Received: 19 September 2022 | Revised: 10 January 2023 | Accepted: 24 January 2023

DOI: 10.1002/ajpa.24711

TECHNICAL NOTE

AMERICAN JOURNAL OF BIOLOGICAL ANTHROPOLOGY The Official Journal of the American Association of Biological Anthropologists

WILEY

Technical note: Application and potentiality of quantitative ultrasonometry for the evaluation of bone mineral density status

Alba Pasini[1] | Natascia Rinaldo[1] | Barbara Bramanti[2,3] | Emanuela Gualdi-Russo[1]

[1]Department of Neuroscience and Rehabilitation, University of Ferrara, Ferrara, Italy

[2]Department of Environmental and Prevention Sciences, University of Ferrara, Ferrara, Italy

[3]University Center for Studies on Gender Medicine, University of Ferrara, Ferrara, Italy

Correspondence
Natascia Rinaldo, Department of Neuroscience and Rehabilitation, University of Ferrara, Corso Ercole I d'Este n.32, 44121, Ferrara, Italy.
Email: natascia.rinaldo@unife.it

Abstract

The evaluation of bone mineral density (BMD) is an important task in paleopathology. Techniques commonly applied in bone quantity assessment, such as DXA or radiogrammetry (XR), suffer from several limitations when applied to skeletal remains. In recently published research, we developed a new methodology and new reference curves for the evaluation of BMD on human skeletal remains, applying for the first time Quantitative Ultrasonometry (QUS), a user-friendly, portable, and reliable clinical technique. This study aims to apply this new methodology to an archeological sample and to compare the results with those obtained through XR. We apply QUS and XR to a sample of 104 adults from Medieval Italian cemeteries. Fragility fractures were recorded. Descriptive statistics and comparisons between sexes, age-at-death cohorts, and individuals with and without fragility fractures were performed. Moreover, univariate and multivariate logistic regression models were used to define the parameters most predictive of fracture risk in past populations. The comparison between sexes showed no significant results concerning BMD parameters, whereas a decrease in BMD with increasing age is confirmed. The comparison between fracture and non-fracture individuals and the logit model demonstrated that QUS parameters, especially UBPI, are more reliable predictors of fracture risk in comparison to XR. Our results confirmed that QUS is a valuable technique that can be efficiently applied to archeological remains, also considering its portability. We also propose a modification of the previously published QUS standard curves, to easily assess osteopenia and osteoporosis in archeological material.

KEYWORDS
biological anthropology, bone mineral density, fracture risk, paleopathology, QUS

1 | INTRODUCTION

Osteoporosis and osteopenia are subclinical metabolic disorders characterized by a loss of bone density in both cortical and spongy bone, which lead to impaired bone strength and an increased risk of fracture (Brickley & Ives, 2008; Tuck et al., 2018; Tu et al., 2018). Typical clinical complications include fractures of the hip, of the distal radius (*Colles' fracture*), and vertebral compression fractures. These are the most affected areas, due to the high content in trabecular bone (Waldron, 2008). Bone Mineral Density (BMD) is expressed as the volumetric amount of bone mineral content (hydroxyapatite) in a specific skeletal area (g/cm^2) (Agarwal, 2019; Akkawi & Zmerly, 2018; Golob & Laya, 2015; Mays, 2007; Waldron, 2008), and can be predictive of an individual's risk of developing osteopenia and osteoporosis (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, 2001; Wüster et al., 2000). The main goal of this work is to compare different methodologies that can be used in the assessment of BMD from dry bones, and more specifically in the diagnosis of osteopenia and osteoporosis in ancient skeletal remains. BMD depends on several intrinsic and extrinsic individual factors, especially age and sex. In fact, BMD increases during growth and reaches its maximum value once the physiological growth process has been completed (Peak Bone Mass, PBM), followed by a period of stabilization and then a physiological decrease (NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, 2001; Weaver et al., 2016). Males and females differ in mean BMD and PBM from puberty, with the greatest divergence starting after 40–50 years of age due to the strong menopausal-related bone resorption processes in women (de Oliveira et al., 2011; Dede & Callan, 2018; Steadman, 2005; Weaver et al., 2016).

Osteoporotic fractures cause higher morbidity, increased risk of other fractures, as well as chronic pain, disability, and a higher risk of dying (de Oliveira et al., 2011; Johnell & Kanis, 2006; Nazrun et al., 2014; Odén et al., 2015). For these reasons, osteoporosis is considered one of the major contemporary health burdens and a current global pandemic (Golob & Laya, 2015b; Madimenos et al., 2015; Oden et al., 2015), although it is known that these disorders have affected human populations since ancient times. In fact, several archeological cases of low BMD have been observed from the Neolithic to the Middle Ages (Agarwal, 2018; Agarwal et al., 2004; Beauchesne & Agarwal, 2017; Brickley & Ives, 2008; Curate, 2014; Curate et al., 2019; Glencross & Agarwal, 2011; Mays et al., 2006; Ryan & Shaw, 2015). A proper analysis of BMD in past populations not only provides data on the occurrence of osteoporosis in human history but can also be a useful and diversified indicator of the health status of a human group (Agarwal, 2018; Curate, 2014).

Macroscopic analysis of putative osteoporotic fractures has been considered the main method for the assessment of BMD for several decades (Brickley & Ives, 2008; Curate et al., 2016; Curate, 2014), and numerous cases are known in the archeological record (Brickley, 2002; Brickley, 2006; Ciesielska & Stark, 2020; Curate et al., 2011; Curate et al., 2013; Ives et al., 2017). However, this method is not considered to be a complete diagnostic criterion for low BMD, as osteoporosis acts as a "silent disorder" also before traumatic or fragility fractures occur (Njeh et al., 1997; Wylie, 2010). In the last few years, the application of biomedical techniques to skeletal remains provided a more systematic approach; the most commonly applied techniques to skeletal remains are dual X-Ray absorptiometry (DXA), Computer Tomography (CT), and radiogrammetry (XR) (Andronowski et al., 2018; Beauchesne & Agarwal, 2017; Curate, 2014; Hale & Ross, 2018). In particular, the micro-CT, providing three-dimensional imaging of the bone, can be used to quantify bone quality (i.e. trabecular structures) in ancient skeletal remains and therefore can be useful for the diagnosis of several pathological conditions, such as osteomalacia (Welsh et al., 2020) and osteoporosis (Nazarian et al., 2008). However, these methods, albeit validated on living subjects, suffer from the lack of a reference model based on a skeletal collection of known age and sex, and their application on archeological skeletons may introduce a bias in the interpretation of the results mainly due to the absence of soft tissue (Andronowski et al., 2018).

A recent study has shown the potential of phalangeal Quantitative Ultrasonometry (QUS) for diagnosing osteoporosis on skeletal remains (Rinaldo et al., 2018). QUS is a reliable, portable, user-friendly, and computer-assisted clinical technique based on ultrasound waves propagation (Agnollitto et al., 2021; Baroncelli, 2008; Drozdzowska et al., 2005; Giavaresi et al., 2004; Guglielmi et al., 2015; Guglielmi & de Terlizzi, 2009; Hadji et al., 2015; Montagnani et al., 2000; Njeh et al., 1997; de Oliveira et al., 2011; Wüster et al., 2009, Wüster et al., 2005), which has never been applied before on forensic or archeological skeletal remains. In the paper of Rinaldo et al. (2018), a protocol specifically adapted for skeletal remains and new reference curves were developed using a sample of 110 skeletons of known age and sex. This allowed providing a standardized and quantitative reference for the diagnosis of bone loss and health status in past populations (Rinaldo et al., 2018).

QUS has been previously tested on skeletal elements through several in vitro studies (de Terlizzi et al., 2000). Nevertheless, its application on skeletonized individuals represented a novelty in anthropological research. To further investigate the diagnostic potential of QUS in archeological specimens, we applied the protocol proposed by Rinaldo et al. (2018) to a large archeological skeletal sample consisting of over 100 individuals from different Italian archeological sites. We then compared the obtained results with those resulting from XR and the macroscopic analysis of osteoporotic fractures and we developed a new cut-off for the prediction of fractures in archeological skeletons. Moreover, we introduced a change to the reference curves from the previous study (Rinaldo et al., 2018) adding the thresholds for the occurrence of osteopenia and osteoporosis.

We aimed to assess whether QUS can be successfully used on archeological remains and whether it can provide a predictive value of fracture for skeletal remains by comparing its results with the XR technique. This finding could expand the possibilities of analyzing human archeological remains with regard to bone loss, health, and human biology of ancient populations.

2 | MATERIALS AND METHODS

2.1 | Sample

The archeological sample included 104 adult individuals (mean age: 40.7 ± 12.2 total sample; 42.7 ± 12.6 males; 38.5 ± 11.4 females) from nine archeological sites of different epochs located in Northern

TABLE 1 Brief description of the examined subsample

Site name	Dating	Archeological context	Males *n*	Females *n*	YA *n*	MA *n*	OA *n*
Chiunsano (Rovigo)	2nd-4th Century	31 inhumations. The burial area was located along the Roman settlement area in the municipality of Gaiba (Rovigo, Italy) (Büsing et al., 1994; Büsing & Büsing Kolbe, 1996).	6	7	6	3	4
Chiesazza (Rovigo)	4th-6th Century	59 inhumations in simple pit burials or wooden coffins located in the city of Ficarolo (Rovigo, Italy) (Büsing et al., 1994; Büsing & Büsing Kolbe, 1996).	7	6	2	9	2
S. Maria in Padovetere (Ferrara)	6th-7th Century	Simple pit burials that are located in the area of the S. Maria in Padovetere church (Comacchio, Ferrara, Italy) (Corti, 2007).	3	1	-	1	3
Imola, via Emilia	7th-8th Century	Single inhumations in brick coffins. These burials were part of a group of three graves dated to the Lombard era, discovered along the Via Emilia (Imola, Bologna, Italy) (Pasini et al., 2018; Rinaldo et al., 2019).	-	2	1	-	1
Crocetta (Ferrara)	Early 15th Century	Single inhumation laid supine inside a rectangular pit at the Oratory of Cento (Ferrara, Italy) (Balboni et al., 2005; Lorenzini, 2001; Onisto & Gualdi-Russo, 2011).	1	-	-	-	1
Imola, via Maghinardo	13th Century	Two single inhumations deposed in coffer graves and located in the city of Imola (Bologna, Italy),	1	-	-	1	-
S. Anna (Ferrara)	15th-16th Century	Several inhumations located in the area of the cloister and the church of S. Anna (Ferrara, Italy) (D'angelo, 2005; Onisto et al., 2006).	1	-	1	-	-
Osservanza (Imola)	17th Century	Four mass graves with 133 individuals were discovered at the Lazzaretto Osservanza (Imola, Bologna) which dated back to the plague outbreak of 1630–1632 in the city of Imola (Bramanti et al., 2018; Guellil et al., 2021; Rinaldo et al., 2019; Rubini et al., 2016)	2	3	2	3	
S. Biagio cemetery (Ravenna)	17th-19th Century	Archeological excavations (2013) of the cemetery adjacent to the church of S. Biagio (Ravenna) returned the human remains of over 200 individuals (Masotti et al., 2017; Scianò et al., 2020; Scianò et al., 2021)	33	31	15	30	19
Total sample			**55**	**49**	**26**	**48**	**30**

Abbreviation: MA, Middle Adult; OA, Old Adult; YA, Young Adult.

Italy (Po river Valley, Veneto, and Emilia-Romagna regions) (Table 1 and Figure 1 Supplementary Material). Among these, 20 individuals had already been considered for applicative purposes in our previous study (Rinaldo et al., 2018). The sub-samples belong to the osteological collection of the University of Ferrara (Laboratory of Archeo-Anthropology and Forensic Anthropology) and were collected from sites with similar sedimentary context to limit as possible the bias of the diagenesis influence on bones. For the same reason, only individuals in a good state of preservation were included in the final analysis. Moreover, only individuals with fully preserved proximal phalanges of the last four fingers of the hand and second metacarpal bones were selected for the study. Individuals with undetermined sex and subadults were excluded.

2.2 | Osteological analysis

Biological profiles (sex, age, and stature) were determined by applying classical anthropological methods (Acsádi & Nemeskéri, 1970; Brooks & Suchey, 1990; Brothwell, 1981; Buikstra & Ubelaker, 1994; Ferembach et al., 1980; Gualdi-Russo, 2007; Gualdi-Russo et al., 2018; Lovejoy et al., 1985; Phenice, 1969; Todd, 1921; Todd, 1920). Individuals were divided into three age cohorts according to Buikstra and Ubelaker (1994): Young Adults (YA, 20–35 years); Middle Adults (MA, 36–50 years); Old Adults (OA, 50+ years of age).

Osteoporotic fractures were recorded following the guidelines of Curate and colleagues (Curate et al., 2016) for vertebral compression fractures, while paleopathological and traumatological analysis of

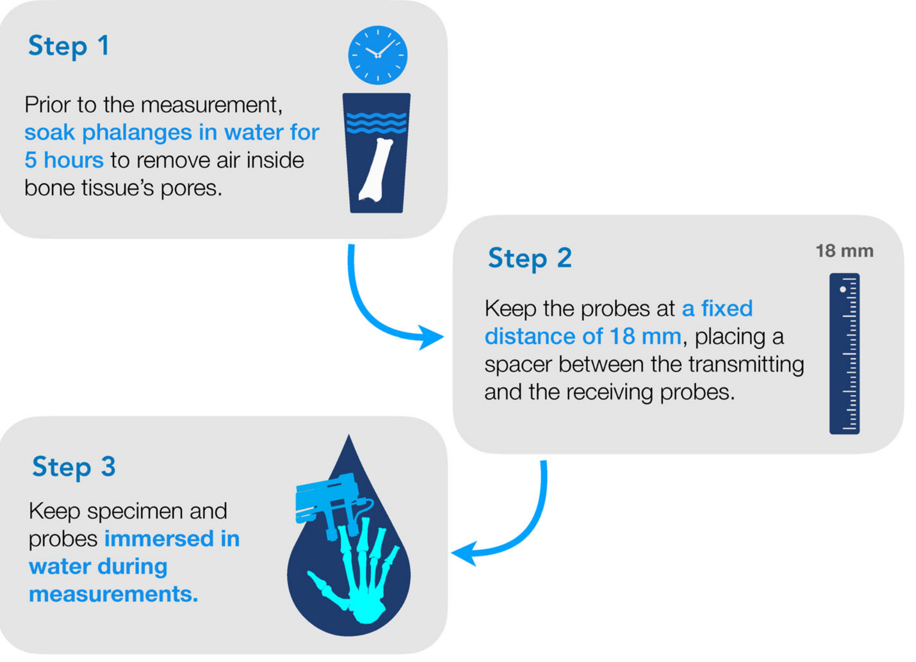

FIGURE 1 Graphical representation of the protocol proposed by Rinaldo et al. (2018).

fracture injuries was applied for the proximal femur and distal radius/ulna (Curate et al., 2013; Lovell, 1997; Ortner, 2003; Scianò et al., 2020).

For each phalanx, we have taken the following measures: total maximal length (TML, mm) and distal maximal width (DMW, mm) – both measured with a sliding caliper –, weight (g), measured with a precision balance, and volume (cm^3), assessed by water immersion using a graduated cylinder. Density was calculated as weight (g)/volume (cm^3).

2.3 | QUS assessment

BMD was assessed following the published specific protocol adapted for skeletal remains (Rinaldo et al., 2018) through phalangeal QUS (DBM Sonic Bone Profiler device, GEA, Carpi, Italy). This methodology involves the application of the probes on the second to fifth finger proximal phalanges of the hand. Phalanges are one of the best proxy areas for BMD detection since they are considered an optimal biomarker due to their very similar characteristics to general bone turnover (Wüster et al., 2005). The high-precision caliper is equipped with two 12-mm diameter transducer probes, which are placed at the lateral and medial portions of the distal metaphysis of the hand phalanges. The protocol proposed by Rinaldo and colleagues involves three steps (Figure 1): (1) Prior to measurement, the phalanges must be soaked in water for 5 h to remove the air within the bone trabeculae. (2) Probes must be set at a fixed distance of 18 mm by using a previously prepared plastic or wooden spacer and positioned at the distal end of the phalanges. (3) Measurements are carried out always keeping the phalanges and probes immersed in water. Water prevents the ultrasounds from dispersing, as suggested by other studies (de Terlizzi et al., 2000; Rinaldo et al., 2018; Wüster et al., 2005). The parameters AD-SoS (m/s, amplitude-dependent speed of sound), BTT (μs, bone transmission time), and UBPI (ultrasound bone profile index, used for the prediction of fracture risk) were registered (Table 2) (Wüster et al., 2000). Samples providing anomalous results (i.e., one or more parameter = 0) were excluded from the study, to avoid possible misinterpretation linked to diagenetic alteration of the bone microstructure.

TABLE 2 Description of each QUS parameter (Baroncelli et al., 2006, 2010; Njeh et al., 1997; Wüster et al., 2000)

Variables	Description
AD-SoS (m/s)	Amplitude dependent speed of sound. The distance between the transducers divided by the time of flight, that is the time from emitted pulse to the received signal. Depends on the velocity and amplitude of the signal received considering the signal that reaches a predetermined minimum amplitude value (2 mV) for the first time.
AD-SoS T-Score	The difference between a measured AD-SoS of an individual and the mean value from a healthy young reference population.
BTT (μs)	Bone transmission time. The difference between the time when the first peak of the received signal reaches its maximum value and the time when the signal reaches 1700 m/s. BTT depends only on bone properties and is not influenced by soft tissue.
UBPI	Ultrasound bone profiler index. An instrument-specific index, which values are between 0 and 1. UBPI is obtained by 3 parameters (fast wave amplitude, dynamic of the ultrasound signal, and time frame). It quantifies the signal characteristics and can is considered as the "fracture- predictive value".

We modified the previously proposed reference curves (Rinaldo et al., 2018) by adding the thresholds for osteopenia (−1 T-score) and osteoporosis (−3.2 T-score). These specific thresholds are selected according to the indications of the DBM Sonic Bone Profiler manufacturer and are based on studies on living populations (Gambacciani et al., 2004; Kanis et al., 2005; Nuzzo et al., 2009; Wüster et al., 2000). T-score is calculated as the number of SDs from the peak of bone mass of the reference population, a value that is usually used in clinical practice for the evaluation of osteopenic or osteoporotic conditions (Kanis & Gluer, 2000).

2.4 | Radiogrammetry assessment

XR measurements were obtained from radiographs taken with the Carestream Health DRX-1 System (S. Maria Maddalena Hospital, Rovigo, Italy) for the left second metacarpal bone of the entire sample. Since previous research has shown no relevant difference between sides, the right second metacarpal bone was selected for individuals lacking the left one (Curate, 2014; Ives & Brickley, 2005). Bone specimens were oriented from an anteroposterior view as suggested by protocols (Ives & Brickley, 2004; Lazenby, 1998; Meema & Meema, 1987; Ortner, 2003). Total length (TL, mm), total width (TW, mm), and medullary width (MW, mm) measurements were performed digitally by Carestream Vue PACS Software; values for cortical thickness (CT, mm) and the cortical index (CI) were obtained using the following formulas:

$$CT = TL - MW$$

$$CI = \frac{(TL - MW)}{TL} \times 100.$$

2.5 | Statistical analysis

The variables were tested for normality using the Shapiro–Wilk test. Descriptive statistics were performed through the calculation of means and SDs for continuous variables, and frequencies for categorical variables. The Student *t*-test or *U*-Mann Whitney test was used when comparing the two sexes, and fractured vs non-fractured individuals, while ANOVA or Kruskal Wallis tests were used in the comparison between age cohorts. Tukey HSD post-hoc test was used to determine the interaction between age-at-death cohorts.

Univariate logistic regression analysis was performed including the following variables: sex (categorical), mean age, MW, CT, CI, AD-SoS, BTT, UBPI, mean weight, mean volume, and mean density. Multivariate backward stepwise logistic regression analysis to evaluate the relationship between dependent and independent variables was performed including the variables with $p < 0.25$ from univariate analysis (Altman, 1991).

Receiver operating characteristic (ROC) curve analysis was performed to identify the optimum cut-off value for predicting fractures in past individuals. The optimal cut-off value was determined by the point on the ROC curve closest to the upper left-hand corner.

A *p*-value <0.05 was considered statistically significant.

All statistical analyses were conducted using STATISTICA (version 11, StatSoft, Tulsa, OK), and MedCalc Statistical Software version 14.8.1 (MedCalc Software bvba, Ostend, Belgium).

3 | RESULTS

A general description of the sample from each site is displayed in Table 1. Comparisons of male and female physical variables for the proximal phalanges have shown several statistically significant differences both when considering all the phalanges (Table 3) and when considering each phalanx separately (Supplementary Material Table 1). Men have significantly longer, wider, and heavier first phalanges in comparison to females. In contrast, the comparison between density values did not result in significant differences between the two sexes.

As regards the macroscopic analysis of osteoporotic fractures, 22 individuals out of 104 showed the presence of fractures that could be interpreted as possible osteoporotic fractures due to their location (femoral neck, wrist, and thoracic or lumbar spine). Most of the recorded traumas were vertebral compression fractures (82%), while femoral neck or wrist fractures were less common (9% each). As an example, we reported in Figure 2 the case of a male from the Older Adults cohort (Crocetta, US11) characterized by healed vertebral fractures of the lumbar trait – wedging type –, and a healed rib fracture (Figure 2a-b). Another male of 30–40 years (St. Biagio, US 162) exhibited an exemplary case of femoral neck fracture characterized by the compression of the femoral neck (Figure 2c). As expected, most fractures were found in the oldest group (47.6%) and no significant differences in their frequency were found between the two sexes (Figure 2, Supplementary Material). For a detailed description of fractures for each individual see Supplementary Material Table 2.

Mean values of osteometric, QUS, and XR parameters for the total sample and separately by sex are reported in Table 3. XR parameters (TW, MW, CT) resulted significantly different between the two sexes, with greater dimensions in males, as expected. However, the CI, the most BMD-related index, did not show differences between males and females. This is in accordance with the results obtained when we compared QUS variables between men and women considering all age groups together, as they did not show significant differences (Table 3). The table also reports bone density status, based on the values of the −1 T score and − 3.2 T score calculated from the reference values and curves proposed for skeletonized individuals by Rinaldo et al. (2018) and separately for each sex (Figure 3). Almost 70% of the individuals examined were below the −1 T-score, i.e. osteopenic, while 10% were categorized as osteoporotic. This high percentage of osteopenic individuals may be due to the higher mean age of the total sample, being majority of the individuals above 35 years of age (Table 3).

TABLE 3 Descriptive statistics of XR, QUS and osteometric parameters, and comparison between males and females. Statistically significant *p* values ($p \le 0.05$) are in bold

Variables	Mean (SD) Total ($n = 104$)	Males ($n = 55$)	Females ($n = 49$)	*p*-value
Osteometric parameters				
TML (mm)	39.12 (2.58)	40.43 (2.2)	37.75 (2.23)	**<0.001**[a]
DMW (mm)	10.8 (1.18)	11.42 (1.11)	10.15 (0.86)	**<0.001**[a]
Weight (g)	2.14 (0.72)	2.45 (0.70)	1.80 (0.59)	**<0.001**[a]
Volume (cm^3)	2.25 (0.58)	2.56 (0.53)	1.91 (0.43)	**<0.001**[a]
Density (g/cm^3)	0.93 (0.18)	0.94 (0.18)	0.93 (0.19)	0.6815[a]
XR parameters				
TW (mm)	8.98 (1.19)	9.62 (1.14)	8.28 (0.79)	**<0.001**[a]
MW (mm)	4.74 (1.10)	5.07 (1.02)	4.38 (1.08)	**0.001**[a]
CT (mm)	4.24 (0.94)	4.55 (0.92)	3.90 (0.85)	**<0.001**[a]
CI	0.47 (0.09)	0.47 (0.08)	0.47 (0.10)	0.9816[a]
QUS parameters				
AD-SoS (m/s)	1741.70 (59.02)	1740.13 (66.60)	1743.47 (49.83)	0.7711[a]
BTT (µs)	0.68 (0.40)	0.66 (0.39)	0.70 (0.40)	0.5821[b]
UBPI	0.25 (0.14)	0.25 (0.14)	0.26 (0.14)	0.6959[b]
Bone density status[d]	**N(%)**	**N(%)**	**N(%)**	0.1411[c]
Below −1 T score	71 (68.3%)	40 (72.7%)	31 (63.3%)	
Below - 3.2 T score	11 (10.6%)	3 (5.4%)	8 (16.3%)	

[a]Comparison performed using independent sample *t* test.
[b]Comparison performed using Mann–Whitney *U* test.
[c]Comparison performed using χ^2 test.
[d]Based on the new proposed thresholds (Figure 3).

TABLE 4 Comparison among age classes for XR, QUS, and osteometric parameters in the total sample. Statistically significant *p* values ($p \le 0.05$) are reported in bold

Variables	Mean (SD) YA $N = 27$	MA $N = 49$	OA $N = 31$	*p*	Post-hoc test
CI	0.50 (0.10)	0.48 (0.07)	0.43 (0.11)	**0.0194**[a]	1 > 3;2 > 3
AD-SoS (m/s)	1767 (47.07)	1742 (58.50)	1719 (61.58)	**0.0030**[a]	1 > 3
BTT (µs)	0.84 (0.47)	0.66 (0.32)	0.57 (0.41)	**0.0385**[b]	1 > 3
UBPI	0.35 (0.18)	0.21 (0.10)	0.23 (0.12)	**0.0003**[b]	1 > 2;1 > 3
Density (g/cm^3)	0.94 (0.16)	0.94 (0.17)	0.93 (0.23)	0.7748[a]	-

Abbreviation: MA, middle adult; OA, old adult; YA, young adult.
[a]Comparison performed using ANOVA.
[b]Comparison perfomed using Kruskal-Wallis test.

TABLE 5 Mean XR, QUS, and osteometric values in individuals presenting and not presenting osteoporotic fractures. Values of $p \le 0.05$ are considered statistically significant

Variables	Means (SD) Fractured ($n = 22$)	Non-fractured ($n = 82$)	*p*
CI	0.46 (0.10)	0.48 (0.09)	0.3380[a]
AD-SoS (m/s)	1719.41 (69.92)	1747.68 (54.69)	**0.0455**[a]
BTT (µs)	0.54 (0.36)	0.72 (0.40)	**0.0498**[a]
UBPI	0.19 (0.10)	0.27 (0.14)	**0.0150**[a]
Density (g/cm^3)	0.94 (0.23)	0.93 (0.17)	0.9560[a]

[a]Comparison performed using Mann–Whitney *U* test.

FIGURE 2 Examples of fracture types observed in the sample: (a) vertebral wedging fracture of the lumbar trait; (b) healed rib fracture; (c) fracture of the medial femoral neck (collapse of the femoral head).

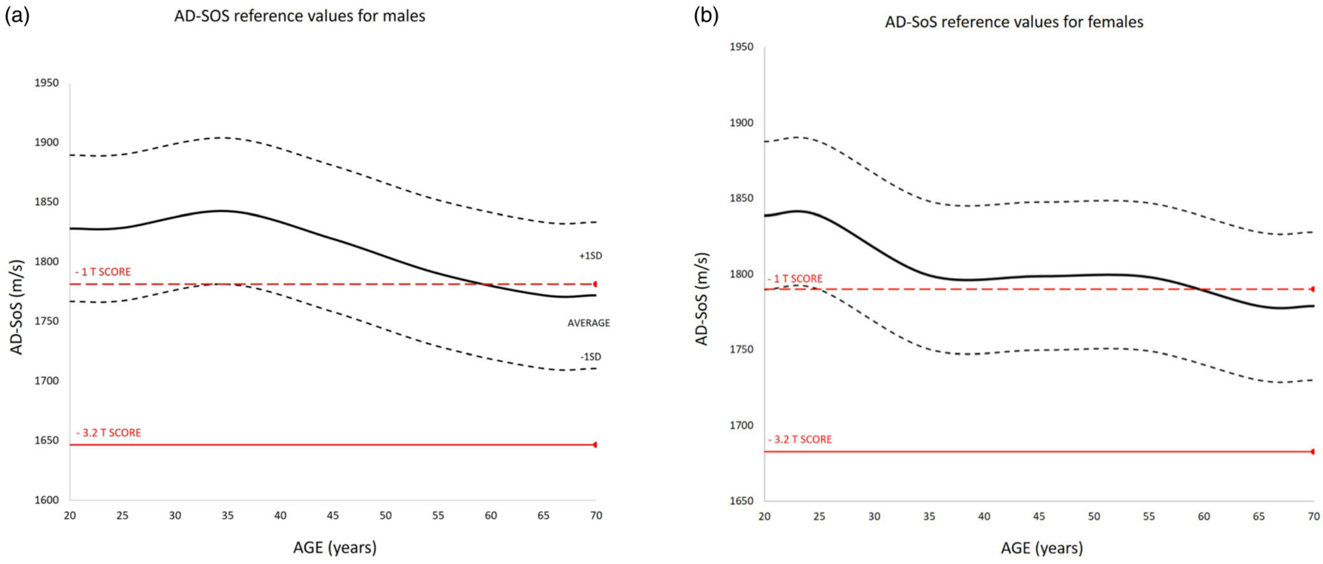

FIGURE 3 Graphs of reference values of AD-SoS in male (a) and female (b) adults proposed by Rinaldo et al. (2018) (reproduced with the kind permission of Elsevier, Inc.) and modified with the inclusion of thresholds for osteopenia and osteoporosis according to the red T-Score lines plotted at −1 and −3.2, respectively.

Considering the results obtained for the comparison between the sexes, the variables found to be statistically different were excluded from the subsequent whole-sample analyses. The results of the analysis of variance for XR, QUS, and osteometric parameters among the three age groups of the total sample are shown in Table 4. CI and QUS parameters resulted statistically different among the age groups. In particular, CI, AD-SoS, and BTT, the parameters most indicative of the BMD status, decrease with increasing age. The greater significant

TABLE 6 Univariate and multivariate logistic regression analysis (with backward method) to predict the fracture risk in the archeological sample. Values of $p \leq 0.05$ are considered statistically significant

	Univariate			Multivariate		
Variables	Odds ratio (95% CI)	Coefficients	*p* value	Odds ratio (95% CI)	Coefficients	*p* value
Sex (males)	1.158 (0.451–2.969)	0.15	0.7603	-	-	-
Age	1.042 (1.000–1.085)	0.04	**0.0439**	-	-	-
CI	0.081 (0.001–13.609	−2.51	0.3343	-	-	-
AD-SoS (m/s)	0.991 (0.982–1.000)	−0.01	**0.0388**	-	-	-
BTT (μs)	0.237 (0.052–1.089)	−1.44	0.0643	-	-	-
UBPI	0.002 (0.000–0.335)	−6.26	**0.0060**	0.002 (0.000–0.335)	−6.21	**0.0060**
Density (g/cm^3)	1.075 (0.084–13.838	0.06	0.9555	-	-	-

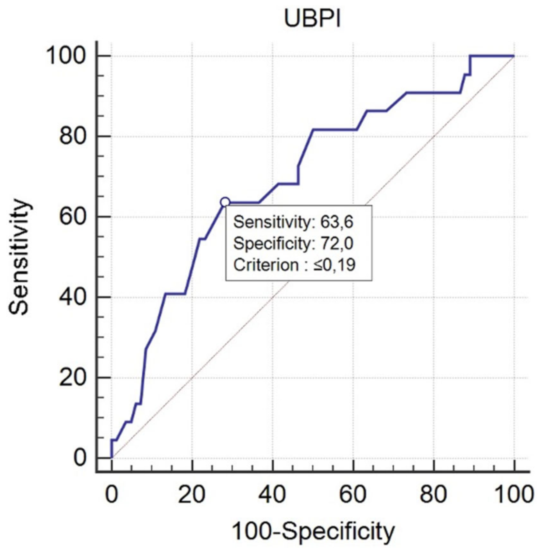

FIGURE 4 Receiver operating characteristic (ROC) curve for the assessment of fracture risk using UBPI.

differences were found between the younger and the older age cohorts. No statistical differences were found when comparing density across age groups (Table 4).

In Table 5, are reported the results of the comparison between fractured and non-fractured individuals. Density and CI did not show any significant difference between the two groups. In contrast, all three QUS parameters (AD-SoS, BTT, and UBPI) resulted significantly lower in fractured individuals (Table 5).

Table 6 shows the results of the univariate and multivariate logistic regression analysis. Univariate analysis showed that the variables significantly associated with greater odds of fractures are mean age (coefficient = 0.04), AD-SoS (coefficient = −0.01), and UBPI (coefficient = −6.26), whereas BTT was almost significant (coefficient = −1.44). In particular, the odds ratio of having an osteoporotic fracture increases with increasing age but decreases with higher values of AD-SoS, BTT, and UBPI, in agreement with the results in Table 4. However, the backward stepwise multivariate logistic regression analysis revealed that only UBPI (coefficient = −6.21, $p = 0.0060$) was a significant independent factor to predict the probability of fractures in archeological skeletons with a constant of 0.0816.

The optimum cut-off value of UBPI was determined using ROC analysis and resulted in ≤0.19 with an area under the ROC curve (AUC) of 0.70, indicating a new fracture risk threshold for skeletal individuals (95% CI = 0.598 to 0.783; sensitivity = 63.6%, specificity = 72.0%, Figure 4).

4 | DISCUSSION

This study aimed to evaluate the diagnostic potential of QUS (in comparison to other traditional methodologies) in archeological skeletons, and its ability to provide new insights into the assessment of bone quality, and the diagnosis of osteopenia and osteoporosis. The results of this evaluation performed on more than 100 individuals from North-Italian archeological sites demonstrate the better performance of QUS when comparing fractured and nonfractured individuals, thus designating the QUS parameters as the most effective and reliable in comparison with osteometric or XR parameters.

As a result of reduced bone mass, osteoporosis occurs, leading to an increased risk of fracture (Christodoulou & Cooper, 2003; Mays et al., 2006). Osteoporosis usually affects mostly postmenopausal women and elderly individuals of both sexes (Díez-Pérez et al., 2003). More in general, an acceleration in bone loss would occur between the fourth and the fifth decade (Curate et al., 2019), mostly due to the enhancement of osteoclastic processes and the reduction of osteoblastic proficiency; this process increases cortical porosity and endocortical resorption (Al-Hourani et al., 2021; Zebaze et al., 2010). This progression starts later in men than in women in physiologic conditions (Khosla et al., 2008).

4.1 | Sex and age influence

In the examined specimens, although differences between sexes for the majority of osteometric or radiogrammetric measures have been detected (except density and CI), there was no statistical difference, on average, in the QUS parameters nor bone density status between males and females of our sample. The absence of significant sex differences in bone maintenance or loss, except for one measure of trabecular bone microarchitecture, has also been found in other archeo-anthropological studies (Beauchesne & Agarwal, 2017; Borrè et al., 2015). Likely, the lower average age (especially in the female sex) compared to current populations affected this result. Indeed, postmenopausal women would be expected to suffer more severely from loss of bone mineral density, even if this trend is not always verified in past populations (Agarwal & Grynpas, 2009). To confirm this particular trend in the past, it is interesting to note that, although age-related bone loss is observed in ancient human remains, the prevalence of osteoporotic fractures is fairly low compared to modern populations (Agarwal, 2018; Mays et al., 2006). This disparity has usually been imputed to shorter life spans and more intense physical activity in past populations (Cho & Stout, 2011). On the other hand, the comparison between groups of different ages in our sample showed, consistently with the literature (among others: Curate et al., 2009; Glencross & Agarwal, 2011), an evident bone loss with age as evidenced by CI (determined by radiogrammetry), AD-SoS, UBPI, and BTT (all three determined by QUS). Bone density (determined osteometrically), instead, did not show any significant difference among different age subsamples, indicating that this parameter (or the method used to determine it) is not suitable for assessing bone mineral density in human archeological remains.

Results from the literature on BMD in ancient skeletons, although generally showing a tendency towards differences with age and sex, are difficult to compare due to both the different methods and the different skeletal elements analyzed. With reference to some studies conducted on ancient Italian populations, age-related bone loss assessed via increased intracortical porosity and endosteal expansion was histologically confirmed on rib and femur specimens in a sample of the Imperial Romans of the Isola Sacra necropolis (Cho & Stout, 2011). In the same study, significant differences emerged between sexes with higher bone loss and turnover rates in the female sex. Conversely, Beauchesne and Agarwal (2017), studying Imperial Romans of Velia with various methodologies (histology of ribs, radiogrammetry of the second metacarpal, CT of vertebral trabecular architecture), did not find any significant difference in bone loss with age but highlighted differences between sexes in the timing of bone loss with age. Considering also results from other European populations, for example, the study on metacarpals in a recent sample of the Portuguese population (Coimbra Identified Skeletal Collection), performed by radiogrammetry and macroscopic analysis, found that endocortical bone loss with age resulted significant only in females (Curate et al., 2019). In the Coimbra collection study (Curate et al., 2019), the incidence of fragility fractures was reported to be influenced by age, whereas metacarpal CI was not found to be an independent risk factor. In a medieval England population at Wharram Percy, a loss of the vertebral trabecular bone has been observed in young adults of both sexes, but this loss would occur earlier in young women and would show little change in bone mineral density in postmenopausal life compared with modern populations (Agarwal & Grynpas, 2009). These different age- and sex-related patterns may depend on the different life habits (dietary and behavioral) of the populations examined but, certainly, the differences in the skeletal segments analyzed, methodologies applied, and variables considered make it difficult to draw a general picture.

4.2 | Bone assessment methods and osteoporosis

Despite the variability among groups in a population, present-day Europeans along with African populations, according to a recent review (Salari et al., 2021), appear to be the most affected by osteoporosis, with a high frequency of osteoporotic fractures (Kanis et al., 2002; Lofthus et al., 2001). Osteoporosis is directly associated both with endogenous and exogenous risk factors, mainly including age and sex, genetics, pathologies, and lifestyle (Dede & Callan, 2018; Golob & Laya, 2015; Waldron, 2008). In particular, genetics and hormones give a major contribution to the onset of the disorder, while lifestyle plays a secondary (yet crucial) role in causing deficiency of vitamin D – induced by insufficient dietary intake and/or lack of sunlight exposure – and enhancing bone resorption processes (Al-Bashaireh et al., 2018; Jamal et al., 1999; Sampson, 1997; Sozen et al., 2017). Therefore, it is important to consider that our sample includes individuals from different archeological sites (albeit all of them from the same geographical area) and different epochs. The majority of fractures (40.1% of all the fractures of the sample) were found in the archeological site of S. Biagio, but it is also the most represented site in our sample; 38.5% of the individuals of Chiesazza, and 50% of the individuals from S.Maria in Padovetere had a fragility fracture. Additional information can be found in Supplementary Material Table 2.

There is no doubt that the analysis of osteopenia and osteoporosis in ancient populations may allow a better understanding of their causes and spread in the past and the present. From a methodological point of view, although a preliminary diagnosis of osteoporosis on skeletal remains is primarily based on the presence of typical fractures in elderly individuals (Curate, 2014), there is a clear need for the development of a quantitative methodology through tools other than macroscopic analysis. A recent review of paleopathological studies concerning osteoporosis and bone density (van Spelde et al., 2021) carried out on ancient human osteological specimens showed that 84 publications over the last 50 years (1969–2021) used 16 different quantitative methods. Specifically, the most frequently used methods were found to be, in order of frequency, DXA (33.3%), radiogrammetry (23.8%), and fracture patterns (13.1%). A shift in the applied methodologies has also been outlined by these authors from the 80 s (photon absorptiometry), to the 90 s and early 2000 s (DXA and radiogrammetry), up to the 2010 s (CT-based scanning methods). However, reference thresholds for the latter methods when applied to the skeleton are lacking, since those used for living people may not be adequate. Indeed, the confounding effect due to the presence of soft tissues, as well as the bone diagenesis and the resulting chemical and biological alterations in the skeletons, can influence and therefore distort the outcomes of the analysis. More generally, non-destructive methods are preferred, while research funding and the possibility of directly using instrumentation in the site where the remains are stored may condition the subsequent choice. Moreover, a lack of reference values for skeletal and archeological populations is usually observed, for example concerning radiogrammetry; many studies have been published during the last decades, yet specific cut-offs for assessing bone loss thresholds are still to be published.

4.3 | QUS and radiogrammetry

Although the application of different methods to different skeletal elements can help in revealing differences in the timing of bone loss with age (Beauchesne & Agarwal, 2017), this approach has obvious limitations. In particular, the difficulty of comparing populations and periods imposed by the different methodologies applied shows the need to identify a reliable method that employs thresholds validated on archeo-anthropological finds and equipment that can be handled directly in the field. This consideration prompted us to develop our research in this area and to propose the use of portable instrumentation such as the QUS, in addition to radiogrammetry and macroscopic analysis of fragility fractures. In fact, DXA, although it can provide accurate assessments of osteodensitometry, requires expensive analyses performed through a complex apparatus, and its widespread use in archeo-anthropology is, therefore, to be ruled out (Van Spelde et al., 2021) especially if a large number of samples have to be tested. Nor, on the other hand, have we resorted to the use of CT-based scanning methods, as they are currently difficult to access (Van Spelde et al., 2021).

Concerning radiogrammetry, this allows the assessment of cortical bone loss, which can be useful in the diagnosis of osteoporosis and fracture risk (Ives & Brickley, 2004). Positive aspects of this technique include its simplicity, low cost, and non-destructive nature (Zhu et al., 2008). Therefore, it has been widely applied in paleopathological studies that evaluated the second metacarpal (sometimes also at the femur and tibia) (Beauchesne & Agarwal, 2014; Curate, 2014; Mays, 1996). XR of the second metacarpal bone is one of the most applied techniques in bioarcheology and is considered a good proxy for age-related cortical bone loss as well as providing good intra-group comparability (Beauchesne & Agarwal, 2014, 2017; Brickley & Ives, 2008; Curate, 2014; Glencross & Agarwal, 2011; Haara et al., 2006; Ives & Brickley, 2004) even if it does not allow fracture risk assessment and osteoporosis diagnosis (Curate, 2014). As well as the phalanges of the hand with the QUS technique, the metacarpal bones are the most appropriate elements for XR due to morphologic factors (tubularity, presence of both cortical and trabecular bone, central medullary canal). Therefore, these elements seem to provide better results than other skeletal areas such as the femur and tibia (Baroncelli et al., 2006; Beauchesne & Agarwal, 2017; Curate, 2014; Ives & Brickley, 2004). Quantitative ultrasound methodologies have been developed for indirect measurement of bone quality and skeletal status in the living person by performing ultrasound measurements at the metaphysis of the proximal phalanx of the last four fingers of the hand preferably (Frost et al., 2000; Nayak et al., 2006; Njeh et al., 1997). As shown in the literature, the performance of the QUS parameters was comparable to DXA, and all QUS parameters were predictive of vertebral fractures (Albanese et al., 2009; Gluer et al., 2004). In the latter study mentioned, UBPI was specifically found to be the most appropriate parameter for clinical practice, reflecting bone changes due to aging. The application of this methodology to archeoanthropological skeletons is very recent (Rinaldo et al., 2018) and therefore further experimental confirmation is needed. Nevertheless, the results of the present study are encouraging.

Radiogrammetry has sometimes been able to demonstrate an association between CI and the risk of osteoporotic fracture (Mays, 1996), contrary to the evidence of other studies (Curate, 2014; Mays, 2006). In our study, the comparison of parameters from different methodologies in fractured and nonfractured subjects suggested that the parameters obtained with QUS may be stronger indicators of fracture risk than XR and osteometric values. Moreover, the application of univariate and multivariate logistic regression analysis methods made it possible to highlight that, once the effect of spurious correlations had been eliminated, the only variable that emerged in the sample examined as an independent predictor of fractures is the UBPI, once again confirming the diagnostic validity of the QUS method. To further confirm this, we evaluated this diagnostic test (UBPI) by plotting sensitivity against specificity (ROC curve) and using the AUC as a measure of accuracy. Importantly, accuracy indices derived from ROC analysis are not affected by fluctuations due to the use of arbitrarily chosen decisional criteria or cut-offs (Hajian-Tilaki, 2013). Most notably, this study demonstrated that the overall diagnostic performance of the test, being the AUC value of 0.70, is to be considered discrete (Swets, 1998). A UBPI value of less than 0.19 was found to be the optimal cut-off to define the risk of fractures in archeological samples. Finally, and in comparison to other methods (especially the osteological observation), QUS allows not only the diagnosis of osteoporosis but also that of osteopenia. Nevertheless, some limitations of this study should be emphasized. Firstly, inter-site differences in BMD patterns have not been analyzed in this research: to test the method, we made use only of the best-preserved individuals from each site. Nevertheless, in an archeological context, preservation issues may also result in an general underestimation of a low BMD (Curate, 2014) due to the exclusion of the most fragile and worst-preserved subjects; therefore the role of diagenesis in bone loss needs to be further investigated. Even though the diagnostic discrimination between diagenetic and pathologic bone loss is beyond the scope of this study, it would be important to investigate possible reasons for preservation issues in subjects with lower BMD. Another point of discussion is the potential invasiveness of the QUS technique. Although the invasiveness of water submersion is minimal, specimens in poor preservation conditions may suffer potential damage. Although the protocol selection per se excludes poorly preserved specimens, since only fully maintained bones can undergo the analysis, it is recommended to check the conservation status of the specimen before applying QUS.

5 | CONCLUSIONS

Our study on bone quality and bone loss in past individuals was addressed through a multi-method approach and allowed us to highlight some QUS parameters as reliable predictors of fracture risk and assessors of the effect of age on bone alterations. Based on the whole sample, an age-related pattern was evident, showing a significant decrease with age in the CI and the three QUS parameters. The comparison between individuals with and without macroscopic fractures showed significant differences in QUS parameters. The UBPI was found to be the main independent risk indicator for osteoporotic fractures in the examined sample and the diagnostic validity of this test has been demonstrated. The standard curves developed by Rinaldo et al. (2018), now implemented with new T-score lines, would seem to hold the necessary reliability and its application would therefore be advisable in the field of archeo-anthropology. However, further confirmation is awaited through investigations carried out on other skeletal populations. Nevertheless, QUS is a reliable, inexpensive, and easy-to-use tool; its portability contributes to making it a useful methodology for investigating archeological remains also in the field. These findings may be of great importance in estimating the health status of past populations, particularly when combined with studies on diet and ecology.

AUTHOR CONTRIBUTIONS

Alba Pasini: Data curation (lead); formal analysis (equal); investigation (lead); writing – original draft (equal). **Natascia Rinaldo:** Data curation (supporting); formal analysis (equal); methodology (lead); project administration (equal); writing – original draft (equal). **Barbara Bramanti:** Resources (equal); visualization (equal); writing – review and editing (equal). **Emanuela Gualdi-Russo:** Conceptualization (lead); project administration (equal); supervision (lead); writing – review and editing (lead).

ACKNOWLEDGMENTS

We would like to thank Roberta Donati for her work in the data collection process. Open Access Funding provided by Universita degli Studi di Ferrara within the CRUI-CARE Agreement.

FUNDING INFORMATION

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

DECLARATIONS OF INTEREST

none.

ORCID

Natascia Rinaldo https://orcid.org/0000-0002-6972-3085
Emanuela Gualdi-Russo https://orcid.org/0000-0002-7274-547X

REFERENCES

Acsádi, G., & Nemeskéri, J. (1970). *History of human life span and mortality*. Akadémiai Kiadó.

Agarwal, S. C. (2018). Light and broken bones: Examining and interpreting bone loss and osteoporosis in past populations. In *Biological Anthropology of the Human Skeleton* (2nd ed., pp. 387–410). John Wiley & Sons, Ltd.. https://doi.org/10.1002/9780470245842.ch12

Agarwal, S. C. (2019). Understanding bone aging, loss and osteoporosis in the past. In *Biological anthropology of the human skeleton* (pp. 385–414). John Wiley & Sons, Ltd. https://doi.org/10.1002/9781119151647.ch11

Agarwal, S. C., Dumitriu, M., Tomlinson, G. A., & Grynpas, M. D. (2004). Medieval trabecular bone architecture: The influence of age, sex, and lifestyle. *American Journal of Physical Anthropology*, *123*, 33–44. https://doi.org/10.1002/ajpa.10335

Agarwal, S. C., & Grynpas, M. D. (2009). Measuring and interpreting age-related loss of vertebral bone mineral density in a medieval population. *American Journal of Physical Anthropology*, *139*(2), 244–252. https://doi.org/10.1002/ajpa.20977

Agnollitto, P. M., De Araújo Braz, G., Spirlandeli, A. L., De Paula, F. J. A., Carneiro, A. A. O., & Nogueira-Barbosa, M. H. (2021). Ex vivo vibro-acoustography characterization of osteoporosis in an experimental mice model. *Quantitative Imaging in Medicine and Surgery*, *11*(2), 586–596. https://doi.org/10.21037/QIMS-20-610

Akkawi, I., & Zmerly, H. (2018). Osteoporosis: Current Concepts. *Joints*, *6*(2), 122–127.

Albanese, C. V., Cepollaro, C., de Terlizzi, F., Brandi, M. L., & Passariello, R. (2009). Performance of five phalangeal QUS parameters in the evaluation of gonadal-status, age and vertebral fracture risk compared with DXA. *Ultrasound in Medicine & Biology*, *35*(4), 537–544. https://doi.org/10.1016/j.ultrasmedbio.2008.09.027

Al-Bashaireh, A. M., Haddad, L. G., Weaver, M., Kelly, D. L., Chengguo, X., & Yoon, S. (2018). The effect of tobacco smoking on musculoskeletal health: A systematic review. *Journal of Environmental and Public Health*, *2018*, 4184190. https://doi.org/10.1155/2018/4184190

Al-Hourani, K., Tsang, S. J., & Simpson, A. H. R. W. (2021). Osteoporosis: current screening methods, novel techniques, and preoperative assessment of bone mineral density. *Bone & Joint Research*, *10*(12), 840–843. https://doi.org/10.1302/2046-3758.1012.BJR-2021-0452.R1

Altman, D. G. (1991). *Practical statistics for medical research*. Chapman & Hall.

Andronowski, J. M., Crowder, C., & Soto Martinez, M. (2018). Recent advancements in the analysis of bone microstructure: New dimensions in forensic anthropology. *Forensic Sciences Research*, *3*(4), 278–293. https://doi.org/10.1080/20961790.2018.1483294

Balboni, B., Borghi, R., Guarnieri, C., & Tassinari, V. (2005). L'oratorio della Crocetta: scoperte e prospettive di ricerca. In *Contributi centesi n°2, collana di studi storici curata dal comune di Cento*. Editore, Cento (Fe).

Baroncelli, G. I. (2008). Quantitative ultrasound methods to assess bone mineral status in children: Technical characteristics, performance, and clinical application. *Pediatric Research*, *63*(3), 220–228. https://doi.org/10.1203/PDR.0b013e318163a286

Baroncelli, G. I., Battini, R., Bertelloni, S., Brunori, E., de Terlizzi, F., Vierucci, F., Cipriani, P., Cioni, G., & Saggese, G. (2010). Analysis of quantitative ultrasound graphic trace and derived variables assessed at proximal phalanges of the hand in healthy subjects and in patients with cerebral palsy or juvenile idiopathic arthritis. *A pilot study. Bone*, *46*(1), 182–189. https://doi.org/10.1016/j.bone.2009.09.010

Baroncelli, G. I., Federico, G., Vignolo, M., Valerio, G., del Puente, A., Maghnie, M., Baserga, M., Farello, G., & Saggese, G. (2006). Cross-sectional reference data for phalangeal quantitative ultrasound from early childhood to young-adulthood according to gender, age, skeletal growth, and pubertal development. *Bone*, *39*(1), 159–173. https://doi.org/10.1016/j.bone.2005.12.010

Beauchesne, P., & Agarwal, S. C. (2014). Age-related cortical bone maintenance and loss in an imperial roman population. *International Journal of Osteoarchaeology*, *24*(1), 15–30. https://doi.org/10.1002/oa.1303

Beauchesne, P., & Agarwal, S. C. (2017). A multi-method assessment of bone maintenance and loss in an Imperial Roman population: Implications for future studies of age-related bone loss in the past. *American Journal of Physical Anthropology*, *164*(1), 41–61. https://doi.org/10.1002/ajpa.23256

Borrè, A., Boano, R., Di Stefano, M., Castiglione, A., Ciccone, G., Isaia, G. C., Panattoni, G. L., & Faletti, C. (2015). X-ray, CT and DXA study of bone loss on medieval remains from North-West Italy. *La Radiologia Medica*, *120*(7), 674–682. https://doi.org/10.1007/s11547-015-0507-3

Bramanti, B., Zedda, N., Rinaldo, N., & Gualdi-Russo, E. (2018). A critical review of anthropological studies on skeletons from European plague pits of different epochs. *Scientific Reports*, *8*(1), 17655. https://doi.org/10.1038/s41598-018-36201-w

Brickley, M. (2002). An investigation of historical and archaeological evidence for age-related bone loss and osteoporosis. *International Journal of Osteoarchaeology*, *12*(5), 364–371. https://doi.org/10.1002/oa.635

Brickley, M., & Ives, R. (2008). The bioarchaeology of metabolic bone disease. In *Understanding bone aging, loss and osteoporosis in the past* (pp. 7–20). Academic Press. https://doi.org/10.1016/B978-0-12-370486-3.00002-0

Brickley, M. B. (2006). Rib fractures in the archaeological record: A useful source of sociocultural information? *International Journal of Osteoarchaeology*, *16*(1), 61–75. https://doi.org/10.1002/oa.809

Brooks, S., & Suchey, J. M. (1990). Skeletal age determination based on the os pubis: A comparison of the Acsádi-Nemeskéri and Suchey-Brooks methods. *Human Evolution*, *5*(3), 227–238. https://doi.org/10.1007/BF02437238

Brothwell, D. R. (1981). *Digging up bones. The excavation, treatment and study of human skeletal remains*. British Museum (Natural History), Cornell University Press.

Buikstra, J. E., & Ubelaker, D. H. (1994). Standards for data collection from human skeletal remains. *Arkansas Archaeological Survey Research Series*, *n.44*.

Büsing, H., & Büsing Kolbe, A. (1996). Sei anni di ricerche archeologiche a Ficarolo Gaiba, vol. XXXI. Padusa, p. 7–17.

Büsing, H., Büsing Kolbe, A., & Bierbrauer, V. (1994). Comuni di Ficarolo e Gaiba, Chiunsano, Rovigo: due tombe ostrogote. In: *I Goti*, pp. 186–188.

Cho, H., & Stout, S. D. (2011). Age-associated bone loss and intraskeletal variability in the Imperial Romans. *Journal of Anthropological Sciences*, *89*, 109–125. https://doi.org/10.4436/jass.89007

Christodoulou, C., & Cooper, C. (2003). What is osteoporosis? *Journal of Postgraduate Medicine*, *79*, 133–138. https://doi.org/10.1136/pmj.79.929.133

Ciesielska, J. A., & Stark, R. J. (2020). Proximal femur fractures among a medieval Christian population of northern Sudan: prevalence and aetiology. *International Journal of Osteoarchaeology*, *30*(5), 642–655. https://doi.org/10.1002/oa.2894

Corti, C. (2007). Santa Maria in Padovetere: la chiesa, la necropoli e l'insediamento circostante. In F. Berti, M. Bollini, S. Gelichi, & J. Ortalli (Eds.), *Genti Nel Delta Da Spina a Comacchio. Uomini, Territorio e Culto Dall'antichità All'Alto Medioevo* (pp. 531–552). Corbo Editore.

Curate, F. (2014). Osteoporosis and paleopathology: A review. *Journal of Anthropological Sciences*, *92*, 119–146. https://doi.org/10.4436/JASS.92003

Curate, F., Albuquerque, A., Correia, J., Ferreira, I., de Lima, J. P., & Cunha, E. M. (2013). A glimpse from the past: Osteoporosis and osteoporotic fractures in a portuguese identified skeletal sample. *Acta Reumatologica Portuguesa*, *38*(1), 20–27.

Curate, F., Assis, S., Lopes, C., & Silva, A. M. (2011). Hip fractures in the Portuguese archaeological record. *Anthropological Science*, *119*(1), 87–93. https://doi.org/10.1537/ase.100211

Curate, F., Perinha, A., Silva, A. M., Cunha, E., Umbelino, C., & Nogueira, C. (2019). Metacarpal cortical bone loss and osteoporotic fractures in the Coimbra Identified Skeletal Collection. *International Journal of Osteoarchaeology*, *29*(1), 73–81. https://doi.org/10.1002/oa.2717

Curate, F., Piombino-Mascali, D., Tavares, A., & Cunha, E. M. (2009). Assottigliamento corticale del femore e fratture da fragilità ossea: uno studio della Collezione Scheletrica Identificata di Coimbra (Portogallo). *Archivio per l'Antropologia e Etnografia*, *139*, 129–146.

Curate, F., Silva, T. F., & Cunha, E. (2016). Vertebral compression fractures: Towards a standard scoring methodology in paleopathology. *International Journal of Osteoarchaeology*, *26*(2), 366–372. https://doi.org/10.1002/oa.2418

D'Angelo, F. (2005). *Archeologia Medievale* (Vol. XXXII). All'insegna del Giglio.

de Oliveira, P. P., Figueiredo Marinheiro, L. P., Osório Wender, M. C., Mendes, J. B., & Roisenberg, F. (2011). Quantitative ultrasound and risk of fractures in elderly women. *Revista Da Associação Médica Brasileira (English Edition)*, *57*(6), 637–642. https://doi.org/10.1016/S2255-4823(11)70129-1

de Terlizzi, F., Battista, S., Cavani, F., Canè, V., & Cadossi, R. (2000). Influence of bone tissue density and elasticity on ultrasound propagation: An in vitro study. *Journal of Bone and Mineral Research*, *15*(12), 2458–2466. https://doi.org/10.1359/jbmr.2000.15.12.2458

Dede, A. D., & Callan, M. (2018). Treatment of osteoporosis: whom, how and for how long? *British Journal of Hospital Medicine (London, Englan: 2005)*, *79*(5), 259–264. https://doi.org/10.12968/hmed.2018.79.5.259

Díez-Pérez, A., Marín, F., Vila, J., Abizanda, M., Cervera, A., Carbonell, C., Alcolea, R. M., Cama, A., Rama, T., Galindo, E., & Olmos, C. (2003). Evaluation of calcaneal quantitative ultrasound in a primary care setting as a screening tool for osteoporosis in postmenopausal women. *Journal of Clinical Densitometry*, *6*(3), 237–245. https://doi.org/10.1385/jcd:6:3:237

Drozdzowska, B., Pluskiewicz, W., Halaba, Z., Misiołek, H., & Beck, B. (2005). Quantitative ultrasound at the hand phalanges in 2850 females aged 7 to 77 yr: A cross-sectional study. *Journal of Clinical Densitometry*, *8*(2), 216–221. https://doi.org/10.1385/JCD:8:2:216

Ferembach, D., Schwydeski, I., & Stloukal, M. (1980). Recommendations for age and sex diagnoses of skeletons. *Journal of Human Evolution*, *9*, 517–549.

Frost, M. L., Blake, G. M., & Fogelman, I. (2000). Can the WHO criteria for diagnosing osteoporosis be applied to calcaneal quantitative ultrasound? *Osteoporosis International*, *11*(4), 321–330. https://doi.org/10.1007/s001980070121

Gambacciani, M., de Aloysio, D., Elia, D., van der Mooren, M. J., Hadji, P., & Wüster, C. (2004). Quantitative ultrasound (QUS) of bone in the management of postmenopausal women. *Maturitas*, *47*(2), 139–149. https://doi.org/10.1016/S0378-5122(03)00245-7

Giavaresi, G., Borsari, V., Fini, M., Martini, L., Tschon, M., De Terlizzi, F., Nicolini, A., & Giardino, R. (2004). Different diagnostic techniques for the assessment of cortical bone on osteoporotic animals. *Biomedicine and Pharmacotherapy*, *58*(9), 494–499. https://doi.org/10.1016/j.biopha.2004.08.017

Glencross, B., & Agarwal, S. C. (2011). An investigation of cortical bone loss and fracture patterns in the neolithic community of Çatalhöyük, Turkey using metacarpal radiogrammetry. *Journal of Archaeological Science*, *38*(3), 513–521. https://doi.org/10.1016/j.jas.2010.10.004

Gluer, C. C., Eastell, R., Reid, D. M., Felsenberg, D., Roux, C., Barkmann, R., Timm, W., Blenk, T., Armbrecht, G., Stewart, A., Clowes, J., Thomasius, F. E., & Kolta, S. (2004). Association of five quantitative ultrasound devices, and bone densitometry with osteoporotic vertebral fractures in a population-based sample: The OPUS study. *Journal of Bone and Mineral Research*, *19*, 782–793.

Golob, A. L., & Laya, M. B. (2015). Osteoporosis: Screening, prevention, and management. *Medical Clinics of North America*, *99*(3), 587–606. https://doi.org/10.1016/j.mcna.2015.01.010

Gualdi-Russo, E. (2007). Sex determination from the talus and calcaneus measurements. *Forensic Science International*, *171*(2–3), 151–156. https://doi.org/10.1016/j.forsciint.2006.10.014

Gualdi-Russo, E., Bramanti, B., & Rinaldo, N. (2018). Stature estimation from tibia percutaneous length: New equations derived from a Mediterranean population. *Science and Justice*, *58*(6), 441–446. https://doi.org/10.1016/j.scijus.2018.08.001

Guellil, M., Rinaldo, N., Zedda, N., Kersten, O., Gonzalez Muro, X., Stenseth, N. C., Gualdi-Russo, E., & Bramanti, B. (2021). Bioarchaeological insights into the last plague of Imola (1630–1632). *Scientific Reports*, *11*(1), 1–12. https://doi.org/10.1038/s41598-021-98214-2

Guglielmi, G., & de Terlizzi, F. (2009). Quantitative ultrasond in the assessment of osteoporosis. *European Journal of Radiology*, *71*(3), 425–431. https://doi.org/10.1016/j.ejrad.2008.04.060

Guglielmi, G., De Terlizzi, F., Nasuto, M., Sinibaldi, L., & Brancati, F. (2015). Quantitative ultrasound at the phalanges in a cohort of monozygotic twins of different ages. *Radiologia Medica*, *120*(3), 277–282. https://doi.org/10.1007/s11547-014-0440-x

Haara, M., Heliövaara, M., Impivaara, O., Arokoski, J. P. A., Manninen, P., Knekt, P., Kärkkäinen, A., Reunanen, A., Aromaa, A., & Kröger, H. (2006). Low metacarpal index predicts hip fracture: a prospective population study of 3,561 subjects with 15 years of follow-up. *Acta Orthopaedica*, *77*(1), 9–14. https://doi.org/10.1080/17453670610045632

Hadji, P., Imani, P., Wüster, C., Hars, O., Albert, U. S., & Kyvernitakis, I. (2015). Comparison of dual-energy X-ray absorptiometry with six quantitative ultrasonometry devices in women with hip fractures. *Climacteric*, *18*(3), 411–418. https://doi.org/10.3109/13697137.2014.984675

Hajian-Tilaki, K. (2013). Receiver operating characteristic (ROC) curve analysis for medical diagnostic test evaluation. *Caspian Journal of Internal Medicine*, *4*(2), 627–635.

Hale, A. R., & Ross, A. H. (2018). Scanning skeletal remains for bone mineral density in forensic contexts. *Journal of Visualized Experiments*, *2018*(131), 1–19. https://doi.org/10.3791/56713

Ives, R., & Brickley, M. (2005). Metacarpal radiogrammetry: A useful indicator of bone loss throughout the skeleton? *Journal of Archaeological Science*, *32*(10), 1552–1559. https://doi.org/10.1016/j.jas.2005.04.008

Ives, R., & Brickley, M. B. (2004). A procedural guide to metacarpal radiogrammetry in archaeology. *International Journal of Osteoarchaeology*, *14*(1), 7–17. https://doi.org/10.1002/oa.709

Ives, R., Mant, M., de la Cova, C., & Brickley, M. (2017). A large-scale palaeopathological study of hip fractures from post-Medieval Urban England. *International Journal of Osteoarchaeology*, *27*(2), 261–275. https://doi.org/10.1002/oa.2536

Jamal, S. A., Ridout, R., Chase, C., Fielding, L., Rubin, L. A., & Hawker, G. A. (1999). Bone mineral density testing and osteoporosis education improve lifestyle behaviors in premenopausal women: A prospective study. *Journal of Bone and Mineral Research*, *14*(12), 2143–2149. https://doi.org/10.1359/jbmr.1999.14.12.2143

Johnell, O., & Kanis, J. A. (2006). An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporosis International.*, *17*(12), 1726–1733. https://doi.org/10.1007/s00198-006-0172-4

Kanis, J. A., & Glüer, C. C. (2000). An update on the diagnosis and assessment of osteoporosis with densitometry. *Osteoporosis International*, *11*(3), 192–202. https://doi.org/10.1007/s001980050281

Kanis, J. A., Johnell, O., De Laet, C., Jonsson, B., Oden, A., & Ogelsby, A. K. (2002). International variations in hip fracture probabilities: implications for risk assessment. *Journal of Bone and Mineral Research*, *17*, 1237–1244.

Kanis, J. A., Johnell, O., Oden, A., de Laet, C., & de Terlizzi, F. (2005). Ten-year probabilities of clinical vertebral fractures according to phalangeal quantitative ultrasonography. *Osteoporosis International*, *16*(9), 1065–1070. https://doi.org/10.1007/s00198-004-1805-0

Khosla, S., Amin, S., & Orwoll, E. (2008). Osteoporosis in men. *Endocrine Reviews*, *29*, 441–464. https://doi.org/10.1210/er.2008-0002

Lazenby, R. A. (1998). Second metacarpal cross-sectional geometry: Rehabilitating a circular argument. *American Jurnal of Human Biology*, *10*(6), 747–756. https://doi.org/10.1002/(SICI)1520-6300(1998)10:6<747::AID-AJHB6>3.0.CO;2-A

Lofthus, C. M., Osnes, E. K., Falch, J. A., Kaastad, T. S., Kristiansen, I. S., Nordsletten, L., Stensvold, I., & Meyer, H. E. (2001). Epidemiology of hip fractures in Oslo, Norway. *Bone*, *29*, 413–418.

Lorenzini, L. (2001). L'oratorio della Crocetta e la confraternita di Santa Croce. In L. Lorenzini (Ed.), *Corti, T* (pp. 62–72). Terra Di Cento.

Lovejoy, C. O., Meindl, R. S., Pryzbeck, T. R., & Mensforth, R. P. (1985). Chronological metamorphosis of the auricular surface of the ilium: A new method for the determination of adult skeletal age at death. *American Journal of Physical Anthropology*, *68*(1), 15–28. https://doi.org/10.1002/ajpa.1330680103

Lovell, N. C. (1997). Trauma analysis in paleopathology. *Yearbook of Physical Anthropology*, *40*, 139–170. https://doi.org/10.1002/(SICI)1096-8644(1997)25+<139::AID-AJPA6>3.0.CO;2

Madimenos, F. C., Liebert, M. A., Cepon-Robins, T. J., Snodgrass, J. J., & Sugiyama, L. S. (2015). Determining osteoporosis risk in older Colono adults from rural amazonian ecuador using calcaneal ultrasonometry. *American Journal of Human Biology*, *27*, 139–142. https://doi.org/10.1002/ajhb.22626

Masotti, S., Melilli, V., Guarnieri, C., & Gualdi-Russo, E. (2017). Tra le braccia della madre. Evidenze antropologiche di morte al parto nella Ravenna del XVIII secolo. In *Nascere. Il parto dalla tarda antichità all'età moderna* (pp. 127–135). Il Mulino.

Mays, S. A. (1996). Age - dependent cortical bone loss in a Medieval population. *International Journal of Osteoarchaeology*, *6*, 144–154.

Mays, S. A. (2006). Age - related cortical bone loss in women from a 3rd –4th century AD population from England. *American Journal of Physical Anthropology*, *528*, 518–528. https://doi.org/10.1002/ajpa

Mays, S. A. (2007). Metabolic bone disease. In *Advances in human palaeopathology* (pp. 215–252). John Wiley & Sons. https://doi.org/10.1002/9780470724187.ch11

Mays, S. A., Turner-Walker, G., & Syversen, U. (2006). Osteoporosis in a population from Medieval Norway. *American Journal of Physical Anthropology*, *131*(3), 343–351. https://doi.org/10.1002/ajpa.20445

Meema, H. E., & Meema, S. (1987). Postmenopausal osteoporosis: simple screening method for diagnosis before structural failure. *Radiology*, *164*(2), 405–410. https://doi.org/10.1148/radiology.164.2.3602377

Montagnani, A., Gonnelli, S., Cepollaro, C., Mangeri, M., Monaco, R., Bruni, D., & Gennari, C. (2000). Quantitative ultrasound at the phalanges in healthy Italian men. *Osteoporosis International*, *11*(6), 499–504. https://doi.org/10.1007/s001980070092

Nayak, S., Olkin, I., Liu, H., Grabe, M., Gould, M. K., Allen, I. E., Owens, D. K., & Bravata, D. M. (2006). Meta-analysis: Accuracy of quantitative ultrasound for identifying patients with osteoporosis. *Annals of Internal Medicine*, *144*(11), 832–841.

Nazarian, A., Snyder, B. D., Zurakowski, D., & Müller, R. (2008). Quantitative micro-computed tomography: a non-invasive method to assess equivalent bone mineral density. *Bone*, *43*(2), 302–311. https://doi.org/10.1016/j.bone.2008.04.009

Nazrun, A. S., Tzar, M. N., Mokhtar, S. A., & Mohamed, I. N. (2014). A systematic review of the outcomes of osteoporotic fracture patients after hospital discharge: Morbidity, subsequent fractures, and mortality.

Therapeutics and Clinical Risk Management, *10*, 937–948. https://doi.org/10.2147/TCRM.S72456

NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. (2001). Osteoporosis prevention, diagnosis, and therapy. *Journal of the American Medical Association*, *285*(6), 785–795. https://doi.org/10.1001/jama.285.6.785

Njeh, C. F., Boivin, C. M., & Langton, C. M. (1997). The role of ultrasound in the assessment of osteoporosis: A review. *Osteoporosis International*, *7*(1), 7–22. https://doi.org/10.1007/BF01623454

Nuzzo, V., de Milita, A. M., Ferraro, T., Monaco, A., Florio, E., Miano, P., Montemarano, E., Zuccoli, A., & de Terlizzi, F. (2009). Analysis of skeletal status by quantitative ultrasonometry in a cohort of postmenopausal women with high blood cholesterol without documented osteoporosis. *Ultrasound in Medicine and Biology*, *35*(5), 717–722. https://doi.org/10.1016/j.ultrasmedbio.2008.11.003

Odén, A., McCloskey, E. V., Kanis, J. A., Harvey, N. C., & Johansson, H. (2015). Burden of high fracture probability worldwide: secular increases 2010–2040. *Osteoporosis International*, *26*(9), 2243–2248. https://doi.org/10.1007/s00198-015-3154-6

Onisto, N., & Gualdi-Russo, E. (2011). Osservazioni antropologiche sui resti scheletrici medievali: analisi osteologica della sepoltura presso la Crocetta. In R. Lambertini & V. Tassinari (Eds.), *L'Oratorio Della Crocetta Tra Storia e Restauri* (pp. 34–40). Siaca Editore.

Onisto, N., Marzi, M., Forlani, L., & Gualdi-Russo, E. (2006). Osservazioni tafonomiche su una sepoltura medievale: la donna con il mazzo di fiori. In *Atti Del XVI Congresso Degli Antropologi Italiani (Genova, 29–31 Ottobre 2005)* (pp. 731–740). Edicolors Publishing.

Ortner, D. J. (2003). Identification of pathological conditions in human skeletal remains (Ortner ed.). *Academic Press.* https://doi.org/10.1016/B978-0-12-528628-2.X5037-6

Pasini, A., Manzon, V. S., Gonzalez-Muro, X., & Gualdi-Russo, E. (2018). Neurosurgery on a pregnant woman with post mortem fetal extrusion: an unusual case from medieval Italy. *World Neurosurgery*, *113*, 78–81. https://doi.org/10.1016/j.wneu.2018.02.044

Phenice, T. W. (1969). A newly developed visual method of sexing the os pubis. *American Journal of Physical Anthropology*, *30*(2), 297–301. https://doi.org/10.1002/ajpa.1330300214

Rinaldo, N., Pasini, A., Donati, R., Belcastro, M. G., & Gualdi-Russo, E. (2018). Quantitative ultrasonometry for the diagnosis of osteoporosis in human skeletal remains: New methods and standards. *Journal of Archaeological Science*, *99*, 153–161. https://doi.org/10.1016/j.jas.2018.09.013

Rinaldo, N., Zedda, N., Bramanti, B., Rosa, I., & Gualdi-Russo, E. (2019). How reliable is the assessment of Porotic Hyperostosis and Cribra Orbitalia in skeletal human remains? A methodological approach for quantitative verification by means of a new evaluation form. *Archaeological and Anthropological Sciences*, *11*(7), 3549–3559. https://doi.org/10.1007/s12520-019-00780-0

Rubini, M., Gualdi-Russo, E., Manzon, V. S., Rinaldo, N., & Bianucci, R. (2016). Mortality risk factors show similar trends in modern and historic populations exposed to plague. *The Journal of Infection in Developing Countries*, *10*(5), 488–493.

Ryan, T. M., & Shaw, C. N. (2015). Gracility of the modern *Homo sapiens* skeleton is the result of decreased biomechanical loading. *Proceedings of the National Academy of Sciences*, *112*(2), 372–377. https://doi.org/10.1073/pnas.1418646112

Salari, N., Ghasemi, H., Mohammadi, L., Behzadi, M. H., Rabieenia, E., Shohaimi, S., & Mohammadi, M. (2021). The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. *Journal of Orthopedic Surgery and Research*, *16*(1), 609. https://doi.org/10.1186/s13018-021-02772-0

Sampson, H. W. (1997). Alcohol, osteoporosis, and bone regulating hormones. *Alcoholism: Clinical and Experimental Research*, *21*(3), 400–403. https://doi.org/10.1111/j.1530-0277.1997.tb03782.x

Scianò, F., Bramanti, B., Manzon, V. S., & Gualdi-Russo, E. (2020). An investigative strategy for assessment of injuries in forensic anthropology. *Legal Medicine*, *42*, 101632. https://doi.org/10.1016/j.legalmed.2019.101632

Scianò, F., Zedda, N., Mongillo, J., Gualdi-Russo, E., & Bramanti, B. (2021). Autopsy or anatomical dissection: evidence of a craniotomy in a 17th-eighteenth century burial site (Ravenna, Italy). *Forensic Science, Medicine and Pathology*, *17*(1), 157–160. https://doi.org/10.1007/s12024-020-00285-6

Sozen, T., Ozisik, L., & Calik Basaran, N. (2017). An overview and management of osteoporosis. *European Journal of Rheumatology*, *4*(1), 46–56. https://doi.org/10.5152/eurjrheum.2016.048

Steadman, D. W. (2005). Bone loss and osteoporosis: an anthropological perspective. *American Journal of Physical Anthropology*, *128*(2), 492–493. https://doi.org/10.1002/ajpa.20143

Swets, J. A. (1998). Measuring the accuracy of diagnostic systems. *Science*, *240*, 1285–1293. https://doi.org/10.1126/science.3287615

Todd, T. W. (1920). Age changes in the pubic bone. I. The male white pubis. *American Journal of Physical Anthropology*, *3*, 285–334. https://doi.org/10.1002/ajpa.1330030301

Todd, T. W. (1921). Ages changes in the pubic bone: III the pubis of the white female. IV the pubis of the female white negro hybrid. *American Journal of Physical Anthropology*, *4*, 1–70.

Tu, K. N., Lie, J. D., Wan, C. K. V., Cameron, M., Austel, A. G., Nguyen, J. K., Van, K., & Hyun, D. (2018). Osteoporosis: A review of treatment options. *Pharmacy and Therapeutics*, *43*(2), 92–104.

Tuck, S., Little, E. A., & Aspray, T. J. (2018). Implications of guidelines for osteoporosis and its treatment. *Age and Ageing*, *47*(3), 334–339. https://doi.org/10.1093/ageing/afx197

van Spelde, A. M., Schroeder, H., Kjellström, A., & Lidén, K. (2021). Approaches to osteoporosis in paleopathology: How did methodology shape bone loss research? *International Journal of Paleopathology*, *33*, 245–257. https://doi.org/10.1016/j.ijpp.2021.05.001

Waldron, T. (2008). *Palaeopathology*. Cambridge University Press. https://doi.org/10.1017/CBO9780511812569

Weaver, C. M., Gordon, C. M., Janz, K. F., Kalkwarf, H. J., Lappe, J. M., Lewis, R., O'Karma, M., Wallace, T. C., & Zemel, B. S. (2016). The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: A systematic review and implementation recommendations. *Osteoporosis International*, *27*(4), 1281–1386. https://doi.org/10.1007/s00198-015-3440-3

Welsh, H., Nelson, A. J., van der Merwe, A. E., de Boer, H. H., & Brickley, M. B. (2020). An investigation of micro-ct analysis of bone as a new diagnostic method for paleopathological cases of osteomalacia. *International Journal of Paleopathology*, *31*, 23–33. https://doi.org/10.1016/j.ijpp.2020.08.004

Wüster, C., Albanese, C., De Aloysio, D., Duboeuf, F., Gambacciani, M., Gonnelli, S., Glüer, C. C., Hans, D., Joly, J., Reginster, J. Y., de Terlizzi, F., & Cadossi, R. (2000). Phalangeal osteosonogrammetry study: Age-related changes, diagnostic sensitivity, and discrimination power. *Journal of Bone and Mineral Resarch*, *15*(8), 1603–1614 https://doi.org/10.1359/jbmr.2000.15.8.1603

Wüster, C., de Terlizzi, F., Becker, S., Cadossi, M., Cadossi, R., & Müller, R. (2005). Usefulness of quantitative ultrasound in evaluating structural and mechanical properties of bone: comparison of ultrasound, dual-energy X-ray absorptiometry, micro-computed tomography, and mechanical testing of human phalanges in vitro. *Technology and Health Care: Official Journal of the European Society for Engineering and Medicine*, *13*(6), 497–510.

Wüster, C., Heilmann, P., Pereira-Lima, J., Schlegel, J., Anstätt, K., & Soballa, T. (2009). Quantitative ultrasonometry (QUS) for the evaluation of osteoporosis risk: Reference data for various measurement sites, limitations and application possibilities. *Experimental and Clinical Endocrinology & Diabetes*, *106*(4), 277–288. https://doi.org/10.1055/s-0029-1211986

Wylie, C. D. (2010). Setting a standard for a "silent" disease: Defining osteoporosis in the 1980 s and 1990 s. *Studies in History and Philosophy of Science Part C :Studies in History and Philosophy of Biological and Biomedical Sciences*, *41*(4), 376–385. https://doi.org/10.1016/j.shpsc.2010.10.015

Zebaze, R. M., Ghasem-Zadeh, A., Bohte, A., Iuliano-Burns, S., Mirams, M., Price, R. I., Mackie, E. J., & Seeman, E. (2010). Intracortical remodelling and porosity in the distal radius and post-mortem femurs of women: A cross-sectional study. *Lancet*, *375*(9727), 1729–1736. https://doi.org/10.1016/S0140-6736(10)60320-0

Zhu, Z. Q., Liu, W., Xu, C. L., Han, S. M., Zu, S. Y., & Zhu, G. J. (2008). Reference data for quantitative ultrasound values of calcaneus in 2927 healthy Chinese men. *Journal of Bone and Mineral Metabolism*, *26*, 165–171. https://doi.org/10.1007/s00774-007-0801-9

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Pasini, A., Rinaldo, N., Bramanti, B., & Gualdi-Russo, E. (2023). Technical note: Application and potentiality of quantitative ultrasonometry for the evaluation of bone mineral density status. *American Journal of Biological Anthropology*, *181*(1), 140–154. https://doi.org/10.1002/ajpa.24711