

Quantification of bone mineral density precision according to repositioning errors in peripheral quantitative computed tomography (pQCT) at the radius and tibia

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Abstract

Peripheral quantitative computed tomography (pQCT) is increasingly being used to measure bone mineral density (BMD) in both research and clinical practice to monitor BMD changes. Repeated measurements in long-term follow-up study are an appropriate method to study the pattern of bone loss and the diagnostic value critically depends upon the precision (reproducibility). Positioning is one of the sources of imprecision. In this study, BMD at the locations around 4% length of the tibia and radius were measured by pQCT. The relationship between the change of BMD and the change of total cross-sectional-area (CSA) of the bone were analyzed in order to promote the follow-up-reproducibility of pQCT measurements. The results showed a decrease of CSA and increase of trabecular BMD from distal to proximal at the human distal radius, while a consistent decrease of CSA and apparent trabecular BMD from distal to proximal at the distal tibia was observed. It is suggested the follow-up location can be considered as the same location as the baseline measurement at the tibia if the CSA changed within $\pm 20 \text{ mm}^2$. As to the radius, the criteria are better to be $\pm 10 \text{ mm}^2$ of the CSA change. Otherwise, it is enough to judge the location only by checking the 4% location when both the 4% and shaft location of the bone are measured at one measurement. And some suggestions are also given to the machine manufacturer.

Keywords: pQCT, Reproducibility, BMD, Radius, Tibia

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Low bone mass estimated by decreased apparent bone mineral density (BMD), which is associated with deterioration of bone microarchitecture, is an established predictor of osteoporotic fracture, as more than 90% of all fractures in elderly individuals are associated with osteoporotic bone changes^{1,2}.

Among the current techniques for the quantitative assessment of the bone mineral status, peripheral quantitative computed tomography (pQCT) offers a number of distinct advantages: in contrast to single or dual X-ray absorptiometry (SXA / DXA), it allows one to assess the trabecular and cortical bone compartments separately, and to measure the volumetric bone mineral density (BMD; in mg/cm^3) rather than the area BMD (mg/cm^2). And it can also provide bone geometry, bone strength, and muscle cross-sectional area. Therefore, pQCT is increasingly being used to measure BMD in both research and clinical practice to monitor BMD changes to evaluate the fracture susceptibility in old people or the effect following therapeutic intervention³. In addition, long-term follow-up with repeated measurements is an appropriate method to study the pattern of bone loss among individuals. In this case, the site (whether it is convenient to be measured) and the reproducibility must be considered.

Besides being convenient to be measured, the anatomy of the radius and tibia (thin cortex with mainly trabecular bone at the distal end and pure cortical bone along the diaphysis)

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enables the examination of both cortical and trabecular bone. Therapeutic effects as well as postmenopausal bone loss can be detected earlier in regions of trabecular bone⁴. Furthermore, it has been suggested that *in vivo* assessment of trabecular bone micro architecture may improve the prediction of fracture risk and the ability to monitor the response to therapeutic intervention⁵. And it has also been suggested that the BMD at the distal radius can be used for predicting osteoporotic fracture^{6,7}.

In our former studies, a decrease of total cross-sectional-area (CSA) was found from distal to proximal at the human distal radius and tibia with apparent trabecular BMD ceaselessly changing. Four percent of the radius and tibia were used to analyze trabecular bone while 60% of the radius and 66% of the tibia was used to analyze cortical bone. The CSA of 4% was used to judge the position because the shape of the distal radius and tibia are changing more sharply than that of the proximal. In the follow-up measurement, it was considered as the same position as that of the baseline measurement if the drift area (change area) of CSA in reference to CSA of the baseline measurement had fallen in the range of ± 20 mm². However, we have no cross-sectional studies describing the interrelationship of the apparent BMD change and with CSA change at the distal tibia and radius. Therefore, the exact range of CSA change has not been found to make sure that the BMD values have been obtained from the same position.

The objective of this study was to find out the range and promote the reproducibility of pQCT in follow-up measurements, that is, how to ensure the same position was measured in diverse operations at the largest degree. BMD of diverse localizations at the distal and shaft of the radius and tibia were measured by pQCT and then the relationship between the change in BMD and the change in total CSA change was evaluated.

Materials and methods

Fresh bones without skin and soft tissues from the same cadaver were examined *in vitro* by XCT 2000 (Stratec, Pforzheim, Germany). The bones were surrounded by particular materials for simulation of surrounding soft tissue. For each specimen, pQCT measurements were performed three times consecutively without repositioning at 11 locations of the distal tibia or at 22 localizations of the distal radius around 4% of the bone length (actually the ulna's length was measured in the same way as in clinical practice).

As a standard procedure the scout view was obtained to locate the desired scan position. A reference line was then placed through the adjacent joint region (articular face of the distal tibia or radius). As the total length of the bone was obtained prior to the measurement, the CT was positioned at 4%.

At the tibia, 11 skeletal localizations around 4% of the bone length were scanned symmetrically and the interval between the adjacent slices was 0.1 mm (that is 4%-0.5 mm, 4%-0.4 mm,

4%-0.3 mm, 4%-0.2 mm, 4%-0.1 mm, 4%, 4%+0.1 mm, 4%+0.2 mm, 4%+0.3 mm, 4%+0.4 mm and 4%+0.5 mm proximal to the distal end of tibia). Accordingly, 11 localizations around 66% in the midshaft region of the tibia were scanned.

At the radius, 22 skeletal localizations around 4% were scanned symmetrically and the interval between the adjacent slices was also 0.1 mm (4%-1.0 mm, 4%-0.9 mm, 4%-0.8 mm, 4%-0.7 mm, 4%-0.6 mm, 4%-0.5 mm, 4%-0.4 mm, 4%-0.3mm, 4%-0.2 mm, 4%-0.1 mm, 4%, 4%+0.1 mm, 4%+0.2 mm, 4%+0.3 mm, 4%+0.4 mm and 4%+0.5 mm, 4%+0.6 mm, 4%+0.7 mm, 4%+0.8 mm, 4%+0.9 mm and 4%+1.0 mm proximal to the distal end of radius). Accordingly, 22 localizations around the 60% in the midshaft region of radius were scanned.

The slice thickness was 2.0 mm at all locations, and the inplane resolution 0.5 mm x 0.5 mm, the image data being analyzed with the software provided by the manufacturer. The trabecular bone compartment was detected with contour mode 1, peel mode 1 and a threshold of 180 mg/cm³. The cortical bone was separated with cortical mode 1 and a threshold of 710 mg/cm³. The following parameters allocated at 4% were evaluated at both the tibia and radius: (a) total bone area in mm² (TOT_A), that is CSA; (b) trabecular density in mg/cm³ (TRAB_DEN). Hence the following parameters were calculated: (1) the drift area of CSA in reference to the 4% CSA (TOT_A_D); (2) the absolute change of trabecular density in reference to the trabecular BMD at the 4% location (TRAB_DEN_C); (3) the change of trabecular density in percent in reference to the trabecular BMD at the 4% location (TRAB_DEN_C%) calculated as $TRAB_DEN_C\% = (TRAB_DEN - TRAB_DEN_{4\%}) / TRAB_DEN_{4\%}$. The similar parameters were also evaluated and calculated at the 66% position of the tibia and 60% of the radius.

Statistical analyses

t-Test was used to compare the mean values of total area or trabecular density of the localization around 4% versus that of 4% position. The level of statistical significance was set at $p < 0.05$. Excel program was used to evaluate the data.

The relationship between CSA change and bone density change in percentage were studied using regression, also between the longitudinal distance and bone density, between longitudinal distance and CSA change.

Results

The sectional total bone area and corresponding trabecular BMD at the tibia and radius are listed in Table 1. At the distal tibia, a consistent decrease of CSA and apparent trabecular BMD from distal to proximal was found. When CSA changes (the drift area, TOT_A_D) were ± 20 mm², the scanned localizations were within 4% ± 0.5 mm along the longitudinal tibia. There were no significant differences in the TOT_A (CSA) between the 4% location and any others within 4% ± 0.5 mm. Also, there were no significant differences in the trabecular bone density between the 4% location and any

Bone	Position	TOT_A ¹⁾ (mm ²) mean±SD	TOT_A_D ²⁾ (mm ²) mean±SD	TRAB_DEN ³⁾ (mg/ccm) mean±SD	TRAB_DEN_C ⁴⁾ (mg/ccm) mean±SD	TRAB_DEN_C% ⁵⁾ mean±SD
Tibia	distal ↑	4%-0.5mm 1201.17±16.00 [#]	21.75±3.12	125.8±0.86 [#]	0.67±0.55	0.53%±0.0044
		4%-0.4mm 1196.25±15.92 [#]	16.83±2.13	125.6±1.06 [#]	0.47±0.60	0.37%±0.0049
		4%-0.3mm 1191.75±14.77 [#]	12.33±0.76	125.4±0.80 [#]	0.33±0.75	0.27%±0.0060
		4%-0.2mm 1186.75±14.53 [#]	7.33±0.72	125.3±0.87 [#]	0.23±0.49	0.19%±0.0040
		4%-0.1mm 1182.83±13.90 [#]	3.42±1.26	125.3±0.55 [#]	0.17±0.55	0.14%±0.0044
	4% 1179.42±14.36	0	125.1±1.06	0	0	
	4%+0.1mm 1174.83±14.32 [#]	-4.58±1.28	124.7±1.36 [#]	-0.43±0.58	-0.35%±0.0046	
	4%+0.2mm 1171.00±15.13 [#]	-8.42±2.24	124.6±1.27 [#]	-0.47±0.67	-0.37%±0.0053	
	4%+0.3mm 1166.58±14.19 [#]	-12.83±0.88	124.4±1.14 [#]	-0.67±0.50	-0.53%±0.0040	
	proximal ↓	4%+0.4mm 1162.50±13.63 [#]	-16.92±1.01	124.3±1.40 [#]	-0.77±0.64	-0.61%±0.0051
	4%+0.5mm 1158.25±12.14 [#]	-21.17±2.60	124.1±1.07 [#]	-0.97±0.55	-0.77%±0.0044	
Radius	distal ↑	4%-1.0mm 371.08±1.88 ^{**}	38.83±1.63	70.23±2.35 [#]	-1.43±1.72	-1.97%±0.02
		4%-0.9mm 367.83±1.88 ^{**}	35.58±1.63	69.77±2.31 [#]	-1.90±0.53	-2.63%±0.01
		4%-0.8mm 363.50±1.80 ^{**}	31.25±1.39	70.30±2.00 [#]	-1.37±0.91	-1.88%±0.01
		4%-0.7mm 356.92±3.74 ^{**}	24.67±6.71	70.07±2.63 [#]	-1.60±0.35	-2.23%±0.00
		4%-0.6mm 357.25±2.61 ^{**}	25.00±0.50	70.00±1.65 [#]	-1.67±1.19	-2.29%±0.02
		4%-0.5mm 352.00±2.14 ^{**}	19.75±1.39	70.03±2.67 [#]	-1.63±0.21	-2.28%±0.00
		4%-0.4mm 346.92±2.93 ^{**}	14.67±0.52	70.10±2.70 [#]	-1.57±0.23	-2.18%±0.00
		4%-0.3mm 344.08±3.61 [*]	11.83±0.58	70.23±2.66 [#]	-1.43±0.81	-1.99%±0.01
		4%-0.2mm 339.25±3.27 [#]	7.00±0.43	71.00±1.57 [#]	-0.67±1.33	-0.88%±0.02
		4%-0.1mm 335.67±3.97 [#]	3.42±0.95	70.47±3.67 [#]	-1.20±0.92	-1.71%±0.01
	4% 332.25±3.03	0	71.67±2.84	0	0	
	4%+0.1mm 328.33±2.10 [#]	-3.92±0.95	72.03±2.68 [#]	0.37±0.38	0.52%±0.01	
	4%+0.2mm 325.50±1.73 [#]	-6.75±1.30	71.63±2.05 [#]	-0.03±1.15	-0.01%±0.02	
	4%+0.3mm 319.83±1.66 ^{**}	-12.42±4.65	71.80±2.78 [#]	0.13±0.59	0.19%±0.01	
	4%+0.4mm 318.42±0.52 [*]	-13.83±2.53	73.23±1.86 [#]	1.57±1.01	2.22%±0.01	
	proximal ↓	4%+0.5mm 315.92±2.45 ^{**}	-16.33±0.58	74.03±2.74 [#]	2.37±0.55	3.31%±0.01
	4%+0.6mm 311.42±1.42 ^{**}	-20.83±1.70	73.83±2.84 [#]	2.17±0.25	3.03%±0.00	
	4%+0.7mm 309.17±0.80 ^{**}	-23.08±2.84	74.40±2.62 [#]	2.73±0.42	3.83%±0.01	
	4%+0.8mm 306.25±1.56 ^{**}	-26.00±1.56	75.13±3.49 [#]	3.47±0.78	4.82%±0.01	
	4%+0.9mm 303.42±1.81 ^{**}	-28.83±1.23	75.00±3.53 [#]	3.33±0.71	4.63%±0.01	
	4%+1.0mm 301.17±2.45 ^{**}	-31.08±0.58	75.80±2.77 [#]	4.13±0.45	5.78%±0.01	

[#] compared with the position of 4%, p>0.05
^{*} compared with the position of 4%, p<0.05
^{**} compared with the position of 4%, p<0.01

Table 1. CSA and trabecular bone density around 4% localizations of tibia and radius.

others within 4%±0.5 mm. The maximal proportional change in trabecular bone density (TRAB_DEN_C%) was less than 1%.

At the distal radius, the pattern of changes in BMD was different in the distal direction as compared with the changes in the proximal direction. There were almost no changes in BMD from 4%-1 mm to 4%-0.1 mm though CSA had a significant change. From 4% to +1 mm, a decrease of CSA and increase of trabecular BMD was found. When the drift area (TOT_A_D) was ±20 mm², the scanned localizations were at around 4%±0.6 mm. In the range of 4%±0.2 mm, the changes of TOT_A were not significant. The corresponding TOT_A_D in this region had fallen in the range of ±10 mm². However, there were significant differences in TOT_A although there were still no significant differences

in trabecular bone density between 4% localization and any others outside the range of 4% ±0.2 mm. The maximal proportional change in trabecular bone density (TRAB_DEN_C %) was less than 1% in the region of 4% ±0.2 mm, about 3% in the region of 4%±0.6 mm and more than 5% in the region of 4%±1.0 mm.

Linear regression analysis at the tibia. At the tibia, linear regression analysis was applied. Figure 1 shows a decrease CSA (TOT_A) from the distal to proximal along the longitudinal tibia. The linear regression formation is y=-42.235x, R²=0.9987. When longitudinal distance (x) is ±0.5 mm, the CSA change (y) is about ±21.12 mm². Figure 2 shows a decrease in trabecular BMD from the distal to proximal along the longitudinal tibia. The linear regression formation is y=-0.0132 x, R²=0.9187. When the longitudinal distance

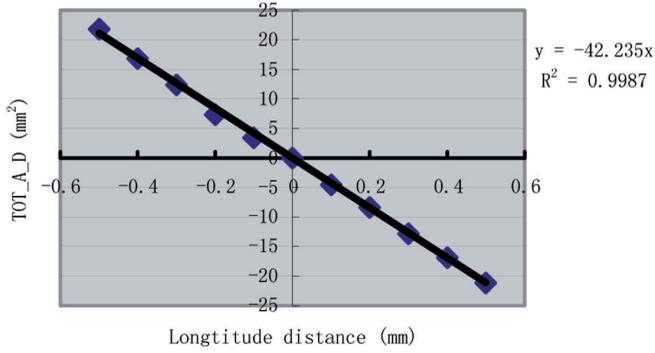


Figure 1. The correlation between longitudinal distance and CSA change at the distal tibia.

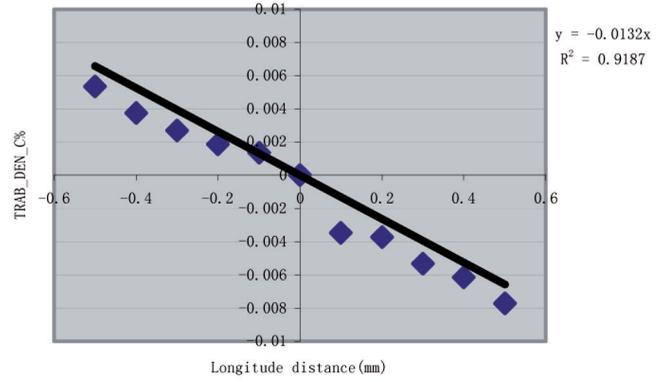


Figure 2. The correlation between longitudinal distance and trabecular bone density change at the distal tibia.

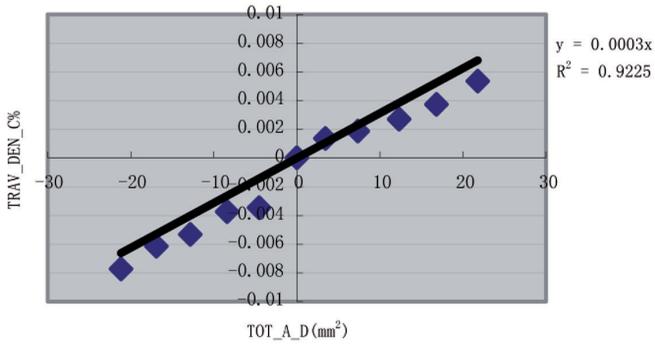


Figure 3. The correlation between CSA change and trabecular bone density change at the distal tibia.

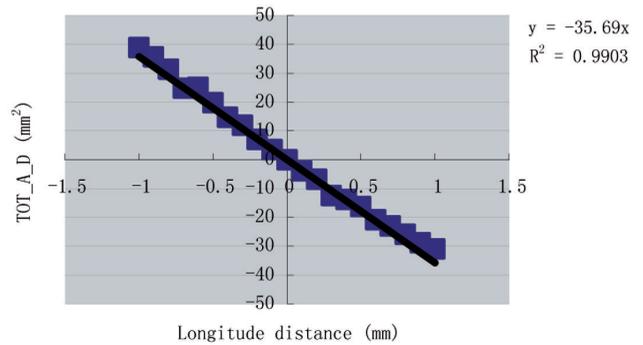


Figure 4. The correlation between longitudinal distance and CSA change at the distal radius.

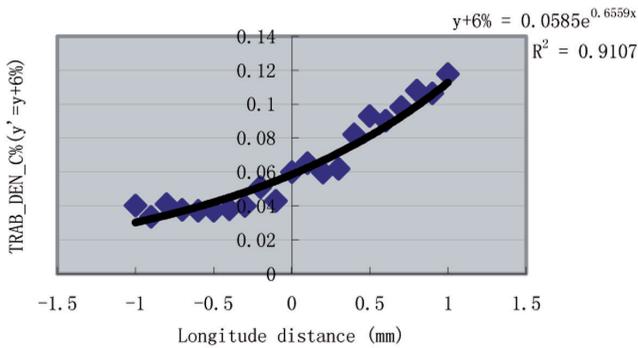


Figure 5. The correlation between longitudinal distance and trabecular bone density change at the radius.

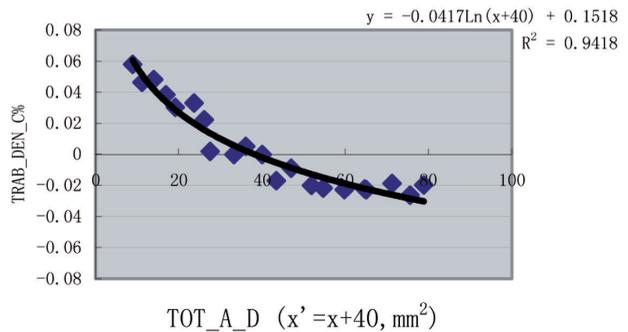


Figure 6. The correlation between CSA change and trabecular bone density change at the distal radius.

(x) is ± 0.5 mm, the trabecular BMD change (y) = $\pm 0.66\%$. Figure 3 shows a consistent increase of CSA and apparent trabecular BMD from the proximal to the distal. The formation is $y = 0.0003x$, $R^2 = 0.9225$. When the CSA change is ± 20 mm², the trabecular BMD change (y) is $\pm 0.6\%$.

Linear and nonlinear regression analysis at the radius. At the radius, Figure 4 shows a decrease in CSA from the distal to proximal along the longitudinal radius. The linear regression formation is $y = -35.69x$, $R^2 = 0.9903$. When longitudinal distance (x) is ± 0.2 mm, CSA change (y) is about ± 7.14 mm² while

Bone	position	TOT_A_D (mm ²)	TRAB_DEN_C%	position	TOT_A_D (mm ²)	CORT_DEN_C%	
Tibia	↑ <i>distal</i>	4%-0.5mm	24.25	0.24%	66%-0.5mm	-1.50	0.44%
		4%-0.4mm	19.00	-0.08%	66%-0.4mm	-1.25	0.26%
		4%-0.3mm	13.00	-0.08%	66%-0.3mm	-0.50	0.55%
		4%-0.2mm	7.75	-0.08%	66%-0.2mm	-1.00	-0.03%
		4%-0.1mm	3.25	0.16%	66%-0.1mm	0.25	0.29%
	↓ <i>proximal</i>	4%	0	0	66%	0.00	0.00%
		4%+0.1mm	-4.25	-0.08%	66%+0.1mm	0.50	-0.46%
		4%+0.2mm	-7.00	-0.96%	66%+0.2mm	0.50	-0.67%
		4%+0.3mm	-12.75	-0.96%	66%+0.3mm	1.75	-0.28%
		4%+0.4mm	-17.50	-1.20%	66%+0.4mm	1.50	-0.70%
	4%+0.5mm	-23.25	-1.20%	66%+0.5mm	2.00	-0.88%	
Radius	↑ <i>distal</i>	4%-1.0mm	37.25	-3.74%	60%-1.0mm	1.75	-0.37%
		4%-0.9mm	34.00	-3.34%	60%-0.9mm	1.00	0.00%
		4%-0.8mm	29.75	-3.20%	60%-0.8mm	1.00	0.09%
		4%-0.7mm	17.00	-2.40%	60%-0.7mm	1.00	-0.20%
		4%-0.6mm	24.50	-4.01%	60%-0.6mm	1.00	-0.22%
		4%-0.5mm	18.50	-2.40%	60%-0.5mm	0.50	0.12%
		4%-0.4mm	14.50	-2.27%	60%-0.4mm	0.75	-0.54%
		4%-0.3mm	12.50	-2.54%	60%-0.3mm	0.75	0.19%
		4%-0.2mm	7.25	-2.94%	60%-0.2mm	1.00	-0.80%
		4%-0.1mm	4.50	-0.27%	60%-0.1mm	0.50	0.06%
	↓ <i>proximal</i>	4%	0	0	60%	0.00	0.00
		4%+0.1mm	-5.00	0.13%	60%+0.1mm	0.25	0.62%
		4%+0.2mm	-8.25	-1.60%	60%+0.2mm	0.25	-0.02%
		4%+0.3mm	-17.75	-0.13%	60%+0.3mm	0.50	0.48%
		4%+0.4mm	-16.75	0.53%	60%+0.4mm	0.50	0.62%
		4%+0.5mm	-17.00	2.85%	60%+0.5mm	0.75	-0.37%
		4%+0.6mm	-22.75	2.94%	60%+0.6mm	0.75	0.64%
		4%+0.7mm	-26.25	3.20%	60%+0.7mm	0.75	0.16%
		4%+0.8mm	-27.75	5.47%	60%+0.8mm	0.50	0.62%
		4%+0.9mm	-30.25	5.47%	60%+0.9mm	0.75	1.59%
	4%+1.0mm	-31.75	5.47%	60%+1.0mm	0.00	2.27%	

Table 2. Comparison of CSA and BMD between the position around 4% versus 66% of the tibia and 4% verse 60% of the radius.

x is ±0.5 mm, y is ±17.85 mm². Figure 5 shows an increase in trabecular BMD from the distal to the proximal along the longitudinal radius approximately. The exponential regression was applied to assess the relationship of BMD change and longitudinal distance at various localizations. The formation is $y=0.0585e^{0.6559x}-0.06$, $R^2=0.9107$. When longitudinal distance (x) is 0.2 mm, the BMD change (y) is 0.67% while $x=-0.2$ mm, $y=-0.87%$; $x=0.5$ mm, $y=2.12%$; $x=-0.5$ mm, $y=-1.79%$. Figure 6 shows a decrease of trabecular BMD and increase of CSA from the proximal to the distal at the human distal radius. The logarithmic regression was applied to assess the relationship of BMD change and CSA change (TOT_A_D) at various localizations. The formation is $y=-0.0417\ln(x+40)+0.1518$, $R^2=0.9418$. When the drift area (x) is 10 mm², the BMD percentage change (y) is -1.13% while $x=-10$ mm², $y=0.997%$; $x=20$ mm², $y=-1.89%$; $x=-20$ mm², $y=2.69%$.

In addition, the CSA change (TOT_A_D) at the shaft position was compared with that of distal position (Table 2). At the tibia, when the drift area around 4% was between ±20

mm², the drift area around 66% was less than ±2 mm². At the radius, when the drift area around 4% was between ±20 mm², the drift area around 60% was less than ±1 mm². This indicates that it is reasonable to control the position only by checking the total area at 4% position, not that of the shaft.

Discussion

Several techniques are currently available for the quantitative assessment of bone mineral status, such as SXA and DXA, quantitative ultrasound, quantitative computed tomography (QCT) and peripheral QCT (pQCT). The DXA technique offers excellent precision *in vivo*, reasonable accuracy, flexibility in applications, short examination time and low radiation exposure to patients, and the ability to predict the fracture risk⁸. DXA has been considered a faster, more precise and more accurate method for quantitative bone assessment compared with the former techniques⁴, such as SPA, DPA and SXA. However,

its status is being challenged by QCT. The advantage of QCT over DXA is that it measures volumetric BMD and the results are given in mg/cm^3 , not in g/cm^2 and assesses the trabecular and cortical bone compartments separately. Special-purpose CT scanners have been developed for imaging the peripheral skeleton. Peripheral quantitative CT (pQCT)'s advantages over QCT are the lower radiation dose and cost, the higher precision, and a potentially higher predictive ability for fractures at peripheral skeletal locations⁹. Therefore, pQCT is anticipated to take the place of DXA in both research and clinical practice.

Precise assessment of bone mineral is one of the most important criteria for depicting responses to therapy. The diagnostic value of bone densitometry techniques in both cross-sectional and longitudinal studies critically depends upon the precision (reproducibility) of the particular method¹. pQCT has also been shown to yield a higher precision than projection techniques such as SXA and DXA^{4,8}. Augat et al.⁴ has reviewed the former articles and compared different techniques, including SPA, DPA, SXA, QCT and pQCT, for quantitative bone assessment at the forearm. For DXA, *in vitro* precision (%CV) of BMD is 0.4%-0.9% and *in vivo* precision of BMC is 0.7%-1.3%. For pQCT, *in vitro* precision (%CV) of BMD is 0.03%-0.3% and *in vivo* precision of BMC and BMD is 1.1%-2.2% and 0.3%-2.2%. In any event, the specific solutions depend on the measurement method but have resulted in an *in vivo* precision error that is less than 2% for all currently available devices^{4,8}.

Precision can be defined as the ability to make reproducible measurements without regard to their accuracy (defined by the difference between the measured value and the true physical property)⁴. One of the sources of imprecision is positioning. Precise patient measurements require exact repositioning to make sure that the same region of bone is scanned. This is especially important in the ultra-distal region where bone density changes rapidly with position along the longitude of the bone.

Imprecision due to repositioning errors can be reduced by methods that automatically select scanning locations and regions of interest⁴. However, during pQCT follow-up measurements the automatically selected scanning locations often differ from the baseline measurement. Evidence suggests that the positioning of the extremity during the follow-up varies too much from the positioning at baseline. In this situation, a manually selected scanning location and even reposition is inevitable. Therefore, rigorous positioning control is necessary.

In earlier studies accomplished by us, the positioning of the forearm or lower leg during the baseline measurements was recorded carefully. These records would be obeyed in all follow-up measurements to make sure the automatically set reference line could be set correctly. Besides that, CSA was used to judge the position. It was considered as the same position as that of the baseline measurement if the drift area (change area) of CSA in reference to CSA of the baseline measurement had fallen in the range of $\pm 20 \text{ mm}^2$. If the CSA change was beyond the range $\pm 20 \text{ mm}^2$, positioning and scanning would be repeated.

The study described here was performed to confirm this

method. The results showed: 1) A decrease of CSA and increase of trabecular BMD from distal to proximal at human distal radius, while a consistent decrease of CSA and apparent trabecular BMD from distal to proximal at the distal tibia. However, it was a little complicated at the distal radius that the pattern of changes in BMD was not so consistent as compared with the changes at the distal tibia. This may be because the shape of the distal radius changes are not so regular and the slice thickness is 2.0 mm and therefore there is a large overlap between the regions. 2) At the distal tibia, the change of trabecular bone density around the ultradistal location of 4% location, showed no significant changes if the CSA change fell within $\pm 20 \text{ mm}^2$ or the longitudinal distance fell within $\pm 0.5 \text{ mm}$. Also, the accordingly appeared change of CSA in this range was not significant. This suggests the former criterion is suitable for the tibia. 3) At the distal radius, CSA and trabecular bone density had no significant difference compared with the 4% when the CSA change was within the range of $\pm 10 \text{ mm}^2$. Within this range, BMD change was less than 0.1%. Beyond this range and within $\pm 20 \text{ mm}^2$, there had been a significant difference of CSA though trabecular bone density had yet no significant difference. The maximal BMD change was large, about 3%. So the former criterion, $\pm 20 \text{ mm}^2$, is not rigorous enough for measurements of the radius. And according to our experience, the CSA change would normally be within $\pm 10 \text{ mm}^2$ if the scanning location looked exactly the same as the baseline measurement. 4) Otherwise, the comparison of CSA change between the 4% and shaft location at the tibia and radius proved that it is reasonable to judge the position only by checking the 4% location when both 4% and shaft locations of tibia or radius are scanned at one measurement. Therefore, $\pm 20 \text{ mm}^2$ of CSA change at 4% of the tibia and $\pm 10 \text{ mm}^2$ at 4% of the radius are suggested to be used to control the same position.

According to the above described, there are another two suggestions regarding the machine. First, it would be better to have the scale marked on the machine wherever the part can be regulated and the precision is at least 0.1 mm. It would be convenient to record the places of the holders and especially better for different investigators to do the follow-up measurement. Second, so far as the software is concerned, it would be better to automatically calculate the CSA change value compared with the baseline measurement. The investigator can then read the change directly and make a judgment immediately and can also avoid calculation mistakes.

Although the results indeed gave some suggestions to perform pQCT in follow-up study, it was an *in vitro* study and the number of specimens was small with bones from just one cadaver. Therefore, further and more experiments should be carried out in the future to confirm the instructions.

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