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Interpreting a DXA Scan in Clinical Practice

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1. 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(Blake and Fogelman 2007). 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)(Kanis 1994; Kanis, Borgstrom et al. 2005). 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(Hans, Downs et al. 2006; Lewiecki, Binkley et al. 2006). A DXA measurement can be completed in about 5 minutes with minimal radiation exposure (about one tenth that of a standard chest x-ray for a quick hips and spine exam).

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

Table 1. WHO Osteoporosis Classification

2. 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(Roux 1998). Physicians not directly involved in the performance and interpretation of DXA should be familiar enough to detect common positioning and 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(Watts 2004).

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 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 (Blake and Fogelman 2002; Blake and Fogelman 2003).

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(Tothill and Avenell 1994) (which can be studied either through cadaver studies(Svendsen, Hassager et al. 1995), CT imaging to delineate the distribution of adipose tissue external to bone(Kuiper, van Kuijk et al. 1996; Lee, Wren et al. 2007) or MRI to measure the percentage of marrow fat inside bone(Griffith, Yeung et al. 2006)). These studies suggest BMD measurement errors of around 5 to 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 (Hans, Downs et al. 2006). 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 paediatric 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 to 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 (Lewiecki and Borges 2006).

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 (Price, Walters et al. 2003). 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)(Watts 2004). 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/cm², the young normal mean is 1.000 g/cm², and the young normal standard deviation is 0.100 g/cm², then this patient's T-score would be (0.700 - 1.000)/0.100, or –0.300/0.100, or –3.0(Watts 2004). 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 post-menopausal 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 standard deviation score(Watts 2004). 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.

3. Who should have a DXA measurement?

Most official groups recommend screening healthy women for osteoporosis at age 65, and testing higher-risk women earlier(Baddoura, Awada et al. 2006). 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 (Hillier, Stone et al. 2007). Such indices, while not identifying all cases of osteoporosis, increase the efficiency of BMD measurement by focusing on subjects who are at increased risk (Cadarette, Jaglal et al. 2000; Gnudi and Sitta 2005; Salaffi, Silveri et al. 2005). 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(Richy, Ethgen et al. 2004; El Maghraoui, Guerboub et al. 2007; El Maghraoui, Habbassi et al. 2007) and men (Adler, Tran et al. 2003; Ghazi, Mounach et al. 2007).

4. Site of measurement of BMD

The ISCD recommends obtaining BMD measurements of the posteroanterior spine and hip(Leib, Binkley et al. 2006). 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(Kanis, Johnell et al. 2000; Kanis, Oden et al. 2001; Kanis 2002; Johnell, Kanis et al. 2005; Kanis, Seeman et al. 2005; Arabi, Baddoura et al. 2007). 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.

5. Interpreting a DXA scan

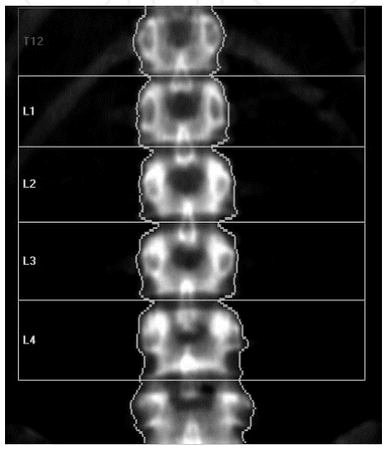
The most important informations to check are the correct identification of the patient, his date of birth and also the sex and ethnicity which are mandatory to calculate T-scores. Sex is used by all manufacturers to calculate T-scores (i.e. T-scores for women are calculated using a female normative database, 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 (Baim, Wilson et al. 2005) 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.

5.1 Positioning

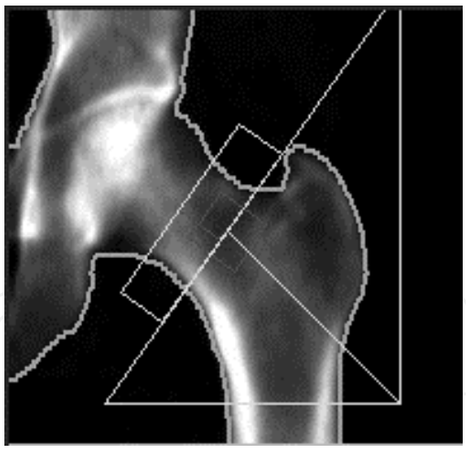
The main purpose of the DXA scan image is to check if the patient is positioned correctly, something that the technologist must determine before the patient leaves the testing centre. Positioning should also be doublechecked by the clinician who interprets the test(Roux 1998). There is many available resources for BMD technologists and physicians training, such as ISCD or International Osteoporosis Foundation (IOF) courses.

A scan with correct positioning of the spine is shown in Fig. 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

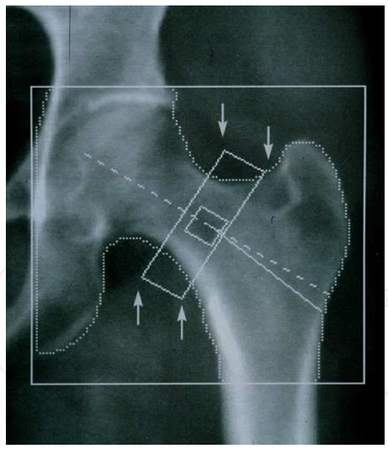
by the use of positioning devices. Internal rotation may be improved by having the patient flex the foot before doing the internal rotation, and then relaxing the foot after the strap is in place. This amount of internal rotation presents the long axis of the femoral neck perpendicular to the X-ray beam, providing the greatest area and the lowest bone mineral content (and the lowest BMD), and is confirmed on the scan by seeing little or none of the lesser trochanter (Fig. 1b)(Lekamwasam and Lenora 2003; 2004). 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 (Hamdy, Kiebzak et al. 2006; Lewiecki, Binkley et al. 2006).



(a)



(b)



(c)

Fig. 1. Correct positioning and analysis of the L1–L4 spine (a) and the proximal femur (Lunar (b) and Hologic (c)).

5.2 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 (Fig. 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 (Fig. 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 the 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 (Fig. 1b). For Hologic the box is on the distal part of the femoral neck (Fig. 1c). This induces a large difference among these 2 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, aortic calcification). Almost all artifacts and local structural change will spuriously elevate BMD(El Maghraoui 2004). 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 recommended. If all vertebrae are affected, the spine should be reported as ''invalid,'' with no BMD or T-score results given. Figure 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 post menopausal osteoporosis.

6. 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 to 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 (Rea, Li et al. 2000; Chapurlat, Duboeuf et al. 2006; Olenginski, Newman et al. 2006). 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,

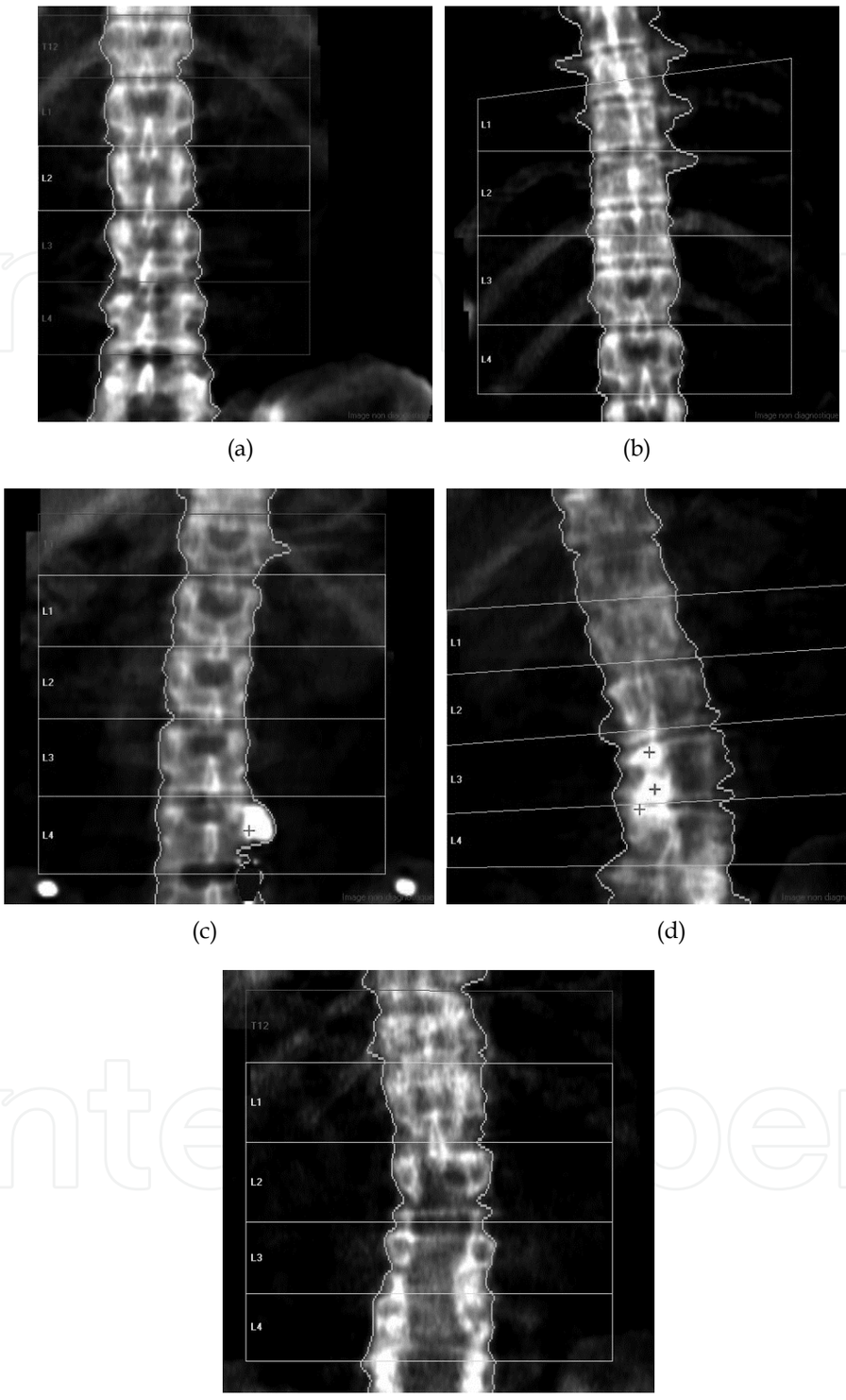


Fig. 2. Examples among some common spine scanning problems: (a) The spine is too close to the right side of the image (b) Vertebral levels are mis-identified (c) Metal button over L4 (d) Scoliosis, and osteophyte at L3–L4 (e) Laminectomy

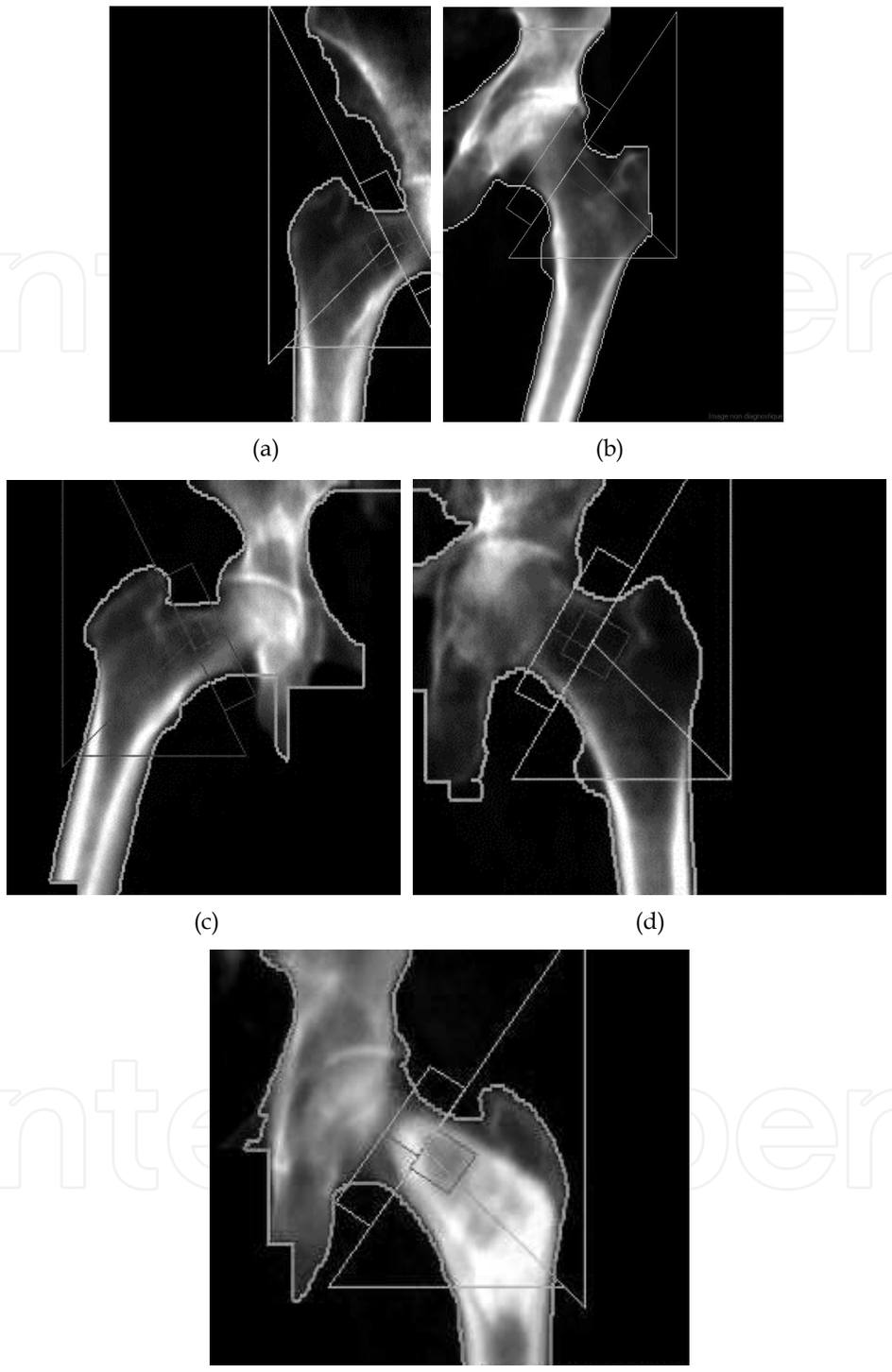


Fig. 3. Examples among some common hip scanning problems: (a) The scan did not go far enough laterally and part of the femoral head is missing. (b) The femur is adducted (c) The femur is abducted (d) Suboptimal internal rotation (too much of the lesser trochanter is showing) (e) Abnormal bone (history of hip fracture and osteosynthesis)

and identify patients likely to benefit from pharmacological therapy who otherwise might not be treated(Olenginski, Newman et al. 2006; Roux, Fechtenbaum et al. 2007). 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(Duboeuf, Bauer et al. 2005; Jacobs-Kosmin, Sandorfi et al. 2005; Chapurlat, Duboeuf et al. 2006; Damiano, Kolta et al. 2006).

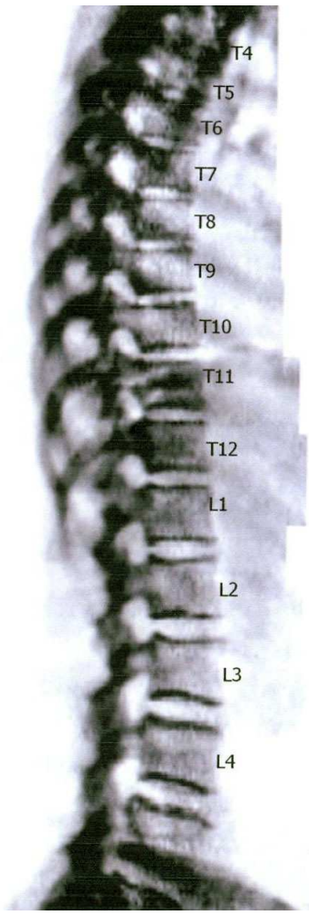


Fig. 4. Vertebral fracture assessment from a dual x-ray absorptiometry image of the spine.

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.

7. 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 densitometery. T-score discordance is the observation that the T-score of an individual patient varies from one key measurement site to another.

7.1 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(Faulkner, von Stetten et al. 1999; Woodson 2000; O'Gradaigh, Debiram et al. 2003; Moayyeri, Soltani et al. 2005). Only two studies focused on risk factors of this commonly observed discordance (Moayyeri, Soltani et al. 2005; El Maghraoui, Mouinga Abayi et al. 2007; El Maghraoui, Mouinga Abayi et al. 2007). Five different causes for occurrence of discordance between the spine and the hip sites have been described(Woodson 2000).

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 non-dominant total hip(Hamdy, Kiebzak et al. 2006). 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 yrs before the hip)(Blank, Malone et al. 2006). And finally, bone loss observed with age in an individual may be more rapid and important in trabecular than cortical bone is another explanation(Agarwal and Camacho 2006). Trabecular bones (typical of lumbar area) are known to have a more rapid rate of deprivation in early post-menopausal state in comparison to 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(Bolotin 2001; Theodorou and Theodorou 2002). Another important cause in younger patients is ankylosing spondylitis syndesmophytes(El Maghraoui, Borderie et al. 1999; Maillefert, Aho et al. 2001; El Maghraoui 2004; El Maghraoui 2004; El Maghraoui, Do Santos Zounon et al. 2005). 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 aetiologies of the secondary osteoporosis (such as glucocorticoid excess, hyperthyroidism, malabsorption, liver disease, rheumatoid arthritis) first affect spinal column(El

Maghraoui 2004; Khan, Hanley et al. 2006). 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 two-fold better in the hips than the spine especially when measuring both hips(El Maghraoui, Do Santos Zounon et al. 2005). Finally, technical discordance can occur due to the normative reference data used by the device software to analyze the test(Liao, Wu et al. 2003; McMahon, Nightingale et al. 2004; Lewiecki, Binkley et al. 2006). 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.

7.2 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.

8. Conclusion

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.

9. Abbreviations

BMC: bone mineral content

BMD: bone mineral density

CV: coefficient of variation

DXA: dual-energy x-ray absorptiometry

IOF: international osteoporosis foundation

ISCD: international society for clinical densitometry

LSC: least significant change

OST: osteoporosis self-assessment tool

PE: precision error

ROI: region of interest

SD: standard deviation

SDD: smallest detectable difference

VFA: vertebral fracture assessment

WHO: world health organization

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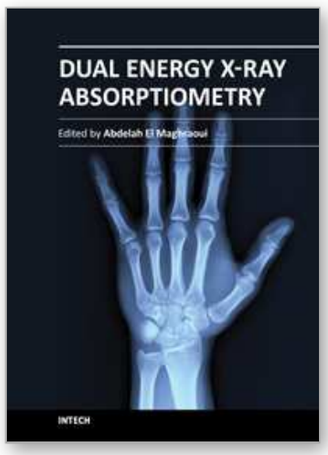

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The World Health Organization (WHO) has established dual-energy x-ray absorptiometry (DXA) as the best densitometric technique for assessing bone mineral density (BMD) in postmenopausal women and has based the definitions of osteopenia and osteoporosis on its results. DXA enables 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, vertebral fracture assessment and body composition assessment, including fat mass and lean soft tissue mass of the whole body and the segments. This book contains reviews and original studies about DXA and its different uses in clinical practice (diagnosis of osteoporosis, monitoring of BMD measurement) and in medical research in several situations (e.g. assessment of morphological asymmetry in athletes, estimation of resting energy expenditure, assessment of vertebral strength and vertebral fracture risk, or study of dry bones such as the ulna).

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