Calcif Tissue Int (2006) 78:186–192
DOI: 10.1007/s00223-005-0191-8

Calcified Tissue International
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PIXImus Bone Densitometer and Associated Technical Measurement Issues of Skeletal Growth in the Young Rat

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Received: 1 August 2005 / Accepted: 12 December 2005 / Online publication: 17 March 2006

Abstract. The PIXImus dual-energy X-ray absorptiometer (DXA) is designed to measure body composition, bone mineral content (BMC), area (BA), and density (BMD) in mice and rats. The aims of this study were to longitudinally measure BMC, BA, and BMD in growing rats and to identify potential technical problems associated with the PIXImus. Total femur and lumbar DXA measurements, body weight, and length of initially 3-week-old rats ($n = 10$) were taken at weeks 5, 9, and 14. BMC and BMD of femoral metaphyseal and diaphyseal regions rich in trabecular and cortical bone, respectively, were obtained. Results showed significant increases in body weight, total femur BMC and BMD, lumbar area, length, BMC, and BMD at each time point. There was a significant positive correlation between body weight and total femur BMD ($r = 0.97$, $P < 0.001$) as well as lumbar BMD ($r = 0.99$, $P < 0.001$). BMD values for the femoral metaphyseal region and the lumbar spine were also positively correlated ($r = 0.96$, $P < 0.01$). Several technical issues (e.g., positioning of animals), difficulties (e.g., in analysis of images), and limitations (e.g., inability to detect underdeveloped calcified bone in growing animals and bone edge detection) of the software pertinent to the PIXImus were evident. In conclusion, despite limitations in the software, the PIXImus is a valuable tool for studying skeletal development of growing rats.

Key words: PIXImus densitometer — Bone mineral content — Growing rat — Femur — Lumbar spine

Bone growth and mineralization during childhood and adolescence are influenced by diet, lifestyle, genotype, and hormonal status [1–3]. The attainment of optimal peak bone mass in early adulthood is believed to reduce the risk of developing osteoporosis later in life as it may offset losses associated with menopause in women and aging in men and women. Studies investigating the determinants of bone growth and mineral accrual in children and adolescents have been cross-sectional [4–6], longitudinal [7–9], or interventional [10–12]. These studies have been extremely valuable in providing insight into some of the determinants of bone mineral accrual. However, the effects of diet on longitudinal skeletal changes from infancy to adolescence are uncertain.

Due to technical, time, and financial constraints associated with conducting human studies from infancy to adolescence, animal models could provide a useful alternative to study mechanisms of bone growth over a shorter time period. Rats have been used extensively to study the effects of hormonal (e.g., estrogen and parathyroid hormone) and drug (e.g., bisphosphonates) treatments on bone [13–17].

The primary end point in these studies has been bone mineral content (BMC) or bone mineral density (BMD) at different skeletal sites, and a number of techniques are available to conduct these measurements both *in vivo* and *ex vivo*. One basic *ex vivo* method includes ashing of excised bones, followed by determination of the calcium content [18]. Bone density can also be determined by the Archimedes principle [18], where the weight of water displaced by the immersed bone is used to determine bone density. The main limitation of both of these techniques is that longitudinal bone measurements of the same animal are not possible.

For a long time, dual-energy X-ray absorptiometry (DXA) has been adapted for rats using specialized small animal software with clinical whole-body DXA machines. It has been reported that this technique is optimized for body weights $>200g$ (Corresponding to the weight of an older growing rat) [19]. Hence, this technique may not be appropriate for the measurement of skeletal changes in young, growing rats. The PIXImus (Lunar, Madison, WI) has recently been designed for measuring BMC in small animals, namely mice, and has also been validated for use in rats [20]. Most studies have used the PIXImus in mice either to quantitatively assess the influence of genotype, [21, 22] hormonal or dietary treatment on BMD [23–26]. A few studies have also been conducted in older rats to examine the effects of dietary or insulin-like growth factor I treatment on

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