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DIAGNOSTIC ACCURACY OF A NOVEL ULTRASOUND-BASED METHODOLOGY FOR SPINAL DENSITOMETRY ON A COHORT OF NORMAL- AND UNDER-WEIGHT WOMEN

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Abstract: Currently, osteoporosis is mainly diagnosed through dual-energy X-ray absorptiometry (DXA). However, DXA cannot be used for early diagnoses through population mass screenings because of issues related to ionizing radiation employment. This paper describes the diagnostic accuracy of a novel ultrasound (US)-based method to perform spinal densitometry without employing X-rays. The proposed innovative methodology is based on a combined analysis of both echographic images and “raw” radiofrequency US signals. The diagnostic output is represented by the same parameters of DXA (bone mineral density (BMD), T-score, Z-score). The actual effectiveness of the proposed methodology was evaluated on a cohort of 350 normal-weight or underweight (body mass index (BMI) < 25 kg/m²) female patients in the age range 45-65 years by a direct comparison with DXA assumed as gold standard. The accuracy of US-based diagnoses ranged from a maximum of 90.5% to a minimum of 74.1%, corresponding to the youngest and oldest patient age category, respectively, with an average of 84.9%. A good correlation was also found between US-estimated BMD and DXA related values ($r=0.69$, $p<0.001$). Obtained results demonstrated the high accuracy of the proposed US approach to spinal bone densitometry compared with DXA. This technique has the potential to become a useful and effective tool in clinical practice improving the current approach to osteoporosis diagnosis.

Keywords: ultrasound; spinal bone densitometry; X-rays; osteoporosis; early diagnosis.

1. INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to increased fragility and augmented fracture risk [1]. Osteoporotic fractures represent a major cause of public health burden in terms of mortality, disability and health care costs, emphasizing the need of more effective methods for early osteoporosis diagnosis and fracture prevention. The worldwide frequency of

osteoporotic fractures is in fact rising [1,2], mainly because of the increased longevity of the population. Therefore, the introduction of novel methods aimed at improving osteoporosis diagnosis and patient management results to be of great importance in preventing bone fractures. Moreover, there exists a large variety of osteoporosis risk factors: first of all, there are statistically significant differences in prevalence between men and women and in the most affected female gender, physical constitution plays an important role [3]. In particular, a low body mass index (BMI) is an important risk factor for osteoporosis and consequent fractures [4-6], probably because of its association with bone size [7]. There is also a significant negative relationship between BMI and baseline bone turnover, which is associated with increased bone loss [7-8]. Then, low bone mass and increased rate of bone loss add to an increased risk of subsequent development of postmenopausal osteoporosis [8]. In this context, the strategies for prevention and timely treatment of osteoporosis gain additional interest, especially if referred to those categories of high-risk patients, as in the case of normal weight or underweight individuals.

Bone densitometry performed through dual X-ray absorptiometry (DXA) provides quantitative measurements of bone mineral density (BMD) and such measurements currently represent the reference indicated by World Health Organization (WHO) for osteoporosis diagnosis. The most frequently investigated anatomical sites are proximal femur and lumbar spine, since it has been demonstrated that BMD measurements on these sites are the most reliable to predict the global fracture risk. In particular, femoral neck BMD is a stronger predictor of hip fracture than BMD measured at other sites [9] and spine BMD is the preferred choice for treatment monitoring due to its high sensitivity to BMD variations [10]. However, DXA cannot be used for early diagnoses through population mass screenings because of the well-known issues related to ionizing radiation employment [11,12].

In the present work, we tested the diagnostic accuracy of a new method for spinal bone densitometry, which does not require ionizing radiation but employs only ultrasound (US) signals.

2. MATERIALS AND METHODS

A. Study population

The study was conducted at the Operative Unit of Rheumatology of "Galateo" Hospital (San Cesario di Lecce, Lecce, Italy). A cohort of 350 female patients was recruited according to the following criteria: 45-65 years, BMI < 25 kg/m², absence of severe deambulation impairments, medical prescription for a spinal DXA, signed informed consent. Enrollment criteria were established taking into account two factors: 1) the considered age range includes the majority of women that are referred for a spinal DXA [13,14]; 2) low BMI is a recognized risk factor for osteoporosis and bone fractures [4-6]. Therefore, the introduction of new methods for diagnosis and prevention of osteoporosis is of more impact in the case of normal weight or underweight individuals with respect to overweight and obese ones.

B. Data acquisition

All the enrolled patients underwent two examinations: a conventional spinal DXA and an abdominal US scan of lumbar spine. Spinal DXA scans were performed using a Hologic Discovery W scanner (Hologic, Waltham, MA, USA), measuring BMD over the lumbar vertebrae L1-L4. Abdominal US scans of lumbar spine were performed employing an innovative US device developed in Lecce (Italy) within the ECHOLIGHT Project through a collaboration between CNR-IFC and Echolight srl, which was equipped with a 3.5-MHz broadband convex transducer and configured to provide both echographic images and unfiltered radiofrequency (RF) signals (Fig. 1). The scan lasted about 1 minute and generated 100 frames of RF data (frame-rate ~1.5 fps) that were acquired and stored in a PC hard-disk for subsequent offline analysis.

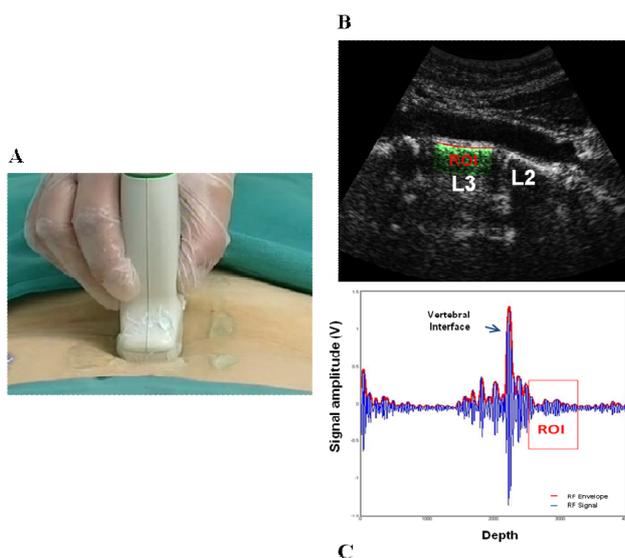


Figure 1. Basic principle of the developed US-method: Abdominal US scan of lumbar spine (A) and processing of both echographic images (B) and unfiltered RF signals (C).

C. US Data analysis

US data were analyzed by a new fully automatic algorithm developed to calculate the same diagnostic parameters provided by DXA (BMD, T-score, Z-score). Starting from the data acquired during the mentioned US scan of the lumbar spine, for each considered patient the algorithm:

- i) processed both echographic images and corresponding "raw" RF signals;
- ii) performed a series of spectral and statistical analyses on the detected regions of interest;
- iii) provided the diagnostic output (BMD, T-score, Z-score) through detailed comparisons with reference models spectra of healthy and osteoporotic vertebrae derived from previous US acquisitions on DXA-classified patients [15].

Diagnostic accuracy of obtained results was evaluated through a direct comparison with corresponding DXA output. Each enrolled patient was classified in one of the three diagnostic categories (osteoporotic, osteopenic, healthy) first according to DXA and then according to US-based analysis. For each considered age range, patients that received the same classification from both DXA and US system were identified as "correct diagnoses". An explanatory scheme of the method used for the comparison of US and DXA diagnoses is shown in Fig. 2.

Pearson coefficient (r) was used to assess the correlation between BMD, T-score and Z-score values calculated by both diagnostic methodologies.

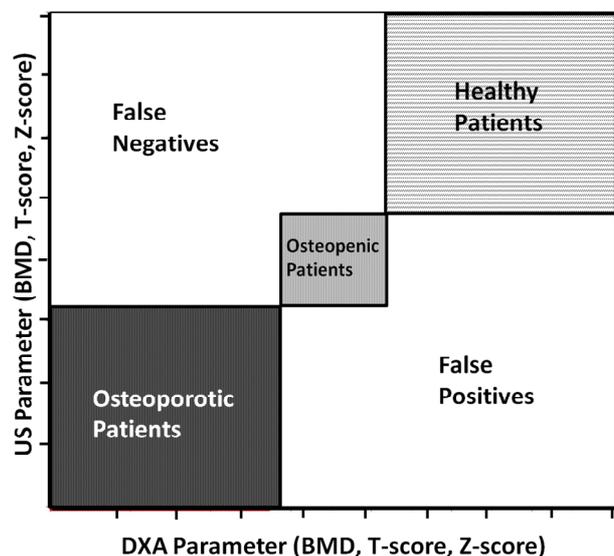


Figure 2. Scheme adopted for the comparison of US and DXA diagnoses.

3. RESULTS

For 84.9% of the cases US diagnosis was the same of the corresponding DXA one. In particular, for each considered 5-year age interval diagnostic accuracy was in the range 74.1%-90.5%, with the maximum in correspondence of the youngest patients (45-50 years) and the minimum in correspondence of the oldest ones (60-65 years) (Table I).

Table I. Diagnostic agreement between US and DXA.

| AGE RANGE | N° of patients | US vs DXA overlapping diagnosis |
|--------------|----------------|---------------------------------|
| 45-50 | 42 | 90.5% |
| 50-55 | 109 | 87.2% |
| 55-60 | 114 | 88.6% |
| 60-65 | 85 | 74.1% |
| Total | 350 | 84.9% |

For each group of patients, Table II shows the average values of BMD calculated with both diagnostic methodologies, together with the percentage difference between these two values.

Table II. Comparison between BMD values calculated with DXA and US.

| AGE RANGE | N° of patients | BMD DXA* (g/cm ²) | BMD US* (g/cm ²) | Difference* (%) |
|--------------|----------------|-------------------------------|------------------------------|-----------------|
| 45-50 | 42 | 0.87±0.12 | 0.88±0.13 | 0.6±9.4 |
| 50-55 | 109 | 0.88±0.11 | 0.88±0.16 | 0.8±13.2 |
| 55-60 | 114 | 0.80±0.11 | 0.80±0.15 | 0.3±13.0 |
| 60-65 | 85 | 0.78±0.12 | 0.79±0.18 | 1.2±19.7 |
| Total | 350 | 0.83±0.12 | 0.83±0.16 | 1.0±14.8 |

*Average value ± standard deviation

For patients in the same age range, Pearson correlation coefficient (r) between DXA and US measurements was also evaluated for each diagnostic parameter (BMD, T-score, Z-score): all the obtained values of r were within the interval 0.53-0.84 (p<0.001) (Table III) and their trends against age qualitatively reflected the observed diagnostic accuracy profile. Therefore, the best correlation (r=0.84) was found in the age range 45-50 years, while the poorest correlation (r=0.53) was again found in correspondence of the oldest considered patients (60-65 years), analogously to what we found for minimum diagnostic accuracy.

Table III. Pearson correlation coefficient (r) between DXA and US measurements for each diagnostic parameter.

| AGE RANGE | N° of patients | BMD | T-score | Z-score |
|--------------|----------------|-------------|-------------|-------------|
| 45-50 | 42 | 0.84 | 0.84 | 0.83 |
| 50-55 | 109 | 0.73 | 0.73 | 0.78 |
| 55-60 | 114 | 0.68 | 0.69 | 0.62 |
| 60-65 | 85 | 0.55 | 0.53 | 0.59 |
| Total | 350 | 0.69 | 0.69 | 0.68 |

Fig. 3 shows the scatterplots relative to Pearson correlation coefficient for all the diagnostic parameters for each age range of patients and the total value of r.

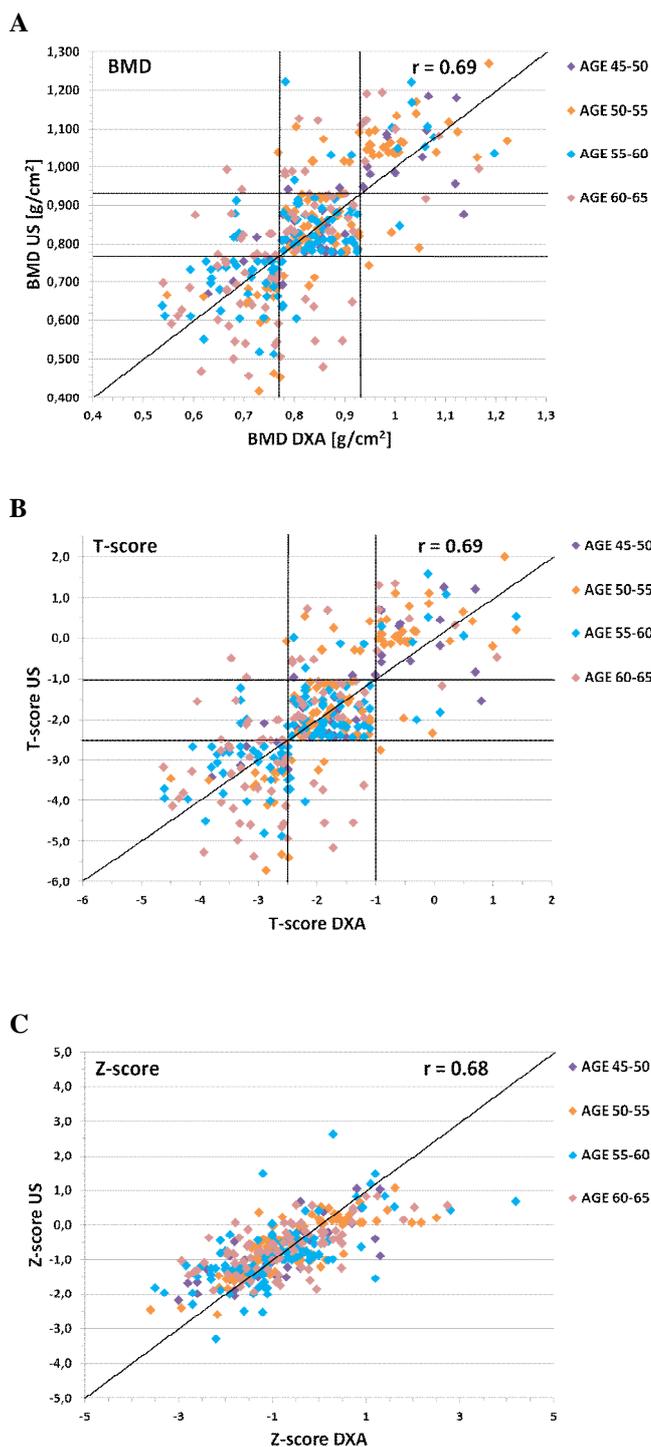


Figure 3. Comparison of BMD (A), T-score (B) and Z-score (C) values measured by US and the corresponding DXA.

4. DISCUSSION

This work demonstrated the feasibility of a new US-based technique for osteoporosis diagnosis on lumbar spine. Starting from an US scan of this bone district, the proposed method provided diagnostic parameters directly correlated with DXA measurements.

The peculiar feature of the introduced method is represented by the exploitation of RF signals acquired during an echographic scan of the target bone structure to determine whether the internal bone architecture can be classified as osteoporotic or healthy through detailed comparisons with reference spectral models.

Diagnostic accuracy of the obtained US outputs, evaluated through a direct comparison with the corresponding DXA ones, resulted pretty high. The percentage of “correct diagnoses” (84.9%) is very good for an US diagnostic method of osteoporosis and the result is even more encouraging if we take into account the applicability of the suggested technique on the same DXA reference site. Much lower accuracy levels are often reported for other quantitative US-based methodologies relative to peripheral sites (radius, tibia, calcaneus, phalanges) [16].

The percentage difference between the average values of US-estimated BMD and DXA-measured one is ever positive in each age range category of patients (Table II). This over-estimation of BMD through US with respect to DXA measurement could be used to set the system in order to have a “safety margin” for osteoporosis diagnosis. In particular, assuming the employment of our system in osteoporosis screening, the intentional shift of the estimated diagnostic parameters to more negative values could be an early indication of BMD decrement, addressing patients to preventive treatments.

It is interesting to observe that maximum agreement between US and DXA diagnoses (90.5%) was found for the youngest considered patients (45-50 years; see Table I), emphasizing the potential of the proposed technique to be applied for population mass screenings on young individuals.

On the other hand, minimum values of diagnostic agreement (74.1%) and BMD correlation ($r=0.55$) were always found for the oldest considered patients (60-65 years; see Table I and Table III). The lower diagnostic agreement in correspondence of these patients is not necessarily due to a lower accuracy of the adopted US methodology, but could be at least partially attributable to a decreased reliability of spinal DXA. It is known [13,14] that, with increasing patient age, spinal degenerations (e.g. calcifications) may affect the accuracy of spinal DXA measurements and in fact, in clinical practice, the preference site for osteoporosis evaluation in elderly people is represented by proximal femur and not by lumbar spine.

In general, for what concerns the age range (45-65 years), the enrolled women cohort includes the majority of patient that are referred for a spinal DXA, since younger women usually do not undergo osteoporosis controls and older women are more frequently referred for femoral DXA for the above mentioned reasons.

Moreover, taking into account that normal-weight or underweight individuals have an increased risk for osteoporosis and bone fractures with respect to overweight and obese ones [4-6], the low BMI of enrolled patients represents a factor of additional interest for the applicability of the presented strategy for diagnosis and prevention of osteoporosis.

5. CONCLUSIONS

The proposed US approach to spinal bone densitometry showed a very good and significant agreement with DXA diagnoses. This innovative non-ionizing approach has the potential to anticipate osteoporosis diagnosis by several years through extended screenings in younger populations and to become a useful tool for therapeutic outcome monitoring.

6. ACKNOWLEDGEMENTS

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