In addition, if not recommended by the manufacturer, the following QC procedures are advised:
     - Periodic (at least once per week) phantom scans are recommended for any DXA system as an independent assessment of system quality assurance
     - Plot and review data from calibration and phantom scans
     - Verify the phantom mean BMD after any service performed on the densitometer
     - Establish and enforce corrective action thresholds that trigger a call for service
     - Maintain service logs
     - Comply with government inspections, radiation surveys, and regulatory requirements

2. Example of Calibration Drift and Shift
   - Daily measurements of phantom – gradual drift or sudden shift may be noted

3. Using Phantom to Create Control Charts
   - 10 phantom scans same day, without repositioning
     - Reflects day-to-day variability in machine values
     - Calculate average BMD and range that represents $\pm 1.5\% (\approx 3SD)$
     - Average $+1.5\%$ and $-1.5\%$ = upper and lower limit for subsequent measurements (control limits)
   - Application of visual check, Shewart charts and CUSUM plot

KK. Why DXA Systems and Data are Not Interchangeable: Same Manufacturer

1. May use different acquisition methods
   - E.g., pencil vs. fan beam
2. May use different software
3. May use different young-normal databases
4. Inter-device variability $\pm 2\%

LL. Why DXA Systems and Data are Not Interchangeable: Different Manufacturers

1. Use different methods for dual energy production
2. Use different methods of X-ray detection
3. Are calibrated differently
4. Use different edge detection software
5. May use different regions of interest
6. Use different young-normal databases
7. Inter-device variability $\pm 5\%-7\%$

MM. Due To These Differences [62]: (Official Position)

1. Direct quantitative comparisons to other machines cannot be made
2. Cross calibration is necessary to compare results
   - For details, see the iscd.org website

NN. Situations Requiring Cross-Calibration [62] (Official Position)

1. New hardware, same manufacturer
2. Entire new system, same or different manufacturer
   • e.g. brand x to brand y; pencil to fan
   • Scan 30 patients on each instrument

OO. Software Changes
1. Check with manufacturer before installing any software upgrades
2. Know the reason for the upgrade
   • Modification of edge detection algorithms
   • Revised reporting systems
   • Normative database updates
   • New features
3. Generally upgrades will not affect BMD results
4. Conversion of patient data between manufacturers should be used with caution
5. There are documented cases in which upgrades have significantly changed BMD or T-scores
6. Example of intentional change:
   • 1997 adoption of NHANES normative database for total hip
   • This was done to improve T-score agreement between manufacturers

PP. Software Changes - Unintentional Consequences [63]
1. GE-Healthcare upgrade enCORE versions 7.x – 8.x
2. NHANES III applied to femoral neck as a result of a recommendation of the International
   Committee for Standards in Bone Measurement
3. Young normal reference SD was not calculated correctly, resulting in a lower mean T-score,
   by about 0.5, for the femoral neck
4. Resulted in over diagnosis of osteoporosis
5. Fixed in enCORE software versions 9.x and higher

QQ. Software Changes
1. After installing new software, compare the new phantom mean with the previous
   phantom mean BMD value
   • Calculate phantom mean BMD with old software
   • Scan the phantom several times with new software
   • Calculate phantom mean BMD with new software
   • The phantom mean BMD should be nearly identical
2. An alternative is to open some old patient scans and compare the BMD and T-score
   obtained with both the old and new software

Section IV PRINCIPLES OF DXA SCAN INTERPRETATION

A. Learning Objectives
1. Discuss patient positioning and scan analysis (PA spine, hip, forearm, total body) and
   recognize common errors in DXA analysis
2. Review skeletal anatomy relevant to DXA
3. Describe principles for interpreting central DXA scans
4. Recognize common artifacts on DXA scan images

B. Always Evaluate the Scan Analysis: Errors Are Not Rare [64]
1. Multicenter trials: Lumbar spine and forearm error rate about 5%; 15% at femoral neck
C. “How often do you see a patient with a previous DXA report interpretation that is incorrect?” [65]
   1. never – 4%
   2. less than one per month – 25%
   3. one per month – 27%;
   4. one per week – 17%;
   5. more than one per week – 22%

D. Positioning: Lumbar Spine
   1. Center patient on scanner table
   2. Align patient with scanner axis
   3. Raise legs with positioning block
   4. Ensure consistent use of positioner
   5. Manufacturer instructions

E. Lumbar Spine: Optimal Positioning
   1. Spine is centered
   2. Spine is straight
      • Not tilted
   3. Both iliac crests are visible
   4. Scan includes
      • Middle of L5
      • Middle of T12

F. Lumbar Spine: Scan Analysis
   1. Verify
      • Lateral vertebral margins (edges)
      • Intervertebral markers
   2. Consistent numbering
      • Count from iliac crest up
   3. Neutralize artifacts

G. Check Intervertebral Markers and Edges
   1. Adjust as required

H. Consistent Vertebral Numbering – Spine Segmentation Study [44]
   1. 375 women, age 50-85
   2. 83.5%
      • 5 lumbar vertebrae
      • Lowest ribs on T12
   3. 7.5%
      • 4 lumbar vertebrae
      • Lowest ribs on T11 or T12
   4. 1.9%
      • 6 lumbar vertebrae
      • Lowest ribs T12 or L1
   5. 7.2%
      • 5 lumbar vertebrae
      • Lowest ribs on T11

I. Vertebral Shape May Help With Correct Labeling (See Figure 2)
   1. L5 often looks like a bow-tie or dog bone
   2. L4 box or X-shaped
   3. L1-L3 U-shaped
J. Summary: Correct Spine Analysis
   1. Edges should include only bone that should be evaluated
   2. Intervertebral markers should be placed in the disc space
   3. Numbering should be correct

K. Positioning: Hip
   1. Place foot (feet) into positioning device
   2. Internally rotate leg to specified angle
   3. Place shaft of femur parallel to scanner axis

L. Proximal Femur: Optimal Positioning
   1. Femoral shaft is straight
   2. Leg internally rotated
      • Lesser trochanter small or not seen
      • The lesser trochanter is a posterior structure; its size is the best indicator of internal rotation
   3. Scan includes
      • Ischium
      • Greater trochanter

M. Proximal Femur Scan Analysis
   1. Check for proper positioning
   2. Check if hip is suited for measurement
      • Hardware, fusion, osteoarthritis, fractures
   3. Visually verify bone edges
   4. Neck ROI should not include greater trochanter
      • Avoid ischium if possible
   5. Exclude artifacts
      • If small, and do not overlay bone

N. Check for errors in positioning, overlap of bone and soft tissue regions with femoral neck box

O. Forearm Scan Positioning
   1. Scan non-dominant forearm
      • Unless fracture or arthritis
   2. Patient in a chair or supine depending on manufacturer’s recommendations
   3. Use positioning device
      • Allows proper alignment
   4. May need to measure forearm length

P. Positioning: Forearm

Q. Forearm: Optimal Positioning
   1. Forearm is centered
   2. Radius and ulna straight
      • Aligned with long axis of table
   3. Distal cortex of radius and ulna visible
   4. No avoidable artifacts

R. Forearm Scan Analysis
   1. Check for proper positioning
   2. Check if forearm is suited for measurement
3. Check for artifacts
4. Visually verify bone edges
5. Use 33% (1/3) site radius for diagnosis

S. **Total (Whole) Body Positioning**
   - Align patient with scanner axis
   - Entire body in scan limits
   - Arms at sides
   - Arms slightly separated from trunk
   - Position of hands and feet previously dependent on manufacturer; NHANES positioning (shown) endorsed by ISCD

T. **Total Body Scan Analysis**
   - Note that the WHO T-score classification does not apply to total body BMD
   - Check for proper positioning/verify entire body in scan field
     - Note if some parts are excluded
   - Check for artifacts including implants
   - ROI placement varies
     - Follow manufacturer recommendations

U. **Do Not Rely on Auto-Analysis**
   - May require manual adjustment
   - This affects regional body composition but has little effect on total body measurements

V. **Bone Composition**
   - Mostly Cancellous
     - Spine
     - Ultradistal radius
     - Calcaneus
   - Mostly Cortical
     - Femoral Neck
     - 1/3 (33%) radius
     - Total body
   - Mixed
     - Total Hip
     - Trochanter
     - Phalanges

W. **Bone Composition: Approximate Percent Cancellous (Trabecular) Bone [66, 67]**
   - Calcaneus 95%
   - PA lumbar spine 66%
   - Ultradistal radius 66%
   - Trochanter 50%
   - Phalanges 40%
   - Femoral neck 25%
   - Total body 20%
   - One-third radius 1%

X. **Which Side to Scan? Extremity Dominance**
   - Forearm
     - Dominant forearm has higher BMD
     - Scan non-dominant forearm [68]
       - Unless asymmetric arthritis or old fracture
   - Hip
• Little difference between hips
• Does not matter which side to scan
  - Unless asymmetric arthritis, old fracture, or other artifact
• ISCD has no position on use of dual-femur

Y. Central DXA Interpretation: Printouts Have Common Features
  1. Patient demographics
  2. Image of skeletal site
  3. Graph (age vs. BMD)
  4. Numerical results

Z. Central DXA Interpretation Principles
  1. Check demographics
  2. Review the image
    • Evaluate positioning, edge placement, labeling, artifacts
  3. Exclude vertebral bodies or regions/sites if artifacts
  4. Utilize the lowest T-score for diagnosis
    • Spine (L1-L4)
    • Hip (neck or total femur) not Ward’s area or trochanter

AA. Check Demographics
  1. Name
  2. Gender
  3. Age
  4. Race

BB. DXA Image
  1. Check patient positioning
  2. Check scan analysis
  3. Identify artifacts
  4. The disclaimer “Image not for diagnosis” is not a mandate to ignore the image

CC. Review the Image
  1. Is positioning correct?
  2. Compare with prior study
  3. Are the proper regions identified?
  4. Are there other problems?
  5. Compression fractures?
  6. Degenerative changes?
  7. Get x-rays if not sure
  8. If possible, delete artifacts

DD. Numerical Results
  1. Region of interest
  2. BMD in g/cm²
    • Used for monitoring
  3. T-score
    • Used for diagnosis
  4. Additional data:
    • %, Z-score, BMC, area, etc
  5. Usually configurable

EE. Numerical Results: Spine
  1. Individual vertebral T-scores should be within 1 SD
2. Do not report individual T-scores
3. Instead, report T-score of L1-L4 if no exclusions

FF. Agreement of Individual Vertebrae
1. BMC and area increase from L1-L4
2. Area may increase disproportionately at L4, so BMD calculation (BMD=BMC/Area) may result in L4 slightly below L3 in some cases.

GG. Discrepancy of Individual Vertebrae
1. Exclude vertebral bodies for cause: more than 1SD difference with structural problems (see ISCD position below)

HH. L1-L4 Is Preferred for Diagnostic Purposes [69](Official Position)
1. Criteria for Exclusion of Vertebrae from Analysis
2. Anatomically abnormal vertebrae may be excluded from analysis if:
   • They are clearly abnormal and non-assessable within the resolution of the system; or
   • There is more than a 1.0 T-score difference between the vertebra in question and adjacent vertebrae
3. When vertebrae are excluded, the BMD of the remaining vertebrae is used to derive the T-score

II. Follow-Up Scans
1. Consistent patient positioning
2. Consistent scan analysis
3. Scan area should be similar

Section V USE OF BONE DENSITOMETRY FOR THE DIAGNOSIS OF OSTEOPOROSIS

A. Learning Objectives
1. Explain how to use central DXA for the diagnosis of osteoporosis
2. State the WHO diagnostic classifications for osteoporosis
3. State and explain the advantages and limitations of WHO classification for densitometric diagnosis
4. Define the standardized scores used in bone densitometry (T-score and Z-score)
5. Compare and contrast use of different skeletal sites and regions of interest for diagnosis
6. Discuss the diagnosis of osteoporosis in: Premenopausal and perimenopausal women, men, non-Caucasians, children
7. Review the use of technologies other than central DXA for diagnosis

B. WHO Classification of Postmenopausal Osteoporosis [42]
1. Published in 1994 by a working group of the WHO
2. Intended to assess the prevalence of the disease in a population
3. Evaluated postmenopausal Caucasian females using DXA of spine, hip or forearm
4. Results were expressed as a standard deviation from the mean predicted bone mass in young adult Caucasian females (which was later expressed as a T-score)

C. WHO Classification of Postmenopausal Osteoporosis [42]
1. Normal: T-score -1.0 or higher
2. Low bone mass (osteopenia): T-score between -1.0 and -2.5
3. Osteoporosis: T-score -2.5 or lower
4. Severe (established) osteoporosis: T-score -2.5 or lower WITH low trauma fracture
D. Why the WHO Chose a T-score of -2.5 [43]
   1. "Such a cutoff value identifies approximately 30% of postmenopausal women as having osteoporosis using measurements made at the spine, hip, or forearm. This is approximately equivalent to the lifetime risk of fracture at these sites."

E. Prevalence of Osteoporosis and Lifetime Fracture Risk in White Women [15, 70]
   1. Femoral neck: 16.2% with T-score at or below -2.5 with site-specific fracture risk of 17.5%
   2. Spine: 16.5% with T-score at or below -2.5 with site-specific clinical fracture risk of 15.6%
   3. Forearm: 17.4% with T-score at or below -2.5 with site-specific risk of 16%
   4. Any of 3 sites: 30.3% with T-score at or below -2.5 and site-specific risk of 39.7%

F. Advantage of T-score Instead of BMD
   1. If there were only one type of densitometer and one skeletal site to measure bone density, absolute BMD criteria would be preferable
   2. Multiple devices exist that use different approaches to BMD measurement
   3. Theoretically, T-score provides a way of using the same diagnostic criteria for all devices and skeletal sites

G. Limitations of 1994 WHO Classification
   1. Not intended as treatment guidelines
   2. Definitions do not necessarily apply to other populations (e.g., men, non-Caucasians, premenopausal women)
   3. Does not recognize that a presumptive diagnosis of osteoporosis can be made by a low-trauma (fragility) fracture regardless of the patient's BMD
   4. Does not differentiate between osteoporosis and other causes of low BMD

T-score Equal to or lower Than -2.5 is Not Always Due to Osteoporosis

H. Examples of Non-Osteoporotic Causes of Low BMD
   1. Osteomalacia
   2. Genetic disorders, e.g., osteogenesis imperfecta
   3. Renal bone disease
   4. Multiple myeloma/other malignancies
   5. Marrow infiltrative diseases, e.g., mastocytosis

I. T-score Calculation
   1. Number of standard deviations patient's BMD is above or below average BMD of young-adult reference population
      \[ \text{BMD patient} - \text{BMD young-normal reference} \]
   2. T-score = \( \frac{\text{BMD patient} - \text{BMD young-normal reference}}{\text{SD young-normal reference}} \)
   3. Used for diagnosis
   4. If low, does not necessarily imply prior bone loss

J. Z-score Calculation [71]
   1. Number of standard deviations patient’s BMD is above or below average BMD of age-matched reference population
      \[ \text{BMD patient} - \text{BMD age-matched reference} \]
   2. Z-score = \( \frac{\text{BMD patient} - \text{BMD age-matched reference}}{\text{SD age-matched reference}} \)
   3. Not used for diagnosis
   4. There is no evidence to support a specific cut-point to evaluate for secondary causes*
5. Secondary causes should always be considered as clinically indicated

K. Why Use T-score Instead of Z-score for Diagnosis?
1. Bone strength related to BMD
2. Risk of fracture related to BMD
3. Using Z-score would suggest that osteoporosis does not increase with age and many “normal” patients (Z-score $³ -1$) have osteoporotic fractures

L. Principles Behind Using T-score to Diagnosis Osteoporosis
1. Dependent on the reference young-normal population selected
   • Manufacturer’s data base vs. NHANES
   • Same race or other
   • For males: male or female database

M. Changing Reference Database can Change the T-score [72]
1. Hologic T-scores (using Hologic database – black line) were $≈ 1$ SD lower than GE-Lunar
2. Applying the NHANES femur database (red line) resulted in a good correlation between Hologic and GE-Lunar machines

N. An Example of How Change in Database Affected a Clinical Trial [73]
1. The number of patients with “osteoporosis” was cut in half in the FIT trial
   • TK 10/25/91 database identified 78.1% of patients with osteoporosis using original Hologic reference values
   • Using NHANES (NHA 2/1/97), 36.8% of patients were classified as having osteoporosis
2. Check your database (should be NHANES at hip) to ensure proper clinical management

O. Principles Behind Using T-score to Diagnosis Osteoporosis
1. Dependent on the reference young-normal population selected
   • Manufacturer’s data base vs. NHANES
   • Same race or other
   • For males: male or female database
2. Dependent on SD of population studied

P. Effect on T-score of Changing the SD: Example with SD of 0.1

<table>
<thead>
<tr>
<th>Patient's BMD – Young-Adult Mean</th>
<th>1 SD of Young Normals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example</td>
<td></td>
</tr>
<tr>
<td>Patient BMD = 0.700 g/cm$^2$</td>
<td>(0.700) – (1.000) = -0.300</td>
</tr>
<tr>
<td>Mean BMD = 1.000 g/cm$^2$</td>
<td>(-0.300) ÷ (0.100)</td>
</tr>
<tr>
<td>SD = 0.100 g/cm$^2$</td>
<td>T-score = -3.0</td>
</tr>
</tbody>
</table>

Q. Effect on T-score of Changing the SD: Example with SD of 0.2

<table>
<thead>
<tr>
<th>Patient's BMD – Young-Adult Mean</th>
<th>1 SD of Young Normals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example</td>
<td></td>
</tr>
<tr>
<td>Patient BMD = 0.700 g/cm$^2$</td>
<td>(0.700) – (1.000) = -0.300</td>
</tr>
<tr>
<td>Mean BMD = 1.000 g/cm$^2$</td>
<td>(-0.300) ÷ (0.200)</td>
</tr>
<tr>
<td>SD = 0.200 g/cm$^2$</td>
<td>T-score = -1.5</td>
</tr>
</tbody>
</table>
R. Effect on T-score of Changing the Young Normal Mean: Example with Young normal = 1.000

\[
\text{Patient's BMD - Young-Adult Mean} = \frac{(0.700) - (1.000)}{0.100} = -3.0
\]

S. Effect on T-score of Changing the Young Normal Mean: Example with Young Normal = 0.900

\[
\text{Patient's BMD - Young-Adult Mean} = \frac{(0.700) - (0.900)}{0.100} = -2.0
\]

T. Principles Behind Using T-score to Diagnose Osteoporosis
1. Dependent on the reference young-normal population selected
   - Manufacturer’s data base vs NHANES
   - Same race or other
   - For males: male or female database
2. Dependent on SD of population studied
3. A low value on one measurement does not imply bone loss, but may be normal peak bone mass for that individual

U. Central DXA for Diagnosis: Skeletal Sites to Measure (Official Position)
1. Measure BMD at both lumbar spine and hip in all patients
2. Measure forearm BMD when:
   - Lumbar spine and/or hip cannot be measured or interpreted
   - Hyperparathyroidism
   - Very obese patients (over the weight limit for DXA table)

V. Central DXA for Diagnosis: Spine Region of Interest (Official Position)
1. Use L1-L4 for spine BMD measurement
2. Use all evaluable vertebrae and only exclude vertebrae affected by structural change or artifact; use 3 vertebrae if 4 cannot be used, and 2 if 3 cannot be used
3. BMD-based diagnostic classification should not be made using a single vertebrae
4. Lateral spine should not be used for diagnosis

W. Central DXA for Diagnosis: Hip Region of Interest (Official Position)
1. Use femoral neck or total proximal femur whichever is lowest
2. BMD may be measured at either hip
3. Do not use Ward’s area or the greater trochanter for diagnosis
4. Mean hip BMD can be used for monitoring with total hip preferred ROI
X. **Central DXA for Diagnosis: Forearm Region of Interest (Official Position)**
   1. Use 33% radius (sometimes called one-third radius) on the non-dominant forearm as alternative site
   2. Other forearm ROIs are not recommended

Y. **Central DXA Diagnosis of Osteoporosis (Official Position)**
   1. Diagnosis is based on the lowest site (lumbar spine, femur neck/total femur or one-third radius) provided:
      • Measurements are technically valid
      • Low bone mass is not due to some other pathology

Z. **Why Measure Spine AND Hip?**
   1. Diagnosis is based on the lowest BMD site
   2. Spine-hip discordance
   3. Fracture prediction
      • Spine BMD for spine fractures
      • Hip BMD for hip fractures
   4. Monitoring response to therapy
      • May lose the ability to continue to monitor an individual site (osteoarthritis, hip fracture)
      • Serial changes at different sites may vary

AA. **Causes of Discordance**
   1. Peak adult bone mass and rate of bone loss are not the same throughout skeleton
   2. In postmenopausal women, the initial rate of bone loss is greater in cancellous bone than cortical bone
   3. Some disorders affect mostly cortical bone (e.g., hyperparathyroidism)
   4. Artifacts (e.g., degenerative disease, fractures)

BB. **Example: Discordance in a Patient Taking Glucocorticoids**
   1. L1-L4
      • T-score −2.4
      • WHO diagnosis
      • LOW BONE DENSITY (OSTEOPENIA)
   2. Total Hip
      • T-score -0.5
      • WHO diagnosis
      • NORMAL

**WHO Classification Should be Limited to Specific Populations, Skeletal Sites and Devices**

CC. **Original Derivation of 1994 WHO Classification (Official Position)**
   1. Only postmenopausal Caucasian women
      • Not men, premenopausal women, children
      • Not other racial or ethnic groups
   2. Only PA spine, hip and forearm DXA
      • Not lateral spine, heel, finger, etc
   3. Only for central DXA and forearm
      • Not peripheral DXA (other than forearm)
      • Not for QCT, QUS, RA, etc

DD. **Diagnosis in Premenopausal Women (age 20 and older) (Official Position)**
   1. WHO classification should not be applied to healthy premenopausal women
2. For women prior to menopause, Z-scores, rather than T-scores, are preferred. This is particularly important in children.
3. A Z-score of -2.0 or lower is defined as “below the expected range for age” and a Z-score above -2.0 is “within the expected range for age.”
4. The diagnosis of osteoporosis in premenopausal women should not be made on the basis of densitometric criteria alone.

EE. Diagnosis in Perimenopausal Women [74]
1. The WHO diagnostic criteria may be applied to women in the menopausal transition.
2. BMD measurement is indicated for women during the menopausal transition who have clinical risk factors for fracture such as low body weight, prior fracture or high-risk medications.

FF. Skeletal Sites to Measure for Diagnosis in Children [75] (Official Position)
1. Patients should have spine and total body less head (TBLH) BMC and areal BMD measured.
2. The total hip is not a reliable site for measurement in growing children due to significant variability in skeletal development and lack of reproducible regions of interest.

GG. Diagnosis in Children and Adolescents: Males and Females Ages 5-19 [76] (Official Position)
1. Should NOT be made on the basis of densitometric criteria alone.
   • The diagnosis of osteoporosis requires the presence of both a clinically significant fracture history and low bone mineral content or bone mineral density.
   • Clinically significant fracture history is defined as:
     - Long bone fracture of the lower extremities, and/or
     - Vertebral compression fracture, and/or
     - Two or more long-bone fractures of the upper extremities.
2. Low BMC or BMD is defined as a Z-score ≤ -2.0 adjusted for age, gender and body size as appropriate.

HH. Example: Your Patient Has a T-score of -5.0 – Is Osteoporosis Treatment Needed?
1. No, This Patient is a Five Year Old Girl!
   • The Z-score is -0.7: this is normal for age T-scores are not appropriate in children.

II. Summary – Children and Adolescents: Males and Females Ages 5-19
1. Osteoporosis diagnosis requires both low bone mineral content or bone mineral density and a clinically significant fracture history.
2. T-scores should not be used and should not appear on DXA printouts in children.
3. Terminology such as “low bone density for chronologic age” may be used if the Z-score is –2.0 or lower.

Diagnosis in Men

JJ. Influence of Sex on BMD
1. Using DXA
   • Young men have areal BMD ~10% higher than women.
   • Mostly because men have generally have larger bones.
2. Male T- and Z-scores were historically based on male reference data resulting in T-scores which, at the same BMD, differed depending on sex.

KK. How to Derive T-scores in Men Has Been Controversial
1. WHO T-score based on data for postmenopausal Caucasian women.
2. Previously ISCD Official Position was to use a:
• Female database to derive T-scores in women
• Male database to derive T-scores in men
3. Basic question: at a given BMD, does the fracture risk differ between men and women?
   • If the fracture risk is the same for men and women, then the T-score should be the same
     - And thus the database to derive the T-score should be the same

LL. Accumulating Data Support Men and Women Fracturing at the Same BMD [77]
1. EPOS: At a given spine bone density, the risk of incident vertebral fracture is similar in men and women
   • 3416 men and women, mean follow-up = 3.8 years (1.4-7.9) [78]
2. CaMOS: At the same BMD, men & women have similar absolute fracture risk
    • 4700 eligible women, 1874 eligible men, follow-up 8 years, one or more fragility fracture: 614 women, 125 men [79]
3. NHANES III: Hazard ratios for major osteoporotic fractures similar using a male or female reference database for femoral neck BMD
    • 380 major osteoporosis related fractures in 2,743 men and women age 65+ [80]

MM. It is Reasonable that Fracture Risk Would Be Comparable at the Same Femoral Neck BMD by DXA, Because Calculated Bone Strength is Similar [81]
1. When aBMD (i.e., DXA) is matched, men have lower vBMD by QCT but larger bone size
2. Matching by areal BMD “leads to quite similar values of both FE-derived femoral strength and load to strength ratio.”

NN. At Equal Femoral Neck BMD, Estimated Fracture Risk by FRAX is Similar in Men and Women [82]
1. Example: US Caucasian
   • Same age (70 year old)
   • Same femoral neck BMD (0.700 g/cm²)
   • Same BMI (24.7)
     - Assumed average height (64” female, 69.5” male)
   • Similar 10 year fracture risks hip/major
     - Male = 3.9/11
     - Female = 3.5/14
2. Note: Since its release, FRAX has utilized female database to generate male T-scores

OO. As a Result, ISCD Now Recommends Using a Female Reference to Derive T-scores in Males
1. Consequences
   • T-scores improve by roughly 0.3 to 0.5 [83]
   • Fewer men with osteoporosis by T-score
     - However, many with osteopenia/low bone mass will still qualify for treatment based on FRAX [84]

PP. Diagnosis in Men [85] (Official Position)
1. Use a uniform Caucasian (non-race adjusted) female reference for men of all ethnic groups.*
2. Age 50 and older
   • T-scores are preferred
   • The WHO densitometric classification is applicable
3. In men younger than age 50
   • Z-scores, not T-scores are preferred
   • A Z-score of -2 or lower is defined as “below the expected range for age” and a Z-score above -2 is “within the expected range for age”
- Osteoporosis cannot be diagnosed on the basis of BMD alone

**Diagnosis in Non-Whites**

**QQ. BMD and Race/Ethnicity (USA Data)**
1. Using DXA, BMD for young normal blacks is ~10% higher than for whites
   - Asians similar to whites
   - Hispanics intermediate
2. Some DXA manufacturers give race-adjusted T-scores, others do not

**RR. Diagnosis in Non-Whites (Official Position)**
1. ISCD recommends using a uniform Caucasian (non-race adjusted) female normative database for women and men of all ethnic groups
2. Z-scores should be population specific where adequate reference data exist
3. For the purpose of Z-score calculation, the patient’s self-reported ethnicity should be used

**SS. Recognize that the Current Recommendations Remain Controversial**
1. Ambiguity about what constitutes a racial or ethnic group
2. Controversy regarding applicability of NHANES to all populations
3. Environmental factors can influence fracture rate, e.g., Asians living in different locations
4. “Application of recommendations may vary according to local requirements.” (ISCD Official Position statement)

**TT. Technologies Other Than Central DXA [86] (Official Position)**
1. The WHO classification system cannot be applied to T-scores from measurements other than DXA at the:
   - Femoral neck
   - Total hip
   - Lumbar spine
   - One-third (33%) radius

**UU. Diagnosis With Technologies Other Than Central DXA [87]**
1. T-scores are not directly comparable to central DXA because:
   - Physical principles of the techniques are different
   - Measuring different skeletal sites (regional differences in rates and times of bone loss)
   - Normative databases are not comparable
2. There are no agreed-upon diagnostic criteria
3. **WHO classification should not be used**

**VV. Diagnosis Using Techniques Other Than Central DXA: Age Dependence of T-scores**
1. QCT – reach 50% at T-score -2.5 or below at age 60
2. DXA spine – reach 50% at T-score -2.5 or below at age 75
3. DXA total hip – reach 50% at T-score -2.5 or below at age 90

**WW. Non-central DXA Bone Mass Measurement Devices [88, 89]**
1. Can predict fragility fracture (discussed in other lecture)
2. Cannot be used for diagnosis using the WHO classification (except with DXA of the 33% radius)

**XX. Summary: Application of WHO Classification for Diagnosis**
1. WHO 1994 applies to postmenopausal Caucasian women only
2. ISCD 2013 applies to postmenopausal women (other ethnic groups as well) and older men of all ethnic groups (use female Caucasian database)
3. No consistent application to premenopausal women, men younger than 50 and using other technologies and sites.

Section VI FRACTURE RISK ASSESSMENT

A. Learning Objectives
1. Understand the use of central DXA for predicting fracture risk
2. Define different ways of expressing risk: absolute risk, relative risk
3. List clinical risk factors for fracture
4. Explain fracture risk assessment combining BMD with clinical risk factors (WHO fracture risk model)
5. Evaluate non-central DXA technologies for predicting fracture risk

B. BMD Correlates With Fracture Risk
1. BMD measured by DXA is highly correlated with bone strength by biomechanical testing
2. In the absence of fracture and treatment, low BMD is the best predictor of fracture in prospective studies

C. Fracture Risk Increases Exponentially with Declining BMD
1. Gradient of risk is characterized by
   • Change in risk (e.g. 2-fold) per change in BMD (e.g. 0.1 g/cm²)
2. Gradient is exponential, e.g.:
   • 2 fold / 0.1 g/cm²
   • 4 fold / 0.2 g/cm²
   • 8 fold / 0.3 g/cm²

D. Fracture Risk Is a Gradient, Not a Threshold
1. Fracture risk is similar for a:
   • T-score = −2.4 (osteopenia) and T-score = −2.6 (osteoporosis) in spite of different diagnostic categories
2. Fracture risk is much higher for a:
   • T-score of −5.0 compared with a T-score of −2.5 in spite of the same diagnostic categories (osteoporosis)

E. Fractures Occur in Patients Without Densitometric Osteoporosis (OFELY Study) [90]
1. 668 patients – 142 with osteoporosis (39% of total fractures fractured); 322 with osteopenia (50% of total fractures); 204 with normal bone density (11% of total fractures).
2. So, 61% of total fractures occurred in patients with osteopenia or normal bone density because the total numbers of these patients were more than the osteoporosis patients.

F. More fractures occur in patients with low bone mass because there are so many more patients in this category. [91]
1. EPISEM study – 6862 postmenopausal white women age 70 and older
2. Mean follow-up 3.2 years with 687 osteoporosis related fractures
3. Fracture rate goes up exponentially as BMD declines as expected.
4. One-third of fractures occurred in patients with a T-score better than −2.5 because more women in the low or normal bone density categories
G. Characterizing Fracture Risk
1. Absolute risk
   - e.g. if 6 of 100 women who smoke have a fracture, absolute risk is 6/100 = 6%

   \[
   \text{Absolute Risk} = \frac{\text{Number of people who develop the disease}}{\text{Number of people at risk}}
   \]

2. Relative risk
   - Ratio of absolute risks for two groups
   - e.g. if absolute risk of fracture in women who smoke is 6% and in women who do not smoke is 2%, relative risk of fracture for smokers is 6/2 = 3

H. Example of Absolute Fracture Risk [92]
1. The 10-year absolute fracture risk is higher for women with lower BMD
2. Exponential relationship femoral neck T-score versus 10 year fracture probability

I. Relative Risk [93]
1. Roughly Doubles for Each Age-adjusted SD Decrease in BMD
2. Marshall data: meta-analysis of 11 prospective studies, 90,000 person years of observation and over 2000 fractures
3. Measurement of BMD at fracture site is advantageous:
   - Radius – hip fracture risk 1.8 fold, vertebral fracture risk 1.7 fold
   - Spine – hip fracture risk 1.6 fold risk, vertebral fracture risk 2.3 fold
   - Proximal radius – hip fracture risk 2.1 fold risk, vertebral fracture 2.2 fold
   - Calcaneus – hip fracture risk 2.0 fold risk, vertebral fracture 2.4 fold
   - Femoral neck – hip fracture risk 2.6 fold, vertebral fracture risk 1.8 fold

J. Relative and Absolute Fracture Risk Are Not The Same
1. Age 50 – hip T-score -2.5 with RR of 10.9 and absolute 10 year risk 6.5%
2. Age 80 – hip T-score -2.5 with RR of 10.9 and absolute 10 year risk of 19.4%
   - Relative risk from Marshall data 2.6^{2.5}
   - Absolute risk from FRAX risk version 3.3

K. Bone Density and Fracture Risk
1. Bone mineral density is important determinant of bone strength
2. Bone strength is important predictor of fracture risk
3. But we need to consider clinical risk factors in addition to BMD

L. Basing Treatment Decisions Solely on T-score Will Miss Over Half of Those Who Will Fracture [94]
1. As noted previously, numerically More Fractures Occur in Those Without Osteoporosis by T-score (Only 44% of women and 21% of men who sustain non-vertebral fractures have osteoporosis by BMD)

M. Multiple Fracture Risk Factors Exist – Which Ones to Use? [95]
1. Age
2. Prior fracture
3. Low body weight
4. Weight loss
5. Inactivity
6. Glucocorticoids
7. Hyperparathyroidism
8. Diabetes type 1
9. Anorexia
10. Gastrectomy
11. Gender (female)
12. Current smoking
13. Low sunlight exposure
14. Family Hx of fracture
15. Surgical menopause
16. Low calcium intake
17. Hyperthyroidism
18. Diabetes type 2
19. Rheumatoid arthritis
N. Age is an Independent Risk Factor for Osteoporotic Fractures [92]
   1. Older age groups have higher fracture risk for a given bone density
   2. Bone architecture (quality) is a major contributing factor

O. Prior Fracture Is a Strong Predictor of Future Fractures (Relative Risk) [25]
   1. A prior wrist fracture increases risk of future wrist fracture 3.3 fold, vertebral fracture 1.7 fold and hip fracture 1.9 fold
   2. A prior vertebral fracture increases risk of wrist fracture 1.4 fold, vertebral fracture 4.4 fold and hip fracture 2.3 fold
   3. A prior hip fracture increases risk of future vertebral fracture 2.5 fold and hip fracture 2.3 fold

P. Prior Fracture Associated With Increased Absolute Risk for Future Fractures [96-99]
   1. Vertebral fracture
      • MORE trial: prevalent fx \(\rightarrow\uparrow20\%\) new vertebral fx/3 yrs
      • VERT trial: incident fx \(\rightarrow\uparrow19\%\) new vertebral fx/1 yr
   2. Hip fracture
      • Rochester: hip fx \(\rightarrow\) 29% contralateral hip fx/20 years
   3. Any fracture predicts fracture
      • For a 65-74 year-old, the 5-year risk of any fracture following:
         - Forearm fracture = 15% (male) 21% (female)
         - Vertebral fracture = 18% (male) 33% (female)

Q. High Bone Turnover May be an Additive Risk Factor for Fracture to BMD [100]
   1. Low hip BMD and high markers increase fracture risk 4.1 to 4.8 fold
   2. Low hip BMD alone increases risk 2.7 fold
   3. High markers alone increases risk 1.9-2.2 fold

R. Some Clinical Factors Increase Fracture Risk Regardless of BMD in Men and Women
   1. Some risk factors are independent of BMD
   2. Non-independent: Obesity (BMI of 30 versus 25) decreases the risk of fracture (risk 0.8) but is not an independent risk factor if BMD is considered (subsumed by the BMD)
   3. Independent: parental history of hip fracture increases fracture risk by about 2 fold and remains at 2 fold when BMD is considered. Other risk factors independent of BMD include low body weight, prior fracture, current smoking, ever use of glucocorticoids, rheumatoid arthritis, and over 2 units of alcohol daily.

S. Assessment of Fracture Risk [101]
   1. Age
   2. BMD
   3. Clinical risk factors
      • Consider those with significant contribution to fracture risk over and above that provided by BMD
         - Previous fracture
         - BMI
         - Family history of fracture
         - Use of glucocorticoids
         - Smoking and alcohol
         - Markers of bone turnover

T. The Greater the Number of Clinical Risk Factors the Higher the Fracture Risk [102]
   1. Adding in more risk factors increases the risk of fracture
U. Combining Risk Factors Improves Osteoporotic Fracture Prediction [103]
   1. Combining risk factors increases the ability to predict fracture

WHO Assessment of Absolute Fracture Risk - FRAX® [82]

V. Criteria Required for Risk Factors in the FRAX® Model [104]
   1. Validated in multiple populations
   2. Easily accessible by primary care practitioners
   3. Be intuitive, rather than counterintuitive, to medical care
   4. Contribute to risk that is amenable to the therapeutic intervention proposed

W. Cohorts Studied to Generate the WHO Fracture Risk Assessment Tool [104]
   1. Twelve studies world-wide
      • EVOS/EPOS, Hiroshima, CaMoS, Rochester, Sheffield, Rotterdam, Gothenberg
        I, Gothenberg II, Dubbo/DOES, EPIDOS, Kuopio, OFELY
   2. N = 59,232; 74% female
   3. Person years = 249,898
   4. Osteoporotic fractures = 3,495
   5. Hip fractures = 957
   6. Validated in 11 cohorts; over 1 million person years

X. FRAX® Risk Factors Estimate 10-year Risk of Fracture [105]
   1. Age (40-90), sex and clinical risk factors
   2. BMI
   3. Prior fragility fracture
   4. Parental history of hip fracture
   5. Current tobacco smoking
   6. Ever long-term use of glucocorticoids
   7. Rheumatoid arthritis or other secondary causes
   8. Alcohol intake 3 or more units daily

Y. FRAX®: The WHO Fracture Risk Assessment Tool [82]
   1. Fracture risk varies in different countries
   2. Hip fracture risk highest Denmark, Sweden, Austria, Norway, Switzerland…
   3. Hip fracture risk mid-range South Korea, Portugal, Japan, USA, Australia, Spain, Chile…
   4. Hip fracture risk lowest in China, India, Ecuador, Tunisia, South Africa…

Z. Benefits of FRAX®
   1. Quantitative assessment of fracture risk rather than qualitative
   2. Fracture probability provides greater clinical utility than relative risk
   3. Application beyond postmenopausal Caucasian women
   4. Applicable to many countries around the world
   5. Can be used with cost-utility analysis to determine cost-effective intervention thresholds

AA. Limitations of FRAX®
   1. Risk factors not considered include falling, rate of bone loss, bone turnover, medications
      other than glucocorticoids, family history of fractures other than parental hip fracture
   2. Limited to certain countries and ethnicities
   3. Secondary osteoporosis is a “dummy” risk factor that does nothing if BMD is provided
   4. BMD input is for hip only
   5. “Dose effect” not considered with “yes” or “no” input for risk factors, e.g., prior fracture
      (number, site, severity), smoking, glucocorticoids, alcohol, RA
   6. Range of uncertainty with fracture risk not clear
7. Applies only to untreated patients
8. Limited to ages 40-90 years
9. Does not apply to premenopausal women
10. Some of these limitations are being addressed as FRAX evolves

BB. Read the FRAX FAQ Section For Additional Information
1. Know the FRAX version you are using and review the frequently asked questions section
2. Note the FRAX version you are using in your reporting

CC. Official Positions on FRAX®
1. ISCD/IOF collaboration (Nov 2010): reviewed evidence for potential modification of current FRAX calculations
2. Evaluated 3 areas:
   • Clinical
   • BMD
   • International
3. 28 statements - Published in Osteoporosis International and the Journal of Clinical Densitometry

DD. Key Clinical Statements
1. The following parameters are associated with increased fracture risk but there is not sufficient evidence to quantify the increased risk
   • Number and type of fracture
   • Severity of vertebral fracture
   • Glucocorticoid dose and duration
   • Frequent falls
   • Impaired functional status in patients with rheumatoid arthritis
   • Dose and duration of tobacco smoking
2. Evidence that bone-turn-over markers predict fracture risk independent of BMD is inconclusive
3. Appropriate replacement doses of glucocorticoids in adrenal insufficiency should not be considered in FRAX calculations

EE. Key BMD Statements
1. Only BMD or T-score at the femoral neck by DXA can be used in FRAX
2. FRAX may underestimate or overestimate major fracture risk when lumbar spine T-score is much lower or higher than femoral neck T-score
3. FRAX with BMD predicts fracture risk better than clinical risk factors or BMD alone
4. It is inappropriate to use FRAX to monitor treatment response

FF. Key International Statements
1. Construction of a country-specific FRAX model requires hip fracture incidence data that are of high quality
2. For countries not included in the current FRAX model, recommendations were made for estimation of fracture risk by using a surrogate country and adjusting for country-specific mortality rates

GG. Multiple Fracture Calculators Exist
1. www.shef.ac.uk/FRAX
3. www.qfracture.org
HH. Estimated Fracture Risk is Being Used to Set Country-Specific Cost-Effective Intervention Thresholds [104]

1. This depends on:
   - Efficacy and cost of therapy
   - Wealth of the nation (GDP/capita)
   - Willingness to pay (health care expenses as % of GDP and health care priorities)

2. For example, the USA spends a greater proportion of its GDP on healthcare than the UK

II. Fracture Risk Estimation is Being Used to Make Intervention Recommendations (NOGG Guidelines)

1. Risk factors - Used in UK (and may be applied to other European countries) for decision making on therapy and when to add a bone density study based on 10 year fracture probability of a major fracture

JJ. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada are different from what is used in the US [106]

1. Low risk (10 year fracture risk <10%) – unlikely to benefit from pharmacotherapy
2. Moderate risk (10 year fracture risk 10-20%) – VFA may help in decision making
3. High risk (10 year fracture risk over 20%) or prior fragility fracture at spine or hip or more than one fragility fracture

KK. Using US-adapted Data, Cost-effective Treatment Thresholds are Suggested in the NOF Clinician’s Guide [107]

LL. NOF Treatment Guidelines: 2013 [107]

1. Postmenopausal women and men age 50 and older presenting with the following should be considered for treatment
   - A hip or vertebral fracture (clinically apparent or found on vertebral imaging)
   - T-score ≤ -2.5 at the femoral neck, total hip or lumbar.
   - Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or lumbar spine) and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on the US-adapted WHO algorithm

Based on these guidelines, the NOF and ISCD have developed a FRAX Implementation Guide to assist in the clinical application of FRAX

MM. The NOF/ISCD FRAX Implementation Guide [108]

1. DXA software provides a “default” FRAX output only when the patient meets NOF criteria for using FRAX to assist with treatment decision i.e.,
   - an untreated postmenopausal woman or a man age 50 or older
   - with low bone mass (T-score between -1.0 and -2.5)
   - with no prior hip or vertebral fracture (clinical or morphometric)
   - and an evaluable hip for DXA study

NN. The NOF/ISCD FRAX Implementation Guide [108]

1. Examples of “untreated” patients include:
   - No ET/HT or SERM for the past one year
   - No calcitomin for the past one year
   - No PTH for the past one year
   - No denosumab for the past one year
   - No bisphosphonate for the past two years (unless it is an oral taken for <2 months)
   - Note: calcium and vitamin D do NOT constitute “treatment” in this context
OO. The NOF/ISCD FRAX Implementation Guide
1. When FRAX results are reported, the software includes a disclaimer along the lines of “This 10-year fracture risk estimate was calculated using FRAX version [X] and a “yes” response for the following FRAX risk factors in this individual: maternal/paternal history of hip fracture, tobacco use, etc.”

PP. Caveats To NOF Guidelines [107]
1. “It is important to note that the recommendations developed in this Guide are intended to serve as a reference point for clinic decision-making with individual patients. They are not intended to be rigid standards, limits or rules. They can be tailored to individual cases.”
2. Clinical Judgment is important

QQ. Important Clinical Judgment Considerations Include Recognition That FRAX Does Not:
1. Consider ALL fragility fractures
   • “Major” fractures include only hip, spine, wrist and humerus
   • Major fractures constitute only 50% of osteoporosis related fractures [109]
2. Take falls into consideration
3. Allow inclusion of multiple fractures
4. Does not include other risk factors, e.g., Diabetes
5. If a number will be helpful, consider the Garvan calculator (garvan.org.au/promotions/bone-fracture-risk/calculator/)

RR. Garvan and FRAX May Yield Markedly Different 10-year Fracture Risk Estimates
1. Considering all fragility fractures and including falls and multiple fractures (as done in Garvan, but not in FRAX) may lead to a much different 10-year fracture risk estimation
2. Garvan may produce results MUCH higher than FRAX when considering falls and all fractures. The use of Garvan may lead to different patient treatment decisions.

SS. Use of Non-Central DXA Technologies
1. CANNOT diagnose osteoporosis
   • WHO diagnostic criteria applies only to femoral neck, total hip, spine and 1/3 radius
2. CAN predict fracture risk

TT. Fracture Assessment Using Non-central DXA Bone Mass Measurement Devices [88, 89](Official Position)
1. Can predict fragility fracture:
   • QUS: Hip, vertebral and global in postmenopausal women; hip and non-vertebral in older men
   • pDXA: Vertebral and global fracture risk in postmenopausal women. Its vertebral fracture predictive ability is weaker than DXA and QUS
   • QCT: Vertebral fractures in postmenopausal women
   • pQCT: Hip fractures in postmenopausal women
   • QUS combined with clinical risk factors can be used to identify a population at low fracture risk

UU. Assessment of Fracture Risk With Peripheral Devices (Official Position)[110]
1. Validated heel QUS devices predict fragility fracture in postmenopausal women (hip, vertebral and global fracture risk) and men over the age of 65 (hip and all non-vertebral fractures) independently of central DXA BMD
2. Measurement by validated pDXA devices can be used to assess vertebral and global fragility fracture risk in postmenopausal women; however, its vertebral fracture predictive...
ability is weaker than central DXA and heel QUS. There is lack of sufficient evidence to support this position for men.

**V. Assessment of Fracture Risk with QCT**[110] (Official Position)

1. Spinal trabecular BMD as measured by QCT has at least the same ability to predict vertebral fractures as AP spinal BMD measured by central DXA in postmenopausal women. There is lack of sufficient evidence to support this position for men.
2. There is lack of sufficient evidence to recommend spine QCT for hip fracture prediction in either women or men.

### Section VII  MONITORING TREATMENT OF OSTEOPOROSIS

**A. Learning Objectives**

1. Describe monitoring of osteoporosis
2. Use of DXA as a monitoring tool
3. State how to calculate precision error and least significant change
4. Discuss which skeletal site to measure, which densitometric method to use, and how often to test
5. Explain clinical relevance of changes in BMD
6. Monitoring using biochemical markers
   - Response to treatment
   - Relationship of biochemical markers with BMD increase and fracture reduction

**B. The Challenge to Monitoring Osteoporosis Therapy**

1. Goal of treatment = reduce fragility fracture occurrence
2. The fragility fracture incidence is low, thus absence of fracture during therapy does not necessarily mean treatment is effective
3. However, fracture occurrence on therapy does not necessarily indicate treatment failure
4. Thus use of surrogates such as BMD and biochemical markers to monitor treatment might be useful
5. Changes in an ideal surrogate marker during therapy should reflect changes in fracture risk

**C. Reasons to Measure Serial BMD[62, 111, 112]**

1. Untreated patients
   - Significant loss may be an indication for treatment and is associated with an increased fracture risk
2. Treated patients
   - To monitor the response to therapy
     - Increase or stable bone density is associated with fracture risk reduction
     - A loss of BMD is cause for concern
       - Consider further evaluation (adherence, secondary causes) for those who are losing BMD

**D. Approach to Monitoring**

1. Compare “apples with apples”
2. Compare the BMD, not the T-score
3. How much of a difference is real?
4. If there is a difference, what does it mean?

**E. Comparing “Apples With Apples”**

1. Look at the DXA images on the two comparison studies
2. The region of interest (ROI) must be the same
3. The measured area should be comparable
4. If the ROI appears the same but the area is different, look for improper positioning, incorrect scan analysis, and/or artifacts (fractures, degenerative changes, etc.)
5. When possible, use the compare feature of your software

F. Compare BMD Values, Not T-scores
   1. T-scores depend on normative database, which may change with software upgrades, and so should not be compared on serial studies
   2. Compare BMD (g/cm²) between two studies
   3. Software may calculate:
      • Change in BMD, percent change in BMD (from initial or previous), or annualized rate of change in BMD

G. How Much of a Difference in BMD is Real?
   1. Know the precision at your center
   2. Calculate least significant change (LSC)

H. Why is Precision Important?[111, 113]
   1. Expresses reproducibility or consistency of repeat measurements
   2. Precision error helps determine how much of a change in BMD is required to know that the difference is real
   3. Significant bone loss increases fracture risk regardless of the BMD

I. Precision Error (%CV): Manufacturer vs. Clinical
   1. ISCD Official Position: The minimum acceptable precision for an individual technologist is:
      • Lumbar spine: 1.9% (LSC = 5.3%)
      • Total hip: 1.8% (LSC = 5.0%)
      • Femoral neck: 2.5% (LSC = 6.9%)

J. Precision Assessment (Official Position)
   1. Each center should determine its precision error and LSC
      • The precision error supplied by the manufacturer should not be used
   2. For more than one technologist
      • Use average precision error from all technologists, if the precision error for each technologist is within a pre-established range of acceptable performance
   3. Each technologist should perform an in vivo precision assessment using patients representative of the clinic’s patient population
   4. Each technologist should do one complete precision assessment after basic scanning skills have been learned and after having performed approximately 100 patient scans
   5. A repeat precision assessment should be done if a new DXA system is installed
   6. A repeat precision assessment should be done if a technologist’s skill level has changed
   7. To perform a precision analysis:
      • Measure 15 patients 3 times, or 30 patients 2 times, repositioning the patients after each scan
      • Calculate precision as the root mean square standard deviation (RMS-SD) or RMS-%CV for the group
      • Calculate least significant change (LSC) for the group at 95% confidence interval
   8. Precision assessment should ideally be standard clinical practice
   9. Precision assessment is not research and may potentially benefit patients
   10. It should not require approval of an IRB
   11. Adherence to local radiologic safety regulations is necessary
   12. Performance of a precision assessment requires the consent of participating patients
K. **How To Calculate Precision** [114] (Official Position) See ISCD.org
   1. Scan
      • 15 patients 3 times
      • 30 patients 2 times
   2. Use patients representative of your typical patient population
   3. Reposition between each scan
   4. Calculate: mean BMD, SD and CV for each patient, then the RMS-SD and RMS-%CV for the group

L. **Calculate Root Mean Square Standard Deviation (RMS-SD) for the Group**
   1. Use EXCEL spreadsheet precision calculator at www.iscd.org
   \[
   RMS \ SD = \sqrt{\frac{\sum_{j=1}^{m} SD_j^2}{m}}
   \]

M. **Calculate Root Mean Square Standard Deviation (RMS-SD) for the Group**
   1. Calculate the SD for each patient
   2. Square SD for each patient
   3. Add them
   4. Divide by number of patients
   5. Take the square root

N. **How To Express Precision Error**
   1. RMS-SD
      • Absolute amount (g/cm²)
      • Absolute amount is recommended for central DXA
   2. RMS-%CV
      • Calculate like RMS-SD, only with %CV instead
      • % coefficient of variation (%CV)
      \[(SD \div \text{Mean}) \times 100\] for each patient

O. **Calculate RMS-%CV for the Group**
   1. Calculate the SD for each patient (as before)
   2. SD ÷ mean for each patient = CV
   3. Square CV for each patient
   4. Add them
   5. Divide by number of patients
   6. Take the square root

P. **Least Significant Change (LSC)**
   1. Precision error at your center
   2. Desired confidence level (95%)
   3. Perform precision study on patients representative of your typical patient population
      • This will help prevent over-calling of significant change
   4. \[\text{LSC} = (\text{precision error}) \times 2.77\] to have 95% confidence that the change is real

Q. **Example: Precision Error (RMS-SD) at One Center**
   1. PA spine
      • Precision error: \[0.010 \text{ g/cm}^2\]
   2. Total hip
- Precision error: 0.012 g/cm²
3. Femoral neck
  - Precision error: 0.022 g/cm²

R. Least Significant Change at Different Sites
1. PA spine
  - 2.77 × precision error
  - 2.77 × 0.010 g/cm² = 0.028 g/cm²
2. Total hip
  - 2.77 × precision error
  - 2.77 × 0.012 g/cm² = 0.033 g/cm²
3. Femoral neck
  - 2.77 × precision error
  - 2.77 × 0.022 g/cm² = 0.060 g/cm²

S. How Much of a Difference in BMD Is Real?
1. Know your facility’s precision in absolute terms (g/cm²)
2. Know your facility’s LSC in absolute terms (g/cm²)
3. Subtract patient’s current BMD from the one you are comparing with (baseline, most recent)
4. See if value meets or exceeds the facility’s LSC
5. If so, report change as significant

T. Serial BMD: Example 1
Baseline spine BMD 0.866 g/cm²
Repeat spine BMD 0.832 g/cm²
Difference 0.034 g/cm²
LSC 0.028 g/cm²
Exceeds or Equals LSC Yes

Change is significant
Note that % change is:
\[-(0.034/0.866) \times 100 = \text{loss of } 4\% \pm \text{LSC} = 4\% \pm 2.8\%\]

U. Serial BMD: Example 2
- 53-year-old woman who is 4 years post menopause
- On HT for 2 years
- BMD measurements performed on the same DXA instrument 18 months apart

<table>
<thead>
<tr>
<th>Date</th>
<th>Lumbar spine</th>
<th>Total hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/22/2007</td>
<td>0.979</td>
<td>0.739</td>
</tr>
<tr>
<td>05/28/2010</td>
<td>0.992</td>
<td>0.728</td>
</tr>
</tbody>
</table>

Actual difference +0.013 -0.011
LSC 0.028NS 0.020NS

V. Grams/cm² or Percent?
1. The absolute value (g/cm²) should be used to express precision
2. This is less affected by BMD than an approach using percent would be
3. EXAMPLE: For a change of .030 g/cm²
   - If BMD = 1.200 g/cm², % change = 2.5% NS
• If BMD = 0.800 g/cm², % change = 3.7%

W. In Summary
   1. Use grams/cm² to determine whether a significant BMD change has occurred
   2. You may wish to report an approximate percent change as this may be more understandable to patients and referring physicians

X. Response to Treatment May Vary According to Skeletal Site[115]
   1. Spine most responsive to therapy
      • Increase in spine BMD >> femoral neck BMD
      • Example: in PEPI trial with estrogen, 4-6% increase in spine BMD over 3 years vs. 1-2% increase in femoral neck. Same differential seen with other meds
      • Note: spine is predominantly trabecular bone (66%) which responds better and faster than the predominant cortical bone seen in the femoral neck (25%)
   2. Total hip usually slower to respond
   3. Forearm does not respond well to therapy

Y. Patients should be encouraged to return to the same center for follow-up scans (Official Position)
   1. Serial results from different machines cannot be compared unless valid cross-calibration has been performed

Z. Selection of Skeletal Site and Region of Interest for Monitoring Changes
   1. PA spine preferred
      • Best precision
      • Most responsive to therapy
      • Use L1-L4 value if possible
   2. If PA spine cannot be used
      • Total hip preferred (better precision)
      • Femoral neck
      • Not Ward’s
      • No ISCD position on dual femur
   3. Forearm (33% or 1/3 radius site)
      • Does not respond well to therapy
      • Useful for hyperparathyroidism
   4. Total body
      • Good precision but does not respond well to therapy
      • Useful in children, when area may change more rapidly than BMC (during growth)

AA. Which Method to Use?
   1. Peripheral densitometry
      • Some peripheral techniques have excellent precision
      • Sites do not increase consistently with treatment
      • Not recommended to monitor
   2. Central DXA is preferred for monitoring

BB. ISCD Position: How Often to Test? (Official Position)
   Note Regulatory Agency Rules/Regulations
   1. Follow-up BMD testing should be done when the expected change in BMD equals or exceeds the least significant change (LSC)
   2. Intervals between BMD testing should be determined according to each patient’s clinical status
• Typically, one year after initiation or change of therapy is appropriate, with longer intervals once therapeutic effect is established
3. In conditions associated with rapid bone loss, such as glucocorticoid therapy, testing more frequently is appropriate

CC. If There Is a Difference in BMD at Follow-up, What Does it Mean?
1. What is a satisfactory response to treatment?
   • Significant gain in BMD?
   • Stable BMD?
2. What is cause for concern?
   • Failure to gain?
   • Significant loss?

DD. Fracture Risk Reduction With Treatment Exceeds that Expected from BMD Gain Alone

EE. Fracture Reduction is Greater Than Would be Predicted by BMD Increase
1. Change in BMD explains less than half of the observed reduction in fractures. This is seen with all drug therapies

FF. Potential Mechanisms for Greater Reduction in Fracture Risk Than Increase in BMD Would Predict
1. Decrease in bone turnover
2. Reduction in stress risers
3. Increased bone mineralization

GG. Greater Increase In BMD Does Not Confer Greater Fracture Reduction[116]
1. Stable or increased bone density are protective against fracture as compared to significant losses

HH. Stable or Increasing BMD is Associated With a Reduction in Fracture Risk
1. Significant increases in BMD are encouraging
2. Stable BMD is OK
3. Significant decreases in BMD are worrisome

II. Monitoring Therapy With BMD: Summary
1. Be sure what you are measuring today is comparable to the previous site
2. Know your precision and LSC
3. Monitor the central skeleton with DXA
   • PA spine is preferred
   • Total hip is alternative site
4. Stable or increasing BMD is acceptable
5. If there is loss of BMD that exceeds LSC (95% confidence)
   • Check compliance with medication
   • Check calcium and vitamin D intake
   • Look for underlying disease or condition
6. Follow-up studies should be done in accord with medical necessity, expected response, and in consideration of regulatory requirements. An initial one year follow-up for patients with osteoporosis on therapy to assess response is reasonable

JJ. In Principle, Markers Change Sooner than BMD but Have more Variability[117]
1. Bone Mineral Density:
   • BMD changes slowly (= static measurement of skeletal status)
   • Low within-person variability
   • Measurement = precise
• BMD measurement used to diagnose OP (WHO definition)
• Small changes in response to antiresorptive therapy

2. Markers
• Dynamic measure of skeletal status
• Larger changes in response to therapy (within months)
• Widely available
• ± great variability

KK. Early Changes in Markers of Bone Turnover are Associated with Long-term Changes in BMD[118]
  1. Decreased bone turnover markers associated with increased BMD

LL. Greater Reduction in BSAP at 1 Year was Associated with Greater Cumulative Fracture Risk Reduction at Years 2.5 - 4.5 in FIT[119]

MM. Teriparatide Increases Bone Turnover Markers[120]

NN. Early Changes in Bone Markers to Predict BMD Response to Parathyroid Hormone Therapy[121]
  1. Increased markers associated with increased BMD changes in anabolic therapy

Section VIII PRINCIPLES OF DXA SCAN REPORTING

A. Learning Objectives
  1. Recognize the standard nomenclature for use in bone densitometry reports
  2. Identify the ISCD basic recommendations for reporting densitometry results
  3. Identify the ISCD optional recommendations for reporting densitometry results
  4. Recognize errors in DXA reporting
  5. Apply the ISCD recommendations using case examples
  6. Clinical History: Screening

B. DXA Nomenclature [122] (Official Position)
  1. Terminology
    • DXA: not DEXA
    • T-score: not T score, t-score, or t score
    • Z-score: not Z score, z-score, or z score
    • VFA – Vertebral Fracture Assessment
  2. Decimal Digits
    • BMD – 3 decimal digits (example 0.927 g/cm²)
    • T-score, Z-score – 1 decimal digit (example -2.1)
    • BMD, area – 2 decimal digits (example 31.76 g)
    • % reference database – integer (example 82%)

C. Baseline DXA Report [122] (Official Position)
  1. Minimum Requirements — Demographics
    • Demographics
      - Name, medical record number, date of birth
      - Race (Caucasian database for T-scores)
      - Sex
      - Height (stadiometer)
      - Weight
        • Z-scores weight adjusted on some machines
2. Minimum Requirements — Other
   • Indications for the test
   • Additional information
     - Prior fractures, family history, glucocorticoids, smoking, rheumatoid arthritis, alcohol
     - Manufacturer and model of instrument used
       • To help determine comparability in absence of a printout

3. Technique/Limitations
   • Technical quality and limitations of the study
     - Is a specific site or ROI invalid or not included?
     - Artifacts: prior back surgery, hip replacement, arthritis, prior known fracture should be noted
     - Poor hip rotation (may be limited by arthritis), scoliosis, prior surgery may limit interpretation

4. Minimum Requirements — Results
   • Sites
     - PA L1-L4 spine and total hip/femoral neck
     - Scan forearm if a site is invalid, cannot be imaged, or if there is a history of hyperparathyroidism
   • Results
     - BMD in g/cm² for each site
     - The T-score and/or Z-score where appropriate
     • Diagnosis based on lowest T-score of spine, total hip or femoral neck; if hip or spine not interpretable, use the 33% site of the forearm
       - Report only one diagnosis
         • Don’t say: "osteoporosis at spine, osteopenia at hip"
     • Use T-scores for diagnosis in postmenopausal women and men age 50+
       - Use Z–scores in children, premenopausal women, and men younger than age 50

D. Baseline DXA Report – Fracture Risk [107]
   1. The ISCD has endorsed the NOF Clinician’s Guide including use of the WHO fracture probability approach (FRAX®)

E. Items That Should Not be Included in a DXA Report [122] (Official Position)
   1. A statement that there is bone loss; unless a comparison is available that shows significant loss
   2. Mention of “mild,” “moderate,” or “marked” osteopenia, or osteoporosis
      • Note: “Severe” or “established” osteoporosis is acceptable to describe postmenopausal women with T-scores at or below -2.5 with a history of fragility fracture
   3. Separate diagnoses for different regions of interest (e.g., osteopenia at the hip and osteoporosis at the spine)
   4. Expressions such as, "She has the bones of an 80-year-old," if the patient is not 80-years-old
   5. Results from skeletal sites that are not technically valid
   6. The change in BMD, if it is not a significant change based on the precision error and LSC

F. Baseline DXA Report – Secondary Causes [122]
   1. A general statement that a medical evaluation for secondary causes of low BMD may be appropriate
   2. No specific Z-score threshold for this statement
   3. Specific recommendations for the evaluation of secondary osteoporosis is optional
G. Follow-Up DXA Report – Follow-up [122] (Official Position)
   1. Statement regarding which previous baseline study and ROI is being used for comparison
   2. Statement about the LSC at your facility and the statistical significance of the comparison
   3. Report significant change, if any, between the current and previous study or studies in grams/cm² and percentage
   4. Recommendations for the necessity and timing of the next BMD study

H. DXA Report: Optional Items [122] (Official Position)
   1. Recommendation for further non-BMD testing, such as x-ray, magnetic resonance imaging, computed tomography, etc
   2. Addition of the percentage compared to a reference population
   3. Recommendations for pharmacological and nonpharmacological interventions
   4. Specific recommendations for evaluation of secondary osteoporosis

I. Components of DXA Report: Initial
   1. Demographics
   2. Requesting provider
   3. Indications for the test
   4. Manufacturer and model of instrument used
   5. Technical quality and limitations of the study, stating why a specific site or ROI is invalid or not included
   6. BMD in g/cm² for each site
   7. The skeletal sites, ROI, and, if appropriate, the side, that were scanned
   8. The T-score and/or Z-score where appropriate
   9. WHO criteria for diagnosis: postmenopausal females and men age 50+
   10. Fracture risk factors
   11. A statement about fracture risk (ISCD endorses FRAX use when appropriate)
   12. A general statement that a medical evaluation for secondary causes of low BMD may be appropriate
   13. Recommendations for the necessity and timing of the next BMD study

J. Components of DXA Report: Follow-up
   1. Statement regarding which previous or baseline study and ROI is being used for comparison
   2. Statement about the LSC at your facility and the statistical significance of the comparison
   3. Report significant change, if any, between the current and previous study or studies in g/cm² and percentage
   4. Comments on any outside study including manufacturer and model on which previous studies were performed and the appropriateness of the comparison
   5. Recommendations for the necessity and timing of the next BMD study

K. Template for reporting – see attached 8.1

Section IX CLINICAL EVALUATION OF BONE HEALTH

A. Learning Objectives
   1. Describe relevant history and physical findings to identify patients at risk for fracture
   2. Recognize secondary causes of osteoporosis and when laboratory testing is appropriate
   3. List the clinical indications and contraindications for bone densitometry
   4. Describe potential clinical uses for measurement of bone densitometry
5. Describe the radiologic findings in patients with osteoporosis including the utility of vertebral fracture assessment

B. The Diagnosis of Osteoporosis Can be Made By:
   1. Fragility fracture
      • Often defined as a fracture occurring with a fall from standing height or less
   2. BMD measurement

C. Routine Procedures Proposed in the Investigation of Osteoporosis [101]
   1. Routine
      • History and physical examination
      • Blood cell count, sedimentation rate, serum calcium, albumin, creatinine, phosphate, alkaline phosphatase and liver transaminases
      • Lateral radiograph of lumbar and thoracic spine
      • Bone densitometry (DXA)
   2. Other procedures
      • X-ray – vertebral fracture assessment
      • Markers of bone turnover, when available

D. Medical History
   1. Symptoms
      • Osteoporosis symptoms: none
      • Fracture symptoms: variable
         - Pain and deformity (hip, spine, forearm, etc.)
         - Frequently no symptoms (vertebral fractures)
   2. Risk factors
      • Risk factors for osteoporosis
      • Risk factors for fracture

E. Clinical Risk Factors for Low Bone Mass [123, 124]
   1. Loss of height
   2. Low body weight
   3. Advanced age
   4. Late age at menarche
   5. Menopausal
   6. Time since menopause
   7. Smoking
   8. Dietary calcium
   9. Alcohol intake
   10. Medications
   11. Inflammatory diseases
   12. Prior fragility fracture

F. Risk Factors for Osteoporotic Fracture Are Not The Same as Risk Factors for Low BMD[93, 125-127]
   1. Low BMD
   2. Advancing age
   3. Prior fragility fracture
   4. Family history of osteoporosis or fragility fracture in a first degree relative (genetics)
   5. Current smoker
   6. Low body weight
   7. Falls
   8. Sarcopenia
   9. Dementia
G. Clinical Risk Factors Are Poor Predictors of Low BMD[128]
1. Review of 9 studies
2. Risk factors accounted for 15-43% of the variability in spine BMD
3. BMD cannot be predicted from clinical risk factors
4. Age and weight accounted for the greatest proportion of the observed variance
5. Conclusion: Clinical risk factors are not a substitute for BMD testing

H. Physical Examination
1. Findings suggesting increased fracture risk:
   • Impaired ambulation
   • Muscle weakness
   • Impaired balance
   • Reduced vision
   • Orthostatic hypotension
2. Signs of prior fracture:
   • Loss of height
   • Kyphosis
   • Chest deformity
   • Protuberant abdomen
   • Rib-pelvis overlap

I. Secondary Causes of Osteoporosis[129]
1. Endocrinopathies
   • Hypercalciuria with or without renal stones
   • Hypogonadism (incl. hyperprolactinemia)
   • Hyperparathyroidism
   • Hyperthyroidism
   • Cushing’s syndrome
   • Acromegaly especially when associated with hypogonadism
2. Drugs
   • Excess glucocorticoids
   • Excess thyroid hormones
   • Anticoagulants (heparin)
   • GnRH agonists
   • Anticonvulsants
   • Aromatase inhibitors
   • Thiazolidinediones
   • Opiates
   • Cyclosporine
   • Rifampicin
   • Exchange resins
   • Methotrexate
   • Alcohol
   • Loop diuretics
3. GI-Tract Disorders
   • Gastrectomy
   • Inflammatory bowel disease
   • Coeliac disease
   • Intestinal bypass surgery
   • Primary biliary cirrhosis
   • Pancreatic insufficiency
4. Bone Marrow based Disorders
   • Multiple myeloma
• Hemolytic anemia, hemoglobinopathies
• Myelo- and lympho-proliferative disorders
• Skeletal metastases (diffuse or localized)
• Gaucher’s disease
• Mastocytosis
5. Inflammatory disorders
• RA
• SLE
• Ankylosing spondylitis
6. Other
• Immobilization
• AIDS/HIV
• Organ transplantation
• COPD
• Anorexia
• Malignancy

J. Vitamin D Insufficiency and Deficiency[130]
1. Lack of sun exposure and dietary vitamin D
2. Age-related decline in cutaneous production
3. Gastrointestinal disease
4. Liver disease
5. Renal disease
6. Drugs (phenytoin, phenobarbital)

K. How Often Is Osteoporosis Associated With Secondary Disorders?[71, 131]
1. In 664 peri/postmenopausal women, T-score < –2.5
2. 53% (355) had secondary osteoporosis by history
3. 47% (309) had no history of secondary etiologies
   • 173/309 had comprehensive lab testing
     - 32% (55/173) previously unrecognized factors
     - 44% (76/173) if low vitamin D is < 20 ng/ml*
4. Conclusion: Previously undiagnosed disorders are common

L. Considerations for Secondary Osteoporosis Evaluation[107] (From NOF Guide)
1. CBC
2. Chemistries (Ca, Creat, PO4, Mg)
3. LFTs
4. TSH
5. 25(OH)D
6. PTH
7. Total testosterone and gonadotropins in younger men
8. 24 hour urine calcium
9. Consider in selected patients: SPEP, serum free light chains, UPEP, tissue transglutaminase, ferritin, homocysteine, tryptase, urinary free cortisol, urinary histamine

M. Osteoporosis – Laboratory Investigation[132]
1. No consensus
2. Considerations: CBC, chemistries (especially Ca, creatinine, phosphate), liver enzymes, TSH, 25-OH vitamin D, PTH, testosterone (FSH, LH, prolactin) in younger men, 24 hour urine calcium (sodium, creatinine), bone turnover markers
3. Other considerations: SPEP, IEF, celiac testing (tissue transglutaminase), urine free cortisol, ferritin, tryptase, homocysteine, urine histamine
N. Patients in Whom More Extensive Lab Evaluation May be Appropriate
   1. Men with osteoporosis
   2. Unexplained fracture
   3. Unexpected low BMD
   4. Poor response to therapy
   5. Clinical suspicion of secondary causes in any patient with osteoporosis

O. Bone Biopsy
   1. Rarely used in clinical practice
   2. Consider in special situations
   3. Renal osteodystrophy
   4. Unexplained osteoporosis in a young person
   5. Extremely low bone mass
   6. Fragility fractures and normal BMD
   7. Non-responders to osteoporosis therapy
   8. Typical method: non-decalcified double tetracycline labeled trans-iliac biopsy

P. Indications for BMD Testing
   1. USPSTF: women 65 or over, menopausal with risk factors and sufficiently high fracture risk by FRAX
   2. NOF: women 65 or over, menopausal over 50 with risk factors, men over 50 with risk factors, men at or over 70, and for monitoring
   3. ISCD: women over 65, postmenopausal with risk factors, men with risk factors, men at or over 70, for monitoring
   4. AACE: women 65 or over, postmenopausal with risk factors, monitoring

Q. Covered Services (CMS)[108, 133]
   1. Estrogen deficient women at clinical risk for osteoporosis
   2. Individuals with vertebral abnormalities on x-rays
   3. Individuals receiving long-term glucocorticoid therapy
   4. Individuals with primary hyperparathyroidism
   5. Individuals being monitored on osteoporosis therapy
   6. Check with your regional CMS carrier to determine the appropriate ICD-9 codes for use in your area!

   1. Primary bone diseases or potential secondary bone diseases
      • e.g., due to chronic inflammatory diseases, endocrine disturbances, history of childhood cancer, or prior transplantation (non-renal)
   2. Thalassemia major
   3. Chronic immobilization
      • e.g., cerebral palsy
   4. Spine and TBLH BMC and areal BMD are preferred for measurement in children
   5. Caution: In children, adolescents, premenopausal women and healthy men under age 50, the diagnosis of osteoporosis should not be made on the basis of densitometric criteria alone.[61]

S. ISCD Assessment in Children and Adolescents with Disease that may affect the skeleton (2013 ISCD Official Position) [134]
   1. DXA measurement is part of a comprehensive skeletal assessment patients with increased risk of fracture
   2. In patients with primary bone disease, or at risk for a secondary bone disease, a DXA should be performed when the patient may benefit from interventions to decrease their
elevated risk of a clinically significant fracture, and the DXA results will influence that management
3. DXA should not be performed if safe and appropriate position of the child cannot be assured.

T. Relative Contraindications for Central DXA
1. Pregnancy
2. Recent contrast study (generally less than 72 hours)
   • Spine measurement only
3. Recent nuclear medicine scan
4. Extensive orthopedic instrumentation
5. Body weight greater than table limit
   • Solution: Measure the forearm

U. Bone Turnover Markers[135]
1. Products of bone remodeling
2. Noninvasive, easily repeated
3. Independent risk factors for fracture
4. Cannot diagnose osteoporosis
5. May be useful in assessing bone dynamics, monitoring response to therapy and promoting adherence
6. Problems: high biological and analytical variability, LSC unclear, reference data not well defined, best marker(s) for testing unclear

V. Bone Turnover Markers
1. Markers of bone resorption
   • N-telopeptide (NTx)
   • C-telopeptide (CTx)
   • Deoxypyridinoline (free, total)
2. Markers of bone formation
   • Bone specific alkaline phosphatase (BSAP)
   • Osteocalcin
   • Procollagen type 1 N-terminal propeptide (P1NP)

W. Biochemical Markers of Bone Turnover
1. Influenced by:
   • Pre-analytical conditions
   • Sample storage
   • Diurnal variation
   • Food intake
   • Within individual variation
   • Assay variation and performance
   • Renal function

X. Increased Bone Resorption Independently Predicts Fracture Risk in Postmenopausal Women
1. EPIDOS: RR 1.9-2.2
2. OFELY: RR 1.9-2.3
3. HOS: RR 1.5
4. Rotterdam: RR 1.9
5. Malmo: RR 2.3

Y. Utility of Conventional Radiography
1. Diagnosis and follow-up of fractures
2. Identification of patients for densitometry
3. Aid in differential diagnosis
   • Multiple myeloma
   • Metastatic disease
   • Osteomalacia

Z. Vertebral Fractures
1. Most common fracture type
2. Often silent
3. Can be progressive
4. Associated with
   • Deformity, height loss, back pain
   • Impaired breathing
   • Increased morbidity and mortality
5. Predict future spine and hip fractures

AA. Not all Fractures are Due to Osteoporosis
1. Consider bone scan or MRI if:
   • Fracture is equivocal
   • Fracture is remote
   • Kyphoplasty/vertebroplasty being considered
2. Consider MRI or biopsy if:
   • Concern of metastatic carcinoma
3. Consider MRI if:
   • Concern of lateral or posterior displacement

BB. Differential Diagnosis of Spinal Fractures Includes:
1. Metastasis
2. Multiple Myeloma
3. Osteoporotic Fracture

CC. Upper T-spine visualization with VFA is inferior to x-ray but isolated fractures above T7 are uncommon: Rotterdam Study of 3469 patients [136]
1. Incident vertebral fracture distribution over 6.3 years in men and women
2. Most fractures at L1 and T12
3. Fractures also often occur L4 through T7

DD. Vertebral Fractures Are Often Unrecognized[24]
1. Only about 1/3 of vertebral fractures found on radiographs come to medical attention and only 10% necessitate admission to the hospital*
2. Radiographs are usually not performed in the course of evaluation of asymptomatic patients with osteoporosis

EE. Clinical vs. Radiographic Fractures[137]
1. Example: MORE study in placebo group
   • Year 0-2: 4% new clinical fractures
   • X-ray at year 2: 8% new radiographic fractures
   • 50% of fractures NOT detected clinically

FF. Even on X-ray, Vertebral Fractures Often Not Diagnosed[138]
1. Studies have shown only about 50% of vertebral fractures present on CXR studies are noted in the report, only 23% noted in summary and only about 7% of patients placed on therapy.
GG. Though Often Unrecognized, Identification of Vertebral Fractures is Important[126]
   1. A vertebral fracture (clinical or morphometric) is an indication for pharmacologic
treatment

HH. The Greater the Number of Prevalent Vertebral Fractures, the Greater the Risk of Future
   Fractures[139]
   1. Number of vertebral deformities at baseline correlates with increased relative risk of
   future vertebral fractures, non-vertebral fractures, and hip fractures.

II. Conclusion: Vertebral Fractures
   1. Important to detect because they:
      • Predict future fractures
      • Are associated with increased mortality and morbidity (reduced quality of life)
   2. Often missed in the course of routine medical care
   3. Can be prevented with appropriate therapy
   4. Traditionally require X-ray for diagnosis
   5. X-ray is usually not obtained
   6. Possible solution: VFA can diagnose fracture at the time of DXA BMD measurement

JJ. What Is VFA?
   1. Vertebral fracture assessment – diagnosing vertebral fractures using a DXA machine
   2. A visual technique – different than the quantitative methodology of DXA for
measurement of BMD
   3. Separate report required

KK. Comparison of spine x-ray and VFA
   1. X-ray spine: effective radiation dose 1800-2000 uSv, requires separate visit, higher cost,
   higher resolution, superior imaging above T7, obliquity common in LS
   2. VFA 30-50 uSv, point of service, lower cost, lower resolution, inferior visualization above
   T7 compared to x-ray, less parallax effect

LL. Appropriate Terminology = VFA
   Manufacturer Terminology Differs (DVA, LVA, IVA, RVA)
   1. 2007 ISCD Official Position:
      • Vertebral Fracture Assessment (VFA) is the correct term to denote densitometric
spine imaging performed for the purpose of detecting vertebral fractures

MM. VFA: Imaging of the Spine for Detection of Vertebral Fractures on DXA Machine
   1. GE-Lunar terminology DVA or LVA
   2. Hologic terminology IVA or RVA

NN. Basic Methods to Diagnose Vertebral Fractures (X-ray or VFA)
   1. Qualitative visual
   2. Quantitative morphometric measurement of vertebral heights
   3. Semiquantitative visual

OO. Qualitative Visual Assessment: The Interpreter (eg: radiologist) Decides if a Vertebra is
   Normal or Fractured
   1. Requires trained interpreter
   2. No method to describe type and severity

PP. Quantitative Morphometry (QM): placing 6 points to delineate the vertebral body
   1. Advantages
• More quantitative (still subjective)
• May be automated

2. Problems
• May over-diagnose abnormalities that are not fracture
• May under-diagnose mild end-plate deformities

3. Need visual assessment to confirm fracture

QQ. Semiquantitative (SQ) Analysis of Genant Visual Grading of Fracture Type and Severity[140]
   1. Combines the advantages of a quantitative method with visual assessment
   2. Grades: normal (grade 0), mild (grade 1, 20-25%), moderate (grade 2, 25-40%), severe (grade 3, 40% or more)
   3. Type: wedge, biconcave, crush

RR. ISCD Indications for Spinal Imaging[108, 126] (Official Position)
   1. Lateral spine imaging with standard radiography or densitometric VFA is indicated when T-score is < -1.0 and one or more of the following is present:
      • Women age ≥ 70 years or men ≥ age 80 years
      • Historical height loss > 4 cm (>1.5 inches)
      • Self-reported but undocumented prior vertebral fracture
      • Glucocorticoid therapy equivalent to ≥ 5 mg of prednisone or equivalent per day for ≥ 3 months

SS. NOF recommendations 2013 Clinician’s Guide[126]
   1. New 2013 recommendations regarding spine imaging are similar, but not identical to ISCD recommendations
   2. Recommend BMD testing and vertebral imaging to those who have had a fracture, to determine degree of disease severity
   3. Measure height annually, preferably with a wall mounted stadiometer
   4. BMD testing should be performed at DXA facilities using accepted quality assurance measures.
References


91. Hans, D. and M.A. Krieg. EPISEM Study. in SSR. 2009. Lausanne, CH.


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Figures and Supplementary Materials

Figure 1.1: Bone structure normal and osteoporosis
Courtesy of David Dempster, PhD

Normal

Osteoporosis
Figure 2.1 – Vertebral anatomy

L5

L1-L3 often “U”

L4 often X or H-shaped
8.1 Reporting template example

US ADULT DXA REPORT TEMPLATE

Dual-Energy X-ray Absorptiometry (DXA)
A DXA scan was performed on (date)____ using a ____ (make/model) __________ densitometer.

Impression:
Based on BMD diagnosis is consistent with ______________(based on WHO criteria)

Indication(s):

Technical Quality:

Clinical History:

Results:
Lumbar Spine
The BMD measured in the (L1-L4, L1-L3- specify levels)_________ region is __________ g/cm².
T-score (and/or Z-score as appropriate)=_______________

Femoral Neck
The BMD measured at the left/right femoral neck is __________ g/cm².
T-score (and/or Z-score as appropriate) =_______________

Total Hip
The BMD measured at the left/right total proximal femur is __________ g/cm².
T-score (and/or Z-score as appropriate) =_______________

1/3 Radius
The BMD measured at the left/right one-third radius is __________ g/cm².
T-score (and/or Z-score as appropriate) =_______________

Interval Change:(if a follow-up study)
Today’s examination is compared to the technically similar prior study of the (site)_________.
In the interim, there has been no change OR a significant increase/decrease__________, of
____ g/cm²,______% at the ______(skeletal site.)

At this facility, the least significant change in BMD with 95% confidence is
________g/cm² at the L1-4 spine, and ________g/cm² at the total hip, ________g/cm² and ________g/cm² at the femoral neck and ________g/cm² at the 1/3 radius.

Fracture Risk: The estimated 10-year risk for a hip fracture is _____% and for a major
osteoporotic fracture is ____%. This fracture risk estimate was calculated using FRAX version
____ and ________ as additional clinical risk factors for fracture.(if FRAX is applicable)

Secondary causes of bone loss should be evaluated if clinically indicated since the etiology of
low BMD cannot be determined by BMD measurement alone.

Treatment Recommendations and Additional Comments:

Follow-up DXA:
Consider repeating this study in ____ years or as clinically indicated to assess bone density
change or response to treatment. Note that Medicare will generally not allow a repeat study
sooner than 2 years unless medically necessary.
Appendix: (Examples of comment statements to be inserted as appropriate - not an exhaustive list)

Note 1:
WHO classification: The T-score compares the patient's BMD to the average BMD of a young adult. The criteria below are from the World Health Organization:
Normal: T-score -1.0 or above
Osteopenia/low bone mass: T-score -1.1 to < -2.5
Osteoporosis: T-score -2.5 or lower
Severe or established osteoporosis: T-score -2.5 or lower plus fragility fracture

Note 2:
According to the International Society for Clinical Densitometry's 2013 consensus conference:
In women prior to menopause and men less than age 50:
- Z-scores, not T-scores are preferred. This is particularly important in children.
- A Z-score of -2.0 or lower is defined as 'below the expected range for age' and a Z-score above -2.0 is 'within the expected range for age.'
- The WHO diagnostic criteria may be applied in women in the menopausal transition.
- Osteoporosis cannot be diagnosed in men under age 50 on the basis of BMD alone.

Note 3:
Approaches to reduce osteoporosis-related fracture risk include optimizing calcium and vitamin D status and fall-prevention measures. The National Osteoporosis Foundation treatment guidelines (http://nof.org/files/nof/public/content/resource/913/files/580.pdf) recommend:
- Initiate pharmacologic treatment in those with hip or vertebral (clinical or asymptomatic)
- Initiate therapy in those with T-scores ≤ -2.5 at the femoral neck, total hip or lumbar spine by DXA, after appropriate evaluation
- Initiate treatment in postmenopausal women and men age 50 and older with low bone mass (T-score between -1.0 and -2.5, osteopenia) at the femoral neck, total hip or lumbar spine by DXA and a 10-year hip fracture probability ≥ 3% or a 10-year major osteoporosis-related fracture probability ≥ 20% based on the U.S.-adapted WHO absolute fracture risk model (FRAX®; www.NOF.org and www.shef.ac.uk/FRAX)

All treatment decisions require clinical judgment and consideration of individual factors including patient preferences, comorbidities, prior drug use, risk factors not captured in the FRAX model (e.g. sarcopenia, falls, vitamin D deficiency, increased bone turnover, interval significant decline in bone density) and possible under or over estimation of fracture risk by FRAX.

Other screening, diagnosis and treatment guidelines may be considered for inclusion depending on the clinical situation:
- Institute for Clinical Systems Improvementhttps://www.icsi.org/guidelines__more/catalog_guidelines_and_more/catalog_guidelines/catalog_musculoskeletal_guidelines/osteoporosis/
- American Family Physician
- American College of Physicians-
  http://www.acponline.org/clinical_information/guidelines/guidelines/
- American College of Obstetrics and Gynecology=
  http://www.acog.org/About_ACOG/News_Room/News_Releases/2012/Osteoporosis_Guidelines_Issued
- NAMS
- USPSTF
  http://www.uspreventiveservicestaskforce.org/3rduspstf/osteoporosis/osteorr.pdf
References

7. Epidemiology. at www.iofbonehealth.org/health-professionals/about-osteoporosis/epidemiology.html.)
12. ISCD Website. International Society for Clinical Densitometry. at www.iscd.org.)
13. 2 Million 2 Many. National Bone Health Alliance. at www.2million2many.org/.


44. Boivin GY, Chavassieux PM, Santora AC, Yates J, Meunier PJ. Alendronate increases bone strength by increasing the mean degree of mineralization of bone tissue in osteoporotic women. Bone 2000;27:687-94.
49. Bonnick SL. Bone Densitometry in Clinical Practice: Application and Interpretation.


65. Chrischilles EA, Butler CD, Davis CS, Wallace RB. A model of lifetime osteoporosis...


98. Finkelstein JS, Wyland JJ, Lee H, Neer RM. Effects of teriparatide, alendronate, or
both in women with postmenopausal osteoporosis. Journal of Clinical Endocrinology & Metabolism 2010;95:1838-45.


116. Hans D, Krieg MA. EPISEM Study. SSR; 2009 Sept 2009; Lausanne, CH.


159. Looker AC. Femur neck bone mineral density and fracture risk by age, sex, and race or Hispanic origin in older US adults from NHANES III. Archives of Osteoporosis 2013;8:141.

162. Luckey M. In: Committee ICU, ed.2009.


222. Tang BMP, Eslick GD, Nowson C, Smith C, Bensoussan A. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. Lancet


