

Improving DXA quality by avoiding common technical and diagnostic pitfalls – Part 1

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Abstract: Dual-energy x-ray absorptiometry (DXA) is an accurate means to assess bone mineral density (BMD), determine the risk of a fragility fracture, and monitor response to therapy. Despite its seemingly straightforward nature – the review of two-to-three non-diagnostic images and a few automatically generated numbers – the proper performance and interpretation of DXA can often be complex. It is complex because it is highly dependent on many factors such as image acquisition, processing, analysis, and subsequent exam interpretation. Each step is subject to potential errors, artifacts, and diagnostic pitfalls; hence meticulous attention must be paid to the technique by both the technologist and interpreting physician to provide high-quality results and, in turn, maximize the exam's clinical utility. This article is part 1 of a two-part series. Part 1 will begin with a review of bone physiology and osteoporosis etiology, followed by a discussion of the principles underlying DXA and the technical procedure. Part 2 will focus on DXA interpretation and discuss scanning pitfalls and clues to recognizing issues and improving scan quality.

Key Words: dual-energy x-ray absorptiometry, DXA, DEXA, bone mineral density, osteoporosis, osteopenia

INTRODUCTION:

Osteoporosis is a skeletal disorder of weakened bone strength resulting in elevated fracture risk. A common but silent disease until a fracture occurs, an estimated half of women and one-fifth of men over age 50 will suffer an osteoporosis-related fracture (1). These fractures are referred to as fragility fractures because they result from low-energy trauma, equal to or less than a fall from standing height. The most common fracture sites are the spine, pelvis, hip, and distal radius. These fractures commonly result in long-term disability, diminished quality of life, and increased mortality; particularly hip fractures, which almost always require hospitalization and have a 20% mortality rate and 50% permanent disability rate (2). With one-third of people in the United States age 50 or older, preventing, detecting, and treating this prevalent disease is critical to the well-being of a substantial portion of the population (3).

Bone strength and, consequently, fracture risk are a function of bone quality and bone mineral density (BMD). Bone quality comprises approximately 30% of bone strength, whereas BMD comprises the remaining 70%. Bone quality refers to a constellation of factors influencing how well a bone resists fracturing. These factors include osseous architecture, accumulated microscopic damage, mineral crystal size, collagen structure, and bone turnover rate (4). BMD is simply the bone mass per area (g/cm^2) (5).

Bone quality cannot be directly measured in the clinical setting. Bone density, however, can be easily measured via dual x-ray absorptiometry (DXA), a quick, inexpensive, and readily available radiological procedure. This article is part one of a two-part series. Part 1 will begin with a review of bone physiology and osteoporosis etiology, followed by a discussion of the principles underlying DXA and the technical procedure. Part 2 will focus on DXA interpretation and discuss scanning pitfalls and clues to recognizing issues and improving scan quality.

BONE PHYSIOLOGY AND OSTEOPOROSIS

Bone Physiology

Normal bone physiology is a process of formation and remodeling (6). Bones grow in both the longitudinal and radial directions, with continuous remodeling throughout life in reaction to microtrauma. It is estimated that most of an adult's skeleton is replaced every 10 years. Bone remodeling is essential because it replenishes bone strength and mineral content, thus averting the accumulation of damaged bone.

There are two types of bone: cortical and trabecular. Cortical bone, also known as compact bone, is the hard outer layer of strong, dense bone. Trabecular bone, also called cancellous bone, is the lighter, less dense, spongy inner network of trabeculae (mesh-like layer of holes connected by thin rods and plates filled with red bone marrow) (7). Approximately 3% of cortical bone is resorbed and replaced each year, compared to 25% of trabecular bone.

Although cortical and trabecular bone differ in their structure, they have similar molecular composition (6). Both have an extracellular matrix, and based on the composition and arrangement, the extracellular matrix determines a bone's mechanical characteristics. Bone strength is influenced by collagenous proteins (tensile strength) and mineralized osteoid (compressive strength).

Bone Cells

Three predominant bone cells include osteocytes, osteoclasts, and osteoblasts. Osteocytes account for 90-95% of total bone cells (8). The adult body has approximately 42 billion. They have a lifespan of up to 25 years. They are often described as terminally differentiated osteoblasts embedded in a mineralized osteoid matrix of calcium and phosphate (hydroxyapatite).

Osteoclasts are responsible for bone resorption, whereas osteoblasts are responsible for bone formation. Their function depends upon one another and are linked in regards to bone remodeling. For resorption, osteoclasts secrete acid and enzymes which digest bone minerals and bone matrix. Osteoblasts secrete and mineralize osteoid bone along with controlling osteoclast resorption. Osteoblasts differentiated into osteocytes appear to control the timing and location of remodeling in response to environmental stress or mechanical strain. Osteoclast resorption of bone, at the microscopic scale, takes weeks, while osteoblast formation of new bone takes 4 to 6 months. Thus, any condition that increases the rate of bone remodeling causes net bone loss over time.

Bone Remodeling Phases

Peak bone mass, representing the greatest amount of bone a person can reach or the bony tissue present at the end of skeletal maturation, occurs between 20 and 30 years of age for men and women, with men typically reaching a higher peak (FIGURE 1) (6). In men, bone mass gradually declines over time until old age. In women, bone mass plateaus until menopause, and then there is an accelerated period of bone loss for several years. After peak bone mass is attained, bone mass and structural integrity are determined by remodeling for the remainder of a person's life.

During remodeling, old bone tissue is replaced by new bone tissue through bone formation and resorption coupling. There are four sequential phases: quiescence/activation, resorption, reversal, and formation. During quiescence/activation, cytokines and growth factors stimulate preosteoclasts which differentiate into mature osteoclasts, which digest old bone during the resorption phase. During reversal, the resorption of the mineral matrix ends, and the osteoclasts produce a "signal" to pre-osteoblasts that initiate bone formation. During the bone formation phase, osteoblasts synthesize new bone by producing an organic matrix of protein and

polysaccharides (osteoid) that becomes bone after mineralization. At the end of formation, the osteoblasts become quiescent and line the newly formed bone surface.

Osteoporosis

Osteoporosis Etiology

Osteoporosis is defined as low bone mass and microstructural weakening of bone tissue leading to increased bone fragility (6). The reduction in bone mass is caused by a decoupling of bone resorption and bone formation. Normally, bone resorption and formation are fairly equally balanced. However, a decrease in bone formation or an increase in bone resorption can result in osteoporosis. In osteoporosis, the coupling mechanism between osteoclasts and osteoblasts does not keep pace with the continuous microtrauma of the trabecular bone. The cause of the imbalance is multifactorial based on genetic, intrinsic, exogenous, and lifestyle factors.

Osteoporosis can be broken down into primary and secondary categories (FIGURE 2). Primary or idiopathic osteoporosis, the most common type, can be further divided into postmenopausal (type I) and age-associated or senile (type II) osteoporosis. A decrease in estrogen mainly causes postmenopausal osteoporosis. Senile osteoporosis is caused by decreased calcium and an aging skeleton. Secondary osteoporosis is caused by disease processes (e.g., renal hypercalciuria, Cushing syndrome), dietary deficiency (e.g., alcoholism, anorexia), or medications (e.g., glucocorticoid, proton pump inhibitors, selective serotonin reuptake inhibitors).

The primary risk factor for osteoporosis is advanced age. However, there are many other identified risk factors such as female gender, white or Asian ethnicity, or family history (TABLE 1).

Osteoporosis Treatment

While there is no cure for osteoporosis, the prognosis is good if it is detected early, and proper treatment is undertaken. Thus, prevention and recognition of the causes are the primary steps to lessen the impact and halt the progression of the disease (6). Treatment includes lifestyle modifications such as increased exercise, smoking cessation, and limiting alcohol consumption. Calcium and vitamin D are also usually prescribed.

Some medications may be helpful, depending on the underlying cause of osteoporosis (TABLE 2). These include antiresorptive agents such as bisphosphonates (e.g., alendronate (Fosamax), risedronate (Actonel), or zoledronic acid (ReClast)), which reduce osteoclast function; selective estrogen receptor modulators (e.g., raloxifene (Evista), bazedoxifene (FRAX)) which act on estrogen receptors to downmodulate osteoclast activity, RANK ligand inhibitors (e.g., denosumab (e.g., Prolia, Xgeva) which block osteoclast maturation, and anabolic agents (e.g., abaloparatide (TYMLOS), teriparatide (Forteo)) which promote new bone formation (9-12).

DXA PRINCIPLES

Newer nuclear medicine technologists may not realize that DXA began as a nuclear medicine procedure, and it is still performed in many nuclear medicine departments today. The systems used in the 1970s to measure BMD were dual-energy photon absorptiometry (DPA) systems that measured the attenuation of monochromatic emissions from the radioisotope gadolinium-153 (13). In 1987, the first DXA scanners became commercially available. DXA uses polychromatic x-ray spectra at different energy levels. Using x-rays shortened the exam time due to the higher photon flux from the x-ray tube resulting in better resolution and precision.

DXA is based on the variable absorption of x-ray photons by different tissues in the body. An x-ray source below the patient produces alternating high (140 kVp) and low (70-100 kVp) energy

pulses. The use of two distinct energy levels enables bone to be measured separately from soft tissue (14). A detector above the patient measures the transmitted low and high-energy photons and calculates bone density based on the difference between the soft tissue and bone attenuation. Although density typically represents mass per unit volume, DXA results are obtained from a planar (two-dimensional) image, and consequently, depth cannot be determined (13). Therefore, density, or more accurately areal density, is reported as mass per unit area (g/cm^2), unlike CT, where traditional density as mass per volume (g/cm^3) is reported.

The calculated BMD results are compared to a normal subjects database. The standard deviation (how much the result varies from the average mean) is reported as a T-score or a Z-score. The scores indicate the relationship between peak bone mass and subsequent bone loss. The results may vary somewhat between manufacturers depending on the database used and differences in the technology.

T-Scores and Z-Scores

The T-score, as defined by the World Health Organization (WHO), represents how a patient's measured BMD differs from that of healthy 30-year-old adult women (presumed peak bone mass) (15). The T-score is used to assess BMD in postmenopausal women and men ages 50 and older. In contrast, younger patients, particularly children, are assessed using a Z-score, which also considers age, gender, and ethnicity.

The T-score, not to be confused with the "t" in the commonly used student's t-test, is determined by taking the difference between the patient's measured BMD and the mean BMD of healthy 30-year-old adults, which is then divided by the 30-year-old adult standard deviation (16).

$$\text{T-score} = \frac{\text{Patient BMD} - \text{Mean healthy 30-year-old adult BMD}}{\text{Healthy 30-year-old standard deviation}}$$

A T-score of -1.0 (standard deviations) or greater is considered normal BMD, and a T-score – 2.5 and below is diagnostic of osteoporosis (15). T-scores less than -1.0 but greater than -2.5 are classified as osteopenia, with ‘low bone density’ also an acceptable term (TABLE 3).

Z-scores are calculated similarly to T-scores; however, Z-scores use the mean age, gender, and ethnicity matched (population-specific) score.

$$\text{Z-score} = \frac{\text{Patient BMD} - \text{Mean population-specific (matched) BMD}}{\text{Population-specific standard deviation}}$$

Z-scores greater than -2.0 are considered normal, while scores equal to or less than -2.0 are considered low bone density for age. Note, Z-scores are not used to formally diagnose osteoporosis; instead, the score serves as a clue to look for a cause of secondary osteoporosis.

DXA ALTERNATIVES

DXA is the preferred technique to measure BMD because of its high precision and accuracy (1-2% margin of error) (17). Note precision refers to the reproducibility of measurement, while accuracy refers to how close a measurement is to the true value. DXA measurements also can be quickly obtained at a relatively low radiation dose. However, other methods are available, including quantitative computed tomography (QCT) and quantitative ultrasound (QUS).

QCT of the lumbar spine, central QCT, is performed on a standard CT machine using specialized protocols. QCT of the forearm, also called peripheral QCT, can be measured using smaller, less sophisticated equipment; however, the measurements correlate poorly with central measures (16). QCT is a three-dimensional technique that calculates the true volume and volumetric bone density (g/cm³) (13). The geometry of the vertebra can be assessed. QCT also allows for the differentiation between cortical and trabecular bone (18). However, one drawback

to QCT is the higher radiation dose. Another drawback is the lack of validated diagnostic criteria.

QUS can assess BMD of the peripheral skeleton, usually the calcaneus. QUS uses ultrasound attenuation instead of x-ray attenuation and the speed of sound. The advantages of QUS are that it is relatively cheap compared to QCT and DXA, and the equipment can be portable. The disadvantage of QUS is that it is less accurate.

DXA PROCEDURE

Indications/Contraindications

The American College of Radiology (ACR), Society for Pediatric Radiology (SPR), and Society for Skeletal Radiology (SSR) practice parameters provide a long list of clinical indications for DXA (see <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/DXA.pdf>). Essentially, DXA is used to diagnose abnormalities of bone mineral density, estimate the risk of fractures, monitor changes in density over time, and assess response to treatment.

There are no absolute contraindications for DXA (14). However, these conditions may result in scans of limited value: recent administration of gastrointestinal contrast or radiopharmaceuticals; severe degenerative changes in the measurement area; fracture; implants or devices in the measurement area, patient's inability to be positioned or remain motionless during the scan, and extremely low or high body mass. Pregnancy is a relative contraindication, and the risks and benefits of a DXA should be discussed with the referring physician.

Patient Preparation

The patient should be pre-screened to ensure they can lie on their back for up to 10 minutes.

The patient should have had no barium or gadolinium oral contrast within two weeks, and they should take no calcium tablets within 24 hours of the scan (18). The patient should wear loose-fitting clothing without metal. Finally, if the patient has had a previous DXA, the patient should bring a copy of the results for comparison.

A detailed patient history is required to perform and interpret a DXA correctly. The history should include risk factors (see above), prior surgery that could affect the accuracy of measurements, previous fractures, endocrine or metabolic diseases, bone marrow-related disorders, and other associated conditions (TABLE 4). (Kaiser) The patient should also be screened for medications associated with bone loss or increased fracture risk (TABLE 5). The International Society of Clinical Densitometry provides patient history questionnaires that can be found at www.iscd.org.

In addition, the WHO fracture risk algorithm can be used to calculate a score from the patient history that can be used to correlate with DXA findings. The Fracture Risk Assessment Tool (FRAX) estimates the 10-year probability of fracture due to osteoporosis in postmenopausal women and men over 50. It evaluates risk factors including age, gender, low body weight, height, previous fracture, parent history of hip fracture, smoking, glucocorticoid use, history of rheumatoid arthritis, menopausal state, and excess alcohol intake (19). The FRAX tool is helpful for risk stratifying osteopenic individuals in order to identify those who are most likely to benefit from therapy.

Acquisition

Equipment

Several manufacturers produce DXA scanners, and the equipment can be full table systems that can measure multiple sites, such as the spine or hip, or peripheral systems that measure the wrist or ankle (20). Full table systems offer the most options and are the preferred osteoporosis assessment and management method.

The first-generation DXA scanners used pencil-beam geometry and a single detector that scanned across the area of interest in a raster pattern (21). Current scanners use fan-beam technology with multiple detectors that sweep the measurement area. One advantage of fan-beam over pencil-beam technology is shorter scan times of 30 seconds for the hip and spine compared to 3 – 10 minutes for pencil-beam technology. (IAEA) The disadvantages of fan-beam scanners include a small amount of image distortion due to magnification of the tissue and increased scanner cost. Another disadvantage of fan-beam scanners is increased scatter.

Quality Control

The accuracy of BMD measurement depends on the consistency of the scanner (22). Quality control procedures vary by manufacturer but usually require scanning a dedicated phantom and automatic analysis that checks and calibrates mechanical function, radiation quality, and absorption coefficient of tissue-equivalent materials. The procedure is performed daily before use and at least three times a week (13). If the results fall outside of the acceptable limits, the scanner should be evaluated by a field service engineer

Cross-calibration procedures are necessary for precise longitudinal assessment when replacing scanners (the same model is usually preferred) or validating measurements between systems

(22). Cross-calibration entails scanning the phantom ten times on each scanner. The measures should be within 1%.

Areas of Study

For routine DXA, the lumbar spine and hip(s) are assessed with measurement of either or both hips considered acceptable technique. Assessment of both hips provides information on the hip with the lowest BMD and allows for the longitudinal evaluation even if one hip is fractured or undergoes surgery in the future (23). In addition, the nondominant forearm BMD should be included in all patients with hyperparathyroidism. The forearm should also be measured when the hip or spine cannot be measured or correctly interpreted due to hardware or other confounding factors. The final diagnosis is made using the lowest score among the measured skeletal sites.

The patient must remove all objects from their pockets in the scan field, such as wallets, cell phones, underwire bras, watches, bracelets, etc.

Positioning

Correct patient positioning is essential to obtaining reliable and reproducible BMD measurements. Incorrect positioning is one of the most common reasons for errors.

Spine

For the spine, posteroanterior images are obtained of L1-L4 with the patient lying supine on the DXA table (24). The lower back should be aligned in the middle of the table with the spine straight compared to the table's long axis and not rotated (FIGURE 3). A tip to ensure the spine is straight is to stand at the patient's head, gently reach under the underarms, and pull the

patient upwards. The legs should be elevated using a foam block -- placed under the patient's lower legs so their thighs are as close to a 90-degree angle to the body as possible – to minimize lordosis and increase intervertebral spacing. The patient should rest their arms and hands comfortably at their sides.

The scan field-of-view extends superiorly to include a portion of the lowest thoracic vertebra (confirmed by the presence of ribs) and inferiorly to show the iliac crests (about the level of the L4–L5 interspace). Usually, proper patient positioning can be achieved by locating the patient's iliac crest and starting the scan two inches below. Most scanners begin the acquisition inferiorly and move superiorly.

As the scan acquires, the technologist monitors the emerging planar image to ensure the entire spine is centered and straight. There should be even amounts of soft tissue on both sides of the spine, and a small part of the iliac crest should be visible in the lower corners of the screen. If the patient is not positioned correctly, the technologist should stop the scan, reposition, and restart the acquisition. The scan can be terminated when ribs attached to the 12th thoracic vertebra (T12) are visualized.

Hip

The hip images must include the entire femoral head, the greater trochanter, and one inch or more of the femoral shaft below the lesser trochanter (Figure 4). The technologist must first locate the patient's greater trochanter to ensure the hip is correctly positioned in the field-of-view. The greater trochanter can be identified by holding the patient's ankle and rotating inwards and outwards while pressing firmly on the thigh with the other hand. The greater trochanter will roll back and forth under the fingertips. An alternative method is to ask the patient to bend at the knee and lift their leg. The crease formed at the top of the leg is approximately in line with the greater trochanter.

A hip positioning device is placed under the patient's lower legs in the midline of the patient's body. The long axis of the femur should be parallel to the long axis of the table. The leg of the hip to be measured is rotated inward and strapped against the positioning device, abducting or internally rotating 15-25 degrees to position the femoral neck axis parallel to the table plane and ensure precise measurement (Figure 5). When rotating the leg, the technologist should place one hand above the knee and the other hand below the knee and gently turn the entire leg, not just the lower portion.

Incorrect leg rotation causes foreshortening of the femoral neck, presenting a smaller cross-sectional area, possibly resulting in a falsely elevated BMD (25). An excess of internal or external rotation as low as 10 degrees can lead to significant changes in measured BMD in approximately 10% of patients (FIGURE 6).

The patient can rest their arms on their chest or outside the scan field. The scan begins at a position two inches below the level of the greater trochanter. A horizontal laser line can ensure the femoral shaft is parallel.

Upon scan completion, the technologist should verify correct hip positioning. The lesser trochanter will be barely visible on a properly aligned and rotated hip, and the shaft of the femur will be straight.

Forearm

When imaging the forearm, the patient sits next to the table with the nondominant forearm, wrist, and hand laid flat, palm side down, secured to a positioning board with a restraining strap (26). The ulnar and radial shafts should be aligned to the long axis of the table with the carpal bones in the top third of the image (FIGURE 7). This position ensures the inclusion of the radius 33% (aka 1/3rd radius), consisting of a 20-mm length of the radial shaft located one-third of the distance between the ulnar styloid and the olecranon. The radius 33% is the recommended

forearm site when either the lumbar spine or hip cannot be assessed or in cases of hyperparathyroidism.

Analysis

The first step in analyzing the DXA image is to confirm positioning and the absence of patient motion on the planar image (27). The image must also be reviewed for artifacts such as metal, overlying hardware, or barium.

Spine

Most DXA scanners utilize automated region of interest (ROI) placement. However, the technologist must manually adjust the ROI to ensure appropriate intervertebral designations. (IAEA) Correct identification and numbering of the lumbar vertebra are critical. Staron et al. found incorrect intervertebral disk space ROI placement was the most common analysis error (28).

The spine measurement region includes L1 through L4, with the box placed at the top of L1 and bottom of L4 (13). The intervertebral lines should be moved and angled as appropriate to ensure the proper numbering of the vertebra. A line drawn from the highest point of one iliac crest to the other iliac crest most commonly traverses the L4–L5 intervertebral disc space and be used as a landmark (29). In addition, there must be adequate soft tissue on both sides of the spine — insufficient soft tissue results in underestimation of the BMD.

Hip

The hip ROI includes the femoral neck, trochanter, and total hip. Although Ward's triangle (not a true anatomic area but a calculated area of the lowest BMD in the femoral head) and the intertrochanteric region are often included in manufacturers' hip BMD results, these regions are

less not relevant and not reported (30). The first step in the hip analysis is to ensure that the line placed midline and parallel through the hip is correctly set. All other ROIs depend on the correct placement of this line. The femoral neck ROI is usually placed halfway between the femoral head and trochanter or on the distal portion of the femoral neck, depending on the DXA manufacturer.

Forearm

The ROI for the forearm must be manually positioned. The three regions of the distal radius must be defined: the ultradistal region (a 15 mm section from the endplate of the radius); the proximal region, also called the one-third distal, (a 20 mm section one-third of the distance between the ulnar styloid and the olecranon); and the intermediate or mid-distal radius (the remaining section between the two other regions) (26).

Longitudinal Measurement Note

Currently available DXA systems use various filters, collimators and detectors, and differing analysis algorithms (18). Thus, it is advisable to perform longitudinal measurements or follow-up scans on the same piece of equipment. When scans are performed on the same stationary equipment, the accuracy is high, with a margin of error of 1-2% (17). In addition, the same skeletal site, ROI, and area size should be used if quantitative comparisons are performed. (ACR) Only qualitative comparisons can be made if follow-up scans are done on a different device.

Radiation Dose

As mentioned, the radiation dose from DXA is relatively low (18). The average dose for a spine plus hip DXA ranges from 1 uSv to 15 uSv depending upon the equipment (31). The dose from pencil-beam systems ranges is usually less about 1 uSv, while fan-beam systems may be up to

15 uSv. For comparison, the average effective dose from a chest x-ray ranges from 20 - 50 uSv, or the average dose from natural background radiation is about 10 uSv per day. The low radiation doses from DXA make serial imaging acceptable if the initial results are abnormal.

CONCLUSION

Osteoporosis is a common skeletal disorder of weakened bone strength, leading to increased bone fragility and elevated fracture risk. Therefore, preventing, detecting, and treating this disease is critical to the well-being of a substantial portion of the US population. Bone strength and, thus, fracture risk can be assessed from the measurement of BMD via DXA.

The precision and accuracy of DXA results depend upon the procedure's proper performance and interpretation. Therefore, correct patient positioning, acquisition, and analysis are essential. This article, part 1 of a two-part series, laid a foundation for performing DXA by first reviewing bone anatomy and physiology along with osteoporosis etiology and treatment. Next, the article explained the principles underlying DXA and the scanner features. Finally, the article detailed the DXA acquisition protocol, including the indications, contraindications, patient preparation, positioning, acquisition, and analysis. Part 2 of the series will review DXA interpretation, using DXA for monitoring changes in BMD, and pitfalls and clues for quality DXA results.

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TABLES

TABLE 1. Osteoporosis Risk Factors

Non-modifiable	Modifiable
>= 50 years old	Physical inactivity
Female gender	Smoking
Asian or white ethnicity	Excessive alcohol consumption
Family history	Low calcium or vitamin D
Thin physique or low weight (<57.6 kg (127 lbs))	
Androgen or estrogen deficiency	
Hypogonadism	
Amenorrhea	
Late menarche	
Early menopause	
Postmenopausal	
Immobility	
Certain medications (e.g., anticonvulsants, steroids, thyroid drugs, heparin, chemotherapy, insulin)	
Dowager hump (focal kyphosis of the upper thoracic spine)	

TABLE 2. Osteoporosis Medications

Type	Function	Examples
Antiresorptive Agents	Reduce osteoclast function	Bisphosphonates: alendronate (Fosamax) risedronate (Actonel) zoledronic acid (ReClast)
Selective Estrogen Receptor Modulators	Act on estrogen receptors to downmodulate osteoclast activity	raloxifene (Evista), bazedoxifene (FRAX)
RANK Ligand Inhibitors	Block osteoclast maturation	denosumab (Prolia, Xgeva)
Anabolic Agents	Promote new bone formation	abaloparatide (TYMLOS) teriparatide (Forteo)

TABLE 3. WHO Osteoporosis T-score Classification*

T-Score	Classification
≥-1	Normal
Between -1.0 and -2.5	Osteopenia
≤-2.5 or lower	Osteoporosis
≤-2.5 (with fragility fracture(s))	Severe or established osteoporosis

*Compared to the mean bone density of young adult women

TABLE 4. Patient Medical History Screening

Category	Condition
Bone Marrow Disorders	Multiple myeloma
	Myelodysplasia
	Systemic mastocytosis
	Thalassemia
Endocrine or Metabolic Diseases	Acromegaly
	Anorexia nervosa
	Cushing syndrome
	Diabetes mellitus type 1
	Hypercalcemia
	Hyperparathyroidism
	Hyperprolactinemia
	Hyperthyroidism
	Hypopituitarism
Other Conditions	Chronic kidney disease
	History of organ transplantation
	Hypercalciuria
	Immobilization (e.g., paraplegia, quadriplegia, muscular dystrophy)
	Inadequate calcium uptake
	Malabsorption (e.g., celiac disease)
	Rheumatoid arthritis
	Secondary hyperparathyroidism due to renal disease
Vitamin D deficiency	

TABLE 5. Medications Causing Bone Loss or Increased Fracture Risk

Bone Loss	Increased Fracture Risk
Anticonvulsants (e.g., phenobarbital, phenytoin)	Benzodiazepines/Z-drugs
Aromatase inhibitors	Insulin with hypoglycemia
Cytotoxic agents	Opioids
Glucocorticoids > 3 months	Thiazolidinediones
Gonadotropin-releasing hormone agonists or antagonists (e.g., androgen deprivation therapy, Lupron)	Selective norepinephrine-reuptake inhibitors
Immunosuppressive agents (e.g., cyclosporine)	Selective serotonin reuptake inhibitors
Intramuscular medroxyprogesterone (Depo-Provera)	SGLT-2 inhibitors
Thyroid hormone excess	

FIGURE LEGEND



FIGURE 1: Normal bone loss over time for men and women. For both men (blue line) and women (green line), peak bone mass occurs between 20-30 years old. Men then begin to lose bone mass over time gradually. Bone mass in women plateaus until menopause, and then there is a rapid period of bone loss for several years.

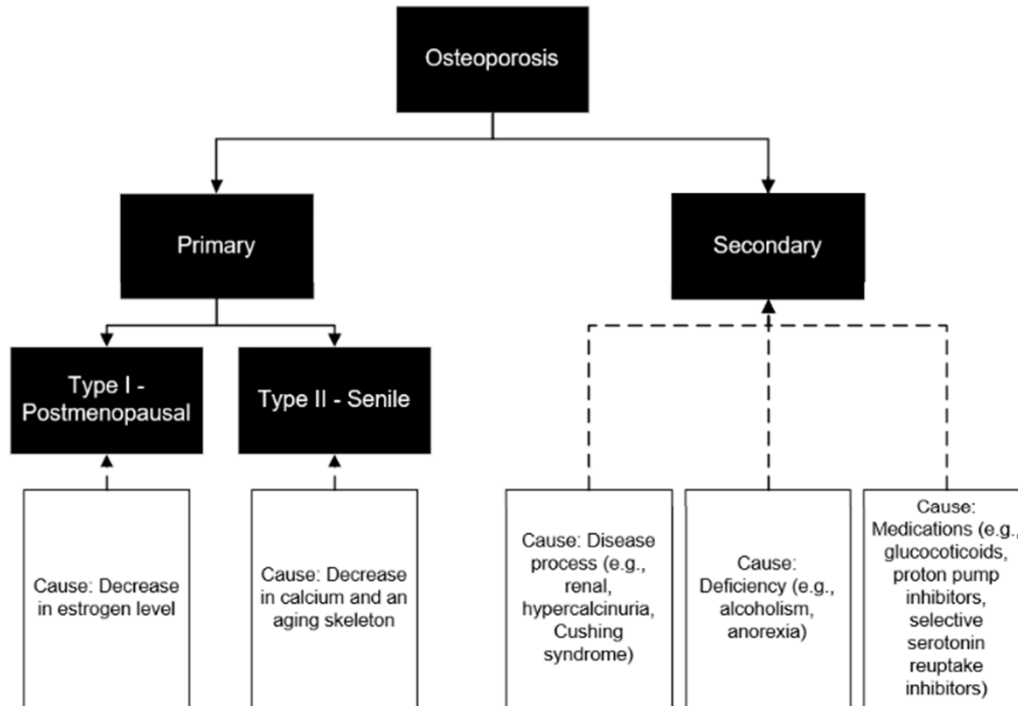


FIGURE 2: Osteoporosis types. Osteoporosis can be broken down into primary and secondary categories. Primary osteoporosis consists of Type 1 or postmenopausal and type II also called senile. Type I osteoporosis is caused by decreases in estrogen levels, while type II is caused by decreased calcium and aging of the skeleton. Secondary osteoporosis is caused by other diseases, diet, or medications.

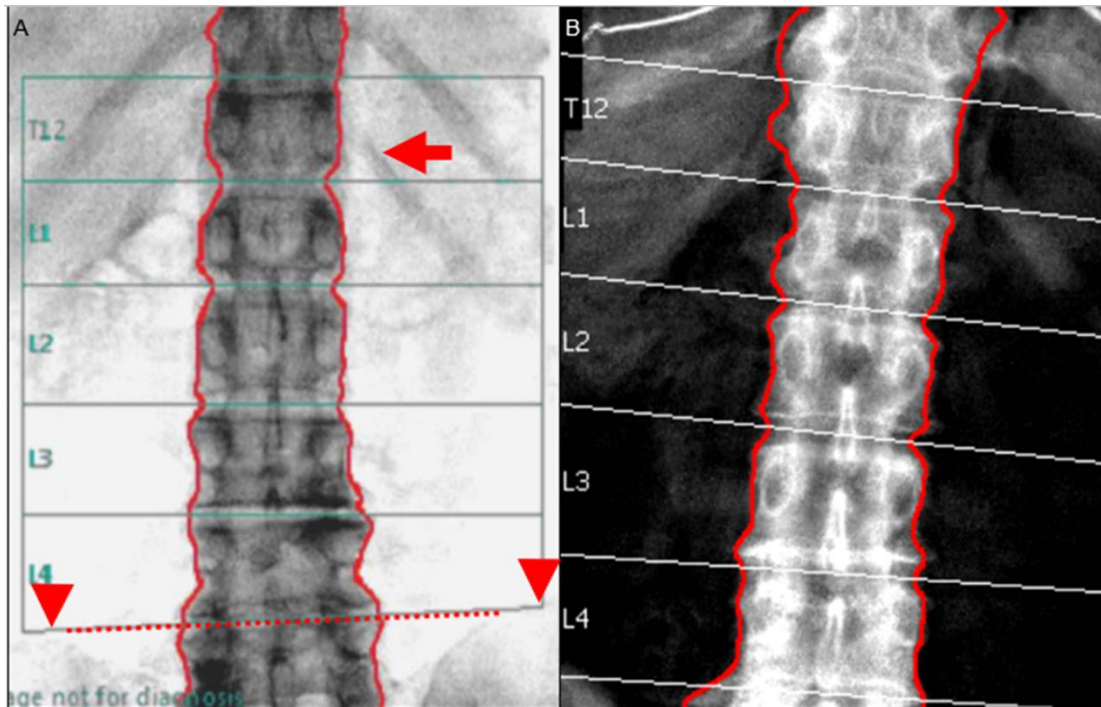


FIGURE 3: (A) Properly positioned PA lumbar spine with appropriate field-of-view (FOV). The spinous processes should be centered straight (midline) and include part of the iliac crest (arrowheads) and part of a vertebra with ribs (arrow). The iliac crests provide a helpful landmark. A line (dashed) connecting this will typically bisect the L4-5 disc space. (B) Incorrectly positioned PA lumbar spine where the spine is angled and the left iliac crest is not visible.

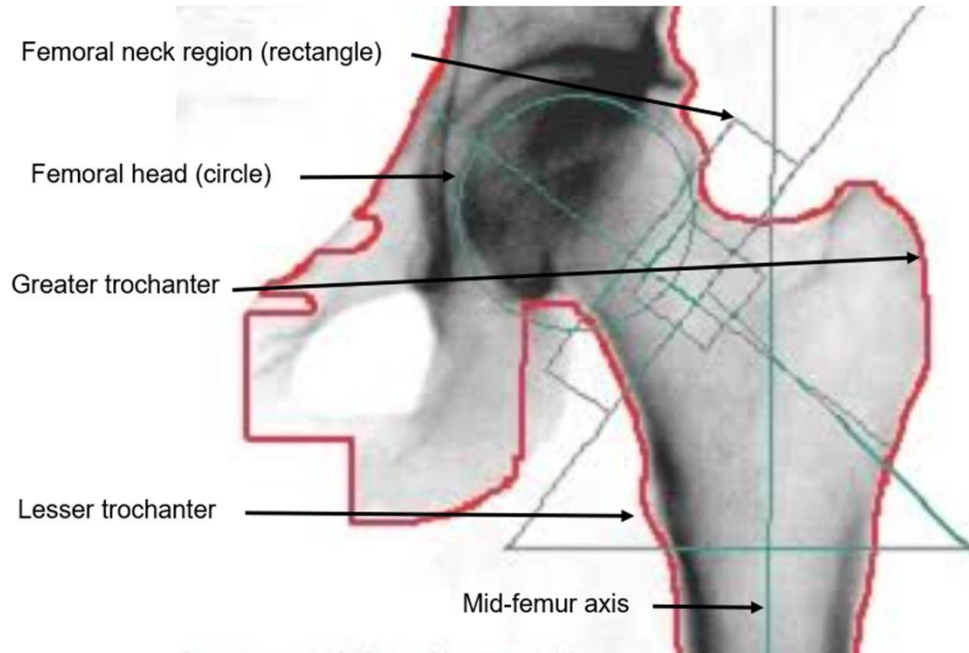


FIGURE 4: Hip anatomy. Essential hip anatomy for proper positioning include the femoral head, femoral neck, greater trochanter, lesser trochanter, and mid-femur axis.

ROI = region of interest

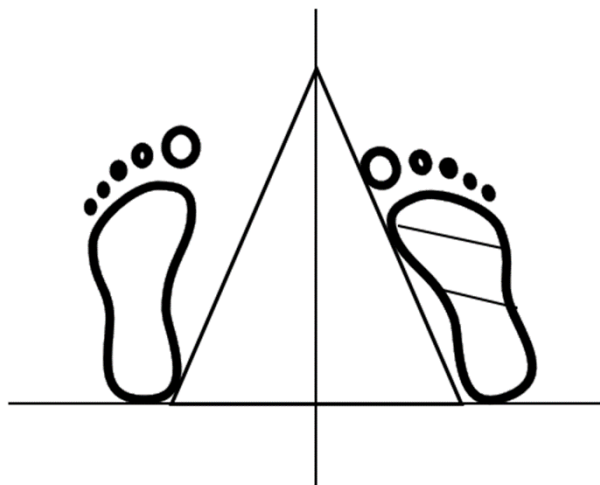


FIGURE 5: Hip positioning device. To properly align the axis of the femoral neck, the must leg be rotated 15-25 degrees inward and strapped to a hip positioning device.

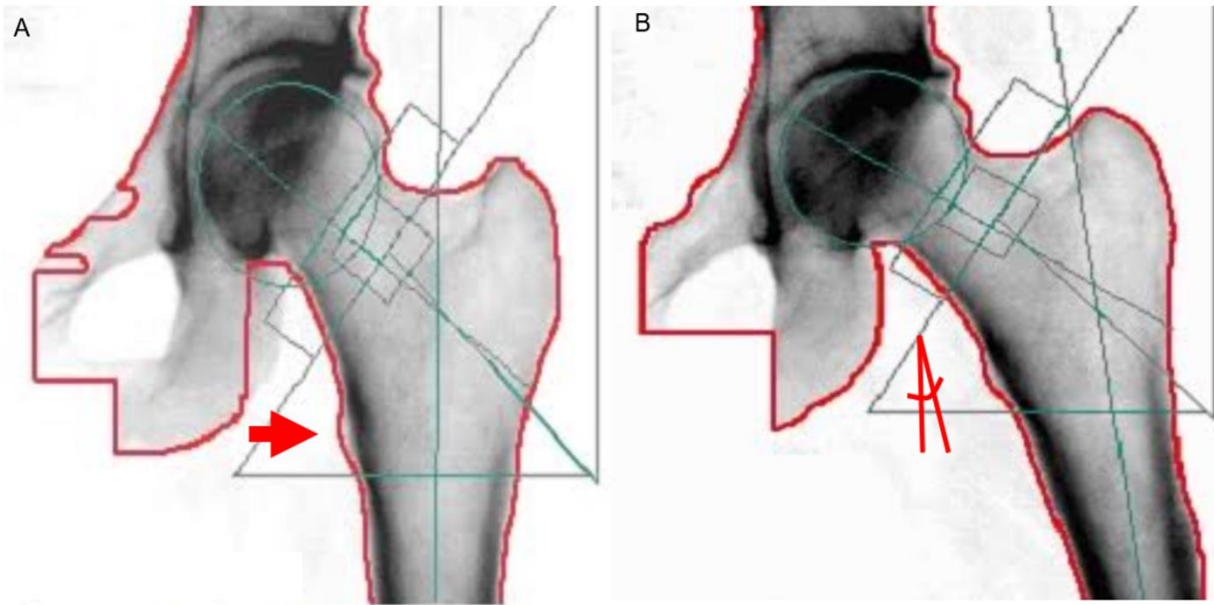


FIGURE 6: (A) Properly positioned hip. Femur shaft is aligned with the cranial-caudal (CC) axis. There is appropriate internal rotation demonstrated by the lesser trochanter (arrow) minimally visualized. The FOV is centered correctly with the greater trochanter at the midway CC point. (B) Improperly positioned hip with the femoral shaft off axis, in 20 degrees of abduction (angle). The incorrect rotation or alignment causes foreshortening of the femoral neck which presents a smaller cross-sectional area, possibly resulting in a falsely elevated BMD. An excess of internal or external rotation as low as 10 degrees can lead to significant changes in measured BMD in approximately 10% of patients (Lekamwasam 2003). Additionally, this incorrect positioning is often not reproduced on follow-up, potentially propagating the error by calculation of a spurious interval change.

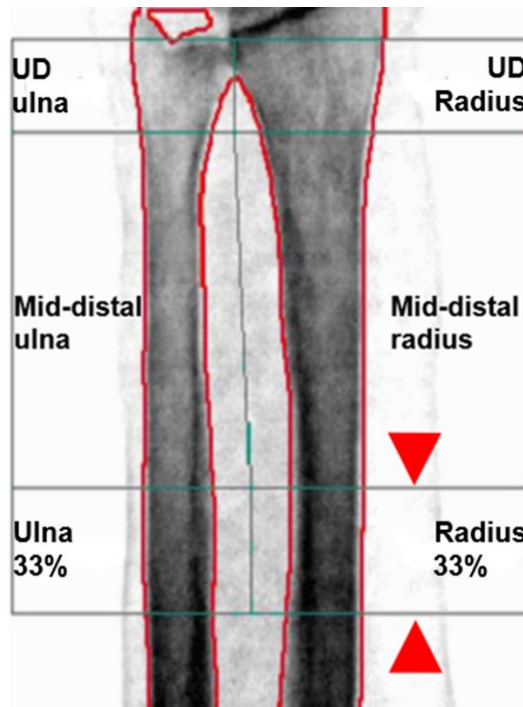


FIGURE 7: Appropriately positioned nondominant forearm. The ulnar and radial shafts are aligned to the long axis of the table with the carpal bones (arrow) in the top third of the image. This position ensures inclusion of the radius 33%, aka 1/3rd radius, consisting of a 20-mm length of the radial shaft located one-third of the distance between the ulnar styloid and the olecranon (arrowheads). UD = ultra-distal