SECTION IV

Investigation of Metabolic Bone Diseases
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Chapter 29. Dxa in Adults and Children

Judith Adams and Nick Bishop

INTRODUCTION

The first DXA scanners were introduced in the late 1980s, and DXA is now the most widely used and available bone densitometry technique; there are ~27,000 central DXA scanners worldwide. Dual-energy X-ray beams are required to correct BMD measurements for overlying soft tissue and are produced by a variety of techniques by different manufacturers, and the energies are selected to optimize separation of mineralized and soft tissue components of the skeletal site analyzed. If a single-energy photon beam is used, this is applicable only to peripheral skeletal sites that have to be placed in a water bath to correct for overlying soft tissues.

Technical Aspects and Developments

Original DXA scanners used a pencil X-ray beam with a single detector, scanning in a rectilinear fashion across the anatomical site (scans times: 5–10 min; spatial resolution = 1 mm). Technical developments have taken place over recent years, which include a fan-beam X-ray source and a bank of detectors that enable faster scanning (1 min/site) with improved image quality and spatial resolution (0.5 mm).

Scanning Sites and Measurements Provided

DXA can be applied to sites of the skeleton at which osteoporotic fractures occur; in the central skeleton, this includes the lumbar spine (L₁–L₄; Fig. 1A) and proximal femur (total hip, femoral neck, trochanter, and Ward’s area; Fig. 1B). DXA can also be applied to peripheral skeletal sites (forearm and calcaneus), using either full-sized or dedicated peripheral DXA scanners. Central DXA measures of lumbar spine, femoral neck, and total hip are currently used as the “gold standard” for the clinical diagnosis of osteoporosis by bone densitometry (Figs. 1A and 1B).

DXA X-ray attenuation values are converted to BMC (g); bone area (BA; cm) is calculated by summing the pixels within the bone edges (software algorithms detect the bone edges). “Areal” BMD (BMDₐ; g/cm²) is calculated by dividing BMC/BA. Because the DXA image is a 2D image of a 3D object, the depth of bones is not taken into account. This fact results in DXA being size-dependent, one of its significant limitations, particular in children in whom the bones change in size and shape during growth, and in patients whose disease might result in small stature or slender bones.

DXA provides BMD of integral (cortical and trabecular) bone. The cortical/trabecular ratios vary in different sites (50/50 postero-anterior [PA] lumbar spine; 10/90 lateral lumbar spine; 60/40 total hip; 80/20 total body; 5/95 calcaneus; 95/5 distal radius; 40/60 ultra-distal radius [depending on site of region of interest]). Because of the different composition of bones and rates of change in various skeletal sites, measurements in different sites in the same individual will not give the same BMD results. Correlations between BMD measurements made in the same patient vary between r = 0.4 and r = 0.9; it is not possible to predict from a DXA BMD measurement made in one site what the BMD will be in another site using DXA or other bone densitometry methods. In research studies, BMD measurements in different anatomical sites and by various bone density methods (DXA, QCT, and quantitative ultrasound [QUS]) may be complementary.

With appropriate software, whole body DXA scanning can be performed, from which is extracted whole body and regional BMC (g) and whole body and regional body composition (lean [muscle] and fat mass; Fig. 2).

Precision

Precision measures the reproducibility of a bone densitometry technique and is usually expressed as a CV or standardized CV (takes into account range of measurements). Precision for DXA total hip and lumbar spine DXA = 1–2%; femoral neck and trochanter CV = 2.5%; and Ward’s area = 2.5–5% (site not applied in clinical practice). In peripheral sites, CV = 1% in the distal forearm, 2.5% in the ultra-distal forearm, and 1.4% in the calcaneus. Measurement sites generally used in clinical diagnosis (in contrast to research) are mean BMD for lumbar spine (L₁–L₄), femoral neck, and total hip; in hyperparathyroidism (primary or secondary), a forearm measurement is relevant, because cortical bone can be lost preferentially from this site. Precision is optimized by using the minimum number of expert, highly motivated, and well-trained technical staff; it is not ideal to have a large number of staff who rotate through different departments and perform BMD scanning only infrequently.

Accuracy

Accuracy is how close the BMD measured by densitometry is to the actual calcium content of the bone (ash weight). The accuracy of DXA lies in the region of 10–15%; the inaccuracies are related to marrow fat and DXA taking soft tissue as a reference. DXA makes some assumptions about body composition and soft tissues, so inaccuracies may occur with excessively under- or overweight subjects and with large changes in weight between scans, but exactly how this can be corrected for in adults is uncertain.

Sensitivity

Sensitivity is the ability of the measurement to discriminate between patients with and without fractures and to measure small changes with time and/or treatment. A statistically significant change in BMD is calculated as 2.77 multiplied by precision (CV) at the site of measurement to provide least significant change (LSC). LSC in the spine = 5.3%; total hip = 5.0% and femoral neck = 6.9%. Because changes in BMD are generally small, it is essential in an individual patient to leave an adequate time interval between DXA measures, usually 18–24 mo.

Fracture Prediction

Because whether a patient develops a fracture depends on factors in addition to BMD (age, whether the patient falls, the nature of the fall, and the patient’s response to the fall), it is impossible for BMD techniques to completely discriminate be-

Dr. Bishop has consulted for Procter & Gamble, Novartis, Roche, and Alliance for Better Bone Health. Dr. Adams states that she has no conflicts of interest.

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between those with and without fractures. However, the lower the DXA BMD, the more at risk the patient is of suffering a fracture.\(^{11}\) DXA BMD measurements made in any skeletal site (central and peripheral) are predictive of fracture, with the risk of fracture increased in individuals with the lower BMD. The relative risk (RR) of fracture per 1 SD decrease in BMD below the age-adjusted mean varies between 1.4 and 2.6.\(^{11}\) This reduction in BMD in predicting fracture is as good as a rise of 1 SD in blood pressure is in predicting stroke and a 1 SD rise in cholesterol is in predicting myocardial infarction. Site-specific measurements are best in predicting fracture in that particular anatomical place.

**Radiation Doses**

DXA involves very low radiation doses (\(p\)DXA: calcaneus, 0.03 \(\mu\)Sv; forearm, 0.5 \(\mu\)Sv; spine, 2-4 \(\mu\)Sv; femur, 2-5 \(\mu\)Sv; whole body, 1–3 \(\mu\)Sv) that are similar to those of natural background radiation (2400 \(\mu\)Sv/yr; \(-7 \mu\)Sv/d).\(^{12,13}\)

**Clinical Applications**

There has been much debate concerning the appropriate use of bone densitometry, particularly in population screening in women at menopause, and the cost-effectiveness of such a program has not been established. However, there is consensus that central DXA bone densitometry is the “gold standard” measurement to make in appropriate individuals to assess fracture risk and make the diagnosis of osteoporosis in terms of bone densitometry.\(^{1,14}\) Bone densitometry has high specificity but low sensitivity. Selection of patients who would most appropriately be referred for DXA bone densitometry is based on a case-finding strategy in those who have had a fragility (low-trauma) fracture or have other strong risk factors (estrogen/testosterone deficiency, primary hypogonadism, height loss, low-trauma fractures, radiographic osteopenia, oral glucocorticoid therapy [prednisolone > 7.5 mg/d for >3 mo], rheumatoid arthritis, and other secondary causes of osteoporosis). There may be national differences in such referral guidelines based on local reimbursement policies and economic constraints.

**Artefacts**

These can cause inaccuracies in DXA and are most common in the lumbar spine in the elderly population. All the calcium in the path of the X-ray beam will contribute to measured BMD. If there is degenerative disc disease with osteophytes, osteoarthritis with hyperostosis of facet joints, or vertebral fracture (same amount of calcium before fracture contained in

**FIG. 1.** (A) DXA of normal lumbar spine L₁–L₄. Results are generally expressed as a mean “areal” density (\(BMD_{\text{a}}\) g/cm²) for all four vertebrae. (B) DXA of left hip; although \(BMD_{\text{a}}\) is provided in a number of different sites (femoral neck, oblong box; Ward’s area, small box; trochanter; and total hip), for clinical diagnosis of osteoporosis (WHO T-score at or below –2.5), femoral neck and total hip are used.

**FIG. 2.** Whole body DXA (in a child) is obtained in ~1 min on fan beam scanners and provides total and regional information about the skeleton (less head) and body composition (lean muscle and fat mass).
TABLE 1. CAUSES OF ARTIFACTS RESULTING IN ERRORS IN DXA BMD

<table>
<thead>
<tr>
<th>Cause of Artifacts</th>
<th>Resulting in Errors in DXA BMD</th>
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<tr>
<td>Overestimation of BMD</td>
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<tr>
<td>Spinal degeneration and hyperostosis (osteophytes)</td>
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<tr>
<td>Vertebral fracture</td>
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<td>Extraneous calcification (lymph nodes, aortic calcification)</td>
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<tr>
<td>Overlying metal (navel rings, surgical rods/plates, Myodil)</td>
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<td>Sclerotic metastases</td>
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<tr>
<td>Vertebral hemangioma</td>
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<tr>
<td>Ankylosis panniculi with paravertebral ossification</td>
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<tr>
<td>Poor positioning of femoral neck (inadequate internal rotation)</td>
<td></td>
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<tr>
<td>Excessive body weight</td>
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<tr>
<td>Strontium ranelate therapy</td>
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<tr>
<td>Underestimation of BMD</td>
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<tr>
<td>Laminectomy</td>
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<td>Lytic metastases</td>
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<tr>
<td>Low body weight</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

DXA will not differentiate low calcium content in bone being caused by osteoporosis (reduced amount of bone; quantitative abnormality) and osteomalacia (reduced calcium/osteoid ratio; qualitative abnormality).

Vertebral fracture (vertebra which is reduced in area) present, BMD will be falsely elevated. Other etiologies can also cause false elevation or underestimation of BMD measured by DXA (Table 1; Figs. 3A and 3B); it is essential that DXA images be scrutinized for such artefacts. Vertebral affected significantly by artefact should be excluded from analysis; however, for clinical diagnosis, a minimum of two vertebrae must be available for analysis. Strontium ranelate is a relatively new oral therapy for osteoporosis; some of the apparent increase in BMD is artefactual, related to the high atomic number of strontium that accumulates in bone and contributes to X-ray attenuation; methods to correct for this have been proposed. It is important to note that DXA will not differentiate low calcium content in bone being caused by osteoporosis (reduced amount of bone; quantitative abnormality) and osteomalacia (reduced calcium/osteoid ratio; qualitative abnormality).

To overcome the problems of degenerative disc disease and hyperostosis in PA DXA of the spine, lateral DXA has been developed. On scanners with “C” arms, lateral scanning can be performed with the patient remaining in the supine position; otherwise, the patient has to be repositioned in the lateral decubitus position, which limits its clinical practicality and precision (CV = 2.8-5.9% in lateral decubitus position, 1.6-2% in the supine position). Because L₁ and L₂ may have ribs superimposed and L₃ is overlain by the iliac crest, L₃ may be the only vertebra that can be analyzed in lateral DXA. Therefore, although lateral DXA may be a more sensitive predictor of vertebral fracture than PA spinal DXA, its limited precision and impracticality means that it is not often performed in clinical practice.

Because of these artefacts on PA DXA of lumbar spine, it has been suggested that, in the elderly population (>65 yr of age), only the proximal femur (femoral neck, total hip) should be scanned. However, monitoring change is performed optimally in the lumbar spine if there are no artefacts.

Interpretation

When a BMD measurement has been made, this has to be interpreted as normal or abnormal and a report must be formulated that will be of assistance to the referring clinician. For this, it is essential that age-, sex-, and ethnically matched reference data are available. The scanner manufacturer supplies such normal reference databases. These databases are predominantly, but not exclusively, drawn from a white American-based population. There is a paucity of appropriate reference ranges for children and certain ethnic minorities (e.g., Asians). A patient’s results can be interpreted in terms of the SD from the mean of either sex-matched peak bone mass (PBM; T-score) or age-matched BMD (Z-score).

The World Health Organization (WHO) has defined osteoporosis in terms of bone densitometry as a T-score at or below -2.5 in the lumbar spine, femoral neck, and total femur. The definition applies to DXA of lumbar spine, proximal femur (femoral neck), and the distal third of the forearm but not to other techniques (e.g., QCT, QUS) or other anatomical sites (e.g., calcaneus). nor is it yet confirmed to be applicable to younger women and men. Until PBM has been reached (i.e., in children and young adults up to 20 yr), interpretation can be made only by comparison with age-matched mean (Z-score). Variations in the mean and SD of reference ranges may alter the number of patients identified as osteoporotic; in DXA of the hip, use of the NHANES reference database is preferred for whites.

Although there is consensus on the definition of osteoporosis in bone densitometry (WHO T-score below -2.5), there is as yet no consensus on levels of BMD that justify therapeutic interventions that are cost-effective. This is perhaps not surprising, because it is the individual patient that is being treated and not the BMD result, and age is a strong independent predictor of fracture. Other factors (e.g., age, previous low trauma fracture over age 50, parental hip fracture, glucocorticoid therapy, rheumatoid arthritis, smoking, alcohol consumption) contribute to prediction of fracture risk. The WHO has recently published algorithms for calculating 10-yr fracture risk for patients from such clinical risk factors that will make the decision to instigate therapy more cost-effective.

Monitoring Change in BMD

Whether DXA should be used to monitor change in BMD with time and therapy is contentious and varies between different countries and their guidelines. In calculating change over time, the absolute BMD values (g/cm²) should be used; statistically significant change is 2.77 × CV%. In longitudinal studies in an individual patient, an adequate interval of time (18-24 mo) between measures is required to show significant change, unless large changes in BMD are anticipated (e.g., after organ transplantation together with large doses of glucocorticoids). Different manufacturers use different edge detection algorithms and analyze different regions of interest (ROIs) for analysis in the hip, so results from different scanners are not interchangeable. In longitudinal studies, it is vital to use the same scanner and software program. With technical developments, it may become necessary to replace a scanner. To cross-calibrate between the old and new scanner, scanning patients (~100, with a spread of BMD from high to low) and phantoms (scanner manufacturer or European Spine Phantom) will generally allow the required calculations to be made.

Research Application

There are other scanning capabilities on central DXA scanners, which currently remain as research applications. These include whole body scanning for total and regional BMC, lean muscle, and fat mass (Fig. 2) in adults, children, and neonates. Software programs are available for measuring BMD around prostheses after hip and knee arthroplasty, in bone...
placed ROIs; these would not be as precise as automated
ning such sites, programs for scanning conventional sites (e.g.,
forearm) can be used, with analysis being performed by hand-
no specific commercial software program available for scan-
tomical sites (hand, mandible). Although there may be
0.62 cm; HAL of 11.0 cm increased hip fracture 2-fold, and
specimens and small animals, and application in novel ana-
tical measurements can also be derived from DXA.
The hip axis length (HAL) has been found to be predictive of
fracture; normal HAL in postmenopausal women is 10.5 ±
0.62 cm; HAL of 11.0 cm increased hip fracture 2-fold, and
HAL of 11.5 cm increased the risk 4-fold. HAL is the dis-
the femoral neck and parallel to its margins. There will be
some magnification of the hip geometry with fan-beam scan-
ers, so that corrections have to be applied. Structural compo-
ents of the proximal femur (size and shape), in combination
with BMD, have been found to improve fracture risk predic-
tion. Hip structure analysis (HSA) has been introduced to
extract geometric strength information from hip DXA, by
making mathematical calculations of the distribution of cal-
cium in DXA cross-sections in the femoral neck, trochanteric
region, and proximal femoral shaft and has been applied
retrospectively in several large research studies. Its application
in clinical practice is still to be defined.

**Vertebral Fracture Assessment**

Lateral views of thoracic and lumbar spine (T4-L4) can be
obtained with fan-beam scanners, using dual- or single-energy
scanning, with the patient either in the supine (“C” arm scanners)
or lateral decubitus position (Fig. 4). From these, a visual
assessment for vertebral fractures or morphometric assessment
of vertebral shape can be made. Such morphometric analysis has the potential for automation by application of
computer analysis techniques (e.g., active shape and appearance
models) that may potentially make them more practical
for use in a clinical setting. Vertebral fracture assessment
(VFA) has several advantages over conventional radiography:
lower dose of ionizing radiation (12 μSv single energy; 42 μSv)
and avoiding problems of the divergent X-ray beam of radi-
ography that can distort vertebral shape causing apparent bi-
concavity of endplates—DXA uses a lateral scan projection
method, with simultaneous movement of X-ray source and
detectors along the spine, so the X-ray beam is always parallel
to the vertebral endplates and avoids the “bean can” artefact
of vertebral endplates caused by the parallax effect on radi-
ographs. Guidelines suggest that elderly patients (women >70
yr; men >80 yr) who have low BMD with historical height loss
of 4 cm (1.6 in) in women, 6 cm (2.4 in) in men) or prospective
height loss of >2 cm (0.8 in) in women (3 cm; 1.2 in in men) and
other risk factors should undergo vertebral fracture assessment
using lateral vertebral assessment (LVA) or instantaneous ver-
tebrae assessment (IVA) by DXA to detect vertebral frac-
tures. (21) The method has been shown to be satisfactory for
excluding vertebral fractures being present. However, more
scientific studies are required to confirm the exact clinical role
of this alternative technology to conventional spinal radiogra-
phy for the identification of vertebral fractures.

**DXA IN CHILDREN**

The purpose of any assessment of bone size or mass in chil-
dren is to provide data relevant to the current, or future, health
of the skeleton. DXA is the most widely used quantitative
bone imaging technique in pediatric practice, but many aspects
of its use, and the interpretation of the data obtained, remain
tenuous. (19–22,37,38)

DXA provides estimates of bone size in two dimensions and
bone mass within that envelope, the value of bone mass ad-
justed for size being BMD (g/cm²). To overcome this limita-
tion to some extent, a “calculated volumetric BMD” (bone
mineral apparent density [BMAD; g/cm³]) can be made in
the spine and femoral neck. Although in adult practice there
is general acceptance that DXA BMD below certain absolute
values are associated with increased fracture risk, there is no
such absolute threshold for children. The fact that this is re-
flected in manufacturer-provided reference values for BMD, which increase in a similar way to height and weight during
childhood and adolescence, clearly indicate that DXA is not
measuring true volumetric BMD, but some composite measure

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of bone size and mass. This is not necessarily a disadvantage because bone size, especially in the tubular bones that children are most prone to fracture, is an important predictor of bone strength.

Advantages of DXA in children are short scan time, low radiation dose, and general widespread availability. DXA measures of bone mass in healthy children are predictive of fracture risk both at the measurement site (in the forearm) and elsewhere; total body less head (TBLH; Fig. 2) BMC, adjusted for weight, height, and bone area, is the measure that has been found, in a prospective cohort study at age 9.9 yr, to be most strongly associated with fracture risk over the following 2 yr. However, there are no data for the predictive value of DXA at other ages in apparently healthy children and no similar data for children with bone disease.

Children are a difficult group to study, because as they grow, their bone mass should increase. They also fracture frequently—by the end of teenage years, up to one half of all boys and one third of girls will have sustained a fracture. A single fracture in an otherwise healthy child should not therefore require study of skeletal health. Most requests for DXA in children will be in the groups thought to be at increased risk of fracture. These include children with primary bone diseases such as osteogenesis imperfecta and idiopathic juvenile osteoporosis; chronic immobilization (cerebral palsy and Duchenne dystrophy); inflammatory conditions (Crohn's disease, cystic fibrosis, and juvenile idiopathic arthritis); endocrine disorders such as anorexia nervosa and Cushing's syndrome (but not Turner's syndrome); after chemotherapy or organ transplantation; and thalassemia major. Other requests come when a child has recurrent fractures in the absence of an obvious underlying predisposition.

In children, when should a DXA scan be performed and should it be repeated? Although there are many studies using DXA to show efficacy of a specific intervention in children, little has been published about the practical application of DXA in the clinical setting. It can be reasonably assumed that a DXA would be only part of an assessment of bone health and would be undertaken either because of a perceived increase in fracture risk or because of bone disease.

Measurement sites for DXA in children are typically the lumbar spine (L₁-L₄) and total body, where precision is similar to that achieved in adults. Forearm and proximal femur have been used in some studies, as has the lateral distal femur where deformity and contracture preclude use of DXA in the normal measurement sites. Normative reference data are available for spine, femoral neck, total body, and lateral distal femur. T-scores must not be used in children who have not yet reached PBM; measurements are usually reported as sex specific and in relation to age (Z-score; at or below -2.0 being reduced in children who are normal in size for their age). The diagnosis of osteoporosis in children should not be made on the basis of densitometric criteria alone. Terminology such as "low BMD for chronological age" may be used if the Z-score is below -2.0; terms such as osteoporosis and osteopenia should not be used. Adjustments have been made in research studies in healthy children to account for the assumed shape of vertebrae (cylindrical, cuboidal) and the femoral

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neck,(39–41) and some reference data using these have been published(45) or the expected relationship of bone size and mass with body size or elements of body composition such as lean body mass. Some of the current generation of scanners provide methods of adjusting for body size at both the spine and total body, but there is a lack of information currently as to which adjustment (if any) should be used in clinical practice. In some studies, adjustment for bone age or pubertal status has been undertaken, but estimation of bone age is a specialized technique, and there is more than one method of assessment in common use. There is a lack of data for ethnic subgroups. It is unclear from the published data whether any one of the proposed adjustments is optimal in terms of either fracture prediction or skeletal health assessment.

In diseases in childhood in which fracture risk is increased, initiation of DXA BMD should be at the discretion of the treating clinician, and the monitoring interval should reflect the severity of the disease. There is little evidence to support monitoring at intervals of <6 mo in any setting. Although there is increased risk of fracture for children receiving glucocorticoid therapy, it is difficult to disentangle the effects of these from those of the underlying bone disease. Currently it does not seem appropriate that DXA should be any more frequent in children receiving such therapy.

Interpretation of DXA results depends on the clinical context. A diagnosis of osteoporosis should not be made on the basis of a bone mass measurement in isolation. If a child presents with recurrent fractures but no clinically apparent underlying disease and bone mass is within the expected range, reassurance can be offered. If there is an underlying problem, further monitoring and additional imaging may be required. Such a clinical setting would be a child with apparently mild osteogenesis imperfecta with bone mass in the normal range who may have occult fractures of thoracic vertebrae. Low bone mass in the presence of vertebral, or recurrent, fractures resulting in loss of independent mobility and chronic bone pain should prompt evaluation of the need for active intervention.

CONCLUSIONS

DXA offers a precise technique, with acceptable accuracy, for measuring BMD in central and peripheral skeletal sites in adults and children, using very low doses of radiation (similar to levels of natural background radiation). DXA is currently regarded as the “gold standard” for BMD measurements for the diagnosis of osteoporosis in adults. However, there are some important limitations (BMD, size dependency, measurement of integral [cortical and trabecular] bone), of which users and operators need to be aware. Good precision depends on scanners being operated by skilled and appropriately trained staff and quality assurance protocols being in place. DXA can be used in adults to diagnose osteoporosis using the WHO threshold (T-score = -2.5 or below in lumbar spine L1–L4, femoral neck, and total hip), predict fractures, contribute to decisions on patient management and therapeutic intervention, and perhaps also monitor change in BMD (except in the forearm). There is potential for visual and morphometric assessment of vertebral fractures from lateral DXA images. There are increasing, and varied, applications of DXA in research studies in novel sites and in both humans and animals. There are particular issues for DXA in children in whom the size dependency is a limitation, and to date, there is no consensus on whether size correction should be applied and which method is optimum.

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