1.1 Essential Prescribing Information

1.1.1 Device Description

The DTU-one measures the broadband ultrasound attenuation (BUA in dB/MHz). The parameter output is expressed both as a T-score (for all patients) and a Z-score (for Caucasian women only – due to the absence of applicable reference databases for other ethnic groups and males).

The scanning method is rectilinear using ultrasonic transducers with a focused beam and bandwidth of 97% (3dB down at 278.1 to 801.9 kHz.), with a scan resolution of 0.6 millimeters over a frequency range of 300 to 650 kHz. The transducers are focused with the focus distance at 33 mm. The center frequency is 540 kHz. The scan time is approx. 3 minutes, using water as a coupling medium. The manufacture of the DTU-one Ultrasound Scanner involves hardware assembly of chassis, power supply, printed circuit boards, power and signal cables, and other components of the device. The operating software is installed/integrated in the hardware and is tested at the systems level on phantoms of known value.

Device Components:

The DTU-one hardware, including accessories, consists of:

- DTU-one Ultrasound Scanner and water container (foot tank).
- Computer and monitor, with the following minimum specifications: Windows NT operating system, 120 MHz clock-rate, 32 MB RAM, and 1 serial and 1 parallel port (e.g.: IBM 330-466DX2 computer and 14L8 15" SVGA monitor. The PC and connected equipment complies with United States FCC rules Part 15 and has the CE mark.
- Printer (optional) e.g.: HP 600 Series (HP 690c).
- DTU-one phantom.
- Heel fixation ring.
- DTU-one Solution. (A mixture of distilled water and a proprietary wetting agent).
- SBR Lipocream.

Cleaning and disinfecting:

The following materials are required for cleaning, disinfecting and maintaining the DTU-one but are not provided by Osteometer MediTech, Inc.:

- Distilled water, 70% Isopropyl Alcohol and 5% Distilled White Vinegar

Electrical service: 115 VAC, 60 Hz or 230 VAC, 50 Hz

Environmental conditions:

The DTU-one Ultrasound Scanner should be placed in an environment where a humidity of 10 to 80% (non-condensing) and a room temperature of 59 to 86°F (15 to 30°C) can be maintained

Computer System configuration:

- Windows NT Platform

1.1.2 Intended Use

The DTU-one is intended to perform a quantitative ultrasound measurement of the calcaneus (the heel bone) the results of which can be used in conjunction with other clinical risk factors as an aid to the physician in diagnosis of osteoporosis (T-score) and in the determination of fracture risk in men and women. The measurement may also be used in Caucasian women to aid in the detection of medical conditions, other than age-related bone loss, that lead to reduced bone density.

1.1.3 Contraindications

None known.

1.1.4 Warnings

- The DTU-one is not intended for measurements on patients under 20 years of age, or patients older than 80 years of age. Reference data is not available for patients below 20 or over 80 years of age. Patients matching these criteria will not receive either a T- or Z-score due to the lack of reference data.

- The DTU-one must be cleaned and disinfected after each patient. Doing so may help prevent transmission of infectious agent between patients.

  Do not use the DTU-one for patients with breached skin or open sores on the foot or heel area. Doing so can increase the risk of transmission of infections.

- Do not operate the DTU-one without first reading the DTU-one Operator's Manual and the Essential Prescribing Information.
- A Quality Control (QC) phantom measurement procedure should be performed every day before patient measurements. If the procedure fails twice, contact your Osteometer MediTech representative or the Osteometer MediTech Service Department for assistance.
- Only trained technicians should operate the DTU-one.

1.1.5 Precautions

- A component of the DTU-one Solution may cause a sensitization reaction in some patients.
- Wear protective gloves when cleaning the DTU-one.
- Soiled material should be disposed of in appropriate waste receptacles.
- Use 70% alcohol when cleaning in a well ventilated area away from open flame or sparks.
- Do not attempt any repairs—there are no user-serviceable parts.
- Do not expose the computer to liquids or moisture.
- Do not put any electric or battery-operated device in the heel bath.
- The connected PC System must be located 6 feet away from the patient to avoid electrical shock.

1.1.6 Potential Adverse Effects On Health

No adverse reactions or deaths were reported in the clinical studies. There have been no reported adverse events associated with the use of, or operation of, the DTU-one ultrasound scanner.

1.1.7 Summary of Clinical Studies

A. Objectives

Clinical studies were conducted to assess the safety and effectiveness of the DTU-one Ultrasound Scanner as an aid in establishing the diagnosis of osteoporosis and assessing risk of osteoporotic fracture. The primary objectives of these studies were to:

1. assess fracture risk,
2. establish a US reference database, and
3. assess precision .

B. Clinical Trials

1. Fracture Risk Study

Two fracture risk studies were performed, one on spinal fractures at the Center for Clinical and Basic Research (CCBR) and the other on hip fractures at Bispebjerg Hospital in Copenhagen, Denmark. The areas (AUC) under the respective receiver operating characteristic (ROC) curves for fracture and non-fracture subjects, measured both by the DTU-one and by DEXA for the two studies are listed below:

CCBR Study of Spinal Fracture

58 Spinal Fractures and 54 No-fracture Controls

DTU-one BUA (Left Heel)		DEXA BMD (Forearm)		DEXA BMD (Spine)		DEXA BMD (Femoral Neck)		DEXA BMD (Total Femur)	
AUC	SE*	AUC	SE	AUC	SE	AUC	SE	AUC	SE
0.713	0.049	0.662	0.051	0.668	0.051	0.622	0.053	0.652	0.052

*Standard Error (SE)

Bispebjerg Study of Falls, With Hip and Without Any Fracture

(Approximately) 23 Falls with Hip Fracture and 21 Falls-without-Fracture Controls

DTU-one BUA (Right Heel)		DTU-one BUA (Left Heel)		DEXA BMD (Forearm)		(Lunar) DEXA BMD (Femoral Neck)		(Lunar) DEXA BMD (Total Femur)	
AUC	SE	AUC	SE	AUC	SE	AUC	SE	AUC	SE
0.684	0.079	0.650	0.082	0.688	0.079	0.802	0.073	0.759	0.080

There were no statistically significant differences detected between the DEXA and DTU-one discriminating ROC curves in either study.

2. US Reference Database Study

For the age group 20-50 years, 217 observations were used to derive the mean value (MBUA) and standard deviation. For the age group 51-80 years, 169 observations were used to derive the following quadratic regression equation to estimate mean BUA (MBUA) at each age:

MBUA (mean of left and right): $34.1648 + \text{Age} \times 0.77948 - (\text{Age}^2 \times 0.00933)$

The mean values for the left calcaneus for ages 20-80 were derived from the following equation:

Left = MBUA + 0.6% of MBUA.

The mean values for the right calcaneus for ages 20-80 were derived from the following equation.

Right = MBUA - 0.6% of MBUA.

Female, left calcaneus, BUA:

The following table shows the mean values of the estimated BUA in the left calcaneus of the reference population over the range of 20 to 80 years of age.

The following data (identified as: "USA Caucasian 1998") will be entered into an existing directory of the DTU-one software program resident on the hard drive under an entry, entitled "Female, left BUA":

20-50 years:	Mean value: 50.13	SD: 6.52

SD for 51-80 years: 7.77

Female, right calcaneus, BUA:

The following table shows the mean value of the estimated broadband ultrasound attenuation in the right calcaneus of the reference population over the range of 20 to 80 years of age.

The following data (identified as: "USA Caucasian 1998") will be entered into an existing directory of the DTU-one software program resident on the hard drive under an entry, entitled "Female, right BUA":

20-50 years:	Mean value: 49.53	SD: 6.52

SD for 51-80: 7.77

3. Precision Study

The precision error in each individual was calculated as the coefficient of variation (CV%) by dividing the standard deviation (SD) by the mean value of the three repeated measurements. The overall CV% was obtained by calculating the pooled within-subject standard deviation (root-mean-square deviation), and dividing by the grand mean. For T-Scores computed from these BUA measurements, the observed-pooled within-subject standard deviation of the replicate T-Scores was 0.17.

The in vivo precision error for BUA, for repositioning only, was found to be:

Precision error BUA: 2.4%	95% Confidence Interval: 2.13-2.66%

The results given above will appear on the computer screen, printed patient report, and in the DTU-one promotional material, which is going to be used in the United States. The standard deviation of the T-score (TSD) is equal to the variability due to repositioning divided by the standard deviation of the young healthy group or 0.177 (of a T-score unit).

C. Adverse Reactions, Patient Discontinuation, Patient Complaints, Device Failures, and Device Replacements Encountered During the Clinical Studies

There were no adverse effects of the device on health during the studies.

1.1.8 Individualization of Treatment

BUA results are expressed as T-scores and Z-scores, which are calculated for the assessment of fracture risk.

1.1.8.1 T-Score and %Young Mean Adult

The T-score represents the patient's BUA result above or below a reference "Young Adult" mean and is expressed in standard deviation (SD) units. The bottom of the yellow region (see figure) marks one standard deviation (-1 SD) below the mean Young Adult value. Fracture risk increases continuously as the BUA values decrease. The "%Young Adult" expresses a patient's BUA value as a percentage of the "Young Adult" mean for women aged 20-50 years.

For example, in Figure 1.1-1 the 60-year-old female patient plotted on the graph has a BUA value -0.77 SD below the Young Adult mean.

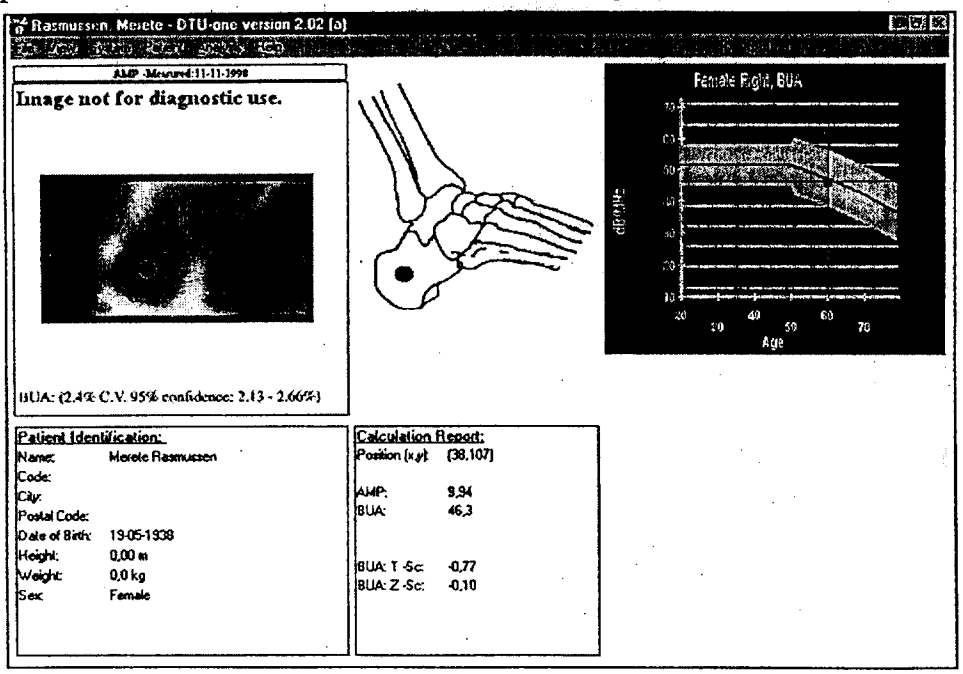

Figure 1.1-1. Reference graph with example: T-score = -0.77 and Z-score = -0.10.

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1.1.8.2 Z-Score and % Age-Matched

The Z-score represents the patient's BUA value above or below the expected Age-Matched value and is expressed in SD relative to the intra-population variation. The reference curve is used in calculation of the expected BUA value at a given age, and the standard error about that curve is used as a measure of variation about that curve. The %Age-Matched value expresses the patient's BUA value as a percentage of the expected values for a reference group of the same age and sex.

For example, in Figure 1.1-1 the BUA value result plotted against Age-Matched data is -0.77 SD below the Young Adult value. However, the value almost falls on the Age-Matched regression line (-0.10). This indicates the patient has an increased risk of fracture, but one that is typical for patients of her age.

BUA values that are 7.77 below that expected at a given age (i.e. Z score worse than -1SD) may suggest that factors in addition to age are affecting the patient's bone. In most cases, low bone density is caused by genetic predisposition, but it may be related to secondary causes listed in Table 1. The physician should consider therapy consistent with the patient's age, physical condition, and other relevant risk factors (refer to NOF Guidelines).

Table 1. Causes of Secondary Osteoporosis

Endocrine Disorders
Hyperthyroidism
Hyperparathyroidism
Hypogonadism
Cushing's syndrome
Growth hormone deficiency
Juvenile diabetes
Renal failure disease
Idiopathic hypercalciuria
Liver disease / failure

Malignancies / Cancer
Multiple myeloma
Metastatic bone disease
Lymphoma

Diet / Malabsorption Syndromes

Gastrectomy
Intestinal bypass
Sprue / celiac disease
Steatorrhea

Drug-Induced (Iatrogenic)
corticosteroids
anticonvulsants
heparin (long-term use)
cancer drugs
glutethimide
thyroid hormone
LHRH, GnRH agonists
cyclosporine
methotrexate
lithium

Heritable Disorders
Turner's syndrome
Klinefelter's syndrome
osteogenesis imperfecta
hypophosphatasia

hemolytic anemia
thalassemia

Other
immobilization

Calcium deficiency	systemic mastocytosis
Vitamin D deficiency	radiation therapy
Vitamin C deficiency	rheumatoid arthritis
Lactose intolerance	alcoholism
Anorexia	

1.1.8.3 Bone Ultrasonometry and Fracture Risk

T-scores for BUA can be used in a manner similar to BMD from X-ray absorptiometry in assessing a patient's risk of osteoporotic fracture. An expert group of the World Health Organization has proposed operation levels at which physicians can recognize increased risk. These are based on "T-scores,". A T-score from -1 to -2.5 is considered to reflect "osteopenia", while a T-score below -2.5 SD is considered to reflect "osteoporosis".

There is no clear demarcation for increased risk of fracture at a specific given level of BMD or BUA value, but rather there is a continuous gradient of risk. BUA values should be considered together with other risk factors (BMD, low body weight, fracture history, corticosteroids use, use of long-acting tranquilizers, history of falling) in patient evaluation. In particular, patients with a prior history of osteoporotic fracture should be considered to have double the risk of future fracture at any density level. The National Osteoporosis Foundation has recently developed practice guidelines for physicians to help in such evaluation. As yet there are no consensus guidelines on how physicians should combine the results of X-ray absorptiometry from different skeletal sites, or from X-ray absorptiometry and ultrasonometry, in patient evaluation. The data from clinical studies suggest that BUA is somewhat independent of X-ray absorptiometry, and provides incremental information on fracture risk.

1.1.8.4 User Assistance

You can get help with any problem you may encounter with the DTU-one: Contact your local authorized OSTEOMETER MEDITECH, INC. representative, or contact OSTEOMETER MEDITECH, INC. directly

Tel:	310-978-3073
Fax:	310-676-0948
e-mail:	info@osteometer.com
website:	www.osteometer.com

1.1.9 Directions for Use

Refer to the "DTU-one Operator's Manual" for detailed directions for use.

1.1.10 Patient Counseling Information

Patient pamphlets are supplied with the DTU-one system. The pamphlet gives a brief summary of the importance of bone density testing and information about the DTU-one imaging ultrasound scanner.

The pamphlet can be readily duplicated, or ordered from OSTEOMETER MEDITECH, INC.

1.1.11 Detailed Device Description

1.1.11.1 DTU-one Ultrasound Scanner

See Figure 1.1-2 and Figure 1.1-3.

- Top plate
- Transducers and transducer arms
- Water Container (blue foot tank)—the patient's foot is submerged in prepared water and the heel is positioned in the water container during a patient measurement.
- Heel Fixation Ring (labeled on the figure as "*Ring for heel Position*") and the Toe Guide—the heel fixation ring is positioned in the water container before a patient measurement. The Heel Fixation Ring and the Toe Guide help align the heel with the transducers and keep the patient's leg stationary so the foot does not move during a patient measurement.

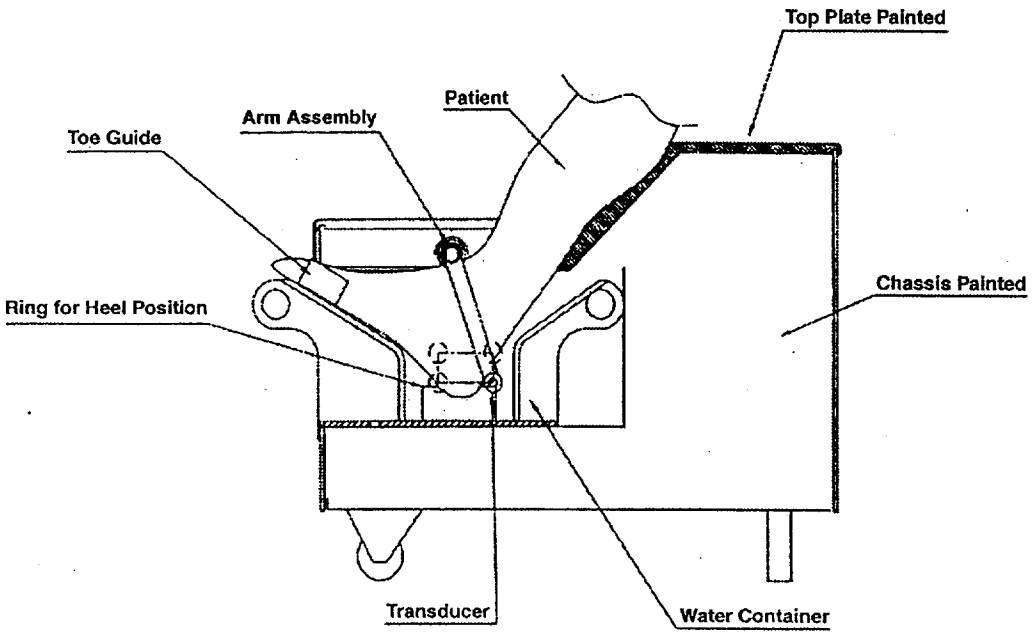

Figure 1.1-2. Side view of the DTU-one

Top Plate
Transducers and transducer arms
Water Container (blue foot tank)- the patient's foot is submerged in prepared water and the heel is positioned in the water container during a patient measurement.
Heel Fixation Ring (labeled on the figure as "Ring for the heel Position") and the Toe Guide-the Heel Fixation Ring is positioned in the water container before a patient's measurement. The Heel Fixation Ring and the Toe Guide help align the heel with the transducers and keep the patient's leg stationary so the foot. does not move during a patient measurement.

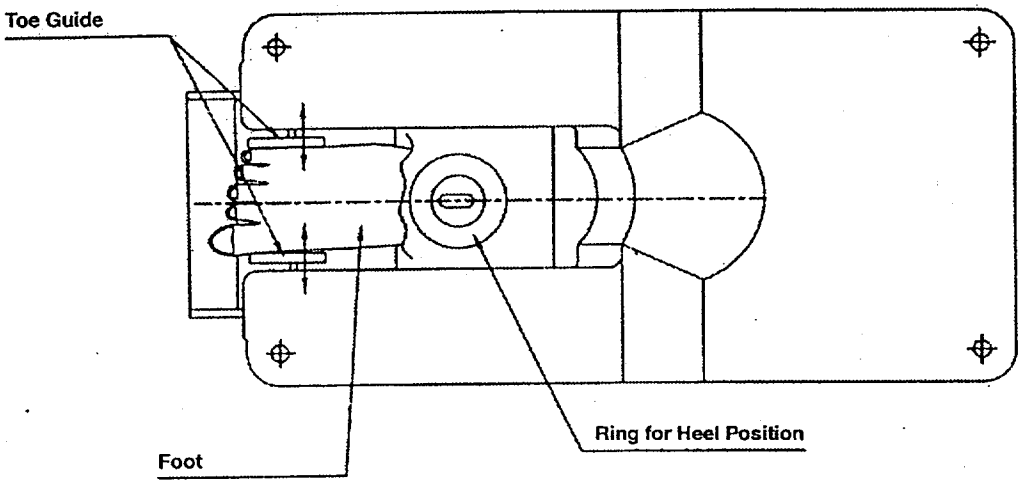

Figure 1.1-3. Top view of the DTU-one

Because the water container and the heel fixation ring/toe guide are in contact with the foot, low-level disinfection procedures must be completed between each patient measurement. Doing so will help prevent possible transmission of infection between patients. For cleaning and disinfecting purposes, 70% isopropyl alcohol is suitable. The entire container surface is thoroughly wiped with the cloth. Make sure that all edges and corners are thoroughly cleaned and disinfected. Refer to Chapter 4 of this manual for procedures. Dispose of soiled materials in appropriate waste receptacle.

1.1.11.2 Power Switch

The power switch (Figure 1.1-4) is located on the back of the DTU-one and is used to turn the DTU-one on and off.

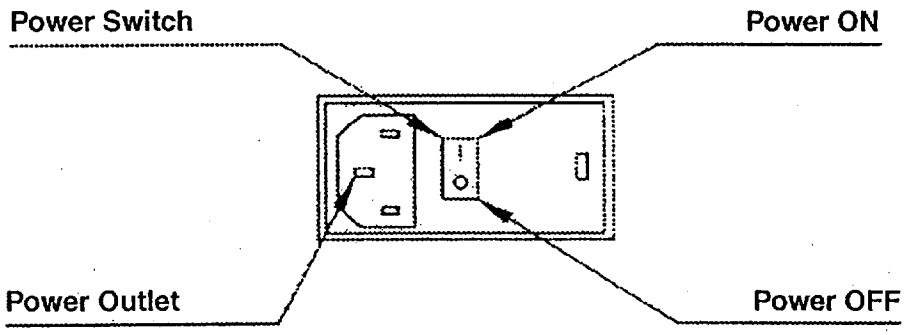

Figure 1.1-4. DTU-one power switch

1.1.11.3 System (QC) Phantom

The system (QC) phantom is used to perform the daily Quality Control procedure. The QC phantom supplied with your DTU-one is calibrated specifically to your system. Phantoms from other systems are not valid for use with your DTU-one. If your clinic possesses more than one DTU-one Ultrasound Scanner, do not interchange their phantoms.

NOTE: The QC phantom should be stored near the DTU-one unit—but not in the water container.

Refer to Chapter 5 of this manual for information about care of your QC phantom.

1.1.12 How Supplied

The DTU-one ultrasound scanner together with personal computer, monitor, keyboard, mouse, and printer are supplied. In addition the DTU-one is supplied both with a complete *DTU-one Operator's Manual* (user guide) and patient educational material.

Refer to Appendix F of this manual for more information.

1.1.12.1 DTU-one Solution

The DTU-one system includes one bottle of DTU-one Solution sufficient for 50 patients. The solution is mixed with distilled water in the water bottle and helps improve coupling of the ultrasound signal.

The DTU-one Solution must be ordered from OSTEOMETER MEDITECH, INC.

1.1.12.2 Distilled Water

Distilled water, i.e. water that does not contain minerals, can be purchased by the user off the shelf from local retail stores.

1.1.12.3 SBR-Lipocream™

SBR-Lipocream™ (NDC: 0496-0819-01) is manufactured by Yamanouchi Europe BV for Ferndale Laboratories, Inc., and can be ordered through your pharmacist.

1.1.12.4 70% Isopropyl alcohol

70% Isopropyl alcohol is used to clean and disinfect the DTU-one system after each patient. It can be purchased by the user from a medical supply store or off the shelf from local retail stores.

1.1.12.5 5% Distilled White Vinegar

5% distilled white vinegar is used to removed any chalky residue which may remain on the surfaces of the water container or transducers and arms. 5% distilled white vinegar can be purchased at local retail or medical supply stores.

1.1.13 References

1.1.13.1 Clinical Studies Using the DTU-one Ultrasound Scanner

1. Jørgensen HL, LV Jørgensen, C Hassager, A Møllgaard, C Christiansen. Quantitative ultrasound (QUS) on a specific Region of Interest (ROI) of the os calcis: A new imaging technique. *Appl Radiat Isot* 1998; 49, No. 5/6: 681-683.
2. Jørgensen HL et al. Improved reproducibility of broadband ultrasound attenuation (BUA) of the os calcis by using a specific region of interest (ROI); *Bone* 1997; 21: 109-112.
3. E Diessel, T Fuerst, CF Njeh, D Hans, S Cheng, HK Genant. Evaluation of an imaging quantitative ultrasound device (DTU-one): Comparison with densitometric measurements (QDR 4500) in the heel and the femur. *Br J Radiol* 1999; Accepted for publication.

1.1.13.2 Comparative Prospective Studies Using DEXA and Ultrasound

1. Bauer DC, Glüer CC, Cauley JA, Vogt TM, Ensrud KE, Genant HK, Black DM. Broadband ultrasound attenuation predicts fractures strongly and independently of densitometry in older women. *Archives of Internal Medicine* 1997; 157: 629-633.
2. Hans D, Dargent-Molina P, Schott AM et al. Ultrasonic heel measurements to predict hip fracture in elderly women: The EPIDOS prospective study. *Lancet* 1996; 348: 511-514.
3. Glüer CC; Cummings SR, Bauer DC et al. Osteoporosis: Association of recent fractures with quantitative US findings. *Radiology* 1996; 199: 725-732.

1.1.13.3 NOF Guidelines

1. Physician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis Foundation, 1998.

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