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Original article

Comparative study of the performances of X-ray and gadolinium 153 bone densitometers at the level of the spine, femoral neck and femoral shaft

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Abstract. We investigated the precision of gadolinium 153 dual photon absorptiometry (DPA) and quantitative digital radiography (QDR) bone densitometers by determining in vitro and in vivo coefficients of variation (CV) of bone mineral density (BMD). In vitro, the long-term CV of spine phantom BMD measured weekly for 40 weeks was 1.2% and 0.7% for DPA and QDR, respectively. Simulating soft-tissue thickness with water, the CV of 6 repeat measurements of spine phantom at depths from 0 to 27 cm in 1 cm steps (a total of 168 measurements) increased from 0.1% at 0 cm of water to 2.5% at 27 cm for DPA, and from 0.2% at 0 cm to 1.4% at 27 cm for QDR; mean CV of the 28 series (0–27 cm) was higher for DPA (1.2% ± 0.8%, mean ± SD) than for QDR (0.7% ± 0.6%; $P < 0.001$). With the hip phantom, femoral neck BMD was determined, and the CV was also dependent on water thickness; mean CV of the 20 series (0–10 cm) was 2.1% ± 1.2% for DPA and 1.3% ± 0.9% for QDR (not significant). In vivo, at the spine level, with DPA, mean CV of BMD measured 6 times after repositioning in 6 healthy volunteers was 3.8% ± 1.9% and 2.1% ± 0.7% with ^{153}Gd activity of 0.46 Ci and 1 Ci, respectively (BMD range: 0.796–1.247 g/cm^2, no significant difference between the two groups). Both values were significantly higher ($P < 0.05$) than mean CV with QDR: 1.0% ± 0.5% (12 subjects, same conditions; BMD range: 0.811–1.124 g/cm^2, no significant difference with the two previous groups). At the femoral neck and shaft levels, the mean CV observed with QDR tended to be lower as compared with DPA (not significant). At the three sites, BMD values obtained with DPA and QDR in 62 patients were highly correlated. In conclusion, our results indicate that the higher precision obtained with QDR is particularly significant at the lumbar spine level, but large biological variations in soft tissue thickness can still influence the degree of precision of BMD measurement.

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Key words: Bone densitometry – Dual photon absorptiometry – Dual energy X-ray absorptiometry

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Introduction

The quantitative assessment of bone mass or bone mineral density (BMD) at sites with particular high fracture incidence represents an important step for evaluating the risk of fracture and the efficacy of any preventive or curative strategy taken against osteoporosis (Mazess 1983; Riggs and Melton 1986; Nilas and Christiansen 1987; Peck et al. 1988; Fogelman 1989). Over the past few years the non-invasive measurement of BMD at the lumbar spine and femoral neck levels has been made possible by dual photon absorptiomery (DPA), using radioisotopes, in particular gadolinium 153 (^{153}Gd) as the dual energy source (Wilson and Madsen 1977; Krolner and Nielsen 1980; Mazess et al. 1988a). More recently, the technique of quantitative digital radiography (QDR) using X-rays as the dual energy source [also designated as DEXA (dual-energy X-ray absorptiometry) or DER (dual-energy radiography)], has been introduced for BMD measurement at both the lumbar spine and femoral neck levels (Pacifici et al. 1988). Reliable assessment of the precision of BMD measurements (i.e. the intrinsic variability of the determination) is an essential requisite to determine the capacity to detect (a) BMD modifications during the follow-up of individual patients and (b) significant differences between cohorts of patients in the setting of clinical trials. Most results available so far concerning the precision of BMD determination have been obtained in vitro with phantoms or in vivo as calculated from duplicate measure-

ments (Nilas et al. 1988; Pacifici et al. 1988; Pouilles et al. 1988; Dawson-Hugues et al. 1989).

In this study, we first compared the precision of a DPA system (Norland 2600) and QDR system (Hologic QDR-1000) by performing repetitive determinations of spine and hip phantoms, and then of healthy volunteers at the lumbar spine and the femoral neck levels and also at the femoral shaft level, a site of weight-bearing cortical bone. The influence on the precision of various depths of water simulating soft tissue was also studied and that of the activity of the isotopic source for the DPA instrument.

Materials and methods

In vitro study

Dual photon absorptiometry. BMD of a specific Norland lumbar spine phantom was measured weekly with a Norland 2600 instrument using a source of ^{153}Gd for 40 weeks. At the end of the 3rd month of the study, the source had an activity of 0.46 Ci and was then changed for a new source (1 Ci).

A thin lumbar spine (contained in a box of plexiglass 5 cm thick) and hip (contained in a box with soft tissue equivalent 5 cm thick) phantoms were scanned in 0–27 cm and in 0–19 cm of water, respectively, to simulate human soft tissue thickness. Phantoms were maintained at the bottom of the water. Six scans were acquired at each centimeter of water. For a given age of the radioactive source, the base line count rate observed in humans was of the same order of magnitude as that obtained within the range of 12–20 cm for the spine and 10–15 cm for the hip. The point resolution and line spacing were 1.5 mm. The scan width was 9.9 cm. The scan speed was 4 to 15 mm/s depending on the depth of water, on the baseline 44 keV count rate through soft tissue and on the manufacturer's scan speed chart. The diameter of the collimator was 8 mm. The same software (Bonestar 3.5.2) was used throughout the study: data were acquired and analysed with the "spine" mode or the "hip" mode set in the software. Baseline and edges were checked and corrected, if necessary. The box that determined the femoral neck BMD was 1.5 cm wide and was placed in the same position as for QDR (Fig. 1).

Quantitative digital radiography. Weekly measurements of BMD of the Hologic lumbar spine phantom were done for 40 weeks. Because of the possibility of acquiring multiple scans by a single procedure and the fast scanning time of the QDR, we also acquired 6 repeated scans every open day for the period of the study in order to evaluate modification over time of the short-term variability. To test in vitro precision, the lumbar spine and hip phantoms previously used with DPA were scanned with QDR in 0–27 cm (spine) and in 0–19 cm (hip) of water. Six scans were acquired at each centimeter of water. The point resolution and the line spacing were 1.0 mm. The diameter of the collimator was 2.0 mm. The same software (version 3.20) was used throughout the study: data were acquired and analysed with the "spine" mode or the "hip" mode set in the software. This analysis is fully automatic. Each step of the analysis including edge definition was checked visually, but corrections were made manually only to modify axes during femoral neck analysis.

In an initial study, repeated measurements of the Hologic hip phantom were done, varying the size and location of the region of interest, while analysing in order to define the best conditions of femoral neck BMD determination. The size of the box (Fig. 1) was set at minimum. Moving this box from the trochanter to the femoral head (6 repeated scans in 1 subject), we observed an increase in CV from 1.3% in position T (near the trochanter), to 1.6% in position M (mid-distance) and to 2.5% in position H (near the femoral head). Furthermore, we also noticed that the mean BMD value itself increased from 0.898 ± 0.012 g/cm^2 in position T, to 1.012 ± 0.016 g/cm^2 in position M and to 1.046 ± 0.026 g/cm^2 in position H. In addition, we observed that from the position T, increasing the size of the box in the H direction did result in an increase of CV and BMD values. As shown in Fig. 1, the best conditions for femoral neck measurement were to set the box perpendicular to the neck axis, the basis of the box sitting on the top of the major trochanter. The width of the box was given by default at 16 pixels.

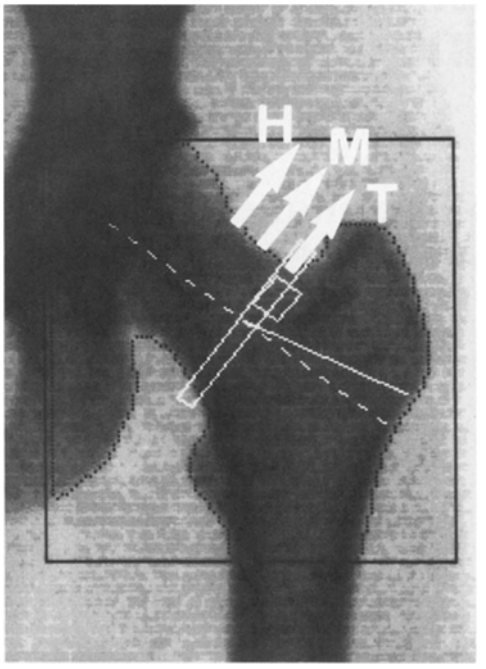


Fig. 1. Influence of the size and the location of the region of interest on bone mineral density (BMD) femoral neck values and precision. The size of the box (see at the level *T*) was set at minimum. The coefficient of variation of repeated measurements was determined when the box was in position *T* (near the trochanter), *M* (mid-distance) and *H* (near the femoral head). The *large rectangle* corresponds to the area measuring femoral neck BMD, and the *small square* corresponds to the area measuring Ward's triangle BMD

In vivo study

Dual photon absorptiometry. BMD of the lumbar spine (L2–L4), femoral neck and femoral shaft of 12 Caucasian volunteers was measured 6 times after repositioning (patients were removed from the table and then asked to climb back on to it). The first group of six subjects with a mean age of 30.3 years (range: 22–51 years) and a mean body mass index [BMI = ratio of weight to square of height (kg/m^2)] of 25.0 (range: 21–29) were scanned at the three sites with a 9-month-old ^{153}Gd source (i.e. an activity of 0.46 Ci), and six others (mean age: 31.1 years, range: 21–45; mean BMI:

22.1, range: 17–26) were scanned with a new 1 Ci source. Standard procedures of acquisition and analysis of the spine and femoral neck sites described by the manufacturer were used; in particular, the legs were maintained in null rotation. The femoral shaft site was scanned for 3 cm in the direction of the patella from a point 22 cm from the top of the patella. Analysis of femoral shaft BMD was done using the "local" mode of analysis provide by the software. All scans were acquired for each subject within 3 weeks.

Quantitative digital radiography. Twelve volunteers (mean age: 29.8 years, range: 21–51 years; mean BMI: 22.7, and range: 17–29) were scanned 6 times after repositioning at the lumbar spine (L2–L4) and femoral neck sites. Standard procedures of acquisition and analysis of the spine and femoral neck sites described by the manufacturer were used. Six additional volunteers were also scanned at the level of the femoral neck with a dedicated contention system provided by the manufacturer (legs maintained with an internal rotation). Furthermore, six other volunteers were scanned only at the femoral shaft site using the spine protocol. The femoral shaft was scanned up to the lower limit of the trochanter minor, starting at a point located 20 cm from the top of the patella. Femoral shaft BMD was determined by using the "spine" mode of analysis provided by the software. The scanned area was divided into four equal parts, the fourth and lowest part was considered as representative of the femoral mid-shaft BMD.

Relationship between QDR and DPA measurements

Spine and femoral neck BDM of 62 patients, and femoral shaft BMD of 24 patients, were measured with both absorptiometers (QDR and DPA) in order to determine a correlation between the two measurements. Each patients was scanned with both apparatuses on the same day.

Statistics

Results were expressed as mean ± 1 SD. The precision of measurement was evaluated by the CV ($CV = 100 \times SD/mean$). Significance of difference between the two groups was tested with a two-tailed, unpaired, Student's t-test. Analysis of variance and Scheffe F-test were used to evaluate the significance of spine and hip phantom BMD modification with depth of water.

Results

In vitro measurements

Comparison of DPA and QDR long-term precision by measuring weekly a specific lumbar spine phantom for 40 weeks is shown in Fig. 2. With DPA, mean BMD was 0.899 ± 0.011 g/cm^2 (range: 0.875–0.920 g/cm^2, $n = 40$), resulting in a CV of 1.2%. With QDR, mean BMD was 1.060 ± 0.007 g/cm^2 (range: 1.044–1.071 g/cm^2, $n = 40$), resulting in a CV of 0.7%. Furthermore, using this latter instrument, mean daily CV as calculated every day from 6 determinations over a period of 137 days was $0.4\% \pm 0.2\%$ (range: 0.1%–0.9%, $n = 137$).

The influence of soft tissue on precision was assessed by measuring BMD of the lumbar spine phantom covered by an increasing depth of water. From 0 to 27 cm of water, an increase of the CV was observed with both DPA and QDR: at 0 cm, CV was 0.1% and 0.2%, and at 27 cm, it was 2.5% and 1.4%, respectively. Thus, the precision of BMD measurement was more dependent on water depth with DPA than with QDR. The mean CV of the 28 series (0–27 cm) was higher for DPA ($1.2\% \pm 0.8\%$) than for QDR ($0.7\% \pm 0.6\%$, $P < 0.001$).

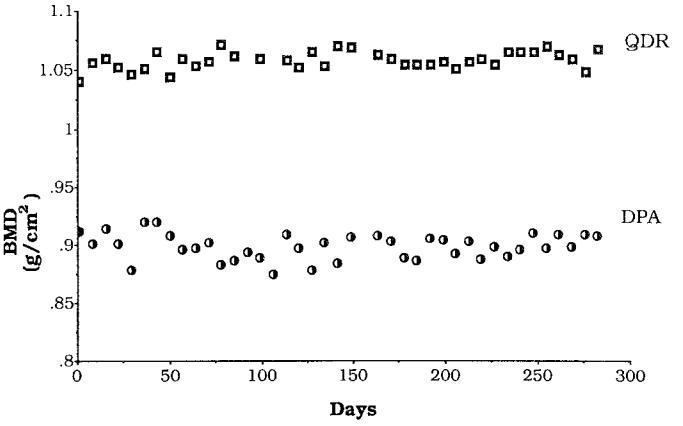


Fig. 2. Comparison of long-term, in vitro precision of bone mineral density (*BMD*) measurement for dual photon absorptiometry (*DPA*) and quantitative digital radiography (*QDR*) using a lumbar spine phantom over a period of 40 weeks

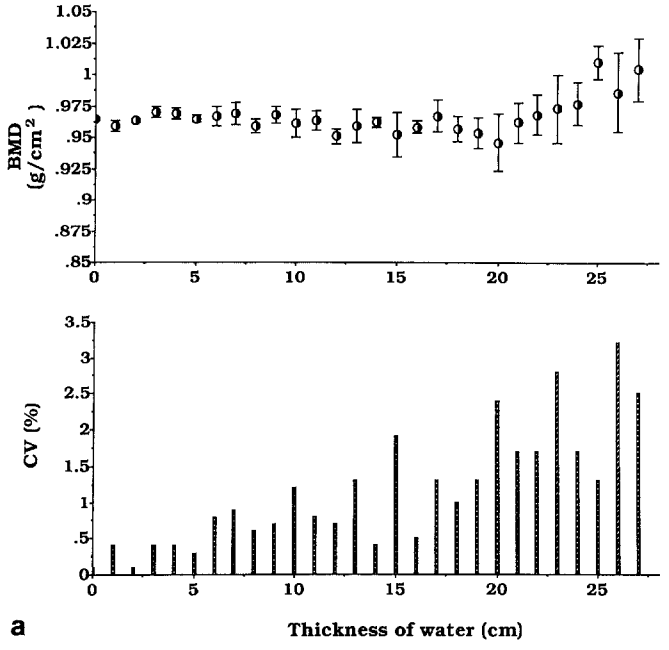
The mean BMD value remained stable between 0 and 22 cm and between 6 and 24 cm of water depth for DPA and QDR, respectively (Fig. 3). Further increase in the water depth resulted in an increment in the mean BDM value. This phenomenon appeared between 22 and 27 cm ($F = 15.5$ and $P < 0.05$ at 27 cm) for DPA and between 24 and 27 cm for QDR ($F = 6.352$ and $P < 0.05$ at 26 cm). In addition, with the QDR instrument, mean BMD tended to increase at depths of water less than 6 cm ($F = 15.5$ and $P < 0.05$ at 1 cm).

Using the hip phantom, the influence of increasing water depth from 0 to 19 cm on the precision of both systems was also assessed. Figure 4 shows that the CV of femoral neck BMD values increased from 1.1% (0 cm) to 6.2% (19 cm) and from 0.6% (0 cm) to 3.1% (19 cm) for DPA and QDR, respectively. The mean CV was $2.1\% \pm 1.2\%$ and $1.3\% \pm 0.9\%$ ($n = 20$, not significant) for DPA and QDR, respectively.

As observed with the spine phantom, increasing the water depth covering the hip phantom resulted in variation of the mean BMD values determined by either DPA or QDR. However, only with QDR at 16 cm of water thickness did mean BMD change significantly ($F = 16.728$, $P < 0.05$).

In vivo measurements

The precision obtained for BMD measurements performed at the level of the lumbar spine, femoral neck and femoral shaft with DPA and QDR in healthy volun-



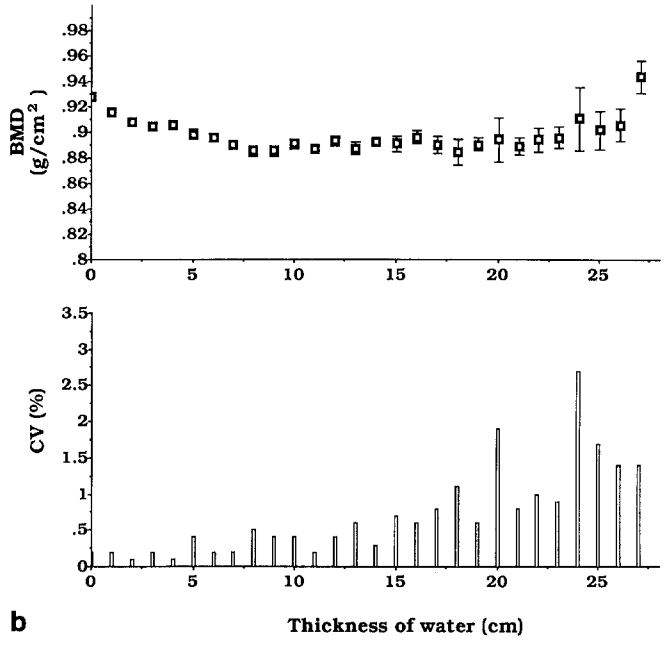
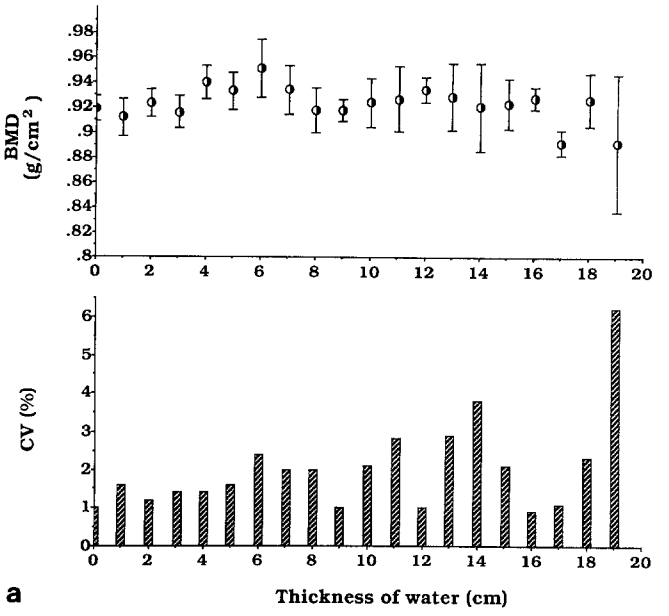


Fig. 3a, b. Influence of varying depth of water on bone mineral density (*BMD*) of a spine phantom measured by DPA (**a**) and QDR (**b**). Coefficient of variation (*CV*) is indicated on the lower panel. Each point represents the mean of six determinations. (plus SD)



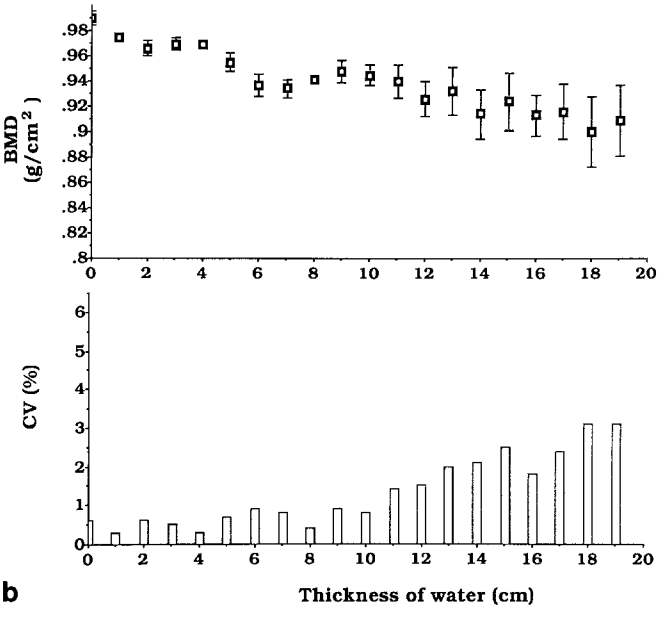


Fig. 4a, b. Influence of varying depth of water on bone mineral density (*BMD*) of a hip phantom measured by DPA (**a**) and QDR (**b**). The coefficient of variation (*CV*) is indicated on the lower panel. Each point represents the mean of 6 determinations (plus SD)

teers is indicated in Table 1. With the DPA system, a 0.46 Ci source was associated with a higher CV as compared with a 1 Ci source, at least at the spine level. The precision for spine BMD was greater with QDR than DPA, even when this latter system was equipped with a new 1 Ci ^{153}Gd source (CV: 2.1% ± 0.7% and 1.0% ± 0.5% for DPA and QDR, respectively; $P<0.001$). CV was independent of BMI with QDR or DPA equipped with a 1 Ci source. However, a positive correlation between BMD and CV was found when BMD was measured by DPA with a 9-month-old ^{153}Gd source (remaining activity of 0.46 Ci) at the spine level ($r=0.821$, $P<0.05$). At the level of the femoral neck and shaft, the use of a higher activity source in the DPA system was associated with a decrease in the CV, which reached the range of those obtained with QDR (Fig. 5). When hip acquisitions were made using the Hologic contention system which maintains coxo-femoral articulations in in-

Table 1. Bone mineral densities (BMD, g/cm^2) and precision (CV) of spine, femoral neck and femoral shaft measurements of 24 volunteers distributed in three groups: 6 for the studies with DPA and an old source, 6 with DPA and a new source and 12 with QDR. Each subject was measured six times after repositioning, and results are presented as mean, minima and maximal values. Different volunteers were used for the three groups

	DPA				QDR	
	Old source (0.46 Ci)		New source (1 Ci)			
Spine						
BMD	1.017	(0.796–1.247)	0.970	(0.863–1.170)	1.014	(0.811–1.124)
CV	3.8	(2.4–7.4)*	2.1	(1.4–3.5)*	1.0	(0.5–2.3)
Femoral neck						
BMD	1.011	(0.794–1.246)	0.796	(0.700–0.898)	0.872	(0.732–1.123)
CV	2.4	(1.6–3.9)	2.0	(0.7–4.1)	1.6	(1.0–2.6)[a]
Femoral shaft						
BMD	1.954	(1.754–2.213)	1.869	(1.702–2.112)	1.937	(1.641–2.170)
CV	2.7	(0.9–4.8)	1.4	(0.7–1.9)	1.5	(1.1–2.1)

* Statistical significance ($P<0.001$) when comparing mean DPA value with mean QDR value

[a] This CV was obtained using the Hologic dedicated contention system. It is not significantly different from the one obtained using our standard procedure: 1.8 (0.6–3.9). See results

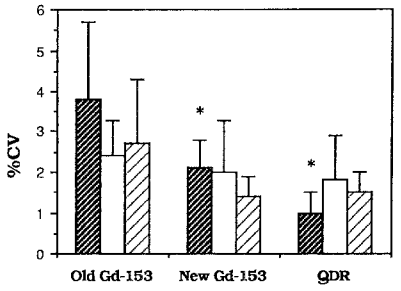
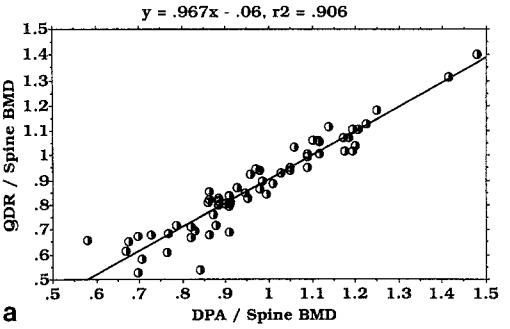
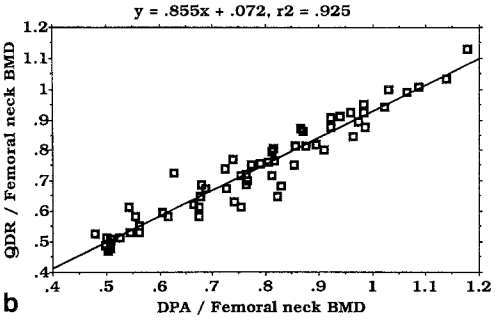


Fig. 5. In vivo precision (% *CV*) of bone mineral density (*BMD*) measurement at three sites with QDR and DPA with an old and new source (6 healthy volunteers for each condition). The results are mean ±SD of 6 determinations. * $P<0.001$ when compared with QDR mean value) ▨ spine; □ femoral neck; ▨ femoral shaft

ternal rotation, mean CV was 1.6% ±0.6%, similar to that obtained using our standard procedure. These values were not significantly different from those obtained with DPA using either an old or new ^{153}Gd source.

As shown in Fig. 6, the values of BMD obtained with DPA and QDR at the three sites in 62 patients were highly correlated for the spine ($r=0.952$) with a standard error of the estimate (SEE) of 0.057 g/cm^2 (Fig. 6a), for the femoral neck ($r=0.962$) with SEE of 0.044 g/cm^2 (Fig. 6b) and for the femoral shaft ($r=0.989$) with SEE of 0.046 g/cm^2 (Fig. 6c).





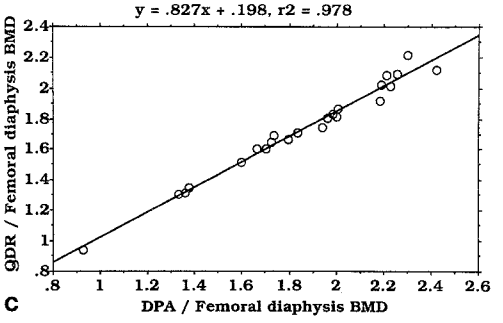


Fig. 6a–c. Relationship between bone mineral density (*BMD*) measurements of the spine (**a**), femoral neck (**b**) and femoral shaft (**c**) performed with DPA and QDR in 62 patients for **a** and **b**, and in 24 patients for **c**

Discussion

During the past decade, non-invasive methods to measure BMD such as DPA have been widely used in both clinical research and practice concerned with the diagnosis, prevention and therapy of osteoporosis (Mazess 1983; Riggs and Melton 1986; Nilas and Christiansen 1987; Peck et al. 1988; Fogelman 1989). In clinical practice, the follow-up of BMD in individual subjects requires methods of high precision (Heaney 1986). As emphasized by Nilas et al. (1988), the difference between two BMD measurements made in a single patient must exceed 2.83 ($2\sqrt{2}$) times the method reproducibility (CV%) in order to be considered significant with a 95% probability. Thus, improvement in method precision from 2.5% to 1.0% would reduce to about one-third the time interval required for assessing the reality of

a change between two BMD values measure in a single patient losing or gaining bone at a constant rate.

BMD at the spine level

Recent assessments of in vitro DPA short-term precision by measuring lumbar spine phantom BMD indicated mean CV values varying from 1.3% to 2.6% (Leblanc et al. 1986; Shipp et al. 1988). In vivo, short-term reproducibility of DPA instruments varied from 1.3% to 3.2% (Leblanc et al. 1986; Lindsay et al. 1987; Nilas et al. 1988; Pouilles et al. 1988; Shipp et al. 1988). Previous assessments of DPA precision of spinal BMD measurement using a torso phantom indicated CVs of about 2%. In addition, the radioactive source decay has been shown to alter measurements in some DPA systems (Lindsay et al. 1987; Nilas et al. 1988; Shipp et al. 1988; Dawson-Hugues et al. 1989). Our in vitro and in vivo results confirm that mean CVs of BMD measured with commercially available DPA are greater than 1%. We also observed a wide range of CV values depending on radioactive ^{153}Gd source decay as well as soft tissue thickness. Other, still unappreciated factors could play a role. Thus, for example, we observed a CV of 7.4% in one healthy subject despite very careful technical acquisition.

The new QDR technology that uses an X-ray tube as the dual energy source has been introduced on the basis of having greater precision than DPA, at least at the spine level (Kelly et al. 1988; Mazess et al. 1988b; Wahner 1988; Wahner et al. 1988; Braillon et al. 1989). Our comparative study using a spine phantom indicates that both the short-term and long-term precision of BMD measurements are greater with the QDR than with the DPA system. In addition, our in vitro data strongly suggest that the influence of soft tissue thickness on the CV of spine BDM is less pronounced than with the DPA system.

The CV value we determined in vivo for lumbar spine BMD is in agreement with very recent reports on the precision of dual-energy X-ray densitometers (Cullum et al. 1988; Kelly et al. 1988; Mazess et al. 1988b; Pacifici et al. 1988; Braillon et al. 1989). The CVs observed in vivo are in the range of those obtained with a phantom under 10–27 cm of water. This range of water depth causes an attenuation of the baseline counts recorded with the DPA system similar to that due to soft tissue in vivo. This correspondence suggests that in vitro testing is adequate for assessing the influence of soft tissue thickness in vivo.

Variation in mean BMD values observed in vitro with a change in water depth raises the problem of the influence of soft tissue on the accuracy of measurement. This issue was not addressed in the present study, but Cullum et al. (1988) observed that BMD is dependent on patient thickness (below 10 cm) and that an apperant 1% change of BMD was produced by replacing 3 mm of soft tissue with fat.

BMD at the femoral level

Unlike the lumbar spine reproducibility, CV of femoral neck or femoral shaft BMD did not achieve 1%, although we still observed a substantial but not statistically significant better precision with the QDR as compared with the DPA apparatus. Software, soft tissue thickness and/or repositioning may be responsible for this relatively lower reproducibility, which has also been observed by Wahner et al. (1988). As described above, small variations in positioning the limits of the femoral neck area could reduce precision, since the cortical inner part of the femoral neck becomes thicker in the direction of the femoral haed. This emphasizes the need to define very strictly the limits of the region of interest. Furthermore, modification in hip angulation after repositioning could also be a factor of variation. The uncomfortable internal rotation positioning achieved by a firm contention system reduced slightly the CV from 1.8% to 1.6%. However, the standard null rotation positioning was selected since we experienced that in clinical practice it is more comfortable and thus better tolerated by elderly patients. In vivo CV for femoral neck BMD corresponds to in vitro CV obtained with a water depth from 10 to 17 cm. This range is equivalent to the soft tissue thickness reflected in vivo by the baseline count attenuation for femoral neck BMD measurement with DPA.

Modification of mean hip BMD values was observed in vitro with change in water depth. The shift seemed to be slightly more pronounced for QDR than for DPA, particularly in the low range of water depth. As mentioned above, the physiological range in adults could correspond to 10–18 cm, i.e. within the plateau of the in vitro BMD measurement. Therefore, variations of soft tissue thickness may not influence to a large extent the accuracy of hip BMD determinations in non-obese adult individuals.

Correlation between DPA and QDR

Finally, we confirmed the good linear relationship between BMD measurements by QDR and DPA at the level of the spine observed by Kelly et al. (1988) and showed that it remained true at the level of the femoral neck and shaft. This should allow the use of the normal or reference range previously established from BMD measurements with DPA Norland 2600 for further clinical application of the QDR system.

In conclusion, because of the short scanning time and the improved reproducibility of the QDR system, the determination of BMD at several sites of interest can be easily envisaged, as well as the determination of significant small changes in BMD for an individual subject. Future developments with QDR should be aimed at achieving a 1% reproducibility at all sites, particularly at the femoral neck level, and preventing a drift in accuracy at both extremes of soft tissue thickness so

that the method could be applied without restriction to infants and obese patients. Among the various options for improvement, the use of a multi-detector system reducing scanning time should allow the duplication or triplication of BMD measurements so that any real change in BMD in the range of 1% or less can be significantly detected at all sites of interest.

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