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Original Articles/นิพนธ์ต้นฉบับ

Cross Calibration of Bone Mineral Density Values among Three Dual Energy X-ray Absorptiometry Systems.

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Abstract

The generalized Least Significant Change (GLSC) is at a 95% confidence interval of precision error in the bone mineral density (BMD). The objectives of the research were to generate the GLSC values among three DXA machines (Lunar Model Prodigy, HOLOGIC Model Discovery A and Discovery W), to predict Bone mineral Density (BMD) values from cross calibration equations, and to compare our predicted BMDs. Our research - derived with equations together with those from the manufacturers equations and observed BMDs from actual measurements. BMD measurements were performed on 30 females (age 20-80 years) at the lumbar spine and proximal femur. Each site was measured with all 3 DXA machines twice with repositioning in between. All measurement and analysis steps complied with the ISCD official position. The GLSCs were as follows: between Lunar Prodigy and Hologic Discovery A at the lumbar spine, the neck of femur and the total hip is at 0.066, 0.088, and 0.066 (g/cm^2), respectively; between Lunar Prodigy and Hologic Discovery W at the lumbar spine, the neck of femur and the total hip is at 0.064, 0.076, and 0.070 (g/cm^2), respectively; between Hologic Discovery A and Hologic Discovery W at the lumbar spine, the neck of femur and the total hip is at 0.020, 0.074, and 0.062 (g/cm^2), respectively. The comparison of the errors from both equations found that the lumbar spine and total hip were statistically significant but not statistically significant at the neck of femur. These errors were larger than GLSCs therefore, the calculation of GLSCs by using the data collection was more appropriate for cross-calibration of the BMDs than the calculated BMDs from both equations.

Keywords: Cross Calibration / DXA/BMD

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Introduction

Osteoporotic fractures have come to be recognized as one of the most serious problems in public health. For a 50-y-old white woman, the lifetime risk of suffering a fragility fracture of the spine, hip, or forearm is estimated to be 30-40%, which compares with the percentages for breast cancer and cardiovascular disease of 9-12% and 30-40%, respectively. For men, the risk of an osteoporotic fracture is about one third of that in women. In the United States in 1995, the total health care costs attributable to osteoporotic fractures exceeded $13 billion, a figure that is expected to rise to between $30 and $40 billion by the year 2020.[1] The post-menopause clinic of Chulalongkorn Hospital in Thailand studied the prevalence of osteoporosis in 1,047 patients, age ranged from 41 to 60 years. The results showed that the prevalence of osteoporosis in women that postmenopause was 11.9% and 21.4% for femoral neck and L-spine, respectively.[2,3] The osteoporosis is the main problem of public health in Thailand. The Bone Mineral Density (BMD) was used for diagnosis and follow up in this disease. Especially, the osteoporosis was recommended to check less than 1 time per year. For analysis, the BMD value of patient was compared with previous value. Thus, the accuracy and precision (reproducibility) of this value should be considered. The change of BMD occurs when the BMD value differ more than 95% Confidence Interval (CI) of precision error that this value is Generalized Least Significant Change (GLSC). For indication of the treatment efficiency, the factor that involve with BMD value was controlled with same parameter in previous check. Furthermore, measurement and calculation techniques of each model and manufacturer are difference. Due to method of generate dual energy x-ray, type of detector, calibration tool and technique, and analysis algorithms. Those factors affect to an intensity of radiation to irradiate patient, a different count value and an equation for calculation. Thus, the compassion of the BMD value with different model and manufacture was tested with patient.[4]

The factors that affect the BMD value in dual energy x-ray absorptiometry (DXA)[5] are as follows;

1. Dual energy x-ray absorptiometry (DXA)
   - 1.1 Methods of generate dual energy x-ray
   - 1.2 Detector type
   - 1.3 Edge detection software
   - 1.4 Calibration technique
   - 1.5 Region Of Interest (ROI)
2. Technologist Precision
   - 2.1 Patient positioning and analysis

Due to there are a lot of factors to the BMDs. Thus, the precision error should be analyzed. And the comparison of the BMDs between machines can be done when Generalized Least Significant Change (GLSC) value was calculated. The GLSCs of the both machines must be more than the GLSCs with same machine.

The main purpose of this study is to generate the GLSC value of three DXA machines at division of Nuclear Medicine, Rama-thibodi Hospital, to diagnosis the change of BMD from the measurement. We have presented an equation to calculate the GLSC(10) between 2 measures on 3 different DXA systems. If the magnitude of the difference between a patient's baseline BMD measured on system 1 and their follow up BMD measured on system 2 is greater than the GLSC, then there is 95% confidence interval that a true change in BMDs has occurred and if the difference between a patient's baseline BMD measure on system 1 and their follow up BMD measure on system 2 is lesser than the GLSC, then there is 95% confidence interval that a variation of measure occurred.

Objective

The objectives of this study are: 2.1 To estimate Generalized Least Significant Change (GLSC) of Dual Energy X-ray Absorptiometry (DXA) from Lunar Prodigy, Hologic Discovery A and Discovery W at

Division of Nuclear Medicine at Ramathibodi Hospital. 2.2 To predicted cross calibration equation from Lunar Prodigy, Hologic Discovery A and Discovery W. 2.3 To study the compare predicted BMDs between research's cross calibration equation and manufac-turer's cross calibration equation.

Methods

Patients aged at least 20 years old sent for DXA examination at Nuclear Medicine Unit, Ramathibodi Hospital were invited to participate in the study. Thirty females who gave written informed consent after being explained and reading the volunteer information sheet about the study were included. Exclusion criterion The subjects were excluded from the study if there was a structural abnormality or artifact at any measurement sites (L1-L4 vertebrae or hip) rendering DXA assessment inaccurate. The protocol of the study was approved by the institutional review board. The subjects completed the questionnaire and underwent BMD measurements at the lumbar spine and proximal femur using all 3 DXA machines (Lunar Prodigy, Hologic Discovery A, and Hologic Discovery W) in random sequences depending on the availability of the machine at the time. With each machine, each site was measured twice with repositioning. The repositioning was done after the subjects had underwent the first measurement, got up from the imaging table, walked about in front of the imaging room, and returned to the imaging table for a second measurement to simulate as close as possible the setting of the follow-up DXA scan. Calculate Generalized Least Significant Change[13-15] between the system 1 and system2 using equation 1 between DXA (Dual Energy X-ray Absorp-tiometry) Lunar Prodigy, Hologic Discovery A and Hologic Discovery W in lumbar spine, neck of femur and total hip. The machine in system 1 and system 2 are listed in table 1.

$$GLSC = 1.96\sqrt{\hat{\sigma}_Y^2 + \frac{(n-1)}{(n-2)}S_Y^2(1-\hat{r}^2)\left(1+\frac{1}{n}+\frac{\frac{S_X^2}{n}+\left(S_X^2-\hat{\sigma}_X^2\right)}{(n-1)S_X^2}\right)+\hat{b}^2\hat{\sigma}_X^2} \quad --(1)$$

Where:

- Old system (System 1) = X
- New system (System 2) = Y
- Precision of old system = sx
- Precision of new system = sy
- Variances of cross-calibration population of old system = Sx
- Variances of cross-calibration population of new system = Sy
- Regression slope = *b*
- Correlation coefficient = r
- Number of subject = n

Plot curve and calculate relationship between BMDs of system 1 and system 2 at lumbar spine, neck of femur and total hip in order to generate cross calibration equation. Compare cross calibration equation from this research and cross calibration equation from manufacturer.

- Random BMDs[16] from first or second measurement for system 1 (lumbar spine, total hip and neck of femur)
- Use cross calibration equation (research) to predicted BMDs from system 1 (random BMD) to system 2
- Compare BMD between predicted BMDs from research cross calibration equation and actual measurement from system 2
- Use Bland & Altman plot reveal a relationship between difference ($BMD_{predicted}$ and $BMD_{observed}$) and mean of BMD ($BMD_{predicted}$ and $BMD_{observed}$)

- $\text{Mean} = \frac{BMD_p + BMD_o}{2}$
- $\text{Difference} = BMD_o - BMD_p$

: $BMD_{predicted}$ (BMD_p) = BMD from cross calibration equation (research)

: $BMD_{observed}$ (BMD_o) = BMD from actual measurement in system 2

- Plot curve between difference and mean
- Calculate 95% limits of agreement (14) of BMD

- Mean Difference = $\frac{\sum \text{Difference}}{30}$
- SD Difference = $\sqrt{\frac{\sum_{i=1}^{n}(\text{Diffi} - \overline{\text{Diff}})^2}{n-1}}$

- Upper 95% limits of agreement
  = Mean Difference + (1.96 x SD Difference)
- Lower 95% limits of agreement
  = Mean Difference - (1.96 x SD Difference)
- Use cross calibration equation (manufacturer) to predicted BMDs from system 1 (random BMD) to system 2
- Compare BMDs between predicted BMDs from manufacturer cross calibration equation and actual measurement from system 2
- Use Bland & Altman plot reveal a relationship between difference ($BMD_{predicted}$ and $BMD_{observed}$) and mean of BMD ($BMD_{predicted}$ and $BMD_{observed}$)
- Plot curve between difference and mean
- Calculate 95% limits of agreement of BMD
- Compare 95% limits of agreement between research and manufacturer cross calibration equation

Results

1. Generalized Least Significant Change of DXA from Lunar Prodigy, Hologic Discovery A and W at division of Nuclear Medicine, Ramathibodi Hospital were shown in table 2.
2. Cross calibration equations from this research shown in the table 3-5
3. The research gives the comparison between research's cross calibration equations and manufacturer's cross calibration equations Manufacturer cross calibration equations

- Lunar Prodigy and Hologic Discovery A,W
  Hologic Discovery A, W = (-0.038) +(0.918 * Lunar Prodigy)
- Hologic Discovery A and Hologic Discovery W
  Hologic Discovery W = (0) + (1 * Hologic Discovery A)

Table 1 Machine in system 1 and system 2

System 1	System 2
Lunar Model Prodigy	Hologic Model Discovery A
Lunar Model Prodigy	Hologic Model Discovery W
Hologic Model Discovery A	Hologic Model Discovery W

Table 2 GLSC from system 1 to system 2

	Lumbar spine	Neck of femur	Total hip
Lunar Prodigy → Hologic Discovery A			
GLSC (g/cm^2)	0.066	0.088	0.066
%CV GLSC	7.2	12.5	7.9
Lunar Prodigy → Hologic Discovery W			
GLSC (g/cm^2)	0.064	0.076	0.070
%CV GLSC	7.3	10.8	8.3
Hologic Discovery → A Hologic Discovery W			
GLSC (g/cm^2)	0.020	0.074	0.062
%CV GLSC	2.2	10.4	7.3

Table 3 Cross calibration equation between Lunar Prodigy and Hologic Discovery A

ROI	Equation
Lumbar spine	Hologic Discovery A = (-0.008) + (0.875 * Lunar Prodigy)
Neck of femur	Hologic Discovery A = (-0.018) + (0.848 * Lunar Prodigy)
Total hip	Hologic Discovery A = (0.043) + (0.848 * Lunar Prodigy)

Table 4 Cross calibration equation between Lunar Prodigy and Hologic Discovery W

ROI	Equation
Lumbar spine	Hologic Discovery W = (-0.044) + (0.881 * Lunar Prodigy)
Neck of femur	Hologic Discovery W = (-0.056) + (0.900 * Lunar Prodigy)
Total hip	Hologic Discovery W = (-0.033) + (0.945 * Lunar Prodigy)

Table 5 Cross calibration equation between Hologic Discovery A and Hologic Discovery W

ROI	Equation
Lumbar spine	Hologic Discovery W)= (-0.029) + (1 * Hologic Discovery A)
Neck of femur	Hologic Discovery W)= (0.003) + (1.003 * Hologic Discovery A)
Total hip	Hologic Discovery W)= (-0.057) + (1.086 * Hologic Discovery A)

Table 6 The 95% confidence interval of difference between observed and predicted BMD using research equations and manufacturer equations (cross calibration equations between Lunar Prodigy and Hologic Discovery A)

	Research Equations **95% confidence interval**	**Manufacturer Equations** **95% confidence interval**
Lumbar spine	-0.0507 - 0.0492	-0.0678 - 0.0359
Neck of femur	-0.0778 - 0.0864	-0.0705 - 0.0944
Total hip	-0.0569 - 0.0534	-0.1003 - 0.0269

Table 7 The 95% confidence interval of difference between observed and predicted BMD using research equations and manufacturer equations (cross calibration equations between Lunar Prodigy and Hologic Discovery W)

	Research Equations **95% confidence interval**	**Manufacturer Equations** **95% confidence interval**
Lumbar spine	-0.0515 - 0.0512	-0.0986 - 0.0085
Neck of femur	-0.0731 - 0.0679	-0.0591 - 0.0811
Total hip	-0.0643 - 0.0562	-0.0854 - 0.0367

Table 8 The 95% confidence interval of difference between observed and predicted BMD using research equations and manufacturer equations (cross calibration equations between Hologic Discovery A and Hologic Discovery W)

	Research Equations 95% confidence interval	Manufacturer Equations 95% confidence interval
Lumbar spine	-0.0348 - 0.0346	-0.0638 - 0.0056
Neck of femur	-0.0634 - 0.0512	-0.0583 - 0.0563
Total hip	-0.0605 - 0.0557	-0.0474 - 0.0721

3.1 The comparison between Lunar Prodigy and Hologic Discovery A were shown in table 6

3.2 The comparison between Lunar Prodigy and Hologic Discovery W were shown in table 7

3.3 The comparison between Hologic Discovery A and Hologic Discovery W were shown in table 8

Discussion

Generalized Least Significant Change (GLSC) has clinical applications in monitoring disease progression or treatment effect in bone mineral density (BMD) and bone mineral content. The main purpose of the research was to generate the GLSC values among three DXA machines at division of Nuclear Medicine, Ramathibodi Hospital. The generated GLSC values would help the clinicians monitoring the BMD to make decision in patient management. If the magnitude of the difference between a patient's baseline BMD measured on system 1 and their follow-up BMD measured on system 2 is greater than the GLSC, then there is 95% confidence that a true change in BMD has occurred and if the difference between a patient's baseline BMD measure on system 1 and their follow up BMD measure on system 2 is less than the GLSC, that is less than 95% confidence interval of the precision error, we cannot conclude that the change is genuine. The next objective was to assess if it was appropriate to use linear regression, cross-calibration equations to predict BMD measurements of one DXA machine from the others. For this, we estimated the difference between the observed (measured) BMDs and the predicted ones. The manufacturer cross-calibration equations were also assessed in the same way. Bland & Altman plots revealed no linear relationship between the differences and the means of the observed and predicted BMDs using either research or manufacturer cross calibration equations. The differences between the measurements form all 3 pair machines scattered relatively evenly about the x-axis without systematic trend, indicating the lack of association between the precision error and the magnitude of the BMDs. This implies that systematic bias is minimal, if at all present. The research's cross calibration equations and manufacturer's cross-calibration equations from Lunar Prodigy to Hologic Discovery A were statistically significant at the lumbar spine (p-value 0.027) and total hip (p-value 0.000) but not statistically significant at the neck of femur (p-value 0.483), Lunar Prodigy to Hologic Discovery W were statistically significant at the lumbar spine (p-value 0.000) and total hip (p-value 0.014) but not statistically significant at the neck of femur (p-value is 0.148). Hologic Discovery A to Hologic Discovery W were statistically significant at the lumbar spine (p-value 0.000) but not statistically significant at the neck of femur (p-values 0.501) and total hip (p-values 0.063).

This study followed the International Society for Clinic Densitometry (ISCD) in vivo cross-calibration protocol. All densitometers were calibrated daily and weekly for quality control in the morning before their use so all measurements were deemed be accurate. One technologist positioned and analyzed volunteers

on all machines, to avoid inter-observer variation. Repeated measurement were performed for all machines, the average measurement for each site may have made for more accurate measurement at each site, and the cross calibration for all DXA systems may have been more accurate. Reposition volunteers were performed when repeated measurement for all DXA systems may have made close to actual measurement in the patients between baseline and follow up measurement Ideally, a patient should be followed-up with the DXA system used at baseline. However, often this is impractical. In general, the manufacturers provide a conversion equation, typically a linear regression, to estimate the BMD values from or to their DXA machine. Nevertheless, the ISCD recommends that the manufacturer's conversion equation should not be used at individual DXA centers. Little is known regarding how manufacturers performed testing. It generally is believed that manufacturers use young normal subjects with no degenerative changes and that expert technologist perform the scans. Furthermore, it is not known how many subjects are used or how many repeat scans are conducted. Overall, the manufacturers may not reflect position data that are commonly encountered in the clinic. The DXA centers should determine and use their own GLSC when comparing measurement performed on 2 different systems. Our attempt to generate conver-sion or predictive equations from one system to another resulted in relatively large differences between the observed and predicted BMDs. Therefore, the prediction method should only be used when there is no alternative. The differences between our equations and the manufactures' were of similar range. However, the latter tend to span over negative values, particularly at the lumbar spine and, more so, the total hip, suggesting systematic bias toward overestimation.

Conclusion

The GLSCs between Lunar Prodigy, Hologic Discovery A and Hologic Discovery W have been estimated. These GLSCs should be used when comparing the BMDs measured from different DXA machines. The cross - calibration equations have also been derived but the prediction errors are larger than the GLSCs. Hence, the GLSCs should be used when comparing the BMDs from different DXA machines.

References

1. Fogelman I, Blake GM. Different approaches to bone densitometry. J Nucl Med 2000;41:2015-25.
2. Taechakraichana N AP, Panyakhamlerd K, Limpaphayom K. Postmenopausal osteoporosis: what is the real magnitude of the problem in the Thai population. J Med Assoc Thai 1998;81:397-401.
3. Limpaphayom K. Health Aging in the 21st century The 6th international menopause society world congress on the menopause. 1999.
4. Hammami M, Picaud J-C, Fusch C, Hockman EM, Rigo J, Koo WWK. Phantoms for Cross-Calibration of Dual Energy X-ray Absorptiometry Measurements in Infants. J Am Coll Nutr 2002;21:328-32.
5. ISCD. International Society for Bone Densitometry Technologist Course Syllabus and Associated reading Materials 8ed2008.
6. Johnson DR. Introductory Anatomy: Bones. 2005; Available from: http://www.leeds.ac.uk/chb/lectures/anatomy3.html.

7. Buckwalter JA. Principles and their application Turek's Orthopedics. 6 ed. Philadelphia: Lippincott Williams & Wilkins; 2005:3-56.
8. Shier D, Butter J, Lewis R. Hole's Human Anatomy Physiology 1996.
9. WHO Scientific group. Prevention and Management of Osteoporosis. Geneva 2003.
10. Lewiecki EM, Baim S, Binkley N, Bilezikian JP, Kendler DL, Hans DB, et al. Report of the International Society for Clinical Densitometry 2007 Adult Position Development Conference and Official Positions. Southern Medical Journal. 2008;101:735-910.
11. Royal AdelaideHospital. 2009; Available from: http://www. rah.sa.gov.au/nucmed/BMD/bmd__equipment.htm.
12. Nelson B. Watts. Fundamentals and pitfalls of bone densitometry using dual-energy X-ray absorptiometry(DXA) Osteopor Int 2004;15:847-54.
13. ISCD. About ISCD. 2009; Available from: http://www.iscd.org/visitors/about/AboutISCD.cfm.
14. Shepherd JA, Lu Y, Wilson K, Fuerst T, Genant H, Hangartner TN, et al. Cross-calibration and minimum precision standards for dual-energy X-ray absorptiometry: the 2005 ISCD Official Positions. J Clin Densitom 2006;9:31-6.
15. Shepherd JA, Lu Y. A generalized least significant change for individuals measured on different DXA systems. J Clin Densitom 2007;10:249-58.
16. GraphPad Software. 2005; Available from: http://www.graphpad.com/quickcalcs/random2.cfm.
17. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 2003;22:85-9.