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Position Statement

Standards and Guidelines for Performing Central Dual-Energy X-Ray Absorptiometry in Premenopausal Women, Men, and Children

A Report From the Canadian Panel[†] of the International Society of Clinical Densitometry

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Abstract

The Canadian Panel of the International Society for Clinical Densitometry has developed standards in order to establish the minimum level of acceptable performance for the practice of bone densitometry in Canada. Previously, this group addressed the performance of densitometry in postmenopausal women. This report addresses the use of densitometry in men, premenopausal women, and children with a focus on dual-energy X-ray absorptiometry.

Key Words: Standards; bone density; premenopausal women; children; men.

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[†]For a listing of the members of the Canadian ISCD Panel please *see* Appendix 1 on p. 60.

Introduction

Standards of care from the Canadian Panel of the International Society for Clinical Densitometry (ISCD) have been developed in order to establish the minimum level of acceptable performance for the practice of bone densitometry in Canada. Measurement of bone mineral density (BMD) is the accepted method for identifying patients at risk for fracture *(1–5)*.

National and international organizations as well as expert panels have developed guidelines for the appropriate use of bone mass measurement in the diagnosis of osteoporosis and for the assessment of fracture risk *(6–12)*.

The Canadian Panel of the ISCD previously published Standards Part I *(13,14)*, which specifically addressed the performance of densitometry in postmenopausal women. Other populations, specifically men, premenopausal women, and children, were not addressed. These populations have not been evaluated as extensively as postmenopausal women. This raises the question of how densitometrists should report findings from bone density testing in these populations.

This manuscript, Standards Part II, was developed by the Canadian Panel of the ISCD and invited international experts from the field of densitometry. The goal of this report is to establish standards in the application of bone densitometry in men, premenopausal women, and children. This document supplements the previous Standards I paper and is to be used in conjunction with the principles outlined previously. The recommendations in this article are based on central DXA measurements and do not address other bone density technologies.

Examination Procedures

DXA Procedure

The guidelines for positioning adult men and younger women undergoing DXA, as well as the preparation for the procedure, are similar to those published previously *(13,14)*. In younger adults, patient positioning is usually easier because of a lower prevalence of degenerative changes and arthropathy.

Bone densitometry is considerably more challenging to perform in growing children. Immobilization is more difficult in children, thus the number of skeletal sites which can be scanned successfully may be limited. The posterior anterior (PA) spine is a preferred site in children, because the scan time is short, anatomic landmarks are consistent, and normative data are most robust. Total body is also recommended in children, however scanning time is longer. Measurements at the total hip and femoral neck are problematic in children, as the standard region of interest (ROI) parameters may be too large and normative data is limited. Moreover, precision at these sites is poorer.

Low-density software (LDS) may be required for edge detection in younger patients with poor mineralization. LDS includes regions of relatively undermineralized bone resulting in a systematically lower BMD than with standard software. These differences have been estimated to be approx 9–11% *(15)*. Any deviations from standard methodology should be reported and repeated with longitudinal studies.

Radiation Safety and Protection

Radiation exposure to the patient from DXA is extremely small. The effective dose equivalent ranges from 0.0005 to 0.0060 millisievert (mSv), whereas the typical annual background radiation dose is 2.5 mSv. Low radiation exposure makes DXA acceptable for examination of children when adequate clinical indications exist. However, fetal radiation exposure should be avoided because of a greater radiosensitivity. All patients of childbearing age should be asked of the possibility of pregnancy. If pregnancy is possible the examination should be deferred until the time of the next normal menstrual period. There is currently no indication for DXA during pregnancy.

Interpretation and Reporting of Results

BMD is calculated from two measured parameters: bone mineral content (BMC), expressed in grams, divided by projected area (cm^2). This areal bone density (g/cm^2) should be distinguished from volumetric bone density (g/cm^3). Currently, only quantitative computed tomography (QCT) directly measures volumetric BMD. Techniques have been described for estimating volumetric BMD from areal DXA measurements. This estimated volumetric

BMD is known as bone mineral apparent density (BMAD). Calculation of BMAD utilizes certain geometric assumptions *(16)*. In most clinical situations, there is no practical limitation to using areal BMD as an index of volumetric BMD. Hip fracture prediction in postmenopausal white women is similar with areal BMD or BMAD measures, although there may be better vertebral fracture prediction with BMAD *(17,18)*.

When bone size varies substantially within a group or between groups, a dissociation between areal BMD and volumetric BMD can emerge. The error is directly proportional to the difference in the unmeasured third dimension, that being depth. Areal DXA thus underestimates BMD in individuals of smaller skeletal size and overestimates BMD in larger individuals. Differences in bone size largely account for the observation that areal BMD is lower in Asians than in Caucasians and higher in men than in women *(19–21)*. This is a reflection of the differences in height between Asians and Caucasians; men and women.

Medical conditions associated with impaired skeletal growth, such as anorexia nervosa, Turner's syndrome, and constitutional delay of puberty also have been shown to complicate the interpretation of DXA measures of areal BMD *(22–24)*. Pediatric patients with chronic illness often experience delays or impairment in growth and puberty. Failure to account for these factors can lead to an overdiagnosis of bone mineral deficits. For patients with growth and/or pubertal retardation, it is reasonable to adjust for skeletal maturation and/or pubertal stage rather than for chronological age when interpreting DXA results. A detailed discussion of bone densitometry in children and adolescence is beyond the scope of this paper and is covered in a separate ISCD publication *(25)*.

Even among normal adult white women, the effect of skeletal size may not be negligible as seen in the positive correlation between body height (a surrogate for skeletal size) and areal BMD (but not BMAD) *(26)*. A seemingly similar paradoxical relationship between areal BMD and fracture risk has been reported in Asians *(27,28)*. Asians have been shown to have a lower fracture risk than whites. However, with correction of BMD for size, Asians actually have a greater BMD than whites, consistent with their lower fracture risk.

Bone geometry is clearly an important biomechanical consideration, as an equal amount of bone mineral distributed across a larger diameter confers increased bone strength *(19)*. There is a limit to the degree of expansion that is beneficial and cortical thinning eventually leads to an unstable structure prone to buckling *(29)*. Bone expansion partially attenuates the loss in skeletal strength that occurs with age-related decreases in BMD *(30)*. Some skeletal anabolic agents influence periosteal bone apposition and may increase bone strength in excess of their effect on BMD *(31,32)*.

Clearly, more data is required to elucidate the complex relationships that link fracture susceptibility with bone density (both areal and volumetric), its principal components (BMC and area), and skeletal geometry. When such detailed information is required, QCT or BMAD calculations may be helpful. Those involved in the practice of DXA should understand the difference between areal and volumetric bone density and exercise caution in the following populations, children, in particular those with delayed growth, as well as in adults at extremed of height.

There are few published reports suggesting how bone density should be reported. However, what has appeared in the literature suggests that healthcare providers desire a description of fracture risk, the percentage reduction in bone density, management suggestions, and recommended follow-up *(33)*. One study found that a detailed letter was preferred by physicians *(34)*. Moreover, such reports can influence treatment *(35)*. Despite the desires of referring physicians, however, most densitometrists do not provide these details *(36)*.

Sending the manufacturer's printout to the referring physician is not sufficient for proper understanding of the test, nor is it adequate for defining appropriate treatment. A report should be detailed and should include the following:

- Properly identify the patient and his or her demographics.
- Properly explain the densitometry technique used and any abnormalities in performing the study.
- Provide BMD in g/cm^2 and the appropriate T-score or Z-score at each assessment site with an explanation of its meaning.
- Provide the diagnostic category.

The Canadian Panel of THE ISCD recommends that the above components constitute bone density reports created by Canadian densitometrists. The appropriate sections of the report are listed in Table

Table 1
The Elements of a Central Densitometry Report

- Demographics
- Additional reporting information
- Factors affecting study validity
- Comments on technique
- Results
- Interpretation (e.g., qualitative fracture risk assessment and significance of serial change)

1. The content of these areas may vary, depending on the center providing the service, but for complete reporting, each section should be present.

In addition to postmenopausal women, these reporting standards apply to premenopausal women, men, and children, although the criteria used for testing and interpretation of the results may vary. The following sections address specific recommendations for BMD testing and reporting in premenopausal women, men, and children.

Premenopausal Women

Background

Although low BMD is a significant risk factor for fracture in the estrogen-deficient woman postmenopause, the significance of low BMD prior to menopause is an issue that needs to be addressed. In the premenopausal woman, low BMD may reflect attainment of a lower peak bone mass, progressive bone loss following achievement of peak bone density, or both. BMD in the young healthy population is approximately gaussian in distribution, regardless of the technique used *(37)*. On a purely statistical basis, approx 15% of young healthy women have a T-score of less than –1, and 0.5% have a T-score of –2.5 or less (the densitometric criteria for osteopenia and osteoporosis, respectively, in postmenopausal women) *(4,38)*. As with fracture risk, the proportion of women affected by osteoporosis at any site increases with age *(4)*.

The majority of studies evaluating BMD prior to the onset of menopause suggest that some bone loss occurs in the premenopausal years following attainment of peak bone mass. The magnitude of premenopausal bone loss, however, is controversial and may be site dependent *(39–46)*. More rapid rates of bone loss have been seen during the perimenopausal transitional period, beginning 2–3 yr prior to the onset of menopause *(47–50)*. This accelerated rate of bone loss ends approx 3–4 yr after the last menses *(51–56)*.

Perimenopausal women with lower bone density are at greater risk of fracture *(57)*, but similar prospective fracture data are not currently available for premenopausal adult women. It is clear that healthy young premenopausal women are at a very low fracture risk even in the presence of low BMD *(58)*, and therefore, BMD alone cannot be used to make a diagnosis of osteoporosis in healthy young premenopausal women in the absence of a fragility fracture. However, premenopausal fractures are a predictor of postmenopausal fractures independent of BMD *(59,60)*.

Menstrual status is an important determinant of peak bone mass as well as the development of bone loss in women prior to the onset of menopause *(61,62)*. Subclinical decreases in circulating gonadal steroids may be associated with a lower peak bone mass and may also contribute to progressive bone loss in otherwise reproductively normal women. Assessment of menstrual status is necessary in the evaluation of low bone density in premenopausal women, as ovulatory disturbances are more common in premenopausal women with low BMD.

A number of diseases and conditions are associated with bone loss and it is necessary to ensure that low BMD in premenopausal women is not secondary to other causes as noted in Table 2. Secondary causes of bone loss should be identified by performing appropriate studies.

There is general agreement that the T-score should not be used for diagnosis in premenopausal women. The World Health Organization (WHO) classification was developed for postmenopausal women. In the premenopausal female population, it is necessary to evaluate BMD in comparison to age-matched peers. Thus, the Z-score should be evaluated. Because the risk of fracture increases with lower body weight, it would not be appropriate to correct the Z-score for weight (a feature with some densitometers). In summary, there are no established densitometric criteria for the diagnosis of osteoporosis in healthy premenopausal women. It is anticipated that prevention of bone loss in perimenopausal

women may decrease current and lifetime fracture risk. However, prospective data are required to further understand the relationship between BMD and fracture risk in the premenopausal period. This risk may be increased in the presence of secondary causes of low bone density.

Recommendations for Premenopausal Women

- BMD assessment in premenopausal women may be considered in the presence of conditions associated with low bone mass (Table 2) in conjunction with other risk factors for fracture.
- DXA assessments are to be avoided in individuals who may be pregnant.
- It is necessary to ensure that women with low bone mass are not experiencing estrogen deficiency either clinically or subclinically. It is also necessary to ensure that other causes of bone loss are not present.
- BMD cannot be used in isolation to make the diagnosis of osteoporosis in healthy premenopausal women. Diagnosis of idiopathic osteoporosis can be made in the presence of fragility fractures in the absence of secondary causes of bone loss.
- The densitometric diagnosis of osteoporosis (Z-score of –2.5 or less) may be made in premenopausal women in the presence of secondary causes of osteoporosis (e.g., glucocorticoid therapy, hypogonadism, or primary hyperparathyroidism) as these women may be at an increased risk of fracture.
- The Z-score, not the T-score, should be used premenopause and should not be weight adjusted.
- Both the hip and spine should be routinely measured. BMD measurement at the spine may be preferred for serial measurement because this site has good precision, it is infrequently affected by osteoarthritis in this age group, and spine BMD decreases rapidly at menopause *(63)*.

Table 2
Secondary Causes of Bone Loss

Diseases/Conditions
• Hypogonadism (primary and secondary)
• Primary hyperparathyroidism
• Thyrotoxicosis
• Hypercortisolism
• Growth hormone deficiency
• Osteomalacia
• Hypophosphatasia
• Mastocytosis
• Myeloproliferative disorders
• Connective tissue disorders
• Malabsorptive states
• Hepatic disorders (primary biliary cirrhosis)
• Inflammatory bowel disease
• Renal disease
• Hypercalciuria
• Osteogenesis imperfecta
Medications
• Glucocorticoids
• Thyroxine (excessive)
• Anticonvulsants (e.g., phenytoin, phenobarbital)
• Heparin (long-term)
• Lithium
• Cytotoxic chemotherapy
• Gonadotropin-releasing hormone (GnRH) agonists
• Depo medroxyprogesterone acetate (DMPA)

Men

Background

Osteoporosis affects men less commonly than women; however, it remains a significant healthcare problem in the male population *(38,64,65)*. Age is associated with increases in both vertebral and hip fracture rates in men as well as in women *(38)*. In some studies, approx 27% of hip fractures occur in men and are associated with a higher mortality than in women *(38,66)*.

Recent data suggest that the overall prevalence of vertebral deformities in men and women is similar *(67,68)*. In a Canadian population-based sample of men and women over age 50 yr, men had a prevalence of vertebral deformities (21.5%) similar to that in women (23.5%) *(67)*. Similar data were reported at a previous ISCD conference *(9)*.

It has also been suggested that prevalent vertebral deformities in men may be caused in part by unrecognized prior trauma *(67,69)*. The presence of one or

two vertebral deformities in men have been weakly associated with risk factors for osteoporosis (e.g., previous hip fracture, lack of exercise, low body mass index, or previous steroid use) *(68)*. The prevalence of multiple deformities, however, rises markedly with age in older men in a pattern similar to that in the female population. This increase is also associated with risk factors for osteoporosis. Thus, the presence of one or two spinal deformities seen in men may be related to heavy physical labor or other trauma, and multiple vertebral deformities are more likely to be related to severe underlying osteoporosis *(68)*. Because data suggest that not all vertebral deformities are a result of osteoporotic fracturing, the criteria for diagnosing osteoporotic fractures in men requires refinement *(70)*.

There are substantial differences in bone metabolism and response to treatment between men and women beyond the obvious differences in hormonal milieu *(71)*. In men, endocortical bone resorption is similar to that in women; however, periosteal bone formation is greater *(72)*. Bone dimensions are greater in men even when corrected for differences in weight and size *(72)*. Thus, DXA measures will tend to overestimate BMD in men relative to women. However, the larger bone size in men may provide a biomechanical advantage *(73)*.

Few data exist relating BMD and fracture risk in men. Such data that do exist nearly all come from cross-sectional studies and not from prospective assessments of fracture incidence *(74–77)*. In addition, there are conflicting data concerning the bone density at which fractures occur. Some studies suggest that, on average, men fracture at greater values of BMD than women *(75)*. Other reports find the BMD-fracture risk relationship to be similar in men and women and suggest that men and women fracture at the same absolute BMD *(78)*. Prospective data is needed to further define the BMD fracture risk relationship in men.

The lifetime risk of fragility fracture in men ages 50 yr and older is approx 13% *(79)*. However, the prevalence of osteoporosis in men is debatable and influenced by the choice of reference database. If a male database is used and the diagnosis predicated on the lowest T-score (–2.5 or less at the hip, spine, or distal radius), then 19% of men age 50 yr or older have osteoporosis *(79)*, comparable with the observed lifetime risk of fragility fracture. In another study of men in the same age group, spine and hip DXA-derived T-scores between –1.8 and –2.3 provided prevalence estimates that corresponded with the lifetime fracture risk *(80)*. Thus, a T-score of –2.5 may underestimate the prevalence of osteoporosis in men. Therefore, prospective data are needed to further refine the BMD definition of osteoporosis in men.

In summary, osteoporosis is an important condition in men. The diagnosis of osteoporosis can be made clinically in the presence of fragility fractures. The relationship between BMD and fracture risk in men is not well understood. This relationship may be different to that in women, in part because of differences in bone size. These differences increase with age as changes in periosteal bone apposition in men provide a degree of biomechanical protection against fracture. Nonetheless, age is associated with an increased risk of fracture in men, and increased vigilance in identifying men with low BMD is recommended.

As in women, the presence of secondary causes of bone loss in men may be associated with an increased fracture risk. In particular, hypogonadism and glucocorticoid exposure, as well as lifestyle factors, including alcohol excess, contribute to progressive increases in bone fragility. BMD and other risk factors for fracture can be integrated to enable identification of men at high risk of bone loss. The presence of secondary causes of bone loss may be associated with increased fracture risk.

T-scores were originally calculated based on the population prevalence of fractures in postmenopausal women. The T-score is widely used to assess the risk of fractures in that population *(81,82)*. In men, the relationship between fracture risk and T-score is less clearly delineated and thus remains controversial. Such a relationship could vary depending upon the presence and location of fractures *(9,75,78)*.

Some have recommended using a T-score of –2.5 derived from a female normative database to determine the risk of hip fracture in men *(83)*. Others have suggested that a male-normative database be used until more information is available *(8,9)*. Using a female-based T-score at the hip and a male-based T-score at the spine would probably create confusion among treating physicians. Therefore, attempts to find one uniform standard for the use of T-scores in men are encouraged and use of a male normative-database is recommended.

Recommendations for Men

- BMD assessment should be obtained in older (senior) men In younger men, BMD assessment should be considered in the presence of secondary causes of low BMD (Table 2) and in conjunction with other risk factors for fracture.
- A densitometric diagnosis of osteoporosis may be made in older (senior) men using the World Health Organization (WHO) classification of osteoporosis (T-score of –2.5 or less) until prospective data defining the BMD-fracture risk relationship in men are available.
- The WHO classification of osteoporosis may be applied to men from ages 20 to 65 yr in the presence of secondary causes of osteoporosis (e.g., steroid therapy, hypogonadism, or hyperparathyroidism) as these conditions may increase fracture risk independent of BMD.
- Osteoporosis in men can be diagnosed clinically in the presence of a fragility fracture
- A complete report should be made with each of the components mentioned previously (Table 1).
- A PA spine and hip study should be performed and reported routinely.
- A T-score derived from a male reference database should be used at this time to determine a diagnosis of normal BMD, osteopenia, or osteoporosis.
- A T-score derived from a male reference database should be used at this time to determine fracture risk.

Children

Background

Fractures are common in otherwise normal children, with a peak incidence between ages 9 and 12 yr in girls and 12 and 14 yr in boys *(84,85)*. The forearm is the most common site for fracture. Some *(86–90)*, but not all *(91,92)*, studies have found lower BMD in children with forearm fractures in comparison to peers without fractures. BMD values have not been linked to fractures at other skeletal sites among healthy children *(90)*.

Chronic disease, glucocorticoid use, and immobilization increase the risk of low bone density and fragility fractures in children as in adults *(93)*. Studies in these patient populations suggest a correlation between low BMD and fractures, but the cohorts are too small to establish a BMD fracture threshold in childhood. Bone densitometry may also be useful to evaluate the deficiency in bone density in chronically ill children. The DXA results must be interpreted with care, however, as alterations in growth, puberty, or body composition commonly occur in these patients. Thus, a diagnosis of childhood osteoporosis cannot be established based upon BMD alone.

The measurement of bone mass in children remains controversial, because bone is in a dynamic state during childhood, with changes in bone size being a major factor in determining bone strength. As the area of a ROI increases, the bone density appears to increase when measured using an areal technique such as DXA, but the true density may not increase. Attempts to circumvent this problem have included reporting BMC or developing a mathematical model of volumetric BMD (BMAD). True bone volume can be measured directly using QCT, but this method requires considerably more ionizing radiation exposure. Peripheral QCT (pQCT) may prove to be a reasonable alternative if precision can be improved and standardized anatomic sites and normative data are developed.

Although controversy persists regarding the best skeletal site to measure with DXA, the spine and/or total body generally are preferred as normative data are most robust for these sites and the bony landmarks are easier to recognize. Some investigators suggest exclusion of the head in total body analyses for children under age 9 yr, as it contributes to greater variability than age in younger children *(94)*. The proximal hip is challenging to evaluate in children because of poor precision and limited normative data.

Many DXA software programs report BMD T-scores regardless of the age. BMD T-scores should not be used in subjects younger than age 18–20 yr as peak bone mass has not yet been reached. Instead, a Z-score should be calculated using age- and sex-specific normative data gathered on DXA equipment from the same manufacturer. Although DXA software programs may lack pediatric reference data for all skeletal sites and ages, limited normative values for age are available in the literature *(95–97)*.

The challenge of defining the limits of normal BMD values extends beyond selection of appropriate reference data. Bone size and maturity affect BMD readings. Because children mature at varying rates, suggestions have been made to compare the BMD to children who are matched for height,

Tanner score, bone age, weight, lean body mass, or chronological age.

There is no agreement on standards for adjusting BMD or BMC for bone size, pubertal stage, skeletal maturity, or body composition. If adjustments are made for these factors, they should be mentioned in the report. Similarly, use of low density software or customized ROI parameters should be specified.

Recommendations for Children

- Bone densitometry may be helpful in assessing skeletal health in children using glucocorticoids or those with chronic disease, radiographic evidence of osteopenia, or recurrent low impact fractures.
- The spine and whole body are preferred sites for BMD measurements in children.
- The value of BMD in predicting childhood fractures has not been established.
- The diagnosis of childhood osteoporosis is made on clinical grounds and cannot be based on BMD alone.
- The spine and whole body are preferred sites for BMD measurements and reporting in children.
- Z-scores rather than T-scores should be reported until peak bone mass is reached (generally at age 20 yr).
- Z-scores should be calculated using the best available pediatric reference datasets for DXA equipment from the manufacturer. The source of reference data should be cited in the report and should be used consistently for subsequent BMD analyses.
- The WHO criteria do not apply to children, and the terms osteopenia and osteoporosis should not be used in reports.
- A Z-score of less than –2 may be reported in qualitative terms such as "low bone density for chronological age."

Serial Assessments

Background

It is common practice for patients to have a repeat DXA study, usually 1–3 yr after the baseline study. This is typically done to monitor the efficacy of pharmacologic therapy for osteoporosis or to evaluate the stability of bone density in untreated patients who are at risk for bone loss. Therefore, if used correctly, serial BMD testing is a helpful clinical tool. To ensure reliability of follow-up testing and interpretation, maintenance of precision data is mandatory for a DXA center. The precision error and least significant change (LSC) are necessary to determine whether a change in BMD is a genuine biological change or measurement error.

Accuracy

Accuracy in bone densitometry is the correlation between measured BMD and true BMD. Calculation of accuracy requires measurement of BMD in a bone sample, followed by ashing to remove nonbone elements, assaying the mineral content, and comparing the results. A low error in accuracy is important to properly diagnose osteoporosis and estimate fracture risk. In general, the accuracy of DXA instruments is excellent in comparison to instruments used to measure other biological variables.

Precision

Precision is the reproducibility of a BMD measurement or the ability of an instrument to obtain the same result with repeated testing of the same patient when no biological change has occurred. Factors influencing precision include the skill of the technologist at positioning the patient, the patient being tested, and the instrument. Precision error is often expressed as the percentage coefficient of variation (% CV) and is usually provided by the manufacturer. The manufacturer's % CV is typically better than what can be expected at a bone densitometry center and should not be used in the management of individual patients. Precision should be calculated for each technologist for each instrument according to the following protocol:

- Measure BMD at each skeletal site and ROI in 30 patients twice or 15 patients three times *(11)*. The demographics (age, sex, and BMD) of these patients should be similar to patients expected to be tested later. Patients should be repositioned between scans by getting off and on the table. All patients should be tested within 1 mo and each individual patient may be tested on one or more days *(98)*.
- Calculate the mean, SD, and CV for each ROI for each patient *(99)*.
- Calculate the root mean square SD (RMS SD) for each ROI for the group. This number is the in vivo precision error and may be expressed as CV,

% CV, or absolute value (g/cm^2). The preferred method of expression is absolute value.
- Precision error and LSC can be calculated easily with the aid of a handheld statistical calculator or with a computer spreadsheet. There are commercially available software products designed for this purpose. A free precision calculating tool is available for use from the ISCD web site at www.iscd.org.

Least Significant Change

The LSC is the minimum change in BMD considered to be a biological change at a specified level of confidence. The ISCD recommends that a 95% level of confidence be used in clinical practice. This value is obtained by multiplying the RMS SD by 2.77. For example, if the RMS SD for L1–L4 is 0.010 g/cm^2, then the LSC is 0.010 g/cm^2 × 2.77, or 0.028 g/cm^2. This means that a BMD change at L1–L4 of at least 0.028 g/cm^2 is required to have a 95% level of confidence that a biological change has occurred.

Comparability

To compare serial BMD tests, the same ROI must be measured in the same way each time. Confirmation of comparability requires visual inspection of the images and review of numerical data, especially for the area measured. The area measured should be similar (i.e., within 2%). For the spine, lumbar vertebral bodies must be labeled in the same way. For the hip, the same hip should be measured each time, and internal rotation and longitudinal orientation of the femoral shaft should be the same. There should be no intervening artifact, such as laminectomy, vertebral compression fracture, or placement of surgical hardware between scans. BMD values and not T-scores should be compared.

Clinical Applications

A low precision error is desirable. This allows for a shorter time between studies so that clinical decisions can be made sooner. The minimum time between studies depends on the expected rate of change of the disease affecting the patient and the LSC at the ROI tested. In the spine, which is typically the skeletal site with the lowest precision error and also the greatest response to pharmacologic intervention, a 1- to 2-yr interval is usually required to see a statistically significant change.

There is a relationship between the BMD response to therapy and reductions in fracture risk *(100)*, a desirable response to therapy is an increase or maintenance of bone density. A significant decline in BMD should trigger an investigation for underlying causes of nonresponse *(101)*. In patients with primary hyperparathyroidism, there may be preferential loss of cortical bone, serial studies of the mid-forearm may show a significant change prior to the spine or hip *(102)*. In patients initiating high-dose glucocorticoid therapy, a significant loss in spine BMD may be seen as early as 6 mo without pharmacologic intervention.

Recommendations

Serial BMD testing has clinical benefit in monitoring response to therapy and in evaluating patients at high risk for progressive bone loss. Calculation of precision error and LSC is necessary to determine whether a change in BMD is a genuine biological change and not simply a reflection of measurement error.

Summary and Conclusions

These standards define the minimum level of acceptable performance in Canada for assessment of BMD in premenopausal women, men, and children. Recommendations are based on the use of DXA at central skeletal sites.

There are no criteria for using BMD alone to diagnose osteoporosis in younger men, premenopausal women, or children; the diagnosis should be made only in the presence of fragility fractures or progressive bone loss. Z-scores rather than T-scores should be used before age 50 yr, and T-scores should never be used in children. A detailed report following the principles outlined in Standards I should be followed with appropriate modification for men, premenopausal women, and children as recommended in this document.

BMD in young people is normally distributed and approx 15% are more than one 1 SD below the mean and about 0.5% are more than 2.5 SD below the mean. Low BMD may be due to a low peak bone mass or to bone loss after skeletal maturity or both. In children, factors to consider in interpreting BMD results include body size (height and weight), skeletal maturity, and pubertal status. BMD should not be routinely measured in healthy young people, but only when there is a clinical indication, such as low

Appendix 1
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trauma fracture, or the presence of a disease, condition, or medication known to cause bone loss or low BMD. BMD testing may not be useful if the region to be measured has been altered by surgery, fracture, or degenerative change.

It is not clear if men and women have similar fracture risk at the same BMD, or if men are more likely to fracture at higher BMD. A male database should be used for calculating T-scores and Z-scores in men, as recommended in the ISCD position paper and consensus reached by the Canadian Panel of the ISCD. This is currently the standard for all densitometry equipment.

Serial BMD testing is useful in monitoring untreated patients for bone loss and for monitoring response to therapy. Each center must determine their precision and calculate the LSC at the 95% confidence level to determine whether a change in BMD at follow-up is real or simply within the error of the measurement. Spine BMD is preferred for monitoring as it has the lowest precision error and is most responsive to treatment. Stable or increasing BMD indicates a satisfactory treatment response. A decrease in BMD signals the need for further investigation.

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