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Evaluation of DXA against the four-component model of body composition in obese children and adolescents aged 5 to 21 years

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Abstract

Background: Body composition is increasingly measured in pediatric obese patients. Although dual-energy X-ray absorptiometry (DXA) is widely available, and is precise, its accuracy for body composition assessment in obese children remains untested.

Objective: We aimed to evaluate DXA against the four component (4C) model in obese children and adolescents in both cross-sectional and longitudinal contexts.

Design: Body composition was measured by DXA (Lunar Prodigy) and the 4C model in 174 obese individuals aged 5-21 years, of whom 66 had a second measurement within 1.4 years. The Bland-Atman method was used to assess agreement between techniques for baseline body composition and change therein.

Results: A significant minority of individuals (n = 21) could not be scanned successfully due to their large size. At baseline, in 153 individuals with complete data, DXA significantly over-estimated fat mass (Δ = 0.9, SD 2.1 kg, $p<0.0001$) and under-estimated lean mass (Δ = −1.0, SD 2.1 kg, $p<0.0001$). Multiple regression analysis showed that gender, puberty status, lean mass and fat mass were associated with the magnitude of the bias. In the longitudinal study of 51 individuals, the mean bias in change in fat or lean mass did not differ significantly from zero (FM: Δ = −0.02, p=0.9; LM: Δ = 0.04 p=0.8), however limits of agreement were wide (FM: ± 3.2 kg; LM ± 3.0 kg). The proportion of variance in the reference values explained by DXA was 76% for change in fat mass and 43% for change in lean mass.

Conclusions: There are limitations to the accuracy of DXA using Lunar Prodigy for assessing body composition or changes therein in obese children. The causes of differential bias include variability in the magnitude of tissue masses, and stage of pubertal development. Further work is required to evaluate this scenario for other DXA models and manufacturers.

Keywords

Body composition; DXA; fat mass; lean mass; childhood obesity

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Introduction

Body composition is increasingly measured in obese children and adolescents, both in research studies and in clinical practice (1;2). While the categorisation of obesity remains based on body mass index (BMI) (3;4), this outcome is not sensitive to variability in adiposity in individuals, and conveys negligible information about changes in body composition during treatment. Many obesity treatment programmes promote both dietary modifications and an increase in physical activity (5). Under these circumstances, changes in the relative contributions of fat and lean tissue to BMI may occur without much change in BMI itself. Alongside interest in establishing the efficacy of weight loss programmes on body composition, there is also interest in monitoring cardiovascular risk (2). Similarly, There is increasing interest in the notion of tailoring some drug dosages to lean mass, because this tissue mass is the primary site of metabolic activity, and because it is highly correlated with the rate of systemic clearance (2). Thus, there is a need for techniques that can accurately quantify both fat mass (FM) and lean mass (LM, used here synonymously with fat-free mass) in pediatric obese patients.

Despite these needs, the measurement of body composition in obese children remains challenging, due both to lack of resources and the limitations of many methodologies. Neither anthropometric nor bio-electrical impedance technologies have high accuracy for body composition assessment in individual obese children (6). Two component methodologies, such as densitometry and isotope dilution, may be adversely affected by alterations in tissue properties that confound the theoretical assumptions on which these techniques rely (6). For example, we have recently shown that obese children have reduced density and increased hydration of LM (7;8), thereby inducing error in calculations of body composition by densitometry and hydrometry in this population. Furthermore, neither of these techniques is widely available in the clinical setting. Magnetic-resonance imaging (MRI) and computed tomography (CT) scanning provide accurate data on adipose tissue distribution, but remain limited to specialist use and are unsuitable for routine clinical application.

Dual energy X-ray absorptiometry is now available in many hospitals, and is relatively easy to use in obese children. Although the technique is well known to have relatively high precision for body composition, studies have questioned its accuracy. Several large studies, using the gold-standard 4-component (4C) model as the reference method, have identified wide limits of agreement in children in both Hologic and Lunar instrumentation across a broad range of nutritional status (9-11). Such studies provide the best evidence on the accuracy of DXA, because the reference method is robust to variability in the properties of LM. However, most assessments of the accuracy of DXA have been conducted in normal-weight populations, and detailed relevant information for those obese remains lacking. We therefore evaluated the accuracy of DXA for body composition assessment, using the 4C model as the reference method, in a sample of 184 obese children and adolescents aged 5 to 21 years. The age range was extended into young adulthood to ensure the entire adolescent age range was addressed.

Methods

The individuals for this study were recruited from obesity management clinics at Great Ormond Street Hospital and University College Hospital (n = 122), or as participants in a study compiling children's body composition reference data (N = 62). The patients were being treated either through a behavioural intervention (95), or with the drug Metformin (27). Those receiving Metformin tended to be older and to have higher BMI. Preliminary results indicate only modest effect of Metformin treatment on body composition. The study

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was open to all obese individuals taking part in either of the studies, and the age range extended up to 22 years in order to ensure the findings were relevant right up to early adulthood. The inclusion criteria were BMI standard deviation score (SDS) >1.64, equivalent to the 95th centile, using UK 1990 reference data (3). Ethical approval for the study was obtained from the Research Ethics Committee of Great Ormond Street Hospital and the UCL Institute of Child Health.

All individuals attended our body composition investigation suite located at Great Ormond Street Hospital for a two hour measurement session. Those participating in longitudinal studies returned for a second session within 1.4 years. Weight and height were measured using standard protocols. Body weight was measured in duplicate as part of the air displacement plethysmography protocol (see below). Height was measured using a wall-mounted stadiometer (Holtain, Dyfed, UK). BMI was calculated as weight (kg) divided by the square of height (m). Anthropometric data were converted to SDS format using UK reference data (3;12). Obesity was categorised using the UK cut-off of BMIS SDS of 1.64 (3). Puberty rating was assessed according to Tanner staging (stages 1-5) by self-report, with the individual selecting a line drawing they felt most closely matched their state.

Measurements of total body water by deuterium dilution, bone mineral content by dual energy X-ray absorptiometry (DXA: Lunar Prodigy; GE Medical Systems, Madison, WI) and body volume (in duplicate) by air displacement plethysmography (Bodpod; Life Measurements, Concord, CA) were obtained as described previously (13). The limt for body weight on our DSXA instrumentation is 115 kg. The 4C model was used to calculate LM and FM as described previously (1;14). Precision of total body water in our laboratory is ~1% (1). Precision of body volume from duplicate measurements was 0.24 litres. Precision of bone mineral content, according to published data, is 1.1% for bone mineral content (15). DXA data for bone and non-bone lean tissue were combined to give a total value for LM, equivalent to that provided by the 4C model.

Statistics

Sex differences in the variables were assessed using independent sample t-tests. Changes within individuals over time were assessed using paired-sample t-tests. The Bland-Altman method (16) involves calculation of the bias (as the difference between DXA and 4C values, assessed for significance using paired sample t-tests), the limits of agreement between techniques (twice the standard deviation as the bias), and the correlation between the bias and the magnitude of the variable (using the average value from DXA and 4C model). Multiple regression analysis was use to identify significant predictors of the bias in FM. Potential factors tested in this model were age, FM and LM (using mean values by the two techniques), hydration, gender, pubertal stage and ethnicity.

Results

A minority of individuals (n = 10) had body weight excessive for the DXA scanning table and had neither 4C data (due to lack of bone mineral mass) nor DXA data available. A total of 174 children and adolescents, 64 boys and 110 girls, had complete datasets for both the 4C model and DXA at baseline, while 66 of these (21 boys, 45 girls) had longitudinal data. However, of those in whom measurements were attempted, a minority were excluded from the analyses because the entire body had not been located within the DXA scanning area. In the cross-sectional sample, 26 individuals were omitted for this reason. These exclusions indicate that of a total of 184 individuals initially recruited to the cross-sectional study, 5% were excluded for excess weight, while 15% of those actually scanned were excluded post-hoc for exceeding the scanner area limits. However, in 5 individuals from the longitudinal sample, who did not have acceptable scans at both time points, the second scan proved

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acceptable and was therefore added to the cross-sectional sample, giving a total of 153 individuals (57 boys, 96 girls) in the final cross-sectional sample.

Of these 153 individuals, 94 were recruited from obesity clinics, and 59 from the general community. Compared to those recruited from the community, those from the clinics had lower mean age (11.2 v 12.2 years, p=0.076), higher mean BMI SDS (3.0 vs 2.2, p<0.0001) and higher fat mass (30.8 v 21.3 kg, p<0.0001) but did not differ significantly in lean mass (39.1 v 38.0, p=0.5). Inability to scan the subject was much commoner in those receiving Metformin (11/27, or 41%) compared to the remainder of the sample (10/147, or 7%). This could be attributed to the greater BMI SDS of the Metformin patients (3.2 ±0.5 versus 2.7 ±0.2 ; p<0.01) as well as their being on average 2 years older.

In the longitudinal sample of 66 individuals, all of whom were clinical patients, 15 subjects had an unacceptable scan at least at one of the two time points, giving a final sample of 51 individuals (18 boys, 33 girls). Those excluded from the analyses had significantly greater weight, body volume and BMI SDS (all p<0.001), and in the longitudinal sample were significantly older (p<0.01). Of these 51, only 5 were being treated with Metformin.

Table 1 presents characteristics of the final cross-sectional sample stratified by sex. The age range spanned 5-21 years, however all but 7 of the sample were aged <18 years. Girls had significantly lower mean total body water, LM by both 4C and DXA than boys, and lower hydration of lean tissue. The range of weight across the entire sample was 24.3 to 112.3 kg. The majority of the sample were categorised as white European (38 boys, 67 girls), with the remaining sample categorised as asian (6 boys, 8 girls), black (6 boys, 13 girls) or “other” (7 boys, 8 girls). The distribution by pubertal stage was 33, 48, 35, 16 and 18 in stages 1-5 respectively.

Table 2 presents the baseline characteristics and their subsequent change in the longitudinal sub-sample. This sample was comprised of 31 white individuals, 7 asian individuals, 7 black individuals, and 6 individuals categorised as “other”. The average duration of follow-up was 0.6 years, ranging from 0.4 to 1.4 years. During this time there was a significant mean decrease in weight SDS and BMI SDS, but significant increases in LM by both techniques, and increases in FM that did not achieve significance by either technique. The apparent contradiction of these findings can be attributed to the fact that the SDS scores take into account growth in the reference data, whereas the absolute tissue mass changes do not.

The bias in weight estimated by DXA was 0.21 (SD 0.57) kg, p<0.0001. Table 3 presents the Bland-Altman statistics for the evaluations of DXA. Compared to the 4C model, DXA significantly over-estimated FM in the entire sample by 0.9 kg. This finding was replicated in each sex when considered separately. The limits of agreements of this bias were ±4.2 kg, but were greater in girls (±4.7 kg) than in boys (±3.1 kg). DXA similarly under-estimated LM by 1.0 kg in the entire sample, with limits of agreement in individuals of ±4.2 kg. Variable bias in weight between individuals accounts for the inconsistency in mean biases for FM and LM. When the sexes were considered separately, the bias was greater in females (−1.2 kg) than males (0.67 kg), though not significantly so. The magnitude of the bias differed significantly by pubertal stage, with both greater bias, and wider limits of agreement, in those of more advanced pubertal stage (Figure 1). The bias was greater in those receiving Metformin (FM: 2.2 ± 3.0 kg versus 0.7 ±1.9 kg, p=0.065; LM: −2.1 ±2.7 kg versus −0.9 ±2.0 kg, p=0.032). However, multiple regression analysis showed that when age and BMI SDS were added to the model, those receiving Metformin did not have significantly greater bias in FM or LM, indicating it was their above-average BMI and age that accounted for the greater bias.

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The bias in FM was significantly related to the magnitude of FM in the whole sample and in each sex. However, the bias in LM was significantly related to the magnitude of LM only in boys. Figure 2 shows the scatter of bias against mean value by both techniques for FM. In the cross-sectional sample, the bias was not significantly different in those recruited from clinics (FM bias: 0.77 SD 2.46 kg; LM bias −0.95 SD 2.48 kg) compared to those recruited from the community (FM bias: 0.98 SD 1.34 kg; LM bias: −1.09 SD 1.30 kg), though the limits of agreement were greater in the clinical sample (FM: ±4.92 v ±2.68 kg; LM: ±4.96 v ±2.60 kg). No age-sex interaction effect on these biases was encountered.

Table 3 also presents Bland-Altman statistics for the change in LM and FM. In view of the smaller sample size, and no indication of differences between the sexes, these analyses were restricted to the whole sample. The average bias was not significantly different from zero for either change in LM, or change in FM, however the limits of agreement in individuals were large (±3 kg) relative to the average change of 1.7 kg in LM or 0.6 kg in FM as estimated by magnitudes of the tissue masses averaged between the two techniques. There were modest correlations between the bias and the magnitude of the change for both outcomes, but these were not significant. Change in FM by DXA accounted for 76% of the variance in change in FM by the 4C model. However, change in LM by DXA accounted for 43% of the variance in change in LM by the 4C model. Figure 3 shows the DXA bias in change for FM.

Table 4 presents statistics for the regression of the DXA bias in FM on potential explanatory variables. Age, pubertal stats, mean FM and LM by both techniques and gender were all significant predictors of the bias. Hydration of lean tissue was positively associated with the bias, but did no achieve significance in the model (p=0.10). Ethnicity showed no significant association with the bias. Two models of similar explanatory strength were obtained. The first, incorporating gender, fat mass, lean mass and hydration, explained 26% of the variance in the FM bias, indicating that factors not addressed in this study were the major determinants. Adding puberty to the model resulted in gender and hydration no longer remaining significant, and explained 28 % of the variance in the FM bias.

Discussion

This study is the first to provide a comprehensive evaluation of the accuracy of DXA for body composition analysis in obese children and adolescents, using the *in vivo* gold standard 4C model as the reference method. Our data indicate firstly that a significant minority of obese individuals cannot be scanned by DXA, either because they exceed the weight limitations, or because their body size exceeds the scanning area. Of those actually scanned, significant biases were apparent in both fat and lean mass, but not in change in fat or lean mass over time. However, for both baseline body composition and its change, there were relatively large limits of agreement between techniques, indicating poor accuracy in individuals. The bias also worsened substantially with pubertal progression.

Technologies for assessing body composition in obese individuals are urgently required. Whilst BMI is predictive of health status, it is a poor index for assessing the efficacy of treatment, especially in the pediatric population in whom changes in adiposity are confounded by growth. Exercise interventions may have antagonistic effects on lean and fat masses that are obscured within the umbrella of BMI. The gold standard technologies for adipose tissue assessment are MRI and CT scanning, however neither is readily available for routine monitoring, and CT further involves exposure to high levels of radiation. There are currently a limited number of options for body composition assessment in the pediatric obese population – DXA, densitometry using whole-body air-displacement plethysmography and isotope dilution (6). Anthropometric approaches and bio-electrical impedance analysis may be valuable clinical tools, but incorporate significant predictive

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error (6). Thus, ideally DXA could play a significant role in this context, but our study indicates further development is required.

The difficulties of scanning larger individuals could be addressed by increasing the weight capacity and scanning area of the instrumentation, as is already occurring. A few of those we rejected from the current analyses due to their image not lying entirely within the scanning area could have been included had greater care been taken when conducting the scan, although this issue is made more difficult by the fact that the area analysed by the software does not match exactly with the guidelines on the scanning table. In such individuals, the loss of tissue from the soft tissue calculations was very minor, however we preferred to conduct our Bland Altman analyses only in those with appropriate raw DXA data. Nevertheless, a significant number of individuals were substantially too large for the scanning area, hence this issue must be addressed by manufacturers. Newer Lunar instrumentation such as the iDXA allows weights up to 200kg. This problem becomes greater with increasing age, due to the larger size of older individuals, and will therefore be particularly apparent in studies of adolescents approaching adulthood.

In those scanned, the limits of agreement for fat mass were equivalent to 3.0 % of the mean value, but the limits of agreement in individuals were ±15.4 %, demonstrating that DXA measures adiposity with substantial error in some obese individuals. Our regression analysis indicated that larger LM increased this error, whereas larger FM decreased it, though the effect of FM was smaller than that of LM. Hydration of lean tissue may also contribute to DXA error, as reported previously in some (17;18) but not all (19) studies, however its effect did not reach significance in our model. The accuracy of DXA is well known to be influenced by tissue depth (20;21), which is likely to account in part for the impact of lean mass, representing physique. Bias was also significantly greater in females compared to males, which may be due to regional differences in the distribution of fat and lean tissue. Our previous analysis of DXA likewise found differential accuracy between the genders, in both children and adults (11). Puberty also was a significant predictor of the bias, with both average bias and its limits of agreement worsening with progression through puberty. This suggests that bias could be particularly problematic for longitudinal studies through puberty, however our own longitudinal analyses covered only a short time span (max 1.4 years).

For assessing change in adiposity over time, our analyses indicated no average bias, which might appear to indicate DXA may be adequate for comparing groups of individuals, for example in randomised trials. However, the limits of agreement in individuals are again large relative to the magnitude of changes taking place, indicating poor accuracy in individuals although ranking was more accurate, indicated by the r^2 value for between-method correlation of 76%. Several studies have previously shown that the accuracy of DXA alters over the range of nutritional status (10;11;19). Thus, for longitudinal changes in body weight that are greater than those observed in this study, accuracy of DXA in groups of individuals cannot be assumed, and further research should be conducted.

Our results are broadly consistent with previous analyses of DXA relative to the 4C model, with relatively limits of agreement in individuals, and a tendency to overestimate adiposity at the upper end of the BMI spectrum (10;11;19) although not all studies have reported this varying bias (9). However, studies of a wide range of nutritional status will not necessarily provide accurate information about the validity of DXA in those obese, a population in whom body composition assessment is particularly important for treatment assessment. Very few studies offer relevant data for such evaluation. In a study of 30 obese children and adolescents, Lunar Prodigy instrumentation over-estimated %fat by 1.9 %, with limits of agreement of ± 4.0 % (22). A study of 14 obese adults (BMI 28.7 to 39.9 kg/m^2) reported no mean bias but poor accuracy in individuals, with this error associated with tissue thickness

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as represented by waist girth (23). Decrease in % fat during weight loss was over-estimated in a study of 27 obese women (24). Our larger pediatric study is consistent in showing limitations of DXA in those obese (though see below for a discussion of variability between DXA instrumentation), and describes with greater confidence the degree of error associated with Lunar DXA in obese children and adolescents.

The main strengths of this study comprise the large sample size, the wide range of adiposity incorporated, and the use of the 4C model as the reference method, as this approach is robust to the alterations in lean tissue composition that we have reported previously (7;8). The main limitation is the lack of statistical power to assess agreement across ethnic groups, however our preliminary analyses offer little indication of such differential bias, and our results are likely to apply broadly to the obese population as a whole. It should not be assumed automatically that our findings apply to other DXA instrumentation, as different manufacturers utilise different algorithms for converting radiographic data to body composition values. The problems indicated here are likely to be in part generic to DXA, and studies of obese individuals using Lunar, Hologic and Norland instrumentation have all shown wide limits of agreement in individuals. However, while some instruments over-estimate adiposity (Lunar: (22); Hologic: (24)), others generate under-estimates (Norland: (25)) and others show no mean bias (Lunar: (23)). Thus, further work is required to establish the validity of DXA for body composition assessment in those obese across the range of instrumentation.

In conclusion, this study highlights the limitations of DXA using Lunar Prodigy instrumentation for body composition assessment in the obese populations. Difficulties in scanning heavier and larger individuals could potentially be addressed by the manufacturers, increasing the weight-bearing capacity and scanning area of the instrumentation. However, the wide limits of agreement in individuals, both for cross-sectional and longitudinal analyses, suggest that Lunar Prodigy instrumentation has significant limitations for high quality research studies investigating the efficacy of obesity weight loss treatment programmes on body composition.

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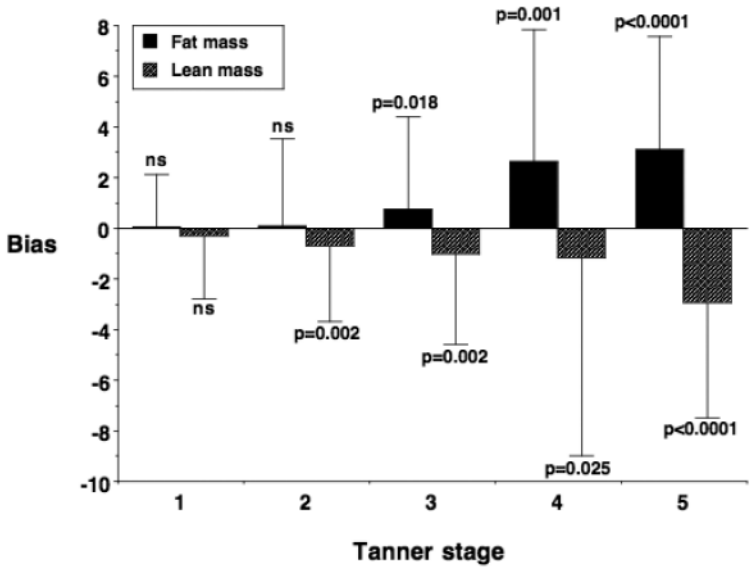

Figure 1.
Mean bias in fat mass and lean mass, calculated as the DXA value – 4C value, according to pubertal stage. The error bars represent the limitations of agreement, calculated as twice the standard deviation of the mean bias.

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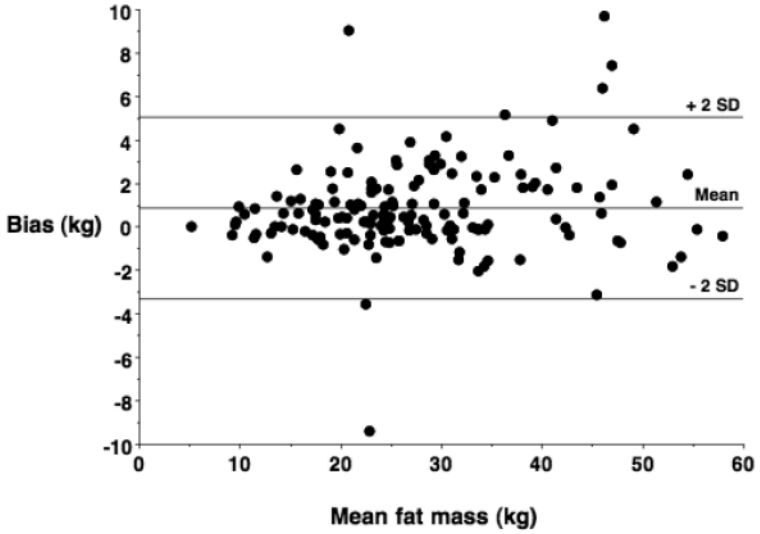

Figure 2.
Bland Altman analysis of the agreement between techniques for fat mass, in 153 individuals. The bias is calculated as DXA value – 4C value.

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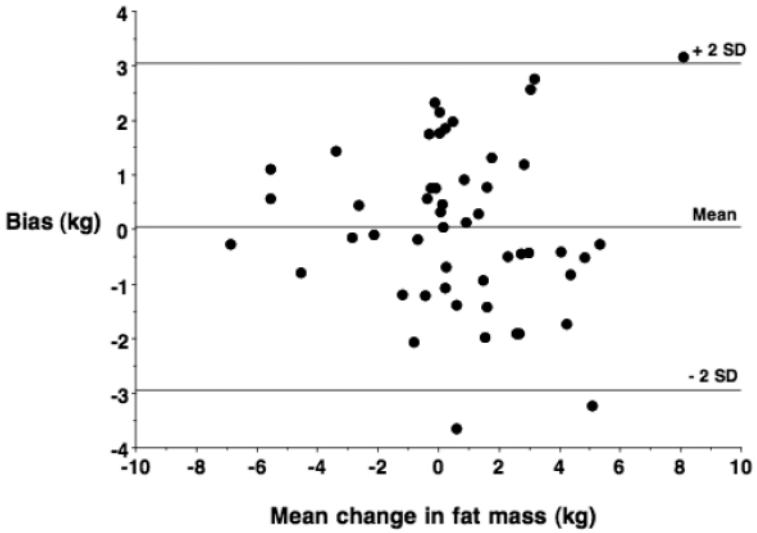

Figure 3.
Bland Altman analysis of the agreement between techniques for change in fat mass, in 51 individuals. The bias is calculated as DXA value – 4C value.

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Table 1

Description of the cross-sectional sample

	Boys (n = 57)			Girls (n = 96)		
	Mean	**SD**	**Range**	**Mean**	**SD**	**Range**
Age (years)	12.0	3.2	5.0, 20.0	11.3	3.3	5.0, 21.7
Weight SDS	2.5	0.9	1.1, 4.8	2.6	0.9	0.9, 4.8
Height SDS	0.8	1.2	−2.2, 3.9	1.0	1.0	−2.1, 3.8
BMI SDS	2.7	0.7	1.7, 4.7	2.7	0.7	1.6, 4.5
Weight (kg)	67.8	20.3	24.3, 107.4	64.7	20.5	28.4, 112.3
Body volume (L)	67.5	20.4	23.6, 109.4	64.6	20.6	28.5, 114.0
Body water (L) *	31.7	9.7	14.5, 50.7	28.3	8.1	12.8, 48.9
Bone mineral (kg)	2.0	0.7	0.8, 3.7	1.9	0.7	0.7, 4.0
4C fat-free mass (kg) *	41.2	12.9	18.8, 68.6	37.2	11.0	16.6, 63.9
4C fat mass (kg)	26.7	10.8	5.1, 55.4	27.4	10.7	9.5, 58.1
Hydration (%) **	77.1	2.2	71.5, 83.9	75.9	2.1	68.0, 81.3
DXA 4C fat-free mass (kg) *	40.5	12.5	18.8, 66.0	36.0	10.0	16.6, 59.4
DXA fat mass (kg)	27.4	10.6	5.2, 55.3	28.4	11.5	9.6, 57.7

BMI - body mass index; SDS – standard deviation score; 4C - 4 component model

* males > females, $p<0.05$

** males > females, $p<0.001$

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Table 2

Details of the baseline characteristics and subsequent change in the longitudinal sample (n = 51)

	Baseline value		Change during longitudinal study			
	Mean	**SD**	**Mean**	**SD**	**Range**	**p** *
Age (years)	10.7	2.2	0.6	0.2	0.4, 1.4	<0.0001
Weight SDS	2.8	0.8	−0.1	0.2	−0.8, 0.3	0.003
BMI SDS	3.0	0.6	−0.1	0.2	−0.9, 0.2	<0.0001
Weight (kg)	65.3	16.9	2.4	3.9	−8.2, 13.0	<0.0001
4C fat-free mass (kg)	36.9	9.0	1.7	2.0	−2.5, 6.6	<0.0001
4C fat mass (kg)	28.5	9.1	0.6	3.0	−6.7, 6.7	0.13
DXA fat-free mass (kg)	35.7	8.5	1.7	1.8	−2.7, 5.4	<0.0001
DXA fat mass (kg)	29.3	9.4	0.7	2.9	−7.0, 9.6	0.1

Sample comprised of 18 boys, 33 girls

* by paired t-test between baseline and follow up values.

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Table 3

Bias and limits of agreement of DXA compared to the 4 component model for baseline body composition and its change (n = 51)

	Fat-free mass					Fat mass				
	Bias (kg)	LOA (kg)	p	r	p	Bias (kg)	LOA (kg)	p	r	p
All	−1.00	4.20	<0.0001	−0.32	<0.0001	0.86	4.19	<0.0001	0.17	0.037
Boys	−0.67	2.96	0.001	−0.24	0.07	0.69	3.07	0.001	−0.19	0.16
Girls	−1.20	4.75	<0.0001	−0.43	<0.0001	0.96	4.74	<0.0001	0.30	0.003
	Change in fat-free mass					Change in fat mass				
	Bias (kg)	LOA (kg)	p	r	p	Bias (kg)	LOA (kg)	p	r	p
All	−0.02	3.16	0.9	−0.18	0.2	0.04	3.00	0.8	−0.06	0.6

LOA – limits of agreement, calculated as twice the standard deviation of the bias. 18 boys, 33 girls.

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Table 4

Multiple regression analysis for the factors associated with DXA bias in fat mass estimation

	B	SE	p
Model 1			
Constant	−13.125	6.082	0.033
Fat-free mass (kg) *	0.131	0.019	<0.0001
Fat mass (kg) *	−0.064	0.020	0.002
Hydration of fat-free tissue (%)	0.119	0.075	0.12
Female sex	1.022	0.342	0.003
Model 2			
Constant	−1.917	0.519	<0.0001
Fat-free mass (kg) *	0.061	0.022	0.006
Fat mass (kg) *	−0.038	0.019	0.042
Pubertal status	0.574	0.160	<0.0001

* average value by DXA and 4C model