Calcif Tissue Int (1991) 49:174–178

Calcified Tissue International
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Precision and Stability of Dual-Energy X-ray Absorptiometry Measurements

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Received April 25, 1990, and in revised form July 30, 1990

Summary. This study was performed to determine the precision and stability of dual-energy X-ray absorptiometry (DEXA) measurements, to compare bone mineral density (BMD) of subjects measured by DEXA and radionuclide dual-photon absorptiometry (DPA), and to evaluate different absorber materials for use with an external standard. Short-term precision (% coefficient of variation, CV) was determined in 6 subjects scanned six times each with repositioning, initially and 9 months later. Mean CV was 1.04% for spine and 2.13% for femoral neck BMD; for whole-body measurements in 5 subjects, mean CV was 0.64% for BMD, 2.2% for fat, and 1.05% for lean body mass. Precision of aluminum phantom measurements made over a 9-month period was 0.89% with the phantom in 15.2 cm, 0.88% in 20.3 cm, and 1.42% in 27.9 cm of water. In 51 subjects, BMD by DEXA and DPA was correlated for the spine (r = 0.98, P = 0.000) and femoral neck (r = 0.91, P = 0.000). Spine BMD was 4.5% lower and femoral neck BMD 3.1% higher by DEXA than by DPA. An aluminum phantom was scanned repeatedly, in both water and in an oil/water (30:70) mixture at thicknesses ranging from 15.2 through 27.9 cm. Phantom BMD was lower at 15.2 cm than at higher thicknesses of both water and oil/water (P = 0.05, ANOVA). The phantom was scanned repeatedly in 15.2, 20.3, and 27.9 cm of water over a 9 month period. In 15.2 and 20.3 cm of water, phantom BMD did not vary significantly whereas in 27.9 cm of water (equivalent to a human over 30 cm thick), phantom BMD increased 2.3% (P = 0.01) over the 9 months.

Key words: Dual-energy X-ray absorptiometry – Precision – Stability.

Dual-energy X-ray absorptiometry (DEXA) is a relatively new method of measuring bone mineral density (BMD). It is gradually replacing radionuclide dual-photon absorptiometry (DPA) because it offers improved precision as well as decreased scan time and decreased radiation exposure. The most important performance features of DEXA are reproducibility *in vivo* and the stability of measurements over time. These are the characteristics that determine its usefulness both in monitoring the treatment of osteoporotic patients and in measuring outcome in longitudinal trials. Short-term *in vivo* precision of DEXA measurements is in the range of 1.0–1.4% (coefficient of variation, CV) for the lumbar spine [1–5], 1.8–1.9% for the hip [3, 5], and 0.5–1.5 for the whole body [3]. Values for the spine and femoral neck are approximately half of those achieved commonly by DPA [2, 5] whereas values for the whole body [3, 6] are similar by the two methods.

Spine BMD measurements by DPA have been reported to drift in relation to source [7, 8], source age [7, 9, 10], and truncal thickness [7]. Drift related to the source age and subject thickness has been diminished by analysis software modifications [7] whereas variation resulting from different gadolinium sources persists [7, 8]. In principle, replacement of ^{153}Gd with an X-ray source should eliminate long-term drift in BMD measurements. However, because the X-ray sources currently in use are fairly new, this remains to be demonstrated. The intent of this initial evaluation of DEXA is to (1) assess short-term precision of spine, femur, and total body measurements *in vivo* and longer-term precision *in vitro;* (2) compare spine and femur BMD by DEXA and DPA; (3) evaluate different soft tissue equivalent materials for use with external standards; and (4) determine the stability of phantom measurements over time.

Subjects and Methods

To evaluate precision *in vivo,* 6 healthy white postmenopausal women had DEXA scans of the lumbar spine (L2–4) and femoral neck performed six times each initially and again 9 months later. Five of the same women had six total body scans at the same intervals. All six scans of each site were performed on the same day, and for each scan the subject was repositioned. At enrollment, these women were 46–71 years of age (mean SD 59 ± 9.7 years) and 1–20 years since menopause, weighed 52–94 kg (mean 65 ± 15.4 kg) and had truncal thickness, measured at the level of the umbilicus with subjects supine, of 16.3–25.0 cm (mean 20.1 ± 3.1 cm).

Spine and femoral neck BMD were measured by DEXA and DPA in 51 healthy white postmenopausal women scanned once on each scanner, on the same day. The women were 43–70 years of age (mean ± SD 61 ± 5.7 years) and 1–30 years since menopause, 44–95 kg in weight (mean 66 ± 11.2 kg), 15.1–27.3 cm thick at the umbilicus (mean 20.7 ± 2.8 cm), and 145–178 cm tall (mean 159 ± 7.1 cm). Two-thirds of the women were taking a 500 mg calcium supplement. None had a vertebral fracture or radiographic abnormality in the scan field.

The Radiation Safety and Human Investigation Review Committees at Tufts University approved the study protocol. Written informed consent was obtained from each participant.

Phantom

An aluminum phantom and two soft tissue equivalents were evaluated for use with an external standard. The phantom is a 16 × 4 × 1 cm aluminum plate sectioned into regions L1–4 (Lunar Radiation Corp. Madison, WI). It was positioned in the bottom of a series of four thin plastic containers which hold up to 28.0 cm of liquid. The

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Table 1. Mean BMD (g/cm^2) and precision (% CV) of BMD measurements conducted initially and repeated 9 months later on 6 subjects scanned six times each

Subject	Thickness (cm)[a]	L2–4 BMD (month 0)	L2–4 % CV (month 0)	L2–4 % CV (month 9)	Femoral neck BMD (month 0)	Femoral neck % CV (month 0)	Femoral neck % CV (month 9)	Total body BMD (month 0)	Total body % CV (month 0)	Total body % CV (month 9)
1	16.3	1.241	0.81	0.42	1.056	0.66	1.63	1.169	0.43	0.43
2	18.6	0.937	0.43	1.19	0.705	2.55	2.76	0.977	0.92	0.52
3	18.9	0.863	0.58	1.76	0.704	3.13	1.33	0.960	0.52	0.84
4	19.7	0.847	1.42	0.91	0.826	2.18	1.95	0.973	0.62	1.02
5	22.5	0.823	2.31	1.15	0.808	1.98	1.81	1.006	0.80	0.29
6	25.0	1.063	0.94	0.60	0.920	2.60	2.95	—[b]	—	—
All	20.2	0.962	1.08	1.01	0.837	2.18	2.07	1.017	0.66	0.62
SD	3.1	0.162	0.69	0.48	0.135	0.84	0.64	0.087	0.20	0.30

[a] Truncal thickness measured at the level of the umbilicus with subjects supine
[b] Subject width exceeded scan field

Table 2. Mean (±SD) weight and precision (% CV) of whole-body bone mineral, lean tissue, and fat tissue

Measurement site	BMC g	BMC % CV	Lean g	Lean % CV	Fat g	Fat % CV
Month 0						
Arms	254 ± 80	1.7 ± 0.7	3,837 ± 605	3.7 ± 1.7	2,421 ± 1,040	6.7 ± 1.7
Legs	783 ± 197	1.1 ± 0.5	13,675 ± 2,313	1.5 ± 0.6	8,460 ± 1,689	2.5 ± 1.2
Trunk	624 ± 202	2.4 ± 0.9	18,451 ± 2,380	1.3 ± 0.4	7,423 ± 2,603	4.1 ± 1.1
Total body	2,132 ± 522	0.8 ± 0.4	38,372 ± 5,213	1.1 ± 0.5	19,723 ± 5,497	2.7 ± 0.8
Month 9						
Arms	265 ± 85	2.0 ± 0.8	3,862 ± 721	2.9 ± 1.3	2,570 ± 1,010	4.3 ± 1.6
Legs	799 ± 193	1.2 ± 0.7	12,977 ± 2,249	1.7 ± 0.6	8,322 ± 1,217	2.4 ± 1.0
Trunk	653 ± 203	2.8 ± 1.2	17,380 ± 2,627	1.4 ± 0.2	7,634 ± 2,014	2.8 ± 0.6
Total body	2,184 ± 520	1.2 ± 0.6	36,570 ± 5,593	1.0 ± 0.5	19,981 ± 4,394	1.7 ± 0.5

aluminum phantom was scanned five times in 15.2, 17.8, 20.3, 22.9, 25.4, and 27.9 cm of water to determine reproducibility. It was also scanned repeatedly over a 9 month period in 15.2, 20.3, and 27.9 cm of water to determine stability. In addition, the aluminum phantom was scanned six times at the different thicknesses in a combination of 30% vegetable oil and 70% water, a mixture meant to simulate human soft tissue.

Densitometry

Dual-energy X-ray absorptiometry is a recently developed technique employing an X-ray source with effective energies at 40 and 70 keV [3]. Scans were performed with a model DPX scanner (Lunar Radiation Corp., Madison, WI) and analyzed with software version 3.1. High keV fluctuated between 621,147 and 661,595 cps and low keV between 383,225 and 409,511 cps over the study period. For the spine and femur, scan speed was 0.8 mm/second for women under 22.0 cm thick at the umbilicus and weighing less than 68 kg, and 0.4 mm/second for women 22.0 cm thick and above or weighing 68 kg or more. Spine scans required 7–14 minutes each and femur scans 5–8 minutes each. Whole-body scans in the 5 women were performed at a scan speed of 0.4 mm/second initially and at a speed of 0.8 mm/second 9 months later. Whole-body scans took 20–30 minutes initially and 15–22 minutes at the faster speed. The phantom was scanned at a speed of 0.8 mm/second for thicknesses of 20.3 cm or less and at 0.4 mm/second for thicknesses of 22.9 cm and above.

The DPA measurements were made with a model DP-3 scanner (Lunar Radiation Corp., Madison, WI) and analyzed with software version 08C. Subjects were scanned at a speed of 5.0 mm/second, a step interval of 4.5 mm, and collimation of 13 mm. The 44 keV air values ranged from 56,584 to 44,581 cps with the first ^{153}Gd source and from 127,235 to 119,817 cps with the second.

Statistical Analyses

Two-way analysis of variance (ANOVA) revealed that the aluminum phantom measurements at different thicknesses for the two soft tissue equivalent materials were not parallel. Thus, one-way ANOVA (with Bonferroni simultaneous confidence intervals) was used to evaluate aluminum phantom measurements at different thicknesses and Student's paired t test was used to compare water alone and water/oil soft tissue equivalents at each thickness. At each thickness, changes in aluminum phantom BMD, BMC, and area over time were evaluated with linear regression equations. The 95% confidence intervals and levels of significance of slopes compared with zero were calculated with an F-test.

Results

Precision of DEXA spine, femur, and total body BMD measurements in 6 women scanned six times each initially and again 9 months later is provided in Table 1. The coefficient of variation (%CV) of the BMD measurements at each site was stable over the 9-month study interval. Total body and femur precision did not vary with subject thickness within the ranges of 16.3–22.5 cm and 16.3–25.0 cm of truncal thickness, respectively. In the first group of scans, abdominal thickness appeared to affect precision of spine BMD measurements, but this phenomenon was not repeated in the second group of scans. Precision tended to be better in those with higher BMD (not significantly). The precision of measurements of mineral, lean tissue, and fat tissue was assessed in 5 of the 6 women (Table 2). As expected, precision

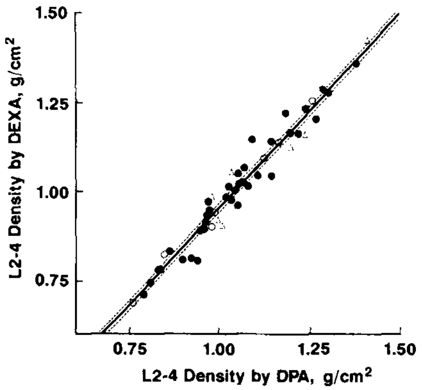

Fig. 1. Spine BMD by DEXA and DPA in 51 women. Correlation coefficient r = 0.98. (----) 95% confidence intervals; (○) women with truncal thickness up to 18.2 cm; (△) truncal thickness 24.2 cm or greater; (●) those in between.

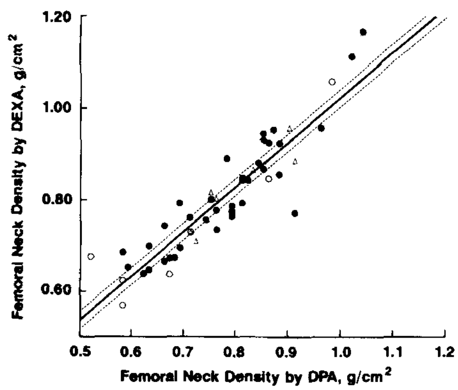

Fig. 2. Femoral neck BMD by DEXA and DPA in 51 women. Correlation coefficient r = 0.91. (----) 95% confidence intervals; (○) volunteers with truncal thickness up to 18.2 cm; (△) truncal thickness 24.2 cm or greater; and (●) those in between.

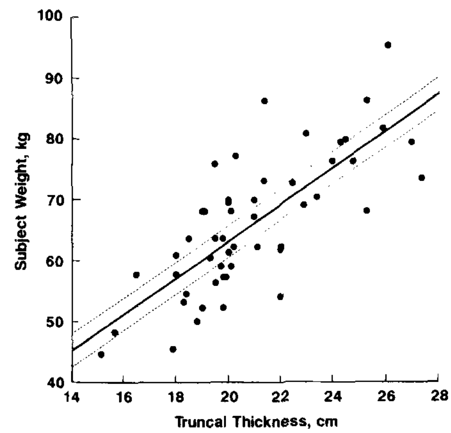

Fig. 3. Relationship of truncal thickness measured at the umbilicus and weight in 51 women. (----) 95% confidence limits; r = 0.76, P = 0.0001; weight = 3.03 × thickness + 2.79.

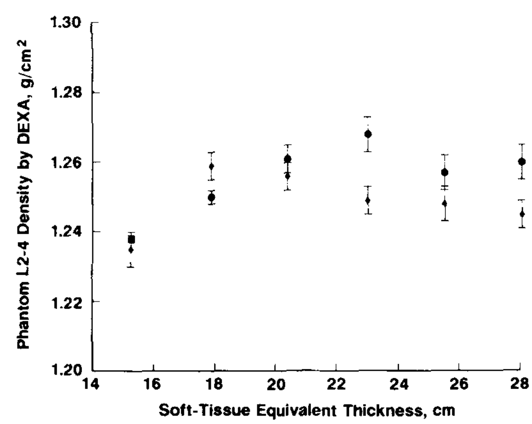

Fig. 4. BMD of aluminum phantom scanned in different thicknesses of water (●) and in a 30:70 oil/water mixture (♦). Each point represents a mean (± SEM) of five (water) or six (oil/water) scans. BMD is significantly lower at 15.2 cm than at higher thicknesses of both water and oil/water ($P < 0.05$, ANOVA). BMD is higher when the phantom is scanned in water than in oil/water at both 22.9 and 27.9 cm of thickness ($P = 0.03$).

of total body was greater than that of regional measurements.

In 51 normal women, measurements of spine and femoral neck BMD by DEXA and DPA were significantly correlated. The correlation coefficient was 0.98 ($P = 0.000$) for the spine (Fig. 1) and 0.91 ($P = 0.000$) for the femoral neck (Fig. 2). Spine BMD measurements on the DEXA were 4.5% lower and femoral neck measurements 3.1% higher than those on the DPA (calculated from the regression lines). Subjects with lowest and highest truncal thickness were evenly distributed around the regression lines (Figs. 1 and 2). As expected, weight and truncal thickness were highly correlated in the 51 women (r = 0.76, $P = 0.0001$, Fig. 3).

Soft-tissue equivalent thickness affects phantom BMD measured by DEXA. The BMD of the aluminum phantom was significantly lower when scanned in 15.2 cm than in thicknesses of 17.8–27.9 cm of water ($P < 0.05$, ANOVA, Fig. 4). BMD of the phantom was also significantly lower in 15.2 cm than in higher thicknesses when it was scanned in the 30:70 oil/water mixture ($P < 0.01$, ANOVA). BMD of the phantom was higher when the phantom was scanned in water than when scanned in oil and water at 22.9 and 27.9 cm of thickness ($P = 0.03$). Overall, BMD of the phantom in both water and oil/water varied up to 2.4% with the different thicknesses.

Stability of phantom measurements was assessed over a 9-month period. When scanned in 15.2 cm of water, aluminum phantom BMD was stable (Fig. 5) although bone mineral content (BMC) increased 0.8% and area increased 1.0%. All measurements of the phantom in 20.3 cm of water were stable. With the phantom in 27.9 cm of water, both BMD and BMC increased significantly over the 9-month period. Specifically, BMD increased 2.3% ($P = 0.01$), BMC increased 3.1% ($P = 0.02$), and area had an upward trend (0.8%, $P = 0.37$). Based on all scans performed over the 9-month period, the coefficient of variation (%CV) of phantom BMD was 0.89% when measured in 15.2 cm of water (n = 32), 0.88% in 20.3 cm of water (n = 52), and 1.42% in 27.9 cm of water (n = 38). For comparison, short-term precision of five phantom scans at each thickness was 0.27% in 15.2 cm, 0.76% in 20.3 cm, and 0.81% in 27.9 cm of water.

Mean percent fat values provided by the spine software (derived from the ratio of low to high energy attenuation in soft tissue) varied widely with soft-tissue equivalent composition. The phantom in water averaged 6.3 ± 1.7 (SD) fat and in oil/water (30:70) it averaged 27.2 ± 1.6% fat. For compar-

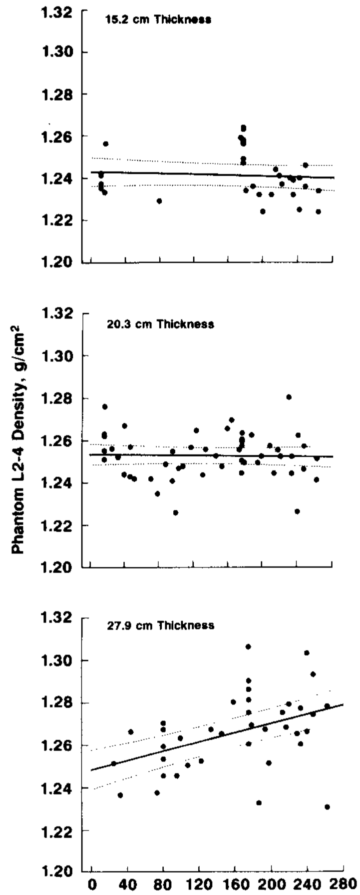

Fig. 5. Aluminum phantom scanned in 15.2, 20.3, and 27.9 cm of water repeatedly over a 9-month period. Regression lines (—) and 95% confidence intervals (----). Slope differs significantly from zero only at 27.9 cm of water (P = 0.01).

ison, mean fat in the spine scan region in 51 of the women in this study was 25.9 ± 8.3 (SD)%. The percent fat values declined slightly as the soft tissue equivalent thickness increased from 15.2 to 27.9 cm (from 7.4 to 5.0% for water and from 28.9 to 26.3% for oil/water.

Discussion

In this evaluation of DEXA, the short-term *in vivo* precision of BMD of the spine, femoral neck, and whole body is similar to that reported by others [1–6]. The improvement in precision over DPA has been attributed largely to the improved resolution of the images. The high degree of reproducibility was maintained when the same subjects were reevaluated after a 9-month interval. These subjects comprised a broad range of both truncal thickness and BMD values. Precision error *in vitro* is inversely related to BMD [4]. This relationship is attenuated *in vivo* because of the substantial fixed contribution of repositioning to precision error at different levels of BMD. Nonetheless, precision error tends to be greater in those most likely to need bone scans, that is, osteopenic patients.

Precision of body composition measurements by DPA and DEXA is similar [6] and compares favorably with precision of other established methods including total-body water, potassium (K-40), and neutron-activation methods for total body calcium and nitrogen. Comparisons of DPA with these methods, in the same subjects, have recently been reported by Heymsfield et al. [11]. In this study, precision of body composition measurements was not compromised by increasing scan speed to 0.8 mm/second.

Variation in phantom measurements was stable over the 9-month period at 20.3 cm of water and increased modestly (to 0.89 and 1.42% CV) at lower and higher thicknesses. Longer-term precision cannot be evaluated in women in this study because of their expected bone loss during the study period.

Soft tissue equivalent composition [3, 12] and thickness [4, 12] have a small but measurable effect on phantom BMD measured by DEXA. As expected, BMD of the phantom tended to be higher when measured in the 30:70 oil/water mixture (read as 27% fat) than in water (6.3% fat) alone. Although mean proportions of fat and lean tissue in the trunk vary somewhat with truncal thickness, the 30:70 oil/water mixture provides a reasonable simulation of soft tissue. BMD measured by DEXA was stable in the thickness range of 17.8–27.9 cm but was slightly lower when the phantom was measured in 15.2 cm of both water (2% lower) and the oil:water mixture (1.3% lower). This thickness effect is modest but could have some impact in direct comparisons of BMD in populations with very low and higher truncal thicknesses or in patients or study subjects who have substantial changes in thickness (weight) during the observation period.

High correlations between measurements of BMD by DPA and DEXA, as observed in this study, have been reported for X-ray instruments made by Hologic, Inc., Waltham, MA [12–14] and by Lunar Radiation Corp., Madison, WI [3]. In most [12–14], but not all [3], of these studies, spine BMD values were lower by DEXA than by DPA, as was observed here. In subjects within the truncal thickness range of 17.8 through 27.9 cm, the relationship between BMD by DEXA and DPA was independent of subject thickness. There were too few thin subjects in this study to allow a comparison of spine BMD by DPA and DEXA at a truncal thickness of around 15.2 cm. On the basis of the phantom measurements, however, spine BMD by DEXA in very thin subjects may be more than 4.5% lower than BMD measured by DPA. Femoral neck measurements by the two methods are also highly correlated in this study and in another [3]. The DEXA values were 3.1% higher than DPA in this study, in contrast to previous findings of no difference [3]. Despite the facts that DEXA and DPA measurements are highly correlated and the mean offset can be adjusted, BMD values of an individual subject can vary substantially on the two instruments. It is therefore preferable not to switch instruments in the course of a longitudinal trial.

Based on nearly 9 months of observation, there appears to be some upward drift in BMC and BMD of the phantom measured by DEXA in the highest thickness of water, 27.9 cm. This is not attributable to variation over time in the count rates. It could be an artifact (e.g., result of a short observation period) or be due to subtle change over time in the energies that is apparent only at the highest thickness of water. The 27.9 cm of water is equivalent to soft-tissue thickness greater than 30 cm, a size rarely encountered. The stability of measurements of the phantom, scanned in the more physiologic 30:70 oil/water mixture, remains to be established. Longer-term surveillance and serial spectral analyses may clarify the source of the observed drift.

In conclusion, the DEXA scanner represents a major advance in bone densitometry. The short-term precision *in vivo* of spine and of whole body mineral and lean tissue measurements is excellent. Precision of femoral neck measurements in these older subjects represents a more modest improvement over DPA. BMD measured by DEXA and DPA are highly correlated. Serial measurements of a phantom in 15.2 and 20.3 cm of water were stable over 9 months. Over this same period, there was some upward drift in phantom BMD measurements at 27.9 cm of water (equivalent to over 30 cm of truncal thickness). Use of an external standard, measured at different soft-tissue equivalent thicknesses, is important as the long-term stability of DEXA measurements is not yet established. In order to be able to use external standard data most effectively, should it turn out to be necessary, the phantom is best scanned at multiple thicknesses through the physiologic range in a material that simulates human soft tissue.

Acknowledgments. This study was supported by the USDA Human Nutrition Research Center on Aging at Tufts University (Contract No. 53-3K06-5-10). The contents of this publication do not necessarily reflect the views or policies of the U.S. Department of Agriculture, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

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