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Least significant change as an essential tool for monitoring of bone mineral density using dual energy X-ray absorptiometry

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KEYWORDS
Least significant change;
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ABSTRACT
Dual-energy X-ray absorptiometry (DXA) scans are the gold standard for measuring bone mineral density (BMD). It is accepted that precision error is crucial in monitoring BMD measurements. The least significant change (LSC) signifies the minimum difference between two consecutive BMD measurements that can confidently indicate a genuine biological change. This value provides direct benefit to patients by aiding clinicians in making clinical decisions based on real change or stability of BMD. This study aimed to determine the LSC for DXA scan used at Udonthani Cancer Hospital. We conducted a cross-sectional study in 150 patients undertaking DXA scans performed by one of our five radio-technologists from March 2023 to September 2023. Each technologist assessed BMD study of 30 participants twice, obtaining paired BMD measurements for the lumbar vertebrae, hip, and forearm. We utilized the copy of region of interest (ROI) software to replicate the ROI. The LSC was calculated with a 95% CI using both the RMS SD and RMS %CV formulas. The obtained LSC were 3.26% for the L1-L4 vertebrae, 4.40% for the femoral neck, 2.30% for the total proximal femur, and 5.30% for the 33% radius, meeting 2019 International Society for Clinical Densitometry (ISCD) standards. Nevertheless, the ISCD 2019 guidelines do not provide acceptable value for determining the LSC at the 33% radius. The higher variability in measurements at the femoral neck and the 33% radius emphasizes the need for continuous professional development and enhanced reproducible methods to improve the precision of BMD measurement using DXA scans.

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Introduction

Dual-energy X-ray absorptiometry (DXA) scan is the gold standard method for measuring bone mineral density (BMD), playing a vital role in diagnosing osteoporosis, assessing risk of fracture, and monitoring changes in BMD over time[1-4]. The core principle of DXA is the measurement of transmission of X-ray with high- and low-energy photons through the body[2]. Precision error becomes particularly critical especially in the monitoring of consecutive BMD measurements using DXA[1].

The least significant change (LSC) represents the least amount of BMD change that can be considered statistically significant. In simpler terms, it signifies the minimum difference between two consecutive measurements that can confidently indicate a genuine biological change, exceeding precision error of the method[3,5]. The LSC helps clinicians make clinical decisions based on real change or stability of BMD. Several factors affect this value, including the instrument used, the characteristics of the patient population, the measurement site, and the skill of the radio-technologist in positioning the patient (radio-technologist's precision). Notably, the radio-technologist's precision is the key factor in determining the LSC[3]. In addition, although the manufacturer-provided LSC is available in each BMD machine, it cannot be accurately applied and used for different settings due to variable skills of patient positioning by different technologists[1]. We aimed to determine the LSC for DXA scan utilized at Udonthani Cancer Hospital.

Materials and methods

Study design and participants

During March 2023 to September 2023, we enrolled new participants referred for DXA scans at Udonthani Cancer Hospital. Inclusion criteria were age ≥ 18 years with good cooperation, whereas exclusion criteria included pregnant women, individuals with disabilities, and those exceeding 159 kg in body weight which is over the machine capacity. Ethical approval for the study was obtained from the local Ethics Committee, and informed written consent was obtained from all participants.

A cross-sectional study was conducted using DXA scan (Lunar Prodigy, GE) to analyze bone mineral density results from 150 participants, with examinations performed by five radio-technologists. Following the 2019 International Society for Clinical Densitometry (ISCD) guidelines[6], each radio-technologist assessed 30 participants twice. Prior to undergoing a second DXA scan, participants were asked to step down from the densitometer and then be repositioned. Paired measurements of BMD were acquired for the lumbar vertebrae, hip, and forearm[6]. In addition, we utilized the copy of region of interest (ROI) software to replicate the ROI from the initial set of images to the subsequent set. The ROIs are shown in figure S1 (supplement data).

We assessed the individual LSC at L1-L4 vertebrae, femoral neck, total proximal femur, and 33% radius for each radio-technologist, as well as our institute LSC. The LSC was calculated with a 95% confidence interval (95% CI) using both the root mean square standard deviation (RMS SD) and root mean square percentage coefficient of variation (RMS %CV) formulas[6].

Research protocol

Participant data, including age, sex, ethnicity, menopausal status, body weight, height, BMI, underlying diseases, and current medications were collected. The characteristics of all participants are summarized in table 1. Table 2 classifies the characteristics of the groups studied by each individual radio-technologist. Table 3 presents details about the radio-technologists, such as their age, duration of experience with DXA, and the number of prior DXA cases before their participation in this study.

Statistical analysis

Continuous variables such as age, weight, height, and BMI were shown as mean ± SD and median (min-max). Categorical variables such as gender, ethnicity, menopausal status, underlying diseases, and current medications were demonstrated in both numbers and percentages. The RMS SD, RMS%CV, and LSC at the 95% confidence interval were computed employing the ISCD Advanced Precision Calculating Tool[(7)]. This calculator expresses precision error as RMS SD (absolute value in g/cm^2), CV or %CV and LSC with a range of confidence levels. It is exclusively indicated for advanced bone densitometrists and should be used in particular clinical practice scenarios or clinical research.

Results

Among the 150 participants, ranging from 20 to 87 years of age, with the mean age of 52.5 years, the majority, 80.7%, were female. Menopausal status was reported in 67.8% of the female participants, while male accounted for 19.3% of the total. More than half of the participants, 96 cases (64%), had underlying diseases, predominantly thyroid cancer and breast cancer, undergoing thyroid hormone suppression, and aromatase inhibitor treatments, respectively. The remaining participants were healthy, as detailed in table 1.

Table 1 Participant characteristics

Variable	Value
Age: years	
Mean ± SD	52.5±11.5
Median (min-max)	52.0 (20.0-87.0)
Sex: (n, %)	
Male	29.0 (19.3)
Female	121.0 (80.7)
Menopausal status (n, %)	
Premenopausal	39.0 (32.3)
Menopausal	82.0 (67.8)
Ethnics (n, %)	
Thai	150.0 (100.0)
BMI: kg/m^2	
Mean ± SD	24.5±4.0
Median (min-max)	23.9 (17.3-37.6)
< 18.5 (Underweight)	8.0 (5.3)
18.5 – 24.9 (Normal weight)	80.0 (53.3)
25.0 – 29.9 (Pre-obesity)	47.0 (31.3)
30.0 – 34.9 (Obesity class I)	13.0 (8.7)
35.0 – 39.9 (Obesity class II)	2.0 (1.3)
$\geq$ 40.0 (Obesity class III)	-

Table 1 Participant characteristics (Cont.)

Variable	Value
Underlying disease (n, %)	
Healthy	54.0 (36.0)
Thyroid cancer	50.0 (33.3)
Breast cancer	23.0 (15.3)
Hyperthyroidism	3.0 (2.0)
Hyperparathyroidism	2.0 (1.4)
Others	18.0 (12.0)
Current medication (n, %)	
No medication	54.0 (36.0)
Thyroid hormone	50.0 (33.3)
Aromatase inhibitor	16.0 (10.7)
Others	30.0 (20.0)

Abbreviation: SD, standard deviation; BMI, Body mass index.

Table 2 illustrates participant characteristics divided into five groups by each radio-technologist. Baseline clinical and demographic characteristics were well balanced among the groups.

Table 2 Participant characteristics divided by each radio-technologist (A, B, C, D, E)

Variable	Radio-technologist				
	A	B	C	D	E
Age (years)					
Mean ± SD	50.2±14.8	52.9±9.6	49.0±9.2	54.3±10.5	55.9±12.1
Median	47.5	52.0	50.0	55.5	55.0
(min-max)	(28.0-87.0)	(34.0-71.0)	(20.0-64.0)	(32.0-85.0)	(23.0-85.0)
Sex:					
Female (n, %)	24.0 (19.8)	22.0 (18.2)	30.0 (24.8)	26.0 (21.5)	19.0 (15.7)
Weight (kg)					
Mean ± SD	59.6±14.2	66.1±11	60.4±12.7	61.3±11.1	60.1±9.8
Median	57.3	66.8	55.1	60.0	59.0
(min-max)	(40.0-96.0)	(44.6-87.0)	(39.5-98.6)	(42.0-87.0)	(42.3-78.0)
Height (cm)					
Mean ± SD	157.4±6.8	160.1±9.2	157.3±5.6	157.2±7.8	160.0±7.2
Median	155.0	158.5	157.0	156.0	160.0
(min-max)	(148.0-175.0)	(143.0-179.0)	(147.0-170.0)	(139.0-174.0)	(145.0-174.0)

Table 2 Participant characteristics divided by each radio-technologist (A, B, C, D, E) (Cont.)

Variable	Radio-technologist				
	A	B	C	D	E
BMI (kg/m^2)					
Mean ± SD	23.9±4.8	25.8±3.5	24.3±4.7	24.8±3.9	23.3±2.7
Median	22.8	25.5	23.1	24.2	23.6
(min-max)	(17.3-35.2)	(19.1-32.7)	(18.3-37.6)	(17.9-32.1)	(17.8-29.1)

Abbreviation: SD, standard deviation; BMI, Body mass index.

The characteristics of each radio-technologist are displayed in table 3. The duration of their work experience with DXA ranges from two to three years. Radio-technologist A has the most experience, with 178 previous DXA cases, while radio-technologist C has the lowest, with 62 previous cases.

Table 3 Characteristics of radio-technologists (A, B, C, D, E)

Variable	Radio-technologist					Mean
	A	B	C	D	E	
Age: years	40	52	48	46	56	48.4
Duration of work experience with DXA scan: years	3	3	2	2	2	2.4
Number of previous DXA cases	178	97	62	63	69	93.8

Abbreviation: DXA, Dual-energy X-ray absorptiometry.

Table 4 The LSC by RMS%CV formula

Site	LSC (%)					
	A	B	C	D	E	Average
L1-L4 vertebrae	3.57	3.14	3.21	3.58	2.80	3.26
Femoral neck	4.91	2.93	5.71	4.07	4.37	4.40
Total proximal femur	2.06	1.62	2.80	2.21	2.81	2.30
33% Radius	4.96	1.62	6.40	4.78	8.75	5.30

Abbreviation: LSC, Least significant change; RMS%CV, root mean square percentage coefficient of variation.

Table 5 The LSC by RMS SD formula

Site	LSC (g/cm^2)					
	A	B	C	D	E	Average
L1-L4 vertebrae	0.037	0.034	0.037	0.038	0.032	0.036
Femoral neck	0.050	0.026	0.054	0.035	0.034	0.040
Total proximal femur	0.018	0.015	0.028	0.019	0.025	0.021
33% Radius	0.041	0.015	0.052	0.037	0.066	0.042

Abbreviation: LSC, Least significant change; RMS SD, root mean square standard deviation.

Discussion

The LSC determined using the RMS%CV formula were as follows: 3.26% for the L1-L4 vertebrae, 4.40% for the femoral neck, 2.30% for the total proximal femur, and 5.30% for the 33% radius. Notably, each of these values falls within the acceptable thresholds established by the ISCD 2019 guidelines, which specifies 5.3% for the L1-L4 vertebrae, 6.9% for the femoral neck, and 5.0% for the total proximal femur(6). However, there are no standard criteria for the 33% radius as this site is not typically included in the routine DXA scan.

A peer review by Wilson et al(8) reported the LSC of 1.22% at the L1-L4 vertebrae and 1.97% at the femoral neck(8), which were lower than those observed for both L1-L4 vertebrae and femoral neck in our study. Moreover, apart from the total proximal femur, the LSC values for nearly all sites in our study were higher than those reported by Nelson et al(9). The LSC values they provided for the L1-L4 vertebrae, the femoral neck, and the total proximal femur were 0.028, 0.030, and 0.021 g/cm^2, respectively(9). Even though Nelson et al(9) analyzed LSC results from eight radio-technologists, which potentially caused larger variability, their LSC results were still better than those observed in our study. This might be due to the relatively less experience of our radio-technologists.

Additionally, the LSC for nearly all sites in our study were higher than those recommended by the manufacturer which specify LSC values of 0.010, 0.014, 0.012, and 0.020 g/cm^2 for the L1-L4 vertebrae, the femoral neck, the total proximal femur, and the 33% radius, respectively. However, there is no disclosure of the sources of the process in obtaining these numbers.

Conclusion

This study determined the LSC among five radio-technologists, with half of participants were cancer patients. The results showed that the LSC values across various sites —specifically the L1-L4 vertebrae, the femoral neck, and the total proximal femur—met ISCD standards. Nevertheless, the ISCD 2019 guidelines do not provide acceptable criteria for determining the LSC at the 33% radius. The higher variability in measurements at the femoral neck and the 33% radius emphasizes the need for ongoing professional development through re-training to improve reproducibility and enhance the precision of BMD measurements using DXA.

Take home messages

Although ISCD 2019 recommends that individual institutions ascertain their own LSC, some face limitations due to the need for sufficient volunteers and additional time required for repeat scans. Therefore, LSC in this study may be a reference standard for institutions sharing patient demographics, numbers, and levels of experience among radio-technologists.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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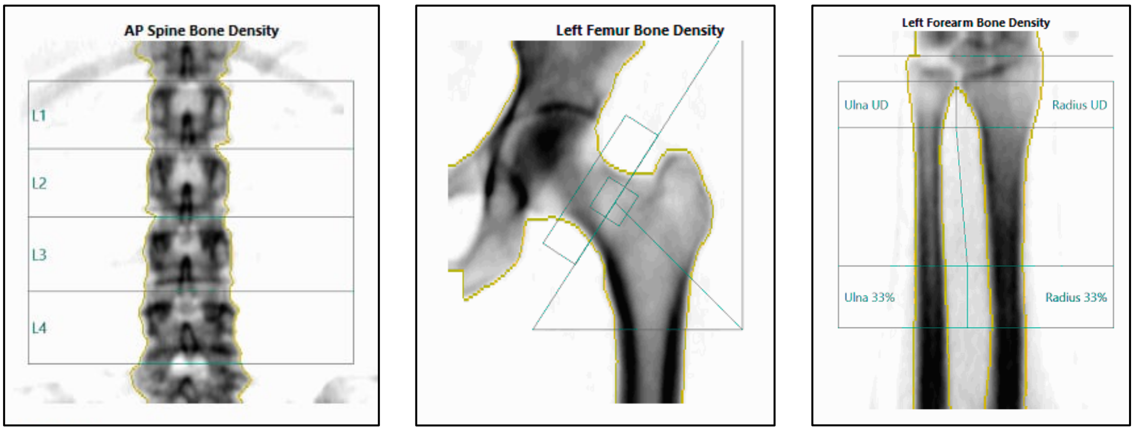
Supplementary



(A) (B) (C)

Figure S1 The ROIs include (A) L1-L4 vertebrae, (B) femoral neck and total proximal femur, and (C) 33% radius.

Abbreviation: ROIs, Region of interest.