Review

QJM

DXA scanning in clinical practice

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Summary

Dual-energy X-ray absorptiometry (DXA) is recognized as the reference method to measure bone mineral density (BMD) with acceptable accuracy errors and good precision and reproducibility. The World Health Organization (WHO) has established DXA as the best densitometric technique for assessing BMD in postmenopausal women and based the definitions of osteopenia and osteoporosis on its results. DXA allows accurate diagnosis of osteoporosis, estimation of fracture risk and monitoring of patients undergoing treatment. However, when DXA studies are performed incorrectly, it can lead to major mistakes in diagnosis and therapy. This article reviews the fundamentals of positioning, scan analysis and interpretation of DXA in clinical practice.

Introduction

Osteoporosis is a metabolic bone disorder characterized by low bone mass and microarchitectural deterioration, with a subsequent increase in bone fragility and susceptibility to fracture. Dual-energy X-ray absorptiometry (DXA) is recognized as the reference method to measure bone mineral density (BMD) with acceptable accuracy errors and good precision and reproducibility.[1] The World Health Organization (WHO) has established DXA as the best densitometric technique for assessing BMD in postmenopausal women and based the definitions of osteopenia and osteoporosis on its results (Table 1).[2,3] DXA allows accurate diagnosis of osteoporosis, estimation of fracture risk and monitoring of patients undergoing treatment. Additional features of DXA include measurement of BMD at multiple skeletal sites, safety of performance, short investigation time and ease of use.[4–6] A DXA measurement can be completed in about 5 min with minimal radiation exposure (about one-tenth that of a standard chest X-ray for a quick hips and spine exam).

Principle of DXA scanning

As with many other diagnostic examinations, DXA scans should be critically assessed by the interpreting physician and densitometrist for abnormalities that may affect BMD measurements. In clinical practice, recognition of diverse artifacts and disease processes that may influence BMD results can be of major importance in the optimal interpretation of DXA scans.[7] Physicians not directly involved in the performance and interpretation of DXA should be familiar enough to detect common positioning and

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Table 1 WHO osteoporosis classification

Diagnosis	T-score
Normal	>-1.0
Osteopenia	$<-1.0, >-2.5$
Osteoporosis	<-2.5
Severe osteoporosis	<-2.5 plus fragility fractures

scanning problems, to know what should appear on a report, what questions to ask if the necessary information is not on the report, how to apply the results in patient management and when to do and how to interpret a second measurement to monitor treatment.[8]

Several different types of DXA systems are available, but they all operate on similar principles. A radiation source is aimed at a radiation detector placed directly opposite to the site to be measured. The patient is placed on a table in the path of the radiation beam. The source/detector assembly is then scanned across the measurement region. The attenuation of the radiation beam is determined and is related to the BMD.[9,10]

Because DXA scanners use two X-ray energies in the presence of three types of tissue (bone mineral, lean tissue and adipose tissue), there are considerable errors arising from the inhomogeneous distribution of adipose tissue in the human body[11] (which can be studied either through cadaver studies,[12] CT imaging to delineate the distribution of adipose tissue external to bone[13,14] or MRI to measure the percentage of marrow fat inside bone[15]). These studies suggest BMD measurement errors of around 5–8%.

DXA technology can measure virtually any skeletal site, but clinical use has been concentrated on the lumbar spine, proximal femur, forearm and total body.[6] DXA systems are available as either full table systems (capable of multiple skeletal measurements, including the spine and hip) or as peripheral systems (limited to measuring the peripheral skeleton). Because of their versatility, and the ability to measure the skeletal sites of greatest clinical interest, full table DXA systems are the current clinical choice for osteoporosis assessment. Peripheral DXA systems, portable and less expensive than full table systems, are more frequently used as screening and early risk assessment tools; they cannot be used for treatments follow-up. Spine and proximal femur scans represent the majority of the clinical measurements performed using DXA. Most full table DXA systems are able to perform additional scans, including lateral spine BMD measurements, body composition study, assessment

of vertebral fractures, measurements of children and infants, assessment of bone around prosthetic implants, small-animal studies and measurements of excised bone specimens. However, for children measurement, the exam should be undertaken by clinicians skilled in interpretation of scans in children in centers that have an adapted pediatric software.

Early DXA systems used a pencil beam geometry and a single detector, which was scanned across the measurement region. Modern full table DXA scanners use a fan-beam source and multiple detectors, which are swept across the measurement region. Fan beam provides the advantage of decreased scan times compared with single-beam systems, but these machines typically cost more because of the need for multiple X-ray detectors. Fan-beam systems use either a single-view or multiview mode to image the skeleton.[16]

In clinical practice, BMD measurements are widely used to diagnose osteoporosis and measurement in bone mass are commonly used as a surrogate for fracture risk.[17] BMD is the measured parameter, and allows the calculation of the bone mineral content (BMC) in grams and the two-dimensional projected area in cm^2 of the bone(s) being measured; thus the units of BMD are g/cm^2. The BMD values (in g/cm^2) are not used for diagnosing osteoporosis. Instead, a working group of the WHO proposed to define osteoporosis on the basis of the T-score [which is the difference between the measured BMD and the mean value of young adults, expressed in standard deviations (SD) for a normal population of the same gender and ethnicity].[8] Despite its limitations; this definition, which concerns only postmenopausal women and men over 50, is currently applied worldwide. Thus, the WHO diagnostic criteria for osteoporosis define osteoporosis in terms of a T-score below -2.5 and osteopenia when T-score is between -2.5 and -1.

The T-score is calculated using the formula: (patient's BMD − young normal mean)/SD of young normal. For example, if a patient has a BMD of $0.700 \, g/cm^2$, the young normal mean is $1.000 \, g/cm^2$, and the young normal SD is $0.100 \, g/cm^2$, then this patient's T-score would be $(0.700-1.000)/0.100$, or $-0.300/0.100$, or -3.0.[8] A T-score of 0 is equal to the young normal mean value, -1.0 is 1 SD low, -2.0 is 2 SD low, etc. Although, the WHO classification was not intended to be applied to individual patients, it works well to define 'normal' (T-score -1.0 and above) and 'osteoporosis' (T-score -2.5 and below). Several large studies have shown an unacceptably high risk of fracture in postmenopausal women who have T-scores of -2.5 and below. Thus, this threshold is

the cornerstone of the patient's assessment. For the therapeutic decisions, however, other risk factors are considered such as prevalent fractures, age and low body mass index.

In addition to the *T*-scores, DXA reports also provide *Z*-scores, which are calculated similarly to the *T*-score, except that the patient's BMD is compared with an age-matched (and race- and gender-matched) mean, and the result expressed as a SD score.[8] In premenopausal women, a low *Z*-score (below −2.0) indicates that bone density is lower than expected and should trigger a search for an underlying cause.

Who should have a DXA measurement?

Most official groups recommend screening healthy women for osteoporosis at age 65, and testing higher-risk women earlier.[18] In Europe the recommendations are to screen for risk factors of osteoporosis and to perform BMD measurement in women with such risks. The International Society for Clinical Densitometry (ISCD) recommends screening men without risk factors for osteoporosis at age 70, and screening higher-risk men earlier. Risk factors include dementia, poor health, recent falls, prolonged immobilization, smoking, alcohol abuse, low body weight, history of fragility fracture in a first-degree relative, estrogen deficiency at an early age (<45 years) and steroid use for more than 3 months. Of course, BMD testing is an appropriate tool in the evaluation of patients who have diseases (e.g. hyperthyroidism, hyperparathyroidism, celiac disease, etc.) or use medications (e.g. glucocorticoids, GnRH agonists, aromatase inhibitors, etc.) that might cause bone loss. Another indication is radiographic evidence of 'osteopenia' (or a vertebral fracture).

Recently, many epidemiological studies have validated risk assessment indices for osteoporosis in women. The purpose of the risk assessment indices is not to diagnose osteoporosis or low BMD, but to identify women who are more likely to have low BMD.[19] Such indices, while not identifying all cases of osteoporosis, increase the efficiency of BMD measurement by focusing on subjects who are at increased risk.[20–22] The easiest to use in clinical practice is certainly the Osteoporosis Self-assessment Tool (OST). The calculated risk index is based on self-reported age and weight: [(weight in kilograms − age in years) × 0.2, truncated to an integer]. It was developed and validated in several studies in Asian and White women[23–25] and men.[26,27]

Site of measurement of BMD

The ISCD recommends obtaining BMD measurements of the posteroanterior spine and hip.[28] The lateral spine and Ward's triangle region of the hip should not be used for diagnosis, because these sites overestimate osteoporosis and results can be false-positive. Evidence suggests that the femur (neck or total hip) is the optimum site for predicting the risk of hip fracture and the spine is the optimum site for monitoring response to treatment. Thus, many authors recommend hip measure alone for the fracture risk assessment.[29–34] In very obese patients, those with primary hyperparathyroidism, or those in whom the hip or the spine, or both, cannot be measured or interpreted, BMD may be measured in the forearm, using a 33% radius on the nondominant forearm.

Interpreting a DXA scan

The most important informations to check are the correct identification of the patient, his date of birth and also the sex and ethnicity which are mandatory to calculate *T*-scores. Sex is used by all manufacturers to calculate *T*-scores (i.e. *T*-scores for women are calculated using a female normative database, while *T*-scores for men are calculated using a male normative database). Although, all manufacturers use race in calculating *Z*-scores, there is inconsistency in the way race is handled when calculating *T*-scores. Norland and Hologic are using race in calculating *T*-scores (i.e. *T*-scores for Caucasians are calculated using a Caucasian normative database, *T*-scores for Blacks are calculated using a normative database for Blacks); however, GE Lunar and recent Hologic machines use the database for young-normal Caucasians to calculate *T*-scores, regardless of the race of the subject. The ISCD recommends the latter approach for use in North America[35] because using race-adjusted *T*-scores results in a similar prevalence of 'osteoporosis' in every racial group, despite the fact that age-specific fracture rates can be very different.

Positioning

The main purpose of the DXA scan image is to check if the patient is positioned correctly, something that the technologist must determine before the patient leaves the testing center. Positioning should also be doublechecked by the clinician who interprets the test.[7] There are many available resources for BMD technologists and physicians training, such as ISCD or International Osteoporosis Foundation (IOF) courses.
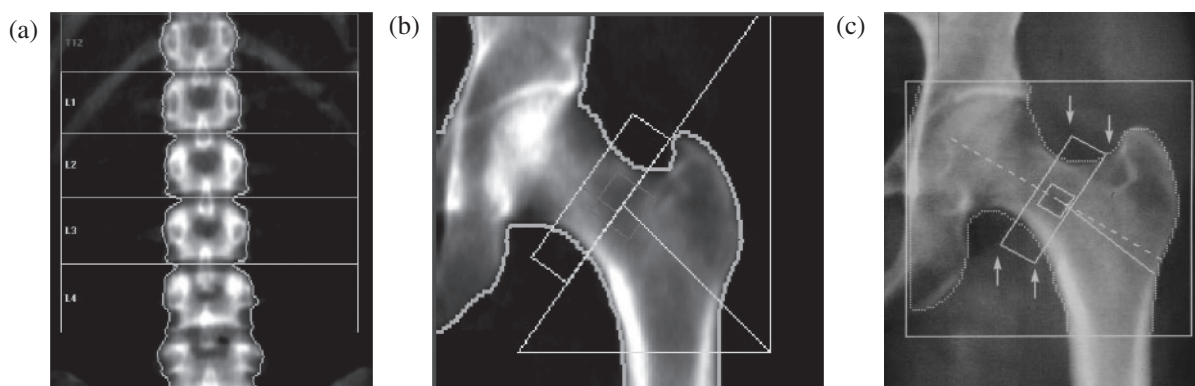
Figure 1. Correct positioning and analysis of the L1–L4 spine **a** and the proximal femur (Lunar **b** and Hologic **c**).

A scan with correct positioning of the spine is shown in Figure 1a the patient is straight on the table (spine is straight on the image), not rotated (spinous processes are centered), and centered in the field (roughly equal soft tissue fields on either side of the spine). Patients with scoliosis cannot be positioned with the spine straight on the table; moreover with severe scoliosis degenerative changes can occur that invalidate the spine measurement. The scan should extend up sufficiently far to include part of the lowest vertebra with ribs (which is usually T12) and low enough to show the pelvic brim (which is usually the level of the L4–L5 interspace). Most testing centers will elevate the patient's knees with a foam block (hip at a 90° angle to the spine) to try to partially flatten the normal lumbar lordosis. For proper positioning of the hip, the patient should have the femur straight on the table (shaft parallel to the edge of the picture), with 15–25° of internal rotation, which can be achieved by the use of positioning devices. Internal rotation may be improved by having the patient flex the foot before doing the internal rotation, and then relaxing the foot after the strap is in place. This amount of internal rotation presents the long axis of the femoral neck perpendicular to the X-ray beam, providing the greatest area and the lowest BMC (and the lowest BMD), and is confirmed on the scan by seeing little or none of the lesser trochanter (Figure 1b).[4,36] If the desired amount of internal rotation cannot be achieved, as is often the case in patients with hip arthritis or short femoral necks, the technologist should place the patient comfortably in a position that is likely to be reproducible in a subsequent scan.[5,37]

DXA scan analysis

The software marks regions of interest in the spine and hip, but the technologist can and should make adjustments if needed. The spine region of interest consists of the L1 through L4 vertebrae (Figure 1a). Correct placement of the top and bottom of the spine 'box' is critical. The intervertebral lines can be moved or angled, if necessary. There must be sufficient soft tissue on both sides of the spine; otherwise BMD will be under estimated. The hip regions of interest include the femoral neck, trochanter and total hip (Figure 1b). Ward's region and the intertrochanteric region are not relevant (and can be deleted from the results reports). The default hip analysis includes a midline that must be placed correctly for the other sites to be identified correctly. The preferred position for the rectangular femoral neck box differs for different manufacturers. For GE Lunar, the femoral neck box is located by the analysis program at the narrowest and lowest density section of the neck; typically this will be about half way between the femoral head and the trochanter (Figure 1b). For Hologic the box is on the distal part of the femoral neck (Figure 1c). This induces a large difference among these two measurements, because of a gradient of BMD all along the femoral neck (the proximal being the highest, the distal being the lowest). Thus careful checking of the femoral neck box is mandatory.

The image should be evaluated for artifacts (e.g. surgical clips, navel rings, barium sulphate, metal from zipper, coin, clip, or other metallic object) or local structural change (e.g. osteophytes, syndesmophytes, compression fractures and aortic calcification). Almost all artifacts and local structural change will spuriously elevate BMD.[38] This is especially true for spinal degenerative change, which can elevate spine BMD by 2, 3, or more *T*-score. In the spine, absent bone (laminectomy or spina bifida) or vertebral rotation (idiopathic scoliosis) will spuriously lower BMD. All evaluable vertebrae should be used, but vertebrae that are affected by local structural change should be deleted from the analysis. Most agree that decisions can be based on two vertebrae; the use of a single vertebra is not
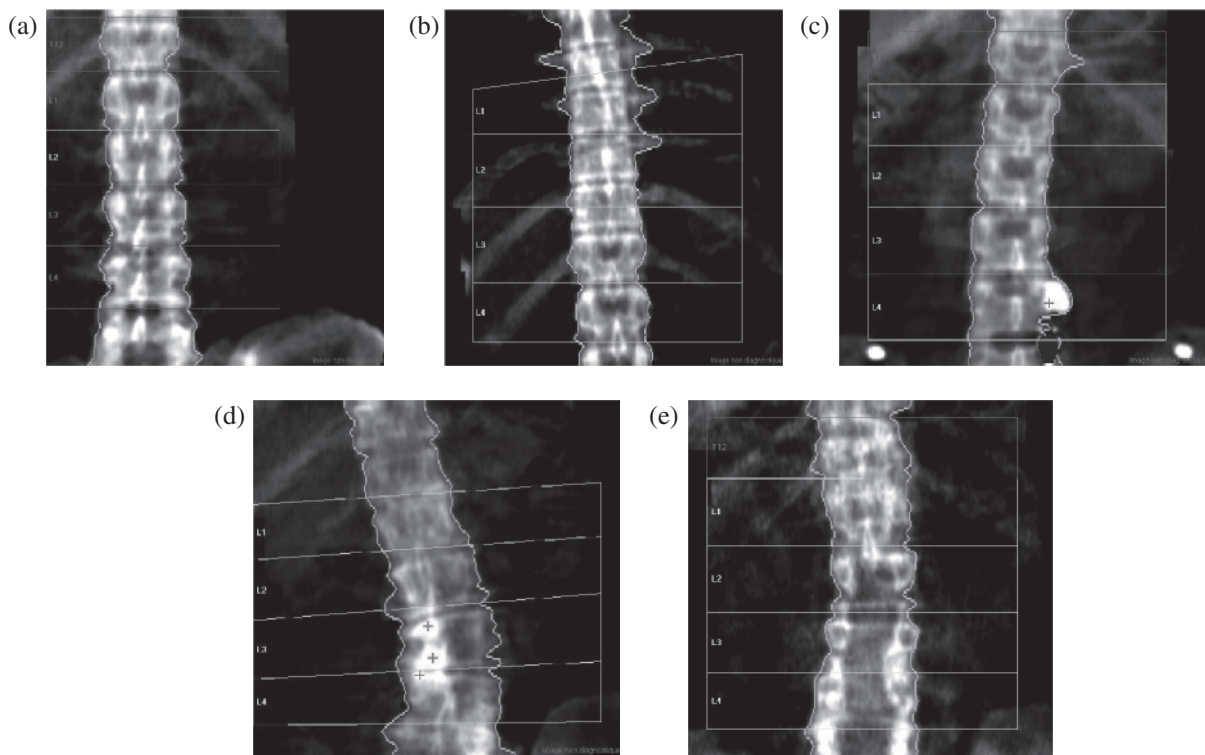
Figure 2. Examples among some common spine scanning problems: **a** The spine is too close to the right side of the image **b** Vertebral levels are mis-identified **c** Metal button over L4 **d** Scoliosis and osteophyte at L3–L4 **e** Laminectomy.
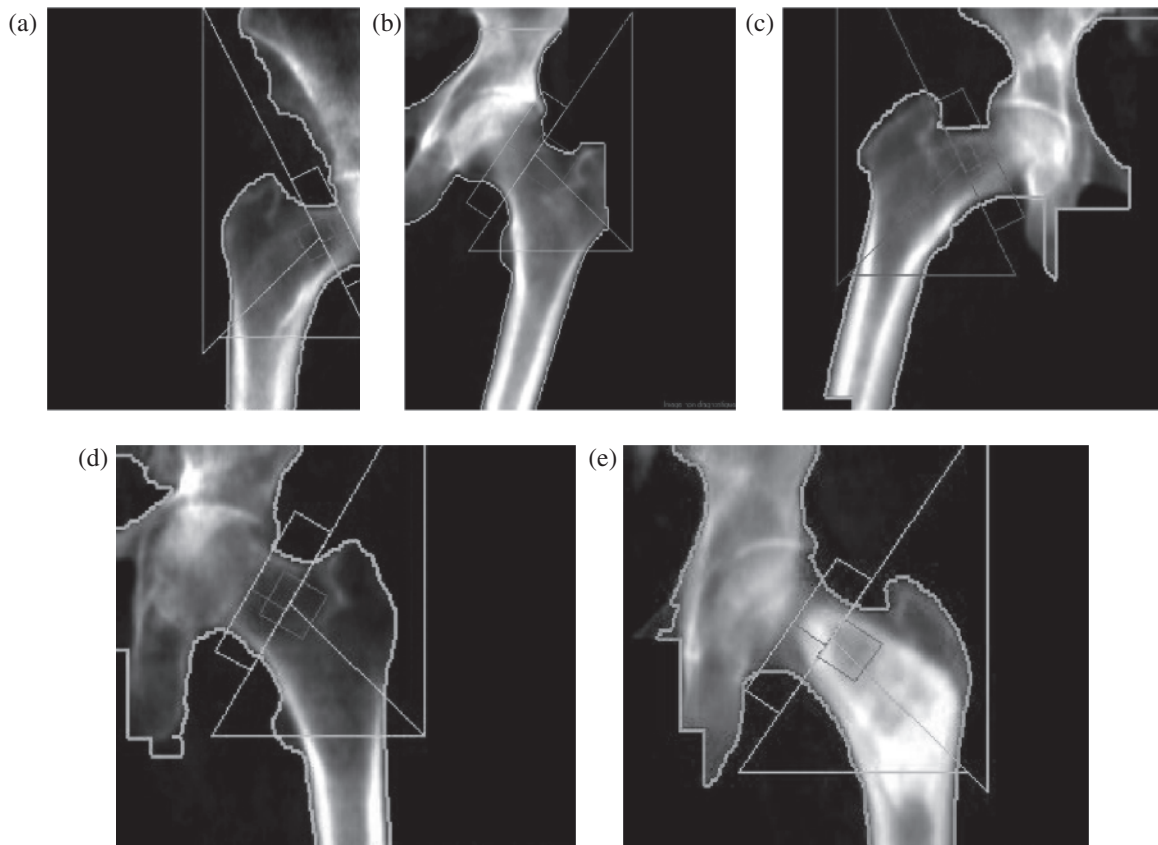

Figure 3. Examples among some common hip scanning problems: **a** The scan did not go far enough laterally and part of the femoral head is missing **b** The femur is adducted **c** The femur is abducted **d** Suboptimal internal rotation (too much of the lesser trochanter is showing) **e** Abnormal bone (history of hip fracture and osteosynthesis).
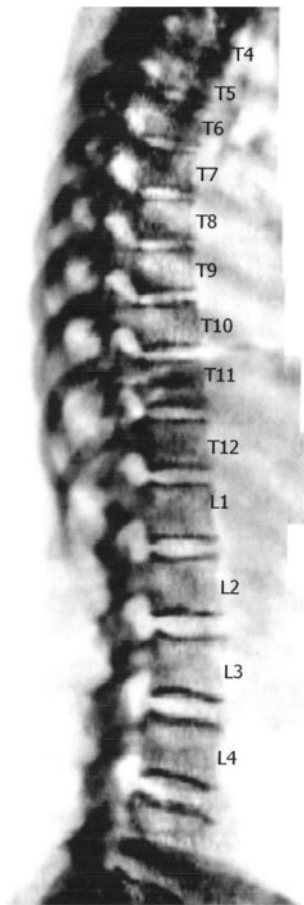
Figure 4. Vertebral fracture assessment from a dual X-ray absorptiometry image of the spine.

recommended. If all vertebrae are affected, the spine should be reported as 'invalid,' with no BMD or *T*-score results given. Figures 2 and 3 show examples from common spine and hips scanning problems.

Finally, physicians must keep in mind to actively look for secondary osteoporosis in front of low BMD value, either by thorough history taking or with biochemical studies before stating about postmenopausal osteoporosis.

Vertebral fracture assessment (VFA)

For assessing vertebral heights (also called vertebral morphometry), a special software is used to determine vertebral body dimensions. The computer (with the help of the technologist) places points on the superior and inferior endplates of each vertebra. The vertebral heights are calculated and compared with each other as well as to the expected normal dimensions. With the advent of higher-resolution DXA systems, visual assessment of fractures is also possible from DXA-based lateral spine images

(Figure 4). In this situation, the DXA system essentially functions as a digital X-ray imaging device. Visual assessment is performed from a computer monitor or high-resolution printout. To optimize the assessment, the use of high-definition dual-energy images has been recommended.[39–41] Using a DXA system for assessing vertebral fracture status has several advantages. The evaluation of spine fractures can be performed without a conventional lateral spine X-ray. This can be done at the same time and at the same place as the BMD measurement, with much less radiation than a conventional spine X-ray. Moreover, VFA is a technology for diagnosing vertebral fractures that may alter diagnostic classification, improve fracture risk stratification, and identify patients likely to benefit from pharmacological therapy who otherwise might not be treated.[39,42] Despite the apparent advantages, the future of VFA using DXA remains unclear. Skeletal radiologists have criticized the technique for being insensitive and inaccurate for detecting vertebral fractures in particular at the upper thoracic spine. A DXA image is of lower resolution than a conventional X-ray and might fail to identify other potential problems or diseases that would be apparent on a spine film. However, VFA allows ruling out vertebral fracture at levels where vertebral fracture is most common, i.e. the lumbar and the mid and lower thoracic levels, and the pencil beam mode of assessment eliminates parallax errors in viewing the vertebral body, which can sometimes make a normal vertebral body appear to have been compressed in a routine spine X-ray.[41,43–45]

At this time, DXA devices are not generally accepted as a surrogate for spinal X-rays, though they may provide a useful screening tool in higher-risk patients when spinal X-rays are unavailable. For example, individuals over 65, subjects reporting significant height loss or patients on long-term glucocorticoid therapy who have not had previous vertebral fractures or spinal radiographs could benefit from a VFA.

Concordance between measurement sites

It is recommended to measure the PA lumbar spine and proximal femur and classifying the patient based on the lowest *T*-score from three sites (lumbar spine, femoral neck and total hip). Although, the BMDs at different anatomic regions are correlated, the agreement between sites is low when it comes to classifying individual subjects as osteoporotic or not. Thus, *T*-score discordance

between the lumbar spine and hip testing sites is a commonly observed phenomenon in densitometry. *T*-score discordance is the observation that the *T*-score of an individual patient varies from one key measurement site to another.

Prevalence and risk factors of *T*-score discordance

Various studies have analyzed the prevalence and impact of *T*-score discordance on the management of osteoporosis.[46–49] Only two studies focused on risk factors of this commonly observed discordance.[46,50,51] Five different causes for occurrence of discordance between the spine and the hip sites have been described.[47]

1. Physiologic discordance is related to the skeleton's natural adaptive reaction to normal external and internal factors and forces. Mechanical strain especially related to weight bearing plays a key role in this kind of discordance. An example of this type of discordance is the difference observed between the dominant and nondominant total hip.[37] The explanation is that weight bearing can cause rise in bone density especially in the hip and femur regions. Moreover, the spine and hips usually start out with different *T*-scores (the spine is said to reach peak at least 5 years before the hip).[52] And finally, bone loss observed with age in an individual may be more rapid and important in trabecular than cortical bone is another explanation.[53] Trabecular bones (typical of lumbar area) are known to have a more rapid rate of deprivation in early postmenopausal state in comparison with cortical bone (typical of proximal femur).

2. The second type of discordance described as pathophysiologic discordance is seen secondary to a disease. Common examples observed in the elderly include vertebral osteophytosis, vertebral end plate and facet sclerosis, osteochondrosis, and aortic calcification.[54,55] Another important cause in younger patients is ankylosing spondylitis syndesmophytes.[38,56–59] The abnormal calcium deposition within the field of the DXA region of interest (ROI) leads to the falsely elevated spine *T*-score. A second subtype is a true discordance resulting from a more decreased BMD in the lumbar spine than the hips. Indeed, most of the etiologiess of the secondary osteoporosis (such as glucocorticoid excess, hyperthyroidism, malabsorption, liver disease and rheumatoid arthritis) first affect spinal column.[60,61] This will lead to higher prevalence of lumbar osteoporosis.

3. Anatomic discordance is owing to differences in the composition of bone envelopes tested. An example is the difference in *T*-scores found for the posteroanterior lumbar spine and the supine lateral lumbar spine in the same patient.

4. Artifactual discordance occurs when dense synthetic manmade substances are within the field of ROI of the test: e.g. barium sulphate, metal from zipper, coin, clip, or other metallic object.

5. And finally, technical discordance occurs because of device errors, technician variability, patients' movements, and variation due to other unpredictable sources. With respect to positioning error, some studies showed that either excessive internal or external rotation of the femur during test acquisition resulted in a BMD difference of as much as 10% compared with correct positioning. We demonstrated in a previous study that DXA *in vivo* reproducibility is 2-fold better in the hips than the spine especially when measuring both hips.[56] Finally, technical discordance can occur due to the normative reference data used by the device software to analyze the test.[5,62,63] This type of discordance occurs when the average BMD of the normative group used to calculate the *T*-score is significantly different from the average value found for the whole population.

Consequences of *T*-score discordance on osteoporosis management

The high prevalence of *T*-score discordance could induce some problems for the physicians in decision-making regarding these patients. In general, high prevalence of discordance between lumbar spine and hip *T*-scores suggests some defects in the cut-off values for definition of osteoporosis and osteopenia proposed with the WHO. The inconsistencies in the diagnostic classification of osteoporosis between skeletal sites lend credence to the notion that BMD should be used as only one of the factors in making therapeutic decisions when evaluating patients with osteoporosis. An international team convened by the WHO is trying to develop a globally applicable measure of absolute fracture risk based upon multiple risk factors including BMD. This could silence much of the controversy regarding the choice of reference data for *T*-score calculation and usefulness of relatively arbitrary densitometric categorizations. However, one can speculate that discordance in individual fracture risk estimation with this new absolute fracture risk will still be observed, as it will be based on different sites BMD.

Monitoring of DXA

It has become more and more common to perform a second DXA measurement to monitor BMD status or the effect of therapeutic intervention. When a second measurement is performed on a patient, the clinician needs to distinguish between a true change in BMD and a random fluctuation related to variability in the

measurement procedure. The reproducibility of DXA measurements is claimed to be good. Such variability is due to multiple causes, such as device errors, technician variability, patients' movements, changing in the area of interest and variation due to other unpredictable sources.[64–68] Under ideal conditions, the same technologist should perform DXA scans on the same densitometer and under similar circumstances.[69]

The precision error (PE) is usually expressed as the coefficient of variation (CV), which is the ratio of the SD to the mean of the measurements, although several other statistics to express reproducibility exist such as the smallest detectable difference (SDD) or the least significant change (LSC). The SDD represents a cut-off that can be measured in an individual and is usually considered more useful than the CV in clinical practice.

Methods of BMD reproducibility measurement

PEs are evaluated by performing repeated scans on a representative set of individuals to characterize the reproducibility of the technique.[70] Most published studies examine the short-term PE, based on repeated measurements of each subject performed over a time period of no more than 2 weeks. Over such a short period, no true change in BMD is expected.

The coefficient of variation

The CV, the most commonly presented measure for BMD variability, is the SD corrected for the mean of paired measurements. CV, expressed as a percentage, is calculated as $CV(\%) = (\sqrt{((\sum (a-b)^2)/2n))}/((Ma+Mb)/2) \times 100$ where a and b are the first and the second measurement, Ma and Mb are the mean values for the two groups and n is the number of paired observations.

Reproducibility is far better for BMD measurement than for most laboratory tests. Reproducibility expressed by the CV is usually 1–2% at the spine on anteroposterior images and 2–3% at the proximal femur in individuals with normal BMD values; the difference between the two sites is ascribable to greater difficulties with repositioning and examining the femur, as compared with the spine. However, these data obtained under nearly experimental conditions may not apply to everyday clinical practice. Reproducibility depends heavily on quality assurance factors, including tests to control the quality and performance of the machine, as well as the experience of the operator. Assessment of machine performance requires daily scanning of a phantom

(which may be anthropomorphic or not), followed by calculation of the *in vitro* CV, which serves to evaluate short-term and long-term performance and to detect drift in measurement accuracy. These *in vitro* data, however, do not necessarily reflect *in vivo* reproducibility, which should be evaluated at each measurement center.[71] Measurements are obtained either thrice in each of 15 patients or twice in each of 30 patients and the CV (m/r) is calculated from the mean (m) and SD (r) of these repeated measurements. The CV is expressed as a percentage and depends on mean BMD values. The SD reflects measurement error, which is a characteristic of machine performance and is independent from the value measured.

The least significant change

For two point measurements in time, a BMD change exceeding $2\sqrt{2}$ times the PE of a technique is considered a significant change (with 95% confidence): the corresponding change criterion has been termed 'least significant change' or LSC. $LSC = 2.8 \times PE$; where PE is the largest precision error of the technique used (or more easily the CV expressed in percentage). This smallest change that is considered statistically significant is also expressed in percentage.

The smallest detectable difference

The measurement error can be calculated using Bland and Altman's 95% limits of agreement method.[72] Precision expressed by this method gives an absolute and metric estimate of random measurement error, also called SDD. In this case, where there are two observations for each subject, the SD of the differences (SD_{diff}) estimates the within variability of the measurements. Most disagreements between measurements are expected to be between limits called 'limits of agreement' defined as $d \pm z_{(1-a/2)} SD_{diff}$ where d is the mean difference between the pairs of measurements and $z_{(1-a/2)}$ is the $100(1-a/2)$ th centile of the normal distribution. The value d is an estimate of the mean systematic bias of measurement 1 to measurement 2. d is expected to be 0 because a true change in BMD is not assumed to occur during the interval between the two BMD measurements. Defining a to be 5%, the limits of agreement are $+1.96 SD_{diff}$ and $-1.96 SD_{diff}$. Thus, about twice the SD of the difference scores gives the 95% limits of agreement for the two measurements by the machine. A test is considered to be capable of detecting a difference, in absolute units, of at least the magnitude of the limits of agreement.

Clinical implications of BMD reproducibility measurement

In clinical practice, two absolute values (g/cm^2) have to be compared, rather than two percentages (*T*-scores). When serial measurements are obtained in a patient, only changes greater than the LSC (in%) or the SDD (in g/cm^2) can be ascribed to treatment effects. Smaller changes may be related to measurement error.

We studied recently the *in vivo* short-term variability of BMD measurement by DXA in three groups of subjects with a wide range of BMD values: healthy young volunteers, postmenopausal women and patients with chronic rheumatic diseases (most of them taking corticosteroids). In all studied subjects, reproducibility expressed by different means was good and independent from clinical and BMD status. Thus, the clinician interpreting a repeated DXA scan of a subject should be aware that a BMD change exceeding the LSC is significant, in our center arising from a BMD change of at least 3.56% at the total hip and 5.60% at the spine. Expressed as SDD, a BMD change should exceed 0.02 g/cm^2 at the total hip and 0.04 g/cm^2 at the spine before it can be considered a significant change.[56] Indeed, it has become usual to perform repeated DXA measurement: in postmenopausal women to monitor efficacy of treatment and in patients with chronic rheumatic diseases where high prevalence of bone loss has been demonstrated especially when long-term corticosteroid therapy is used. It has been shown that reproducibility expressed using the SDD is independent of the BMD value whereas reproducibility expressed using the CV or the derived LSC depend on the BMD value. Influence of age on BMD reproducibility is controversial. Previous studies have suggested that BMD measurement errors were independent of age even some studies suggested that SDD may vary in extreme ages (children and elderly) probably because of age-related factors other than BMD. However, few data exist for reproducibility of DXA in women over 70. Ravaud *et al.*[73] data, as well as those of Fuleihan,[67] show that the measurement error is greater in older osteoporotic subjects. Several factors such as difficulties in repositioning could explain the increase of measurement error in this kind of patients. Therefore, the use of the SDD in the evaluation of an apparent BMD change gives a more conservative approach than the use of the CV at low BMD. Because of its independence from the BMD level and its expression in absolute units, the SDD is a preferable measure for use in daily clinical practice as compared with the CV and the derived LSC.

In contrast with all previous publications about DXA reproducibility, we found in our center better results for the hip BMD variability than the lumbar spine. This is due to the fact that our study was the first to use the mean measure of the two femurs (dual femur). In this study, we showed in a group of young healthy volunteers that the SDD was 0.0218 g/cm^2 when both femurs were measured whereas it was 0.0339 g/cm^2 when only one femur was measured. Thus, these results enhance to encourage the use of the measurement of both hips to improve the reproducibility of DXA at this site.[56,74]

In summary, reproducibility of BMD measurement by DXA in different kinds of patients (postmenopausal women, patients with chronic rheumatic diseases, elderly, etc.) expressed by different means is good at a group level. However, the clinician must remain aware that an apparent BMD change in an individual patient may represent a PE. At each measurement center, the SDD should be calculated from *in vivo* reproducibility data. In clinical practice, the SDD should be used to estimate the significance of observed changes, in absolute values.

Other factors influencing DXA monitoring

The first factor is the time interval between two measurements in the same patient, which must be long enough to allow occurrence of a change greater than the SDD or the LSC. Therefore, it depends on the expected rate of change in BMD measurement (which varies according to whether the measurement site is composed predominantly of trabecular or of cortical bone) and the reproducibility of BMD measurement at that site. Thus, in clinical practice, a treatment-induced BMD increase can only be detected in general after 2 years.[35] However, in patients receiving long-term steroid therapy, the changes in BMD may be so important that they can be detected after 1 year. Thus, although the spine may not be the best site for the diagnosis of osteoporosis given the high prevalence of spinal degenerative disease, it may be the most sensitive site for detecting changes over time.

The changes in BMD measurements are influenced by the ability of osteoporosis treatments to increase the BMD at the different skeletal sites.[75] For some treatments such as teriparatide and strontium ranelate, significant changes in spine BMD occur on time scales of 1–2 years in the majority of patients,[76] although for other treatments, the changes are often not large enough to be statistically significant. Thus, with the exception of HRT, treatment dosages cannot be adjusted on the basis of BMD changes. Moreover, there is no proof that repeating BMD

measurements improves compliance to treatment, as most patients discontinue antiresorptive medications after a few months because of administration constraints, side effects, cost of medications or lack of interest.[77]

Above all, BMD is used as a surrogate marker for the fracture risk, although BMD increases do not reliably reflect a reduction in the fracture risk.[3] Although bisphosphonates, raloxifene and HRT have not been compared in the same study, they seem to produce comparable reductions in the risk of vertebral fractures, of about 30–50%, whereas BMD changes differ markedly across medications. Studies have shown that BMD gains explain only a small proportion of the vertebral fracture risk reduction: 28% with risedronate,[78] 16% with alendronate and 4% with raloxifene.[79] It has been suggested that the percentage of BMD change may be related to the change in the relative risk of fracture. In one study, a linear relationship was found between these two parameters, but a 1% increase in spinal BMD was associated with an only 3% decrease in the relative risk of vertebral fracture.[80] The only exception for peripheral fractures, in contrast, the risk reduction is clearly related to the BMD gain.[81] Common sense indicates that a BMD increase during treatment should be preferable over a BMD decrease. However, recent data showing that the fracture risk may decrease despite a slight decrease in BMD under treatment have been reported.[82,83] It has also been shown that the fracture risk was more heavily dependent on BMD at baseline than on BMD changes during treatment.[2,19] A significant BMD decrease while taking a treatment indicates either a compliance problem or a lack of efficacy. The measurement of bone markers may be more helpful in monitoring treatment besides BMD.[70]

Conclusions

Correct performance of BMD measurements using DXA requires rigorous attention to detail in positioning and analysis. When DXA studies are performed incorrectly, it can lead to major mistakes in diagnosis and therapy. Measurement error must be considered when evaluating serial assessments. A clear understanding of the interpretation of serial measurements and the statistical principles impacting upon their interpretation is necessary to determine whether a change is real and not simply random fluctuation. Moreover, it is important to keep in mind that fracture-protection benefit may be realized before BMD gains are detected. Physicians interested in osteoporosis management, even if not directly involved in the performance and interpretation of DXA, should be familiar with the principles outlined here to minimize serious errors and allow proper use of bone densitometry.

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