#### **ORIGINAL RESEARCH**



# Radiofrequency Echographic Multispectrometry (REMS) can Overcome the Effects of Structural Internal Artifacts and Evaluate Bone Fragility Accurately

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#### **Abstract**

**Purpose** This study measured bone mineral density (BMD) in a Japanese population using the novel non-ionizing system using radiofrequency echographic multispectrometry (REMS) and compared the results with those obtained using traditional dual-energy X-ray absorptiometry (DXA). We aimed to identify any discrepancies between measurements obtained using these instruments and identify the influencing factors.

**Methods** This cross-sectional study examined patients with osteoporosis treated at a single center from April to August 2023. We examined BMD assessment by DXA and REMS in lumbar spine and proximal femur. Patients were categorized into two groups: those with discrepancies between lumbar spine BMD measured by DXA and REMS, and those without. Semiquantitative evaluation of vertebral fractures and abdominal aortic calcification scoring were also performed and compared between the two groups, along with various patient characteristics.

Results A total of 70 patients (88.6% female; mean age  $78.39 \pm 9.50$  years) undergoing osteoporosis treatment were included in the study. A significant difference was noted between DXA and REMS measurement of BMD and T-scores, with REMS recording consistently lower values. The discrepancy group exhibited a higher incidence of multiple vertebral fractures and increased vascular calcification than the non-discrepancy group. Multivariate analysis indicated that diabetes mellitus, severe vertebral fractures, and increased abdominal aortic calcification scores were significantly associated with discrepancies in lumbar spine T-scores.

**Conclusion** This study suggests that REMS may offer a more accurate measurement of BMD, overcoming the overestimation of BMD by DXA owing to factors such as vertebral deformities, abdominal aortic calcification, and diabetes mellitus.

 $\textbf{Keywords} \ \ Abdominal \ a ortic \ calcification \cdot Bone \ mineral \ density \cdot Dual-energy \ X-ray \ absorptiometry \cdot REMS \cdot Semi-quantitative \ grading \ of \ vertebral \ fractures$ 

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#### Introduction

Osteoporosis is a common skeletal disorder characterized by reduced bone mineral density (BMD) [1]; individuals with osteoporosis are therefore susceptible to fragility fractures [2, 3]. These fractures often precipitate a decline in the activities of daily living, imposing a significant burden on healthcare systems [4, 5]. In aging populations, the incidence of osteoporosis and associated fragility fractures increases. However, fragility fractures often occur before a diagnosis of osteoporosis is made. Therefore, an early, economical, and accurate diagnostic approach is required to allow prompt intervention [6].



The established gold standard for determining the risk of fragility fractures is the assessment of BMD through dual-energy X-ray absorptiometry (DXA) [7]. However, it has been shown that the diagnostic sensitivity of DXA can be undermined by internal artifacts [8, 9]. Given that DXA provides a two-dimensional anteroposterior projection of the lumbar spine, the areal BMD measurements may be influenced by structural abnormalities, such as osteophytes and vertebral deformities, often resulting from vertebral compression fractures [10]. Additionally, it has been reported that abdominal aortic calcification can lead to BMD overestimation [11]. This limited recognition of structural abnormalities may result in an overestimation of BMD, and therefore a significant underestimation of fracture risk.

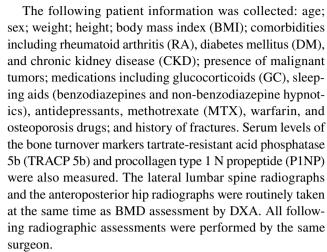
Recently, radiofrequency echographic multispectrometry (REMS) has emerged as a revolutionary non-ionizing tool for BMD assessment; this system is radiation-free, portable, and cost-effective. It analyzes raw radiofrequency ultrasound signals obtained during lumbar spine and proximal femur scans, capturing detailed tissue property data that are typically missed by conventional B-mode imaging [12]. European studies have demonstrated the diagnostic precision and reliability of REMS compared to DXA [13, 14]. An Italian study in a Caucasian female population showed that REMS effectively overcame common DXA artifacts, such as osteoarthritis (OA) and vertebral fractures [15]. Moreover, Fassio et al. found a positive correlation between discrepancies in DXA and REMS results and the extent of abdominal aortic calcification [16]. However, these results require verification in Asian populations. In addition, the multifaceted nature of BMD assessment by DXA and REMS is yet to be extensively explored.

We hypothesized that multiple factors influence the discrepancy between BMD measured by REMS and DXA, and aimed to determine this discrepancy and identify its influencing factors.

#### **Materials and Methods**

# **Study Design and Subjects**

This was a cross-sectional study involving patients who received osteoporosis treatment and BMD assessment by DXA at a single center between April and August 2023. Patients who were unable to lie supine due to spinal deformities or comorbidities were excluded. Because we have a BMD assessment biannually at our facility, all patients had only one BMD assessment during the period. This study was approved by the local ethics committee of Iwamizawa Hokushokai Hospital (0023-001). Informed consent was obtained from all participants included in the study.



Semi-quantitative grading of lateral lumbar spine radiographs was used to evaluate vertebral fractures and deformities [17]. The 1st–4th lumbar vertebrae were graded by visual inspection without direct vertebral measurement as follows: normal, grade 0; mildly deformed, grade 1 (20–25% reduction in anterior, middle, and/or posterior height and a 10–20% reduction in area); moderately deformed, grade 2 (25–40% reduction in any height and a 20–40% reduction in area); and severely deformed, grade 3 (>40% reduction in any height and area).

Semi-quantitative evaluation of abdominal aortic calcification was performed using the abdominal aortic calcification score (AACS) [18]. The value of this score has been reported in the assessment of cardiovascular events, and complications in patients undergoing dialysis [19, 20]. Calcific deposits were assessed separately for the posterior and anterior walls of the abdominal aorta, which were scored as follows: 0, no aortic calcific deposits; 1, small scattered calcific deposits filling less than one-third of the longitudinal wall of the aorta; 2, calcification of more than one-third, but less than two-thirds, of the longitudinal wall of the aorta; and 3, calcification of two-thirds or more of the longitudinal wall of the aorta. Scoring was performed at eight locations on the anterior and posterior walls of the 1st–4th vertebrae, with a resulting total score of 0–24.

OA of the hip joint was assessed using the Kellgren-Lawrence (KL) classification, applied to anteroposterior hip radiographs [21]. Each radiograph received a grade between 0 to 4, reflecting the progression of OA severity—with Grade 0 indicating no OA and Grade 4 indicating severe OA. The KL grade was determined for the same unilateral femur for which BMD was measured.

BMD assessment in all patients was measured using both DXA (PRODIGY Fuga-C, GE Healthcare, Madison, WI, USA) and REMS (Echos system, Echolight SPA, Lecce, Italy). BMD and T-score discrepancies between the two instruments were calculated. We divided the patients into two groups: a discrepancy group (D group) and a



non-discrepancy group (ND group), based on a  $\Delta$  Lumbar spine T-score of 2.0. All BMD measurements using REMS were performed by the same surgeon who was judged by a third-party organization to have a stable learning curve after appropriate practice.

## **Statistics Analysis**

Categorical variables are presented as frequencies (percentages) and were evaluated using the chi-square test, whereas continuous variables are presented as the mean (standard error of the mean) and were analyzed using an independent Student's t-test. Univariate and multivariate analyses were performed to calculate the odds ratio (OR) and 95% confidence intervals (CI) for the  $\Delta$  Lumbar spine T-score. Multivariate analyses were conducted using a logistic regression model adjusted for age, weight, and height. When the power, alpha error, and effect size were set at 0.8, 0.05, and 0.8, respectively, the statistically required sample size for  $\Delta$  Lumbar spine T-score analysis in this study was 26 cases per group. All statistical analyses were performed using JMP Pro version 17.0.0 (SAS Institute, Cary, NC, USA), with the significance level set at P > 0.05.

## Results

### **Patient Characteristics**

A comprehensive registration of 70 patients undergoing osteoporosis treatment was conducted between April and August 2023. Their characteristics are presented in Table 1. The study population had a mean age of  $78.39 \pm 9.50$  years at the time of assessment; the majority of patients (88.6%) were female. Participants exhibited the following mean anthropometric parameters: body weight,  $51.62 \pm 9.55$  kg; height,  $150.63 \pm 7.44$  cm; and BMI,  $22.66 \pm 3.29$  kg/m². Analysis of preexisting medical conditions revealed the following distributions: RA, 7.1%; DM, 12.9%; CKD, 7.1%; and malignant tumors, 10.0%. Medication data revealed that 1.4% of patients were taking GC, 14.3% were using sleeping aids, 2.9% were on antidepressants, 1.4% were taking warfarin, and 1.4% were on MTX.

The vast majority of patients (91.4%) were undergoing osteoporosis treatment, with the following medications being administered: bisphosphonate, 11.4%; denosumab, 45.7%; parathyroid hormone, 4.3%; selective estrogen receptor modulators, 12.9%; romosozumab, 11.4%; and active vitamin D3 only, 5.7%. Biochemical analyses revealed mean serum concentrations of TRACP 5b and P1NP to be 322.18

**Table 1** Clinical characteristics of the study participants

	All participants $(N=70)$
Sex, male: female	8: 62
Mean age, years	78.39 (9.50)
Weight, kg	51.62 (9.55)
Height, cm	150.63 (7.44)
Body mass index, kg/m <sup>2</sup>	22.66 (3.29)
Present illness, no. of cases (%)	
RA	5 (7.1%)
DM	9 (12.9%)
CKD	5 (7.1%)
Malignant tumor	7 (10.0%)
Medication, no. of cases (%)	
GC	1 (1.4%)
Sleeping pills	10 (14.3%)
Antidepressant	2 (2.9%)
Warfarin	1 (1.4%)
Methotrexate	1 (1.4%)
Osteoporosis treatment	64 (91.4%)
BP	8 (11.4%)
DMAb	32 (45.7%)
PTH	3 (4.3%)
SERM	9 (12.9%)
ROMO	8 (11.4%)
VD alone	4 (5.7%)
TRACP-5b (mU/dL)	322.18 (157.5)
Total P1NP (µg/L)	41.72 (21.24)
History of fractures (%)	39 (55.7%)

RA rheumatoid arthritis, DM diabetes mellitus, CKD chronic kidney disease, GC glucocorticoids, BP bisphosphonate, DMAb denosumab, PTH parathyroid hormone, SERM selective estrogen receptor modulator, ROMO: romosozumab, VD: vitamin D3 preparation, TRACP-5b: tartrate-resistant acid phosphatase 5b, P1NP type 1 procollagen-N-propeptide

Data presented as mean (standard error of the mean or percentage)

U/L and 41.72 ng/mL, respectively. The majority of patients (55.7%) had a history of fractures.

# Semi-Quantitative Assessment of Vertebral Fractures, KL Grade of Hip OA, and AACS

A semi-quantitative analysis was conducted on fractures of the L1–L4 lumbar vertebrae, with grading classifications ranging from 0 to 3 with increasing severity. For all four vertebrae, the majority of patients had grades of 0 or 1 (Table 2). The KL grading for hip OA was applied on a scale from 0 to 4, with higher values representing greater severity. Over 30% of the patients were assessed with a KL grade of 2 (findings of osteosclerosis) or more. The mean total AACS was 4.27 (4.31).



Table 2 Semi-quantitative grading for vertebral fractures, and KL grade of hip OA, and abdominal aortic calcification score of all study participants

Semi-quantitative grading, no. of cases (%)	All participants ( $N=70$ )							
	0		1		2		3	
1st lumbar spine	34 (48.6%)		24 (34.3%)		6 (8.6%)		6 (8.6%)	
2nd lumbar spine	36 (34.3%)		26 (37.1%)		6 (8.6%)		2 (2.9%)	
3rd lumbar spine	30 (42.9%)		27 (38.6%)		12 (17.1%)		1 (1.4%)	
4th lumbar spine	25 (35.7%)		34 (48.6%)		8 (11.4%)		3 (4.3%)	
	0	1		2		3		4
KL grade of hip OA no. of cases (%)	5 (7.1%)	35 (50.0%)		13 (18.6%)		9 (12.9%)		2 (2.9%)
AACS	4.27 (4.31)							

*KL* Kellgren-Lawrence, *OA* osteoarthritis, *AACS* abdominal aortic calcification score Data presented as mean (standard error of the mean)

# BMD and T-Scores as Measured by DXA and REMS

We evaluated BMD and T-scores using DXA and REMS and compared the results. REMS reported notably lower average lumbar spine, femoral neck, and total proximal femur BMD and T-scores than DXA (Table 3). Internal artifacts, including vertebral fractures and abdominal aortic calcifications, are known to directly impact lumbar spine BMD measurements obtained via DXA. Consistent with expectations, the greatest discrepancies were observed in lumbar spine BMD readings, where REMS registered a BMD of 0.623 and a T-score of -3.20, while DXA reported a BMD of 0.966 and a T-score of - 1.30, with these differences being statistically significant (P < 0.001). Similar trends were observed in the femoral neck (P < 0.001) and total proximal femur (P < 0.001). Positive correlations were found between the BMD as measured by DXA and REMS in the lumbar spine (r=0.471, P<0.001), femoral neck (r=0.361, P<0.001),

and total proximal femur (r = 0.429, P = 0.003) regions (Fig. 1). Osteoporosis diagnosis based solely on BMD and T-score was established in 72.9% of patients with DXA and in 90.0% with REMS, respectively, with a statistically significant difference (P = 0.009).

# Correlation of $\Delta$ Proximal Femoral T-Score and KL Grade of Hip OA

We divided into two groups according to KL grade: low KL grade (< grade 2) and high KL grade ( $\ge$  grade 2). 40 patients were classified as low KL grade; 30 patients were classified as high KL grade.  $\Delta$  femoral neck T-score was significantly larger in the high KL grade (0.61 vs 1.83; P < 0.001), and  $\Delta$  total proximal femur T-score was also significantly larger in the high KL grade (0.34 vs 1.39; P < 0.001) (Supplementary Table 1).

Table 3 Comparison of bone mineral density and T score of all participants by between DXA and REMS

	All participants (N=70)			
	DXA	REMS	P-value	
Lumbar spine BMD (g/cm <sup>2</sup> )	0.966 (0.203)	0.623 (0.090)	< 0.001*	
Femoral neck BMD (g/cm <sup>2</sup> )	0.689 (0.128)	0.488 (0.080)	< 0.001*	
Total proximal femur BMD (g/cm <sup>2</sup> )	0.729 (0.141)	0.612 (0.092)	< 0.001*	
Lumbar spine T score (g/cm <sup>2</sup> )	- 1.30 (1.47)	- 3.20 (0.79)	< 0.001*	
Femoral neck T score (g/cm <sup>2</sup> )	- 2.25 (1.09)	- 3.35 (0.89)	< 0.001*	
Total proximal femur T score (g/cm <sup>2</sup> )	- 1.86 (1.05)	- 2.63 (0.92)	< 0.001*	

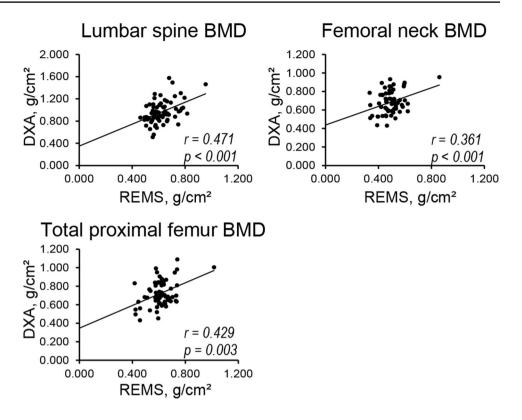
Data presented as mean (standard error of the mean)

DXA dual-energy X-ray Absorptiometry, REMS: radiofrequency echographic multispectrometry

\*P<0.05: significant differences between two groups



Fig. 1 Correlation between BMD measured by DXA and REMS. BMD in the lumbar spine, femoral neck, and total proximal femur, as measured by DXA and REMS and presented as scatter plots and lines of best fit. BMD, bone mineral density; DXA, dual-energy X-ray absorptiometry



# Patient Characteristics and Semi-Quantitative Evaluations in the D and ND Groups

Based on the discrepancy between DXA and REMS, patients were divided into D (N=31) and ND (N=39) groups. The clinical characteristics of each group are presented in Table 4. The two groups exhibited no significant differences in sex distribution, age, weight, or height. However, a notable disparity was observed in BMI, which was higher in the D group than in the ND group (23.55 vs 21.96 kg/m²; P=0.045). DM was more prevalent in the D group, affecting 22.6% of individuals, than in the ND group (5.1% of individuals; P=0.030). In contrast, no significant differences in medication use, fracture history, or bone turnover marker levels were found.

The D group exhibited a higher incidence of multiple vertebral fractures and increased vascular calcification than the ND group (Fig. 2). Significant differences in BMD were observed at all sites when measured by DXA, whereas no significant differences were detected in BMD measurements obtained by REMS. A higher proportion of patients in the D group than in the ND group had a fracture grade  $\geq 2$  in at least 2 vertebrae (29.0% vs 7.9%; P=0.019) (Table 4). In addition, the AACS was significantly elevated in the D group compared to the ND group (6.81 vs 2.26; P < 0.001) (Table 4). Moreover, a positive correlation was found between the AACS and the  $\Delta$  Lumbar spine T-score (r=0.378, P=0.002). A higher AACS was also observed in

patients with DM than in those without the condition (7.67 vs 3.77; P = 0.011).

# Univariate and Multivariate Analyses of $\Delta$ Lumbar Spine T-Scores

Univariate and multivariate analyses were performed to identify factors associated with  $\Delta$  Lumbar spine T-scores (Table 5). In the univariate analysis, BMI, DM, grade > 2 in at least 2 vertebrae, and the AACS were significantly associated with increased  $\Delta$  Lumbar spine T-scores (OR 1.167, 95% CI 1.005–1.380, P=0.042; OR 5.396, 95% CI 1.187–38.301, P=0.028; OR 5.333, 95% CI 1.392–26.417, P=0.014; and OR: 1.429, 95% CI 1.206–1.778, P<0.001, respectively). Following multivariate analysis, DM, grade > 2 in at least 2 vertebrae, and the AACS remained significantly associated with increased  $\Delta$  Lumbar spine T-scores (OR 5.749, 95% CI 1.142–45.123, P=0.033; OR 4.235 95% CI 1.043–21.720, P=0.043; and OR 1.707, 95% CI 1.325–2.394, P<0.001, respectively).

# **Discussion**

This cross-sectional study conducted in Japan explored the disparity between BMD as measured by DXA and REMS, with a particular focus on identifying the factors influencing this discrepancy. While BMD as assessed by



Table 4 Comparison of clinical characteristics of participants with and without lumbar spine BMD deviation between DXA and REMS

	D group ( <i>N</i> =31)	ND group ( <i>N</i> =39)	P-value	
Sex, male: female	4: 27	5: 34	0.992	
Mean age, years	79.52 (10.25)	77.49 (8.74)	0.382	
Weight, kg	52.50 (9.86)	50.93 (9.23)	0.499	
Height, cm	148.98 (7.65)	151.94 (6.99)	0.101	
Body mass index, kg/m <sup>2</sup>	23.55 (3.29)	21.96 (3.12)	0.045*	
Present illness, no. of cases (%)				
RA	1 (3.2%)	4 (10.3%)	0.257	
DM	7 (22.6%)	2 (5.1%)	0.030*	
CKD	3 (9.7%)	2 (5.1%)	0.463	
Malignant tumor	3 (9.7%)	4 (10.3%)	0.936	
Medication, no. of cases (%)				
GC	0 (0.0%)	1 (2.6%)	-	
Sleeping pills	5 (16.1%)	5 (12.8%)	0.694	
Antidepressant	1 (3.2%)	1 (2.6%)	0.869	
Warfarin	1 (3.2%)	0 (0.0%)	_	
Methotrexate	0 (0.0%)	1 (2.6%)	_	
Osteoporosis treatment	26 (83.9%)	38 (97.4%)	0.765	
BP	3	5		
DMAb	13	19		
РТН	0	3		
SERM	4	5		
ROMO	4	4		
VD alone	2	2		
TRACP-5b (mU/dL)	305.48 (148.08)	333.87 (162.76)	0.536	
Total P1NP (μg/L)	35.61 (19.53)	46.04 (21.34)	0.067	
History of fractures (%)	18 (58.1%)	21 (53.85%)	0.724	
Lumbar spine BMD (g/cm <sup>2</sup> )				
by DXA	1.137 (0.183)	0.849 (0.129)	< 0.001*	
by REMS	0.615 (0.100)	0.629 (0.080)	0.507	
Femoral neck BMD (g/cm <sup>2</sup> )				
by DXA	0.732 (0.129)	0.653 (0.115)	0.011*	
by REMS	0.497 (0.093)	0.481 (0.067)	0.441	
Total proximal femur BMD (g/cm <sup>2</sup> )				
by DXA	0.782 (0.137)	0.684 (0.129)	0.004*	
by REMS	0.625 (0.104)	0.602 (0.080)	0.303	
Semi-quantitative grading, cases				
More than grade $2 \ge 2$ vertebrae	9 (29.0%)	3 (7.9%)	0.019*	
AACS	6.81 (4.85)	2.26 (2.35)	< 0.001*	

Data presented as mean (standard error of the mean)

BMD bone mineral density, DXA dual-energy X-ray absorptiometry, REMS radiofrequency echographic multispectrometry, D group discrepancy group, ND group non-discrepancy group, RA rheumatoid arthritis, DM diabetes mellitus, CKD chronic kidney disease, GC glucocorticoids, BP bisphosphonate, DMAb denosumab, PTH parathyroid hormone, SERM selective estrogen receptor modulator, ROMO romosozumab, VD vitamin D3 preparation, TRACP-5b Tartrate-resistant Acid Phosphatase 5b, P1NP type 1 procollagen-N-propeptide, AACS abdominal aortic calcification score

REMS were positively correlated with those measured by DXA, REMS recorded consistently lower values for both BMD and T-scores across all measured regions. Although the discrepancy was larger in this study than in previous

reports where erroneous scans due to poor quality acquisitions were excluded, the same trend was observed in previous reports [15, 16, 22]. The greatest discrepancy was observed in the lumbar spine region, with the presence of



<sup>\*</sup>P<0.05: there were significant differences between two groups

## Discrepancy Group

# Non-Discrepancy Group





**Fig. 2** Representative lumbar spine radiographs from each group. Left: lateral lumbar spine radiograph of a patient with a discrepancy in BMD assessment by DXA and REMS. Right: lateral lumbar spine radiograph of a patient with no discrepancy in BMD assessment by DXA and REMS. SQ grade, semiquantitative grade; AACS, abdominal aortic calcification score

multiple vertebral deformities, an increased AACS, and DM emerging as significant contributing factors. A multivariate analysis identified DM as a novel factor influencing lumbar spine T-scores, alongside the previously established factors vertebral deformities and the AACS. Moreover, a significant association was found between the KL grade of hip OA and the discrepancy in the proximal femoral T-score. This study indicates that REMS effectively reduces the effect of internal artifacts, such as vertebral deformity, abdominal aortic calcification, and hip OA—factors that are known to affect BMD measurements

by DXA. Thus, REMS potentially provides a more accurate evaluation of bone fragility.

Internal artifacts, including vertebral deformities, osteophytes, and ossification of spinal ligaments, have been shown to affect BMD as measured by DXA [23–26]. Consequently, DXA may overestimate lumbar spine BMD in patients with an exceptionally high risk of fractures due to osteoporosis. In contrast, REMS may assess BMD with greater accuracy in these high-risk individuals, thereby facilitating the selection of more appropriate osteoporosis treatment strategies.

In this study, a significant correlation was noted between the discrepancy in lumbar spine T-scores determined by DXA and REMS and factors including the AACS and DM. Abdominal aortic calcification has been implicated in several diseases, including CKD, dialysis-associated complications, hyperparathyroidism, and primary hyperaldosteronism [27–29]. The elevated AACS observed in patients with DM in our study is explained by the previous identification of DM as an independent risk factor for abdominal aortic calcification [30]. This association underscores a paradox in which, despite the established role of abdominal aortic calcification in bone fragility, it tends to cause an overestimation of BMD assessed by DXA. This highlights the necessity for auxiliary validation using lateral imaging and other diagnostic tests such as quantitative computed tomography [31–33]. REMS has emerged as a viable tool to rectify this paradox, offering a radiation-free and cost-effective alternative to DXA for accurate bone fragility evaluation.

Previous research has explored the relationship between OA and osteoporosis, traditionally considered to be mutually exclusive conditions. However, recent studies have begun to report overlaps between these conditions [34, 35]. While BMD is typically higher in patients with OA [36–38], the

**Table 5** ORs for the lumbar spine BMD deviation between DXA and REMS

	Univariate analysis			Multivariate analysis <sup>a</sup>		
	P-value	95% CI	OR	P-value	95% CI	OR
Age	0.378	0.973-1.080	1.023			
Weight	0.494	0.968 - 1.072	1.018			
Height	0.105	0.880 - 1.009	0.946			
BMI	0.042*	1.005-1.380	1.167	0.389	0.425-10.501	1.972
DM	0.028*	1.187-38.301	5.396	0.033*	1.142-45.123	5.749
Semi-quantitative gra	ding					
More than grade 2 ≥ 2 vertebrae	0.014*	1.392–26.417	5.333	0.043*	1.043-21.720	4.235
AACS	< 0.001*	1.206–1.778	1.429	< 0.001*	1.325-2.394	1.707

Data presented as mean (standard error of the mean)

BMD bone mineral density, DXA dual-energy X-ray absorptiometry, REMS radiofrequency echographic multispectrometry, CI confidence interval, OR odds ratio, BMI body mass index, DM diabetes mellitus, AACS abdominal aortic calcification score



<sup>&</sup>lt;sup>a</sup>Adjusted by age, weight, height

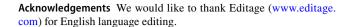
<sup>\*</sup>P < 0.05: the item significantly affected the lumbar BMD deviation

impact of artifacts such as osteosclerosis and osteophytes on these measurements has not been thoroughly investigated. Additionally, most prior BMD assessments have utilized DXA. In our study, we found that BMD measurements of the proximal femur obtained via REMS were significantly lower than those obtained using DXA. Moreover, a significant correlation was observed between the KL grade of hip OA and discrepancies in the proximal femoral T-score. These findings suggest that REMS may not be influenced by the same artifacts that affect DXA measurements and could potentially provide a more precise evaluation of bone fragility. Looking ahead, to further investigate the relationship between bone fragility and REMS measurements, future studies should focus on analyzing fracture rates.

This study has several limitations. First, it was a singlecenter study with a patient cohort that lacked diversity, which may affect the generalizability of the findings. The cohort consisted predominantly of individuals with a history of fractures, and the prescription patterns for osteoporosis medications may have been influenced by the preference of a single physician. Second, certain critical factors such as ossification of the spinal ligaments and the presence of osteophytes were not assessed. Given the challenge of quantitatively evaluating these from radiographs, we prioritized the analysis of vertebral deformity and abdominal aortic calcification, both of which permit semi-quantitative assessment. In the future, it would be beneficial to incorporate quantitative evaluations using computed tomography into our analysis. Third, this study could not delineate between primary and secondary osteoporosis, indicating the need for expanded case studies that provide a detailed exploration of these variants. Future research should increase the sample size and perform a more comprehensive investigation to address these limitations. Finally, we performed only unilateral femoral BMD measurements in this study. We speculated that it would be important to measure both femoral sites to eliminate the effects of femoral deformity and microfractures.

In conclusion, our study underscores the roles of multiple vertebral deformities, AACS, and DM in contributing to the observed discrepancies in lumbar spine BMD when measured by DXA compared to REMS. Furthermore, the KL grade of hip OA was found to be significantly associated with discrepancies in the proximal femoral T-score. These results imply that REMS proficiently navigates around the common artifacts that typically affect BMD measurements via DXA, including vertebral deformity, abdominal aortic calcification, and hip OA. Consequently, REMS may offer a more accurate evaluation of bone fragility, highlighting its potential as a valuable tool in clinical practice.

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Data availability Not applicable.

Code availability Not applicable.

### **Declarations**

Conflict of interest Hotaka Ishizu, Tomohiro Shimizu, Yuki Sakamoto, Fumi Toyama, Keita Kitahara, Hiroki Takayama, Moritaka Miyamoto and Norimasa Iwasaki declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Iwamizawa Hokushokai Hospital Institutional Review Board (0023–001).

**Informed Consent** Informed consent was obtained from all participants included in the study.

**Consent for Publication** Not applicable.

#### References

- Song S, Guo Y, Yang Y, Fu D (2022) Advances in pathogenesis and therapeutic strategies for osteoporosis. Pharmacol Ther 237:108168
- Adami G, Fassio A, Rossini M, Caimmi C, Giollo A, Orsolini G, Viapiana O, Gatti D (2019) Osteoporosis in rheumatic diseases. Int J Mol Sci 20:5867
- Curtis EM, Moon RJ, Harvey NC, Cooper C (2017) The impact of fragility fracture and approaches to osteoporosis risk assessment worldwide. Bone 104:29–38
- Gupta A, Maslen C, Vindlacheruvu M, Abel RL, Bhattacharya P, Bromiley PA, Clark EM, Compston JE, Crabtree N, Gregory JS, Kariki EP, Harvey NC, McCloskey E, Ward KA, Poole KES (2022) Digital health interventions for osteoporosis and post-fragility fracture care. Ther Adv Musculoskelet Dis 14:1759720X221083523
- Keen R (2007) Osteoporosis: strategies for prevention and management. Best Pract Res Clin Rheumatol 21:109–122
- Langton CM, Njeh CF (1999) Acoustic and ultrasonic tissue characterization—assessment of osteoporosis. Proc Inst Mech Eng H 213:261–269
- Carey JJ, Chih-Hsing WuP, Bergin D (2022) Risk assessment tools for osteoporosis and fractures in 2022. Best Pract Res Clin Rheumatol 36:101775
- Martineau P, Bazarjani S, Zuckier LS (2015) Artifacts and incidental findings encountered on dual-energy X-ray absorptiometry: atlas and analysis. Semin Nucl Med 45:458–469
- Morgan SL, Prater GL (2017) Quality in dual-energy X-ray absorptiometry scans. Bone 104:13–28
- Frye MA, Melton LJ 3rd, Bryant SC, Fitzpatrick LA, Wahner HW, Schwartz RS, Riggs BL (1992) Osteoporosis and calcification of the aorta. Bone Miner 19:185–194
- Stewart A, Black AJ (2000) Bone mineral density in osteoarthritis. Curr Opin Rheumatol 12:464–467



- Conversano F, Franchini R, Greco A, Soloperto G, Chiriacò F, Casciaro E, Aventaggiato M, Renna MD, Pisani P, Di Paola M, Grimaldi A, Quarta L, Quarta E, Muratore M, Laugier P, Casciaro S (2015) A novel ultrasound methodology for estimating spine mineral density. Ultrasound Med Biol 41:281–300
- 13. Di Paola M, Gatti D, Viapiana O, Cianferotti L, Cavalli L, Caffarelli C, Conversano F, Quarta E, Pisani P, Girasole G, Giusti A, Manfredini M, Arioli G, Matucci-Cerinic M, Bianchi G, Nuti R, Gonnelli S, Brandi ML, Muratore M, Rossini M (2019) Radiofrequency echographic multispectrometry compared with dual X-ray absorptiometry for osteoporosis diagnosis on lumbar spine and femoral neck. Osteoporos Int 30:391–402
- 14. Diez-Perez A, Brandi ML, Al-Daghri N, Branco JC, Bruyère O, Cavalli L, Cooper C, Cortet B, Dawson-Hughes B, Dimai HP, Gonnelli S, Hadji P, Halbout P, Kaufman JM, Kurth A, Locquet M, Maggi S, Matijevic R, Reginster JY, Rizzoli R, Thierry T (2019) Radiofrequency echographic multi-spectrometry for the in-vivo assessment of bone strength: state of the art-outcomes of an expert consensus meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Aging Clin Exp Res 31:1375–1389
- Caffarelli C, Tomai Pitinca MD, Al Refaie A, De Vita M, Catapano S, Gonnelli S (2022) Could radiofrequency echographic multispectrometry (REMS) overcome the overestimation in BMD by dual-energy X-ray absorptiometry (DXA) at the lumbar spine? BMC Musculoskelet Disord 23:469
- Fassio A, Andreola S, Gatti D, Bianco B, Gatti M, Gambaro G, Rossini M, Viapiana O, Negrelli R, Adami G (2023) Radiofrequency echographic multi-spectrometry and DXA for the evaluation of bone mineral density in a peritoneal dialysis setting. Aging Clin Exp Res 35:185–192
- Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–1148
- Kauppila LI, Polak JF, Cupples LA, Hannan MT, Kiel DP, Wilson PW (1997) New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis 132:245–250
- Hashimoto H, Iijima K, Hashimoto M, Son BK, Ota H, Ogawa S, Eto M, Akishita M, Ouchi Y (2009) Validity and usefulness of aortic arch calcification in chest X-ray. J Atheroscler Thromb 16:256–264
- Ma D, Yan H, Yang X, Yu Z, Ni Z, Fang W (2020) Abdominal aortic calcification score as a predictor of clinical outcome in peritoneal dialysis patients: a prospective cohort study. BMC Nephrol 21:151
- Kellgren JH, Lawrence JS (1957) Radiological assessment of osteo-arthrosis. Ann Rheum Dis 16:494–502
- 22. Caffarelli C, Al Refaie A, Mondillo C, Versienti A, Baldassini L, De Vita M, Tomai Pitinca MD, Gonnelli S (2023) Radiofrequency echographic multispectrometry (REMS): a new option in the assessment bone status in adults with osteogenesis imperfecta. J Imaging 9(10):210
- Albano D, Agnollitto PM, Petrini M, Biacca A, Ulivieri FM, Sconfienza LM, Messina C (2021) Operator-related errors and pitfalls in dual energy X-ray absorptiometry: how to recognize and avoid them. Acad Radiol 28:1272–1286
- Gupta A, Upadhyaya S, Patel A, Fogel HA, Cha T, Schwab J, Bono C, Hershman S (2020) DEXA sensitivity analysis in patients with adult spinal deformity. Spine J 20:174–180
- Marcus R, Wang O, Satterwhite J, Mitlak B (2003) The skeletal response to teriparatide is largely independent of age, initial bone mineral density, and prevalent vertebral fractures in postmenopausal women with osteoporosis. J Bone Miner Res 18:18–23
- Shiraki M, Kuroda T, Miyakawa N, Fujinawa N, Tanzawa K, Ishizuka A, Tanaka S, Tanaka Y, Hosoi T, Itoi E, Morimoto S,

- Itabashi A, Sugimoto T, Yamashita T, Gorai I, Mori S, Kishimoto H, Mizunuma H, Endo N, Nishizawa Y, Takaoka K, Ohashi Y, Ohta H, Fukunaga M, Nakamura T, Orimo H (2011) Design of a pragmatic approach to evaluate the effectiveness of concurrent treatment for the prevention of osteoporotic fractures: rationale, aims and organization of a Japanese osteoporosis intervention trial (JOINT) initiated by the Research Group of Adequate Treatment of Osteoporosis (A-TOP). J Bone Miner Metab 29:37–43
- Kim K, Song SH, Kim IJ, Jeon YK (2021) Is dual-energy absorptiometry accurate in the assessment of bone status of patients with chronic kidney disease? Osteoporos Int 32:1859–1868
- Pepe J, Diacinti D, Fratini E, Nofroni I, D'Angelo A, Pilotto R, Savoriti C, Colangelo L, Raimo O, Cilli M, Cipriani C, Minisola S (2016) High prevalence of abdominal aortic calcification in patients with primary hyperparathyroidism as evaluated by Kauppila score. Eur J Endocrinol 175:95–100
- Tuersun T, Luo Q, Zhang Z, Wang G, Zhang D, Wang M, Wu T, Zhou K, Yue N, Li N (2020) Abdominal aortic calcification is more severe in unilateral primary aldosteronism patients and is associated with elevated aldosterone and parathyroid hormone levels. Hypertens Res 43:1413–1420
- Bendix EF, Johansen E, Ringgaard T, Wolder M, Starup-Linde J (2018) Diabetes and abdominal aortic calcification-a systematic review. Curr Osteoporos Rep 16:42–57
- Li N, Li XM, Xu L, Sun WJ, Cheng XG, Tian W (2013) Comparison of QCT and DXA: osteoporosis detection rates in postmenopausal women. Int J Endocrinol 2013:895474
- Reid S, Schousboe JT, Kimelman D, Monchka BA, Jafari Jozani M, Leslie WD (2021) Machine learning for automated abdominal aortic calcification scoring of DXA vertebral fracture assessment images: a pilot study. Bone 148:115943
- Schousboe JT, Wilson KE, Kiel DP (2006) Detection of abdominal aortic calcification with lateral spine imaging using DXA. J Clin Densitom 9:302–308
- Kim D, Pirshahid AA, Li Y, Varghese T, Pope JE (2022) Prevalence of osteoporosis in osteoarthritis: a systematic review and meta-analysis. Osteoporos Int 33:1687–1693
- Tarantino U, Celi M, Rao C, Feola M, Cerocchi I, Gasbarra E, Ferlosio A, Orlandi A (2014) Hip osteoarthritis and osteoporosis: clinical and histomorphometric considerations. Int J Endocrinol 2014;372021
- Jiang L, Jiang Y, Wang A, Wu C, Shen Y (2022) The causal association between bone mineral density and risk of osteoarthritis:
  a Mendelian randomization study. Front Endocrinol (Lausanne) 13:1021083
- Karlsson MK, Magnusson H, Cöster MC, Vonschewelov T, Karlsson C, Rosengren BE (2014) Patients with hip osteoarthritis have a phenotype with high bone mass and low lean body mass. Clin Orthop Relat Res 472:1224–1229
- Zucker BE, Ebsim R, Lindner C, Hardcastle S, Cootes T, Tobias JH, Whitehouse MR, Gregson CL, Faber BG, Hartley AE (2022) High bone mass and cam morphology are independently related to hip osteoarthritis: findings from the high bone mass cohort. BMC Musculoskelet Disord 23:757

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