Women's Health Issues and Nuclear Medicine, Part III: Women and Osteoporosis

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Objective: This article is the third in a 4-part series on women's health issues and nuclear medicine. After reading this article the technologist should be able to: (a) state potential risk factors for osteoporosis; (b) describe osteoporosis and its natural history; and (c) identify methods for detecting normal and abnormal bone mineral density results.

Key Words: osteoporosis; bone densitometry

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Osteoporosis is recognized as one of the most serious problems in public health, threatening 28 million Americans of whom 80% are women (*1–6*). Annually osteoporosis leads to 1.5 million fractures, including 300,000 hip fractures, 700,000 vertebral fractures and 250,000 wrist fractures, accounting for $14 billion in health care costs (*1–5*). Approximately 50% of women over 50 y of age have osteoporosis and will suffer an osteoporosis-related fracture in their lifetime (*3–5*). The risk of fracture in women due to osteoporosis is equal to the risk of suffering a myocardial infarction and the risk of hip fracture alone is equal to the combined risk of developing breast, uterine and ovarian cancer (*6,7*). Osteoporosis is the primary cause of hip fractures in women and 1 in 3 women will suffer a vertebral fracture (*3–6*). Women who suffer hip fractures have a 20% mortality rate after 1 y and 50% suffer from reduced functional capacity (*2–8*). Currently there are no cures or preventive measures for osteoporosis, but early detection and treatment can delay the onset and severity of the disease.

BONE TISSUE

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in fragility and susceptibility to fracture (*1,2,7,9,10*). Although it affects the whole skeleton, some bones are more likely to fracture than others. The development of osteoporosis occurs over a lifetime.

Bone tissue consists of several fibers including collagen, a protein that provides a soft framework. This collagen framework is hardened with calcium, phosphorus and other minerals, which add strength to the framework. The combination of these substances makes bones strong yet flexible to withstand stress (*4,5*).

Throughout a person's lifetime bone tissue goes through a process called remodeling. There are 2 functions that occur during this process: formation, whereby new bone is added, and resorption, whereby old bone is removed. There are 2 cell types involved: osteoclasts, which break down bone, and osteoblasts, which rebuild bone, as well as many hormones that are responsible for balancing this process (*4,5*).

Formation occurs much faster than resorption during childhood and adolescence until peak bone mass (maximum bone density and strength) is reached (*4,5*). Ninety-eight percent of peak bone mass is reached by age 20 for boys and by age 18 for girls (*2,9,11*). Approximately another 5% is added before age 28, when mineral acquisition is complete. After age 30, bone resorption starts to exceed bone formation and bone mass declines. Osteoporosis develops when bone resorption occurs too quickly or if bone formation occurs too slowly.

RISK FACTORS

Certain risk factors have been linked with the likelihood of developing osteoporosis, however, some individuals with osteoporosis will not present with any risk factors. Some risk factors can be modified, while others cannot.

Two major risk factors for osteoporosis, which cannot be modified, are gender and age (*4,5,9*). Women have a much greater chance of developing osteoporosis than men. This is because women tend to build less bone mass and the decline of estrogen at menopause causes bones to break down more rapidly. By age 65, some women have lost half their skeletal mass (*4*). Other risk factors that cannot be modified include: ethnic heritage, body size and family history. Risk factors that can be modified include: a sedentary lifestyle, smoking, excessive use of alcohol, use of certain medications, and diet.

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DETECTING OSTEOPOROSIS

Osteoporosis is sometimes referred to as the ''silent disease'' because bone loss occurs without symptoms (*5*). People may not be aware they have osteoporosis until they suffer a fracture. Bone densitometry (bone mass measurements) has become a precise and accurate tool to assess risk of fracture, detect low bone density before fractures occur, confirm a diagnosis of osteoporosis after a fracture, predict chances for future fractures, determine the rate of bone loss, and monitor treatment (*2,4,5,9*). Bone mineral density at the site of measurement is the best predictor of fracture risk for any bone (*7,12*). This is important because the most common sites of fracture that occur with osteoporosis are the vertebrae and femoral neck. Bone densitometry is used most often to assess patients who are at increased risk for osteoporosis. Examples of such patients include women who are postmenopausal, women and men with a medical or surgical disorder known to cause osteoporosis, and individuals who have had atraumatic fractures before age 50 (*2,7*). It also can be used to monitor an individual's response to certain treatments.

Bone densitometry has experienced a rapid evolution over the past 10 y (*13,14*). It can be performed with several techniques including: single- or dual-energy absorptiometry, conventional radiography, quantitative computerized tomography, radiographic absorptiometry, and ultrasound (*1,2,7,9*). All bone densitometry procedures, except ultrasound, use a radiation source (x- or gamma ray) (*2*). These methods are based on the principle that attenuation of x- and/or gamma rays is related to the thickness and composition of tissue in its path (*1,2,11*). Bone thickness is the dominant cause of attenuation at most skeletal sites, however, some sites have a smaller variation in soft-tissue thickness than others (*1,2*). Converting attenuation values to equivalent mineral thickness and comparing these values to population-based normal subjects determines bone mineral density (*2*).

Conventional Radiography

Conventional radiography can detect decalcification of the bone. Decalcification must be marked and osteopenia can be detected only after a 20%–40% loss of bone mass has occurred (*2*). Conventional radiography does not allow early diagnosis or detection of small changes in bone density (*2*).

Quantitative Computerized Tomography

Quantitative computerized tomography is the only method that can provide true bone density measurements (*15*). It can distinguish between cortical and trabecular bone compartments because transaxial images of the body can be acquired. Volumetric measures (gm/cm^3) of bone mineral density can be obtained for the lumbar spine and peripheral bones, such as the radius, ulna and tibia (*2,7,16*). However, quantitative computerized tomography currently cannot provide measurements for the femur and requires large doses of radiation (*2,7,17*).

Radiographic Absorptiometry

Radiographic absorptiometry has been used as an alternative to dual-energy absorptiometry. A radiograph of the hand is simultaneously obtained with a reference aluminum wedge (*2,18*). The density of the wedge is compared to the densities of the second, third and fourth fingers and bone mineral densities are analyzed using a optical dosimeter and computer. It is considered fast, inexpensive and involves low levels of radiation, however, this technique can be inaccurate (*2,18*).

Ultrasound

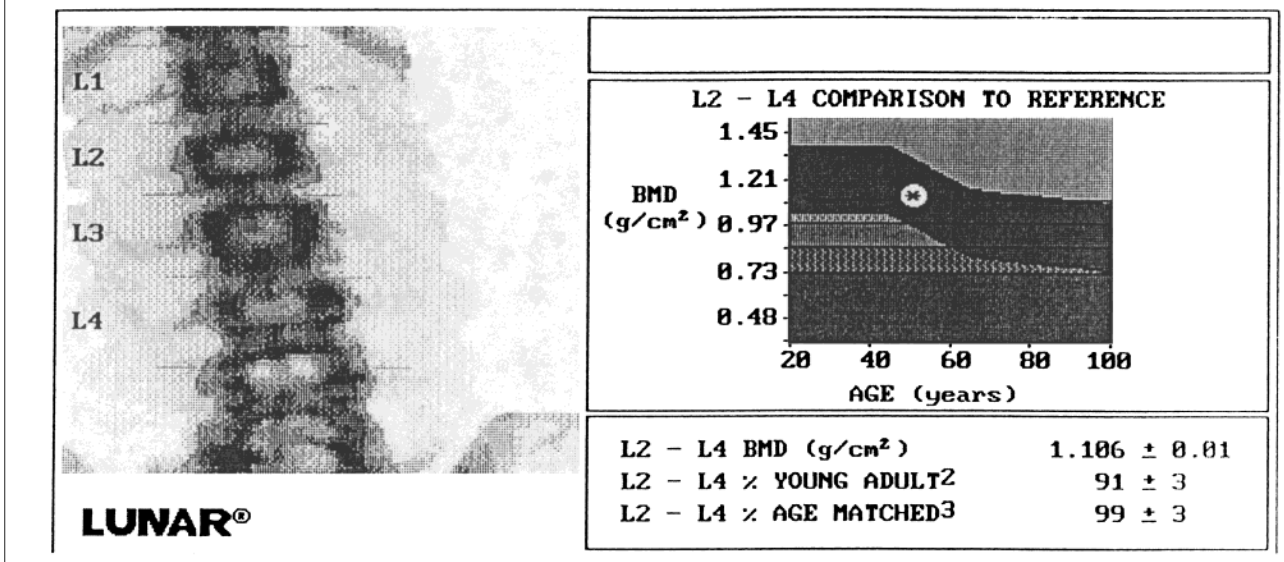
Ultrasound is a mechanical wave, which measures the broadband ultrasonic attenuation and velocity of sound across bone (*1,2,7*). It determines not only mineral properties but also structural properties of the bone (*1,7*). Ultrasound is considered both fast and safe. There is no radiation dose to the patient. Studies have shown good correlation with both dual-energy absorptiometry and quantitative CT for determining bone mineral density. The bone density correlation was not sufficient to predict the risk of fracture in the spine and femur in individual subjects (*7,19,20*). Most measurements are performed on the calcaneus and the results may vary depending on the position of the foot. This results in poor reproducibility and eliminates its use for assessment in response to treatment (*2*).

Single- and Dual-Energy Absorptiometry

Photon or x-ray absorptiometry uses a beam or beams of energy that scan the area of interest opposite a detector. Earlier instruments included a single source of energy (single-energy absorptiometry) and could be used only for peripheral sites, such as the forearm which has only a small variation in tissue thickness. Newer absorptiometry techniques involve 2 beams of distinct energy (dual-energy absorptiometry), which allows the correction of soft-tissue attenuation. This allows scanning of both peripheral (forearm) and axial (hip and spine) sites (*2,13*).

Single-energy absorptiometry used a radioactive source of ^{125}I, which has an energy of 29 keV (*21*). The low energy prevented this method from being useful in larger areas, such as the spine and femur. The first dual-energy techniques introduced used a radioactive source of ^{153}Gd (*1,7,13,21*). Gadolinium-153 yields energies of 44 keV and 100 keV, which creates dual beams for acquisition. This dual-energy technique allows accurate measurements at larger bone sites. These devices were placed in nuclear medicine laboratories because of the radioactive sources.

X-ray absorptiometry, which uses 2 x-ray energy windows, was introduced later. Both the single- and dual-energy system yield a precision error as low as 1% and some x-ray systems have errors as low as 0.5% (*21*). Radiation exposure is very low for both systems, however, scanning time is less for the x-ray system, allowing faster patient throughput. Another advantage of the x-ray systems is the photon flux remains consistent, whereas the systems using radioactive sources decay over time and require replacement (*13,21*). Although some ^{153}Gd systems still may exist, the majority of scanners now are x-ray systems. This procedure, however, still resides in a large number of nuclear medicine laboratories throughout the country.



Age (years).....	51	Large Standard.....	275.36	Scan Mode.....	Medium
Sex.....	Female	Medium Standard.....	204.28	Scan Type.....	DPX
Weight (lb).....	130.0	Small Standard.....	145.50	Source Collimation (mm).	1.68
Height (in).....	68	Low keV Air (cps)...	846919	Sample Size (mm).....	1.2x1.2
Ethnic.....	White	High keV Air (cps)..	501834		
System.....	6218	Rvalue (%Fat).....	1.381(5.6)		

REGION	BMD g/cm²	% Young² Adult	% Age³ Matched
L1	1.032 ± 0.03	94	102
L2	1.090 ± 0.03	90	97
L3	1.166 ± 0.03	96	104
L4	1.070 ± 0.03	88	95
L1 - L2	1.061 ± 0.02	92	100
L1 - L3	1.100 ± 0.01	94	102
L1 - L4	1.091 ± 0.01	92	100
L2 - L3	1.131 ± 0.02	93	101
L2 - L4	1.106 ± 0.01	91	99
L3 - L4	1.112 ± 0.02	92	99

2 - USA AP Spine Reference Population, Ages 20-40. See Appendices.
3 - Matched for Age, Weight, Ethnic. See Appendices.

FIGURE 1. Example of a normal dual-energy absorptiometry study of the lumbar spine. This study was performed on a dual x-ray absorptiometry instrument (DPX system; Lunar, Madison, WI).

Dual-energy absorptiometry is the method of choice for bone mineral density measurements (*1,2,7,13,21*). Results are highly reproducible and accurate and this technique can be used to measure both peripheral and axial sites.

ACQUIRING AND PROCESSING DUAL-ENERGY ABSORPTIOMETRY

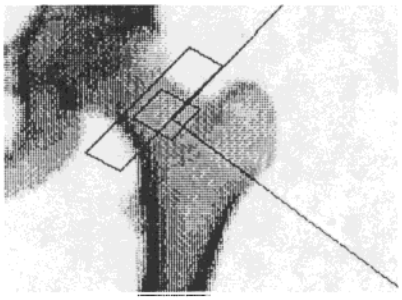
Dual-energy absorptiometry is easy to perform. No special patient preparation is required. The patient should be instructed to remove any metallic items that may be in the scan path, including any articles of clothing that have metallic items attached such as metal zippers and buttons. It is also important to inquire whether the patient has had a recent gastrointestinal study involving barium because this may interfere with imaging results.

To acquire images of the lumbar spine, the patient is placed supine on the imaging table and a cushion is placed under the legs to elevate the lower extremities, separate the lumbar

regions, and press the pelvis and lumbar regions flat against the imaging table. It is important to ensure that the patient is straight and instruct the patient not to move during imaging. In a rectilinear fashion, images are acquired from L1 to L5.

Imaging also may be performed on the femur similar to the spine. The patient lays supine on the table, the legs are straight and a brace is placed on the foot to straighten out the leg and rotate the femoral neck in an outward position. An image is acquired from the mid to lower pelvis bone to just below the femoral head. On completion of imaging, computer processing is performed to calculate bone mineral density results.

Processing of bone mineral densities is easy to perform and can vary slightly from system to system. Processing of the lumbar spine involves applying an edge detection algorithm to find the bone edges. The total projected area of bone can be derived by summing the pixels within the bone edges (Fig. 1). The reported values of the bone mineral density are calculated as mean bone mineral density over all of the pixels of identified bone (*1*).



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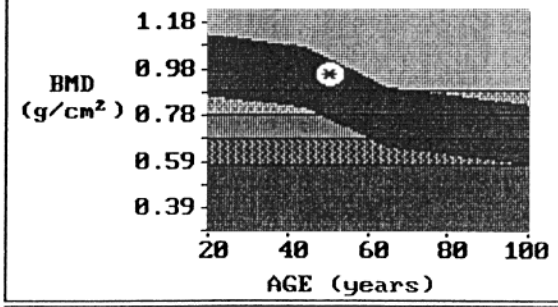
NECK COMPARISON TO REFERENCE



NECK BMD (g/cm²)	0.943 ± 0.02
NECK % YOUNG ADULT[2]	96 ± 3
NECK % AGE MATCHED[3]	107 ± 3

LUNAR®

Age (years).....	51	Large Standard.....	275.36	Scan Mode.....	Medium
Sex.....	Female	Medium Standard.....	204.28	Scan Type.....	DPX
Weight (lb).....	130.0	Small Standard.....	145.50	Source Collimation (mm).	1.68
Height (in).....	68	Low keV Air (cps)...	846919	Sample Size (mm).....	1.2x1.2
Ethnic.....	White	High keV Air (cps)..	501834	Region height (mm).....	60.0
System.....	6218	Rvalue (%Fat).....	1.353(19.6)	Region width (mm).....	15.0
Side.....	Left			Region angle (deg).....	53

NECK	: BMC (grams) =	4.77	AREA (cm²) =	5.06
WARDS	: BMC (grams) =	2.30	AREA (cm²) =	2.84
TROCH	: BMC (grams) =	8.38	AREA (cm²) =	10.77

REGION	BMD g/cm²	% Young[2] Adult	% Age[3] Matched
NECK	0.943 ± 0.02	96	107
WARDS	0.810 ± 0.02	89	106
TROCH	0.778 ± 0.02	101	108

2 - USA Femur Reference Population, Ages 20-40. See Appendices.

3 - Matched for Age, Weight, Ethnic. See Appendices.

FIGURE 2. Example of a normal dual-energy absorptiometry study of the femur. This study was performed on a dual x-ray absorptiometry instrument (DPX system; Lunar, Madison, WI).

Processing of the femur involves determining several regions of interest, including the femoral neck, trochanter, intertrochanteric and Ward's triangle (area in the center of the femoral neck) (Fig. 2). Bone mineral densities are calculated for each of the regions and the total hip bone mineral density is the weighted mean for the femoral neck, trochanter and intertrochanteric sites (*1*).

INTERPRETING DUAL-ENERGY ABSORPTIOMETRY

Dual-energy absorptiometry measurements of bone mineral density generally are expressed as absolute values of mass of bone mineral per unit projected area (g/cm^2) over the region of interest included in the analysis box (*1,2,7,22*). These measurements follow a Gaussian distribution and can be defined in terms of mean and SD. The normal range for bone mineral density can be expressed as the normal population ± 2 SDs (*2*). These values also can be specified as particular to age population (Z-score) or to healthy young adults (T-score) (*1,2,7,22*).

In 1994 the World Health Organization (WHO) reviewed worldwide data on bone density testing and the risk of fracture in a report titled, ''Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis'' (*23*). This report indicated that it would be more appropriate to report bone density values in relation to the peak mean of young normal controls (T-scores) rather than to age-matched controls (Z-Scores). WHO defines bone mineral density values as follows: T-score $\leqq$1.0 SD as normal, $<$1.0–2.5 SD as osteopenia (low bone mass) and $<$ 2.5 SD as osteoporosis.

T scores and Z scores sometimes can present problems because they are not widely understood. An alternative is to present values as a percentage of the mean values for either a young adult or age-matched population (*22*). Reporting in this manner does not take into account the range of values present in the population and has no implications in terms of fracture risk.

It is important to remember that bone density values may vary slightly between systems. If a patient is being followed for treatment, it is important to repeat the bone densitometry study on the same system to prevent measurements that show false improvements.

CONCLUSION

Osteoporosis is considered one of the largest public health problems today. Osteoporosis-related fractures account for more than $14 million in health care costs annually. Bone densitometry has established an important role in diagnosing and treating osteoporosis. It is a precise and accurate tool to assess the risk of fracture, determine a diagnosis of osteoporosis after a fracture, determine low bone mass before a fracture, and measure bone mass in response to treatment.

Dual-energy absorptiometry is the most reliable and accurate method to measure bone mineral density. It remains one of the most commonly ordered procedures in nuclear medicine today. It is easy to perform and standardization of interpretation methods makes the procedure results easy for referring physicians to interpret.

REFERENCES

1. Blake GM, Fogelman I. Applications of bone densitometry for osteoporosis. *Endocrinol Metab Clin North Am*. 1998;27:267–288.
2. Levis S, Altman R. Bone densitometry: clinical consideration. *Arthritis Rheum*. 1998;41:577–587.
3. Merck and Co., Inc. *Osteoporosis Outreach Program*. Whitehouse Station, NJ: Merck and Co., Inc.; 1995.
4. Strange CJ. *Boning Up on Osteoporosis.* Rockville, MD: US Food and Drug Administration; 1997. Available at: www.fda.gov/fdac/features/796_bone.html.
5. National Institutes of Health, Osteoporosis and Related Bone Diseases National Resource Center. *Osteoporosis Overview.* Washington, DC: National Institutes of Health; 1998. Available at: www.osteo.org/osteo.html.
6. Amarillo Medical Specialists, LLP. *Osteoporosis*. Amarillo, TX: Amarillo Medical Specialists; 1998. Available at: www.amarillomed.com/osteopor.htm.
7. Davey DA. Osteoporosis in clinical practice—bone densitometry and fracture risk. *S Afr Med J*. 1998;88:1419–1423.
8. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ III. Population-based study of survival after osteoporotic fractures. *Am J Epidemiol*. 1993;137:1001–1005.
9. The Foundation for Osteoporosis Research and Education. *Guidelines of Care on Osteoporosis for Primary Care Physicians.* San Francisco, CA: The Foundation for Osteoporosis Research and Education; 1998. Available at: http://208.206.61.237/guide/g_intro.html.
10. Consensus Development Conference: diagnosis, prophylaxis and treatment of osteoporosis. *Am J Med.* 1993;94:646–650.
11. Recker RR, Davies KM, Hinders SM, et al. Bone gain in young adult women. *JAMA.* 1992;268:2403–2408.
12. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. *Lancet.* 1993;341:72–75.
13. Blake GM, Fogelman I. Technical principles of dual energy x-ray absorptiometry. *Semin Nucl Med.* 1997;27:210–228.
14. Genant HK, Engelke K, Fuerst T, et al. Noninvasive assessment of bone mineral and structure: state of the art. *J Bone Min Res*. 1996;11:707–730.
15. Guglielmi G, Schneider P, Lang TF, et al. Quantitative computed tomography at the axial and peripheral skeleton. *Eur Radiol.* 1997;7:S32–S42.
16. Ito M, Tsurusaki K, Hayashi K. Peripheral QCT for the diagnosis of osteoporosis. *Osteoporosis Int.* 1997;7:S120–S127.
17. Kalender WA. Effective dose values in bone mineral measurements by photon absorptiometry and computed tomography. *Osteoporosis Int.* 1992;2:82–87.
18. Yates AJ, Ross PD, Lydick E, Epstein RS. Radiographic absorptiometry in the diagnosis of osteoporosis. *Am J Med.* 1995;98:41S-47S.
19. Cunningham JL, Fordham JN, Hewitt TA, Speed CA. Ultrasound velocity and attenuation at different skeletal sites compared with bone mineral density measured using dual energy x-ray absorptiometry. *Br J Radiol*. 1996;69:25–32.
20. Laugier P, Droin P, Laval-Jeantet AM, Berger G. In vitro assessment of the relationship between acoustic properties and bone mass density of the calcaneus by comparison of ultrasound parametric imaging and quantitative computed tomography. *Bone*. 1997;20:157–165.
21. Robinson RG. Measurement studies. In: Early PJ, Sodee DB, eds: *Principles and Practice of Nuclear Medicine.* 2nd ed. Chapter 17: Bone. St. Louis, MO: Mosby-Year Book, Inc.; 1995:363–369.
22. Blake GM, Fogelman I. Interpretation of bone density studies. *Semin Nucl Med.* 1997;27:248–260.
23. World Health Organization. *Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis*. Technical report series 843. Geneva, Switzerland: World Health Organization; 1994.