
Precision of Dual-Energy X-Ray Absorptiometry in Determining Bone Mineral Density and Content of Various Skeletal Sites

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Repeated measurements of bone mineral density (BMD) by dual-energy x-ray absorptiometry (DEXA) reliably indicate changes in the bone mineral content (BMC) of the lumbar spine and proximal femur, but its applicability to other sites has not been properly determined. The in-vivo day-to-day precision of DEXA (Norland XR-26) for lumbar spine, femoral neck, distal femur, patella, proximal tibia, calcaneus and distal radius was evaluated for 15 subjects who were scanned three times for 2 wk. Intra- and interobserver errors were also determined for image analysis. For clearly defined regions of interest, the following precision values were obtained for BMD with low intra- and interobserver error: 1.7% (lumbar spine), 1.3% (femoral neck), 1.2% (distal femur), 1.0% (patella), 0.7% (proximal tibia), 1.3% (calcaneus) and 1.9% (distal radius). The precision for BMC was lower. The results indicate that DEXA can successfully and precisely measure BMD of sites not commonly assessed by this technique.

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Bone densitometry is a sensitive noninvasive method that permits the early detection of trabecular bone loss before symptomatic disease appears. It is also a useful method with which to evaluate the osteogenic effect of various interventions on bone properties. Several techniques are commonly used for measuring bone mineral density (BMD) and bone mineral content (BMC), including single-photon absorptiometry (SPA), dual-photon absorptiometry (DPA), dual-energy x-ray absorptiometry (DEXA) and quantitative computed tomography (QCT) (1-7). For accuracy, precision, stability, cost, subject radiation dose and compliance, freedom to select skeletal sites, speed and ease of scanning, DEXA seems to be the most appropriate choice.

Of the aforementioned parameters, precision is the most important with respect to whether temporal difference in either the BMD or BMC of an individual subject is real. Many factors influence the precision of DEXA and should

be recognized. They include instrument-, operator- and subject-dependent factors, of which the last two can be beneficially affected by proper quality control and measurement procedures (8,9).

In longitudinal trials and intervention studies, our laboratory has used a commercial DEXA densitometer for about 2 yr and has performed over 2000 scans at a variety of skeletal sites. The sites measured include the conventional clinical regions of interest (ROIs) and those not commonly assessed by DEXA. The objectives of this study were to demonstrate the potential usefulness of DEXA in the assessment of BMD and BMC at various skeletal sites and to establish our procedures for measuring BMD and BMC in lumbar spine, femoral neck, knee, calcaneus and distal radius by introducing consistent and precise ROIs for image analysis and for proper subject positioning during the measurements.

MATERIALS AND METHODS

Fifteen volunteers (3 men, 12 women) participated in the study. They had a mean age of 38.1 yr (s.d., 12.3, range, 23-61), a mean height of 167.5 cm (s.d., 10.3, range, 153-186) cm and a mean weight of 68.5 kg (s.d., 16.2, range, 50-98).

BMD and BMC were measured with a DEXA bone densitometer (Norland XR-26, Norland Corp.) that uses an x-ray tube (focal spot size 0.9 mm²) operating at 100 kV_p (1.0 mA) coupled with a K-edge samarium filter module. This system gave effective energies of 46.8 and 80 keV. The samarium module consists of four components (samarium composition in brackets), of which one is fixed (0.6 g/cm²) and the rest are optional (0.12 g/cm², 0.24 g/cm², 0.48 g/cm²). This arrangement provides increased filtration in steps with an aluminum equivalent from 8.9 mm up to 64.0 mm at 100 kV_p. This multistage filter (eight different filters) permits the intensity of the x-ray beam to be optimized for patient thickness, while allowing the tube to operate at constant power.

The source collimator is 4 mm in diameter and is located above the filter assembly, 16 cm above the focal spot. The x-ray beam is about 6 mm in diameter at the table level (23 cm above the focal spot) and widens to about 12 mm at the detector. The detector collimator has two apertures: the lower one is 8 mm in diameter (68 cm above the focal spot) and the upper one is 8.5 mm in diameter (72.3 cm above the focal spot). The detector itself consists of a low-energy detector (0.3 mm NaI) 76.1 cm

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above the focal spot and a high-energy detector (7 mm NaI) 81.2 cm above the focal spot.

The densitometer was calibrated daily by a dual-material standard according to the manufacturer's recommendations. Daily determinations of the BMD and BMC of a lumbar spine phantom at exactly the same location on the table were used to control measurement quality. The total BMC of the phantom, which simulated vertebrae L2–L4 embedded in a 2.2-cm thick acrylic block, was 35.28 g, the total area was 38.71 cm², and the mean BMD was 0.911 g/cm². Based on results from about 300 daily measurements, the long-term precision (coefficient of variation) was 0.7%, and there were no significant trends during this period. The short-term precision obtained from 10 consecutive measurements of the phantom done at exactly the same location on the same day was 0.7% for both BMD and BMC. The variation in the area was 0.4%. These precision data can be regarded as indicating the best possible precision of our densitometer, and they were affected only by the technical performance of the apparatus.

Not only were standard lumbar spine and hip scans assessed, but modified calcaneus, distal radius scans and lateral scans of the knee region were also obtained with the general scan option (software version 2.1.1). The time required for each type of scan depended on the scan speed, the selected pixel size and the width of the scan. It varied from about 2 min for the distal radius scan up to about 10 min for the lateral knee scan. The spatial resolution of the scan was dependent on scan-line spacing and point resolution and was indicated by pixel size. The skin entrance dose was determined based on the type of scan. It was the highest (230 μSv at maximum with a body thickness over 22 cm) in the hip scan, much lower in the lumbar spine and lateral knee scans and only marginal in the calcaneus and distal radius scans.

The average BMD and BMC values were determined for vertebrae L2–L4, right femoral neck, right calcaneus, right distal radius, right distal femur, right patella and right proximal tibia. Subject positioning, determination of the ROIs for each skeletal site and scan analysis were carried out consistently by the operator according to the methods described for each skeletal site.

Procedures for Different Skeletal Sites

Lumbar Spine Scan. Subjects were positioned with appropriate support blocks according to the manufacturer's recommendations for lumbar spine measurements. The starting point was the palpated apex of the processus xiphoideus. The end point was located at the level of the iliac crest. The width of the scan was 10 cm, and its pixel size was 1.5 × 1.5 mm. The scan speed was 60 mm/sec. The ROI was defined as the area between two parallel lines located in intervertebral spaces of L1–L2 and L4–L5 (Fig. 1a). Special attention was given to reliably identifying the Th12/L1 and L5 vertebrae.

Hip Scan. Subjects were positioned with appropriate support blocks according to the manufacturer's recommendations for proximal femur measurements, and images were acquired using the procedure for the standard right hip scan with a pixel size of 1 × 1 mm. The scan speed was 45 mm/sec. The ROI was defined as a region between two parallel lines, the upper located 1 mm (one pixel) distal to the recognizable base of the femoral neck, and the lower one 1 mm proximal to the recognizable base of the trochanter major (Fig. 1b).

Calcaneus Scan. The subject laid comfortably on his or her right side with the lower leg fixed at a 120° knee angle by two specific support blocks at the anterior and posterior sides of the knee, and with the upper leg resting on the posterior support block. The hip angle was approximately 150°. The starting point was located above the Achilles' tendon approximately at the malleolar level and the end point was below the calcaneus (Fig. 1c). The baseline point was located approximately 1 cm inferior to the starting point. The width of the scan was 6 cm and its pixel size was 1 × 1 mm. The scan speed was 45 mm/sec. The ROI was defined as a rectangle whose proximal side was located parallel to the posterior edge of the talus. The area of the rectangle was determined based on the dimensions of the distal calcaneus (Fig. 1c).

Distal Radius Scan. The subject was positioned comfortably on a chair beside the scan table with the volar side of his or her slightly clenched hand and the upper arm resting on the table. The starting point was located approximately 1 cm above the

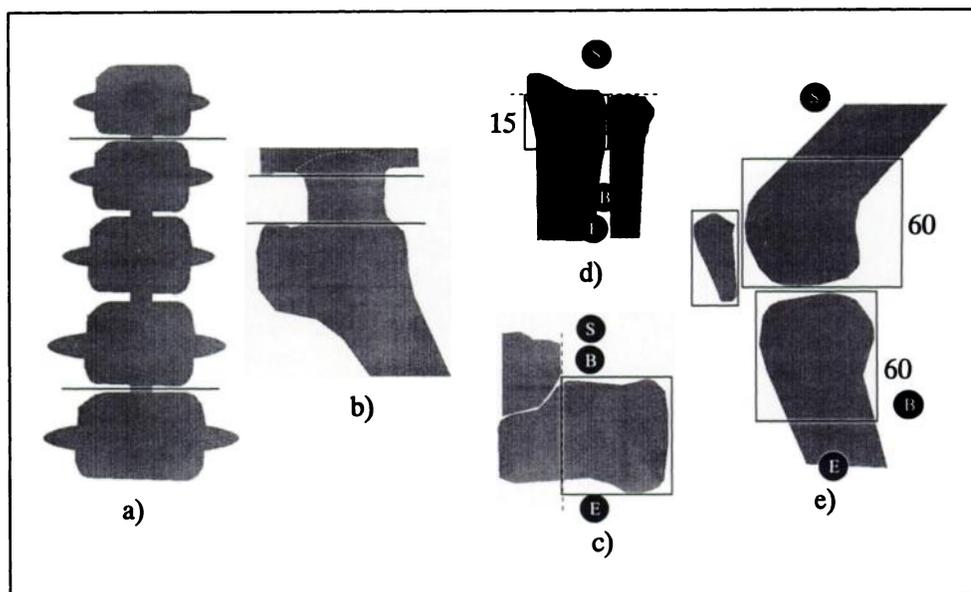


FIGURE 1. Definitions of the ROIs for (a) lumbar spine, (b) femoral neck, (c) calcaneus, (d) distal radius and (e) knee (for further details, see the text). The approximate starting, end and baseline points of a scan are indicated by "S", "E" and "B", respectively.

palpated proximal wrist joint, and the end point was approximately 8 cm in the proximal direction (Fig. 1d). The baseline point was located between the radius and ulna approximately 1 cm distal to the end point. The width of the scan was 6 cm, and its pixel size was 1 × 1 mm. The scan speed was 45 mm/sec. Scanning was terminated when a sufficient length of the radius was imaged. The ROI was defined as a rectangle with the upper side located parallel to the end of the distal ulna and the lower side 15 mm in the proximal direction. The width was determined based on the width of the distal radius (Fig. 1d).

Lateral Knee Scan. The subject was positioned and supported following the procedure used in the calcaneus scan. The starting point was located approximately 1 cm internal to the anterior edge of the thigh, 3–5 cm proximal to the superior edge of the patella, and the end point was approximately 10 cm distal to the knee joint parallel to the tibia (Fig. 1e). The baseline point was located posterior to the tibia and fibula, approximately 5 cm distal to the knee joint. The width of the scan was 15 cm, and its pixel size was 1.5 × 1.5 mm. The scan speed was 45 mm/sec. Scanning was terminated when a sufficient length of the tibia was imaged. The ROI for the distal femur was defined as a rectangle whose lower side was located at the extreme edge of the distal femur and whose upper side was 60 mm in the proximal direction. The width of the rectangle was determined based on the dimensions of the distal femur (Fig. 1e). The ROI for the patella was defined as a rectangle whose size was determined based on the dimensions of the patella (Fig. 1e). The ROI for the proximal tibia was defined as a rectangle whose upper side was located at the extreme edge of the proximal tibia and whose lower side was 60 mm in the distal direction; the width of the rectangle was determined based on the width of the proximal tibia (Fig. 1e). Special attention was paid to the exclusion of the fibular region.

Study Protocol

BMD and BMC measurements for each subject were repeated three times by the same experienced technician (#1) within 2 wk. The mean distance between the first and the last scan was 8 days (s.d., 4.5, range, 2–14). Scanning and image analysis were done according to the procedures previously described. During image analysis, no side-by-side comparison was allowed. Coefficients of variation (CV) for BMD and BMC measurements were calculated for each site measured for each subject. The mean of the individual CVs for each site was then obtained. These values represented the overall precision of BMD and BMC measurements in relation to such factors as subject positioning, image analysis and scanner precision, but not physiological variation.

We confirmed the general applicability of the precision obtained (i.e., that there was no significant dependence between

variability and the size of the individual measurements) by comparing the precision values of the low BMD and BMC measurements (< the mean) with those of the high BMD and BMC measurements (≥ the mean) for each site.

In order to evaluate the objective positioning of the ROI in each skeletal site, we randomly selected 10 scans representing each site. The scans were initially analyzed by the technician (#1) who made the scans. The scans were reanalyzed about 3 wk after the initial analysis by the same technician, after which another less experienced technician (#2) analyzed the same scans twice 1 wk apart. Before the replicate analysis, the ROIs were arbitrarily repositioned and their dimensions were changed. The two technicians were not informed about these changes. Because of its obvious sensitivity to changes in the scanned bone volume, the variability of the BMC was used as the index for the objective repositioning of the ROI. This index has been reported as the mean intra- and interobserver CV of the BMC of each skeletal site.

The mean, standard deviations, ranges and 95% confidence intervals are given as descriptive statistics when appropriate. The precision of the measurement is described by the CV, that is, the standard deviation as a percentage of the mean. The nonparametric Wilcoxon test and Mann-Whitney test were used to compare the paired and unpaired data, respectively.

RESULTS

The BMD and BMC values of the study population are summarized in Table 1. When these values were compared with the mean BMD values obtained for our young female reference population (age < 35 yr, n = 61, unpublished data), the following ranges were observed: –17% to +15% for the lumbar spine, –25% to +15% for the femoral neck, –24% to +31% for the calcaneus and –13% to +66% for the distal radius. The corresponding standard deviations of the reference population were 11%, 12%, 14% and 14%, expressed as the fraction of the corresponding average BMD. Therefore, the BMD and BMC values observed in this study covered the majority of variations found among healthy young women.

Table 2 gives the in-vivo day-to-day precision of BMD and BMC measurements for a variety of skeletal sites. It became obvious that the BMC analysis was less precise than that of the BMD in all sites, although the differences were not significant for the lumbar spine, the distal radius or the distal femur. It was also obvious that the precision

TABLE 1
Average BMD and BMC for Study Population

Skeletal site	BMD (g/cm ²)		BMC (g)	
	Mean (s.d.)	Range	Mean (s.d.)	Range
Lumbar spine	1.050 (0.106)	0.877-1.219	48.08 (8.61)	36.31-66.24
Femoral neck	0.894 (0.097)	0.711-1.085	4.73 (0.90)	2.92-6.59
Calcaneus	0.671 (0.113)	0.498-0.853	9.58 (2.23)	6.05-13.24
Distal radius	0.401 (0.089)	0.306-0.582	1.81 (0.56)	1.05-2.91
Distal femur	1.291 (0.205)	1.075-1.641	40.80 (9.11)	33.19-54.31
Patella	1.154 (0.189)	0.966-1.487	7.44 (2.04)	4.44-10.21
Proximal tibia	1.138 (0.199)	0.862-1.458	33.76 (7.79)	25.01-44.48

TABLE 2
In-Vivo Day-to-Day Precision of BMD and BMC Measurements for Various Skeletal Sites

Skeletal site	No. of subjects	Total no. of scans	CV (%) for BMD 95% confidence		CV (%) for BMC 95% confidence	
			Mean	Interval	Mean	Interval
Lumbar spine	15	45	1.7	1.0-2.4	1.9	0.9-2.9
Femoral neck	15	45	1.3	0.9-1.7	3.5	0.2-6.7*
Calcaneus	15	45	1.3	0.8-1.8	5.3	3.3-7.3 [‡]
Distal radius	15	45	1.9	1.3-2.5	2.2	1.2-3.2
Distal femur	8	24	1.2	0.4-2.0	1.9	0.6-3.2
Patella	8	24	1.0	0.3-1.7	10.7	0.0-23.8*
Proximal tibia	8	24	0.7	0.2-1.2	4.0	0.7-7.3 [‡]

Significance of the difference between the precision of the BMD and BMC measurements: * p < 0.05, † p < 0.01, ‡ p < 0.001.

of the BMD measurement was less affected by subject positioning and image analysis.

Despite the fact that only a few practice scans were obtained before this study, the lateral knee scan turned out to be very precise for BMD measurements. The mean CV for this type of scan was 1.0%. The precision for the femoral neck and calcaneus scans was also remarkably good (1.3%).

Table 3 shows the precision of the BMD and BMC values in relation to the mean value for each skeletal site. The individual CV determined for these ranges did not show any significant difference for either BMD or BMC, with the exception of the BMD for the distal femur (p < 0.05). Furthermore, there was no significant negative correlation between the individual CV and the corresponding measurement for any skeletal site. In other words, the relative precision did not significantly improve as the size of the measurement increased.

Table 4 summarizes the intra- and interobserver variability for the two technicians' ratings of BMC as a result of repositioning the ROI. The performance of the first technician was generally consistent with little variability, except for the few exceptional mispositionings indicated by the large standard deviation and a relatively low mean

intraobserver CV. The second technician had more irregular repositioning of the ROI for some skeletal sites, for which the replicate results differed significantly (p < 0.01) in the analyses of the distal femur and proximal tibia data. However, the average performance of both technicians did not differ significantly.

For interobserver variability, there was no significant and systematic deviation in the repositioning of the ROI for any skeletal site except the lumbar spine (p < 0.01) and possibly the distal femur (p < 0.05).

DISCUSSION

Since modern commercial DEXA scanners are practically stable throughout their operating life and since their precision and accuracy rely on high technology and advanced digital signal processing techniques (10,11), a scanner's effect on overall precision remains relatively small and constant. Therefore, a potential improvement in overall precision can be achieved with proper quality control, reproducible and careful subject positioning and more objective image analysis. However, automatic positioning of the ROI occasionally gave aberrant results, making manual repositioning of the ROI necessary. Therefore, to

TABLE 3
Size Dependence of the Precision of BMD and BMC Measurements

Skeletal site	CV (%) for BMD				CV (%) for BMC			
	Low values		High values		Low values		High values	
	N	Mean (s.d.)	N	Mean (s.d.)	N	Mean (s.d.)	N	Mean (s.d.)
Lumbar spine	6	1.5 (0.7)	9	1.8 (1.5)	8	1.3 (0.9)	7	2.4 (2.3)
Femoral neck	7	1.3 (0.9)	8	1.3 (0.7)	7	5.6 (8.0)	8	1.6 (1.1)
Calcaneus	7	1.6 (1.0)	8	1.0 (0.8)	8	4.7 (3.3)	7	5.9 (3.9)
Distal radius	8	1.9 (1.3)	7	1.8 (1.0)	10	2.2 (1.9)	5	2.2 (1.3)
Distal femur	5	1.7 (0.9)	3	0.5 (0.3)*	5	1.7 (1.9)	3	2.0 (1.1)
Patella	4	0.7 (0.5)	4	1.3 (1.0)	5	13.7 (18.2)	3	5.6 (4.6)
Proximal tibia	4	0.6 (0.5)	4	0.6 (0.5)	4	6.0 (4.2)	4	1.9 (1.7)

Significance of the difference of the precision in relation to the low (<the mean) and high (≥the mean). BMD and BMC values: * p < 0.05.

TABLE 4
Intra- and Interobserver Precision of BMC Measurements

Skeletal site	Intraobserver CV (%)		Interobserver CV (%)
	Technician (#1) Mean (s.d.)	Technician (#2) Mean (s.d.)	Mean (s.d.)
Lumbar spine	0.1 (0.2)	0.3 (0.5)	0.4 (0.3) [†]
Femoral neck	0.0 (0.0)	0.1 (0.2)	0.0 (0.2)
Calcaneus	0.6 (1.4)	0.4 (0.9)	1.7 (3.7)
Distal radius	0.3 (0.6)	0.0 (0.0)	0.5 (1.1)
Distal femur	0.6 (1.1)	0.7 (0.6) [†]	0.7 (0.9) [*]
Patella	3.9 (8.9)	1.2 (1.9)	2.4 (7.3)
Proximal tibia	1.5 (3.0)	1.0 (0.8) [†]	1.3 (2.2)

Ten scans were analyzed twice by both technicians.
Significance of the deviation from CV (%) = 0: * $p < 0.05$, [†] $p < 0.01$.

guarantee continuous and systematic consistency for image analysis of all subjects, we chose a manual method with clearly defined rules for ROI positioning. To minimize additional interobserver error, however, an automatic method with more refined rules would be optimal.

The BMD values of the subjects in our study represent a relatively wide range of normal BMD values, and therefore the precision values achieved with these ROIs can be generally applicable for this type of DEXA scanner without reconsideration of the individual BMD. This conclusion is further confirmed by the results presented in Table 3, in which the precision of a BMD measurement was not significantly size-dependent, except for the lateral scan of the distal femur ($p < 0.05$). Furthermore, low and consistent intra- and interobserver variability indicated objective repositioning of the ROI. In general, the principle of manual positioning was efficiently adopted by a less experienced technician, and image analysis by a different observer did not introduce significant error. In this case, the difference observed for the lumbar spine was probably due to the individual technician's recognition of the intervertebral spaces. As for the discordant result obtained for the distal femur, some action by the less experienced technician probably played a role. Generally, an ROI can be positioned consistently only on the basis of positioning rules specific for each type of scan, regardless of the level of experience of the technician. Some problematic scans with indistinct anatomy, however, may require some modification of the rules. To minimize errors, each observer should be properly trained and should apply similar measurement principles.

If the in-vivo day-to-day precision values of our study are compared with those obtained elsewhere for DPA, QCT or DEXA with compatible materials (1-6), our values are about the same or slightly better for the lumbar spine and femoral neck (2%-3% on average). There are few precision data available for other skeletal sites with respect to DEXA; to our knowledge, precision data have only been reported for the BMD of the distal radius (1.7% on average) (12). In comparison with SPA, our method

provided compatible precision for the distal radius and the calcaneus (1%-3% on average) (1-3,13). We extensively applied DEXA to a variety of skeletal sites, including standard sites of clinical interest as well as sites that may be potentially important when the effects of independent or combined exercise and dietary interventions on bone are being assessed.

There are at least three "observer-controllable" factors that may affect the overall precision of BMD and BMC measurements: reproducibility of subject repositioning, selection of the baseline area (an area where only soft tissue is present), repeatability of baseline area selection and ROI repositioning. The precision of measurements for irregular skeletal sites with inhomogeneous structures is probably the most susceptible to subject positioning because variances, if any, it can cause a change in the bone volume measured and thus yield a misleading change in BMC, and possibly in BMD. Therefore, appropriate support blocks are indispensable for providing sufficient reproducible positioning. On the other hand, meticulous positioning with exactly the same angles for every subject may cause discomfort to some subjects and indirectly reduce overall precision. Consequently, individual but sufficiently repeatable positioning is probably the more favorable procedure with which to obtain more precise results. Accurate positioning of the baseline point has only a minor effect on overall precision since the soft-tissue region close to the bone can be determined by palpation with acceptable accuracy. In this case, the multistage filter of the XR-26 densitometer further reduces variability caused by different soft-tissue thicknesses at various skeletal sites. Actually, no adverse effect on BMD was found when a baseline point was deliberately positioned on a bone (unpublished observations). The repeatability of ROI repositioning can be improved if definite anatomical landmarks are used and if the size of the ROI is properly selected. Distinct anatomy is obviously required for precise positioning, whereas the size of the ROI dictates its sensitivity to inhomogeneities in the bone and to the changed position of a particular bone. In general, the larger the ROI, the more precise the

results obtained, provided that the ROI is reasonably selected (i.e., the majority of bone tissue at the site in question is trabecular). This principle has been the cornerstone for ROI size applied in our study.

BMD measurement is evidently more insensitive to subject repositioning than BMC measurement, and therefore BMD is a more precise and preferable variable for longitudinal studies of all skeletal sites. A similar conclusion was drawn for the lumbar spine by LeBlanc et al. (6). This conclusion is especially true for sites consisting of nonsymmetric bone structures such as the calcaneus, the patella and both ends of the femur as well as the proximal end of the tibia. For these sites, we found the precision of the BMD measurement to be markedly better than that of the BMC measurement, probably due to the more complex and, therefore, more variable subject positioning that could have resulted in a partially different scanned bone volume and different BMC. In contrast, the precision of the BMD measurement was not adversely affected, probably due to a relatively high homogeneity of trabecular bone at these sites.

The replicate measurements were obtained as they are routinely done in our normal research projects without meticulous subject repositioning. Furthermore, during image analysis, no side-by-side comparison of the first scan was allowed, so that the objectivity of the ROI could be demonstrated. However, as is always true for unclear cases and for optimal precision, side-by-side comparison is necessary to prevent undue repositioning imprecision of an ROI that occurred in some individual sites in this study, especially for the patella and proximal tibia. If this comparison technique had been applied in our study, the precision values obtained might have improved, at least in these last two sites.

In conclusion, our method provided an objective and precise procedure for determining BMD of the lumbar spine, femoral neck, knee, calcaneus and distal radius with a DEXA scanner. The principle for ROI positioning can be easily adopted, even by a less experienced observer, for each skeletal site since the rules for positioning are relatively simple and unambiguous. With careful subject po-

sitioning and proper quality control, this application of DEXA makes it possible to precisely measure BMD for a variety of skeletal sites that may be affected by various interventions.

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