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Adaptation of the Lateral Distal Femur DXA Scan Technique to Adults with Disabilities

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INTRODUCTION

It has been well established that children and adolescents with neuromuscular impairments that limit or preclude ambulation have low bone mineral density (BMD), and many will sustain fractures with minimal trauma. While multiple aspects of bone health have been

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examined in reasonably large series of children with conditions such as cerebral palsy (CP) (1), very little has been published looking at these same issues in even smaller groups of adults with CP (2,3).

One obstacle to assessing bone health in persons with CP has been the difficulty in obtaining DXA scans that are both technically feasible and clinically relevant. Joint contractures, scoliosis, hip dysplasia, and metallic implants frequently prevent reliable measures of BMD by DXA in the whole body, proximal femur, and lumbar spine where BMD is commonly measured. However, a more subtle issue often overlooked is whether the particular BMD assessment is at all relevant to the clinical problem of fractures in that specific population. In children with disabilities, it is not clear whether there is in fact a relationship between DXA measures of lumbar spine BMD and fracture risk (4-5). Further, it has been found that quantitative computed tomography (QCT) measures of volumetric bone density in the lumbar spine of children with CP do not correlate with the degree of motor impairment, and thus clearly do not reflect skeletal fragility (6).

In order to address these difficulties in obtaining clinically meaningful assessments of bone density, a new technique was developed utilizing DXA measurements of the distal femur projected in the lateral plane (7, 8). The distal femur is the most common site of fracture in persons with severely limited mobility, and metallic fixation is uncommon in this region. While the lateral distal femur (LDF) DXA scan is obtainable in persons without neurological disability, even those with contractures can usually be appropriately and comfortably positioned. The proven relationship between distal femur BMD and fracture risk (5), the technical feasibility of obtaining a reliable assessment of BMD in the distal femur, and the publication of more robust normal pediatric reference data (9) establish the LDF DXA as the clear technique of choice for assessment of BMD in children and adolescents with neuromuscular disabilities or significantly impaired mobility.

However, it is critical to note that the LDF DXA protocol and Regions of Interest (ROI) were developed for the pediatric age group, and the published analysis technique relies on the growth plate as a reference point (8). The purpose of this current study is to describe the adaptation and application of the LDF DXA scan technique to adults with CP, and to assess reproducibility and precision of these measures in this population.

MATERIALS AND METHODS

As part of on-going studies looking at health and fitness in adults with CP there were 100 adult subjects with CP who had distal femur DXA scans obtained as part of their evaluation; a subset of 31 subjects were selected for this study. This subset of subjects had the scans obtained by one of two technologists, had no metallic implants in the scanned regions, and were willing to undergo duplicate scans of both the right and left distal femurs. Duplicate scans of each distal femur were obtained with repositioning of the subject between every scan. Bilateral duplicate scans in 31 patients provided 124 total scans of the distal femur. DXA scans were acquired on a Hologic Discovery A scanner (Bedford, MA, USA) utilizing APEX software version 3.3. The study was approved by the University of North Carolina at Chapel Hill IRB and informed consent obtained from all participants.

The mean age of the 31 subjects was 27.8 ± 8.5 years ($\pm$ SD), ranging from 21.4 to 58.8 years. Seven subjects were female (23%), 25 were Caucasian (81%), 4 were African-American (13%), and 1 each were Hispanic and Asian. Severity of CP is commonly graded Level I through V based on the Gross Motor Functional Classification System (GMFCS) (10). Eleven subjects (35%) were GMFCS Level I at the time of the evaluation, meaning they were fully ambulatory with no significant limitations. Thirteen subjects (42%) were GMFCS Level II with some impairment in ambulation; these subjects generally ambulate with external supports or braces, and may utilize a wheelchair for long distances out in the community. Five subjects (16%) were GMFCS Level III, meaning that external supports were needed for ambulation and a wheelchair was consistently utilized out of doors and for long distances. Two subjects (6%) were GMFCS Level IV; these persons are wheelchair dependent and require significant external support to be in a standing position and usually some support even to sit. No subjects were at the most severely involved end of the spectrum (GMFCS Level V).

Technique for Scan Acquisition

The LDF scan is acquired using the forearm mode on the DXA scanner. The subject is placed on the table in a side-lying position on the side being measured. The femoral shaft follows the center longitudinal axis of the scanner table. The limb on top, which is not being scanned, is flexed forward and supported on foam blocks so it will not directly overlay the lower scanned limb. Sandbags and additional foam blocks are used as needed to help comfortably stabilize the patient. The technologist assures that the knee is in a true lateral position to avoid technical issues encountered with femoral rotation. Figure 1A shows a well-positioned distal femur scan and contrasts with Figure 1B showing a rotated and poorly aligned scan.

Technique for Scan Analysis

The principles of analysis for the LDF remain the same for scans acquired on adults; during scan analysis the technologist creates 3 regions of interest (ROIs) by using subregion analysis software, starting distally and moving up the shaft proximally. The ROIs are proportionate to the width of the femoral shaft; femoral shaft width is used to determine the height of the ROIs. The three ROIs contain significantly different proportions of cortical and cancellous bone and, therefore, results from each ROI are treated independently.

In a child, the base of Region 1 is defined by the growth plate (8, 9). In adults, however, that landmark is not available, so the base of Region 1 is defined by the point where the condyles join the femoral shaft posteriorly. Figure 2 shows the landmark used in the adult LDF analysis. Further details and instructions for scan acquisition and analysis can be found at www.lateraldistalfemur.org.

Scan Analyses

Three clinical centers that use DXA scanning in adults with neuromuscular movements participated in this project. The experience of the technologist at each center involved in this work ranged widely. The lead technologist (HHK) has been extensively involved in the development of the lateral distal femur DXA method since its inception over 10 years ago,

and has trained numerous others in the technique. Another technician (BAN) is a registered radiology technologist with certification in DXA, and over 7 years of DXA experience. The third technician (BAH) is a clinical research assistant with no formal DXA or radiology technician training or certification, and roughly 1 year of experience with DXA.

The series of unanalyzed LDF scans were downloaded to a CD disc and provided to each of the 3 technologists. Each technologist analyzed all 124 scans independently and then each technologist reanalyzed all scans after an interval of no less than 2 weeks. All analyses were done independently; the 'compare' feature in the analysis software was not utilized. It is important to note that prior to analyzing the study scans, the lead technician (HHK) utilized a separate training series of adult LDF DXA scans to teach and evaluate the other two technologists (BAN and BAH). A 'back and forth' exchange process involving over 50 scan analyses occurred before the technicians were considered qualified to do the analyses.

When assessing precision, there are two components to consider: 1) precision of the analysis affected by consistent ROI placement and 2) precision of the acquisition affected by patient positioning. Assessment of duplicate analyses of each scan focuses specifically on the consistency of analysis. Obtaining and analyzing duplicate scans of a limb assesses the reproducibility of both acquisition and analysis. This latter combination is what is typically considered for assessment of precision error.

Scan Quality

Persons with neuromuscular disabilities are a challenging group on which to obtain optimal quality DXA scans at any body site. Contractures can make positioning difficult, though proper positioning for scanning of the LDF is generally the most comfortable and therefore least difficult body site to successfully measure. Cognitive limitations in understanding and cooperation, exaggerated startle reflexes, and involuntary movement, sometimes result in unwanted motion during the scan. If motion was considered excessive, the scan was restarted.

RESULTS

One potential source of variability is lack of consistency in analysis of the scan. Consistency was assessed by comparing duplicate analyses of the same scan. Table 1 summarizes the findings for the three technologists individually for each of the three regions of the distal femur. There was a small, but statistically significant difference between the technologists in the precision of scan analysis, precision improves with experience. The precision of the analyses also varied with each Region of Interest in the distal femur. Precision in Regions 2 and 3 was similar, with a mean absolute difference between analysis #1 and analysis #2 of 0.4% with the most experienced technician, to roughly 1.0% with the least experienced technician. However, significantly greater variability of 1.3% (most experienced technician) to 2.3% (least experienced technician) was found with duplicate analyses of Region 1 where the borders and landmarks are typically less sharply defined.

In clinical practice and research, the sensitivity to detect true change in BMD over time is dependent on the precision of the measurement. Precision is best assessed by repeated scans

obtained on the same day, with complete repositioning between scans (subject removed and then replaced on the scanner). The 31 subjects participating in this study provided duplicate DXA scans of 62 distal femurs with which the precision of the measurement could be examined. Table 2 shows the difference in BMD between analysis #1 of scan #1 and analysis #1 of scan #2, for each of the three technologists and comparing the three regions of the LDF.

As expected, there was greater precision (less variability) with duplicate analyses of the same scan as compared to the reproducibility of analyzing duplicate scans. In Region 1 the precision of duplicate scans was 7.1%, compared to a precision of 1.8% for duplicate analysis of the same scan (all technologists). Similarly, in Regions 2 and 3 the precision of duplicate scans was 2.4%, compared to 0.7% for duplicate analyses. Therefore, most of the variability seen with duplicate scans can be accounted for by variability in the scan acquisition, or process of positioning the subject and obtaining the scan, rather than in the scan analysis.

The International Society for Clinical Densitometry (ISCD) has established useful guidelines for assessing precision in routine clinical practice, and points out that the anatomic region, clinical population, and specific technician involved are relevant variables. The ISCD recommends that 20 representative patients be scanned 3 times, or 30 patients be scanned twice in order to assess precision. The ISCD also provides an on-line calculator to assess precision according to these guidelines (<http://www.iscd.org/resources/calculators/>).

To simulate this important routine quality control process, the ISCD precision calculator was applied to the 31 left distal femurs scanned in duplicate and those results are presented in Table 3. Note that full simulation of this process would include that each technologist acquires and analyzes the repeated scans, allowing for a determination of precision for that particular technologist. In this study, all scans were acquired at one institution while the analyses occurred at three different centers. The results in Table 3 demonstrate the point that the least significant change, meaning the amount of change in serial measures of BMD necessary to be confident that there has been a true change in BMD, is dependent on both the technician involved and the region of interest.

In order to simplify a bone density evaluation, consideration is sometimes given to scanning only one limb. This raises the issue of how reliably BMD measures in one limb accurately reflect the contralateral limb. Based on analysis #1 of scan #1 by the most experienced technologist, the mean ($\pm$ SE) absolute % difference between right and left sides was 7.7% $\pm$ 1.7% in Region 1, 5.3% $\pm$ 0.9% in Region 2, and 5.6% $\pm$ 1.0% in Region 3. For Region 1 the variability with duplicate scans of the same limb is relatively large (7.4%, Table 2), and comparable to the side-to-side difference of 7.7%. However, with Regions 2 and 3 where the precision of measurement is much better (2.2% Table 2), the side to side differences of over 5% are more than double the precision of duplicate measures of the same limb.

DISCUSSION

In a recent review of aging and bone health in persons with disabilities the authors outlined the significant problem of skeletal fragility in this population, and the relative paucity of

information that is available (11). These authors also noted the considerable challenges in obtaining assessments of BMD in this population. These challenges encountered in working with children with neuromuscular impairments led to the development of the LDF DXA scanning technique (7, 8). Feasibility, proven relevance to fracture risk, and available age-matched reference norms clearly establishes DXA scanning of the LDF as the method of choice for bone density assessment in children with neuromuscular impairments. The purpose of this current study was to begin the process of adapting and evaluating the distal femur technique for use in the assessment of bone health in adults with neuromuscular disabilities.

One of the advantages of the LDF scan technique is the 3 separate ROIs, which range from predominately cancellous bone in the distal femoral metaphysis (Region 1), to the cortical bone of the femoral shaft (Region 3). The ability to detect change, such as loss of bone over time or the impact of interventions, depends on the rate of change in BMD and the precision of the measurements. Cancellous bone is generally the most metabolically active, and therefore typically the most sensitive to changes. For example, BMD increased an average of 39% in Region 1 as compared to 21% in Region 3 over 18 months in a randomized, placebo-controlled clinical trial of bisphosphonates in children with CP (12). However, the precision of measurement in Region 1 is significantly less than in Regions 2 and 3. The clinical relevance of this is reflected in the amount of change necessary to be confident that a measured change is a true change, or the 'least significant change'. The least significant change in Region 1 is more than twice that of Regions 2 and 3, so while Region 1 is metabolically more responsive to change, a greater amount of change is required in order to be confident that the change is real. The reported precision errors when assessing adult women by DXA are approximately 0.9 – 2.6% in the lumbar spine and 0.9 – 2.5% in the proximal femur (new ref: Fuleihan, G. E.-H., Testa, M. A., Angelini, J. E., Porrino, N. and Leboff, M. S. (1995) Reproducibility of DXA absorptiometry: A model for bone loss estimates. *J Bone Miner Res.* 10: 1004–1014. doi: 10.1002/jbmr.5650100704). The trend for greater variability in LDF Region 1 has been reported in other studies: Henderson, et al reported 3% variation at Region 1 in 250 children with CP (8) and Mueske, et al reported 9% variation at Region 1 in a group of 15 adults and children (ref. Mueske NM, Chan LS, Wren TA. Reliability of Lateral Distal Femur Dual-Energy X-Ray Absorptiometry Measures. *J Clin Densitom.* 2013 Mar 26. pii: S1094-6950(13)00032-2. doi: 10.1016/j.jocd.2013.02.010. [Epub ahead of print]). Particularly in Region 1, very low bone density and challenges with proper, consistent positioning contribute to the diminished precision being reported with DXA measures in the distal femur of adults with CP.

Additional details about the technique and instructions for obtaining and analyzing distal femur scans in adults and children are available at www.lateraldistalfemur.org. We the authors, feel it important to emphasize the value of hands-on training on the LDF technique for institutions less familiar in scanning children and/or in scanning patients with neuromuscular disabilities. Clinical experience with DXA and CBDR (Certified Bone Density Technologist) certification alone may not be adequate to prepare a technologist to obtain and analyze reliable LDF DXA scans in adults with neuromuscular disabilities. Contractures, deformities, and limited understanding and cooperation can considerably increase the difficulty of obtaining DXA scans in persons with neuromuscular impairment,

as compared to postmenopausal women undergoing osteoporosis screening. In addition, even after a training series of over 10 scans, an experienced, certified DXA technologist (GAN) still did not analyze scans with quite the same degree of precision as someone who had years of experience working with the distal femur scan in persons with neuromuscular disabilities (HHK).

Another important limitation is that age-matched reference norms do not currently exist for distal femur scans in adults. The available reference data extends only up to age 18 years (9), so age and gender-matched BMD Z-scores cannot be provided for distal femur DXA scans in adults. However, BMD is usually referenced against typically developing young adults for the T-score. Therefore, in the absence of adult LDF norms, some clinicians may choose to use the 18-year-old norms as the reference to estimate a T-score. It is also common to use the first scan as a baseline and assess change with serial studies. Clearly, reference norms for distal femur BMD in adults need to be determined.

Bone density assessment in adults with neuromuscular impairments poses some unique challenges. It should not be assumed that principles, practices, and experience measuring BMD in osteoporotic, but otherwise typical elderly adults freely transfers to working with persons who have neuromuscular impairment. The lateral distal femur DXA scan technique was originally developed for use in children. With some modifications and an appreciation of the precision data outlined in this paper, the LDF DXA scan can be used in adults with neuromuscular disabilities by those interested in obtaining the necessary training and experience.

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Figure 1

A well-positioned (1A) and poorly positioned (1B) scan of an adult distal femur. Figure 1B is the most poorly positioned scan in the series: the patient should have been repositioned and rescanned. The limbo is not longitudinally aligned with the axis of the scan, and malrotation is reflected by both overlapping of the patella with the condyles and the oblique projection of the medial condyle on the lateral condyle.

Figure 2
Landmark for placement of the bottom of Region 1 for the adult LDF DXA: the upper margin of the posterior femoral condyle where it joins the shaft (arrow). Dashed line indicates the bottom of Region 1.

Table 1
Precision of Duplicate Analyses by Each Technician

	Technician			p values ³
	A (most experience)	B	C (least experience)	
Region 1				
mean BMD g/cm ²	0.890	0.893	0.870	
mean difference ± SE ¹	0.010 ±0.002	0.014 ±0.003	0.019 ±0.003	B vs C p=0.1
mean % difference ± SE ²	1.0% ±0.3%	1.7% ±0.5%	2.3% ±0.5%	A vs B&C p<0.005
Region 2				
mean BMD g/cm ²	1.135	1.131	1.129	
mean difference ± SE ¹	0.004 ±0.001	0.006 ±0.001	0.010 ±0.002	all pairs p<0.005
mean % difference ± SE ²	0.4% ±0.1%	0.6% ±0.1%	0.9% ±0.2%	
Region 3				
mean BMD g/cm ²	1.215	1.211	1.213	
mean difference ± SE ¹	0.005 ±0.001	0.009 ±0.002	0.013 ±0.003	all pairs p≤0.01
mean % difference ± SE ²	0.4% ±0.1%	0.7% ±0.2%	1.0% ±0.2%	

Note: The precision of duplicate analyses differed between Region 1 and Region 2 and 3 ($p<0.005$), but precision in Region 2 and Region 3 did not differ ($p>0.4$); Wilcoxon rank sum test.

¹ mean absolute difference in BMD between analysis #1 and analysis #2; n=124 scans

² % difference = absolute difference ÷ mean BMD analysis #1 and #2 × 100%

³ Wilcoxon rank sum non-parametric test comparing technicians in their differences between duplicate analyses

Table 2

Precision of Duplicate Scans

	Technician			p values ³
	A (most experience)	B	C (least experience)	
Region 1				
mean BMD g/cm ²	0.892	0.889	0.872	
mean difference ± SE ¹	0.003 ±0.032	0.057 ±0.052	0.061 ±0.031	all pairs p>0.3
mean % difference ± SE ²	0.4% ±4.1%	6.7% ±4.1%	7.2% ±3.8%	
Region 2				
mean BMD g/cm ²	1.135	1.131	1.129	
mean difference ± SE ¹	0.024 ±0.008	0.027 ±0.009	0.029 ±0.009	all pairs p>0.3
mean % difference ± SE ²	2.1% ±0.5%	2.4% ±0.7%	2.6% ±0.7%	
Region 3				
mean BMD g/cm ²	1.215	1.212	1.215	
mean difference ± SE ¹	0.028 ±0.006	0.031 ±0.007	0.033 ±0.006	all pairs p>0.3
mean % difference ± SE ²	2.3% ±0.5%	2.4% ±0.5%	2.5% ±0.6%	

Notes: The precision of duplicate scans did not differ between Region 2 and Region 3 ($p>0.3$ for all techs). The precision of duplicate scans did differ between Region 1 and Region 2 for techs A and C ($p\leq 0.04$) but not tech B ($p=0.2$).

The precision of duplicate scans did differ between Region 1 and Region 3 for tech A ($p=0.04$), but not techs B and C ($p\geq 0.06$).

¹ mean absolute difference in BMD between scan #1 and scan #2 for all 62 distal femurs

² % difference = absolute difference ÷ mean BMD scan #1 and scan #2 × 100%

³ Wilcoxon rank sum non-parametric test comparing technicians in their differences between duplicate scans

Table 2
 ISCD Recommended Routine Assessment of Precision*

	Technician		
	A (most experience)	B	C (least experience)
Region 1			
RMS SD (g/cm ²)	0.044	0.044	0.057
%CV	4.34%	4.37%	6.02%
LSC (g/cm ²)	0.122	0.122	0.158
Region 2			
RMS SD (g/cm ²)	0.017	0.017	0.021
%CV	1.59%	1.63%	1.92%
LSC (g/cm ²)	0.047	0.047	0.058
Region 3			
RMS SD (g/cm ²)	0.020	0.022	0.019
%CV	1.62%	1.74%	1.57%
LSC (g/cm ²)	0.055	0.061	0.053

* Based on analysis #1 of scans #1 and #2 of the 31 left distal femur scans input into the online ISCD precision calculator.

RMS SD: root mean square standard deviation

%CV: percent coefficient of variation

LSC: least significant change at the 95% confidence level = RMS SD × 2.77