Accepted Article

J Musculoskelet Neuronal Interact 2024

Journal of Musculoskeletal and Neuronal Interactions JMNI

Original Article

Precision Errors of Lower Leg Measurement by pQCT in Children With Medical Conditions: Bone Density, Mass, Dimensions, Mechanostat Parameters and Soft Tissue Composition

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Abstract

Objectives: The one of the developing methods in paediatric densitometry field is peripheral quantitative computed tomography (pQCT), however, very little is known about its precision in children. The aim of presented study was to evaluate the precision errors for bone density, mass, dimensions, strength and mechanostat parameters as well as for soft tissue composition in children with medical conditions. **Methods**: Stratec XCT 2000L apparatus was used. The measurement sites were 4%, 14%, 38% and 66% of the lower leg length. The study group comprised of 60 patients (30 girls) aged 5,0-18,0 yrs. **Results**: Relative precision errors (CV%RMS) were from 0,25% for tibia 38% cortical bone density to 5,49% for fat cross-sectional area to muscle cross-sectional area ratio. Least significant change (LSC) was from 0,70% to 15,20%, respectively. Weak to moderate correlations between precision errors and body size, with r from -0,43 to 0,71, have been observed. **Conclusion**: Presented study revealed pQCT method at the lower leg in children with medical conditions as relatively precise technique. Obtained results provides an attainable basis for design and interpretation of pQCT studies in children with medical conditions.

Keywords: Bone Density, Diseased Children, Lower Leg, pQCT, Precision Error

Introduction

Precision is the measure of agreement among replicated measurements on the same objects under unchanged conditions and arises from random variability of the results[1]. Precision error is one of the main parameters characterising performance of the method. Its low value is crucial for the technique's ability to detect skeletal longitudinal changes[2]. For this purposes International Society for Clinical Densitometry defines "least significant change" (LSC)[3], the so directly derived from the precision error. LSC is the least amount of result's change that can be judged as clinically relevant, i.e. exceeding random variability of the results. In the case of children LSC allows not only to distinguish between real and apparent change but, additionally, to state whether rate of the change in patients is lower/higher than in healthy ones[4,5].

The one of developing method in paediatric densitometry field is peripheral quantitative computed tomography (pQCT). The method allows measurements of the cortical and trabecular bone density and mass as well as bone geometry and strength[6-9]. At the same procedure pQCT is able to measure soft tissue composition and muscle to bone ratio as a measure of the functional muscle-bone unit[10,11]. Besides of these, pQCT enables calculation of so-called longitudinal shape indexes[12] which compare bone mass (or areas) in certain bone slices. They measure longitudinal shape of the bone and characterise decreasing of metaphysis diameter by periosteal resorption and thickening of bone cortex by endosteal apposition of bony tissue (metaphyseal inwaisting)[13,14]. Finally, pQCT method avoid systemic irradiation[6,7], thus the

The authors have no conflict of interest.

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Edited by: G. Lyritis
Accepted 27 August 2024

effective dose for the patient is very low, less than a daily dose from natural sources of radiation[6,7,12]. Taking these into consideration, the pQCT method seems to be a suitable one for an extensive assessment of various skeletal properties of the bone in children and adolescents. However, very little is known about precision of the lower leg measurement results and data concerning factors affecting precision errors is scarce[15-17]. Since in the children's population growth affects a lot of measures, anthropometric parameters are strong natural candidate for being such factors. It should be taken, planning precision assessment procedure, that International Society for Clinical Densitometry requires to assess precision using population representative to the patients seen in routine clinical measurement[18].

Therefore, the aim of presented study was to evaluate the precision errors of 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 changes for pQCT measures in children with medical conditions of wide age range (5-18 yr), typical patients of our lab, at the lower leg, using Stratec XCT-2000L machine.

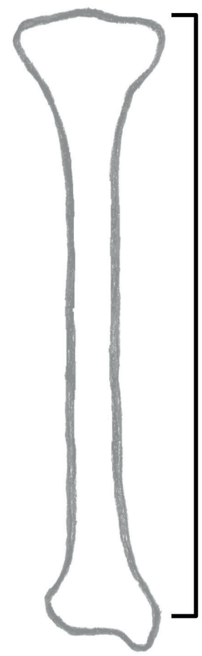

Figure 1. Scheme of the tibia length measurement.

Materials and Methods

All measurements were done on a non-dominant lower leg[12] on Stratec XCT 2000L (Stratec Medizintechnik, Pforzheim, Germany) apparatus with software v. 6.20. Dominance was determined by the participant's report. The measurement sites were 4%, 14%, 38%, and 66% of the tibia length[12]. The tibia length was measured with the ruler from the middle of the inner ankle to the tibial plateau (Figure 1)[12]. The scout view was used to determine the start position as follows: if the growth plate was visible, the reference line was placed in the middle of the growth plate; if the growth plate had fused, the reference line was placed in the middle of the distal end of the tibia. The scan lines were automatically placed at a distances of 4%, 14%, 38%, and 66% of the tibia length, proximal to the reference line. Scan speed, slice thickness, and voxel size were 20 mm/s, 2,3 mm, and 0,4x0,4mm, respectively[12]. 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 with using the CALCBD analysis algorithm, contour mode 1, peel mode 1, and threshold of 181 mg/cm^3. Area was set as 45% (central) for trabecular volumetric bone mineral density determination[12]. At the 14% and 38% sites, the 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) and cortical cross-sectional area (mm^2), while threshold 280 mg/cm^3 was used for polar strength strain index (mm^3) calculation. The same threshold (280 mg/cm^3) with the contour mode 1 and peel mode 1 was used for total bone cross-sectional area (mm^2) determination[12]. At the 66% site, the CALCBD algorithm was used, with threshold of -53 mg/cm^3 (contour mode 3 and peel mode 1) for the determination of total lower leg cross-sectional area; with threshold of 40 mg/cm^3 (contour mode 3, peel mode 1, and filter F03F05) for muscle+bone area; with threshold of 280 mg/cm^3 (contour mode1 and peel mode 2) for bone area[12]. Muscle cross-sectional area (mm^2) was calculated by the subtraction of bone cross-sectional area from muscle+bone cross-sectional area, and fat cross-sectional area (mm^2) was calculated by subtraction of muscle+bone cross-sectional area from total lower leg cross-sectional area[12].

Table 1. Characteristics of studied group, female n=30, male n=30.

	Mean (SD)
Age [yrs]	12,37 (3,84)
Height [cm]	151,6 (20,8)
Weight [kg]	44,60 (17,43)
BMI [kg/m^2]	18,57 (3,55)
Z-score height	-0,04 (1,29)
Z-score weight	-0,15 (1,04)
Z-score BMI	-0,15 (0,98)

BMI - body mass index.

The bone mass per 1 running centimetre was calculated as

Table 2. Raw data of the first and second measurements in the whole group of patients (n=60; mean and SD).

	First measurement	Second measurement
Bone mineral densities:		
tibia 4% trabecular bone density [mg/cm^3]	199,1 (28,2)	198,3 (28,8)
tibia 4% total bone density [mg/cm^3]	284,6 (33,6)	283,9 (33,4)
tibia 14% cortical bone density [mg/cm^3]	1048,2 (64,9)	1046,7 (64,6)
tibia 38% cortical bone density [mg/cm^3]	1095,2 (59,3)	1094,9 (59,3)
Bone masses:		
tibia 4% bone mass [g]	2,233 (0,842)	2,224 (0,840)
tibia 14% bone mass [g]	1,766 (0,595)	1,762 (0,595)
tibia 38% bone mass [g]	2,479 (0,845)	2,474 (0,844)
Cross-sectional dimensions:		
tibia 14% inner cortical bone circumference [mm]	53,43 (11,58)	53,34 (11,51)
tibia 38% inner cortical bone circumference [mm]	36,50 (7,05)	36,50 (7,10)
tibia 14% outer cortical bone circumference [mm]	66,49 (12,10)	66,44 (12,08)
tibia 38% outer cortical bone circumference [mm]	62,08 (10,35)	62,04 (10,33)
tibia 14% cortical shell thickness [mm]	2,078 (0,425)	2,085 (0,429)
tibia 38% cortical shell thickness [mm]	4,071 (0,828)	4,065 (0,826)
tibia 14% cortical bone cross-sectional area [mm^2]	125,6 (38,5)	125,9 (39,0)
tibia 38% cortical bone cross-sectional area [mm^2]	205,2 (69,1)	204,7 (68,8)
tibia 4% total bone cross-sectional area [mm^2]	790,3 (305,8)	788,7 (301,6)
tibia 14% total bone cross-sectional area [mm^2]	363,3 (129,9)	362,7 (129,0)
tibia 38% total bone cross-sectional area [mm^2]	315,1 (102,3)	314,7 (102,0)
Longitudinal shape indexes:		
tibia 4% bone mass/tibia 38% bone mass	0,894 (0,084)	0,891 (0,084)
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	16,60 (3,19)	16,66 (3,20)
Strength strain index:		
tibia 14% polar SSI [mm^3]	997,7 (494,9)	996,5 (499,6)
tibia 38% polar SSI [mm^3]	1062,6 (506,7)	1048,5 (485,1)
Muscle and bone:		
lower leg 66% muscle cross-sectional area [mm^2]	4837 (1734)	4791 (1686)
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	5,359 (0,826)	5,392 (0,806)
Fat:		
lower leg 66% fat cross-sectional area [mm^2]	2150 (874)	2149 (878)
lower leg 66% fat cross-sectional area/muscle cross-sectional area	47,57 (18,63)	47,94 (19,02)

SSI - Strength strain index.

multiplication of the density and cross-sectional area of bone in the particular slice and expressed in grams[12]. Outer cortical bone circumference, inner cortical bone circumference and cortical shell thickness were calculated basing on the circular ring model[19]. Finally, the following ratios were calculated: tibia 14% cortical bone cross-sectional area to tibia 4% total bone cross-sectional area and tibia 4% bone mass to tibia 38% bone mass as a measure of the longwise bone shape[12], lower leg 66% total cortical cross-sectional area to muscle cross-sectional area as a measure of the bone/muscle relationship[10,11], and fat cross-sectional area to muscle cross-sectional area as a measure of soft tissue composition[12].

Quality of each slice was inspected by the operator according to visual scale[20]. All slices were considered as technically valid. All participants were measured twice (including tibia length), with full reposition between the measurements. Time between measurements was approximately 30 minutes. All measurements were done between February 2017 and September 2022 by the same operator on the same unit.

The effective doses involved in the procedure are as follows: scout view: 0,08 microSv; CT scans at 4%, 14%, 38, and 66% sites: 0,88 microSv (4 x 0,22 microSv); total dose: 0,96 microSv[12].

The routine quality assurance procedures were carried out, basing on the phantom supplied by the manufacturer.

Table 3. Absolute precision errors (CV_{RMS}) and absolute least significant change (LSC) of pQCT measures in studied group (n=60).

	Precision error	LSC
Bone mineral densities:		
tibia 4% trabecular bone density [mg/cm^3]	2,11	5,86
tibia 4% total bone density [mg/cm^3]	2,26	6,27
tibia 14% cortical bone density [mg/cm^3]	3,84	10,64
tibia 38% cortical bone density [mg/cm^3]	2,81	7,78
Bone masses:		
tibia 4% bone mass [g]	0,0242	0,0669
tibia 14% bone mass [g]	0,0079	0,0218
tibia 38% bone mass [g]	0,0140	0,0388
Cross-sectional dimensions:		
tibia 14% inner cortical bone circumference [mm]	0,372	1,030
tibia 38% inner cortical bone circumference [mm]	0,266	0,736
tibia 14% outer cortical bone circumference [mm]	0,234	0,647
tibia 38% outer cortical bone circumference [mm]	0,156	0,433
tibia 14% cortical shell thickness [mm]	0,031	0,086
tibia 38% cortical shell thickness [mm]	0,042	0,116
tibia 14% cortical bone cross-sectional area [mm^2]	1,63	4,52
tibia 38% cortical bone cross-sectional area [mm^2]	1,89	5,22
tibia 4% total bone cross-sectional area [mm^2]	13,37	37,03
tibia 14% total bone cross-sectional area [mm^2]	2,84	7,86
tibia 38% total bone cross-sectional area [mm^2]	1,61	4,47
Longitudinal shape indexes:		
tibia 4% bone mass/tibia 38% bone mass	0,0116	0,0321
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	0,372	1,030
Strength strain index:		
tibia 14% polar SSI [mm^3]	29,6	82,0
tibia 38% polar SSI [mm^3]	63,4	175,6
Muscle and bone:		
lower leg 66% muscle cross-sectional area [mm^2]	101,6	281,4
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,083	0,229
Fat:		
lower leg 66% fat cross-sectional area [mm^2]	64,7	179,1
lower leg 66% fat cross-sectional area/muscle cross-sectional area	1,86	5,16
SSI - Strength strain index.		

The phantom comprises two parts: "standard" and "cone". The standard part of the phantom was measured each day when patients were measured. The cone part of the phantom was measured monthly. The measurement errors were (CV%, standard phantom) 0.35% for total density, 0.44% for trabecular density, and 0.37% 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

Mean and SD were calculated and presented as descriptive statistics. Absolute (CV_{RMS}) and relative ($CV\%_{RMS}$) coefficients of variation for group were calculated as root mean square[1] (Eq. 4a and 5a, respectively]. Absolute (LSC) and relative (LSC%) least significant changes were calculated with 95% confidence level, by multiplying respective coefficients of variation by the factor of 2,77[3]. The relationships between precision errors of pQCT outcomes and anthropometric parameters were tested using Spearman rank correlation. LMS Growth v. 2.77 (Medical Research Council, UK) was used for calculation of Z-scores for anthropometric data, basing

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

	Precision error (%)	LSC (%)
Bone mineral densities:		
tibia 4% trabecular bone density	1,12	3,11
tibia 4% total bone density	0,81	2,25
tibia 14% cortical bone density	0,36	1,01
tibia 38% cortical bone density	0,25	0,71
Bone masses:		
tibia 4% bone mass	1,14	3,17
tibia 14% bone mass	0,61	1,69
tibia 38% bone mass	0,58	1,62
Cross-sectional dimensions:		
tibia 14% inner cortical bone circumference	0,69	1,92
tibia 38% inner cortical bone circumference	0,78	2,17
tibia 14% outer cortical bone circumference	0,34	0,93
tibia 38% outer cortical bone circumference	0,25	0,70
tibia 14% cortical shell thickness	1,52	4,20
tibia 38% cortical shell thickness	1,04	2,89
tibia 14% cortical bone cross-sectional area	1,19	3,30
tibia 38% cortical bone cross-sectional area	0,91	2,51
tibia 4% total bone cross-sectional area	1,60	4,43
tibia 14% total bone cross-sectional area	0,67	1,86
tibia 38% total bone cross-sectional area	0,50	1,40
Longitudinal shape indexes:		
tibia 4% bone mass/tibia 38% bone mass	1,29	3,57
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	2,35	6,51
Strength strain index:		
tibia 14% polar SSI	2,66	7,36
tibia 38% polar SSI	4,53	12,55
Muscle and bone:		
lower leg 66% muscle cross-sectional area	1,72	4,77
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	1,56	4,32
Fat:		
lower leg 66% fat cross-sectional area	4,43	12,28
lower leg 66% fat cross-sectional area/muscle cross-sectional area	5,49	15,20

SSI - Strength strain index.

on local reference data[21]. Statistical calculations were done with Statistica 10,0 PL. A p values lower than 0,05 were considered as significant.

Participants

Studied group is a part of 3 arms cohort designed for measure reproducibility of the pQCT and mechanography methods and was described elsewhere[22]. Briefly, 60 children (30 girls), aged 5-18 yrs were recruited from typical patients of the Densitometry Lab. The exclusion criteria were: 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 (32), liver diseases (12), gastrointestinal diseases (5), allergy (4), calcium-phosphate disorders (2), multiple fracture (2), hypertension (2), Cushing syndrome (1), diabetes mellitus type 1 (1), hypercalcemia (1), hypobetalipoproteinemia (1), homocystinuria (1), tyrosinemia (1), preterm birth (1), Asperger syndrome (1), habitual constipation (1) and 1 patient was during diagnostics. Characteristics of studied group are presented in Table 1. Raw data for both measurements in the whole group are presented in Table 2.

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

	Age [yrs]	Height [cm]	Weight [kg]	Lower leg length [mm]
Bone mineral densities:				
tibia 4% trabecular bone density [mg/cm³]	-0,26*	-0,29*	-0,20	-0,25
tibia 4% total bone density [mg/cm³]	-0,19	-0,14	-0,08	-0,09
tibia 14% cortical bone density [mg/cm³]	-0,02	-0,05	0,01	-0,05
tibia 38% cortical bone density [mg/cm³]	-0,01	-0,09	-0,06	-0,07
Bone masses:				
tibia 4% bone mass [g]	-0,03	-0,02	0,09	-0,02
tibia 14% bone mass [g]	0,15	0,12	0,17	0,05
tibia 38% bone mass [g]	0,29*	0,31*	0,38*	0,34*
Cross-sectional dimensions:				
tibia 14% inner cortical bone circumference [mm]	-0,06	-0,13	-0,02	-0,11
tibia 38% inner cortical bone circumference [mm]	-0,09	-0,07	0,03	-0,09
tibia 14% outer cortical bone circumference [mm]	-0,13	-0,20	-0,03	-0,16
tibia 38% outer cortical bone circumference [mm]	0,03	-0,02	0,10	0,02
tibia 14% cortical shell thickness [mm]	-0,13	-0,14	-0,05	-0,11
tibia 38% cortical shell thickness [mm]	-0,08	-0,04	0,01	-0,03
tibia 14% cortical bone cross-sectional area [mm²]	-0,01	0,06	0,15	0,08
tibia 38% cortical bone cross-sectional area [mm²]	0,16	0,16	0,24	0,20
tibia 4% total bone cross-sectional area [mm²]	-0,04	-0,01	0,10	0,03
tibia 14% total bone cross-sectional area [mm²]	0,02	-0,04	0,12	-0,02
tibia 38% total bone cross-sectional area [mm²]	0,15	0,11	0,24	0,15
Longitudinal shape indexes:				
tibia 4% bone mass/tibia 38% bone mass	-0,33*	-0,37*	-0,21	-0,32*
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	-0,27*	-0,34*	-0,26*	-0,32*
Strength strain index:				
tibia 14% polar SSI [mm³]	0,50*	0,43*	0,53*	0,41*
tibia 38% polar SSI [mm³]	0,71*	0,68*	0,70*	0,67*
Muscle and bone:				
lower leg 66% muscle cross-sectional area [mm²]	0,46*	0,37*	0,43*	0,32*
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,19	0,07	0,12	0,03
Fat:				
lower leg 66% fat cross-sectional area [mm²]	0,43*	0,33*	0,42*	0,29*
lower leg 66% fat cross-sectional area/muscle				
** - p<0,05. SSI - Strength strain index.*				

Results

Coefficients of variation were calculated for pQCT outcomes and expressed as absolute and relative precision errors. Table 3 presented absolute (CV_{RMS}) and Table 4 relative ($CV\%_{RMS}$) precision errors. Absolute precision errors were from 2,11 mg/cm³ to 3,84 mg/cm³, with corresponding LSC amounted from 5,86 mg/cm³ to 10,64 mg/cm³ for bone densities, from 0,0079 g to 0,0242 g for bone masses (LSC 0,0218 g to 0,0669 g), from 0,031 mm to 0,372 mm (LSC 0,086 mm to 1,030 mm) for bone cross-sectional dimensions, from 1,61 mm² to 13,37 mm² (LSC 4,47 mm² to 37,03 mm²) for cross-sectional areas, from 0,0116 to 0,372 (LSC 0,0321 to 1,030) for longitudinal bone indexes, from 29,6 mm³ to 63,4 mm³ (LSC 82,0 mm³ to 175,6 mm³) for polar SSI and from 64,7 mm² to 101,6 mm² (LSC 179,1 mm² to 281,4 mm²) for fat and muscle cross-sectional area, and 0,083 (LSC 0,229) for total cortical bone cross-sectional area to muscle cross-sectional area ratio. Relative precision errors ($CV\%_{RMS}$) (Table 4) for bone densities were from

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

	Age [yrs]	Height [cm]	Weight [kg]	Lower leg length [mm]
Bone mineral densities:				
tibia 4% trabecular bone density	-0,32*	-0,34*	-0,26*	-0,28*
tibia 4% total bone density	-0,20	-0,14	-0,08	-0,09
tibia 14% cortical bone density	-0,05	-0,08	-0,02	-0,08
tibia 38% cortical bone density	-0,04	-0,10	-0,08	-0,08
Bone masses:				
tibia 4% bone mass	-0,41*	-0,43*	-0,30*	-0,41*
tibia 14% bone mass	-0,02	-0,08	-0,02	-0,12
tibia 38% bone mass	0,00	-0,03	0,05	0,01
Cross-sectional dimensions:				
tibia 14% inner cortical bone circumference	-0,19	-0,29*	-0,19	-0,26*
tibia 38% inner cortical bone circumference	-0,21	-0,23	-0,14	-0,26*
tibia 14% outer cortical bone circumference	-0,27*	-0,34*	-0,18	-0,30*
tibia 38% outer cortical bone circumference	-0,11	-0,18	-0,05	-0,14
tibia 14% cortical shell thickness	-0,25	-0,27*	-0,15	-0,24
tibia 38% cortical shell thickness	-0,22	-0,20	-0,15	-0,18
tibia 14% cortical bone cross-sectional area	-0,27*	-0,23	-0,12	-0,21
tibia 38% cortical bone cross-sectional area	-0,12	-0,17	-0,08	-0,13
tibia 4% total bone cross-sectional area	-0,29*	-0,29*	-0,18	-0,25
tibia 14% total bone cross-sectional area	-0,27*	-0,34*	-0,17	-0,30*
tibia 38% total bone cross-sectional area	-0,12	-0,18	-0,06	-0,14
Longitudinal shape indexes:				
tibia 4% bone mass/tibia 38% bone mass	-0,36*	-0,40*	-0,25	-0,35*
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	-0,19	-0,25	-0,16	-0,24
Strength strain index:				
tibia 14% polar SSI	0,09	0,00	0,12	-0,01
tibia 38% polar SSI	0,48*	0,40*	0,44*	0,40*
Muscle and bone:				
lower leg 66% muscle cross-sectional area	0,17	0,04	0,11	-0,01
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,21	0,06	0,13	0,02
Fat:				
lower leg 66% fat cross-sectional area	0,30*	0,20	0,23	0,13
lower leg 66% fat cross-sectional area/muscle				
cross-sectional area	0,32*	0,26*	0,32*	0,20
** - p<0,05. SSI - Strength strain index.*				

0,25% for tibia 38% cortical bone density to 1,12% for tibia 4% trabecular bone density while for bone masses their values were from 0,58% for tibia 38% bone mass to 1,14% for tibia 4% bone mass. In the case of cross-sectional dimensions relative precision error was from 0,25% for tibia 38% outer cortical bone circumference to 1,60% for tibia 4% total bone cross-sectional area. Longitudinal shape indexes showed relative precision errors from 1,29% to 2,35% while for polar SSI $CV\%_{RMS}$ were from 2,66% to 4,53%. For "muscle and bone"

Table 7. Absolute (CV_{RMS}) and relative precision errors ($CV\%_{RMS}$) of lower leg length in studied group (n=60).

Absolute precision error	
Lower leg length [mm]	CV_{RMS}
	1,92
Relative precision error	
Lower leg length [%]	$CV\%_{RMS}$
	0,62

parameters relative precision errors were 1,56% for lower leg 66% total cortical bone cross-sectional area to muscle cross-sectional area ratio to 1,72% for lower leg 66% muscle cross-sectional area while for fat cross-sectional area and for fat cross-sectional area to muscle cross-sectional area ratio they were 4,43% and 5,49%, respectively. Concordantly (Table 4) relative least significant change (LSC%) values for bone densities were from 0,71% (tibia 38% cortical bone density) to 3,11% (tibia 4% trabecular bone density); for bone masses from 1,62% (tibia 38% bone mass) to 3,17% (tibia 4% bone mass); for cross-sectional dimensions from 0,70% (tibia 38% outer cortical bone circumference) to 4,43% (tibia 4% total bone cross-sectional area); for longitudinal shape indexes from 3,57% (tibia 4% bone mass/tibia 38% bone mass) to 6,51% (tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area); from 7,36% (tibia 14% polar SSI) to 12,55% (tibia 38% polar SSI); for "muscle and bone" from 4,32% (lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area) to 4,77% (lower leg 66% muscle cross-sectional area) and 12,28% and 15,20% for lower leg 66% fat cross-sectional area and lower leg 66% 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 positive correlations between absolute precision error and all anthropometric parameters (including lower leg length) were noted for tibia 38% bone mass, polar SSI (for both: 14% and 38% of the tibia length), muscle and fat cross-sectional area, with r value from 0,29 to 0,71. Significant negative correlations between absolute precision error and anthropometric parameters were observed for ratios: tibia 14% cortical bone cross-sectional area to tibia 4% total bone cross-sectional area (all anthropometric parameters, r from -0,26 to -0,34) and tibia 4% bone mass to tibia 38% bone mass (with exception of weight, r from -0,32 to -0,37). Weak negative correlations were observed also for tibia 4% trabecular bone density with age and height, r = -0,26 and 0,29, respectively. In the case of relative errors (Table 6) positive correlations were observed only for tibia 38% polar SSI (with all anthropometric parameters, r from 0,40 to 0,48), lower leg 66% fat cross-sectional area (with age, r = 0,30) and for ratio: lower leg 66% fat cross-sectional area to muscle cross-sectional area (with age, height and weight, r = 0,32, 0,26 and 0,32, respectively). Negative correlations with all anthropometric measures were observed for tibia 4% trabecular bone density and tibia 4% bone mass (r from -0,26 to -0,43) while tibia 4% bone mass to tibia 38% bone mass ratio correlated significantly with age, height and lower leg length (r = -0,36, -0,40 and -0,35, respectively). Individual weak but significant correlations were observed for some cross-sectional bone dimensions and selected anthropometric measures, with r values ranged from -0,26 to -0,34.

Table 7 provided absolute and relative precision errors for lower leg length measurement. Absolute precision error (CV_{RMS}) was 1,92 mm and relative precision error was 0,62%.

Table 8 presented Spearman rank correlation between absolute errors of lower leg length and pQCT outcomes. Significant correlations were noted for lower leg 66% fat cross-sectional area to muscle cross-sectional area ratio (r=0,31), only. Table 9 presented Spearman rank correlation for relative errors. Relative errors of lower leg length

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

	Lower leg length [mm]
Bone mineral densities:	
tibia 4% trabecular bone density [mg/cm^3]	0,11
tibia 4% total bone density [mg/cm3]	-0,11
tibia 14% cortical bone density [mg/cm^3]	0,11
tibia 38% cortical bone density [mg/cm^3]	0,06
Bone masses:	
tibia 4% bone mass [g]	0,18
tibia 14% bone mass [g]	-0,22
tibia 38% bone mass [g]	0,15
Cross-sectional dimensions:	
tibia 14% inner cortical bone circumference [mm]	-0,05
tibia 38% inner cortical bone circumference [mm]	0,16
tibia 14% outer cortical bone circumference [mm]	0,04
tibia 38% outer cortical bone circumference [mm]	0,05
tibia 14% cortical shell thickness [mm]	-0,05
tibia 38% cortical shell thickness [mm]	0,24
tibia 14% cortical bone cross-sectional area [mm^2]	0,05
tibia 38% cortical bone cross-sectional area [mm^2]	0,21
tibia 4% total bone cross-sectional area [mm^2]	0,17
tibia 14% total bone cross-sectional area [mm^2]	0,05
tibia 38% total bone cross-sectional area [mm^2]	0,04
Longitudinal shape indexes:	
tibia 4% bone mass/tibia 38% bone mass	0,21
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	0,09
Strength strain index:	
tibia 14% polar SSI [mm3]	-0,01
tibia 38% polar SSI [mm3]	-0,03
Muscle and bone:	
lower leg 66% muscle cross-sectional area [mm^2]	0,23
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,07
Fat:	
lower leg 66% fat cross-sectional area [mm^2]	0,25
lower leg 66% fat cross-sectional area/muscle cross-sectional area	0,31*

** - p<0,05. SSI - Strength strain index.*

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

	Lower leg length [mm]
Bone mineral densities:	
tibia 4% trabecular bone density	0,20
tibia 4% total bone density	-0,08
tibia 14% cortical bone density	0,10
tibia 38% cortical bone density	0,05
Bone masses:	
tibia 4% bone mass	0,31*
tibia 14% bone mass	-0,19
tibia 38% bone mass	0,13
Cross-sectional dimensions:	
tibia 14% inner cortical bone circumference	-0,02
tibia 38% inner cortical bone circumference	0,19
tibia 14% outer cortical bone circumference	0,10
tibia 38% outer cortical bone circumference	0,07
tibia 14% cortical shell thickness	0,05
tibia 38% cortical shell thickness	0,20
tibia 14% cortical bone cross-sectional area	0,13
tibia 38% cortical bone cross-sectional area	0,20
tibia 4% total bone cross-sectional area	0,17
tibia 14% total bone cross-sectional area	0,09
tibia 38% total bone cross-sectional area	0,07
Longitudinal shape indexes:	
tibia 4% bone mass/tibia 38% bone mass	0,26*
tibia 14% cortical bone cross-sectional area/tibia 4% total bone cross-sectional area	0,18
Strength strain index:	
tibia 14% polar SSI	-0,03
tibia 38% polar SSI	-0,11
Muscle and bone:	
lower leg 66% muscle cross-sectional area	0,27*
lower leg 66% total cortical bone cross-sectional area/muscle cross-sectional area	0,07
Fat:	
lower leg 66% fat cross-sectional area	0,21
lower leg 66% fat cross-sectional area/muscle cross-sectional area	0,20

** - p<0,05. SSI - Strength strain index.*

correlated with relative error of tibia 4% bone mass (r=0,31), tibia 4% bone mass to tibia 38% bone mass ratio (r=0,26) and with lower leg 66% muscle cross-sectional area (r=0,27).

Discussion

To the best of the authors knowledge, this is the first study presented precision errors of bone density, size and strength by pQCT of lower leg in children with medical conditions. Besides of the current study only Duff et al.[15] and Zheng et al.[17] presented data for lower leg in healthy children while Swinford et al.[16] for healthy young adults. Interestingly, precision errors values ($CV\%_{RMS}$) in our patients were similar to these reported by Swinford et al.[16] in healthy young adults and lower than presented by Duff et al.[15] and Zheng et al.[17] in healthy children. In our group $CV\%_{RMS}$ were from 0,25% to 4,43% while in Swinford's group $CV\%_{RMS}$ were from 0,32% to 2,67% for mutual measures and in Duff's group $CV\%_{RMS}$ were from 1,9% to 8,9% in comparison to 0,5% to 4,5% in our patients for measures utilised in both groups. Accordingly, Zheng et al. showed $CV\%_{RMS}$ for muscle cross-sectional area equals to 3,3% while in our group $CV\%_{RMS}$ was 1,72%. Since the specifics of the measurement's technology (i.e. scan speed, slice thickness, voxel size, etc.) were almost the same, observed differences may be at least partially explained by longer period between repeated scans in Duff et al.[15] work (one month) and Zheng et al.[17] (28 days) in comparison to Swinford et al.[16] (one week) and to presented study (0,5 hour). As was described by Swinford et al.[16] time between scans is a significant factor determining precision error. On the other hand, Duff et al.[15] show rather high number of excluded, due to poor quality, scans, as high as 9% for distal tibia and 6% for tibia shaft scans, while we do not exclude any scan. It seems that prone to the involuntary movement may be an additional factor increasing precision error in the population studied by Duff et al.[15]. Another possible cause may be that Duff et al.[15] measured the tibia length once while in the presented study we measured it twice, the same as in Swinford et al. study[16]. However, tibia measurement length error seems not to be a strong determinant of the precision error of pQCT outcomes. In the presented study the precision error of tibia length measurement emerged as weak (r from 0,26 to 0,31) determinant of the precision errors of pQCT outcomes for 4 out of 26 measures, only. Similar results were showed by Sun et al.[23] who pointed out positioning error as determinant for cross-sectional bone area, but not for density.

We found precision error of the pQCT measurement dependent on the subjects' body size (age, height, weight and lower leg length). Absolute errors of trabecular bone density and longitudinal ratios (tibia 4% bone mass to tibia 38% bone mass and tibia 14% cortical bone cross-sectional area to tibia 4% total bone cross-sectional area) diminished with increasing body size, however the strength of the dependency was weak, with r values from -0,26 to -0,37. At the same time tibia 38% bone mass, SSI (14% and 38% of the tibia length), muscle cross-sectional area and fat cross-sectional area absolute errors escalate with the body size, with r values from 0,29 to 0,71. Similarly, Swinford et al.[16] found absolute errors of bone mass, cortical area and polar moment of inertia dependent on the body size, with r values from 0,34 to 0,69. Accordingly, in the presented data, relative error diminishes with increasing body size for trabecular bone density, bone mass (4% slice), some bone dimensions and for ratio of tibia 4% bone mass to 38% bone mass. The relationships were weak, too, with r value from -0,26 to -0,43. On the contrary, polar SSI (38% slice) and lower leg 66% fat cross-sectional area to muscle cross-sectional area ratio show increased relative errors with increasing body size. Similarly, Duff et al.[15] reported diminishing with increasing age relative errors for total area, total and trabecular content, total density and trabecular area. The observed diminishing with body size precision errors may be related to higher level of cooperation in the older children than in younger ones, and to fact, that greater bones are less susceptible to the partial volume effect[24]. On the contrary, opposite effect of body size (i.e. increasing precision error) may be partially resulted from higher repositioning error connected with difficulties in positioning of the lower leg without touching the sides of the gantry, as was hypothesised by Swinford et al.[16].

Presented study has limitations. Firstly, the studied group comprised patients in which standard measurement procedure can be employed, so presented results may not be directly applied to the patients required non-standard measurement procedure. Nevertheless, these patients are not typical patients of the densitometry lab, since such a patient always needed the individual decision concerning reasonability of admission order to the bone densitometry. Secondly, the duplicated measurements were done with relatively short time span, which may underestimate the precision error[16]. However, procedure with full reposition between scans and with duplicated forearm length measurement was carried out, which may mitigate the aforementioned effect. Thirdly, all measurements and scan analyses were done by one operator. Probably, it is questionable limitation since well-trained operators can conduct measurements with comparable quality, with no effect on the precision error[16]. Finally, the presented results are, at least in parts, specific 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 the wide range group (5-18 yrs) of children, typical patients of the densitometry lab. These fulfil ISCD requirement[18] and ensure, that assessed precision errors is not underestimated, since healthy young subjects are likely to show better precision than diseased ones, partially due to easier positioning and better cooperation[25]. It is more pronounced in the case of percentage precision error when lower measured values lead to higher percent changes compared with normal patients with similar absolute change[26]. The recruiting procedure was blinded. During the recruitment recruiter did not know for which arm of the study participant will fall – forearm, lower leg or mechanography. It allows to minimize bias of the selection of the participants. The number of patients is relatively high, with overall degrees of freedom equals 60, which is two times greater than minimal degrees of freedom recommended by the International Society for Clinical Densitometry[2]. To avoid underestimating of the precision errors, rather conservative measure, root mean square coefficients of variation[1] were presented. Least significant changes were calculated in the conservative manner, too, with the 95% confidence level.

Presented study reveal pQCT method at the lower leg in children with medical conditions as relatively precise technique, with $CV\%_{RMS}$ from 0,25% to 5,49% and LSC (95%) from 0,70% to 15,2%. Obtained results provide an attainable basis for design and interpretation of pQCT studies in children with medical conditions.

Ethics Approval

The study protocol was approved by the Bioethical Commission of The Children's Memorial Health Institute, decision number 61/KBE/2016.

Consent to participate

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.

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.

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