

Prevalence of osteoporosis using bone mineral measurements at the calcaneus by dual X-ray and laser (DXL)

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Abstract Using manufacturers reference data the prevalence of osteoporosis using a *T*-score threshold of -2.5 for heel measurements by DXL technology was compared to dual-energy X-ray absorptiometry (DXA) measurements at the femoral neck, spine and forearm. The prevalence of osteoporosis for women aged 50 years or older was 28% for DXL measurements of the heel bone and 30, 22 and 32% for DXA measurements of the lumbar spine, femoral neck and forearm respectively. Bone mineral density (BMD) was also measured by DXL in the heel bone and by DXA in spine and femoral neck in 251 women (mean age 62 ± 14.5 years) when attending an osteoporosis clinic. The sensitivity and specificity for osteoporosis and osteopenia for the DXL measurements were calculated assuming a low *T*-score at the spine or femoral neck as the criterion for a correct diagnosis. The sensitivity was found to be 80% for osteoporosis and 82% for osteopenia and the specificity was 82% for osteoporosis and 89% for osteopenia. We conclude that DXL measurement at the heel bone, using a *T*-score threshold of -2.5 for classification of osteoporosis, is in concordance with the World Health Organization (WHO) definition of osteoporosis.

Keywords Bone mineral density (BMD) · Calcaneus
Dual X-ray and laser (DXL) · *T*-scores · WHO criteria

Introduction

Fracture is the clinical manifestation of osteoporosis. Measurement of bone mass by DXA is the most frequent applied technology for classifying the individual risk of

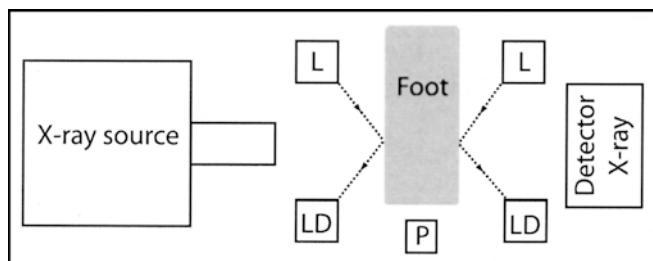
sustaining a fracture. Conventional DXA technology assumes a two-component tissue model consisting of only bone mineral and soft tissue. However, the absorption properties of adipose tissue are significantly different from those of both bone mineral and lean soft tissue. This gives rise to accuracy errors of between 10 and 20% in conventional DXA technology [1,2,3,4]. A more realistic model of tissues is a three-component model consisting of bone mineral, lean soft tissues and adipose tissues. The volume of marrow adipose tissue increases with age and is particularly large in patients with osteoporosis [5]. In order to be able to measure the bone mineral content without the influence of adipose tissue both inside and outside the measured bone, three different measured quantities has to be used. DXL technology has been developed with this in mind using two X-ray energies in combination with laser measurement of the object thickness in order to determine all three tissue components (Fig. 1). Since the total linear thickness of the object being measured is composed of the individual thickness of bone mineral, lean soft tissue and adipose tissue, it is possible to combine the thickness measurement with the two X-ray measurements and get a unique solution of the three different components at the measurement site [6].

Normalization of measurements of bone mineral content (BMC) and bone mineral density (BMD) can be achieved by calculating *T*-score, which is a gender specific normalization using the skeletal status of young normal adults as the “gold standard” [$T\text{-score} = (\text{measured BMD} - \text{young adult mean BMD}) / \text{SD of young adults}$].

Measurements at the lumbar spine, femoral neck and forearm have been applied for the diagnosis of osteoporosis and osteopenia. In the original document from the World Health Organization (WHO) [7], a measured value (*T*-score) of bone mineral > 2.5 SD below the mean for young healthy adult women at spine, femoral neck or mid-radius identifies 30% of all postmenopausal women as having osteoporosis and for hip alone 16%. According to the WHO document the diagnostic criteria

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L = Laser diode
 LD = Laser Detector
 P = Internal aluminum phantom for calibration

Fig. 1 Schematic diagram of the DXL Calscan method. The measurement time is < 1 min and effective dose to the patient less than 0.2 μ Sv

for osteoporosis should yield prevalence estimates that roughly reflect the lifetime risk of fracture. However, the intended use of the WHO criteria was for epidemiological purposes, to compare populations, and not for individual diagnosis of osteoporosis.

In clinical practice, a measurement of BMD is useful only when the fracture risk can be estimated from the measurement. It is important to distinguish assessments of fracture risk from the diagnosis of the disease osteoporosis. Several studies have revealed that the relative risk of all fractures estimated from heel BMD measurements is similar to that from DXA measurements in the hip and lumbar spine [8,9,10]. For vertebral fracture prediction, heel BMD measurements are similar to those made in the spine, and better than those made in the forearm and hip [10].

In this study, we wanted to derive *T*-scores according to the WHO procedure for DXL applied on bone mineral measurements of the heel bone. We also wanted to study whether the diagnostic criteria for osteoporosis from DXL measurements of BMD in the heel bone yielded prevalence estimates in concordance with the WHO definition and was in agreement with measurements at the femoral neck, spine and forearm.

Materials and methods

Two different populations were used in this study.

Group A

To calculate *T*-scores, reference data for Caucasian women were obtained from the product information published by equipment manufacturers, for hip (total and femoral neck) from NHANES III [11], spine and forearm (total region) DXA (Hologic) and heel DXL (Demetech). For the DXL technology, 1051 healthy women aged 15–85 years were included in the reference database. The subjects were recruited from workplaces, universities, nursing homes and pensioner associations in southern Sweden. Exclusion criteria that were applied during the data analysis were: history of osteoporosis treatment by active agents such as bisphosphonate or calcitonin, use of corticosteroids for more than 3 months, and extended bed rest. The study was approved from ethics committee

Table 1 Age-dependent BMD values with standard deviations for women for DXL Calscan

| Age group (years) | Number | Mean age (years) | SD (years) | BMD (g/cm^2) | SD (g/cm^2) |
|-------------------|--------|------------------|------------|--------------------------------|-------------------------------|
| 15–19 | 90 | 16.7 | 1.2 | 0.464 | 0.054 |
| 20–29 | 95 | 24.9 | 2.7 | 0.477 | 0.069 |
| 30–39 | 140 | 35.1 | 2.9 | 0.466 | 0.064 |
| 40–49 | 246 | 44.6 | 2.9 | 0.454 | 0.060 |
| 50–59 | 288 | 54.4 | 2.7 | 0.428 | 0.066 |
| 60–69 | 93 | 63.3 | 2.8 | 0.401 | 0.065 |
| 70–79 | 78 | 74.1 | 2.7 | 0.339 | 0.069 |
| 80–85 | 21 | 82.4 | 2.3 | 0.306 | 0.085 |

and informed written consent was obtained from all subjects. The age-dependent BMD values in 10-year age groups are shown in Table 1.

Group B

In order to compare the results from different equipment in terms of *T*-scores on patient measurements, 251 women (mean age 61.8 ± 14.5 years) attending an osteoporosis clinic were measured by DXL Calscan in the heel bone and by DXA (Lunar DPX-L) in spine and femoral neck. Among these patients, 110 were diagnosed as having osteoporosis from previous DXA measurements; 99 were participating in studies of patients with diabetes, acromegaly, and inflammatory bowel disease where BMD was one of the endpoints; and 42 were referred for investigation of osteoporosis.

Results

For group A, the young adult mean BMD values and standard deviations for the different regions of the skeleton as given by the manufacturers are shown in Table 2. From these data the mean *T*-scores for women 40–85 years of age were determined from manufacturers' data (Fig. 2). Since the peak bone mass for the DXL technology was attained at an age of 22 years the young adult reference mean and standard deviation were derived from the age interval between 18 and 27 years.

Figure 2 shows that the *T*-scores calculated from the DXL measurements at the heel bone are in close concordance with the age decline in *T*-scores from measurements of the femoral neck and spine. This also applies to the forearm measurements, up to the age of 70. That is, DXL measured mean *T*-scores at the heel bone have a close agreement to the mean *T*-scores at the sites included in the WHO definition of osteoporosis and osteopenia. However, the total hip *T*-scores show a different age decline, and the difference between spine and total hip *T*-scores is greater than between spine and DXL heel *T*-scores.

The expected percentage of Swedish Caucasian women aged 50 years and older with *T*-scores below -2.5 was calculated from manufacturers' data (group A) for different measurement sites and techniques (see Table 3). It was assumed that the normative data were normally distributed at all ages. The total number of women aged 50 years and older in Sweden was

Table 2 Peak bone mass values used in this study for DXA of the femoral neck, Total hip, spine (L1–L4) and forearm and DXL heel. Data were obtained from NHANES III [11] for femoral neck and total hip and from Hologic (USA) for Spine and Demetech

| | Femoral neck DXA (g/cm ²) | Total hip DXA (g/cm ²) | Spine DXA (g/cm ²) | Total forearm DXA (g/cm ²) | Heel DXL (g/cm ²) |
|------------------------------|--|---------------------------------------|-----------------------------------|---|----------------------------------|
| Peak bone mass | 0.858 | 0.942 | 1.040 | 0.561 | 0.483 |
| Standard deviation | 0.12 | 0.122 | 0.110 | 0.051 | 0.062 |
| SD as percent of young adult | 14.0 | 13.0 | 10.6 | 9.1 | 12.8 |

(Sweden) for heel bone. The standard deviation of the population is shown both in density units and as a percent of the young adult value

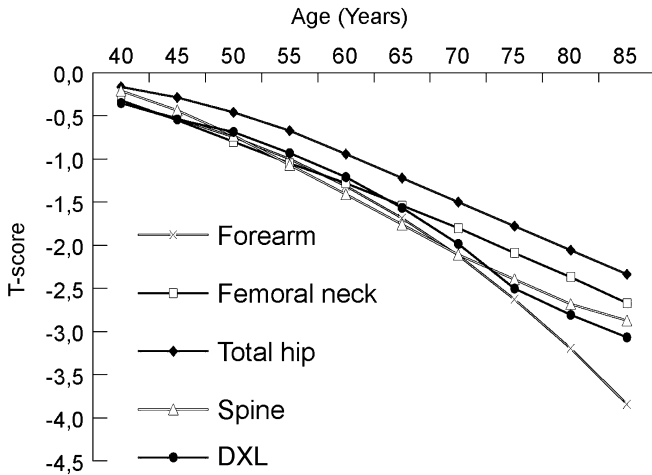


Fig. 2 Age-related decline in *T*-scores for bone mineral measurements by DXA at the spine, femoral neck, total hip, forearm and heel using DXL

Table 3 Percentage of Swedish women over the age of 50 falling at or below a *T*-score of -2.5 , by measurement site and method

| Measurement site | Percentage of women |
|-------------------|---------------------|
| Femoral neck, DXA | 22 |
| Total hip, DXA | 14 |
| Lumbar spine, DXA | 30 |
| Forearm, DXA | 32 |
| Heel, DXL | 28 |

1.523 million (year 1992) [12]. It can be seen from Table 3 that there is a close agreement between the results for femoral neck, forearm, lumbar spine and DXL heel.

The prevalence of osteoporosis for 65-year-old Caucasian women using data from group A and a *T*-score of -2.5 SD below that of young healthy women is presented in Table 4.

From Table 4 it can be seen that the femoral neck, spine, forearm and DXL heel indicate about the same prevalence of osteoporosis. The total hip gave a much lower prevalence, and probably would miss diagnoses of osteoporosis.

Assuming a low *T*-score at the spine or femoral neck is the criterion for a correct diagnosis the sensitivity, specificity, positive predictive value and negative predictive value for osteoporosis (*T*-score less than -2.5)

Table 4 Percentage of 65-year-old Caucasian women with *T*-scores below the WHO cut-off level of -2.5 SD

| | Femoral neck DXA | Total hip DXA | Spine DXA | Total forearm DXA | Heel DXL |
|------------------------|---------------------|------------------|--------------|----------------------|-------------|
| <i>T</i> -score -2.5 | 17 | 10 | 24 | 22 | 18 |

Table 5 Sensitivity, specificity, positive predictive value and negative predictive value (%) for DXL Calscan assuming a *T*-score of -2.5 or less at the femoral neck or lumbar spine as the criterion for a correct diagnosis of osteoporosis and between -1 and -2.5 for osteopenia

| | Osteoporosis | Osteopenia |
|---------------------------|--------------|------------|
| Sensitivity | 80 | 82 |
| Specificity | 82 | 89 |
| Positive predictive value | 82 | 85 |
| Negative predictive value | 81 | 69 |

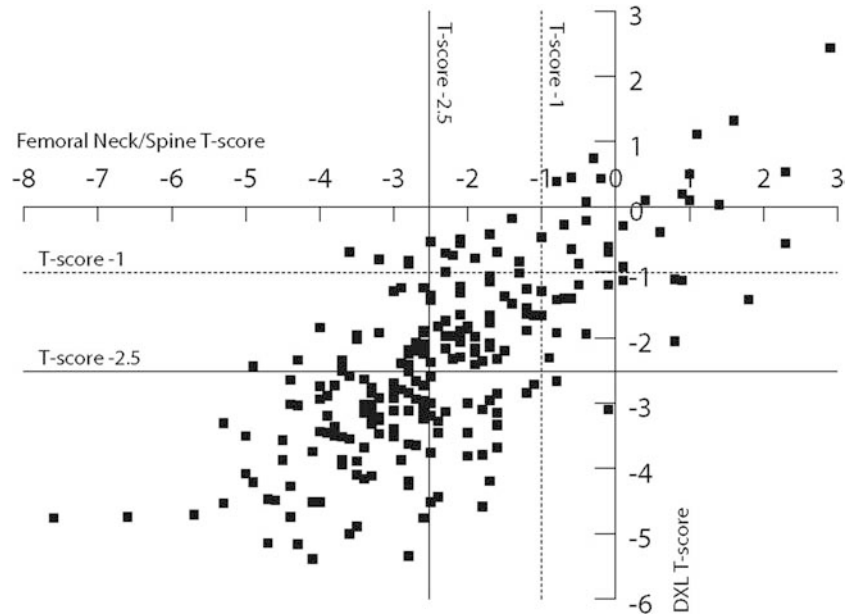
and osteopenia (*T*-score between -1 and -2.5) for DXL Calscan at the heel were calculated for the 251 patients in group B (Table 5). Figure 3 shows the DXL *T*-scores plotted against the spine and femoral neck *T*-scores for group B. The negative predictive value was lower than the positive predictive value, however, this may be an effect of the low number of individuals that were healthy in group B. The kappa score for the DXL technology was 0.62, which could be compared to the kappa score for femoral neck BMD against lumbar spine BMD, which was 0.49.

The short-term in-vivo precision for the DXL Calscan device, as assessed by duplicate measurements on the same day on 35 healthy individuals (mean age 52 years, range 25–72 years), was 1.2% (root-mean-square CV).

Discussion

In this study, we have demonstrated that the DXL measurement technology at the heel bone shows a similar pattern in terms of *T*-scores as axial measures and forearm measures, and thus may be used for diagnosis equally as well as axial DXA. The diagnostic capabilities of the DXL measurements are confirmed by the high

Fig. 3 DXL T -scores plotted against DXA T -scores for the femoral neck or spine. For the femoral neck and spine the lowest T -score value was used as the criterion for a correct diagnosis. The *solid line* represents a T -score of -2.5 and the *dotted line* a T -score of -1



sensitivity and specificity found when spine and femoral neck are used for diagnosis. A cut-off T -score of -2.5 or less for DXL technology identifies about the same number of women as osteoporotic, as do measurements at the femoral neck, lumbar spine or forearm, which suggests that the WHO threshold can be applied to this new technology.

BMD measurements should be used together with other risk factors for fracture as the basis for the decision of treatment. The clinical use of BMD measurements in an accurate and precise way is important for diagnosis, regardless of which technology is used, as long as it gives a good assessment of fracture risk. Axial DXA has over time become an established technology for measurements of BMD. The cut-off value of -2.5 SD below the average of the healthy young reference range is appropriate at any site if measurements at that site identify approximately the same proportion of adult women as having osteoporosis (and the lifetime risk of fracture at hip, spine or forearm) as the WHO defined sites do.

Several analyses have shown a distinct relationship between reduced BMD and increased risk of fracture [13,14,15,16]. A decrease of 1 SD in the BMD results in a doubling of the fracture risk. One meta-analysis [10], based only on prospective studies, shows that the predictive power for any fracture for a BMD value one standard deviation below age adjusted mean was equally strong for all measurement sites and techniques. For hip fracture prediction, a measurement at the hip was the best site and the heel the second best site. For vertebral fracture prediction, heel bone measurement was just as good as measurement at the spine, and better than those made at the forearm or hip. However, the fracture prediction capabilities of the DXL technology have not yet been established and the results from this meta-analysis may not be applicable to DXL technology.

For the forearm, the T -scores decreased more rapidly than the DXL heel T -scores after the age of 70. This may be an effect of the enlarging of the tubular bones as a function of age. This will enlarge the integrated area and thus produce a smaller BMD value [17].

The WHO definition of osteoporosis from BMD measurements is based on the premise that a diagnostic criterion should identify a proportion of subjects that is equal to the lifetime risk for common fractures in the same population. Table 6 shows the lifetime risk for different types of fractures resulting from osteoporosis for Swedish women aged 50 years and older [12].

As can be seen from Table 6, about 50% of the Swedish women over the age of 50 years will suffer an osteoporotic fracture. With the current definition of osteoporosis based on T -scores, about 20–30% of women aged 50 years or older will be identified as having osteoporosis if measurements are made in the femoral neck, forearm or spine by DXA or heel by DXL. If measurements are made at total hip by DXA 15% will be identified as having osteoporosis. This can be regarded as a significant under-diagnosis.

The discrepancies in the prevalence of osteoporosis found at different measurement locations are a result of many factors. Among those are differences in the reference population, amount of cortical and trabecular bone and technology based differences [18]. These discrepancies are greater for different locations in the

Table 6 Lifetime risk of different fractures in Sweden [12]

| Location | Lifetime risk (%) |
|---------------------------|-------------------|
| Hip | 25 |
| Vertebral body | 25 |
| Forearm | 40 |
| Any osteoporotic fracture | 50 |

axial skeleton compared to the differences between heel bone measurements by DXL and axial measurements by DXA. According to WHO [7], the measurements of spine, hip and forearm gave a prevalence of osteoporosis of 30% and for hip alone 16% when a *T*-score threshold of -2.5 was used. If single hip measurements are performed, as when lumbar osteoarthritis is present, about 25% fewer patients will be identified as osteoporotic. If only total hip measurements are used, then a *T*-score of -2.1 should have been used in order to have a prevalence of osteoporosis of 30%.

By using the WHO criteria for total hip, one will consistently under-diagnose osteoporosis. However, if measurements are made in the femoral neck, forearm or spine by DXA or heel by DXL these will be in concordance with the WHO document.

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