J Musculoskelet Neuronal Interact 2023; 23(4):397-406

Journal of Musculoskeletal and Neuronal Interactions JMNI

Original Article

Precision errors and least significant changes in paediatric forearm measurements of bone density, mass, dimensions, mechanostat parameters and soft tissue composition by Stratec XCT-2000L

Maciej Jaworski, Maria Kobylińska

Department of Biochemistry, Radioimmunology and Experimental Medicine, The Children's Memorial Health Institute, Warsaw, Poland

Abstract

Objectives: The peripheral quantitative computed tomography (pQCT) is gaining popularity in the field of paediatric densitometry, however, very little is known about the precision errors of this method in diseased children. The aim of the study was to evaluate the precision errors of bone density, mass, dimensions, strength, mechanostat parameters and soft tissue at the forearm in diseased children. **Methods**: Stratec XCT 2000L apparatus was used. The measurement sites were 4% and 66% of the forearm length. The study group consisted of 60 patients (31 girls) aged 5,7-18,0 yrs. **Results**: We observed week relationships between precision errors and body size with r from -0,37 to 0,28. Relative precision errors ($CV\%_{RMS}$) were from 0,85% for radius 66% cortical bone density to 3,82% for fat cross-sectional area to muscle cross-sectional area ratio. Least significant change (LSC) was from 2,73% to 10,59%, respectively. **Conclusion**: Presented study reveal pQCT method at the forearm in diseased children as relatively precise technique. The results may help with planning and interpretation of pQCT studies in diseased children.

Keywords: Bone, Diseased Children, Forearm, pQCT, Precision Error

Introduction

The peripheral quantitative computed tomography (pQCT) is gaining popularity in the field of paediatric densitometry. Its popularity has to do with the measurement of true volumetric bone mineral density, bone dimensions and strength as well as fat and muscle areas, simultaneously[1-4]. Providing both information about the bone and the muscle, the pQCT method enables an evaluation of the functional muscle-bone unit[4-6]. Finally, the procedure involves only a small radiation dose, as compared to the other X-ray imaging modalities and avoid systemic irradiation[1,2], i.e. the effective dose for the patient is less than the dose received daily from natural sources of radiation[7,8].

The most important parameter characterising basic method performance is the precision error[9]. Precision error serves as an important factor in the interpretation of single measurement, but it is crucial for the interpretation of the serial measurements[10]. The so, called "least significant change" (LSC), according to the International Society for Clinical Densitometry definition[11], is the least amount of result's change that can be considered statistically significant, i.e. it is the least change between 2 consecutive measurements that may be judged as ''true'' change, that is exceeding the precision error of the measurement. The implementation of LSC in the children is more complicated than in the adults. However, it allows not only to distinguish between real and apparent change but, additionally, to compare rate of the change in patients with expected rate derived from the reference values[12,13], i.e. it allows to state whether the accretion of bone mass/density is faster or slower (or the same) as in healthy ones.

Therefore, the aim was to evaluate the precision

The authors have no conflict of interest.

Corresponding author: Maciej Jaworski, Department of Biochemistry, Radioimmunology and Experimental Medicine, The Children's Memorial Health Institute, Al. Dzieci Polskich 20, 04-730 Warsaw, Poland
E-mail: m.jaworski@ipczd.pl

Edited by: G. Lyritis
Accepted 26 June 2023

Table 1. Characteristics of studied group, female n=31, male n=29.

	Median	Minimum	Maximum
Age [yrs]	12,1	5,7	18,0
Height [cm]	152	112	185
Weight [kg]	42	16	80
BMI [kg/m^2]	17,2	12,6	24,0
Z-score height	-0,07	-2,79	3,92
Z-score weight	-0,49	-2,94	2,47
Z-score BMI	-0,29	-2,60	1,82
BMI - body mass index			

Table 2. Absolute precision errors of pQCT measures in studied group (n=60).

	Median	Minimum	Maximum
Bone Mineral Densities:			
Radius 4% Trabecular Bone Density [mg/cm^3]	1,156	0,028	9,991
Radius 4% Total Bone Density [mg/cm^3]	2,150	0,028	13,866
Radius 66% Cortical Bone Density [mg/cm^3]	4,154	0,092	27,125
Bone Masses:			
Radius 4% Bone Mass [g]	0,00707	0,00000	0,03536
Radius 66% Bone Mass [g]	0,00354	0,00000	0,02121
Cross-Sectional Dimensions:			
Radius 4% Total Bone Cross-Sectional Area [mm^2]	3,712	0,000	15,026
Radius 66% Inner Cortical Bone Circumference [mm]	0,3090	0,0000	2,1949
Radius 66% Outer Cortical Bone Circumference [mm]	0,1838	0,0000	1,4057
Radius 66% Cortical Shell Thickness [mm]	0,03536	0,00000	0,12657
Radius 66% Cortical Bone Cross-Sectional Area [mm^2]	0,7071	0,0000	2,6517
Radius 66% Total Bone Cross-Sectional Area [mm^2]	1,061	0,000	9,192
Longitudinal Shape Indexes:			
Radius 66% Cortical Bone Cross-Sectional Area/Radius 4% Total Bone Cross-Sectional Area	0,4437	0,0000	1,7697
Radius 4% Bone Mass/Radius 66% Bone Mass	0,01164	0,00000	0,06149
Strength Strain Index:			
Radius 66% Polar SSI [mm^3]	2,740	0,035	14,347
Muscle And Bone:			
Forearm 66% Muscle Cross-Sectional Area [mm^2]	13,44	0,53	91,92
Forearm 66% Total Cortical Bone Cross-Sectional Area/Muscle Cross-Sectional Area	0,07071	0,00707	0,34648
Fat:			
Fat Cross-Sectional Area [mm^2]	8,397	0,177	85,737
Fat Cross-Sectional Area/Muscle Cross-Sectional Area	0,7637	0,0212	8,0257

errors for bone density, mass, dimensions, strength and mechanostat parameters as well as for soft tissue composition, to assess the relationships between precision errors and anthropometric parameters, and to calculate least significant change for pQCT measures in children of wide age range (5-18 yr) in the forearm, using Stratec XCT-2000L machine.

Materials and Methods

Participants

Studied group was a part of a larger, 3 arms cohort recruited to elaborate reproducibility of the pQCT method (forearm and shank) and mechanography. Participants were recruited from typical patients of our Densitometry Lab. After recruitment, patients were randomly assigned,

Table 3. Relative precision errors (CV%) of pQCT measures in studied group (n=60).

	Median	Minimum	Maximum
Bone mineral densities:			
Radius 4% trabecular bone density	0,737	0,017	5,776
Radius 4% total bone density	0,751	0,012	4,723
Radius 66% cortical bone density	0,411	0,010	2,726
Bone masses:			
Radius 4% bone mass	0,969	0,000	5,398
Radius 66% bone mass	0,314	0,000	5,370
Cross-sectional dimensions:			
Radius 4% total bone cross-sectional area	1,575	0,000	6,894
Radius 66% inner cortical bone circumference	1,112	0,000	7,351
Radius 66% outer cortical bone circumference	0,490	0,000	4,338
Radius 66% cortical shell thickness	2,008	0,000	9,767
Radius 66% cortical bone cross-sectional area	1,387	0,000	5,558
Radius 66% total bone cross-sectional area	0,981	0,000	8,667
Longitudinal shape indexes:			
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	2,265	0,000	8,103
Radius 4% bone mass/radius 66% bone mass	1,150	0,000	6,428
Strength strain index:			
Radius 66% polar SSI	1,634	0,027	5,780
Muscle and bone:			
Forearm 66% muscle cross-sectional area	0,786	0,039	3,701
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	1,190	0,088	6,052
Fat:			
Fat cross-sectional area	0,856	0,017	9,999
Fat cross-sectional area/muscle cross-sectional area	1,180	0,027	13,674

with stratification by age and sex, to a specific arm of the cohort. Full cohort comprised 180 patients, while studied group numbered 60 children (31 girls), aged 5,7-18,0. Exclusion criteria were as follows: the presence of tremors or involuntary movements, impaired personal communication, mobility impairment, considerable body deformation, significant obesity or any other circumstances which would require applying a non-standard measurement procedure. Diagnoses were: kidney diseases (33), liver diseases (12), gastrointestinal diseases (11), calcium-phosphate disorder (5), thyroid diseases (2), rheumatoid diseases (2), allergy (2) and other (14). Characteristics of studied group are presented in Table 1.

Methods

All measurements were done on a non-dominant forearm[14] on Stratec XCT 2000L (Stratec Medizintechnik, Pforzheim, Germany) apparatus with software v. 6.20. Forearm length was measured with the ruler from the ulnar styloid process to the olecranon. The scout view was used to determine start position as follows: if the growth plate was visible the reference line was placed through the most distal portion of the growth plate; if the growth plate had fused the reference line was placed through the middle of horizontal part of the articular surface of the radius. The scan lines were automatically placed at distances of 4% and 66% of the forearm length, proximal to the reference line[7]. Scan speed, slice thickness and voxel size were 30 mm/s, 2,3 mm and 0,5x0,5 mm, respectively. At the 4% site trabecular volumetric bone mineral density (mg/cm^3), total volumetric bone mineral density (mg/cm^3) and total bone cross-sectional area (mm^2) were measured. CALCBD algorithm was used, with contour mode 1, peel mode 1 and threshold of 280 mg/cm^3. Area was set as 45% (central) in the case of trabecular volumetric bone mineral density determination. At the 66% site CORTBD algorithm with separation mode 1 and threshold of 711 mg/cm^3 was used for determining cortical volumetric bone mineral density (mg/cm^3), cortical cross-sectional area (mm^2) and total bone cross-sectional area (mm^2). For the polar strength strain index (SSI) (mm^3) calculation threshold of 280 mg/mm^3 was used. The CALCBD algorithm was used with threshold 40 mg/cm^3, contour mode 1, peel mode 2 and filter F03F05 for determination of muscle+bone cross-sectional area and with threshold 280 mg/cm^3, contour mode1 and peel mode 2 for bone cross-

Table 4. Relative precision errors (RMS CV%) and least significant change (LSC%) of pQCT measures in studied group (n=60).

	Precision error (%)	LSC (%)
Bone mineral densities:		
Radius 4% trabecular bone density	1,59	4,39
Radius 4% total bone density	1,32	3,65
Radius 66% cortical bone density	0,85	2,37
Bone masses:		
Radius 4% bone mass	1,61	4,47
Radius 66% bone mass	1,04	2,87
Cross-sectional dimensions:		
Radius 4% total bone cross-sectional area	2,32	6,42
Radius 66% inner cortical bone circumference	2,28	6,33
Radius 66% outer cortical bone circumference	1,09	3,01
Radius 66% cortical shell thickness	3,26	9,02
Radius 66% cortical bone cross-sectional area	2,25	6,24
Radius 66% total bone cross-sectional area	2,17	6,02
Longitudinal shape indexes:		
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	3,30	9,15
Radius 4% bone mass/radius 66% bone mass	2,08	5,75
Strength strain index:		
Radius 66% polar SSI	2,38	6,59
Muscle and bone:		
Forearm 66% muscle cross-sectional area	1,34	3,72
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	2,05	5,69
Fat:		
Fat cross-sectional area	2,79	7,73
Fat cross-sectional area/muscle cross-sectional area	3,82	10,59

sectional area. The muscle cross-sectional area (mm^2) was calculated by the subtraction of the bone cross-sectional area from muscle+bone cross-sectional area. Bone mass (g) was calculated as the multiplication of total bone cross-sectional area by the total bone density at the particular bone slice. Outer cortical bone circumference, inner cortical bone circumference and cortical shell thickness were calculated basing on the circular ring model with CALCBD algorithm with contour mode 1, threshold 710 mg/cm^3, peel mode 2 and inner threshold 710 mg/cm^3 [15]. Lastly, the following ratios were calculated: radius 66% cortical cross-sectional area to radius 4% total cross-sectional area and radius 4% bone mass to radius 66% bone mass as a measures of longwise bone shape[7] and forearm 66% total cortical cross-sectional area to muscle cross-sectional area as a measure of bone/muscle relationship[5,6]. Quality of each slice was inspected by the operator according to visual scale[16]. All slices were considered as technically valid. All participant was measured twice (including forearm length), with full reposition between measurements. Time between measurements was about 30 minutes. All measurements were done between February 2017 and September 2022 by the same operator on the same unit.

Effective doses involved in the procedure were as follows[7]: scout view – 0,08 μSv; CT scan 4% site – 0,22 μSv; CT scan 66% site – 0,22%; total dose per 1 measurement – 0,52 μSv, total dose per patient – 1,04 μSv.

Routine quality assurance procedures were carried out, basing on the phantom supplied by the manufacturer. The phantom comprises two "parts": standard and cone. Standard phantom was measured at least each day when patients were measured. Cone phantom was measured monthly. Measurement errors were (CV%, standard phantom): 1,04% for total density, 1,30% for trabecular density and 0,93% for cortical density in the whole study period.

Body height (cm) and weight (kg) were measured in the standing position using stadiometer with medical scale (Tryb, Bydgoszcz, Poland). Body mass index (kg/m^2) was calculated as body weight divided by squared height. Age of each participant was calculated from birth and examination dates.

Statistical Analysis

Statistical analyses were done with Statistica 10,0 (StatSoft Inc., Tulsa, USA). Non-parametric statistics were used. Descriptive statistics were presented as median,

Table 5. Correlations between absolute error of pQCT variables and anthropometric parameters (coefficients of correlations r).

	Age [yrs]	Height [cm]	Weight [kg]	Forearm length [mm]
Bone mineral densities:				
Radius 4% trabecular bone density [mg/cm³]	-0,34*	-0,26*	-0,18	-0,25
Radius 4% total bone density [mg/cm³]	0,23	0,10	0,20	0,11
Radius 66% cortical bone density [mg/cm³]	-0,09	-0,06	-0,08	-0,07
Bone masses:				
Radius 4% bone mass [g]	-0,08	0,03	0,13	0,00
Radius 66% bone mass [g]	0,24	0,25*	0,28*	0,28*
Cross-sectional dimensions:				
Radius 4% total bone cross-sectional area [mm²]	0,20	0,13	0,23	0,10
Radius 66% inner cortical bone circumference [mm]	-0,16	-0,22	-0,21	-0,23
Radius 66% outer cortical bone circumference [mm]	-0,21	-0,14	-0,09	-0,12
Radius 66% cortical shell thickness [mm]	-0,07	-0,07	-0,13	-0,08
Radius 66% cortical bone cross-sectional area [mm²]	0,15	0,14	0,15	0,13
Radius 66% total bone cross-sectional area [mm²]	-0,14	-0,06	0,00	-0,05
Longitudinal shape indexes:				
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	0,02	-0,02	0,04	-0,01
Radius 4% bone mass/radius 66% bone mass	-0,15	-0,07	-0,01	-0,08
Strength strain index:				
Radius 66% polar SSI [mm³]	0,19	0,24	0,23	0,23
Muscle and bone:				
Forearm 66% muscle cross-sectional area [mm²]	-0,01	0,01	0,03	-0,01
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	-0,31*	-0,33*	-0,36*	-0,37*
Fat:				
Fat cross-sectional area [mm²]	0,14	0,13	0,21	0,08
Fat cross-sectional area/muscle cross-sectional area	-0,26*	-0,27*	-0,15	-0,28*
** - p<0,05*				

minimum and maximum. Relationships between outcomes were tested using Spearman rank correlation. Coefficient of variation for group was calculated as median (CV) and as root mean square (CVRMS)[9]. Least significant change (LSC) was calculated with 95% confidence level, by multiplying the precision error by factor of 2.77[11]. P values lower than 0.05 were considered significant.

Results

Coefficient of variation was calculated for each outcome for whole group and expressed as absolute and relative precision errors. Table 2 presented absolute precision errors while Table 3 presented relative precision errors. Absolute precision errors (median) were from 1,156 to 4,454 mg/cm³ for bone densities, from 0,7071 to 13,44 mm² for cross-sectional areas, from 0,03536 to 0,3090 mm for bone dimensions, from 0,00354 to 0,00707 g for bone masses, from 0,01164 to 0,7637 for indexes and 2,740 mm³ for polar SSI. Relative precision errors (median) for bone densities were from 0,411% for radius 66% cortical bone density to 0,751% for radius 4% total bone density. For bone masses relative precision error was smaller for radius 66% bone mass than for radius 4% bone mass: 0,314% in comparison with 0,969%, respectively. In the case of cross-sectional dimensions relative precision error was from 0,490% for radius 66% outer cortical bone circumference to 2,008% for radius 66% cortical shell thickness. Longitudinal shape indexes showed relative precision errors from 1,150% to 2,265% while for radius 66% polar SSI CV% amounted 1,634%. For "muscle and bone" parameters relative precision errors were 0,786% for forearm 66% muscle cross-sectional area and 1,190% for forearm 66% total cortical bone cross-sectional area to muscle cross-sectional area ratio while for fat cross-sectional area and for fat cross-sectional area to muscle cross-sectional area ratio they were 0,856% and 1,180%, respectively. Accordingly (Table 4),

Table 6. Correlations between relative error of pQCT variables and anthropometric parameters (coefficients of correlations r).

	Age [yrs]	Height [cm]	Weight [kg]	Forearm length [mm]
Bone mineral densities:				
Radius 4% trabecular bone density	-0,34*	-0,29*	-0,22	-0,29*
Radius 4% total bone density	0,21	0,06	0,15	0,07
Radius 66% cortical bone density	-0,14	-0,10	-0,12	-0,11
Bone masses:				
Radius 4% bone mass	-0,35*	-0,26*	-0,17	-0,28*
Radius 66% bone mass	0,04	0,06	0,07	0,08
Cross-sectional dimensions:				
Radius 4% total bone cross-sectional area	-0,10	-0,16	-0,08	-0,18
Radius 66% inner cortical bone circumference	-0,19	-0,25	-0,26*	-0,26*
Radius 66% outer cortical bone circumference	-0,28*	-0,23	-0,20	-0,21
Radius 66% cortical shell thickness	-0,22	-0,24	-0,30*	-0,26*
Radius 66% cortical bone cross-sectional area	-0,12	-0,16	-0,16	-0,18
Radius 66% total bone cross-sectional area	-0,28*	-0,23	-0,20	-0,21
Longitudinal shape indexes:				
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	0,01	-0,03	0,02	-0,05
Radius 4% bone mass/radius 66% bone mass	-0,17	-0,09	-0,03	-0,11
Strength strain index:				
Radius 66% polar SSI	-0,21	-0,19	-0,20	-0,18
Muscle and bone:				
Forearm 66% muscle cross-sectional area	-0,29*	-0,29*	-0,27*	-0,30*
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	-0,27*	-0,29*	-0,32*	-0,35*
Fat:				
Fat cross-sectional area	0,07	0,08	0,08	0,03
Fat cross-sectional area/muscle cross-sectional area	-0,12	-0,10	-0,04	-0,12
** - p<0,05*				

least significant change (LSC) values for bone densities were from 2,37% (radius 66% cortical bone density) to 4,39% (radius 4% trabecular bone density); for bone masses from 2,87% (radius 66% bone mass) to 4,47% (radius 4% bone mass); for cross-sectional dimensions from 3,01% (radius 66% outer cortical bone circumference) to 9,02% (radius 66% cortical shell thickness); for longitudinal shape indexes from 5,75% (radius 4% bone mass/radius 66% bone mass) to 9,15% (radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area); 6,59% for radius 66% polar SSI; for "muscle and bone" from 3,72% (forearm 66% muscle cross-sectional area) to 5,69% (forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area) and 7,73% and 10,59% for fat cross-sectional area and fat cross-sectional area/muscle cross-sectional area, respectively.

Spearman rank correlation coefficients (r values) were calculated for the relationships between absolute (Table 5) and relative (Table 6) precision errors and anthropometric data. Significant negative correlations between absolute precision error and all anthropometric parameters were noted for ratios: forearm 66% total cortical bone cross-sectional area to muscle cross-sectional area and fat cross-sectional area to muscle cross-sectional area, with r values from -0,26 to -0,37, while radius 4% trabecular bone density correlated only with age and height, with r values -0,34 and -0,26, respectively. Significant positive correlations between absolute precision error and height, weight and forearm length were noted for radius 66% bone mass, only, with r ranged from 0,25 to 0,28. In the case of relative errors there were no positive correlations with anthropometric measures. Negative correlations were observed between forearm 66% muscle cross-sectional area, forearm 66% total cortical bone cross-sectional area to muscle cross-sectional area ratio and all anthropometric measures, i.e. height, weight and forearm length, with r value ranged from -0,27 to -0,35; radius 4% trabecular bone density and radius 4% bone mass correlated similarly with these measures (r from -0,26 to -0,35) with

Table 7. Absolute and relative precision errors (CV%) of forearm length in studied group (n=60).

	Median	Minimum	Maximum
Absolute precision error			
Forearm length [mm]	0,707	0,000	3,536
Relative precision error			
Forearm length	0,343	0,000	1,406

Table 8. Correlations between absolute error of pQCT variables and absolute error of forearm length (coefficients of correlations r).

	Forearm length [mm]
Bone mineral densities:	
Radius 4% trabecular bone density [mg/cm^3]	-0,14
Radius 4% total bone density [mg/cm^3]	0,25*
Radius 66% cortical bone density [mg/cm^3]	0,15
Bone masses:	
Radius 4% bone mass [g]	0,19
Radius 66% bone mass [g]	0,18
Cross-sectional dimensions:	
Radius 4% total bone cross-sectional area [mm^2]	0,24
Radius 66% inner cortical bone circumference [mm]	0,13
Radius 66% outer cortical bone circumference [mm]	0,21
Radius 66% cortical shell thickness [mm]	0,17
Radius 66% cortical bone cross-sectional area [mm^2]	0,29*
Radius 66% total bone cross-sectional area [mm^2]	0,24
Longitudinal shape indexes:	
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	0,19
Radius 4% bone mass/radius 66% bone mass	0,11
Strength strain index:	
Radius 66% polar SSI [mm^3]	0,10
Muscle and bone:	
Forearm 66% muscle cross-sectional area [mm^2]	0,20
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	-0,01
Fat:	
Fat cross-sectional area [mm^2]	-0,02
Fat cross-sectional area/muscle cross-sectional area	-0,06

the exception of weight, when no statistically significant correlations were observed. Individual correlations were observed for bone cross-sectional dimensions: radius 66% inner cortical bone circumference with weight and forearm length (r=-0,26 for both), radius 66% cortical shell thickness with the same anthropometric measures (r=-0,30 and -0,26, respectively) and the last ones: radius 66% outer cortical bone circumference and radius 66% total bone cross-sectional area with age (r=-0,28 for both).

Table 7 provided absolute and relative precision errors for forearm length measurement. Absolute precision error (median) was 0,707 mm and relative precision error was 0,343%.

Table 8 presented Spearman rank correlation between absolute errors of forearm length and pQCT measures. Significant correlations were noted for radius 4% total bone density (r=0,25) and for radius 66% cortical bone cross-sectional area (r=0,29). Accordingly, Table 9 presented Spearman rank correlation for relative errors. Relative errors of forearm length correlated with relative error of radius 4%

Table 9. Correlations between relative error of pQCT variables and relative error of forearm length (coefficients of correlations r).

	Forearm length
Bone mineral densities:	
Radius 4% trabecular bone density	-0,08
Radius 4% total bone density	0,24
Radius 66% cortical bone density	0,16
Bone masses:	
Radius 4% bone mass	0,17
Radius 66% bone mass	0,13
Cross-sectional dimensions:	
Radius 4% total bone cross-sectional area	0,27*
Radius 66% inner cortical bone circumference	0,14
Radius 66% outer cortical bone circumference	0,21
Radius 66% cortical shell thickness	0,20
Radius 66% cortical bone cross-sectional area	0,26*
Radius 66% total bone cross-sectional area	0,21
Longitudinal shape indexes:	
Radius 66% cortical bone cross-sectional area/radius 4% total bone cross-sectional area	0,22
Radius 4% bone mass/radius 66% bone mass	0,12
Strength strain index:	
Radius 66% polar SSI	0,00
Muscle and bone:	
Forearm 66% muscle cross-sectional area	0,23
Forearm 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,12
Fat:	
Fat cross-sectional area	0,04
Fat cross-sectional area/muscle cross-sectional area	0,05

total bone cross-sectional area (r=0,27) and with relative error of radius 66% cortical bone cross-sectional area (r=0,26).

Discussion

To the best of the authors knowledge, this is the first study presented precision errors of bone density, size and strength by the pQCT method in diseased children. Besides of the current study only Duff et al.[17] presented data for children, however, that work concerns healthy children. Interestingly, precision errors values ($CV\%_{RMS}$) in our patients were lower than in healthy children presented by Duff et al.[17]. In our group they were from 1,0% to 3,3% while in Duff's group they were from 4,2% to 10,5%, for measures utilized in the both works. Observed discrepancies may be attributed to longer period between repeated scans in Duff et al. study than in the presented study (1 month in comparison with 0,5 hour). As was shown by Swinford et al.[18] time between scans is a significant factor determining precision error. Additionally, Duff's participants[17] seem to be more prone to involuntary movement and because of this, a bit of a handful to measure, despite of that they were healthy. Duff et al. excluded 7% of distal radius and 10% of radius shaft scans while our scans are mostly 1-2 grade according to Blew et al.[16] and no exclusion was done. Another difference is that Duff et al.[17] measured the forearm length once while in the presented study we measured it twice. However, forearm length measurement error seems not to be a strong determinant of the precision error. In the presented study CV of forearm length appeared as week determinant (r from 0,25 to 0,29) for 3 out of 18 measures, only. Similar results were presented by Sun et al.[19] who indicated positioning error as determinant for cross sectional bone area, but not for density.

We found dependence of the precision error of the pQCT measurement on the subjects body size (age, height and weight). Absolute error of trabecular bone density and for ratios (total cortical bone cross-sectional area to muscle cross-sectional area and fat cross-sectional area to muscle cross-sectional area) diminished with increasing body size, however the strength of the dependency was weak, with r values from -0,26 to -0,36. Accordingly, relative error diminishes with increasing body size for trabecular bone density, bone mass, bone dimensions, muscle cross-sectional area and for ratio of total cortical bone cross-sectional area to muscle cross-sectional area. The relationships were weak, too, with r value from -0,26 to -0,35. The same phenomenon was observed by Duff et al.[17]. It may be attributed to the fact that the older children are more cooperative than younger ones, thereby less prone to involuntary movements and that greater bones are less susceptible to the partial volume effect[20]. On the contrary, absolute precision error for 66% bone mass increased with body size (r value 0,25 to 0,28). The last one is in accordance with Swinford et al.[18], who reported positive association between the absolute measurement errors and body size in the tibia measurement. They assumed that the phenomenon may partially resulted from greater repositioning error related to difficulties in positioning of the lower extremity without touching the sides of the gantry. In the case of forearm measurement gantry diameter is not an issue so we observed positive correlation only for 66% bone mass while for other measures correlations between precision error (relative and absolute) and body size were negative.

Presented study has limitations. Firstly, the measurements were done at the same day, which may underestimate the precision error[18]. However, we applied procedure with full reposition between measurements and with second forearm length measurement, which may mitigate the effect of “the same day” measurement. Secondly, all measurements and analysis were done by the same operator. It seems debatable limitation since well trained operators can conduct measurements equally, with no effects on the precision error[18]. Thirdly, the studied group did not comprise patients with the presence of tremors or involuntary movements, impaired personal communication, mobility impairment, considerable body deformation or significant obesity, in the main patients which would require a non-standard measurement procedure. However, such children always needed the individual decision prior to the admission order to the bone densitometry, after taking into consideration advantages and disadvantages and are not typical patients of the densitometry lab. Finally, our findings were limited to the used pQCT methodology, including voxel size, scan speed, filtering and thresholding as well as skeletal sites and population.

Presented study shows the precision errors in group of diseased children, typical patients of the densitometry lab, in wide age range of 5-18 yrs. The recruitment procedure was blinded. During the procedure the recruiter did not know for which arm of the study participant will fall – forearm measurement, shank measurement or mechanography. It allows us to minimize bias of the selection of the patients. The number of patients was relatively high, with overall degrees of freedom equals 60, which is two times greater than minimal sample size recommended by the International Society for Clinical Densitometry[10]. To avoid underestimating of the precision errors, rather conservative measure, root mean square coefficients of variation[9] were presented. Least significant changes were calculated in the conservative manner, too, with the 95% confidence level.

This study reveals pQCT method at the forearm in diseased children as relatively precise technique, with $CV\%_{RMS}$ from 0,8% to 3,8% and LSC (95%) from 2,4% to 10,6%. The results may help with planning and interpretation of pQCT studies in diseased children.

Authors' contributions

MJ and MK are responsible for subject enrolment; MJ and MK drafted the manuscript and completed manuscript revision; MJ is responsible for study design, outcome assessment, data collection, statistical analysis, data interpretation, literature search and funds collection; MJ takes responsibility for the integrity of the data analysis.

Ethics approval

The study was conducted with permission of the local Ethics Committee (Warsaw, Poland). Informed written consents were obtained from the parents or legal guardians of the patients.

Funding

This study is supported by specific-user subvention from Ministry of Science and Higher Education to Children's Memorial Health Institute for research activity; Children's Memorial Health Institute's statutory research task No: 240/2016.

Acquiring of Stratec XCT 2000L was cofinanced by ERDF (EU Structural Funds) project POIG.02.01.00-14-059/09.

References

1. Binkley TL, Berry R, Specker BL. Methods for measurement of pediatric bone. Rev Endocr Metab Disord 2008;9:95-106.
2. Zemel BS. Quantitative computed tomography and computed tomography in children. Curr Osteoporos Rep 2011;9:284-90.
3. Stagi S, Cavalli L, Iurato C, Seminara S, Brandi ML, de Martino M. Bone health in children and adolescents: the available imaging techniques. Clin Cases Miner Bone Metab 2013;10:166-71.
4. Stagi S, Cavalli L, Cavalli T, de Martino M, Brandi ML. Peripheral quantitative computed tomography (pQCT) for the assessment of bone strength in most of bone affecting conditions in developmental age: a review. Ital J Pediatr 2016 Sep 26;42(1):88.
5. Schoenau E, Neu CM, Beck B, Manz F, Rauch F. Bone mineral content per muscle cross-sectional area as an index of the functional muscle-bone unit. J Bone Miner Res 2002;17:1095-101.
6. Schoenau E, Neu MC, Manz F. Muscle mass during childhood - relationship to skeletal development. J Musculoskelet Neuronal Interact 2004;4:105-8.
7. Stratec XCT 2000L manual. Stratec Medizintechnik 2011.
8. Di Iorgi N, Maruca K, Patti G, Mora S. Update on bone density measurements and their interpretation in children and adolescents. Best Pract Res Clin Endocrinol Metab 2018;32(4):477-498.
9. Glüer CC, Blake G, Lu Y, Blunt BA, Jergas M, Genant

HK. Accurate assessment of precision errors: how to measure the reproducibility of bone densitometry techniques. Osteoporos Int 1995;5(4):262-70.
10. Baim S, Binkley N, Bilezikian JP, Kendler DL, Hans DB, Lewiecki EM, Silverman S. Official Positions of the International Society for Clinical Densitometry and executive summary of the 2007 ISCD Position Development Conference. J Clin Densitom 2008; 11(1):75-91.
11. Shuhart CR, Yeap SS, Anderson PA, Jankowski LG, Lewiecki EM, Morse LR, Rosen HN, Weber DR, Zemel BS, Shepherd JA. Executive Summary of the 2019 ISCD Position Development Conference on Monitoring Treatment, DXA Cross-calibration and Least Significant Change, Spinal Cord Injury, Peri-prosthetic and Orthopedic Bone Health, Transgender Medicine, and Pediatrics. J Clin Densitom 2019;22(4):453-471.
12. Jaworski M, Karczmarewicz E, Pawlowska J, et al. Application of least significant change (LSC) in interpretation of serial bone mineral density and bone size measurements in children after liver transplantation. Calcif Tissue Int 2008;82(1 Suppl):s66.
13. Jaworski M, Pludowski P. Specific interpretation of bone mineral density and body composition measurements in children and adolescentsdcategorized and continuous normative data for mechanostat. Standardy Medyczne 2009;6(2):292-303.
14. Adams JE, Engelke K, Zemel BS, Ward KA. International Society of Clinical Densitometry. Quantitative computer tomography in children and adolescents: the 2013 ISCD Pediatric Official Positions. J Clin Densitom 2014;17:258-74.
15. Louis O, Willnecker J, Soykens S, Van den Winkel P,Osteaux M. Cortical thickness assessed by peripheral quantitative computed tomography: accuracy evaluated on radius specimens. Osteoporos Int 1995;5(6):446-9.
16. Blew RM, Lee VR, Farr JN, Schiferl DJ, Going SB. Standardizing evaluation of pQCT image quality in the presence of subject movement: qualitative versus quantitative assessment. Calcif Tissue Int 2014;94:202-11.
17. Duff WRD, Björkman KM, Kawalilak CE, Kehrig AM, Wiebe S, Kontulainen S. Precision of pQCT-measured total, trabecular and cortical bone area, content, density and estimated bone strength in children. J Musculoskelet Neuronal Interact 2017;17(2):59-68.
18. Swinford RR, Warden SJ. Factors affecting short-term precision of musculoskeletal measures using peripheral quantitative computed tomography (pQCT). Osteoporos Int 2010;21(11):1863-70.
19. Sun L, Beller G, Felsenberg D. Quantification of bone mineral density precision according to repositioning errors in peripheral quantitative computed tomography (pQCT) at the radius and tibia. J Musculoskelet Neuronal Interact 2009;9(1):18-24.
20. Binkley TL, Specker BL. pQCT measurement of bone parameters in young children: validation of technique. J Clin Densitom 2000;3:9-14.