Dual-Energy X-Ray Absorptiometry Scanning in Practice, Technical Aspects, and Precision Testing

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Department of Endocrinology, Christian Medical College, Vellore, Tamil Nadu, ¹Department of Gynaecology, Tanvir Hospital, Hyderabad, Telangana, India The last three decades have witnessed considerable progress in the field of bone densitometry. Osteoporosis may be diagnosed in postmenopausal women and in men aged 50 and older if the bone mineral density (BMD) T-scores of the lumbar spine, total hip, or femoral neck are -2.5 or less. For reporting T-scores, the Hologic dual-energy X-ray absorptiometry (DXA) scanner uses the Caucasian (nonrace adjusted) female normative database for women and men of all ethnic groups although reference database used does have an impact on the categorization of BMD and must be chosen judiciously considering the regional and ethnic characteristics of the population. The quality control for DXA systems should be periodically done in accordance with manufacturer guidelines for DXA. Beyond conventional BMD assessment, DXA may also be utilized to assess the trabecular bone score, hip structural analysis, vertebral fractures, and body composition.

Keywords: Bone mineral density, database, dual-energy X-ray absorptiometry,

hip structural analysis, quality control, trabecular bone score TBS

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INTRODUCTION

The increase in life expectancy of the Indian population has witnessed an increase in the prevalence of several noncommunicable diseases such as diabetes, obesity, cardiovascular disease, and osteoporosis. Osteoporosis, however, continues to be under-recognized and inadequately treated in many parts of the country. The unfortunate consequence of untreated osteoporosis is a fragility fracture which is associated with high societal costs and is a burden on the patient and the community at large.^[1] It is thus imperative that osteoporosis be identified early so as to facilitate timely and appropriate treatment for the same.

The gold standard in the diagnosis of osteoporosis is the assessment of bone mineral density (BMD) using the dual-energy X-ray absorptiometry (DXA) scan.^[2] The utility of DXA in the comprehensive assessment of bone health cannot be overemphasized. The various aspects of bone densitometry including availability and applicability of DXA, technical details, quality control (QC), and additional uses are described below.

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HISTORY AND EVOLUTION OF DUAL-ENERGY X-RAY ABSORPTIOMETRY

In the early years of measurement of BMD, conventional X-rays were used. However, the inherent disadvantage of using X-rays was that changes were apparent only after 30%–40% of the bone had been lost, during which time the patient would have suffered fractures. This led to the development of single-photon absorptiometry and dual-photon absorptiometry, both of which used high-energy radio-isotopes to assess BMD. In the 1980s, the co-founders of Hologic Dr. David Ellenbogen and Dr. Jay Stein began their work of developing the DXA. In 1987, Hologic developed the first bone densitometry with its proprietary DXA quantitative digital radiography, which has managed to set high-performance standards in the subsequent years.

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The X-ray source of the DXA system generates alternating high- and low-energy waves in a thin beam that passes through Hologic's patented automatic internal reference system. By continually comparing the patient's bone density to a known value contained in the internal reference standard, Hologic systems automatically calibrate each data pixel on every scan. At the time of conception of the DXA systems, a rectilinear pencil beam of X-rays was used; subsequently, the fan beam of X-rays was developed, which helped to reduce scan time and improve efficiency.^[3] As of today, the three major manufacturers of DXA are the Hologic (Waltham, Mass.), Lunar (Madison, Wis.), and Norland (Fort Atkinson, Wis.) systems.

Assessment of Bone Mineral Density and Diagnosis of Osteoporosis

Osteoporosis may be diagnosed in postmenopausal women and in men aged 50 and older if the T-scores of the lumbar spine, total hip, or femoral neck (FN) are -2.5 or less [Table 1]. The distal one-third forearm is used in the diagnosis of osteoporosis only when the hip and spine are nonevaluable in cases of hyperparathyroidism and in very obese subjects who exceed the weight limit for the DXA table.^[4]

T-scores are calculated as the number of standard deviations that the patient's BMD is above or below the young adult reference mean. Similarly, Z-scores are estimated as number of standard deviations that the patient's BMD is above or below the reference mean of the age-matched group. In premenopausal women and men younger than 50 years of age, Z-scores are preferred. A Z-score that is -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]" Although the International Society for Clinical Densitometry (ISCD) recommends screening for all postmenopausal women aged 65 years and above for osteoporosis, the Indian Menopause Society recommends screening of all women

Table 1: Categorization of bone mineral density	
BMD category	Definition
Normal BMD	Spinal or hip BMD within 1.0 SD below the young adult female reference mean (T-score \geq -1.0)
Osteopenia	Spinal or hip BMD between 1.0 and 2.5 SDs below the young adult female reference mean
Osteoporosis	(T-score <-1.0 and >-2.5) Spinal or hip BMD \geq 2.5 SDs below the young adult female reference mean (T-score \leq -2.5)
Severe osteoporosis	BMD ≥2.5 SDs below the young adult female reference mean and the presence of one or more fragility fractures

BMD: Bone mineral density, SD: Standard deviation

5 years after menopause or the presence of other risk factors if within 5 years of menopause.^[5]

Pregnancy is a contraindication to DXA scanning. Other limitations in the use of clinical DXA for total body composition or BMD are body weight exceeding the weight limit of the DXA table, recent administration of contrast material, and/or artifact. Radiopharmaceutical agents may interfere with accuracy of results using systems from some DXA manufacturers.^[4]

DATABASE USED

The Hologic DXA scanner uses the Caucasian (nonrace adjusted) female normative database for women and men of all ethnic groups for computing T-scores. It is recommended that manufacturers continue to use the Third National Health and Nutrition Examination Survey data as the reference standard for FN and total hip T-scores. However, for the lumbar spine, manufacturers may use their own databases as the reference standard for T-scores. In the case of Z-scores, ideally population- and ethnicity-specific data should be used when available.^[4]

The Indian Council of Medical Research (ICMR) has recently published the normative reference for BMD assessment by DXA. The impact of using this database in comparison with the Caucasian database in the categorization of osteoporosis was recently assessed in a study done at the authors' center. Among 2976 subjects, of which 316 had a low impact hip fracture, it was found that there was perfect agreement between the two databases for the diagnosis of osteoporosis at the hip (κ = -0.82, *P* < 0.0001) in all subjects, and a moderate relationship existed in those with hip fracture (κ = -0.65, *P* < 0.0001). Seventy-three of 316 hip fracture subjects (23.5%) defined as osteoporosis according to the Hologic database were classified as osteopenia according to ICMR.^[6]

In another study undertaken by the authors, the influence of various databases in the categorization of BMD in postmenopausal women from southern India was assessed. It was found that among 211 women with FN fractures, osteoporosis at FN was found in 72% with Caucasian, 88% with North Indian, 56% with Italian, and 45% with Korean database. On comparing manufacturer-provided database with the other population-specific reference, there were perfect agreement with North Indian ($\kappa = 0.81$ [FN], $\kappa = 0.82$ [LS]) and good agreement with the Italian database ($\kappa = 0.78$ [FN], $\kappa = 0.74$ [LS]).^[7] Thus, the reference database used does have an impact on the categorization of BMD and must be chosen judiciously considering the regional and ethnic characteristics of the population.

SERIAL BONE MINERAL DENSITY ASSESSMENT

Serial BMD evaluation in combination with clinical assessment of fracture risk, bone turnover markers, and other factors including height loss and trabecular bone score, may be used to determine whether treatment should be initiated in untreated patients, according to locally applicable guidelines. Serial assessment of BMD is also used to monitor response to therapy and to monitor individuals following cessation of anti-osteoporotic therapy. While on treatment, the loss of bone density that is detected on repeat BMD evaluation, indicates the need for assessment of treatment adherence, evaluation of secondary causes of osteoporosis, and re-evaluation of treatment options. Intervals between BMD testing should be determined according to each patient's clinical status; usually, this is 1 year after initiation or change of therapy with longer intervals once therapeutic effect is established. In conditions associated with rapid bone loss, such as chronic glucocorticoid use, more frequent testing may be warranted.^[4]

RADIATION SAFETY

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The effective dose from a DXA scan (<10 microsieverts) is among the lowest of all the radiological investigations. In comparison, a conventional X-ray of the chest in PA and lateral views require 60 uSi, a mammogram about 130 uSv, and a computed tomography (CT) scan of the pelvis about 5000 uSv. Thus, DXA scan is a lowcost and safe procedure which may be used not only to monitor BMD but also to assess the efficacy of therapy and in making assessments pertaining to precision of the equipment.^[8]

ACCURACY, PRECISION, AND QUALITY CONTROL

Accuracy is defined as how well the measured value reflects the true value of the object measured. Accuracy is calculated as the difference between the true and measured values compared to the true value of the quantity measured expressed in percent. Usually, the accuracy error of a DXA instrument is better than 10% and is sufficient for the clinical assessment of facture risk and the diagnosis of osteoporosis according to the World Health Organization criteria.

Precision, on the other hand, refers to reproducibility and refers to the ability of the DXA scan to produce the same numerical result on a repeat test done in an identical fashion. For DXA, the ISCD recommends that the precision be calculated as the root mean squared standard deviation. The least significant change in BMD that can be recognized with 95% confidence is 2.77 times the precision. For example, if the precision error of a DXA scan is 2%, then, the difference between two consecutive BMD readings should exceed 5.54% (2.77 * 2%) to demonstrate that the BMD difference is significant. At the authors' center, the precision error of measurement of BMD at the lumbar spine and hip is <1% and 1%–2%, respectively.

The QC for DXA systems is done in accordance with manufacturer guidelines for DXA. It is recommended that periodic phantom scans be performed for the purpose of system calibration. The anthropomorphic lumbar spine phantom mean BMD should be verified from time to time and corrective action should be enforced at thresholds that trigger a call for service.^[8]

AVAILABILITY

Osteoporosis is a common public health problem, and is unrecognized in most parts of the country. The gold standard in the diagnosis of osteoporosis is the DXA scan, the availability of which across the country is grossly inadequate.^[9] It is important to improve awareness on osteoporosis among physicians as well as patients.^[10,11] The consequences of untreated osteoporosis are fragility fractures of the spine and hip which are associated with high morbidity and mortality and increased societal costs. Improving the accessibility and availability of DXA will enable the early screening and diagnosis of osteoporosis, the treatment of which will improve the quality of life of at-risk individuals.

Additional Uses

Besides conventional BMD assessment, the DXA systems are also equipped with additional software which enables a more comprehensive assessment of bone health. Body composition analysis may also be performed using the DXA scan. These additional tools are elaborated below.

Trabecular bone score

Trabecular bone score (TBS) is a novel method that assesses skeletal micro-architecture from the lumbar spine DXA images.^[12,13] TBS may help in improving fracture risk prediction beyond BMD assessment and can be incorporated to the Fracture Risk Assessment Tool to enhance fracture prediction.^[14] There is insufficient evidence that TBS can be used to monitor treatment with bisphosphonates. A recent study undertaken at the authors' center demonstrated that the TBS remained stable on bisphosphonate therapy in postmenopausal women with osteoporosis at 2 years of follow-up.^[15] TBS may also be particularly helpful to assess fracture risk in diabetes.^[16]

Hip structural analysis

Apart from BMD, bone strength is also determined by biomechanical and geometric properties of the bone, as well as the direction and magnitude of the force applied. The hip structural analysis (HSA) program was introduced to extract information on geometric strength of the hip from archived DXA images.^[17] The components of the HSA are shown in Table 2. The HSA program may find additional benefit in certain disease cohorts where mere assessment of BMD may not convey ample information about all aspects of bone health.^[16,18]

Vertebral fracture assessment

Vertebral fracture assessment (VFA) is a densitometric technique to image the spine for the purpose of detecting vertebral fractures. A VFA is indicated when the lumbar spine T-score is $\langle -1.0 \rangle$ and any one of the following risk factors is present: (i) women aged $\geq 70 \rangle$ years or men aged $\geq 80 \rangle$ years, (ii) historical height loss $\geq 4 \rangle$ cm (≥ 1.5 "), (iii) self-reported but undocumented prior vertebral fracture, and (iv) glucocorticoid therapy equivalent to $\geq 5 \rangle$ mg of prednisone or equivalent per day for $\geq 3 \rangle$ months. The Genant visual semi-quantitative method is the current clinical technique of choice for diagnosing vertebral fracture with VFA.^[14,19]

Screening for atypical femoral fracture

DXA may also be used to detect abnormalities in the spectrum of atypical femoral fracture (AFF). The scans obtained should include full-length femur images (FFIs) and state the presence or absence of focal cortical abnormalities. Bilateral FFI should be done in subjects who have received bisphosphonates or denosumab or have discontinued it within the last year, with a

Table 2: Components of the hip structural analysis program with definitions

Component	Definition
of HSA	
CSA (cm ²)	Excludes soft spaces in the marrow and pores
	and is an index of resistance to axial forces
CSMI (cm ⁴)	Provides an estimate of resistance to bending
	forces in a cross-section
Section	Index of strength calculated as the CSMI+the
modulus (Z)	distance from the bone edge to the centroid
(cm ³)	(assumed here to be half the subperiosteal width)
BR	Index of susceptibility to local cortical buckling
	under compressive loads. A buckling ratio (NN)
	of >10 was considered to be deleterious (7)
HAL (mm)	Distance from the pelvic rim to the outer margin
	of greater trochanter along the neck axis
NSA	Angle between derived axis of neck and shaft
HSA: Hip strue	ctural analysis, CSA: Cross-sectional area,

CSMI: Cross-sectional moment of inertia, BR: Buckling ratio, HAL: Hip axis length, NSA: Neck shaft angle, NN: Narrow neck cumulative exposure of 3 or more years, and especially those on glucocorticoids. $\ensuremath{^{[4]}}$

Body composition assessment

DXA scans may also be utilized to perform a body composition analysis, and it is recommended that total body (with head) values of BMI, BMD, bone mineral content, total mass, total lean mass, total fat mass, and percent fat mass should appear on all reports. Other measures of adiposity and lean mass include visceral adipose tissue, appendicular lean mass (ALM) index (ALM divided by height squared [ALM/height²]), android/gynoid percent fat mass ratio, trunk-to-leg fat mass ratio, lean mass index (total lean mass/height²), and fat mass index (fat mass/height2). The use of DXA adiposity measures (percent fat mass or fat mass index) may be useful in risk-stratifying patients for cardiometabolic outcomes. Low lean mass could be defined using ALM/height² with Z-scores derived from a young adult-, race-, and sex-matched population.^[4]

ALTERNATE SYSTEMS TO ASSESS BONE Health

These include the quantitative CT (QCT), peripheral QCT, quantitative ultrasound, and the peripheral DXA. Bone density measurements from different devices cannot be directly compared.^[20] These systems should be independently validated for fracture risk prediction from prospective trials or by demonstration of equivalence to a validated standard device. A detailed description of these is beyond the scope of this review.

CONCLUSION

DXA has been commercially available for more than three decades. The advantages of DXA as compared to its predecessors include reduced radiation exposure, faster scan acquisition, and increased precision of measurements. DXA continues to be a comprehensive platform for assessment of bone health as well as body composition in current clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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