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A New Ultrasonic Method for Lumbar Spine Densitometry

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Abstract—**Aim of this work was to carry out a first clinical validation of a new ultrasound (US)-based approach to bone densitometry of lumbar spine. A total of 290 female patients were enrolled for this study (45-75 years of age, body mass index (BMI)<40 kg/m^2) and all of them underwent two different diagnostic investigations: a lumbar DXA (dual-energy X-ray absorptiometry) and an US scan of the same vertebras, performed with an echographic device configured for the acquisition of both echographic images and unfiltered radiofrequency signals. US data analysis was carried out through an innovative algorithm, whose main features include: a) measurements are always performed on a specific region of interest of the vertebra, identified on the basis of both morphologic and spectral characteristics; b) analysis takes into account patient BMI; c) the algorithm is integrated with a reference database containing model acquisitions for different combinations of patient age, sex and BMI. Accuracy of final algorithm output, represented by the same diagnostic parameters of a DXA investigation, was evaluated through a direct comparison with DXA results. For 84.5% of the patients US diagnosis (osteoporotic, osteopenic, healthy) coincided with the corresponding DXA one and this accuracy level was not appreciably influenced by patient age nor by BMI. The proposed approach represents the first US method for osteoporosis diagnosis which is directly applicable on spine and has the potential to be effectively used for population mass screenings.**

Keywords - bone densitometry; osteoporosis diagnosis; radiofrequency signal processing; ultrasound imaging; biomedical image processing.

I. INTRODUCTION

Osteoporosis is the most common bone disease, causing increased bone fragility and augmented fracture risk, with related huge social and economic costs [1]-[2]. The most effective way to reduce these costs would be an earlier osteoporosis diagnosis through population mass screenings.

Unfortunately, the only method to reliably predict main osteoporotic fractures is currently represented by bone mineral density (BMD) measurements performed on lumbar vertebras or femur through dual-energy X-ray absorptiometry (DXA), which cannot be used for population screenings because of radiation-related issues.

We developed a new ultrasound (US)-based approach to bone densitometry of lumbar spine and femur, capable of providing diagnostic accuracies comparable to DXA investigations without employing X-rays. Aim of this work was to carry out a first clinical validation of this novel approach applied to spinal densitometry.

II. METHODS

A. Patients

The study was conducted at the Operative Unit of Rheumatology of "Galateo" Hospital (San Cesario di Lecce, Lecce, Italy) and included a total of 290 consecutive female patients, according to the following inclusion criteria: Caucasian ethnicity, 45-75 years of age, body mass index (BMI)<40 kg/m^2, medical prescription for a spinal DXA. All the enrolled patients underwent two different investigations: a lumbar spine DXA and an abdominal US scan of the same vertebras, as detailed in the following paragraphs.

The study protocol was approved by the Hospital Ethics Review Board and all patients gave informed consent.

B. DXA Measurements

DXA scans were performed on the lumbar spine (L1-L4) using a Hologic Discovery W scanner (Hologic, Waltham, MA, USA). Measurement results were expressed both as BMD and as T-score values, where T-score value is defined as the number of standard deviations (SDs) from the peak BMD of young women belonging to the considered ethnicity.

According to the operational definition of osteoporosis given by the World Health Organization (WHO), patients were classified as "osteoporotic" if T-score $\leq$ -2.5, "osteopenic" if -2.5 < T-score < -1.0 or "healthy" if T-score $\geq$ -1.0.

C. Ultrasound Acquisitions

US scans of lumbar vertebras were performed through an echographic device (Echo Blaster 128, Telemed Medical Systems srl, Milan, Italy), equipped with a 3.5-MHz broadband convex transducer (C3.5/60/128Z, Telemed Medical Systems srl) and configured to provide both echographic images and unfiltered radiofrequency (RF) signals.

Each patient underwent a sagittal abdominal scan of lumbar spine which lasted about 70 s and generated 100 frames of RF signals, that were high-pass filtered, amplified, digitized (40 MHz, 16 bits) and stored on a PC hard-disk for offline analysis. Transducer focus and scan depth were each time adjusted in order to have vertebral interfaces in the beam focal zone and in the central area of the image. Other acquisition parameters were: echograph power = 75%; mechanical index (MI) = 0.4; gain = 0 dB; linear TGC (time gain compensation).

D. Ultrasound Data Analysis

US data analysis was carried out through our new fully automatic algorithm, characterized by the following innovative features with respect to previous US-based approaches for osteoporosis diagnosis:

- diagnostic measurements are always performed on a specific region of interest (ROI) of the vertebra, identified on the basis of both morphologic and spectral characteristics;
- data analysis takes into account patient BMI;
- the algorithm is integrated with a reference database containing model acquisitions for each combination of anatomical site, patient age and sex.

Algorithm working principle is based on a complex patented method [3]-[4] which is herein summarized.

First, the algorithm automatically identifies vertebral interfaces within the sequence of echographic images acquired on the considered patient through the following steps, performed on each acquired frame:

1. selection of a "search region" corresponding to the central part of the image and exclusion of "noisy" frames on the basis of search region histogram analysis;
2. pre-processing of retained search regions based on thresholding operations and selection of clusters of pixels resembling the geometrical features of vertebral interfaces;
3. spectral analysis of RF signals corresponding to each "possible" vertebra identified by a selected cluster of pixels through a comparison with reference models of vertebral spectra;
4. identification of the "actual" vertebras based on previous step results.

After the completion of this identification process, the algorithm performs diagnostic parameter calculations on RF signal segments corresponding to specific ROIs internal to the identified vertebras. In this process, the algorithm compares RF spectra of the considered patient with reference model spectra of healthy and osteoporotic vertebras derived from previous US acquisitions on DXA-classified patients. Reference model spectra are in fact taken from a preliminarily built database in which specific models are available for different combinations of patient sex, BMI interval and age range. For each analyzed patient, the algorithm provides as a final output the same diagnostic parameters of a DXA investigation: BMD, T-score and Z-score (where Z-score is defined as the number of SDs from the average BMD of women of the same age belonging to the considered ethnicity).

In this study, algorithm accuracy was assessed through a direct comparison with DXA results (assumed as a "gold standard" reference) according to the evaluation scheme reported in Fig. 1.

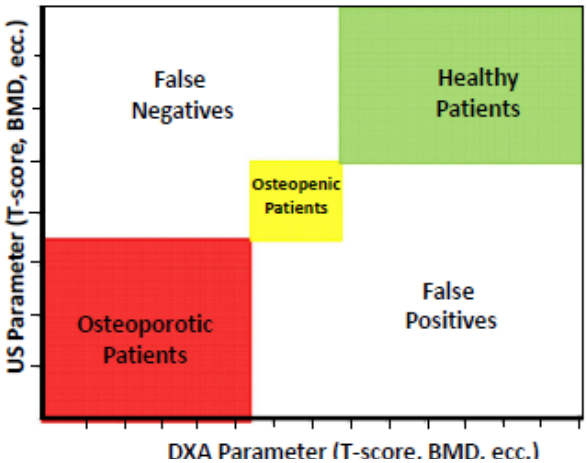

Figure 1. Evaluation scheme adopted for the assessment of US diagnostic accuracy against DXA.

III. RESULTS

For 84.5% of the analyzed patients US diagnosis (osteoporotic, osteopenic, healthy) coincided with the corresponding DXA one, as visually emphasized by the graphs reported in Fig. 2 and Fig. 3.

Fig. 4 shows the corresponding graph obtained for Z-score values. In this case, taking into account the definition of Z-score and the operational definition of osteoporosis, it is not possible the direct identification on the graph of correctly diagnosed patients, false negatives and false positives. However, a strong and statistically significant correlation between US output and corresponding DXA parameter values was found also for Z-score ($r = 0.81$, $p<0.001$).

Assessing the diagnostic accuracy (*i.e.,* number of correct diagnoses/analyzed patients) as a function of patient BMI, we obtained: 85.2% for patients with BMI<25 kg/m^2 (n=162), 87.2% for those having BMI in the range 25-30 kg/m^2 (n=86) and 76.2% for those with BMI in the range 30-40 kg/m^2 (n=42).

Regarding diagnostic accuracy as a function of patient age, we found: 83.1% for patients in the range 45-55 y (n=71), 84.9% in 56-65 y (n=166), 84.9% in 66-75 y (n=53).

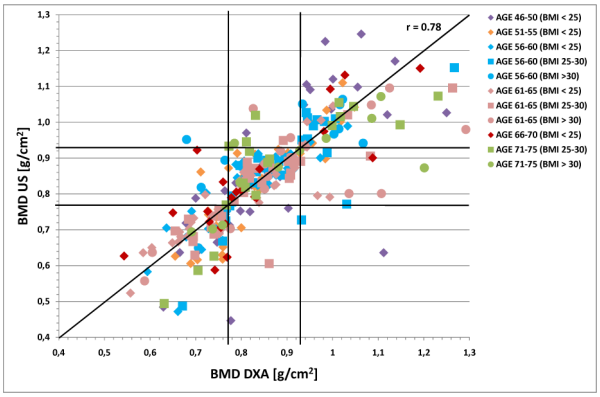

Figure 2. US-measured BMD against the corresponding DXA values for all the studied patients. ($p<0.001$; please refer to the evaluation scheme in Fig. 1 to identify correctly diagnosed parients, false negatives and false positives)

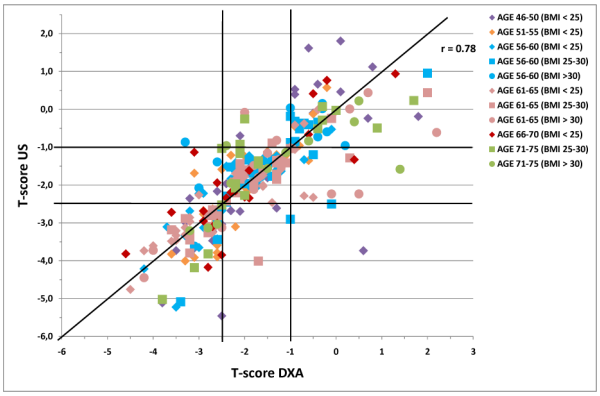

Figure 3. US-measured T-score values against the corresponding DXA values for all the studied patients. ($p<0.001$; please refer to the evaluation scheme in Fig. 1 to identify correctly diagnosed parients, false negatives and false positives)

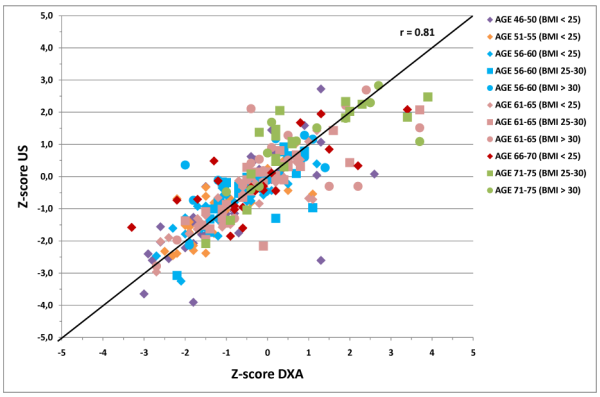

Figure 4. US-measured Z-score values against the corresponding DXA values for all the studied patients ($p<0.001$).

Table 1 illustrates the comparison between BMD values calculated with both the diagnostic methodologies as a function of age range, showing that for each considered age range the average difference between BMD values provided by DXA and US is always within the 1% limit.

TABLE I. COMPARISON OF DXA AND US MEASUREMENTS OF BMD AS A FUNCTION OF AGE RANGE

Age range	n	BMD DXA[a] (g/cm^2)	BMD US[a] (g/cm^2)	Difference[a] (%)
46-50	36	0.88±0.15	0.88±0.22	-0.8% ± 15.2%
51-55	35	0.84±0.10	0.83±0.13	-0.6% ± 8.9%
56-60	82	0.81±0.10	0.80±0.11	-0.8% ± 8.7%
61-65	84	0.79±0.13	0.78±0.12	-1.0% ± 7.9%
66-70	21	0.82±0.15	0.83±0.15	+0.9% ± 11.9%
71-75	32	0.88±0.15	0.88±0.16	0.0% ± 11.8%

IV. DISCUSSION

Ultrasound techniques are currently experiencing an increasing diffusion in different biomedical fields thanks to the combination of their well-known advantages (absence of ionizing radiation, portability, low costs) with recent research achievements that are providing such techniques with more standardized and less operator-dependent results, in some cases obtained also through the development of innovative image processing strategies involving microbubble- or nanoparticle-based contrast agents [5]-[13].

In this context, quantitative US (QUS) methods have been investigated also for osteoporosis screening purposes, searching for a non-ionizing and cheaper alternative to DXA investigations [14]-[18]. Actually, the currently available QUS methods have several advantages over DXA (absence of ionizing radiation, portable machines, lower costs), but they are only applicable to peripheral anatomical sites (*e.g.*, calcaneus) and there is not yet consensus regarding their accuracy in identifying osteoporotic patients [16],[18]-[22]. As a consequence, the widely accepted physician opinion is that osteoporosis cannot be reliably diagnosed by QUS methods, which can be actually useful only as a preliminary test for non-vertebral fracture risk to be followed by a DXA confirmation [22]-[24].

The present study demonstrated the feasibility of a novel US approach for osteoporosis diagnosis directly applicable to lumbar spine. Assuming DXA as the gold standard reference, US-based identification of osteoporotic, osteopenic and healthy patients resulted correct in 84.5% of the analyzed cases (n=290) and this accuracy level was not appreciably influenced by patient age nor by BMI. Furthermore, US-measured BMD values showed a good correlation with the corresponding DXA values and the adopted method did not show the tendency to overestimate nor to underestimate BMD in any of the considered age ranges (see Tab. 1).

To the best of our knowledge, the proposed method represents the first US-based approach for osteoporosis diagnosis directly applicable on spine. This fact, combined

with the exploitation of RF signal analysis to determine the microscopic characteristics of the considered bone, resulted in diagnostic agreements and parameter correlations with spinal DXA measurements which are unprecedented for an US technique.

V. Conclusion

We presented a novel US-based approach for spinal densitometry, showing its significant diagnostic agreement with the reference gold standard represented by DXA outputs.

Thanks to the observed accuracy levels, combined with the full automation of the diagnosis procedure and with the absence of ionizing radiation, the illustrated method has the potential to become actually useful for routine population mass screenings for early osteoporosis diagnosis.

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