Advanced Analysis Techniques Improve Infant Bone and Body Composition Measures by Dual-Energy X-Ray Absorptiometry

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Objective To evaluate a novel technique designed to reduce the negative impact of motion artifacts in infant dual-energy X-ray absorptiometry (DXA) scans.

Study design Using cross-sectional data from a large multicenter study, we developed and tested advanced methods for infant scan analysis. Newborns (n = 750) received spine and whole-body DXA scans with up to 3 attempts to acquire a motion free scan. Precision of infant DXA was estimated from visits with multiple valid scans. Accuracy of regional reflection, fusion, and omission techniques was estimated by comparing modified scans to unmodified valid scans. The effectiveness of the acquisition and analysis protocol was represented by the reduction in rate of failure to acquire valid results from infant visits.

Results For infant whole-body DXA, arm reflection and all fusion techniques caused no significant changes to bone mineral content, bone mineral density, bone area, total mass, fat mass, lean mass, and percentage fat. Leg reflection and arm/leg dual-reflection caused significant changes to total mass, but the percentage change remained small. For infant spine DXA, fusion and omission caused no significant changes. Advanced analysis techniques reduced the failure rate of whole-body scanning from 20.8% to 9.3% and the failure rate of spine scanning from 8.9% to 2.4%.

Conclusions Advanced analysis techniques significantly reduced the impact of motion artifacts on infant DXA scans. We suggest this protocol be used in future infant DXA research and clinical practice. *(J Pediatr 2017;181:248-53).*

Dual-energy X-ray absorptiometry (DXA) is the gold standard for measuring bone and body composition status in adults because of its high reproducibility and precision.[1] The precision of adult spine bone mineral density (BMD) and whole-body percentage fat are typically better than 1%.[2,3] Evaluations of bone health are also needed to identify infants, children, and adolescents who may benefit from interventions to decrease their risk of fracture.[1] A reliable method of measuring bone health during early life is necessary to optimize intervention strategies.[4] In a comprehensive overview of body composition measurement modalities, Demerath and Fields[5] found DXA to be ideal for use in children because of its high precision and low radiation dose. However, the precision of DXA BMD measures in children has been reported to be worse than that of adults most likely because of smaller bone sizes, lower bone densities, and movement artifacts.[6] Nevertheless, the International Society for Clinical Densitometry (ISCD) considers DXA a valid method for assessing bone health in infants and recommends that spine and whole-body DXA scans be performed for pediatric bone evaluations. Several studies have found that infant bone and body composition are important markers of immediate and lifelong health.[7-10] Though anthropometric measures can be used to assess infant growth in relation to World Health Organization standards, body composition varies substantially at birth.[4] Body weight alone does not adequately reflect disease risk. DXA can provide a more reliable indicator of infant health in efforts to optimize intervention strategies, and DXA results have been validated to infant weight of <2 kg.[11]

Previous studies have shown that motion artifacts introduce unpredictable variance into DXA measurements.[12,13] The official positions of the ISCD recommend that all artifacts be removed from DXA scans whenever possible.[14] Various methods have been used to mitigate motion artifacts including swaddling, timing of the scan while the infant sleeps, and light sedatives.[15] However, pervasive motion artifacts still represent a significant barrier to infant DXA assessment.[16-19]

ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
BMC	Bone mineral content
BMD	Bone mineral density
DXA	Dual-energy X-ray absorptiometry
ISCD	International Society for Clinical Densitometry
ROI	Region of interest
RMS	Root-mean-square
%CV	Coefficient of variation

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For this study, we created guidelines on positioning and analysis for improved accuracy and precision of spine and whole-body infant DXA scanning. We evaluated the precision of infant spine and whole-body DXA scans, as well as the accuracy of regional omission, reflection, and fusion techniques. Our guidelines should improve the usability of infant DXA bone health measurements by reducing the negative influence of motion artifacts.

Methods

We performed a cross-sectional observational substudy on an existing cohort of infants who underwent spine and whole-body DXA scans. Between August 2011 and June 2014, we recruited 784 infants as part of the International Maternal Pediatric Adolescent AIDS Clinical Trials P1084s study in Africa to assess the potential impact on bone of antiretroviral drugs taken by pregnant women for prevention of HIV vertical transmission. The details to the recruitment and study design can be found elsewhere.[20] To acquire motion-free DXA scans, infants received up to 3 whole-body and spine scans at birth (0-21 days of age) and at 26 weeks of age. However, in this report, we examined only the scans taken at birth. Study visits were scheduled for the morning or when the infant was napping. Infants were checked to ensure they were dry, clean, and wearing comfortable loose fitting clothing with no metal components such as buttons, pins, or snaps. Infants were allowed to use a pacifier if necessary. Infants were well fed to ensure they were as comfortable as possible during the scans. Written informed consent was obtained from all mothers in the study.

DXA Scan Acquisition

Participants from 10 study sites were scanned using 1 of 6 DXA systems; 5 were Hologic Discovery/Wi and 1 was Hologic Discovery/W (Hologic, Marlborough, Massachusetts). To minimize measurement bias because of differences in scanners and software, all DXA systems were cross-calibrated according to ISCD protocol. At no point during scanning were infants unattended. All DXA technologists received training specific to the protocol by the DXA quality assurance center at the University of California at San Francisco, California.

For spine acquisition, the infant was placed in the center of the DXA table (**Figure 1**; available at www.jpeds.com). The technologist felt for the top of the iliac crest, then centered the laser 2 cm below the iliac crest. Scans were taken with the fast array anteoposterior lumbar spine scan mode. The scan image was reviewed by the technologist for scan quality, including movement in the L1-L4 regions. If necessary, light restraint to the infant's arms and/or lower body was used to keep the infant still. The restrainer's hands were placed outside of the scan field. Images were reviewed by the technologist to ensure the spine was centrally positioned and that the top of the iliac crests, all of L5, and at least 5 vertebral bodies were included in the study (**Figure 2**; available at www.jpeds.com). If the image was not clearly visible because of low BMD, the scan was continued and assessed for quality after acquisition. Scans were repeated up to 2 times if movement was visible on the image or if the image quality was otherwise questionable. If the infant was noncooperative, scans were attempted again at a later time. No more than 3 attempts were made to acquire a valid infant spine scan. Properly analyzed examples of valid and invalid lumbar spine scans are shown in **Figure 2**.

For whole-body acquisition, the infant was swaddled in a blanket and placed near the top of the table (**Figure 1**). The swaddling technique is shown in **Figure 3** (available at www.jpeds.com). A folded towel was used to keep the head straight. Arms and legs were placed in a relaxed position to avoid overlap with any other part of the body. Scans were taken with the infant whole-body scan mode. The caregiver remained in the examination room during the scan. Scans were repeated up to 2 additional times if movement was visible on the scan image or if the image quality was otherwise questionable. If the infant was noncooperative, scans were attempted again at a later time.

The maximum infant radiation dose for the baseline scan protocol was estimated using the calculations of Thomas et al[21] and Blake et al.[22] For the instance of an infant having to have the maximum of 3 whole-body and 3 lumbar spine DXA scans at baseline, the maximum radiation exposure to infants was less than or equal to 4.9 mrem, roughly equivalent to 5 days of radiation from natural sources at sea level. There are several international guidelines for dose to research subjects. One of the most detailed guideline is that used by the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA). ARPANSA guidelines are consistent with the recommendations from the International Commission on Radiologic Protection. ARPANSA states that annual research dose levels for a child in the age range from birth to 18 years should be constrained to not exceed 50 mrem (0.5 mSv).[23] The maximum of 4.9 mrem this protocol could deliver to the infant is well below the most stringent upper constraint for the annual research radiation dose.

DXA Scan Analysis

Scan analysis was performed centrally at University of California at San Francisco using Hologic software v Apex 3.4. Spine scans were analyzed using a standard 4 vertebrae (region of interest [ROI]) analysis method (**Figure 2**). Any discontinuity in bone or soft tissue was coded as motion. Advanced analysis techniques were applied to regional data from standard lumbar spine ROIs. Interscan vertebral fusion replaced data for 1 or more invalid vertebrae with valid data from scans within the same visit. Intrascan omission estimated BMD by omitting invalid vertebrae within a single scan. Intrascan omission cannot be used to calculate total spine bone mineral content (BMC).

Whole-body scans were analyzed using 6 ROIs to isolate the arms, legs, head, and trunk (**Figure 4**; available at www.jpeds.com). Advanced analysis techniques were applied to data from scans with invalid regions. Intrascan limb reflection replaced data for an invalid limb region with data from its movement-free counterpart within the same DXA scan. Interscan fusion replaced data for invalidated head or trunk regions valid head or trunk region data from scans within the