# DIAGNOSTIC PERFORMANCE OF ULTRASONOMETER FOR EVALUATION OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

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## ABSTRACT

**Objects:** To evaluate the diagnostic performance of quantitative ultrasound (QUS)
**Study design:** A diagnostic test (Cross-sectional descriptive study)
**Methods:** 324 postmenopausal women were evaluated for bone mineral density (BMD) at the lumbar spine and femoral neck by dual energy X-ray absorptiometry (DEXA) at Nuclear Medicine Division, Bangkok Metropolitan Administration and Vajira Hospital from January 2003–November 2004. BMDs were interpreted as osteoporosis by WHO criteria. The speed of sound (SOS) was also measured at the distal third of radius by quantitative ultrasound (QUS).
**Results:** The prevalence of osteoporosis in our study was 30.8%, sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratio were 62%, 91.5%, 76.5%, 84.4% and 7 respectively.
**Conclusion:** SOS measurement at the distal third of radius by QUS had moderate sensitivity, but had high specificity when use DEXA as a gold standard and use WHO T-score as a reference. The highly specific test has been useful to confirm a diagnosis that has been suggested by other clinical data.

**Key words:** Osteoporosis, Dual energy X-ray absorptiometry, Quantitative ultrasound

**Foot notes:**
**QUS** = Quantitative Ultrasound
**DEXA** = Dual Energy X-ray Absorptiometry
**SOS** = Speed of sound
**BMD** = Bone Mineral Density

Osteoporosis is systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.[1] It is a significant cause of morbidity and mortality among postmenopausal women and has a major effect on the health economy worldwide.[2] Osteoporosis is a growing concern due to the increased in the percentage of aging in our population. It is therefore become imperative to evaluate and diagnose patients with osteoporosis so that preventive or therapeutic can be instituted as soon as possible.

The clinical management of osteoporosis relies heavily on the use of bone mass measurements, including quantitative computerized tomography, dual photon absorptiometry, radiographic absorptiometry, and dual-energy X-ray absorptiometry (DEXA). DEXA of the hip and spine has become the most widely accepted technique for evaluation of the skeleton status. DEXA measurements have good precision and accuracy, low radiation exposure, and are associated with hip and vertebral fracture risk.[3] However, owing to these machines require dedicated office space and can be expensive, they are not

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always accessible and tend to be located mainly in urban areas. To this end, several safe, precise, and accurate methods have been developed. The use of quantitative ultrasound (QUS) for the assessment of skeleton status has been to be a continued interest in recent years.[4-9] The attractiveness of QUS lies in its low cost, portability, ease of use, and freedom from ionizing radiation. It is possible that QUS may provide additional information on bone property (structure and strength) that is independent of BMD.[10-12] These benefits combined with preliminary clinical results showing good diagnostic sensitivity for fracture discrimination have encouraged further basic investigation.

There are essentially two approaches ultrasound assessment of bone: the first uses ultrasound velocity or speed of sound (SOS) and the second uses the frequency dependent attenuation. Ultrasound velocity is determined as the quotient of transit time and body part width or length and is quoted in meters per second (m/s), it is commonly measured at the calcaneus, tibia, patella, and phalanges. For frequency dependent attenuation, it is determined at the calcaneus. The attenuation parameter BUA is defined as the slope of attenuation versus frequency in this range and is reported in units of decibels per megahurtz. SOS and attenuation are both correlated with bone density and strength. Therefore, healthy bone will have a higher SOS and attenuation whereas osteoporotic bone will have a slower SOS and attenuation. In general, velocity is easier to measure and results in greater precision. Measurement of attenuation usually requires more complex hardware and results in less precised data.[4]

Recently, a quantitative ultrasound device that measures speed of sound (SOS) at multiple skeletal sites was introduced. Preliminary reports suggested that of the different skeletal sites measured by this device, the distal third of the radius is the preferred measurement site for osteoporosis.[13-14] In contrast to commonly used calcaneal QUS devices that evaluate ultrasound properties perpendicular to the load vector, determination of SOS along the radius seems more relevant to the mechanical load that is applied along the arm.

However, there is scarce studies in SOS measurement at the distal third of the radius. The aim of this study was to assess the diagnostic performance of quantitative ultrasound (SOS) at the distal third of the radius in detecting osteoporosis in Thai postmenopausal women using dual energy x-ray absorptiometry as the gold standard.

## SUBJECTS AND METHODS

### Subjects

The study included 324 Thai postmenopausal women who attended Bangkok Metopolitan Administration and Vajira Hospital from January 2003 to November 2004. The study has been approved by the Medical Ethics Committee of Bangkok Metropolitan Administration, and written informed consent is obtained from participants. Baseline data consist of both demographic and clinical variables such as age, height, weight, date of the last priod and duration of postmenopause. Postmenopausal duration was the period after the final menstrual period regardless of whether it was spontaneous or induced, that was duration of current age in years minus age at menopause. Menopause was indicated after 12 consecutive months of amenorrhea, regardless of pathological or physiological cause. The study subject consisted of two groups, osteoporotic and non-osteoporotic. The osteoporotic group (n=100) was comprised of postmenopausal females with a BMD more than 2.5 standard deviations (SD) below the mean young normal bone mass (T-score) at the lumbar spine and/or femoral neck as determined by the Lunar normative database. Vital signs, height, and weight were

**BMD** = Bone Mineral Density, **BUA** = Broad band Ultrasound Attenuation, **SOS** = Speed of Sound,
**SD** = Standard Diviation, **QUS** = Quantitative Ultrasound

collected. Subjects who met all inclusion and exclusion criteria underwent a DEXA scan of the hip and posteroanterior spine and quantitative ultrasound (SOS) of the left distal third of the radius.

Exclusion criteria included diseases or conditions known to affect bone health, including chronic kidney disease, long-term immobilization, smoking, and medications (fluoride, calcitonin, bisphosphonates, corticosteroids, thiazides, anticoagulants). Appropriate informed consent forms were obtained from every subject. Each postmenopausal women was undergone both DEXA and QUS measurements by independent radiological technologist.

**Quantitative ultrasound (bone sonometry)**

Measurements of the velocity of the ultrasound wave, expressed as speed of sound (SOS) in m/s, were done using quantitative ultrasound (The Sunlight Omnisense™ 7000S Bone sonometer device, Israel) at distal third of radius. It is designed to measure SOS of ultrasonic waves axially transmitted along bones. The ultrasound wave are conducted along the bone and then detected by two different transducers assembled within the probe. By measuring the propagation times along the different trajectories, originating at one of the transmitting transducers and arriving at one of the receiving transducers, the SOS of the bone is determined. The non-dominant side was uniformly used for examination, left usually, unless a history of fracture was present. Each value recorded was the mean of 3 consecutive determinations. The total scanning time with analysis took no more than 5 minutes.

QUS quality controls suggested by the manufacturer were carried out daily before the examinations. To quantify the precision error of this instrument, the instrument precision underwent a total of three measurements without repositioning in 18 subjects. The repositioning/interobserver precision underwent a total of three measurements of each in the same day by three technologists. The short term precision underwent one measurement on 5 separate days within one week period in 10 subjects. The instrument precision was 0.47%. The interobserver precision was 0.38-0.47%. The short term precision was 0.43%.

**Dual energy x-ray absorptiometric measurements**

Bone mineral measurements with DEXA were performed with a bone densitometer with a Lunar DPX-L (Lunar Radiation Corporation, Madison, WI, USA) at the lumbar spine (L2-L4) and the left proximal femur (femoral neck). The machine was calibrated daily using a quality assurance phantom. The precision error of the technique expressed as CV was 0.5% for the lumbar spine phantom and 1.3% for the hip phantom.

To ascertain whether the SOS values could identify osteoporotic and non-osteoporotic groups, the SOS mean and standard deviation were calculated for each group. Comparison between groups was made using an unpaired two-tailed Student's t-test. The Pearson correlation coefficients were calculated for weight, BMI, SOS, lumbar spine BMD and proximal femoral BMD. Data are expressed as mean ±SD. A p value < 0.05 was considered statistically significant.

**DEXA** = Dual energy X-ray Absorptiometry, **SOS** = Speed of Sound, **QUS** = Quantitative Ultrasound,
**CV** = Coeffieient of Variation, **BMI** = Body Mass Index

## RESULTS

**TABLE 1** Demographic of study population (n=324 ) (mean±SD, range)

| | | |
|---|---|---|
| Age (years) | 59.6±10.19 | 39 to 97 |
| Years since menopause | 10.7±8.96 | 1 to 50 |
| Age at menopause | 48.9±3.06 | 33 to 55 |
| Body weight (Kg) | 55.7±9.28 | 32 to 92 |
| Height (cm) | 152.1±8.19 | 152 to172 |
| Body mass index (Kg/m$^2$) | 23.9±3.79 | 16 to 40.3 |
| L-spine BMD (g/cm$^2$) | 0.980±0.19 | 0.959 to 1.002 |
| L-spine BMD (T-score) | -1.163±1.59 | -1.347 to -0.993 |
| FN BMD (g/cm$^2$) | 0.645±0.66 | 0.572 to 0.718 |
| FN BMD (T-score) | -1.169±1.25 | -1.312to -1.034 |
| Left forearm SOS (m/s) | 4043.39±157.13 | 3658 to 4468 |
| Left forearm T-score | -1.255±1.37 | -1.406 to -1.105 |

**TABLE 2** WHO criteria for lumbar spine/ Femoral neck BMD

| | Non-osteoporosis (n=224) T-score ≥ -2.5 | Osteoporosis (n=100) T-score < -2.5 | p-value |
|---|---|---|---|
| Age (years) | 56.1±7.73 | 67.2±10.39 | <0.001 |
| Years since menopause | 7.8±6.86 | 17.4±9.56 | <0.001 |
| Age at menopause | 48.3±3.02 | 50.3±2.68 | <0.001 |
| Body weight (Kg) | 57.4±9.11 | 51.3±5.7 | <0.001 |
| Body mass index (Kg/m$^2$) | 24.3±3.82 | 23.2±4.29 | <0.05 |
| L- spine BMD (g/cm$^2$) | 1.064±0.16 | 0.788±0.11 | <0.001 |
| L- spine BMD (T-score) | -0.46±1.51 | -2.75 ±0.91 | <0.001 |
| FN BMD | 0.824±0.122 | 0.611±9.72 | <0.001 |
| FN BMD (T-score) | -0.634 ±1.00 | -2.371±0.86 | <0.001 |
| Left forearm SOS (m/s) | 4099±124 | 3919±151 | <0.001 |
| Left forearm (T-score) | 0.77±1.08 | -2.34±1.34 | <0.001 |

Values are the mean±SD, LS= lumbar spine; FN= femoral neck; BMD= bone mineral density

**DEXA** = Dual Energy X-ray Absorptionretry, **QUS** = Quantitative Ultrasound, **FN** = Fermoral Neek
**SOS (m/s)** = Speed of Sound (meter/sec), **CV** = Coeffieient of Variation, **BMI** = Body Mass Index

**TABLE 3** The characteristics of diagnostic performance taking QUS and DEXA-BMD

| QUS (Test) | DEXA | | Total |
|---|---|---|---|
| | T-score<-2.5 | T-score>-2.5 | |
| T-score<-2.5 | 62 | 19 | 81 |
| T-score>-2.5 | 38 | 205 | 243 |
| Total | 100 | 224 | 324 |

QUS = Ouantitative Ultrasound
DEXA = Dual energy X-ray Absorptiometry
FN = Femoral neek

**TABLE 4** Correlation coefficients between age, body weight, BMI, LS and FN BMD, and wrist SOS

| | | Age | Meno dura | Wt | BMI | Wr-SOS | BMD_FN | BMD-LS |
|---|---|---|---|---|---|---|---|---|
| Wr-SOS | Pearson Correlation | -.507* | -.466* | .105 | .007 | 1.000 | .068 | .527* |
| | Sig. (2-tailed) | .000 | .000 | .059 | .898 | . | .225 | .000 |
| | N | 322 | 322 | 322 | 322 | 322 | 318 | 321 |
| BMD-FN | Pearson Correlation | -.115 | -.070 | .225 | .209 | .068 | 1.000 | .363 |
| | Sig. (2-tailed) | .039 | .214 | .000 | .000 | .225 | . | .000 |
| | N | 320 | 320 | 320 | 320 | 318 | 320 | 318 |
| BMD-LS | Pearson Correlation | -.454* | -.450* | .378 | .222 | .527 | .363* | 1.000 |
| | Sig. (2-tailed) | .000 | .000 | .000 | .000 | .000 | .000 | . |
| | N | 322 | 322 | 322 | 322 | 321 | 318 | 322 |
| Wt | Pearson Correlation | -.243 | -.248 | 1.000 | .874 | .105 | .225 | .378 |
| | Sig. (2-tailed) | .000 | .000 | . | .000 | .059 | .000 | .000 |
| | N | 324 | 324 | 324 | 324 | 322 | 320 | 322 |
| BMI | Pearson Correlation | -.048 | -.047 | .874 | 1.000 | .007 | .209 | .222 |
| | Sig. (2-tailed) | .387 | .403 | .000 | . | .898 | .000 | .000 |
| | N | 324 | 324 | 324 | 324 | 322 | 320 | 322 |

* Correlation is significant at the 0.05 level (2-tailed).
Meno dura = duration of menopause, Wt= weight, BMD=bone mineral density, LS=lumbar spine, FN=femoral neck, BMI=body mass index, Wr = Wrist

A total of 324 postmenopausal women in Bangkok Metropolitan Administration Medical College and Vajira Hospital were participated. As shown in Table 1, their average age, BMI, age at menopause, duration of menopause, lumbar spine and femoral neck BMD, and SOS at the wrist, were 59.6 years, 23.9, 48.9 years, 10.7 years, 0.980±0.96 g/m$^2$, 0.645±0.57 g/m$^2$ and 4043m/sec respectively.

As displayed in Table 2, the women were classified by the WHO criteria for BMD at the lumbar spine and/or femoral neck to non-osteoporosis and osteoporosis. There were significant differences among the groups in term of age, years since menopause, age at menopause, BMI, SOS and BMD at the lumbar spine and femoral neck.

BMDs were measured in 324 postmenopausal women by DEXA as a gold standard and by QUS measurement as a new diagnostic test. The prevalence of osteoporosis was 30.8%. False positive rate is 8.4%, and false negative rate is 38%. The sensitivity of QUS using DEXA as the gold standard was moderate (62%) but had high specificity (91.5%). The probability that the subjects with a positive test result would have the osteoporosis (positive predictive value) was 76.5% and the probability that an individual with a negative test result would not have the osteoporosis (negative predictive value) was 84.4%. The chance of test positive if the subject has disease (LR+) is 7 times to the chance of a positive result if the subjects do not have disease (Table 3).

Correlation coefficients for BMD and SOS between different anatomic sites are shown in Table 4.Lumbar spine and femoral neck BMD had a correlation of 0.363. SOS correlated better with lumbar spine BMD (0.527) than with femoral neck BMD. Both age and duration of menopause were negatively correlated with SOS (-0.507 and -0.466) and lumbar BMD (-0.454 and –0.450).

## DISCUSSION

Much less has been published about QUS (SOS) at the distal third of the radius.

In our study, SOS and BMDs (lumbar spine and femoral neck) have been shown to be significantly decreased in women with osteoporosis which compatible with many studies.[14-16] Our results are similar to study of Weiss et al[14] who used the same method and site.

The objective of this study is to determine the diagnostic performance of QUS (SOS) radius measurement in the case finding of osteoporosis in postmenopausal women using DEXA as gold standard. To assess the diagnostic performance, we use the accuracy of the test, which is the correspondence with sensitivity and specificity. In this study we found that QUS at the distal third of radius had a moderate sensitivity (62%) for predicting BMD- osteoporosis, but had a high specificity (91.5%). In study of Benitez CL et al,[16] the sensitivity and specificity were 84% and 50% respectively. They studied QUS (SOS) at the proximal phalanxes in 206 postmenopausal Mexican-American women. Massie A et al[17] found that only 44% of the perimenopausal women whose spinal DEXA falls within the lowest quartile being in the lowest quartile of BUA of the calcaneus. Difference in results might be from population, measurement technique and site. In our study the high specific test (QUS) has been useful to confirm (rule in) a diagnosis that has been suggested by other clinical data. This is because highly specific test is rarely positive in the absence of disease - that is, it gives low false positive results. Therefore, DEXA examination could be avoided if procedure with QUS is performed at the beginning of a diagnostic work-up. In this study positive predictive value (76.5 %) was relatively low for QUS as a predictor of BMD -defined osteoporosis. This might be because of a test with high specificity (low false positive among the

**BMD** = Bone Mineral Density, **SOS** = Speed of Sound, **DEXA** = Dual energy X-ray Absorptionretry, **(LR+)** = positive Lihulthood Ratio disease free) could have low positive predictive value if the ratio of disease-free to disease subjects was high.[18]

The likelihood ratio for a particular ratio of a diagnostic test is defined as the probability of that test result in people with disease divided by the probability of the result in people without disease. Likelihood expresses how many times more (less) likely a test reszult is to be found in disease compared with non-disease people.[18] In this study the positive likelihood ratio was 7.0 which meant that a subject with positive test was 7 times more likely to occur osteoporosis than one without it. A high likelihood ratio for a positive result has shown that the test (QUS) provided useful information.

The correlation of radius QUS and DEXA at the lumbar spine was modest (0.53) and was better than at the femoral neck. One of the reasons for different correlation between sites is probably bone composition. The correlation between QUS and BMD measurements has been examined in several studies. Depending on the population studied, method (SOS or BUA) and the site of measurement (calcaneus, radius, phalanx), correlation was ranged from 0.29 to 0.90.[15,17,19-21]

DEXA is presently the standard method for assessing BMD. The technique provides an apparent area density (BMD) calculated as bone mineral content /bone area and expresses density as $g/cm^2$, therefore the standard DEXA technique measures not true bone mineral density ($g/cm^3$), but rather areal density($g/cm^2$). In contrast to bone density measurements, QUS which is mechanical wave may have greater potential to assess of three dimensional structure and strength.[12] This advantage is especially significant for some chronic (rheumatic) disorders associated with bone growth; when comparing 2 bones of different sizes but with the same mineral content, the larger will show artificially higher BMD than the smaller one. Thus, QUS appeared to be less dependent on anthropometric parameters.

In conclusion, our study was a cross-sectional study on a postmenopausal population that needs to be further validated with larger groups. However, promising results were seen in the application of radius QUS as to confirm (rule in) a diagnosis of osteoporosis that has been suggested by other clinical data. The application of QUS will help to prevent unnecessary DEXA. A low cost, portable and radiation-free screening tool would also be beneficial for the assessment of the skeletal status in much of the population.

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**BUA** = Broad band Ultrasound Attennation, **SOS** = Speed of Sound

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