Diagnostic agreement between radiofrequency echographic multispectrometry and dual-energy X-ray absorptiometry in the assessment of osteoporosis in a Polish group of patients

Authors: Anna Nowakowska-Płaza, Jakub Wroński, Mateusz Płaza, Iwona Sudol-Szopińska, Piotr Głuszko

Article type: Original article

Received: May 13, 2021.

Accepted: June 20, 2021.

Published online: June 25, 2021.

ISSN: 1897-9483
Diagnostic agreement between radiofrequency echographic multispectrometry and dual-energy X-ray absorptiometry in the assessment of osteoporosis in a Polish group of patients

Anna Nowakowska-Plaza¹, Jakub Wroński¹, Mateusz Plaza², Iwona Sudol-Szopińska², Piotr Głużko¹

¹ Department of Rheumatology, National Institute of Geriatrics, Rheumatology, and Rehabilitation, Warsaw, Poland
² Department of Radiology, National Institute of Geriatrics, Rheumatology, and Rehabilitation, Warsaw, Poland

Short title: Diagnostic agreement between REMS and DXA

Correspondence to: Jakub Wroński, Ph.D., M.D., Department of Rheumatology, National Institute of Geriatrics, Rheumatology, and Rehabilitation, Spartańska 1, 02-637 Warsaw, Poland, phone: +48 22 670 92 13, email: jakub-wronski@wp.pl

Conflict of interest: None declared

Keywords: osteoporosis, bone mineral density, radiofrequency echographic multispectrometry
What’s new?

Osteoporosis is still under-diagnosed in many countries and there is the need for new widely available diagnostic techniques. Radiofrequency echographic multispectrometry (REMS) is a novel quantitative ultrasound technique, that shows a significant diagnostic agreement with dual-energy X-ray absorptiometry (DXA) measurements. Furthermore, REMS is easy to learn and automatically eliminates a significant part of erroneous results often associated with classic DXA. Our study confirms the usefulness of REMS in the assessment of osteoporosis.
Abstract

Introduction: Osteoporosis is still under-diagnosed in Poland, among others due to limited accessibility to gold standard diagnostic technique, dual X-ray absorptiometry (DXA) of the proximal femur and lumbar spine. Radiofrequency echographic multispectrometry (REMS) might be of particular interest because the technique is nonionizing, devices are portable and utilization relatively cheap.

Objectives: The aim of this study was to assess the agreement between a novel quantitative technique REMS, and DXA in bone mineral density evaluation and the diagnosis of osteoporosis.

Patients and methods: All recruited patients (116) underwent DXA and REMS of the proximal femur and lumbar spine. The diagnostic agreement of REMS was assessed through a direct comparison with DXA results, with separate analysis for the proximal femur and lumbar spine scans. Additional sub-analysis of the impact of gender, age, and BMI was performed.

Results: After the exclusion of patients due to significant skeletal impairments, missing results, and erroneous reports, 66 results of the femur and 58 reports of the lumbar spine were analyzed. The diagnostic agreement between DXA and REMS results was 82.8% in the lumbar spine group and 84.8% in the femur group. Strong correlations between REMS and DXA results were found, both in the lumbar spine and femur groups. The correlations between REMS and DXA scores remained strong regardless of gender, age, and BMI.

Conclusion: REMS showed a significant diagnostic agreement with the corresponding DXA measurements. The study confirms further the usefulness of REMS in the assessment of osteoporosis.
Introduction

Osteoporosis is a chronic skeletal disease characterized by reduced bone mass and deteriorated bone microarchitecture, which results in an increased risk of fractures. It is estimated that about 50% of Caucasian women and about 20% of men will experience an osteoporosis-related fracture at some point in their lifetime[1]. Osteoporotic fractures result in disability, impaired quality of life, and increased mortality, and are a tremendous burden, both personal and economic[2–4]. The total health burden, measured in terms of lost quality-adjusted life years (QALYs), was estimated at one million lost QALYs in 2017 for the five largest EU countries and Sweden (EU6)[3]. Disability-adjusted life years caused by osteoporotic fractures were outranged only by lung cancer, dementia, and ischemic heart disease. 2.7 million fractures that caused this health burden also attributed to the direct cost of 37.5 billion Euro. In Poland, about 120,000 patients experience an osteoporotic fracture annually, with only direct costs amounting to 473 million Polish Zloty (~ 104 million Euro)[5]. The annual mortality after fractures of the proximal femur in Poland was 29.4% in 2017[5]. The number of Years of Life Lost that can be directly attributed to these fractures is about 20,000.

Unfortunately, osteoporosis is an under-diagnosed disease[3, 5, 6]. In EU6 countries 73% of women and 63% of men eligible for osteoporosis treatment do not receive it[3]. In Poland, it is estimated that 74% of Polish patients with osteoporosis are undiagnosed – from 2.1 million Poles with osteoporosis only 0.55 million are diagnosed with the disease[5]. Although the bone mineral density (BMD) assessment alone is insufficient for identification of patients at risk of fracture (novel techniques are used to assess also bone microarchitecture[7], and the key role is played by assessing the individualized fracture risk with questionnaires, such as country-specific FRAX®), the dual X-ray absorptiometry (DXA) of the proximal femur and lumbar spine remains gold standard technique for osteoporosis.
diagnosis per definition [3, 4, 6, 8]. To improve the recognition of osteoporosis, better access
to DXA is needed[4, 6]. Still, accessibility to DXA examinations in Poland is highly limited.
The availability of DXA units in Poland is one of the worst in Europe (5th from the bottom
out of 27 European countries in 2010)[4]. In 2017, DXA was performed only in 176,000
patients[5].

For these reasons, the search for novel diagnostic techniques is continued[6].
Ultrasound methods may be of particular interest because such techniques are nonionizing,
and the devices are portable and relatively cheap[9] (although the price of the device is similar
to DXA device, it is characterized by lower utilization costs). Techniques of quantitative
ultrasound (QUS) of bone density have been studied for many years and meta-analysis of
these studies showed the value of QUS in predicting fractures[10]. Still, QUS has not yet
entered widespread clinical use and the role QUS could play in diagnosing osteoporosis
remains unexploited. An equally important problem as the availability of DXA is the fact that
DXA requires technical and interpretive excellence, scrupulous adherence to equipment
calibration protocols, and the assessment of measurement precision[4, 6, 11]. Failure to
adhere to strict DXA measurement principles can lead to a high percentage of erroneous BMD
reports in everyday clinical practice[12, 13]. Radiofrequency Echographic Multi Spectrometry
(REMS), an innovative quantitative ultrasound technique for osteoporosis diagnosis in the
proximal femur and lumbar spine, has been recently validated in a few clinical studies,
showing promising results[14–16]. REMS has been approved by the Food and Drug
Administration in October 2018 and rated as a valuable approach for osteoporosis diagnosis
and fracture risk prediction by ESCEO[17].

The aim of our study was to evaluate the diagnostic agreement of REMS in
comparison to DXA for the assessment of proximal femur and lumbar spine bone density in a
Polish group of patients.
Patients and methods

The study was conducted at the Department of Radiology in the National Institute of Geriatrics, Rheumatology, and Rehabilitation in Warsaw, Poland. The inclusion criteria were: Caucasian ethnicity, age between 40-87 years, and the existence of indications for femoral and lumbar spine DXA (age >65 in women and >70 in men or postmenopausal age in women and >50 in men with fracture risk factors, low-trauma spine or hip fracture history in people aged >50, and patients with risk of secondary osteoporosis regardless of age). The exclusion criterion was a significant skeletal impairment not allowing proper execution of DXA and/or REMS. All recruited patients underwent DXA and REMS of the proximal femur and lumbar spine. The study protocol has been approved by the hospital bioethics committee (number KBT-7/1/2017). All participants (116 patients - 98 females, 18 males) have signed informed consent for inclusion in the study. The study was conducted according to the Declaration of Helsinki.

DXA and REMS reports included the BMD (bone mineral density) value, expressed as grams per square centimeter (g/cm²), and the T-score values. According to the WHO definitions[18], osteoporosis was diagnosed in patients with T-score ≤-2.5 SD, osteopenia with T-score <-1 and >-2.5 SD, or “healthy” with T-score ≥-1.0. All DXA and REMS reports were reviewed for possible errors by two independent experts (according to the methodology described by Di Paola et al.[14]), and only error-free reports were in the statistical analysis. Errors were categorized as errors in data analysis, patient positioning, artifacts, or incorrect personal data entry.

DXA scans were performed using Hologic Discovery A densitometer. REMS scans were performed using EchoStation with the dedicated software EchoStudio (by Echolight
Spa, Italy). The device used in REMS is equipped with a 3.5 MHz broadband convex ultrasound transducer and configured to provide both echographic images and “raw” unfiltered radiofrequency signals, sampled at 40 MS/s. Using REMS EchoStation the probe is placed in the hip area during the examination of the proximal femur. While examining the lumbar spine, the probe is placed in the abdominal wall starting from the xiphoid process of the sternum and moved centrally down – with automated identification of the regions of interest. Examination of the spine lasts approximately 80 seconds and the proximal femur about 40 seconds (with the progress of the test signaled by video and sounds). All scans are performed in a supine position. Acquired ultrasonographic data is analyzed through an automatic algorithm that performs a series of spectral and statistical analyses. The analysis of both the echographic images (Figure 1a) and the native radiofrequency signals allows for the calculation of BMD (Figure 1b). T-score and Z-score for REMS results are calculated using the NHANES reference database[19] (same as Hologic DXA devices).

**Statistical analysis**

REMS diagnostic agreement on the obtained results was assessed by calculating the diagnostic agreement percent and Cohen’s kappa between DXA and REMS results, with separate analysis for the proximal femur and spine scans. Additionally, DXA-REMS correlation coefficient and Bland-Altman plots (of differences between DXA and REMS measurements plotted against the averages of the two measurements) were obtained as supportive methods for comparing the results of REMS and DXA. The compliance of the data with the normal distribution was assessed using the Shapiro-Wilk test. The correlation was assessed using Spearman's rank correlation coefficient due to the non-parametric nature of the variables. Additional sub-analysis of the impact of gender, age, and BMI were performed - the significance of observed differences between correlations in different groups
was measured using Fisher’s r to z transformation. Statistical significance was set at p<0.05. Statistical analysis was performed using Statistica 13.1 software.

Results

After the exclusion of patients due to significant skeletal impairments, missing results, and erroneous reports in the statistical analysis, 66 results of the proximal femur and 58 reports of the lumbar spine were included (Figure 2). Only 23.4% of all erroneous reports in the femur group and 20% in the lumbar spine group were excluded due to REMS errors. The remaining reports were excluded due to DXA errors - primarily wrong data analysis.

The characteristics of patients included in the statistical analysis are shown in Table 1a (lumbar spine group) and 1b (femur group). The diagnostic agreement between DXA and REMS results (diagnosed as healthy, osteopenic, or osteoporotic) was 82.8% and Cohen’s k=0.611 in the lumbar spine group, and 84.8% and Cohen’s k=0.667 in the femur group. Statistically significant strong correlations (Spearman's coefficient) between REMS and DXA results (BMD and T-scores) were found, both in the lumbar spine and in the femur groups (r and p values are presented in Tables 1a and 1b, figures in Supplementary Material). Scatter diagrams of the differences between DXA and REMS measurements plotted against the averages of the two measurements are presented in Bland-Altman plots in Figures 3a and 3b (lumbar spine group) and Figures 3c and 3d (femur group).

The effects of the patient’s sex, age, and BMI on obtained results were studied in detail and are reported in Table 2a (lumbar spine group) and 2b (femur group). The correlations between REMS and DXA scores remained statistically significantly strong, both in young and old (age <60 and ≥60), as well in patients with normal body weight and the overweight ones (BMI <25 and ≥25). Spearman's coefficient was not calculated for the men
group with lumbar spine scans due to lack of power (too small group – 5 results) but remained significant in men with femur scans. No statistically significant differences were observed between all sub-groups correlations.

**Discussion**

We found a significant diagnostic agreement between REMS and DXA measurements in all patients, irrespective of sex, age, and BMI. In our study, the diagnostic concordance was 84.8% for the femoral neck and 82.8% for the lumbar spine. These results are in line with the results of two large multicenter studies comparing DXA and REMS. In the Italian study involving 1914 postmenopausal women, the diagnostic agreement between DXA and REMS was 88.2% for the femoral neck and 88.8% for the lumbar spine[14]. In the most recent and largest up today international study of 4307 women aged 30-90 years the diagnostic concordance was 86% for the femoral neck and 86.6% for the lumbar spine[16]. Despite these promising results, the use of REMS should be treated with caution. In our study, 7 patients in the lumbar group with DXA osteopenia were diagnosed with REMS as healthy.

In our study, all reports, both DXA and REMS, were carefully checked for possible errors. Our observation shows that automatic algorithm used in REMS, by the exclusion of nondiagnostic scans, help to eliminate most technical DXA errors (like wrong positioning of the patients, or erroneous data analysis), which is in accordance with the previous study by Messina et al.[13]. While DXA remains the gold standard for assessing bone density, DXA requires excellent technique to avoid erroneous results[4, 6]. According to the study by Krueger et al. technical errors can be identified in 90% of DXA scans[12]. Similar results were shown by the study by Messina et al. - more than 90% of DXA reports present one or more errors, mostly related to wrong data analysis or patient positioning[13]. In contrast,
REMS proper technique is quite easy to master after a short training, as examination requires the operator to set only 2 parameters – transducer depth and focus. The advantage of REMS in the automatic elimination of erroneous reports can be useful especially in the evaluation of lumbar spine scans. Structures like osteophytes, calcifications (e.g. atherosclerotic plaques in the abdominal aorta), or compression fractures may result in a false increment of BMD, causing false automatic DXA reports. In standard DXA it is essential to analyze thoroughly each vertebra and a minimum of two vertebrae should be assessed to obtain reliable results according to ISCD guidelines[11]. The same principle applies to REMS but it is done automatically. Indeed, in our study the Bland-Altman plot for the T-score in the lumbar region shows the increasing difference between the measurements for higher T-scores, suggesting falsely elevated DXA results by the presence of degenerative changes. Errors in wrong patient positioning can affect both spine and femur DXA results. Usually, the spine is not centered or straight in the image field, and the femur is adducted or abducted and in an inadequate internal rotation. REMS automatic algorithm eliminates patient positioning errors through selective analysis of trabecular bone (by comparison of spectral features of tested area with the spectral model of the trabecular bone)[20] - if the received image is inadequate, the result is not obtained and the exam should be repeated. These advantages of REMS have been recognized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO)[17].

Our experience shows that to obtain a good image, the REMS examination of the spine has to be done after fasting like for abdominal ultrasound (intestinal gas can interfere with imaging of the vertebrae). REMS also has a limitation in assessing obese patients - the maximal distance separating the bone surface from the ultrasound probe should be 210 mm for the spine and 150 mm for the femur neck (the „depth” regulated by the operator). In a previous study, it was shown that diagnostic accuracy between REMS and DXA can be
slightly lower in elderly patients (aged >65 years) with BMI >25 kg/m$^2$ - 69.6% vs 81.5% in younger patients[19]. Still, this result may be due to degenerative changes in the spine and the associated false-negative DXA results - in a study where DXA and REMS reports were assessed for possible errors, REMS was assessed as feasible for all the patients without extremely obesity (BMI up to 40 kg/m$^2$)[14]. Similarly, in our study, there was no difference in correlations between DXA and REMS spine results of patients with normal body weight and overweight.

The observed correlations between DXA and REMS results found in our study add evidence to support the opinion about the usefulness of the REMS as an alternative to classic densitometry in BMD imaging. The strength of our study is the validation of obtained results (exclusion of reports with errors). It was also a real-life study, and patients were not specifically selected for this short investigation. The biggest limitation is a small sample size. However, the groups were large enough given the observed differences – the statistical power was sufficient to evaluate the significance of expected correlation coefficients higher than 0.8 (except for the male subgroup with lumbar spine scans). The other limitation is the cross-sectional character of the study. Prospective studies that can demonstrate the usefulness of REMS in predicting osteoporotic fractures would have the greatest clinical value. Up to date, only one study by Adami et al. assessed that issue prospectively, showing promising results[15]. Finally, we did not assess the intra-operator repeatability. Still, according to the previous study by di Paola et al., the precision error of REMS (root-mean-square coefficient of variation) was 0.32% for the femur neck and 0.38% for the lumbar spine[14], which is a much smaller error compared to DXA (estimated to be 1.47%[21] for femur neck and 1.26% for spine[22]).

REMS is a novel densitometric method showing a significant diagnostic agreement with traditional DXA. REMS accuracy is acceptable irrespective of age and BMI and could be
particularly useful in the diagnosis of osteoporosis in the elderly, as it does not give falsely overestimated values of BMD by omitting degenerative changes and aortic plaques. REMS, having the advantages of quantitative ultrasound and automatically eliminating a significant part of erroneous results, could be a useful technique in routine clinical practice. ESCEO has already rated REMS as a clinically available and valuable technology for osteoporosis diagnosis and fracture risk assessment[17]. Nevertheless, further studies are required. The clinical utility of REMS in particular groups of patients, including patients who should avoid ionizing radiation (pediatric and pregnant women) and those at increased risk of developing secondary osteoporosis (with chronic steroid therapy, diabetes mellitus, rheumatic diseases, chronic kidney disease, or oncological diseases) should be examined.

**Contribution statement:** AN-P designed the study, was responsible for the acquisition and interpretation of data and prepared the draft of the paper. JW was responsible for statistical analysis and interpretation of the data and prepared the draft of the paper. MP was responsible for the acquisition and interpretation of data and prepared the draft of the paper. IS-S and PG contributed with the conception of the work and revised it critically. All authors approved the final version and agree to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper are investigated and properly resolved.

**Acknowledgments:** Many thanks to Paola Pisani and her team for the critical review of the work.
References

1. US Department of Health and Human Services. Bone health and osteoporosis: a report of the Surgeon General. US Heal Hum Serv. 2004.

2. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician’s Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014; 25: 2359–2381.

3. Borgström F, Karlsson L, Ortsäter G, et al. Fragility fractures in Europe: burden, management and opportunities. Arch Osteoporos. 2020; 15: 59.

4. Kanis JA, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2019; 30: 3–44.

5. Centrala Narodowego Funduszu Zdrowia. Departament Analiz i Strategii. NFZ o zdrowiu Osteoporoza. 2019.

6. Lems WF, Raterman HG. Critical issues and current challenges in osteoporosis and fracture prevention. An overview of unmet needs. Ther Adv Musculoskelet Dis. 2017; 9: 299–316.

7. Nowakowska-Płaza A, Płaza M, Sudol-Szopińska I, Głuszko P. Usefulness of trabecular bone score in a misdiagnosed case of osteoporosis: clinical image of a woman with multiple fractures. Pol Arch Intern Med. 2020; 130: 150-152.

8. Lorenc R, Głuszko P, Franek E, et al. Guidelines for the diagnosis and management of osteoporosis in Poland: Update 2017. Endokrynol Pol. 2017; 68: 604–9.

9. Glüer CC. Quantitative ultrasound techniques for the assessment of osteoporosis: Expert agreement on current status. J Bone Miner Res. 1997; 12: 1280–1288.

10. Moayyeri A, Adams JE, Adler RA, et al. Quantitative ultrasound of the heel and fracture risk assessment: An updated meta-analysis. Osteoporos Int. 2012; 23: 143–153.

11. 2019 ISCD Official Positions - Adult - International Society for Clinical Densitometry
12. Krueger D, Shives E, Siglinsky E, et al. DXA Errors Are Common and Reduced by Use of a Reporting Template. J Clin Densitom. 2019; 22: 115–124.

13. Messina C, Bandirali M, Sconfienza LM, et al. Prevalence and type of errors in dual-energy x-ray absorptiometry. Eur Radiol. 2015; 25: 1504–1511.

14. Di Paola M, Gatti D, Viapiana O, et al. Radiofrequency echographic multispectrometry compared with dual X-ray absorptiometry for osteoporosis diagnosis on lumbar spine and femoral neck. Osteoporos Int. 2019; 30: 391–402.

15. Adami G, Arioli G, Bianchi G, et al. Radiofrequency echographic multi spectrometry for the prediction of incident fragility fractures: A 5-year follow-up study. Bone. 2020; 134: 115297.

16. Cortet B, Dennison E, Diez-Perez A, et al. Radiofrequency Echographic Multi Spectrometry (REMS) for the diagnosis of osteoporosis in a European multicenter clinical context. Bone. 2021; 143: 115786.

17. Diez-Perez A, Brandi ML, Al-Daghri N, et al. Radiofrequency echographic multispectrometry 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. 2019; 31: 1375–1389.

18. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ. Tech Rep Ser. 1994; 843: 1–129.

19. Casciaro S, Pisani P, Conversano F, et al. Innovative ultrasound approach to estimate spinal mineral density: Diagnostic assessment on overweight and obese women. IET
20. De Marco T, Peccarisi M, Conversano F, et al. A new approach for measuring the trabecular bone density through the echosound backscattering: An ex vivo validation on human femoral heads. Meas J Int Meas Confed. 2016; 87: 51–61.

21. Ravaud P, Reny JL, Giraudeau B, et al. Individual Smallest Detectable Difference in Bone Mineral Density Measurements. J Bone Miner Res. 1999; 14: 1449–1456.

22. Hopkins SJ, Welsman JR, Knapp KM. Short-term Precision Error in Dual Energy X-Ray Absorptiometry, Bone Mineral Density and Trabecular Bone Score Measurements; and Effects of Obesity on Precision Error. J Biomed Graph Comput. 2014; 4: 8.
**Table 1a:** Characteristics of the lumbar spine group with error-free scans. BMD – bone mineral density, DXA - dual-energy X-ray absorptiometry, REMS - radiofrequency echographic multispectrometry.

| Lumbar spine group |          |
|--------------------|----------|
| Sex, females number (%) | 53 (91.4%) |
| Age, median (min, max) | 61 (40, 87) |
| BMI, median (min, max) | 25.95 (18.2, 42.6) |
| Diagnosis, number (%) | DXA | REMS |
| Osteoporosis | 7 (12.1%) | 4 (6.9%) |
| Osteopenia | 33 (56.9%) | 30 (51.7%) |
| Healthy | 18 (31%) | 24 (41.4%) |
| Diagnostic agreement | | | 82.8% |
| Cohen’s kappa | | | 0.611 |
| BMD, median g/cm2 (min, max) | DXA | REMS | Spearman's correlation |
| | 0.873 (0.642, 1.300) | 0.914 (0.673, 1.107) | R=0.839, P<0.001 |
| T-score, median (min, max) | -1.6 (-3.7, 2.3) | -1.2 (-3.4, 0.2) | R=0.846, P<0.001 |

**Table 1b:** Characteristics of the femur group with error-free scans. BMD – bone mineral density, DXA - dual-energy X-ray absorptiometry, REMS - radiofrequency echographic multispectrometry.

| Femur group |          |
|-------------|----------|
| Sex, females number (%) | 53 (80.3%) |
| Age, median (min, max) | 62 (40, 85) |
| BMI, median (min, max) | 26.65 (19.4, 36.6) |
| Diagnosis, number (%) | DXA | REMS |
| Osteoporosis | 3 (4.6%) | 4 (6.1%) |
| Osteopenia | 32 (48.5%) | 35 (53%) |
| Healthy | 31 (46.9%) | 27 (40.9%) |
| Diagnostic agreement | | | 84.8% |
| Cohen’s kappa | | | 0.667 |
| BMD, median g/cm2 (min, max) | DXA | REMS | Spearman's correlation |
| | 0.748 (0.455, 1.151) | 0.720 (0.500, 1.053) | R=0.867, P<0.001 |
| T-score, median (min, max) | -1.1 (-3.6, 2.7) | -1.15 (-3.1, 1) | R=0.871, P<0.001 |
Table 2a Sub analysis of the lumbar spine group. BMD – bone mineral density, n – number; significance tested with Fisher’s r to z transformation.

|          | Lumbar spine group | T-score Spearman's correlation |
|----------|--------------------|-------------------------------|
|          | Diagnostic agreement | BMD Spearman's correlation    |
| Sex      |                    |                              |
| Male (n=5) | 100%               | analysis not performed - lack of power |
| Female (n=53) | 79.2%           | analysis not performed - lack of power |
| Age      |                    |                              |
| <60 (n=25) | 80%                | R=0.781 P<0.001             | R= 0.791 P<0.001 |
| ≥60 (n=33) | 81.8%              | R=0.834 P<0.001             | R= 0.848 P<0.001 |
| difference| P=0.293            | P=0.267                      |
| BMI      |                    |                              |
| <25 (n=23) | 87%                | R=0.858 P<0.001             | R= 0.869 P<0.001 |
| ≥25 (n=35) | 77.1%              | R=0.776 P<0.001             | R= 0.784 P<0.001 |
| difference| P=0.19             | P=0.169                      |

Table 2b Sub analysis of the femur group. BMD – bone mineral density, n – number; significance tested with Fisher’s r to z transformation.

|          | Femur group | T-score Spearman's correlation |
|----------|-------------|-------------------------------|
|          | Diagnostic agreement | BMD Spearman's correlation    |
| Sex      |              |                               |
| Male (n=13) | 76.9%       | R=0.714 P=0.006               | R=0.765 P=0.002 |
| Female (n=53) | 84.9%     | R=0.854 P<0.001               | R= 0.862 P<0.001 |
| difference| P=0.139    | P=0.199                      |
| Age      |              |                               |
| <60 (n=22) | 81.8%       | R=0.778 P<0.001               | R= 0.818 P<0.001 |
| ≥60 (n=44) | 84.1%       | R=0.88 P<0.001                | R= 0.877 P<0.001 |
| difference| P=0.113    | P=0.223                      |
| BMI      |              |                               |
| <25 (n=23) | 78.3%       | R=0.789 P<0.001               | R= 0.718 P<0.001 |
| ≥25 (n=43) | 86%         | R=0.848 P<0.001               | R= 0.846 P<0.001 |
| difference| P=0.255    | P=0.108                      |
Figure 1a Ultrasound image obtained during radiofrequency echographic multispectrometry examination of the lumbar spine

Figure 1b Automatically generated final report obtained during radiofrequency echographic multispectrometry examination of the lumbar spine
Figure 2 Patients enrolment and data validation
Figure 3a Bland-Altman plots of the differences between dual-energy X-ray absorptiometry and radiofrequency echographic multispectrometry measurements of bone mineral density plotted against the averages of the two measurements in the lumbar spine group.

Figure 3b Bland-Altman plots of the differences between dual-energy X-ray absorptiometry and radiofrequency echographic multispectrometry measurements of T-scores plotted against the averages of the two measurements in the lumbar spine group.
Figure 3c Bland-Altman plot of the differences between dual-energy X-ray absorptiometry and radiofrequency echographic multispectrometry measurements of bone mineral density plotted against the averages of the two measurements in the femur group.

Figure 3d Bland-Altman plot of the differences between dual-energy X-ray absorptiometry and radiofrequency echographic multispectrometry measurements of T-scores plotted against the averages of the two measurements in the femur group.