Published in final edited form as:

J Clin Densitom. 2018 ; 21(2): 281–294. doi:10.1016/j.jocd.2017.01.007.

Cross-calibrated DXA Scanners Demonstrate Systematic Bias in Pediatric and Young Adult Females

Jodi N. Dowthwaite, Ph.D.^{1,2}, Kristen A. Dunsmore, M.S.², Dongliang Wang, Ph.D.³, Paula F. Rosenbaum, Ph.D.³, and Tamara A. Scerpella, M.D.^{1,4}

¹Dept. of Orthopedic Surgery, SUNY Upstate Medical University, Syracuse, NY

²Dept. of Exercise Science, Syracuse University, Syracuse, NY

³Dept. of Public Health and Preventive Medicine, SUNY Upstate Medical University, Syracuse, NY

⁴Dept. of Orthopedics and Rehabilitation, University of Wisconsin, Madison, WI

Abstract

Background—Consistency of DXA scan results is critical for data integrity. For pediatric subjects, the extent to which cross-calibration of DXA scanners alleviates model to model scanner differences is unclear. In the current study, DXA bone outcomes were compared for same-day measurements performed using different scanners, cross-calibrated to alleviate discrepancies (Hologic: Discovery A (DISCO); QDR 4500W (QDR)).

Methods—Inter-scanner differences were evaluated in approximately 130 females, age 8 to 24 years. Scans were performed in a single session on both QDR and DISCO scanners to compare projected area, bone mineral content (BMC), and areal bone mineral density (BMD) output for whole body (total, sub-head, head, arm, leg), forearm (1/3 and ultradistal radius), lumbar spine (vertebra L3; L1–L4) and proximal femur (femoral neck). Paired t-tests evaluated inter-scanner differences; concordance correlation coefficients evaluated inter-scanner correlations. Root mean square error coefficients of variation (RMSECVs) were compared to same-day duplicate DISCO scan RMSECVs for approximately 30 adult females. Deming regression equations were generated for conversion of QDR to DISCO results and vice versa.

Results—Inter-scanner correlations were very high (95% CI for CCC > 0.90), for all outcomes except femoral neck area and sub-head area, (95% CI for CCC = 0.83 to 0.94; 0.57 to 0.73).

However, QDR values were systematically lower than Discovery values ($p < 0.05$), except head area, head BMC, head BMD, ultradistal BMD (QDR > Discovery, $p = 0.05$) and L1–L4 area, L3 area, femoral neck BMD (no differences). Most Bland-Altman and Deming regression plots indicated good inter-scanner agreement, with little systematic variation based on bone/body size.

Corresponding Author: Jodi N. Dowthwaite, Ph.D., Department of Orthopedic Surgery, SUNY Upstate Medical University, 750 E. Adams St., Syracuse, NY, 13210, Phone: (315) 464-9981; Fax: (315) 464-6638; dowthwaj@upstate.edu.

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The authors have no conflicts of interest to disclose.

Conclusion—In pediatric and young adult females, subtle but systematic differences were noted between scans obtained on DISCO and QDR scanners, despite cross-calibration, such that most outcomes are systematically higher for Discovery A than QDR 4500W. Use of conversion equations is warranted.

Keywords

Analysis Quantitation of Bone; DXA; Quality Control; Pediatric; Female

INTRODUCTION

Densitometry relies upon consistent DXA scan results to evaluate stability of patient status with progression of time. In particular, when patients are monitored to determine treatment efficacy, it is important to know whether differences between assessments exceed the least significant change or smallest detectable difference, indicating an actual difference between measurements, or whether the difference between assessments falls within expected measurement error.^(1,2) When patients are tracked across time using a single scanner, inter-measurement error is presumed to be fairly consistent and without systematic bias. However, when a facility replaces or upgrades aging equipment with a newer scanner model, a systematic bias may be introduced, generating a predictable distinction between scans performed using the old versus the new scanner. While scans from older scanner models may be reanalyzed using new software to reduce software-based differences, reanalysis cannot compensate for hardware differences. Cross-calibration of the new scanner with the old scanner is recommended to minimize variability between scanners, but hardware-related differences may persist despite cross-calibration.⁽³⁾ Accordingly, it is important to compare repeated DXA measurements performed on different scanner models, evaluating them in the context of repeated measurements on a single scanner model.

Most DXA precision studies have been performed in adults,^(2,4–9) due to concerns about the accumulation of radiation doses in immature, growing subjects.^(10,11) Accordingly, although there are published studies evaluating intra-scanner error in infants⁽¹²⁾ and pediatric subjects,^(13–15) we are not aware of any published studies evaluating scanner model-related bias in pediatric subjects. The evaluation of precision error is important in children and adolescents, as repeated measurements are expected to change over time due to growth.⁽¹⁵⁾ In this population, growth in area and bone mineral content is potentially large; thus, it is essential to determine variability in bone outcomes that is associated solely with improvements in bone edge detection as a result of hardware changes. For the small bones of immature subjects, we hypothesize that a minor difference in edge detection-related bone geometry and mass may result in a relatively large percent difference for these key outcomes. Thus, we performed the current study to evaluate differences between repeated scans performed on the same day, using a Hologic QDR scanner and a cross-calibrated Hologic DISCO scanner; the latter has been purposefully improved to enhance edge-detection.

MATERIALS AND METHODS

Prior to study commencement, all protocols were approved by our Institutional Review Board. The research was performed in accordance with the Declaration of Helsinki. In order to thoroughly evaluate potential effects of age and body size on inter-scanner variability, we evaluated 133 females, approximately 8 to 24 years of age, representing pre-puberty through young adulthood (pre-peak bone mass=PRE-PBM). Mature participants had been participating in an ongoing longitudinal study of bone growth for at least 5 years, with all prior scans performed on the QDR4500W scanner. Immature subjects were new recruits for the longitudinal study with no prior DXA data. Scans of the entire age and body size range were performed to develop a correction equation for application to pre-existing QDR4500W scans of mature participants (spanning age 8 to 24 years). In this manner, future longitudinal growth analyses comprising scans from all study participants would account for inter-scanner discrepancies, as all scan data could be converted to be “Discovery A equivalent”. In addition, approximately 30 pre- and post-menopausal adult women (post-peak bone mass=ADULT), age 37 to 58 years, participated in same-day, duplicate scans, with repositioning between scans, to allow comparisons of inter-scanner versus intra-scanner variation. To minimize radiation exposure, PRE-PBM participants were not subjected to additional duplicate scans using the DISCO scanner, as these females are participants in a long-term, longitudinal study of bone growth that includes repeated, annual DXA scans.

Same day scans of whole body (total, sub-head, arms and legs), non-dominant radius (1/3 and ultradistal), lumbar spine (vertebrae L1–L4 (total); isolated vertebra L3 for evaluation of paired postero-anterior – lateral scan data) and left proximal femur (femoral neck) were performed on each PRE-PBM participant using the Hologic QDR and DISCO scanner models. All scans were performed using “array mode” (mode 11), except for a subset of hip (n= 24/130) and spine (n=23/132) scans (fast array mode= mode 12). These exceptions represent approximately 50% of pre-PBM hip and spine scans performed in “mature” subjects, age 15.9 to 23.9 years. On this basis, discrepancies between DISCO array and QDR fast array results were specifically evaluated within that age group using independent samples t-tests.

By definition, subjects were re-positioned between scans, as the subject had to move from one machine to the other. As recommended by the 2013 ISCD Position Statement [<http://www.iscd.org/official-positions/2013-iscd-official-positions-adult/>], these duplicate scans represent the work of both of our New York State certified DXA technologists who routinely perform scans for our longitudinal bone growth study, thereby reflecting a composite of the general lab operating procedures.

Scans were analyzed by a single investigator on the DISCO scanner, using Apex software version 12.7.3; thus, any discrepancies between models are not attributable to software differences or to inter-observer analysis error (intra-observer analysis error only). This investigator was trained in scan analysis by Hologic personnel (10/2008) and completed the ISCD Pediatric Densitometry Course (2009); she has routinely analyzed all longitudinal bone growth study DXA scans since completing that training, reanalyzing all prior scans (1998–2008) on the DISCO scanner using Hologic software version 12.7.3. The “compare”

feature was not used on duplicate scans; this feature is not used in our longitudinal bone growth study, as the morphological changes that occur from pre-puberty to adulthood are deemed too extreme to make appropriate use of this feature. To maximize comparability of results with immature scan analyses, we did not use compare mode in adult scan analyses. To maximize concordance of regions of interest, scan pairs for each participant and region of interest were analyzed back-to-back in the same analysis session (e.g. Subject X: QDR proximal femur and DISCO proximal femur). One subtle difference between our analysis method for radius scans and standard adult Hologic positioning methods is that we base region of interest positioning on the **radius alone** to avoid problems generated by inter- and intra-subject variability in the relative positions of the distal articular surfaces of the radius and ulna during growth. These radius scan positioning methods were used on all subjects, both pre-PBM and post-PBM. Using these methods, DXA model outcomes were compared for projected area, bone mineral content (BMC), and areal bone mineral density (BMD).

Statistical Analysis

Subject characteristics are presented as means and standard deviations, with frequencies for Tanner stages. We performed paired t-tests to evaluate the significance and direction of inter-scanner differences. We used independent samples t-tests to evaluate differences between array and fast array mode scans in mature subjects; we also compared mean differences for these scan sub-groups against those of immature subjects (consistent array mode scans). Concordance correlation coefficients were calculated to measure the correlation and agreement between QDR and DISCO results. We performed Deming regressions to generate reversible conversion equations for translating QDR results to DISCO results (and vice versa), incorporating estimates of measurement error for both measurement methods, with measurement errors assumed to be independent and normally distributed.

In addition, inter-scanner agreement for DXA bone outcomes was evaluated using Bland-Altman plots of mean bone outcome (X axis) versus inter-scanner difference (Y-axis, subtracting QDR results from DISCO scanner results; $\text{Diff} = \text{DISCO bone outcome} - \text{QDR bone outcome}$). Mean differences and ± 2 standard deviation intervals for differences were calculated (Table 3) and plotted (Figures 1, 2, 3, and 4). For Bland-Altman plots (Figures 1–4), X-axis scales were set to accommodate the largest and smallest means for each bone outcome; Y-axes were centered at zero difference, set to match the X-axis spread.

The method of Glüer and colleagues (16) was used to calculate root mean square error coefficients of variation (RMSECVs) to assess inter-scanner differences for DXA bone outcomes for the pre-PBM group as a whole, and separately, for pediatric (8–12 yrs) and late adolescent (13–24 yrs) subgroups. Separate RMSECVs were calculated in the ADULT cohort to allow comparison of *inter*-scanner differences in the pre-PBM cohort against *intra*-scanner differences in the ADULT cohort.

RESULTS

One hundred thirty-three young (PRE-PBM) participants were scanned for the main body of the current analyses. PRE-PBM subject characteristics are shown in Table 1. Chronological age ranged from 7.8 to 23.9 years of age (mean 13.4, sd 4.9). Biological age ranged from at

least 5.7 years pre-menarche to 11.0 years post-menarche (some subject menarche dates remain unknown). The comparison group of adult women (ADULT) for DISCO same-day duplicate RMSECVs (intra-scanner variation) was comprised primarily of pre-menopausal women, aged 37.5 to 57.8 years of age (POST-PBM mean: 45.6 years, sd: 4.7).

Table 2 presents paired t-test results. For most bone outcomes, results from separate scanners were significantly different. In general, DISCO values were higher than QDR values ($p < 0.03$). However, DISCO results were lower than QDR for: head area, head BMC, head BMD ($p < 0.001$) and ultradistal radius BMD ($p = 0.03$). Significant differences were not detected between DISCO and QDR results for femoral neck BMD ($p = 0.485$) or lumbar spine area (L1-L4 or L3, $p = 0.590$).

Table 3 presents inter-scanner concordance correlation coefficients, as well as mean differences (± 2 standard deviations) between scanner models for all outcomes. Whole body, lumbar spine, femoral neck and distal radius outcomes demonstrated extremely high positive inter-scanner correlations ($CCC > 0.90$, 95% CI > 0.90), except sub-head area and femoral neck area; the latter correlations were moderate ($CCC = 0.66$, 95% CI = 0.57 to 0.73) and strong ($CCC > 0.89$, 95% CI = 0.83 to 0.94), respectively.

Mean differences are also depicted in Bland-Altman plots (Figures 1–4). As noted above, other than for ultradistal BMD, lumbar spine area (L1–L4 and L3) and head outcomes, mean DISCO minus QDR differences are positive. Based on Bland-Altman plots, inter-scanner bias appears to be consistent based on body size and bone properties, other than subtle indications of greater QDR underestimations of BMC in larger bodies for sub-head and arm regions of interest. Deming regression plots depict these relationships in an alternative manner, accounting for measurement errors of both methods and depicting 95% confidence intervals for the lines of best fit (Supplementary Figures 5–16). Deming regression coefficients (Table 4) are often statistically significant, indicating that to convert QDR 4500W scanner results to “Discovery A Equivalent” scan results, one must account for subtle but systematic differences. In some cases, these differences are mild, but slightly more severe, in subjects of larger body size. For a detailed analysis of these differences, and to view the Deming regressions plots, see supplementary materials.

Table 5 presents the RMSECVs for each bone outcome (intra-scanner: ADULT; inter-scanner: PRE-PBM; pediatric, adolescent). In most cases, the inter-scanner coefficients of variation for PRE-PBM are much higher than the intra-scanner coefficients of variation for ADULT. As discussed below, for most outcomes, these RMSECV comparisons present a misleading indication of the magnitude of inter-scanner vs. intra-scanner discrepancies. As shown in the Bland-Altman plots (Figures 1–4) and Deming regression plots, for most sites, the mean differences for BMC and BMD are close to zero, with relatively little spread around the Y-axis origin, or line of identity, respectively.

The contribution of scan mode to differences was evaluated using independent samples t-tests for subjects age 15 to 24 years (fast array vs. array mode), with mean differences compared against those of immature subjects (consistent scan mode-array only). Femoral neck scanner discrepancies did not differ based on scan mode within this cohort,

biologically mature age group ($p > 0.48$). In contrast, lumbar spine scanner discrepancies did differ based on scan mode for L3 area, L3 BMD, LS area and LS BMC ($p < 0.05$). Area was overestimated by fast array mode (mean difference: L3 area 0.24 cm^2 ; LS area 0.20), rather than underestimated by array mode (mean difference: L3 area -0.19 cm^2 ; LS area -0.97). Effectively, immature subjects' mean scanner differences for area were closer to zero, between fast array and array results (age 8.0 to 14 years: mean difference: L3 area -0.05 cm^2 ; LS area 0.08 cm^2). LSBMC was overestimated to a greater extent by fast array mode (mean difference: L3BMC 0.54 g , LSBMC 1.57 g) than by array mode (mean difference: L3BMC 0.34 g , LSBMC 0.66 g); once again, immature subjects' BMC scanner discrepancies were smaller and more in line with mature subject array mode (array only, mean difference L3BMC 0.20 g , LSBMC 0.72). For L3 BMD, fast array mode mean differences were actually smaller than those for array mode (fast array: 0.02 g/cm^2 ; array 0.04 g/cm^2); immature subject scanner discrepancies were in line with fast array mode (0.02 g/cm^2). Thus, on the whole, lumbar spine BMD results were similarly reliable regardless of scan mode and subject age, but lumbar spine area and BMC results were more adversely affected by fast array scan modes in mature subjects of larger body sizes; femoral neck scanner discrepancies did not appear to be differentially affected by scan mode.

DISCUSSION

Bland-Altman plots (Figures 1–4) and associated mean differences (Table 3) present relevant indications of the level of inter-scanner discrepancies and their systematic nature, corroborated by significant paired t-test results. As indicated by Deming regressions, for most variables, even if differences are significant, the mean difference between scanners is relatively low and close to zero. In cases where there were apparently systematic differences based on body size, these slope differences were subtle, $\sim 5\%$, except for whole body sub-regions (arm area and BMC (8–12%), head BMC (6%)). One can compensate for these systematic differentials using regression equations to convert QDR to DISCO results, and vice versa, achieving extremely high correlations in most cases (Deming Regression coefficients, Table 4; supplementary figures). For whole body, sub-head, radius and lumbar spine, inter-scanner agreement was excellent for all outcomes, as was agreement for FNBMC and FNBMD. As would be expected, in all cases, our *inter*-scanner coefficients of variation are higher than comparable *intra*-scanner coefficients of variation, as reported by Shepherd et al.⁽¹⁵⁾ For variables where the influence of bone geometric variability and positioning was large (for both subject and analysis boxes), the inter-scanner discordance was also larger (e.g. FN area, whole body sub-regions); this phenomenon was generally supported by parallel elevation of intra-scanner discordance in ADULT results (Table 5).

Because all scans were analyzed on the DISCO machine, using Apex software version 12.7.3, inter-scanner differences cannot be attributed to software discrepancies. The broadly positive differentials between DISCO and QDR results may represent the hardware improvements made by Hologic engineers to yield superior bone edge detection; for most regions of interest, hardware differences result in Discovery detection of higher bone areas, bone mineral contents and areal densities that increase in proportion with body size (ie. larger bones, larger QDR underestimates). The QDR4500W has a fixed 1mm aperture, with less than half the number of detectors and detectors twice the size of those utilized in

Discovery A scanners. Furthermore, the Discovery A has the added improvement of a selectable aperture that is set at 1 mm for hip, spine and WB (fast or array scans), but is set at 0.5mm for forearm scans. As a result of its technical limitations, the QDR4500W averages data from the two nearest detectors; in contrast, the Discovery A has more detectors with narrower fields and the capacity for finer aperture selection. Accordingly, the Discovery A edge detection improvement is a function of the use of twice as many “true pixels” compared to the QDR4500W. This hardware improvement clearly yields superior image quality as sensed by the human eye, but to our knowledge, studies in adults have not noted systematic scanner-related differences in results between cross-calibrated scanners. To our knowledge, our results are the first evidence of a subtle difference in densitometric results in vivo for comparisons of these scanner models.

The main exceptions to higher results in DISCO vs. QDR scans are for head outcomes. For the head, it may be that the bone edges in this hyper-dense region of interest are blurred by QDR thresholding and “rounded up”, leading to inclusion of non-bone tissue in area and bone mass readings (QDR>DISCO). In contrast, most other regions of interest are of lower overall density, so blurred edges appear to be “rounded down” by QDR thresholding, leading to exclusion of bone tissue from area and BMC readings (QDR<DISCO). For the head region of interest, pediatric positional variability may play a very large role, in both subject scan and analysis box positioning, thereby inflating inter-scan variability regardless of scanner model variability (e.g. subtle differences in head position (greater maxilla/mandible projected area)). For lumbar spine area, DISCO-QDR differences are negative; this may be due to differences in DISCO analysis box positioning to accommodate bone geometric properties based upon supine lateral paired scans, which are NOT discernible using the QDR scanner (postero-anterior view only).

Interestingly, whole body area, BMC and BMD agreement was superior to agreement for sub-head outcomes. These findings call into question the ISCD recommended practice of using total body less head (sub-head) BMC rather than whole body BMC for pediatric assessment.^(17,18) It is clear that the head dominates BMC assessments very early in growth, contributes a significantly decreasing proportion of BMC in the whole body region as growth progresses, and, at younger ages, inclusion of the head may mask important decrements in post-cranial bone mass that are more relevant to overall fracture risk. However, when assessing older girls (age 9.0 and higher), these issues appear to be of lower concern, as the head contributes a smaller proportion of bone mass to the whole body assessment, and the variability of the head to whole body BMC ratio across time is less extreme. We have used a subset of our substantial longitudinal DXA database (n=98), for subjects with known menarche dates and data representing growth from at least 1 year pre-menarche (age <12.0 years) beyond menarche to evaluate this concern, including numerous late-maturing individuals (16% age at menarche >14.0 years). In our sample, head to whole body BMC ratio stabilizes by menarche (varies by less than 5% of “adult” ratio, for all but one subject). Few subjects exhibited more than a 10% difference in head BMC to whole body BMC ratio, relative to their adult ratio (n=7); and the maximum differential in ratio was 13%. Most differentials >10% were exhibited in subjects <9.0 years old (n=4). By age 12 years, no subjects exhibited a deficit of 10% in head to whole body BMC ratio relative to their latest post-menarcheal assessment (“adult” proportion). On this basis, it may be

preferred to monitor girls age 9.0 years or greater using full whole body measures rather than sub-head measures, as positional variability (subject and analysis box) appear to be more influential than immature head to whole body BMC proportions in this age group, and sub-head data reliability is lower than reliability for whole body data. Our data cannot be generalized to males, who mature over a longer timescale.

Limitations

To minimize radiation exposure for PRE-PBM participants in the longitudinal study of bone growth, we did not subject them to a third same day scan (duplicate scan on DISCO scanner). Accordingly, the use of comparison data from ADULT subjects may have affected our RMSECV comparisons. As shown in Table 5, the RMSECVs for inter-scanner comparisons (PRE-PBM subjects) are much higher than those for intra-scanner comparisons (ADULT subjects). However, in some cases, this may be partly a function of there being much higher variability and lower grand mean values for each bone outcome among PRE-PBM subjects than among ADULT subjects. Since the root mean square error (numerator=function of total sample variability) is divided by the grand mean value (denominator), the RMSECV is always higher for inter-scanner comparisons in the PRE-PBM subjects than for intra-scanner comparisons in the ADULT subjects. In other words, mathematically, a larger value divided by a smaller value will always yield a larger value than a smaller value divided by a larger value. Thus, the high variability across different PRE-PBM subjects (inter-individual variation) and the low grand mean values for PRE-PBM subjects may sometimes be a factor in the higher inter-scanner RMSECV relative to intra-scanner RMSECVs for ADULT subjects. Our inter-scan discrepancies may be elevated relative to other labs due to our decision not to use the compare analysis feature; however, we do not believe that this is the source of the observed systematic inter-scanner biases. Finally, our Deming regression equations should only be used for conversions between Hologic scanners of these two model types (QDR4500W and Discovery A).

Conclusion

Most Bland-Altman plots indicated good agreement between measurements obtained on Discovery A and QDR4500W scanners. In PRE-PBM subjects, systematic differences were noted, despite cross-calibration, with most outcomes being systematically higher for DISCO than QDR. In the event that substitution of scanners is required for serial measurements of patients or research subjects, it would be advisable to repeat measurements on each scanner within a single session to evaluate and address any systematic bias. Our regression-based conversion equations may provide a relatively simple method to address systematic scanner bias for DISCO A and QDR 4500W models, when duplicate assessments of pediatric and young adult subjects are not possible. Additional studies in young males are necessary.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

All of the authors have approved final version. This research was supported by NIAMS R01 and by bridge funding from XXXXX. The sponsors had no influence upon any aspect of study conduct or presentation of results.

References

1. Blake GM, Fogelman I. How important are BMD accuracy errors for the clinical interpretation of DXA scans? *J Bone Miner Res*. 2008; 23(4):457–462. [PubMed: 18052754]
2. El Maghraoui A, Do Santos Zounon AA, Jroundi I, Nouijai A, Ghazi M, Achemlal L, et al. Reproducibility of bone mineral density measurements using dual X-ray absorptiometry in daily clinical practice. *Osteoporos Int*. 2005; 16(12):1742–1748. [PubMed: 15937633]
3. Blake GM. Replacing DXA scanners: cross-calibration with phantoms may be misleading. *Calcif Tissue Int*. 1996; 59(1):1–5. [PubMed: 8661987]
4. Fan B, Lewiecki EM, Sherman M, Lu Y, Miller PD, Genant HK, et al. Improved precision with Hologic Apex software. *Osteoporos Int*. 2008; 19(11):1597–1602. [PubMed: 18373054]
5. Knapp KM, Welsman JR, Hopkins SJ, Fogelman I, Blake GM. Obesity increases precision errors in dual-energy X-ray absorptiometry measurements. *J Clin Densitom*. 2012; 15(3):315–319. [PubMed: 22402120]
6. Knapp KM, Welsman JR, Hopkins SJ, Shallcross A, Fogelman I, Blake GM. Obesity Increases Precision Errors in Total Body Dual-Energy X-Ray Absorptiometry Measurements. *J Clin Densitom*. 2014 2014 Jul 31.
7. Rajamanohara R, Robinson J, Rymer J, Patel R, Fogelman I, Blake GM. The effect of weight and weight change on the long-term precision of spine and hip DXA measurements. *Osteoporos Int*. 2011; 22(5):1503–1512. [PubMed: 20700581]
8. Shepherd JA, Fan B, Lu Y, Lewiecki EM, Miller P, Genant HK. Comparison of BMD precision for Prodigy and Delphi spine and femur scans. *Osteoporos Int*. 2006; 17(9):1303–1308. [PubMed: 16823544]
9. Shepherd JA, Lu Y. A generalized least significant change for individuals measured on different DXA systems. *J Clin Densitom*. 2007; 10(3):249–258. [PubMed: 17616413]
10. Blake GM, Naeem M, Boutros M. Comparison of effective dose to children and adults from dual X-ray absorptiometry examinations. *Bone*. 2006; 38(6):935–942. [PubMed: 16376161]
11. Linet MS, Kim KP, Rajaraman P. Children's exposure to diagnostic medical radiation and cancer risk: epidemiologic and dosimetric considerations. *Pediatr Radiol*. 2009; 39(Suppl 1):S4–26. [PubMed: 19083224]
12. de Knecht VE, Carlsen EM, Bech Jensen JE, Lade Rasmussen AM, Pryds O. DXA performance in a pediatric population: precision of body composition measurements in healthy term-born infants using dual-energy X-ray absorptiometry. *J Clin Densitom*. 2015; 18(1):117–123. [PubMed: 25439455]
13. Jaworski M, Pludowski P. Precision errors, least significant change, and monitoring time interval in pediatric measurements of bone mineral density, body composition, and mechanostat parameters by GE lunar prodigy. *J Clin Densitom*. 2013; 16(4):562–569. [PubMed: 23452871]
14. Leonard CM, Roza MA, Barr RD, Webber CE. Reproducibility of DXA measurements of bone mineral density and body composition in children. *Pediatr Radiol*. 2009; 39(2):148–154. [PubMed: 19052738]
15. Shepherd JA, Wang L, Fan B, Gilsanz V, Kalkwarf HJ, Lappe J, et al. Optimal monitoring time interval between DXA measures in children. *J Bone Miner Res*. 2011; 26(11):2745–2752. [PubMed: 21773995]
16. Gluer 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):262–270. [PubMed: 7492865]
17. Schousboe JT, Shepherd JA, Bilezikian JP, Baim S. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry. *J Clin Densitom*. 2013; 16(4):455–466. [PubMed: 24183638]

18. 2013 Official Positions-Pediatric. Available at: <http://www.iscd.org/official-positions/2013-iscd-official-positions-pediatric/> Accessed 10/24/16

Figure 1. Distal Radius: Discovery A vs. QDR 4500W Bland-Altman Plots. The associated plots present the mean of Discovery and QDR measurements (X-axis) plotted against the

difference between the Discovery and QDR measurements (DISCO – QDR). The mean difference between the two measurements is plotted on the X-axis (bold grey line), with ± 2 standard deviation range plotted using dotted lines. The scale range of the X-axis has been plotted as equivalent to the Y-axis scale range for appropriate context.

Figure 2.

Lumbar Spine: Discovery A vs. QDR 4500W Bland-Altman Plots. The associated plots present the mean of Discovery and QDR measurements (X-axis) plotted against the difference between the Discovery and QDR measurements (DISCO – QDR). The mean difference between the two measurements is plotted on the X-axis (bold grey line), with ± 2 standard deviation range plotted using dotted lines. The scale range of the X-axis has been plotted as equivalent to the Y-axis scale range for appropriate context.

Figure 3.

Femoral Neck: Discovery A vs. QDR 4500W Bland-Altman Plots. The associated plots present the mean of Discovery and QDR measurements (X-axis) plotted against the difference between the Discovery and QDR measurements (DISCO – QDR). The mean difference between the two measurements is plotted on the X-axis (bold grey line), with ± 2 standard deviation range plotted using dotted lines. The scale range of the X-axis has been plotted as equivalent to the Y-axis scale range for appropriate context.

Figure 4.

Whole Body Bone: Discovery A vs. QDR 4500W Bland-Altman Plots. The associated plots present the mean of Discovery and QDR measurements (X-axis) plotted against the difference between the Discovery and QDR measurements (DISCO – QDR). The mean difference between the two measurements is plotted on the X-axis (bold grey line), with ± 2 standard deviation range plotted using dotted lines. The scale range of the X-axis has been plotted as equivalent to the Y-axis scale range for appropriate context.

Table 1

Pre-Peak Bone Mass, Subject Characteristics

Variable	Mean or % Frequency	Standard Deviation	Minimum	Maximum
Chronological Age (years)	13.3	4.9	7.8	23.9
Tanner Breast Stage (% frequency)	I= 42.3%; II= 18.5%; III= 6.2%; IV= 7.7%; V= 25.4%		I	V
Tanner Pubic Stage (% frequency)	I= 50.0%; II= 10.0%; III= 5.4%; IV= 10.8%; V= 23.8%		I	V
Height (m)	146.8	15.14	116.0	178.5
Mass (kg)	42.9	14.7	20.4	91.2
Body Mass Index (kg/m ²)	19.3	3.5	13.5	29.0
Whole Body Percent Fat (%)	24.1	5.7	14.2	40.1
Waist Girth (cm)	64.5	9.7	49.0	110.5
Hip Girth (cm)	80.4	12.9	58.0	112.0

Table 2

Paired T-test Results for Mean Difference: Discovery A - QDR 4500W

Variable	Mean (sd)	median	range	Significance (p)
RADIUS (n=133)				
1/3 Radius Area	0.03 (0.07)	0.03	(-0.17, 0.25)	<0.001
1/3 Radius BMC	0.06 (0.04)	0.06	(-0.03, 0.16)	<0.001
1/3 Radius BMD	0.02 (0.01)	0.02	(-0.02, 0.06)	<0.001
UD Radius Area	0.11 (0.09)	0.11	(-0.27, 0.29)	<0.001
UD Radius BMC	0.04 (0.03)	0.04	(-0.12, 0.12)	<0.001
UD Radius BMD	-0.002 (0.01)	0.00	(-0.02, 0.02)	0.029
LUMBAR SPINE (n=132)				
L1-L4 Area	-0.08 (1.63)	-0.07	(-8.39, 4.82)	0.59
L1-L4 BMC	0.86 (1.22)	0.81	(-4.27, 5.28)	<0.001
L1-L4 BMD	0.02 (0.02)	0.02	(-0.07, 0.07)	<0.001
L3 Area	-0.02 (0.47)	-0.02	(-2.06, 1.07)	0.648
L3 BMC	0.28 (0.43)	0.26	(-1.11, 1.87)	<0.001
L3 BMD	0.02 (0.02)	0.02	(-0.04, 0.1)	<0.001
FEMORAL NECK AND NARROW NECK (n=130)				
FN Area	0.07 (0.21)	0.08	(-0.87, 1.09)	<0.001
FN BMC	0.05 (0.18)	0.05	(-0.35, 0.87)	0.001
FN BMD	0 (0.03)	0	(-0.07, 0.11)	0.485
WHOLE BODY (n=132)				
WB Area	20.27 (30.31)	18.97	(-52.79, 171.23)	<0.001
WB BMC	62.61 (35.25)	59.53	(-4.62, 207.8)	<0.001
WB BMD	0.03 (0.01)	0.03	(-0.01, 0.07)	<0.001
Sub-head Area	27.96 (30.56)	27.62	(-35.56, 180.05)	<0.001
Sub-head BMC	80.18 (36.44)	73.49	(14.43, 213.19)	<0.001
Sub-head BMD	0.04 (0.01)	0.04	(0, 0.08)	<0.001
Head Area	-7.69 (9.29)	-6.83	(-35.5, 17.31)	<0.001
Head BMC	-17.56 (16.6)	-18.3	(-82.9, 29.95)	<0.001
Head BMD	-0.02 (0.06)	-0.02	(-0.23, 0.12)	<0.001
Left Arm Area	12.29 (7.43)	11.74	(-7.72, 38.16)	<0.001
Left Arm BMC	10.8 (5.02)	10.04	(1.67, 26.58)	<0.001
Left Arm BMD	0.02 (0.02)	0.02	(-0.04, 0.08)	<0.001
Sum Arm BMC	23.95 (11.65)	22.08	(5.63, 71.46)	<0.001
Left Leg Area	11.68 (8.93)	11.82	(-19.19, 32.29)	<0.001
Left Leg BMC	22.54 (8.23)	22.53	(0.95, 54.2)	<0.001
Left Leg BMD	0.04 (0.03)	0.04	(-0.05, 0.14)	<0.001
Sum Leg BMC	43.3 (17.04)	40.32	(6.83, 88.31)	<0.001

Bold outcomes are lower in Discovery A than QDR4500W; Bold italic differences are not statistically significant

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Table 3

Concordance Correlation Coefficients with 95% Confidence Intervals and Inter-DXA mean differences ± 2 standard deviations

DXA Bone Outcomes	Concordance Correlation Coefficients		Discovery A minus QDR 4500W	
	CCC	95% CI	Mean Difference	(-2 sd to +2 sd)
RADIUS (n=133)				
1/3 Area (cm ²)	0.974	(0.963, 0.982)	+0.035	(-0.108 to +0.177)
1/3 BMC (g)	0.987	(0.984, 0.989)	+0.064	(-0.009 to +0.136)
1/3 BMD (g/cm ²)	0.979	(0.973, 0.983)	+0.018	(-0.010 to +0.047)
UD Area (cm ²)	0.964	(0.955, 0.972)	+0.106	(-0.071 to +0.284)
UD BMC (g)	0.994	(0.992, 0.995)	+0.036	(-0.026 to +0.098)
UD BMD (g/cm ²)	0.995	(0.994, 0.997)	-0.002	(-0.019 to +0.015)
LUMBAR SPINE (n=132)				
L1-L4 Area (cm ²)	0.987	(0.979, 0.992)	-0.077	(-3.337, +3.184)
L1-L4 BMC (g)	0.996	(0.995, 0.998)	+0.856	(-1.574, +3.287)
L1-L4 BMD (g/cm ²)	0.991	(0.988, 0.993)	+0.020	(-0.018, +0.058)
L3 Area (cm ²)	0.985	(0.978, 0.990)	-0.019	(-0.963, +0.926)
L3 BMC (g)	0.994	(0.992, 0.996)	+0.279	(-0.572, +1.129)
L3 BMD (g/cm ²)	0.987	(0.982, 0.990)	+0.023	(-0.024, +0.071)
FEMORAL NECK (n=130)				
FN Area (cm ²)	0.895	(0.833, 0.935)	+0.065	(-0.350 to +0.481)
FN BMC (g)	0.981	(0.971, 0.988)	+0.054	(-0.310 to +0.418)
FN BMD (g/cm ²)	0.986	(0.978, 0.991)	+0.002	(-0.054 to +0.057)
WHOLE BODY (n=132)				
WB Area (cm ²)	0.989	(0.984 - 0.993)	+20.531	(-40.147 to +81.209)
WB BMC (g)	0.982	(0.978 - 0.985)	+62.488	(-8.118 to +133.094)
WB BMD (g/cm ²)	0.966	(0.959 - 0.972)	+0.027	(-0.003 to +0.056)
Sub-head Area (cm ²)	0.660	(0.570 - 0.734)	+28.320	(-32.937 to +89.578)
Sub-head BMC (g)	0.966	(0.956 - 0.974)	+80.172	(+6.802 to +153.543)
Sub-head BMD (g/cm ²)	0.985	(0.981 - 0.989)	+0.041	(+0.013 to +0.069)
Head Area (cm ²)	0.923	(0.907 - 0.936)	-7.788	(-26.135 to +10.559)
Head BMC (g)	0.956	(0.947 - 0.964)	-17.685	(-50.795 to +15.426)
Head BMD (g/cm ²)	0.971	(0.962 - 0.978)	-0.022	(-0.143 to +0.100)
Left Arm Area (cm ²)	0.948	(0.936 - 0.958)	+12.504	(-1.986 to +26.994)
Left Arm BMC (g)	0.989	(0.984 - 0.993)	+10.877	(+0.831 to +20.923)
Left Arm BMD (g/cm ²)	0.982	(0.978 - 0.985)	+0.019	(-0.024 to +0.062)
Left Leg Area (cm ²)	0.966	(0.956, 0.974)	+11.678	(-6.292 to +29.648)
Left Leg BMC (g)	0.975	(0.970, 0.980)	+22.557	(+6.068 to +39.046)
Left Leg BMD (g/cm ²)	0.969	(0.960, 0.976)	+0.042	(-0.013 to +0.097)

CI= confidence intervals; sd= standard deviation; 1/3= 1/3 distal; UD= ultradistal; BMC= bone mineral content; BMD= areal bone mineral density; L1–L4, L3= lumbar vertebrae 1 – 4, vertebra 3; FN= femoral neck; WB= whole body

Bold italic =correlation coefficient < 0.89. **Bold** =negative mean difference.

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Table 4

Deming Regression Coefficients (Intercept, Slope)

DXA Bone Outcome	Intercept 95% CI			Slope 95% CI		
	β	Lower bound	Upper bound	β	Lower bound	Upper bound
Radius n = 133						
1/3 Area (cm ²)	-0.05	-0.13, 0.03		1.03		1, 1.07
1/3 BMC (g)	0.03	0.01, 0.04		1.03		1.01, 1.04
1/3 BMD (g/cm ²)	0.02	0.01, 0.03		0.99		0.97, 1.01
UD Area (cm ²)	0.13	0.04, 0.21		0.99		0.96, 1.02
UD BMC (g)	0.02	0.01, 0.03		1.01		1, 1.02
UD BMD (g/cm ²)	0	-0.01, 0		1		0.98, 1.02
Lumbar Spine n = 132						
L1-L4 Area (cm ²)	1.15	-0.19, 2.34		0.97		0.95, 1
L1-L4 BMC (g)	0.45	-0.02, 0.88		1.01		1, 1.02
L1-L4 BMD (g/cm ²)	0	-0.02, 0.01		1.03		1.02, 1.04
L3 Area (cm ²)	-0.15	-0.53, 0.22		1.01		0.98, 1.04
L3 BMC (g)	-0.01	-0.19, 0.15		1.03		1.01, 1.05
L3 BMD (g/cm ²)	0.01	-0.01, 0.02		1.02		1, 1.04
Femoral Neck n = 130						
FN Area (cm ²)	0.02	-0.49, 0.47		1.01		0.91, 1.13
FN BMC (g)	0.13	0.02, 0.25		0.98		0.94, 1.01
FN BMD (g/cm ²)	0.04	0.02, 0.06		0.95		0.92, 0.98
Whole Body n = 132						
WB Area (cm ²)	6.09	-22.06, 32.18		1.01		0.99, 1.03
WB BMC (g)	12.16	-2.5, 27.98		1.03		1.02, 1.04
WB BMD (g/cm ²)	0.01	-0.01, 0.03		1.02		1, 1.04
Sub-head Area (cm ²)	8.49	-15.73, 31.3		1.01		1, 1.03
Sub-head BMC (g)	20.28	7.14, 33.2		1.05		1.04, 1.07
Sub-head BMD (g/cm ²)	0.02	0.01, 0.04		1.02		1, 1.04

DXA Bone Outcome	Intercept 95% CI			Slope 95% CI		
	β	Lower bound	Upper bound	β	Lower bound	Upper bound
Head Area (cm ²)	16.9	-13.92, 38.68		0.89	0.79, 1.03	
Head BMC (g)	3.25	-6.45, 14.4		0.94	0.91, 0.97	
Head BMD (g/cm ²)	0	-0.05, 0.06		0.99	0.95, 1.02	
Left Arm Area (cm ²)	1.77	-3.14, 6.77		1.08	1.04, 1.12	
Left Arm BMC (g)	2.61	1.04, 3.97		1.09	1.07, 1.11	
Left Arm BMD (g/cm ²)	0.02	0, 0.04		1	0.97, 1.04	
Sum Arm BMC (g)	3.02	-1.27, 7.4		1.12	1.09, 1.15	
Left Leg Area (cm ²)	6.27	-0.33, 12.96		1.02	1, 1.04	
Left Leg BMC (g)	13.04	9.99, 16.09		1.04	1.02, 1.05	
Left Leg BMD (g/cm ²)	0.07	0.05, 0.09		0.97	0.95, 1	
Sum Leg BMC (g)	18.9	13.86, 24.73		1.05	1.03, 1.06	

95% CI= 95% confidence intervals; sd= standard deviation; 1/3= 1/3 distal radius; UD= ultradistal radius; Area= bone projected area; BMC= bone mineral content; BMD= areal bone mineral density; L1= L4= lumbar spine vertebrae 1 through 4; L3= lumbar spine vertebra 3; FN= femoral neck; WB= whole body

Table 5

a. Radius Root Mean Square Error Coefficients of Variation: IntraDXA (Adult, Disco A) and InterDXA (Pre-PBM, Pediatric, Adolescent)				
Radius ROI	Adult Discovery A (post-PBM: age 37–57 y)	Pre-PBM (age 8–24 y)	Pediatric (age 8–12 y)	Adolescent (age 13–24 y)
1/3 Area	1.2%	2.4%	2.8%	2.1%
1/3 BMC	1.0%	3.6%	3.5%	3.8%
1/3 BMD	1.0%	2.6%	2.8%	3.0%
UD Area	1.3%	3.5%	3.7%	3.7%
UD BMC	1.0%	3.0%	3.1%	3.2%
UD BMD	0.9%	1.6%	1.6%	1.6%

b. Lumbar Root Mean Square Error Coefficients of Variation: IntraDXA (Adult, Disco A) and InterDXA (Pre-PBM, Pediatric, Adolescent)				
Lumbar ROI	Adult Disco A (post-PBM)	Pre-PBM (8–24 y)	Pediatric (8–12 y)	Adolescent (13–24 y)
L1–L4 Area (total)	0.8%	2.5%	2.2%	3.1%
L1–L4 BMC	1.0%	2.8%	2.6%	2.9%
L1–L4 BMD	0.9%	2.4%	2.6%	2.2%
L3 Area	2.4%	2.8%	2.5%	3.1%
L3 BMC	2.8%	3.5%	3.5%	3.3%
L3 BMD	1.3%	2.9%	3.1%	2.6%

c. Proximal Femur Root Mean Square Error Coefficients of Variation: IntraDXA (Adult, Disco A) and InterDXA (Pre-PBM, Pediatric, Adolescent)				
Femoral Neck ROI	Adult (post-PBM)	Pre-PBM (8–24 y)	Pediatric (8–12 y)	Adolescent (13–25 y)
Neck Area	2.5%	3.7%	4.1%	3.2%
Neck BMC	3.0%	4.0%	5.1%	3.1%
Neck BMD	1.9%	2.5%	3.2%	1.6%

d. Whole Body Root Mean Square Error Coefficients of Variation: IntraDXA (Adult, Disco A) and InterDXA (Pre-PBM, Pediatric, Adolescent)				
Whole Body ROI	Adult (post-PBM)	Pre-PBM (8–24 y)	Pediatric (8–12 y)	Adolescent (13–24 y)
Whole Body Area	0.9%	1.6%	1.6%	1.6%
WB BMC	0.8%	3.4%	3.5%	3.0%
WB BMD	0.7%	2.3%	2.4%	2.1%
Sub-head Area	1.0%	2.2%	2.2%	2.1%
Sub-head BMC	1.0%	5.4%	5.7%	4.8%
Sub-head BMD	0.8%	3.7%	4.0%	3.3%
Head Area	1.8%	4.0%	4.0%	4.1%
Head BMC	1.8%	4.8%	4.8%	4.7%
Head BMD	1.5%	2.7%	2.6%	2.7%
L Arm Area	2.7%	7.2%	7.5%	6.8%

d. Whole Body Root Mean Square Error Coefficients of Variation: IntraDXA (Adult, Disco A) and InterDXA (Pre-PBM, Pediatric, Adolescent)				
Whole Body ROI	Adult (post-PBM)	Pre-PBM (8–24 y)	Pediatric (8–12 y)	Adolescent (13–24 y)
L Arm BMC	1.8%	9.0%	9.3%	8.1%
Sum Arm BMC	1.4%	9.8%	10.0%	8.9%
L Arm BMD	2.0%	3.2%	3.7%	2.6%
L Leg Area	2.0%	3.8%	4.1%	3.4%
L Leg BMC	1.8%	6.2%	7.5%	5.0%
L Leg BMD	1.2%	3.7%	4.4%	2.8%
Sum Leg BMC	1.2%	5.9%	7.1%	4.9%