

# Bone Mineral Density Determination in Children

## Evaluation of a novel method and application to Duchenne muscular dystrophy

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- I Söderpalm A-C, Kullenberg R, Albertsson Wikland K, Swolin-Eide D. **Pediatric Reference Data for Bone Mineral Density in the Calcaneus for Healthy Children 2, 4 and 7 Years of Age by Dual-Energy X-Ray Absorptiometry and Laser.** J Clin Densitom. 2005; 8(3):303-313.
- II Söderpalm A-C, Kullenberg R, Swolin-Eide D. **The Relationship Between Dual-Energy X-Ray Absorptiometry (DXA) and DXA With Laser (DXL) Measurements in Children.** J Clin Densitom. 2008; 11 (4):555-560.
- III Söderpalm A-C, Magnusson P, Åhlander A-C, Karlsson J, Kroksmark A-K, Tulinius M, Swolin-Eide D. **Low bone mineral density and decreased bone turnover in Duchenne muscular dystrophy.** Neuromuscul Disord. 2007; 17(11-12):919-928.
- IV Söderpalm A-C, Magnusson P, Åhlander A-C, Karlsson J, Kroksmark A-K, Tulinius M, Swolin-Eide D. **Bone mass in Duchenne and Becker muscular dystrophies: A four-year longitudinal study.** Submitted Ms. No. NMD-D-09-00181, under revision.



UNIVERSITY OF GOTHENBURG

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## Evaluation of a novel method and application to Duchenne muscular dystrophy

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**Aims:** The overall aims of this thesis were to evaluate the dual-energy X-ray and laser (DXL) method for bone densitometry measurements of the calcaneus in children, to provide reference data for bone mineral density (BMD) in the heel bone in young children and to apply the DXL technique to patients with Duchenne muscular dystrophy (DMD) and conduct a survey about bone health of DMD patients.

**Study populations and methods:** The DXL Calscan method was modified and adapted for measurements in children and applied to bone densitometry in all subsequent studies. To provide percentile reference data for the DXL measurements, a total of 334 healthy children aged 2, 4 and 7 years were measured (Study I). Measurement data were collected from 112 individuals, aged 2-21 years, to evaluate the relationship between the heel DXL measurements and whole-body dual-energy X-ray absorptiometry (DXA) measurements (Study II). In a cross-sectional study, 24 DMD patients, aged 2-20 years, were compared with 24 healthy age- and gender-matched controls with special emphasis on bone mass assessed at different skeletal sites and bone turnover (Study III). In a longitudinal study, 18 DMD patients from Study III and 6 patients with Becker muscular dystrophy (MD) were followed for 4 years with the emphasis on bone mass development, body composition, muscle strength and motor function (Study IV).

**Results:** The DXL method was readily applied, both in the very young children and in the children with various disabilities. Reference data for BMD were provided as percentile values for children aged 2, 4 and 7. Additional data (a total of 645 DXL Calscan measurements (328 girls/317 boys)) from a follow-up study enabled the presentation of BMD reference curves (mean  $\pm$  2 SD) for children (girls and boys respectively) between 2 and 10 years of age. A high correlation was found between the heel DXL measurements and DXA measurements in the hip, in the spine and in the total body. The DXL measurements predicted the lowest DXA-determined BMD values at these sites with high sensitivity (0.9-1.0) and high specificity (0.86-0.95). In the DMD patients, the BMD levels were generally lower compared with the healthy controls. These differences increased with increasing age and were particularly evident in the hip and the heel. Biochemical markers of bone turnover demonstrated reduced bone formation as well as reduced bone resorption in the DMD patients. The fracture rate was no higher in the DMD group compared with the control group, but the fractures were more frequently located in the lower extremities in the patient group. The BMD values were significantly reduced in the DMD patients, even when compared with Becker MD patients. The Becker MD patients, in turn, showed significantly reduced BMD levels compared with healthy controls at most sites. A significant association was found between the changes in lean mass (muscle mass) and bone mass with time and there was also a strong association between BMD measurements and muscle function parameters.

**Conclusions:** It is feasible to perform DXL bone densitometry measurements of the calcaneus in very young children as well as in children with disabilities. The DXL measurements can predict low BMD values as measured by whole-body DXA. DMD patients had both reduced bone turnover and reduced BMD values compared with healthy controls. The impaired muscle strength and reduced motor function, as observed in the DMD patients, were associated with reduced bone mass during growth. The level of disability appeared to have a major effect on skeletal development, which was, for example, demonstrated as a decrease in hip BMD in the DMD patients with time.

**Keywords:** adolescents, age- and gender-matched, Becker, bone densitometry, bone markers, bone mineral density, calciotropic hormones, children, DXA, DXL, Duchenne, glucocorticoids, muscular dystrophy, normative, reference values, skeleton