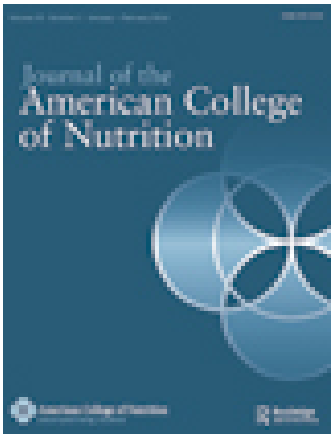

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Phantoms for Cross-Calibration of Dual Energy X-ray Absorptiometry Measurements in Infants

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Original Research

Phantoms for Cross-Calibration of Dual Energy X-ray Absorptiometry Measurements in Infants

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Key words: phantom, body composition, fat, lean, bone, infant

Objective: To test the suitability of phantoms to cross-calibrate body composition measurements in small subjects among different dual energy X-ray absorptiometry (DXA) instruments.

Methods: A set of four phantoms with total weights 1520g, 3140g, 4650g and 7490g were made with low cost and easily available materials. Each phantom was made from assembling polyethylene bottles (100 to 1000 mL) filled with either pure olive oil or electrolyte solution in different combinations, and borosilicate tubes (3 and 5 mL) and flexible polypropylene tubing filled with calcium carbonate. Triplicate measurements of each of the four phantoms were performed with three pencil beam densitometers made by the same manufacturer (Hologic Inc., Waltham, MA): two QDR 2000 (University of Liege, Liege, Belgium, and Wayne State University, Detroit, Michigan) and a QDR1500 (University Children's Hospital, Greifswald, Germany) using infant whole body-scanning mode and analyzed with software V5.73P.

Results: DXA measured total weight, or bone, lean and fat masses, from one center were highly predictive of DXA measurements from the other centers with an adjusted r^2 of 0.94 to 1.00, $p < 0.001$. This was the case whether the measurements from single scan or from average of triplicate scans were used in the analysis.

Conclusions: Systematic corrections, in the form of linear transformations, are possible to allow comparison of clinical data generated from different centers. Different size phantoms can be made to accommodate the varying range of weights and body composition of study subjects.

INTRODUCTION

Dual energy X-ray absorptiometry (DXA) is the recognized standard for bone measurements and is increasingly being used for the measurement of soft tissue body composition in adults [1] and children [2] including infants [3]. However, it is well known that DXA measurements varied with instruments from different manufacturers [4–6] and even within the same manufacturer [7] because of differences in scanner design, materials used for calibration and analysis algorithms. Thus, in order to determine the comparability of results generated from different centers, it is essential to test all the properties of scanner performance as a whole with the use of phantoms and/or human subjects. With increasing availability of DXA technique for studies in infants, it is imperative to determine whether different instruments used to measure body composition in infants can be cross-calibrated to allow meaningful comparison of data generated from different institutions, although no such study has been reported. We therefore aim to test the suitability of a set of phantoms to cross-calibrate body composition measurements in small subjects among different DXA instruments.

METHODS

Phantoms

Pure olive oil (Salov North America Corp, Hackensack, NJ), an electrolyte solution containing a mixture of sodium

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chloride and potassium mono-basic phosphate (Sigma Aldrich Inc., St. Louis, MO) and calcium carbonate powder (Sigma Aldrich Inc, St. Louis, MO) were used to mimic fat, lean and bone. Polyethylene bottles (Nalge Nunc International, Rochester, NY) of different shapes and capacities (100 to 1000 mL) were filled with either pure olive oil or electrolyte solution. Different size borosilicate tubes (3 and 5 mL, Becton Dickinson Vacutainer Systems, Rutherford, NJ) and flexible polypropylene tubing (Nalge Nunc International, Rochester, NY) were filled with calcium carbonate. Bottles and tubes were taped together in layers to form nine blocks. Each block contained different quantities of oil, electrolyte solution and calcium carbonate. The blocks were assembled contiguously with one another in a predetermined fashion to form four phantoms with total weights 1520g, 3140g, 4650g and 7490g as determined by an electronic scale (Seca model 727, Toledo Scale Corp., Toledo, OH). The maximum dimensions of the four phantoms varied between 28 to 58 cm in length, 12 to 32 cm in width and 11 to 15 cm thick. All blocks were kept in a box at room temperature between DXA measurements.

DXA Scans

Three densitometers from three centers were assessed in this study. All densitometers were from the same manufacturer (Hologic Inc., Waltham, MA): two QDR 2000 (one located at University of Liege (UL), Liege, Belgium, and the other located at Wayne State University (WSU), Detroit, MI, USA) and a QDR1500 located at the Neonatal unit of University Children's Hospital (UCH), Greifswald, Germany. Quality control scans for each densitometer were performed daily using a manufacturer-supplied anthropomorphic spine phantom. The *in vitro* coefficients of variation (CV) for >1 year for the determination of bone mineral content, bone area and bone mineral density were 0.43%, 0.42% and 0.46%, respectively at UL, were 0.38%, 0.30% and 0.34% at WSU, and were 0.35%, 0.35% and 0.31%, respectively at UCH.

All densitometers were operated in the pencil beam mode, the only technique freely available for body composition studies in infants. The four phantoms were scanned in triplicate on each densitometer using infant whole body-scanning mode and analyzed with manufacturer-supplied software V5.73P. One investigator (J.-C.P.) familiar with the agreed layout of the phantoms was present at each site to insure the correct assembly and placement of the phantoms for DXA measurements. Each center used its own operator for scan acquisition and analysis. Phantoms were transported personally or shipped between centers via commercial courier.

Statistical Analysis

DXA measured total weight, lean mass, fat mass, bone mineral content, bone area and bone mineral density were used in data analysis. Percent of fat was presented as descriptive data and not analyzed further since it was calculated from fat mass and total weight. Repeated measures analysis of variance was used to determine the equivalence of the triplicate DXA measurements (within subject factor) among the four phantoms (between subject factor) and whether there was interaction between DXA measurements from different size phantoms from different instruments.

Regression analyses were performed to determine the ability of DXA measurements from UL and UCH to predict the DXA measurements of the same phantoms at WSU. Univariate analysis of variance with Helmert contrasts was used to analyze comparability of residuals from each prediction equation based on UL and UCH data respectively. The same procedures were repeated to determine the regression equation for prediction of DXA measurements of the same phantoms at the other centers from WSU DXA measurements.

The same procedures were repeated using the first of the triplicate measurements to mimic the clinical situation of generating one satisfactory scan per subject. This was done to determine whether the same relationships exist with the use of data from one or three DXA scan. All statistical tests were performed with SPSS 10.0 (SPSS Inc., Chicago, IL) for windows at an adopted significance level of 0.05.

RESULTS

A representative phantom and its corresponding scan are shown in Fig. 1. DXA measurements of the four phantoms from the study sites are shown in Table 1. DXA measurements were highly correlated (adjusted $r^2 = 0.96$ to 1.00) with weight of the components and total weight of each phantom. There was no significant difference among triplicate DXA measurements of the phantoms. Therefore averages across the three measurements were used in further analyses. There was no interaction among DXA measurements from different size phantoms using the three instruments.

DXA measurements from UL and UCH were highly predictive (adjusted $r^2 = 0.94$ to 1.00, $p < 0.001$) of DXA measurements of the same phantoms at WSU (Table 2).

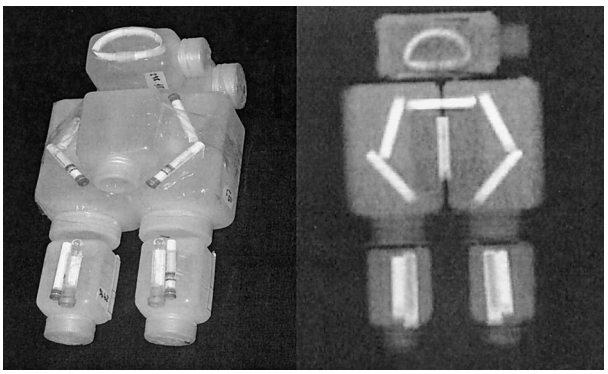

Fig. 1. A 5 kg phantom assembled from various blocks (left) and the resultant dual energy X-ray absorptiometry scan (right).

Table 1. Triplicate Measurements* of Phantoms Using Dual Energy X-ray Absorptiometry

	UL			UCH			WSU		
	Mean	SD	CV%	Mean	SD	CV%	Mean	SD	CV%
Phantom 1.5 kg									
Total g	1507	1.2	0.08	1499	2.3	0.15	1506	1.6	0.11
Lean Mass g	982	6.9	0.70	1034	21.4	2.07	1037	15.1	1.46
Fat Mass g	490	6.4	1.30	432	22.3	5.15	435	16.1	3.71
BMC g	34.4	0.15	0.42	32.9	1.39	4.23	34.4	1.79	5.20
Bone Area cm^2	170	2.2	1.32	165	7.0	4.23	163	8.2	5.05
BMD g/cm^2	0.202	0.002	0.76	0.199	0.001	0.58	0.211	0.003	1.25
Phantom 3 kg									
Total g	3156	5.2	0.16	3147	4.9	0.15	3157	3.1	0.10
Lean Mass g	1965	25.5	1.30	2005	67.1	3.35	2049	89.4	4.37
Fat Mass g	1116	23.9	2.14	1074	70.7	6.58	1037	93.0	8.97
BMC g	75.1	1.08	1.44	68.9	1.24	1.80	72.1	3.37	4.67
Bone Area cm^2	285	4.6	1.60	271	2.7	1.00	277	5.9	2.13
BMD g/cm^2	0.264	0.004	1.58	0.254	0.004	1.64	0.260	0.009	3.63
Phantom 5 kg									
Total g	4664	9.1	0.19	4677	3.6	0.08	4670	7.7	0.16
Lean Mass g	3178	61.2	1.93	3174	100.5	3.17	3349	71.0	2.12
Fat Mass g	1373	68.9	5.02	1395	101.1	7.25	1218	81.4	6.68
BMC g	113.2	1.19	1.05	107.4	0.94	0.87	102.9	7.43	7.22
Bone Area cm^2	364	4.4	1.21	341	5.1	1.49	350	3.8	1.09
BMD g/cm^2	0.311	0.001	0.32	0.316	0.003	0.80	0.294	0.019	6.59
Phantom 7 kg									
Total g	7513	9.5	0.13	7521	9.9	0.13	7563	5.5	0.07
Lean Mass g	5364	45.7	0.85	5600	99.8	1.78	5695	19.3	0.34
Fat Mass g	1991	36.3	1.82	1755	91.2	5.20	1700	19.9	1.17
BMC g	182.2	1.54	0.85†	165.7	1.58	0.96	168.3	0.87	0.51
Bone Area cm^2	631	3.1	0.49	588	9.5	1.61	590	4.6	0.77
BMD g/cm^2	0.290	0.002	0.73†	0.282	0.004	1.44	0.285	0.002	0.61

Abbreviation: UL = University of Liege, Belgium, UCH = University Children Hospital, Germany, and WSU = Wayne State University, USA, BMC = bone mineral content, BMD = bone mineral density.

* Average of triplicate measurements.

† Excluded one BMC and one BMD value at ~50% lower than the value generated from the other two scans.

Helmert contrasts in analysis of variance confirmed that the residuals from UL and UCH taken together did not differ from WSU (as zero), nor did UL and UCH residuals differ from each other.

Similar results were found when using the first value instead of the average of the triplicate DXA measurements for the prediction of DXA measurements among the three institutions with an adjusted $r^2 = 0.94$ to 1.00, $p < 0.001$. These findings were applicable to the determination of predicted mean, standard error of estimate and the slope of the prediction equations regardless of the DXA parameter measured. The differences in the slope of the predicted equation were <1% in all cases whether the first or average of triplicate measurements were used in the prediction equations.

DISCUSSION

To advance the understanding of physiologic and pathologic effects on body composition in infants and young children, it is imperative that a system exists to determine the validity of data generated from different centers using different instruments. It would be useful to have *in vivo* studies to cross-calibrate different instruments as has been done with human adults [4–7]. However, the use of human infants for this purpose is impractical under most circumstances, especially since the three instruments employed for this study are located in widely separated geographic regions. Thus, the use of phantoms would be the most practical means to cross-calibrate different instruments in the study of body composition in small subjects particularly infants. However, phantoms suitable for use in older children [8] and adults [4–7] are inappropriate for the assessment of body composition in small subjects because of major differences in the acquisition and analysis of scans.

Our goal for this study was to develop a set of phantoms that can be made easily and inexpensively and have sufficient flexibility for any investigator to further modify or adjust the components to create different size phantoms with varied body composition. The primary purpose for the use of these phantoms is to determine the interrelationship of the DXA measurements among different densitometers rather than the comparison of absolute accuracy of the DXA densitometers. This is

Table 2. Prediction of Dual Energy X-ray Absorptiometry (DXA) Measurements at Wayne State University (WSU), USA from DXA Measurements Obtained from Densitometers at University of Liege (UL), Belgium, and University Children Hospital (UCH), Germany, Using Average of Triplicate Scans of the Same Phantoms

	UL	UCH
Total weight (Total) g	1.008 Total* − 21.5	1.005 Total* − 9.4
Adjusted r^2	1.000	1.000
Predicted mean/SEE	4224/11.4	4224/18.7
Lean mass (LM) g	1.065 LM* − 26.8	1.021 LM* + 17.4
Adjusted r^2	1.000	0.999
Predicted mean/SEE	3032/19.5	3032/75.3
Fat mass (FM) g	0.839 FM† + 54.9	0.924 FM† + 22.6
Adjusted r^2	0.993	0.977
Predicted mean/SEE	1097/44.1	1097/78.8
Bone mineral content (BMC) g	0.901 BMC† + 3.25	0.995 BMC† + 1.15
Adjusted r^2	0.999	0.994
Predicted mean/SEE	94.4/2.0	94.4/4.3
Bone area (BA) cm^2	0.923 BA* + 10.5	1.006 BA* + 1.8
Adjusted r^2	0.999	0.999
Predicted mean/SEE	345/4.9	345/5.7
Bone mineral density (BMD) g/cm^2	0.789 BMD† + 0.052	0.744 BMD‡ + 0.067
Adjusted r^2	0.990	0.941
Predicted mean/SEE	0.263/0.004	0.263/0.009

* $p \leq 0.001$; † $p \leq 0.01$; ‡ $p = 0.02$.

All intercepts had $p > 0.05$ although the intercept for the BMD prediction equation from UL had $p = 0.051$.

SEE = Standard error of the estimate.

consistent with the means to obtain standardized DXA measurements of the spine using instruments from different manufacturers that are known to provide different values for the same subject [9]. The design of our phantoms also satisfied the recommendations of the International DXA Standardization Committee that cross-calibration among different instruments should not be based on the use of a single phantom [9].

We have independently reported [10–12] the validity of the pencil beam DXA technique for the measurement of body composition using instruments from the same manufacturer based on animal tissue studies, and it was not our intention to reproduce the anatomically correct or exact duplication of body composition of infants, since there are great differences among infants and it would be prohibitively expensive and time consuming to achieve these goals. In any case, the physical dimensions and body composition values of our phantoms can be modified to accommodate the wide range of weights and body composition in clinical subjects, thus allowing cross comparison of any clinical studies involving small subjects.

In this study, the strongly predictive relationships of DXA measurements among the three instruments would support that data generated from different densitometers made by the same manufacturer employing the same DXA pencil beam technique and the same software are comparable. Furthermore, systematic corrections in the form of linear transformations are possible to allow comparison of clinical data generated from different studies. It is also possible that our system of phantoms can be used to determine whether these relationships remain true for data generated from the use of other DXA techniques or the use of instruments from different manufacturers.

That the intercepts of the regression equations for the prediction of DXA measurements among various centers were not significantly different from zero would support the absence of systematic difference among the densitometers tested, although the intercept for BMD prediction equation derived from UL approached significance. Even if there was a systematic difference in BMD measurements among different densitometers, it is still possible to compare data among different centers since the slope of the relationship in BMD measurements remain significantly highly correlated with an adjusted r^2 of ≥ 0.94. By way of clarification, the conversion of Celsius to Fahrenheit or vice versa would show a different intercept, but the slope would indicate that these two measurements are highly significantly related. In any case, BMD as an index of bone mass measurement is inappropriate in growing individuals such as infants [13,14]. Furthermore, since DXA bone mass measurement was validated for adults based on the mass of hydroxyapatite or other material [15] and for infants was based on the mass of carcass ash and calcium [10–12], i.e., not based on density, the potential clinical significance of any discrepancy in BMD measurements would be limited.

The same predictive ability among DXA measurements for the various components and total weight of phantoms whether using data from first or average of multiple DXA scans has major clinical implications. Thus the generation of a single good quality DXA scan, specifically without movement artifact, is likely to be adequate for clinical studies in infants. This results in reduction of radiation exposure, time and cost of clinical studies. In contrast, it is theoretically possible that a transient variability in the output X-ray source may have led to

the one outlier in the triplicate measurement of one phantom. If this was the case, then the use of one DXA scan may be inadequate to determine the existence of this problem during any clinical study. The occurrence of the outlier measurement was unlikely the result of operator error since no repositioning was performed between the three scans. In any case, it is critical to maintain the instrument in optimal operating condition, remain vigilant to the assurance of uninterrupted X-ray energy output, consistent approach in data acquisition and analysis, avoidance of motion artifact and strict adherence to all aspects of quality assurance including duplicate scans on a sample of subjects in any DXA study.

CONCLUSION

We have demonstrated that phantoms of various sizes can be made from easily available and low cost materials and can be used to cross-calibrate different DXA instruments to allow meaningful comparison of data among different centers.

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