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ORIGINAL ARTICLE

Calculating In-vivo Short-term Precision Error of Dual-Energy X-ray Absorptiometry in Human and Animal: A Technical Report

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ABSTRAK

Pengukuran ketumpatan mineral tulang oleh 'Dual-energy X-ray Absorptiometry' (DXA) adalah penting untuk mengenalpasti osteoporosis. Ralat ketepatan DXA adalah ukuran yang penting untuk menentukan perubahan sebenar dalam nilai ketumpatan mineral tulang. Kajian ini bertujuan untuk mengkaji pekali variasi jangka pendek mesin QDR Wi DXA Discovery Hologic. Ketumpatan mineral tulang pinggul dan tulang belakang untuk lima belas sukarelawan (purata umur: 30.67 ± 10.41 tahun) dan ketumpatan tulang keseluruhan badan untuk lima belas ekor tikus Sprague-Dawley betina (berusia tiga bulan) diimbas menggunakan mesin HDR Discover QDR Wi DXA. Setiap sukarelawan dan tikus menjalani imbasan sebanyak tiga kali untuk menilai kebolehulangan nilai ketumpatan tulang. Imbasan untuk subjek manusia dilakukan dalam tempoh 1 hingga 12 minggu. Untuk sampel haiwan, imbasan diulang pada hari yang sama selepas posisi semula. Ralat kepersisan dinyatakan sebagai peratusan pekali variasi (%CV). %CV diperolehi untuk tulang belakang lumbar adalah 1.8% dan 1.2% untuk tulang pinggul. %CV untuk keseluruhan BMD tikus adalah 1.4%. %CV jangka pendek yang ditunjukkan untuk kedua-dua manusia dan haiwan dalam kajian ini adalah setanding. Ralat kepersisan DXA mesti dipantau untuk memastikan prestasi yang optimum.

Kata kunci: dual-energy-X-ray absorptiometry, in vivo, ketumpatan mineral tulang, ralat kepersisan

ABSTRACT

Bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry

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(DXA) is important in diagnosing osteoporosis. Precision error of DXA is a useful measure to determine a true change in BMD value. This study aimed to investigate the short-term coefficient of variance of Hologic Discovery QDR Wi DXA machine. The lumbar spine and hip BMD of fifteen healthy volunteers (mean age: 30.67 ± 10.41 years) and the whole body BMD of fifteen female *Sprague-Dawley* rats (aged three months old) were scanned using Hologic Discovery QDR Wi DXA machine. Each volunteer and rat underwent triplicate scans to assess the reproducibility of BMD values. The interval between the scans ranged within 1 to 12 weeks for human subjects. For animal samples, the scans were repeated on the same day after repositioning. The precision error was expressed as a percentage coefficient of variance (%CV). The %CV obtained for lumbar spine and hip BMD for human were 1.8% and 1.2%, respectively. The %CV for whole body BMD of rats was 1.4%. The short-term CV demonstrated for both human and animal in the present study were comparable. The precision error of DXA must be monitored to ensure optimal performance of the device.

Keywords: bone mineral density, dual-energy-X-ray absorptiometry, in vivo, precision

INTRODUCTION

Assessment of bone mineral density (BMD) is an important step to determine bone loss in an individual. Dual-energy X-ray absorptiometry (DXA) is known to be the gold standard technique to assess BMD (World Health Organization 1994). The physicians need to identify a true change on BMD when a second scan is performed on a patient (El Maghraoui et al. 2005). Therefore, the measurement of precision of DXA is important in determining whether the change in BMD was random or significant due to interventions. The precision of a diagnostic test indicates the reproducibility of its measurements. Short-term precision of a DXA machine is established by repeated BMD measurements carried out over a short period of time (El Maghraoui et al. 2005). It may involve 30 subjects, each with two repeated scans, or 15 subjects, each with three repeated scans (Kim & Yang 2014). The precision error is commonly expressed as the coefficient of variation (CV) which is the ratio of the standard deviation (SD) to the mean of the measurements (Boutsen et al. 2001). Previous reports indicated that a change in BMD greater than 2√2 %CV should be considered as a true change (Fuleihan et al. 1995). DXA also has been used to measure BMD in small animals (Lochmüller et al. 2001). The BMD of small animals, such as rats and mice, has been difficult to measure with the DXA technique because of their small bone size and relative lack of machine sensitivity. Thus, it is important to minimize the technical errors between measurements to enhance its accuracy. However, there

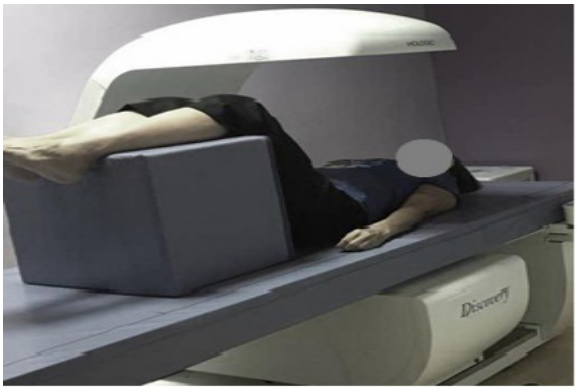

Figure 1: Position for spine BMD measurement by DXA

is a paucity of data on %CV values of DXA in small animals.

This paper aimed to demonstrate how the short term in-vivo precision of DXA in human and animal studies was calculated, using Hologic Discovery QDR Wi DXA machine as an example. Hologic Discovery QDR Wi DXA machine is one of the most widely used DXA model currently. The manufacturer provided a short-term %CV value of 1%. We hypothesize that we would obtain a slightly larger %CV value in the real world setting.

MATERIALS AND METHODS

BMD was measured using Hologic Discovery QDR Wi DXA machine (MA, USA) with 13.5.3 analysis software. Calibration of the machine was performed before each scanning session using a Hologic calibration phantom. The same operator performed all the scanning and analysis. The scanning was repeated three times for each human subject and rat.

Human subjects

A total of 15 healthy nongravid volunteers aged 23-45 (mean age=30.67 $\pm$ 10.41 years; men=6, women=9) without any metal implants on the site of assessment were recruited conveniently at a university in Kuala Lumpur, Malaysia. Informed consent was obtained from each volunteer prior to the scanning. BMD of their lumbar spine (L1-L4) and left hip was measured as per the standard protocol. For spine BMD scan, volunteers lied down in a supine position and a block provided by the manufacturer was used to elevate the legs (Figure 1). For the left hip measurement, the left leg of the subject was rotated internally and the foot was strapped onto the positioning device to prevent movement while the subject remained in the supine position (Figure 2). Each volunteer was scanned three times on a different day within 1 to 12 weeks.

Animal samples

Fifteen female *Sprague-Dawley* rats aged 3 months old weighing between 200-250 g were procured from the Laboratory Animal Resource Unit,

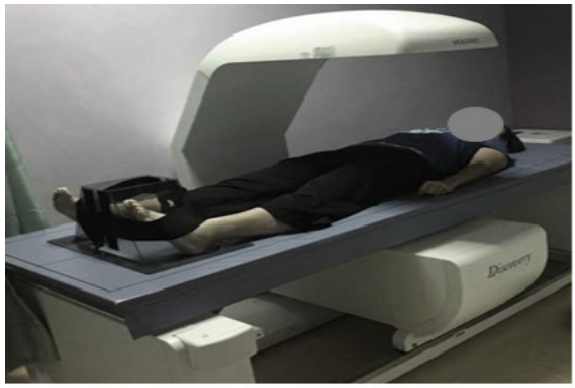

Figure 2: Position for left hip BMD measurement by DXA

Universiti Kebangsaan Malaysia Medical Centre (Kuala Lumpur, Malaysia). Whole body scan was performed onto the rats in a prone position when they were anaesthetized using a mixture of ketamine/xylazine. The scan began from the nose and extending to the end of the tail (Figure 3). Rats were scanned three times by repositioning immediately after the first scan (4 minutes later).

Ethical Consideration

The current study was part of the projects GUP-2017-012 and GUP-2017-060. The protocols of the main studies have been reviewed and approved by the Ethics Committee of Universiti Kebangsaan Malaysia (approval code: UKM PPI/111/8/JEP-2017-761 and FAR/PP/2018/IMA NIRWANA/23-JAN./898-MAR.-2018-FEB.-2020).

Figure 3: Image of the total body scan of the rats from the nose to the tail by DXA

Short-term Precision Equation

Data analysis was computed using Microsoft Excel 2013 (Redmond, Washington). BMD measurement was done three times on each sample to achieve a degree of freedom (df) of 30 as recommended by the International Society of Clinical Densitometry (ISCD). The df for the study is determined by the following formula: (number of measurements on each individual – 1) x (number of individuals in the study). The characteristics of human subjects and rats were reported as the mean and standard deviation. Precision was expressed as the percentage coefficient of variance (%CV) where:

$$\%CV = \frac{\text{Standard deviation}}{\text{Mean}} \times 100$$

RESULTS

The mean height, weight and body mass index (BMI) of the volunteers were 161 ± 5.19 cm, 58.40 ± 7.74 kg and 22.3 ± 2.8 kg/m^2, respectively. Table 1 and Table 2 show the short-term in vivo precision of measurements for the spine and left hip BMD of the volunteers, respectively. The mean %CV varied between 0.30 and 4.0 % for spinal BMD while for hip BMD, the mean %CV varied from 0.2 and 2.5%. Table 3 shows the short-term in vivo precision of measurements for the whole body BMD of the rats. The mean %CV of whole body BMD in rats also varied from 0.20% and 2.44%.

DISCUSSION

This paper demonstrated the precision of BMD analysis for both spine and hip region of human subject and the whole body of rats using Hologic Discovery QDR Wi DXA machine. The short-term %CV obtained for human in the present study was 1.8% for spinal BMD and 1.2% for total hip BMD. Several epidemiological studies using Hologic Discovery QDR Wi reported similar %CV values (Ho-Pham et al. 2011; Limpaphayom et al. 2001). Wapniarz et al. (1994) found a lower %CV for spinal BMD (1.02%) and femoral neck BMD (1.72%) among forty-eight patients (Wapniarz et al. 1994). The %CV values generated from the current study showed good reproducibility of

Table 1: In vivo precision for spine BMD of human

Volunteer	Reading 1	Reading 2	Reading 3	%CV (SD in g/cm^2)
1	0.908	0.878	0.853	3.1(0.028)
2	0.9	0.872	0.86	2.3(0.021)
3	0.935	0.915	0.988	4.0(0.038)
4	0.724	0.731	0.737	0.9(0.007)
5	1.163	1.175	1.177	0.6(0.008)
6	0.874	0.898	0.891	1.4(0.012)
7	0.973	0.949	0.95	1.4(0.014)
8	1.041	1.034	1.031	0.5(0.005)
9	1.04	0.964	1.016	3.9 (0.039)
10	0.947	0.93	0.908	2.1(0.020)
11	0.829	0.857	0.812	2.7(0.023)
12	1.049	1.045	1.091	2.4(0.025)
13	0.806	0.805	0.801	0.3(0.003)
14	1.177	1.184	1.155	1.3(0.015)
15	1.067	1.066	1.057	0.5(0.006)
Range				0.3-4.0
%CV				1.8

Abbreviation: CV: Coefficient of variance; SD: Standard deviation

Table 2: In vivo precision for left hip BMD of human

Volunteer	Reading 1	Reading 2	Reading 3	%CV (SD in g/cm^2)
1	0.851	0.848	0.852	0.2(0.002)
2	0.778	0.778	0.763	1.1(0.009)
3	0.803	0.797	0.806	0.6(0.005)
4	0.669	0.661	0.655	1.1(0.007)
5	1.063	1.091	1.04	2.4(0.026)
6	0.811	0.812	0.819	0.5(0.004)
7	0.92	0.897	0.881	2.2(0.020)
8	0.959	0.945	0.954	0.7(0.007)
9	0.926	0.928	0.942	0.9(0.009)
10	0.77	0.792	0.787	1.5(0.012)
11	0.728	0.726	0.712	1.2(0.009)
12	0.857	0.879	0.86	1.4(0.012)
13	0.709	0.692	0.708	1.4(0.010)
14	0.782	0.779	0.814	2.5(0.019)
15	0.831	0.825	0.815	1.0(0.008)
Range				0.2-2.5
%CV				1.2

Abbreviation: CV: Coefficient of variance; SD: Standard deviation

BMD measurement especially for hip measurement. This might be due to the recruitment of younger subjects in our study, which made the hip rotation to be easier during scans. A similar finding has been observed in a previous study involving 47 Caucasian subjects (13 younger postmenopausal women; 17 elderly women; 17 men) whereby the measurement error for femur among younger subjects was smaller than that of the elderly subjects (Maggio et al. 1998). Generally, the %CV at the spine is usually 1-2% and 2-3% at the proximal femur. These values vary depending on various factors, such as the type of machines used and experience of the technician (El Maghraoui & Roux 2008).

Studies reporting in vivo bone densitometry measurement of the rats using DXA Hologic Discovery QDR Wi are limited. Therefore, comparison was made with studies using other models of DXA in the following discussion. The %CV observed in our present study for the whole body BMD of 15 female Sprague Dawley rats was 1.4%. This value was similar to the 1.4% reported by Karahan et al. (2002) using a DPX-L DXA model (Lunar Corp, Madison, Wisconsin) for the whole body BMD in 12 male Wistar rats (Karahan et al. 2002). It was also comparable to the %CV of 1.5% reported in 10 Wistar rats (5 male and 5 female) using Hologic QDR 1000®, software version 5.52 (Casez et al. 1994). In addition, Ammann et al. (1992) demonstrated that the %CV varies depending on the

Table 3: In vivo precision for the whole body BMD of rats

Volunteer	Reading 1	Reading 2	Reading 3	%CV (SD in g/cm^2)
1	0.182	0.183	0.184	0.7 (0.001)
2	0.178	0.180	0.183	1.2 (0.002)
3	0.171	0.166	0.170	1.3(0.002)
4	0.162	0.167	0.166	1.5(0.003)
5	0.189	0.196	0.193	1.8(0.004)
6	0.181	0.182	0.184	0.2(<0.001)
7	0.188	0.193	0.188	1.5(0.003)
8	0.185	0.191	0.188	1.7(0.003)
9	0.181	0.180	0.185	1.5(0.003)
10	0.190	0.186	0.185	1.3(0.002)
11	0.186	0.184	0.186	0.4(0.001)
12	0.177	0.184	0.178	2.1(0.003)
13	0.167	0.161	0.168	2.3(0.004)
14	0.183	0.190	0.181	2.4(0.004)
15	0.179	0.175	0.176	1.4(0.002)
Range				0.2-2.4
%CV				1.4

Abbreviation: CV: Coefficient of variance; SD: Standard deviation

site of measurement. They reported CV values of 0.66%, 3.10% and 1.36% for lumbar spine, proximal tail and tibia, respectively in 7 female Sprague Dawley rats, using a similar DXA scanning (Ammann et al. 1992). The low value of %CV for whole body BMD in rats indicated that the measurements were reproducible. However, we did not perform segmental BMD analysis like previous studies.

Quantum noise, changes in soft tissue composition, patient movement during the scans and scan analysis can influence the precision of DXA (Engelke et al. 1995). Correct positioning of patients or animals during a DXA scan is important in ensuring reproducible BMD results. Proper skills and training in positioning the subjects and intuition are required to obtain the best objective measurement (Carey & Delaney 2017). To our knowledge, this is the first study to report the short-term coefficient of variance for small animal BMD using Hologic Discovery QDR Wi DXA machine.

CONCLUSION

Overall, the short-term precision of spinal and hip BMD of human and whole body BMD of rats using Hologic Discovery QDR Wi DXA was acceptable. The random error should be considered when interpreting the BMD results obtained in longitudinal studies.

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