Original article

Cross calibration between two dual energy X-ray absorptiometry systems: Horizon A and Discovery A

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Background: When the department installed the new dual energy X-ray absorptiometry (DXA) system, cross calibration as the international society for clinical densitometry (ISCD) recommendation has to be implemented. The generalized least significant change (GLSC) and percentage of generalized least significant change (%GLSC) value must be determined for comparing the bone mineral density (BMD) values between 2 systems.
Objective: To determine the generalized least significant change (GLSC) and %GLSC values and compare the BMD relationship between Hologic Horizon A and Discovery A through the cross calibration.
Methods: Thirty women subjects (56 - 67 years) were scanned at the lumbar spine and femur on both systems. The linear regression and Bland-Altman analysis were used to reveal the relationship and agreement. The least significant change (LSC) was calculated on the individually DXA system and for cross-calibration between the two systems, the GLSC and %GLSC were presented.
Results: The relationship was highly correlated in BMD. Bland-Altman analysis presented good agreement. The LSC values in lumbar spine, femoral neck, and total femur were 1.6%, 2.8% and 1.2% for Horizon A and 2.1%, 2.6% and 1.8% for Discovery A, respectively. The LSC of both systems in all sites were within the minimum acceptable precision according to the recommendation from ISCD. The GLSC and %GLSC values between two systems in lumbar spine, femoral neck, and total femur were 0.015 g/cm^2 and 1.8%, 0.017 g/cm^2 and 2.6%, and 0.013 g/cm^2 and 1.6%, respectively.
Conclusion: The stated GLSC from two different systems could be used to interpret the true change of the BMD, when the magnitude of the difference of BMD between systems is greater than the GLSC value.

Keywords: DXA, cross calibration, precision, GLSC.

Dual energy X-ray absorptiometry (DXA) is the gold standard and is generally used to evaluate bone mineral density (BMD). The World Health Organization (WHO) recommended the sites of the lumbar spine (L1 - L4) and femur DXA measurement for osteoporosis diagnosis. (1) The DXA measurement is also used to monitor the long-term changes of BMD for the bone status follow up and to evaluate the response to intervention. The follow up BMD measurement should be performed on the same DXA system. The interpretation of the true loss or gain in BMD can be accomplished by the clinician when the difference of BMD exceeds the least significant change value (LSC).

In the DXA measurement, the sources of variation are the patient, technologist, and instrument (2), which all effects to the LSC value. However, in the case of the long-term operation, the replacement by the new DXA system might be required due to the deterioration of the old system. The follow up BMD measurement on the different DXA systems require the cross calibration to determine the generalize least significant change value (GLSC) and percentage of generalize least significant change (%GLSC) for comparing BMD values.(1, 3 - 5)

The International Society for Clinical Densitometry (ISCD) recommends cross-calibration(6) at the time of replacement due to the systematic

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differences between systems that may exceed the biological BMD changes. The Horizon A is the latest model of the DXA system (Hologic, Inc., Bedford, MA) which improves technology from the Discovery A (Hologic, Inc., Bedford, MA). The using of the gadolinium sulfoxylate scintillation detectors in Horizon A instead of the cadmium tungstate scintillation detectors in Discovery A offers a higher signal-to-noise performance.[7]

The purpose of this study was to determine the GLSC and %GLSC values and compare the BMD relationship between Hologic Horizon A and Discovery A through the cross calibration.

Materials and methods

Subjects

Thirty female subjects were recruited in this study. Exclusion criteria included lumbar spine and femur prosthesis, the historical of the fracture at the lumbar spine and/or femur, severe scoliosis at the lumbar spine, within seven days of oral contrast administration. This study was approved by the Institutional Review Board (IRB), the Faculty of Medicine Ramathibodi Hospital, Mahidol University (Research Ethics Code COA. MURA2020/572). The subject's demographic was shown in Table 1.

DXA measurement

All subjects were required to make two visits with the duration of within two weeks and one hour for each visit. All measurements were conducted by the same technologist and using the same scanning mode (fast array). The subjects were instructed about the entire measurement and signed written informed consent. They were asked to change to hospital light clothing and remove all metal and/or plastic artifacts before DXA measurement.

In the first visit, the subjects were scanned on Discovery A and Horizon A in the second visit. At each visit, the lumbar spine (L1 - L4) and femur were scanned two times. The subjects were released and repositioned for the second scan. The positioning of the lumbar spine scans, subject lied back down on the bed (make sure the lumbar spine (L1 - L4) is in the scanned area). The leg support block was introduced to reduce the curvature of the spine. The localized laser was set about 1 - 2 inches below the iliac crest and at the mid-line of the body. After the completion of the lumbar spine (L1 - L4) scan, the femur scan (left femur for all subjects) was acquired. The triangle block was used as the foot stabilization to turn the leg rolled inward about 25 degrees. The localized laser was placed at 3 inches below the greater trochanter and 1 inch medial to the shaft of the femur. The positioning was followed the manufacturer's recommendation.[8]

All scans on Discovery A were analyzed using Apex Software version 13.4.2 (Hologic, Inc., Bedford, MA) and Horizon A using Apex Software version 13.6.0.7 (Hologic, Inc., Bedford, MA). A quality control test was performed daily before collecting the data and the results were passed. The spine phantom was scan 10 times on each system, without repositioning, the variation of BMD, bone mineral content (BMC) and area value was within 0.2%.

Statistical analysis

The descriptive data of all subjects were reported as mean ± standard deviation (SD). Linear regression and Bland-Altman analysis were used to reveal the relationship and agreement between the two systems.[9] P – value < 0.05 was consider as statistically significant. Linear regression analysis was performed for deriving the cross-calibration equations. The mean BMD differences of Horizon A and Discovery A were plotted against the mean values of BMD. Limits of agreement were calculated using the formula mean ± 1.96 SD. The LSC was calculated on the individually DXA machine in terms of root mean square standard deviation (RMS - SD), coefficient of variation (CV), and percent coefficient of variation (%CV) were calculated by multiplying the SD of measurement errors by 2.77 (95% confidence level), as recommended by the ISCD.[10] The Wilcoxon signed-rank test was used for comparing precision between two systems.[11] The cross-calibration between two systems (Horizon A and Discovery A) was presented in GLSC and %GLSC values, which uses the ISCD DXA Machine Cross Calibration Calculating Tool to calculated.[12] The determination of GLSC and %GLSC was performed using the equation (1) and (2), respectively.[5]

Table 1. Demographic data of the subjects (n = 30).

	Mean ± SD	**Range**
Age (years)	58.8 ± 4.0	56.0 – 67.0
Height (cm)	155.0 ± 5.2	158 - 167
Weight (kg)	57.4 ± 8.6	59.8 - 80.0
BMI (kg /m²)	23.9 ± 3.6	16.8 - 32.1
BMD in Discovery A		
Lumbar spine (L1 - L4) (g/cm²)	0.862 ± 0.161	0.820 - 1.469
Femoral neck (g/cm²)	0.658 ± 0.109	0.724 - 0.892
Total femur (g/cm²)	0.816 ± 0.120	0.837 - 1.128
BMD in Horizon A		
Lumbar spine (L1 - L4) (g/cm²)	0.857 ± 0.158	0.794 - 1.459
Femoral neck (g/cm²)	0.657 ± 0.109	0.723 - 0.893
Total femur (g/cm²)	0.825 ± 0.121	0.850 - 1.134

SD: Standard deviation, BMI: Body mass index, BMD: Bone mineral density

$$GLSC = 1.96\sqrt{\hat{\sigma}_y^2 + \frac{(n-1)}{(n-2)}\, S_y^2(1-\hat{r})\left(1+\frac{1}{n}+\frac{\frac{s_x^2}{n}+(s_x^2-\hat{\sigma}_x^2)}{(n-1)s_x^2}\right)+\hat{b}^2\hat{\sigma}_x^2} \tag{1}$$

and

$$\%GLSC = 1.96\frac{\sqrt{\hat{\sigma}_y^2 + \frac{(n-1)}{(n-2)}\, S_y^2(1-\hat{r})\left(1+\frac{1}{n}+\frac{\frac{s_x^2}{n}+(s_x^2-\hat{\sigma}_x^2)}{(n-1)s_x^2}\right)+\hat{b}^2\hat{\sigma}_x^2}}{\hat{a}+\hat{b}\mu_x}\times 100\% \tag{2}$$

Where:

X = Old system (Discovery A)
Y = New system (Horizon A)
σ_x = Precision of old system
σ_y = Precision of new system
S_x = Variances of cross-calibration population of old system
S_y = Variances of cross-calibration population of old system
b = Regression slope
r = Correlation coefficient
n = Number of subject

Results

The demographic data of all subjects were given in Table 1. The relationship of BMD between Horizon A and Discovery A highly correlated with the r^2 values of 0.986, 0.981 and 0.984 for the lumbar spine, femoral neck and total femur, respectively is presented in Figure 1. The cross-calibration equations obtained by linear regression analysis is shown in Table 2. Bland-Altman plots for the lumbar spine, femoral neck, and total femur (limits of agreements = mean ± 1.96 × SD) are shown in Figure 2. All LSC (%CV) for each system was within the minimum acceptable precision according to the ISCD position recommended [13] and is shown in Table 3. As for the comparison of LSC (%CV), we observed no significant difference in precision between Horizon A and Discovery A. (*P* - value of lumbar spine, femoral neck and total femur were 0.080, 0.337 and 0.067, respectively). The GLSC and %GLSC values between systems in the lumbar spine, femoral neck, and total femur were 0.015 g/cm² and 1.8%, 0.017 g/cm² and 2.6%, and 0.013 g/cm² and 1.6%, respectively, as shown in Table 4.

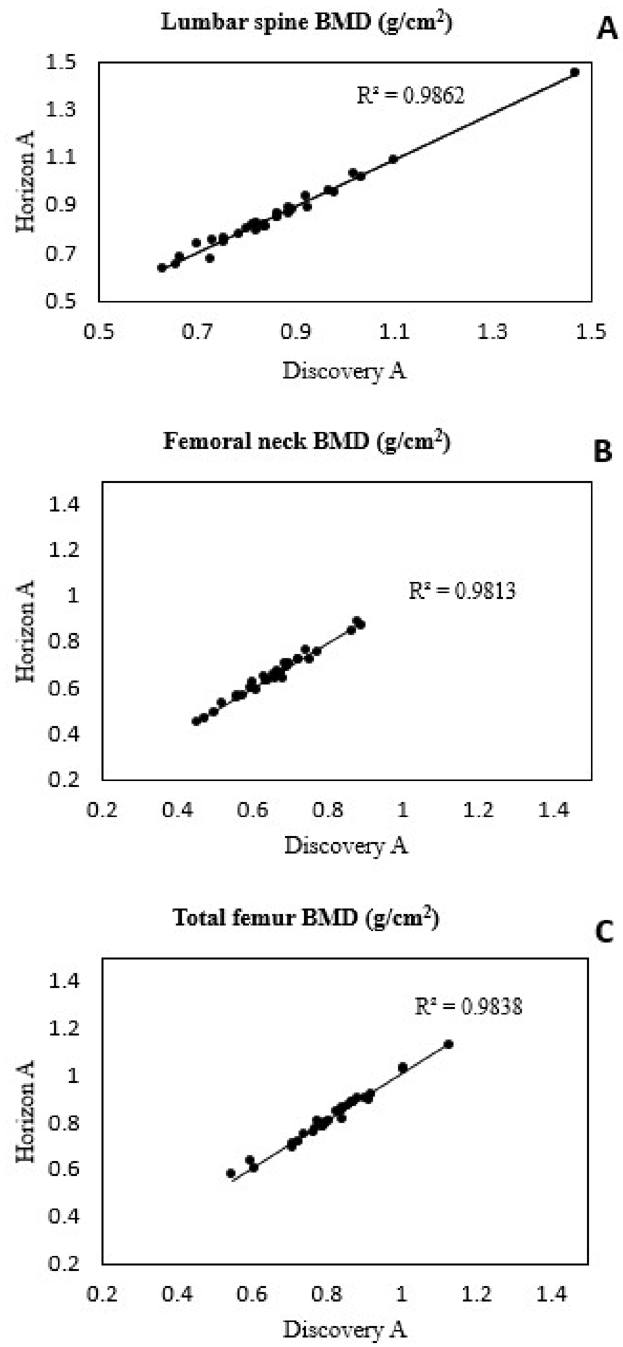

Figure 1. Correlation of BMD at the lumbar spine (A), femoral neck (B), and total femur (C) obtained on Discovery A and Horizon A.

Table 2. Cross calibration equation of BMD between Horizon A and Discovery A (n = 30).

Site	Cross calibration equation (Horizon A and Discovery A)	R-square	Slope
Lumbar spine (L1 - L4)	Horizon A = 0.015 + 0.977 × Discovery A	0.9862	0.977
Femoral neck	Horizon A = 0.012 + 0.980 × Discovery A	0.9813	0.980
Total femur	Horizon A = 0.009 + 1.000 × Discovery A	0.9838	1.000

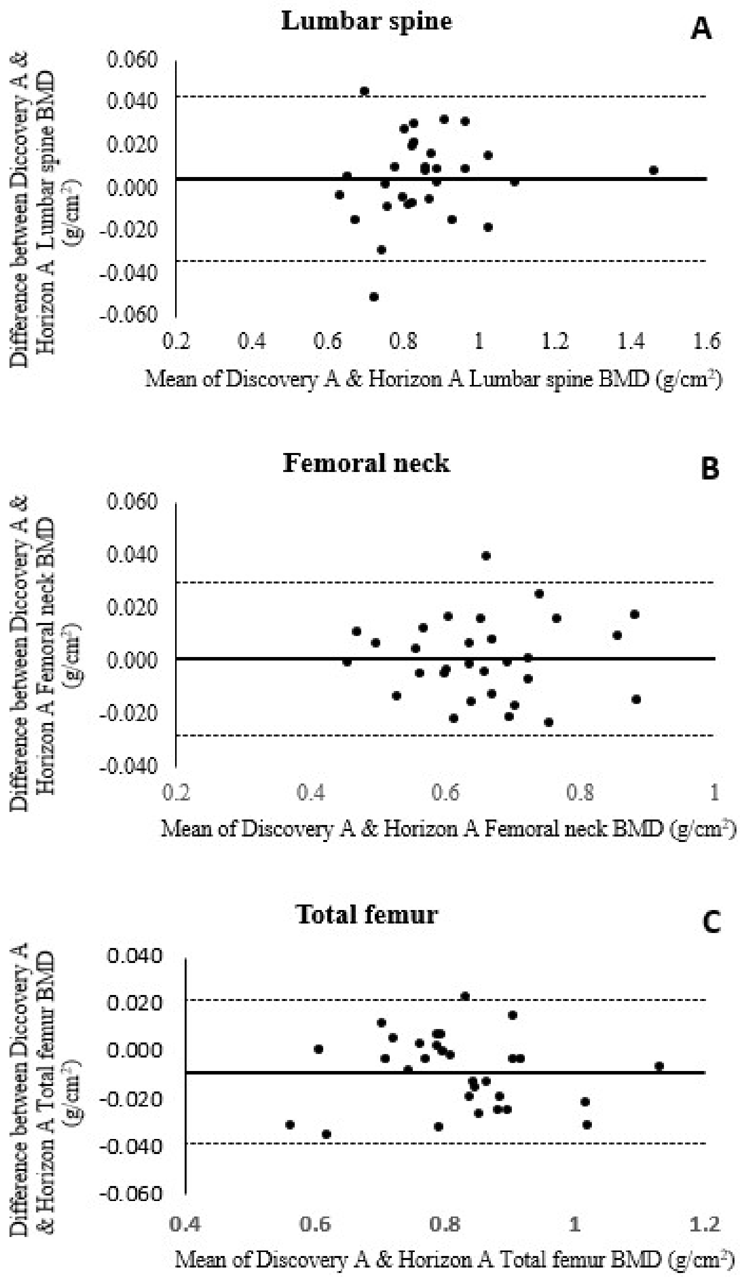

Figure 2. Agreement between BMD values of the lumbar spine (A), femoral neck (B), and total femur (C) obtained on Discovery A and Horizon A by Bland and Altman analysis. Solid line = mean difference and dashed lines = limits of agreement (mean difference ± 1.96 × SD).

Table 3. The least significant of individual DXA systems (Discovery A and Horizon A), (n = 30).

Site	Discovery A			Horizon A		
	RMS SD	CV	%CV	RMS SD	CV	%CV
Lumbar spine (L1 - L4)	0.018	0.021	2.07	0.013	0.016	1.60
Femoral neck	0.016	0.026	2.64	0.018	0.028	2.81
Total femur	0.015	0.018	1.84	0.010	0.012	1.16

RMS-SD: Root mean square standard deviation, CV: Coefficient of variation, %CV: Percent coefficient of variation $P < 0.05$

Table 4. Generalized least significant change between Horizon A and Discovery A.

Site	Discovery A to Horizon A	
	GLSC (g/cm^2)	% GLSC
Lumbar spine (L1 - L4)	0.015	1.8
Femoral neck	0.017	2.6
Total femur	0.013	1.6

GLSC: Generalize least significant change, %GLSC: Percent of generalize least significant change $P < 0.05$

Discussion

This study compared BMD values between two DXA systems (Horizon A and Discovery A) and developed cross calibration equations to convert BMD values from Discovery A to Horizon A. The BMD values were quite similar in both systems at all sites. The linear regression analysis showed an excellent correlation with r^2 of more than 0.98. The Bland-Altman analysis also presented good agreement.

The precision of Horizon A and Discovery A in this study is quite identical and no significant difference, similar to that of Whittaker LG, *et al.* [14] The performing of one technologist (the LSC value less than 3.0% for all studied sites) with more than 10 years' experience in BMD measurement by DXA followed ISCD standard performed all scans throughout the entire study might enhanced the accuracy of the precision in our study.

The discovered precision was within the ISCD recommendation with the value of 5.3%, 6.9%, and 5.0% for the lumbar spine, femoral neck and total femur, respectively. While the significantly better precision on Horizon A than Discovery A was reported in the lumbar spine from McNamara EA, *et al.* [15] and in the phantom study of Jankowski L, *et al.* [16]

For comparison data between two systems (Horizon A and Discovery A), we calculated the GLSC value for assisting the clinicians to monitor the BMD to make decision in patient management. The true change in the magnitude of the BMD could be interpreted when the difference between follow up BMD measured on Horizon A and baseline BMD measured on Discovery A greater than GLSC (95% confidence interval). Moreover, for the percentage change of BMD, the greater than %GLSC can be clarified as the true change. As for example, with the baseline on Discovery A, the significant change of the BMD in lumbar spine follow-up can be considered when the GLSC (%GLSC) was larger than 0.018 g/cm^2 (2.1%) and 0.015 g/cm^2 (1.8%) for Discovery A and Horizon A, respectively.

Ideally, ISCD recommends the representative population of the patient in the department for cross calibration. [13] However, there were some difficulties in making an appointment with the patients. The nominated participants in this study were the healthy female which might lead to our limitations. First, the average age of 58.8 years old was rather younger than that of the patients. The repositioning of the younger healthy participants shown higher reproducibility and smaller measurement error when compared to older population. [17] Second, all participants in this study were female. However, the study from Krueger D, *et al.* showed no significant difference in BMD precision between females and males [18] and no recommendation on gender for DXA cross calibration from ISCD. [19]

Conclusion

This study, the GLSC between Horizon A and Discovery A were calculated. The GLSC and %GLSC value were important to be used for comparing BMD values and the percentage of change of BMD that obtained between DXA systems, which different technology model and/or manufacturer. If the magnitude of the BMD difference between DXA system is greater than GLSC, the true change in BMD has occurred. To summarize, the cross calibration could minimize the discrepancies between devices and allows the accurate interpretation on BMD follow up from different DXA systems.

Conflict of interest

The authors, hereby, declare no conflict of interest.

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