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Original Article

Accuracy and Precision Study In Vitro for Peripheral Quantitative Computed Tomography

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Abstract. We evaluated the accuracy and precision of a peripheral quantitative computed tomography (pQCT) scanner, the Stratec XCT-960, using 12 human cadaveric forearms. The accuracy was determined by comparing the total bone mineral content (BMC) with the ash weight (AW). We scanned and ashed three consecutive slices (thickness 2.5 mm) at the standard position (s-position) and at 2.5 mm both proximal and distal to the s-position. The correlation coefficient between the AW and total BMC using slices at the s-position was $r = 0.87$ with an accuracy error (random component) of 15.5%. The correlation coefficient using all slices was $r = 0.90$ with an accuracy error of 14.3%. The correlation coefficient improved to $r = 0.95$ with an accuracy error of 9.7% after averaging the results of all three slices for each forearm. The short-term precision error expressed as the coefficient of variation (CV) of bone mineral density (BMD) and BMC was determined by measuring the forearms five times either with repositioning or without repositioning. The CVs with repositioning were 2.77 and 1.15 for total BMD and BMC, 1.85 for trabecular BMD; without repositioning they were 0.29, 0.58 and 0.69 respectively. To further evaluate the influence of positioning, additional scans were performed at 1, 2 and 5 mm proximal, and 1 and 2 mm distal to the s-position. BMD and BMC were greatly influenced by the scan location; for example, the percentage differences in trabecular BMD 1 mm distal and proximal relative to the s-position were 2.5% ± 5.1% and 0.18% ± 6.3%, respectively. The Stratec XCT-960 appears to be a moderately accurate and highly precise scanner with potential usefulness for evaluating BMC and BMD of ultradistal radius.

Keywords: Accuracy; Ash weight; Bone mineral measurement; Peripheral quantitative computed tomography (pQCT); Precision; Radius

Introduction

Bone mineral measurement of the radius has been used for many years in the evaluation of osteoporosis. Currently, bone mineral density (BMD) is measured at this site mainly by dual X-ray absorptiometry (DXA) and single X-ray absorptiometry (SXA) as well as by the older method of single photon absorptiometry (SPA) [1–7]. An alternative technique, peripheral quantitative computed tomography (pQCT), which has been used on a research basis since 1976 [8], recently became commercially available for measuring the ultradistal radius [9–11]. In contrast to projection techniques such as DXA or SPA, pQCT measures the true volumetric BMD (mg/cm^3) and allows for separate assessment of trabecular and cortical bone. In this paper we evaluated the Stratec XCT-960 pQCT scanner (Stratec, Berkenfeld, Germany) [11] using human cadaveric forearms. The accuracy of pQCT has been evaluated using computer simulation and phantoms [8,12]. However, to our knowledge, no previous report has directly addressed the accuracy of the radial measurement by pQCT. In this study we evaluated the in vitro accuracy and precision. In addition, we analyzed the impact of scan location on BMD, BMC and area measurements.

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Materials and Methods

Subjects

Twelve frozen cadaveric forearms (8 right, 4 left; further demographic information unavailable) which were obtained from the Department of Orthopedic Surgery, University of California San Francisco were used. This study was approved by the Committee on Human Research, University of California San Francisco.

Bone Mass Measurement

A Stratec XCT-960 pQCT scanner (distributed in USA by Norland, Fort Atkinson, WI) was used for this study. The following standard scan protocol was used: before initiating a scan, the forearm was secured at the wrist by a fixture and at the elbow by a block with a Velcro strap that maintained the elbow at 90° flexion. Then a coronal scout scan was performed. On this scout view, the operator manually placed a reference line at the medial end of the radial endplate. Using this line the software automatically found the standard scan position (s-position) for the CT scan (Fig. 1A). It was located proximal to the distal medial end of the radius by 4% of the distance from the ulnar styloid to the olecranon process. One slice was obtained (Fig. 1B). The slice thickness was 2.5 mm.

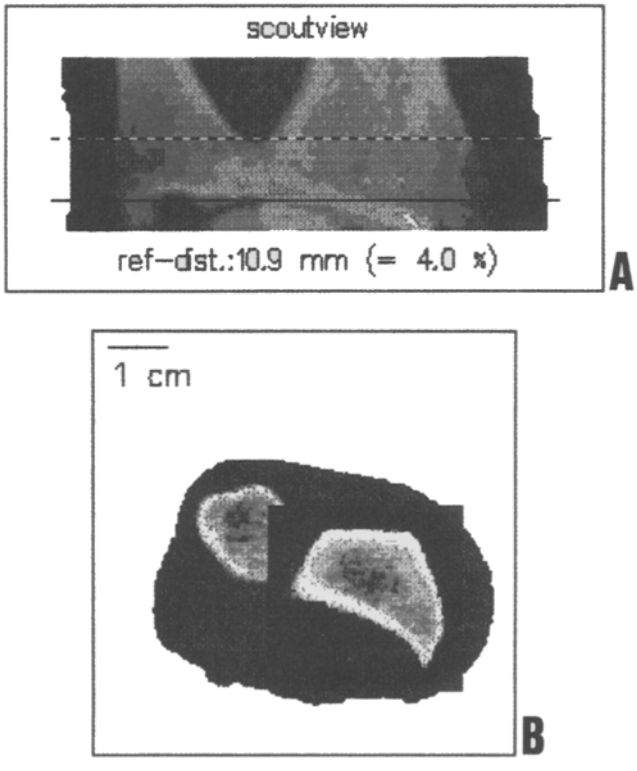

Fig. 1. A A printed image of a coronal scout scan with one of the cadaveric forearms. On the scout view the operator manually places a reference line (*continuous line*) at the medial end of the radius. Then the software automatically finds the standard scan position (*dotted line*) for the CT scan. **B** A printed CT image obtained from the same forearm.

The projection data were collected with five detectors that were incrementally angled 2.5° each. Fifteen different positions of the detector ensemble resulting in 75 projections were equally spread over 180°. The pixel size was 0.59 mm × 0.59 mm for normal forearms and 0.69 mm × 0.69 mm for large forearms. The maximum scan diameter was 73 mm and 88 mm, respectively. In this study the smaller pixel size of 0.59 mm × 0.59 mm was used for all forearms. The radius was segmented from the surrounding soft tissue with the help of a thresholding algorithm (linear attenuation coefficient 0.40–0.67 cm^{-1} = 112–377 mg/cm^3 hydroxyapatite as set by the manufacturer) [11], and then the total BMD was computed. Fifty-five percent of the area used for the calculation of the total BMD was peeled off concentrically. The trabecular BMD corresponded to the mean bone density within the remaining 45% of this area [11,13].

Accuracy Study

Seven of 12 forearms were used. Three scans per forearm were performed at the s-position, and at 2.5 mm both proximal and distal to the s-position without repositioning. After the pQCT measurements had been obtained, the distal one-third of the cadaveric radius was dissected. The dissected radius was put on a table in the same way as in the scout view, and then the line corresponding to the measurement at the s-position was marked on the radius by measuring the 4% distance used in the scout view from the medial end of the radius using a ruler. The slice (thickness 2.5 mm) corresponding to the measurement at the s-position of the cadaveric radius was dissected using an Isomet (Buehler Ltd., Lake Bluff, IL; blade thickness 0.40 mm), and then the two slices both proximal and distal to the first slice were also dissected. These two slices corresponded to the measurements at 2.5 mm both proximal and distal to the s-position. No attempt was made to remove bone marrow fat. All dissected slices were ashed at 650 °C for 24 h.

A linear regression analysis was performed to determine the correlation between the ash weights (AWs) and total bone mineral content (BMC). First, for each forearm, the total BMC results of the measurements at the s-position were compared with the AW results of the corresponding slices. Secondly, the BMC values of all 21 slices were compared with the AWs of the corresponding slices. In addition, the same analysis was performed after averaging the AWs of all three slices for each forearm. BMC (g) was calculated by BMD (g/cm^3) × Area (cm^2) × thickness × 0.25 (cm). Two components of the accuracy error must be distinguished. The systematic component manifests itself by a slope different from 1 and an intercept different from 0 and is mainly caused by a calibration offset. The random

component of the accuracy error is the scatter around the linear regression and was given as the coefficient of variation (CV) in percentage of the linear regression [(standard error of estimate (SEE) of the regression) / (mean of the dependent variable) × 100]. Unless the intercept was significantly different from 0, the CV was recalculated by forcing the intercept to 0.

Precision Study

Seven of 12 forearms were used, two of which were the same as those used for the accuracy study. The short-term precision error expressed as the root mean square of the CV in percentage of the total BMD, total BMC and trabecular BMD was determined by measuring the forearms consecutively five times with repositioning and five times without repositioning at the s-position.

Evaluation of the Influence of Positioning

Seven of the 12 forearms were used (the same ones as were used for the precision study). Additional scans were performed at 1, 2 and 5 mm proximal, and 1 and 2 mm distal to the s-position without repositioning. The differences in total BMD, total BMC, trabecular BMD and total area between the s-position and each of the additional scan positions were represented as the percentage deviations from values of the s-position. A paired *t*-test was performed to investigate whether these percentage deviations were significantly different from 0.

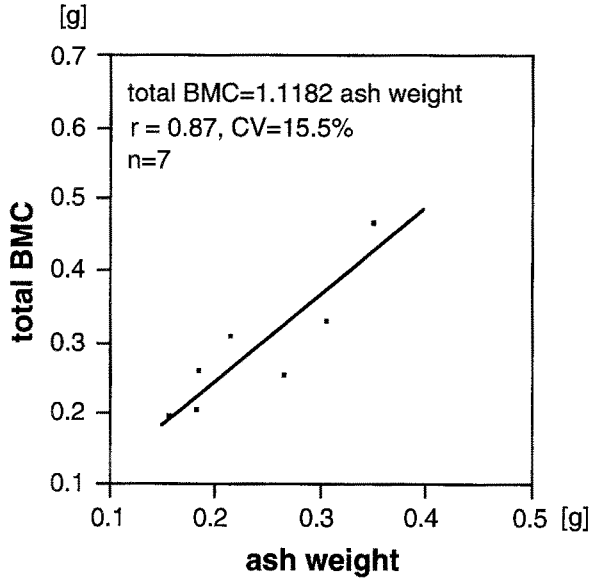

Fig. 2. The correlations between ash weights (AWs) and total BMCs of one slice per cadaveric forearm taken at the standard position (n = 7 cadavers). The random component of the accuracy error is given as the coefficient of variation (CV) in percentage of the linear regression [(standard error of estimate (SEE) of the regression)/(mean of the dependent variable) × 100] and by forcing the intercept to 0. All correlations were significant ($p<0.001$).

Results

The correlations between the AWs and the corresponding total BMC values at the s-position per forearm are shown in Fig. 2. The correlation coefficient was $r = 0.87$ with an accuracy error (random component) of 15.5%. The correlation between the AWs of all 21 slices in the 7 forearms and their total BMC values are shown in Fig. 3a. The correlation coefficient was $r = 0.90$ with an accuracy error of 14.3%. As shown in Fig. 3b, the correlation coefficient improved to $r = 0.95$ with an accuracy error of 9.7% after averaging the results of all three slices for each forearm. All correlations were significant ($p<0.001$). For all linear results presented

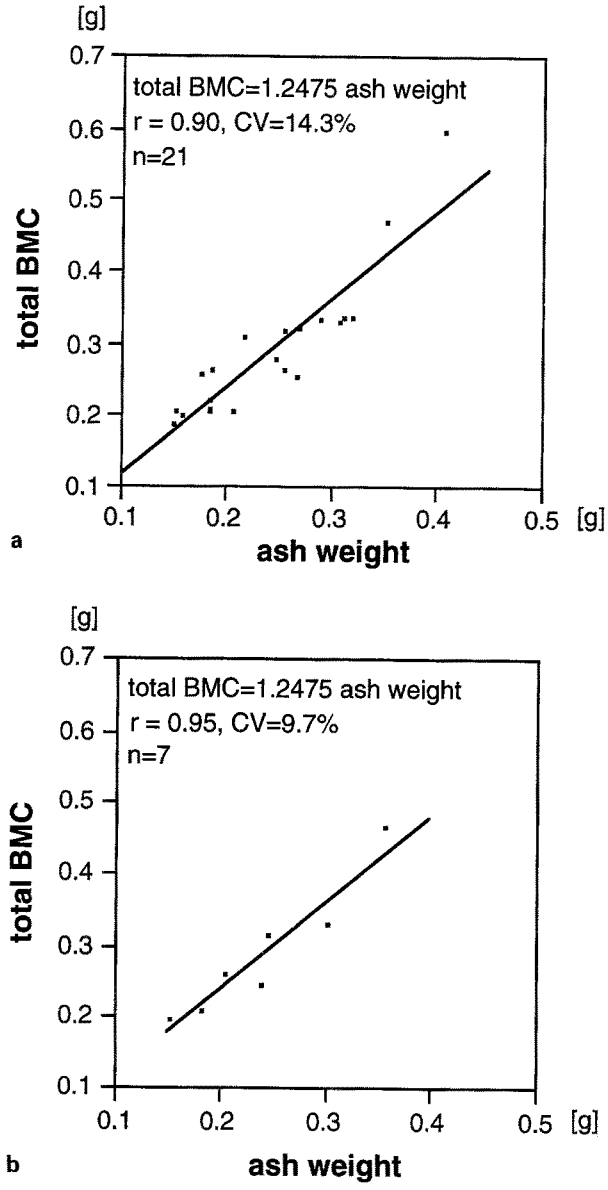

Fig. 3. a The correlations between AWs and total BMCs of all 21 slices in the 7 cadaveric forearms. **b** The correlations between AWs and total BMCs after averaging the results of all three slices for each forearm. The accuracy error is given in the same way as in Fig. 2 and all correlations were significant ($p<0.001$).

Table 1. The short-term in vitro precision error (CV in %)

	With repositioning	Without repositioning
Total BMD	2.77	0.29
Total BMC	1.15	0.58
Trabecular BMD	1.85	0.69

here the regression lines were forced through 0 (intercept = 0) because none of the intercepts was significantly different from 0.

The short-term in vitro precision errors (Table 1) ranged from 0.29% to 2.77% for BMD, and from 0.58% to 1.15% for BMC. As shown in Table 2, total BMD and area changed dramatically when the reference line was shifted by only 1 mm. The changes in trabecular BMD showed a large standard variation but BMD distal or proximal to the s-position was not statistically different from BMD at the s-position. Moving the scan location from distal to proximal away from the wrist resulted in increasing total BMD values and decreasing total areas in all forearms. Compared with the other parameters, changes in total BMC compared with the s-position were relatively small.

Discussion

In the accuracy study we found a random component of the accuracy error of 15.5% when comparing the total BMC with AW at the s-position. With regard to the systematic component of the accuracy error, the slope of the regression between the total BMC and AW was significantly different from 1, consistent with the fact that the pQCT calibration is based on hydroxyapatite using the COMAC European forearm phantom [14] and not on AW. Part of the random component of the accuracy error can certainly be attributed to our methodology, because it is difficult to dissect the exact slice that a pQCT scanner measures. We have to consider that slipping 1 or 2 mm during the dissection may cause some errors in the total BMCs. Those errors are up to 2% according to Table 2. Other likely factors affecting accuracy errors are marrow fat and beam hardening. It is a known problem in single-energy QCT, and thus a problem of current pQCT scanners, that marrow fat causes an underestimation of the actual BMC [15]. Also beam hardening problems are more pronounced in single-energy compared with dual-energy QCT. A random component of accuracy errors of 13.2% [15] has been reported for single-energy QCT using cadaveric vertebrae. Considering these potential error sources, the random part of the accuracy error of 15.5% in total BMC appears to be understandable and acceptable.

When comparing the total BMCs with the AWs in all 21 slices, we found a better accuracy error of 14.3%. In this case, we have to consider that the blade thickness (0.4 mm) caused some error in the total BMCs at 2.5 mm both proximal and distal to the s-position. Assuming that the s-position sample was cut at the correct position, the other samples were shifted by 0.4 mm. The true accuracy of this regression is probably less than our measured 14.3%. Comparing the total BMCs with the AWs after averaging the results of all three slices for each forearm in all 21 slices, the correlation coefficient and accuracy error were improved. When comparing the accuracy results before and after averaging, the methodological errors caused by the finite blade thickness are probably minor.

The short-term precision error for total BMC with repositioning in this study was 1.15%, and thus the improvement of accuracy errors by scanning three slices per forearm indicates that it is preferable for highly accurate measurements to use a larger volume of the radius. This is also supported by a study from our group comparing ash weights with DXA values of three different machines in the distal one-third radius. In this DXA study the correlation coefficients ranged from 0.97 to 0.98 with a random component of the accuracy errors ranging from 4.4% to 5.2% in the cadaveric radii in which segments 20 mm in length were assessed [16]. These issues deserve further discussion regarding sampling errors and adequacy of a single slice of 2.5 mm thickness; nevertheless the Stratec XCT-960, at least for total bone, can be considered a moderately accurate pQCT scanner.

The precision errors of the Stratec pQCT scanner for trabecular BMD in vivo with repositioning have been reported in the literature to range from 0.71% to 1.67% [11,17,18]. However, young women were enrolled in these studies. This resulted in relatively high trabecular

Table 2. The percentage differences in BMD, BMC and area from the standard position

	2 mm distal	1 mm distal	1 mm proximal	2 mm proximal	5 mm proximal
Total BMD	−10.2±0.8[a]	−5.5 ±0.7[b]	6.4 ±1.7[b]	13.7 ± 3.0[c]	31.0 ±10.4[d]
Total BMC	2.0±2.6	0.85±1.8	0.20±1.3	0.84± 2.6	−0.61± 4.6
Trabecular BMD	2.3±5.6	2.5 ±5.1	0.18±6.3	1.3 ±11.5	2.8 ±23.5
Total area	13.6±3.3[a]	6.7 ±1.9[b]	−5.8 ±2.0[b]	−11.3 ± 2.2[c]	−23.1 ± 3.3[d]

The values (mean ± SD) are represented as the percentage difference between the shifted and standard position.
[a] $p<0.001$ versus 1 mm distal; [b] $p<0.001$ versus the standard position, [c] $p<0.001$ versus 1 mm proximal; [d] $p<0.001$ versus 2 mm proximal.

BMD of forearms. At our center, Grampp et al. [19] recently carried out a study of 20 premenopausal women aged 31 ± 6 years (mean ± SD), 20 postmenopausal women aged 62 ± 10 years, and 20 postmenopausal osteoporotic women aged 69 ± 8 years. For the two consecutive measurements with repositioning, the CVs for each group were 0.9%, 1.8% and 2.1% for trabecular BMD, and 1.1%, 2.2% and 2.1% for total BMD, respectively. In our in vitro study presented here, the average and standard deviation of trabecular and total BMD of 7 forearms were 182 ± 46 mg/cm^3 and 323 ± 68 mg/cm^3, respectively. These values are close to those of postmenopausal healthy women in Grampp et al.'s study: 173 ± 55 mg/cm^3 and 323 ± 66 mg/cm^3, respectively. Our in vitro CV result for trabecular bone was the same as Grampp et al.'s in vivo result for postmenopausal healthy women: 1.85% versus 1.8%. Our in vitro CV results for total BMD were slightly higher compared with the corresponding in vivo CV results: 2.77% versus 2.2%. Considering these matters, given the uncertainty in the age of our cadavers, our in vitro CV results can be considered typical in clinical use.

In this in vitro study the CV for the total BMD with repositioning was worse than that of the trabecular BMD. This tendency was consistent with in vivo results from Grampp et al.'s study [19]. One reason may be that along the longitudinal axis of the radius the changes in total BMD are much higher than those in trabecular BMD (see Table 2). On the other hand, the CV result for total BMC with repositioning was better than that of total and trabecular BMD. The reason may be that the total BMC, mainly influenced by the cortical shell, varies less than either the total or trabecular BMD (see Table 2). Given these difficult anatomical relations, the magnitude of the precision errors appears to be understandable. We found much better precision values when scanning the cadaveric forearms without repositioning, indicating excellent machine precision.

From the study evaluating the influence of positioning, we found that the values of total BMD and area were most affected by the positioning. The results in Table 2 suggests that positioning may have a dramatic impact on precision errors of these parameters. Total BMC and trabecular BMD were less affected. The measurement of several slices may potentially reduce the errors caused by positioning. The Densiscan pQCT system from Scanco (Zurich, Switzerland), which is also commercially available, uses multiple slices at the ultradistal radius and the manufacturer has reported very low precision errors for trabecular BMD: 0.3%, 0.6% and 0.9% in normal, osteoporotic and severely osteoporotic women, respectively [20]. Newer versions of the Stratec scanners can also measure multiple slices. Using the single slice technique considerable care must be exercised in placing a reference line in order to scan the same slice in subsequent measurements.

In summary, our in vitro results indicate that the Stratec XCT-960 is a moderately accurate and highly precise scanner with potential usefulness for evaluating BMC and BMD of ultradistal radius.

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