



P970040

JUN 26 1998

Food and Drug Administration  
9200 Corporate Boulevard  
Rockville MD 20850

Kenneth D. Buroker  
Lunar  
313 W. Beltline Highway  
Madison, Wisconsin 53713

Re: P970040  
Achilles+ Bone Sonometer  
Filed: September 2, 1997  
Amended: December 8, 1997, February 20, March 11, June 2, 15 and 24, 1998

Dear Mr. Buroker:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Bone Sonometer. This device is indicated as follows:

The Achilles+ultrasonometer measures ultrasound variables of the os calcis to provide a clinical measure called Stiffness Index. The Stiffness Index indicates risk of osteoporotic fracture in postmenopausal women comparable to bone mineral density (BMD) as measured by X-ray absorptiometry at the spine or hip.

Stiffness Index results expressed as T-scores are used to assist the physicians in the diagnosis of osteoporosis in the same way as are T-scores or obtained by X-ray absorptiometry. Either the Stiffness Index T-score or X-ray absorptiometry T-score can be utilized by a physician, in conjunction with other clinical risk factors, to provide a comprehensive skeletal assessment.

The Stiffness Index has a precision error in older women comparable to that of x-ray absorptiometry, which makes it suitable for monitoring bone changes.

We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

CDRH will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

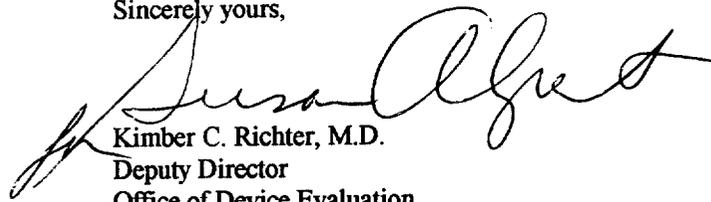
Page - 2 - Mr. Kenneth Buroker

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
9200 Corporate Blvd.  
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Jack Monahan at (301) 594-1212.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Kimber C. Richter", written over a horizontal line.

Kimber C. Richter, M.D.  
Deputy Director  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

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Issued: 3-4-98

#### CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effectuated" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effectuated" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effectuated." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

(a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

(b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mix-up of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

(3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984. This regulation was replaced by the reporting requirements of the Safe Medical Devices Act of 1990 which became effective July 31, 1996 and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to the FDA whenever they receive or otherwise become aware of information, from any source, that reasonably suggests that a device marketed by the manufacturer or importer:

- (1) May have caused or contributed to a death or serious injury; or
- (2) Has malfunctioned and such device or similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for a PMA, the manufacturer shall submit the appropriate reports required by the MDR Regulation within the time frames as identified in 21 CFR 803.10(c) using FDA Form 3500A, i.e., 30 days after becoming aware of a reportable death, serious injury, or malfunction as described in 21 CFR 803.50 and 21 CFR 803.52 and 5 days after becoming aware that a reportable MDR event requires remedial action to prevent an unreasonable risk of substantial harm to the public health. The manufacturer is responsible for submitting a baseline report on FDA Form 3417 for a device when the device model is first reported under 21 CFR 803.50. This baseline report is to include the PMA reference number. Any written report and its envelope is to be specifically identified, e.g., "Manufacturer Report," "5-Day Report," "Baseline Report," etc. Any written report is to be submitted to:

Food and Drug Administration  
Center for Devices and Radiological Health  
Medical Device Reporting  
PO Box 3002  
Rockville, Maryland 20847-3002

Copies of the MDR Regulation (FOD # 336&1336) and FDA publications entitled "An Overview of the Medical Device Reporting Regulation" (FOD # 509) and "Medical Device Reporting for Manufacturers" (FOD #987) are available on the CDRH WWW

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Home Page. They are also available through CDRH's Fact-On-Demand (F-O-D) at 800-899-0381. Written requests for information can be made by sending a facsimile to CDRH's Division of Small Manufacturers Assistance (DSMA) at 301-443-8818.

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## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### 1. GENERAL INFORMATION

Device Generic Name      Bone Sonometer

Device Trade Name:      Achilles+ Ultrasonometer  
Applicant's Name:      Lunar Corporation  
313 W. Beltline Highway  
Madison, Wisconsin 53713

608-274-2663

Premarket Approval Application (PMA) Number: P970040

Date of Notice of Approval to the Applicant: June 26, 1998

### II. INDICATIONS FOR USE

The Achilles+ measures ultrasound variables of the os calcis to provide a clinical measure called Stiffness Index. The Stiffness Index indicates risk of osteoporotic fracture in postmenopausal women comparable to bone mineral density (BMD) as measured by X-ray absorptiometry at the spine or hip.

Stiffness Index results expressed as T-scores are used to assist physicians in the diagnosis of osteoporosis in the same way as are T-scores obtained by X-ray absorptiometry. Either the Stiffness Index T-score or X-ray absorptiometry T-score can be utilized by the physician, in conjunction with other clinical risk factors, to provide a comprehensive skeletal assessment.

The Stiffness Index has a precision error in older women comparable to that of X-ray absorptiometry, which makes it suitable for monitoring bone changes.

### III. DEVICE DESCRIPTION

The Achilles+ is a bone ultrasonometer that uses high frequency sound waves (ultrasound) to evaluate bone status in the heel (the os calcis). Achilles+ measurements are performed with the patient seated and with their foot placed into the heel bath of the Achilles+. The heel is surrounded by 100 cc of warm water; water is the optimum medium for the transmission of ultrasound. A transducer on one side of the heel bath converts an electrical signal into a sound wave which passes through the water and the patient's heel. A transducer on the opposite side

passes through the water and the patient's heel. A transducer on the opposite side of the heel receives the sound wave and converts it to an electrical signal that is analyzed by the Achilles+ program. The Achilles+ measures speed of sound (SOS) and the frequency-dependent attenuation of the sound waves (broadband ultrasound attenuation, BUA) and combines them to form a clinical measure called the Stiffness Index.

The Achilles+ consists of the following components:

**Control Board:** The control board coordinates all internal functions, digitizes transducer outputs, and calculates ultrasound parameters. Software is stored on ROM (Read Only Memory). This board also interfaces with the internal printer, the liquid crystal display (LCD) screen, and the optional external computer.

**Foot-well:** The subject places their heel in the foot-well for measurement. The foot-well receives water to act as a coupling medium for the ultrasound signal.

**Sending Transducer:** The sending transducer is the ultrasound transducer which emits the sound waves used in measurement. This transducer converts an electrical pulse into a sound wave.

**Receiving Transducer:** The receiving transducer receives the sound waves from the transducer. This transducer converts the sound wave into an electrical signal.

**Fill Water Bottle:** The fill water bottle is a water reservoir which supplies fresh water to the foot-well.

**Heater:** The heater warms the water to approximately 37°C before entry into the foot-well.

**Drain Water Bottle:** The drain bottle receives water from the foot-well after completion of the measurement.

**Optional Computer:** When operated from the external computer (i.e., Intel 486 or better), the Achilles+ relies on the computer for primary control and operator interface. The computer provides an additional benefit of database functions, and full-size report printing.

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The ultrasound signal is emitted from the Send Transducer and propagates through the water and heel. The signal is detected by the Receive Transducer. The signal is digitized by the Control Board for analysis or data transfer to the computer. All data analysis is performed digitally. The algorithms are identical, whether performed by the internal control board, or via the external computer. The digitized data are analyzed to calculate speed of sound (SOS) and broadband ultrasound attenuation (BUA) values.

Measurement of SOS in the heel involves accurate determination of the transit time of a sound wave as it passes through the heel. Transit time is the amount of elapsed time between the beginning of the transmitted wave pulse (trigger pulse) and the beginning of the received wave pulse (received signal).

SOS is directly related to the mass of material (in this case tissue and bone) in the ultrasound beam. SOS values are referenced to water, which has a known value at any given temperature. The precision error of SOS in vivo on the heel is about 4 m/s. A typical value of SOS in trabecular bone is ~1520 m/s.

Measurement of BUA involves sending a broadband ultrasound pulse through the heel and measuring the attenuation of discrete frequencies. Sending a voltage spike into the ultrasound transducer generates a sound wave with a broad frequency spectrum. The received frequency spectrum is mathematically processed to quantify discrete frequencies in a function called Discrete Fourier Transform (DFT).

The net attenuation at each frequency between 250 and 550 kHz is provided by subtracting the values in this broad frequency spectrum from values obtained by transmitting a sound wave through a weakly attenuating reference medium, such as water. A regression line is then drawn through the points on the net attenuation curve to obtain the attenuation slope (dB/MHz). The slope of the regression line is the BUA value. The Achilles+ measures BUA with a precision error of approximately 1.7 dB/MHz in vivo.

Achilles+ combines SOS and BUA values into a unitless clinical measure called Stiffness Index. This Index is calculated as  $(0.68 \text{ BUA} + 0.28 \text{ SOS}) - 420$ . This formula is constructed so that BUA and SOS make approximately equal contributions to the Stiffness Index over the range of expected clinical values. For example, at typical values of BUA and SOS in young normal women (120 dB/MHz and 1560 m/s), BUA and SOS each contribute 50%; at typical values in the elderly (100 dB/MHz and 1520 m/s), each variable again contributes 50%.

The Achilles+ provides an output of the patient's Stiffness Index with associated precision error (for example  $92 \pm 2$ ). The precision error has been derived from a

large number of independent studies. The Achilles+ also plots a patient's Stiffness Index compared to reference values. Reference values are derived from a population database composed of non-Hispanic Caucasian women between 20 and 35 years of age (See Clinical Study BF3501). The bars on the reference graph are used to compare the patient's Stiffness Index results to the expected results for a 20-35 year old subject. The expected young adult value for a 20-35 year old female is a Stiffness Index of 100. Each bar represents one standard deviation from the young adult value. The patient's ultrasound T-score is calculated by the number of standard deviations from the young adult value.

#### **IV. CONTRAINDICATIONS**

There are no known contraindications associated with the use of the Achilles+.

#### **V. WARNINGS AND PRECAUTIONS**

Warnings:

1. Do not operate the Achilles+ without first reading the Operator's Manual.
2. Read the Essential Prescribing Information before prescribing the Achilles+ or interpreting results.
3. The Achilles+ is not intended for measurement of patients under 20 years of age. Reference data is not available for patients who are less than 20 years old.
4. Do not use the Achilles+ for subjects with breached skin or open sores on the foot or heel area. Doing so can increase the risk of transmission of infection between patients.
5. The Achilles+ is a Non-Critical Patient Contact Device. It requires low-level disinfection (reprocessing) between patient measurements. Doing so can help prevent transmission of infection between patients.
6. Make sure the Computer is at least 1.5 meters (5 feet) from the patient to prevent electrical shock during PC operation. The patient must not touch the computer when their foot is positioned in the heel bath.

Precautions:

1. You must complete a quality assurance (QA) procedure each week. If the procedure fails two times, contact the LUNAR Service Department or your LUNAR distributor
2. Do not attempt any repairs. The Achilles+ contains no user-serviceable parts.
3. Do not let liquids touch the computer when operated from an external computer.
4. Do not put any electric or battery-operated devices in the heel bath.

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

Traditional methods used for the estimation of BMD expose the patient and operator to ionizing radiation. These methodologies include single energy X-ray absorptiometry (SXA), dual energy X-ray absorptiometry (DXA or DEXA), quantitative computed tomography (QCT), single photon absorptiometry (SPA) and dual photon absorptiometry (DPA). Of these techniques SXA,DXA and SPA have been used specifically for the estimation of BMD of the calcaneus.

Of the traditional x-ray based methods for assessing bone density, DXA and SXA techniques are the most widely used. These established techniques estimate BMD at a variety of anatomical sides including the heel, by measuring the attenuation of X-rays due to passage through the bone. In addition, there are several bone sonometers that are currently being marketed for assessment of a patient's skeletal status (fracture risk).

## VII. MARKETING HISTORY

The Achilles+ Sonometer has been commercially available to markets outside the United States since late 1991. Over 800 sonometers have been manufactured by Lunar in the U.S. for export to Japan under 801E export approval. European sales of the Achilles+ have been based on units manufactured by Lunar GmbH (a subsidiary in Germany). A summary of the distribution of Achilles+ by country is provided in Table 1.

**Table 1. Achilles+ Marketing History by Country**

EUROPE*		ASIA PACIFIC		LATIN AMERICA		N. AMERICA	
Germany	218	Japan	862	Brazil	15	US**	11
Italy	61	Korea*	162	Columbia	13	Canada	11
Poland	39	Australia	15	Other	20		
France	34	Taiwan	11				
Spain	25	Other	15				
Sweden	25						
Other	115						
TOTAL	516	TOTAL	1065	TOTAL	48	TOTAL	22

\*Manufactured by LUNAR GmbH \*\* For investigational use only

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

There have been no reported adverse effects associated with the use of the Achilles+. The device has not been withdrawn from marketing in any country for any reason related to safety or use.

## **IX. SUMMARY OF PRECLINICAL STUDIES**

The Achilles+ sonometer is considered a non-critical, reusable medical device which externally contacts with patients for 3-5 minutes per measurement. There were four general areas of potential patient risk identified with the operation of the Achilles+:

1. Transference of disease via patient contact with the Achilles+.

A "Cleaning Effectiveness Study" was conducted in order to validate the Achilles+ cleaning (reprocessing) procedures. Product labeling for reprocessing has been developed in accordance with FDA labeling regulations 21 CFR 801. The test was conducted in accordance with the requirements of the FDA Good Laboratory Practice (GLP) Regulations, 21 CFR 58. The results of the study demonstrated that by performing the cleaning procedure between patients as specified in the Operator's manual, challenge organisms were reduced by >99%.

2. Bio-compatibility of Achilles+ components which contact patients.

The potential exists for adverse reaction due to contact with components of the Achilles+. The composition of contact components are controlled and specified in the LUNAR manufacturing process. They verified that the supplier of the material which comprises all contact surfaces on the Achilles+, routinely performs appropriate tests for external contact devices, contacting with intact surfaces, for transient periods (<5 minutes). The results of this testing demonstrated that under the test conditions CYCOLAC HP-30-2679F is a non-irritant, shows no evidence of delayed contact dermal sensitization, and is non-toxic.

3. Potential for electric shock

The Achilles+ has been certified to pass IEC-60601 guidelines for electrical safety and electromagnetic compatibility (EMC).

4. Biologic effect of ultrasonic transmission through the heel.

The use of ultrasound in medical instrumentation is well documented and considered to be safe. The Achilles+ has been tested to meet AIUM guidelines for diagnostic acoustic output.

## **X. SUMMARY OF CLINICAL STUDIES**

Three clinical studies were performed to meet the following objectives:

1. compare the Stiffness Index results to calcaneal bone mineral density determined by X-ray absorptiometry;
2. assess the precision of the Stiffness Index versus calcaneal BMD by X-ray absorptiometry in elderly women;
3. compare the Stiffness Index versus axial BMD to indicate the risk of osteoporotic fracture in post menopausal women;
4. obtain reference data on >600 normal white adult women between the ages of 20 and 79; and
5. determine the safety of the Achilles+ Sonometer.

### FOSAMAX 349 Study

Fosamax 349 was a multicenter study conducted in the USA to investigate calcaneal absorptiometry and calcaneal ultrasonometers. It was designed to examine the precision and correlation of calcaneal bone densitometers in comparison to results obtained using dual energy X-ray absorptiometry in ~150 Caucasian women, age 25 to ~80 years. The population consisted of 3 equal size groups: one young control group, and 2 osteoporotic test groups. One osteoporotic group consisted of women >55 years old with BMD more than 2.5 standard deviations below normal at the femoral neck, trochanter or lumbar spine, and with no history of osteoporotic fracture. The other osteoporotic group consisted of women >55 years old with BMD more than 2.5 standard deviations below normal at the femoral neck, trochanter or lumbar spine, and who had suffered at least one osteoporotic fracture.

The study employed sonometers from 4 manufacturers and 2 X-ray densitometers, as seen in Table 2, to measure each study participant.

**Table 2. Test Instrument Summary**

Technology	Instrument	Manufacturer	Diagnostic Result
QUS*	Achilles+	Lunar	BMD <sub>QUS</sub> , a combination of speed of sound (SOS, m/s) and broadband ultrasound attenuation (BUA, dB/MHz)
QUS	UBA575+	Hologic	BUA
QUS	CUBA	McCue	BUA
QUS	Ultrasonometer	OsteoScience	Ultrasound Bone Index (UBI)
X-ray (SXA)	OsteoAnalyzer	Dove Medical	Bone Mineral Content (BMC, g)
X-ray (DXA)	QDR 1500/2000	Hologic	Bone Mineral Density (BMD, g/cm <sup>2</sup> )

\*QUS = quantitative ultrasound

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## Results

Short-term precision (%CV) was evaluated by measuring each subject five times over one week. The precision error was standardized (%SCV) using 95% of the range of individual variation as a denominator (Table 3). There were a significant number of scans deleted from the "per protocol" precision analysis for the OsteoAnalyzer. This reduced its precision error from 5.9% to 2.0%. No measurements were deleted for the Achilles+. The standardized precision error of Stiffness Index was significantly lower than that for Achilles+ BUA, and was comparable to the precision for BMD.

**Table 3. Comparison of Short-term Precision**

	All Scans		Per Protocol	
	% CV	% SCV	% CV	% SCV
Achilles+ (BUA)	1.8	4.0	1.8	4.0
Achilles+ (SOS)	0.3	2.7	0.3	2.7
Achilles+ (Stiffness)	2.4	2.5	2.4	2.5
OsteoAnalyzer (BMD)	5.9	5.2	2.0	1.8
QDR (BMD)	2.0	2.3	2.0	2.4
CUBA (BUA)	5.2	4.3	5.2	4.3
UBA575 (BUA)	6.6	5.3	6.6	5.3
Ultrasonometer (UBI)	7.3	7.0	7.0	6.8

The precision error of the Achilles+ was significantly lower ( $p < 0.05$ ) than that of other QUS instruments, but did not differ ( $p > 0.05$ ) from that of BMD using the QDR.

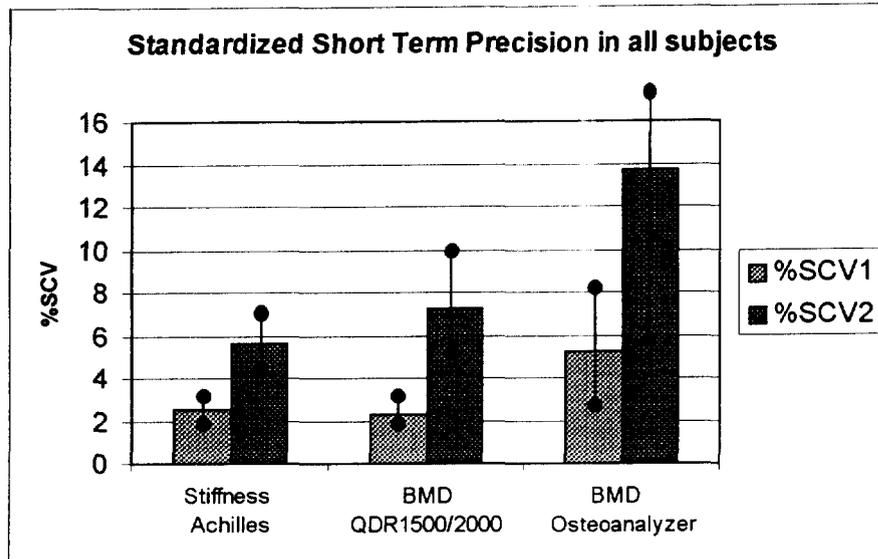
The FOSAMAX 349 study demonstrated that the short-term standardized precision error (%SCV) of the Stiffness Index was comparable ( $P > 0.05$ ) to the %SCV of os calcis BMD (see Figure 1).

The FOSAMAX 349 study also compared the short-term precision (%CV) in osteoporotic subjects, versus the %CV in young adult controls. The Stiffness Index demonstrated equivalent %CV in the osteoporotic cohort versus young adults (2.3% vs. 2.4%,  $p = 0.78$ ). BMD by both the QDR1500/2000 and the OsteoAnalyzer exhibited a higher precision error in osteoporotic subjects versus young controls (see Figure 2), which in the case of the OsteoAnalyzer was statistically significant ( $p < 0.001$ ).

The precision of the Stiffness Index is nominally 2% (the average among 27 studies was 1.7%). The detailed study by Rosenthal [25] showed a precision error of 2.0% in 408 subjects who had T-scores for Stiffness Index that were less than -2.0, versus 2.15% in 200 subjects with T-scores  $> -1$ . These studies confirm the findings of

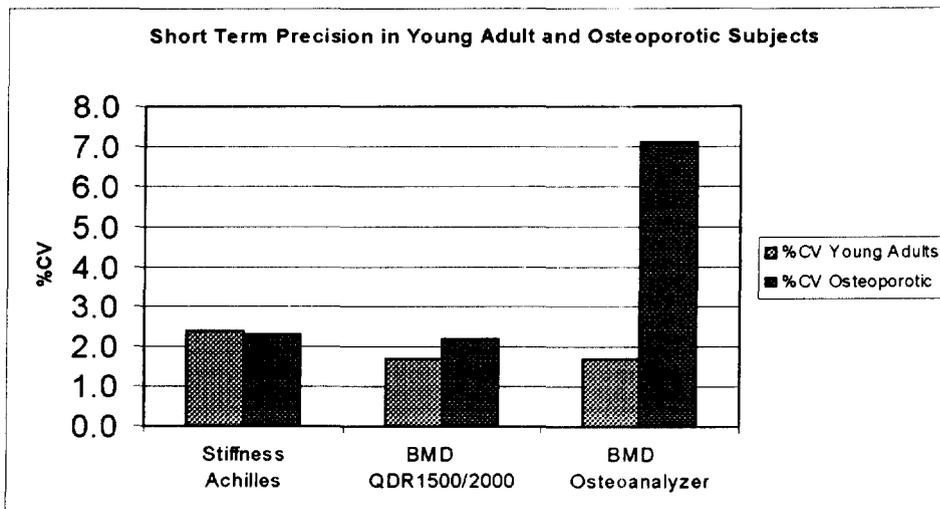
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FOSAMAX 349 that the Stiffness Index provides equivalent precision error in subjects with low density versus those with normal density.



**Figure 1. Standardized precision comparison, pooled cohorts, Stiffness Index Vs BMD, and 95% CI**

%SCV1=SD/95% range, %SCV2=SD/(young adult mean - osteoporotic group mean)



**Figure 2. FOSAMAX 349 %CV in young adult versus osteoporotic subjects**

Note: Standardized precision not required for precision comparison across cohorts.

Based on the information FDA concluded that the Stiffness Index has a precision error in older women comparable to that of X-ray absorptiometry. This precision error is not significantly different in osteoporotic subjects compared to young

adults. The short term standardized precision of the Stiffness Index is equivalent to that of BMD of the os calcis measured by X-ray absorptiometry and the %CV is nominally 2%.

Fracture risk was assessed using T-scores, Z-scores, and ROC analysis. The T-score is a commonly used index to clinically assess fracture risk. The ability to correctly classify the test group subjects (osteoporotic) from controls was assessed using two criteria: 1) T-score <-2.5; and 2) T-score <-2.0. In all cases, the Achilles+ correctly identified more osteoporotic subjects (with and without fractures) than the QDR-1500/2000. The ability of Stiffness Index to differentiate osteoporotic subjects from young normal controls was equivalent or superior ( $p < 0.05$ ) to calcaneal X-ray absorptiometry using T-score thresholds of  $T < -2.0$  and  $T < -2.5$ .

Another method of assessing fracture risk uses the Z-score. Z-score is defined as the difference of the direct measurement and the mean of an age matched reference, divided by the standard deviation of the age matched reference. The Z-score inherently adjusts for age. In the case of Fosamax 349, the Z-score also adjusts for age and BMD as all test subjects are >55 years old and meet minimum BMD threshold. The Z-score was calculated for osteoporotic subjects with fractures for all instruments. The Achilles+ demonstrated the lowest Z-score versus X-ray absorptiometry as seen in Table 4.

**Table 4. Z-Scores derived by Sonometry and X-ray Absorptiometry**

	Mean Osteoporotic non-fracture	SD Osteoporotic non-fracture	Mean Osteoporotic with fracture	Z-score Osteoporotic with fractures
Achilles+ (BUA)	102.1	7.9	97.2	-0.63
Achilles+ (SOS)	1527	26.2	1510	-0.64
Achilles+ (Stiffness)	75.6	11.9	67.7	-0.67
OsteoAnalyzer (BMD)	300	64.8	260.4	-0.61
QDR (BMD)	0.43	0.09	0.39	-0.48

ROC curves were generated for classifying test subjects from controls. Curves were generated by varying the criteria for correct classification and calculating the true positive fraction (TPF) and false positive fraction (FPF) each time.

**Table 5. Area under ROC Curves**

	Osteoporotic subjects vs Young Controls	Osteoporotic with fractures vs Osteoporotic non-fracture
Achilles+ (Stiffness)	0.93	0.71
OsteoAnalyzer (BMC)	0.88	0.65
QDR 1500/2000 (BMD)	0.88	0.63

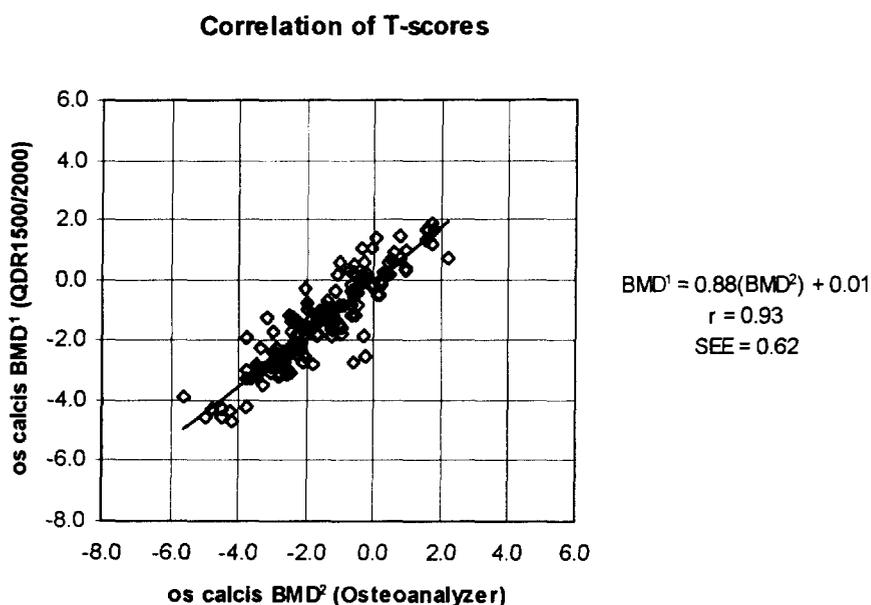
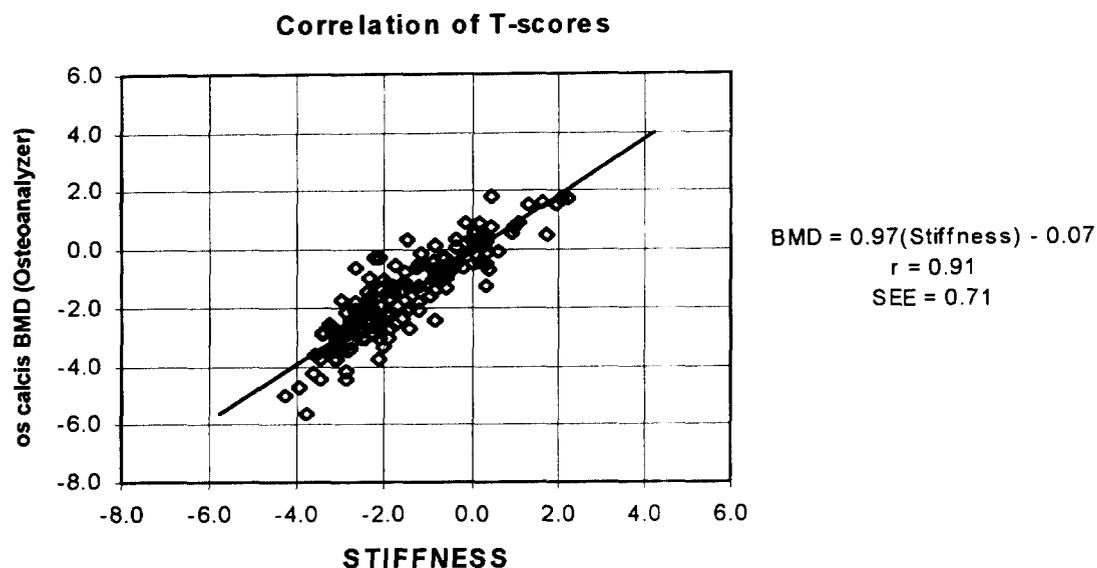
The FOSAMAX 349 study compared discrimination using area under ROC curves (Table 5). The ability of Stiffness Index to discriminate osteoporotic subjects from young adult controls was not different ( $p>0.05$ ) than BMD of the spine, femur or os calcis. None of the X-ray densitometers or ultrasonometers were able to significantly distinguish between osteoporotic fracture and non-fracture subjects using ROC analysis, due to: (a) the non-fracture group had been selected for low BMD values, and (b) the small sample sizes of the groups ( $n=50$ ).

The FOSAMAX 349 study demonstrated that Stiffness Index correlates with os calcis BMD by X-ray absorptiometry ( $r=0.91$ ). This correlation was not significantly different ( $p>0.05$ ) than the correlation ( $r=0.93$ ) of os calcis BMD as measured by two different X-ray absorptiometers (Table 6). The ultrasound T-score for Stiffness Index predicted the T-score using X-ray absorptiometry with a small standard error of the estimate ( $SEE=0.7$ ) that was not significantly different ( $p>0.05$ ) than the SEE between two different X-ray absorptiometers at the same site ( $SEE=0.6$ ).

**Table 6. Correlation Stiffness Index versus BMD by X-ray absorptiometry**

	Pearson Correlation		SEE (T-score)	
	BMD OsteoAnalyzer	BMD QDR1500/2000	BMD OsteoAnalyzer	BMD QDR1500/2000
Stiffness Achilles+	0.91	0.86	0.71	0.76
BMD OsteoAnalyzer		0.93		0.62

The FOSAMAX 349 study also showed that the regression of T-scores by Stiffness Index versus T-scores by os calcis BMD was not significantly different from unity (slope = 0.97,  $SEE=0.04$ ), thus demonstrating equivalent scaling and intra-population SD (Figure 3).

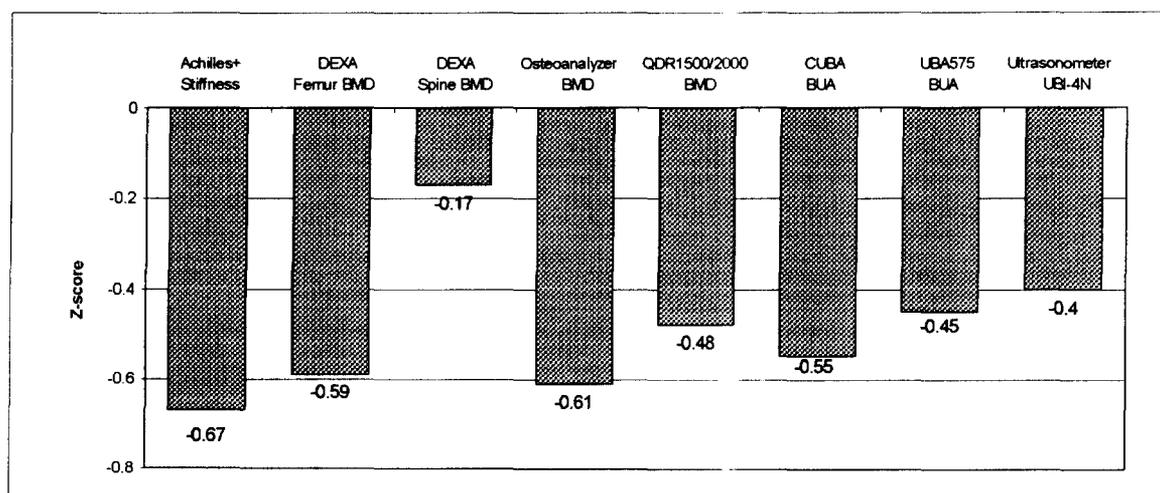


**Figure 3. Relationship of Stiffness Index and BMD from FOSAMAX 349**

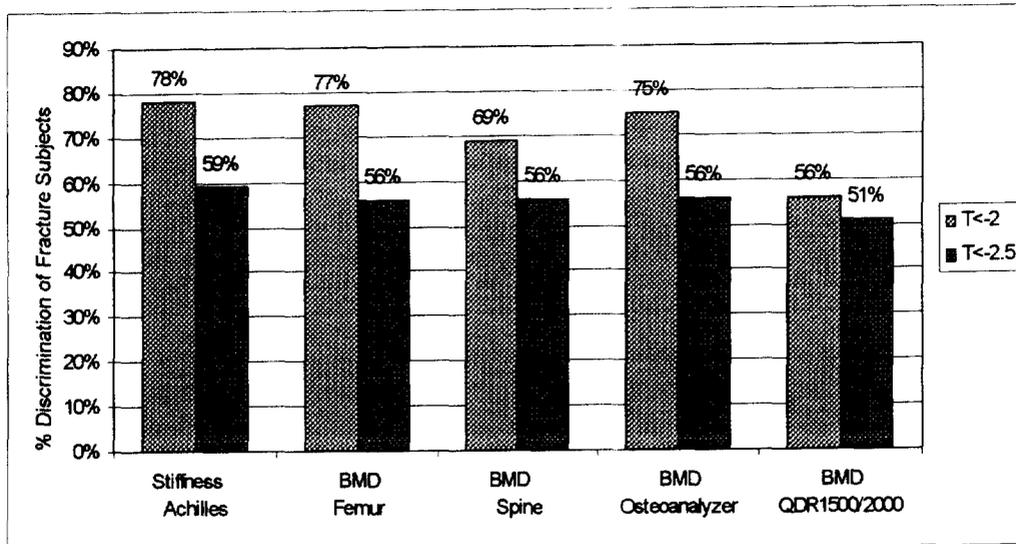
FDA concluded that the Stiffness Index can estimate BMD as determined by X-ray absorptiometry of the os calcis in adult women. This is based on the correlation ( $r=0.9$ ) of the Stiffness Index with BMD. This correlation is similar to that observed between BMD values determined by two different X-ray densitometers at the same site. The Stiffness Index also appears to predict the T-score of the os calcis BMD with similar SEE compared to two X-ray absorptiometers from different manufacturers.

The FOSAMAX 349 study adds an additional level of control. Both the fracture and non-fracture test groups of postmenopausal women had low BMD at the femur neck or trochanter. Stiffness Index demonstrated the lowest Z-score, although differences between Stiffness Index and os calcis BMD did not reach statistical significance ( $p=0.07$ ). The SD for Stiffness Index was 11.9 which is comparable to the SD (13.0) in a group of 70-79 year old women as found in the BF3501 study. The Z-score (-0.67) as calculated from FOSAMAX 349 is therefore somewhat comparable to that which would be expected (-1.0) if the non-fracture controls in FOSAMAX 349 had not selected for low BMD (Figure 4).

The FOSAMAX 349 study also tested the ability of Stiffness Index and BMD to discriminate osteoporotic subjects with fractures from young adult controls using T-score thresholds of  $T < -2$  and  $< -2.5$  (Figure 5). The discriminatory ability of Stiffness Index was not significantly different than BMD by X-ray absorptiometry at the spine, femur, or at the os calcis (using the OsteoAnalyzer). Stiffness Index was superior ( $p=0.025$ ) to os calcis BMD measured with the QDR using a T-score threshold of -2.0.



**Figure 4. FOSAMAX 349 Comparison of Z-scores of osteoporotic subjects with fractures**



**Figure 5. FOSAMAX 349 Comparison of Fracture Discrimination by T-score Thresholds**

### EPIDOS Study

EPIDOS was a multicenter prospective study conducted in France. The study was sponsored by INSERM to assess the value of calcaneal ultrasonometry and DEXA of the femur in prospectively assessing fracture risk in elderly females (>75 years old). It is the largest prospective study to date comparing DEXA and ultrasonometry in assessing fracture risk. Five centers in France participated.

A total of 5662 subjects received ultrasound and DEXA measurements over the course of 3 years. Follow-up occurred every 4 months by means of a questionnaire. Subjects were encouraged to report all falls and fractures at which time an extensive interview would occur. The maximum follow-up duration was defined as 3 years, 3 months. Fewer ultrasound measurements were taken because the Achilles+ system was not available during the initial portion of the study. Therefore the mean follow-up for the Achilles+ data is 2 years.

### Results

The estimation of relative risk of fracture was calculated using three different criteria: (1) Cox proportional regression model; (2) fracture incidence by combined variables BMD and Stiffness; and (3) ROC analysis. The Cox proportional regression model was used to estimate the relative risk of first hip fracture. The follow-up time for fracture subjects was recorded as time between baseline and the fracture occurrence. The relative fracture risk was estimated for one SD reduction in the bone variable. The results are shown in Table 7. The estimated relative risk was similar for all of the bone variables ( $p>0.05$ ).

**Table 7. Relative Risk by Bone Variable**

	Relative Risk
Femur Neck BMD	2.1
Stiffness	2.1
BUA	2.1
SOS	1.9

The incidence of fracture was calculated for subjects falling above and below the medians for both BMD and Stiffness. Fracture incidence was calculated in a 4x4 matrix. The results are shown in Table 8.

**Table 8. Fracture Incidence by BMD and Stiffness Index**

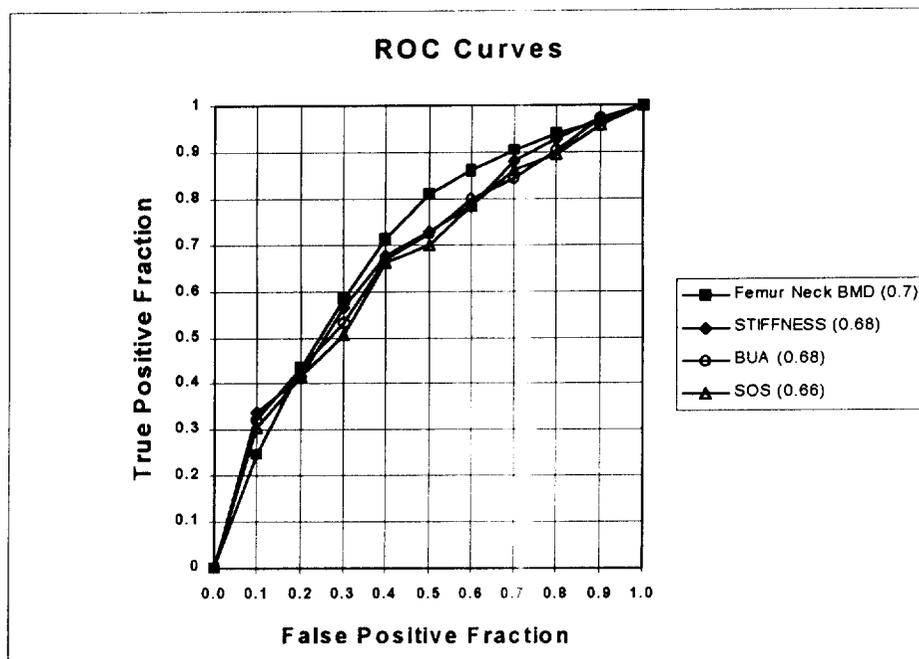
	BMD Above Median (>0.703 g/cm <sup>2</sup> )				BMD Below Median			
	Non-Fractured	Fractures	woman years (k)	rate/1k years	Non-Fractured	Fractures	woman years (k)	rate/1k years
STIFFNESS ABOVE MEDIAN	1807	9	3.7	2.5	993	22	2.07	10.6
STIFFNESS BELOW MEDIAN	1004	13	2.0	6.4	1743	71	3.53	20.1

Median Stiffness = 65.09

The combination of BMD and Stiffness Index demonstrated the highest risk stratification with women in the highest risk group (low BMD and low Stiffness) having 8 times the incidence of fracture versus the lowest risk group (high BMD and high Stiffness). This is contrasted to a gradient of only 4.3 using the median of BMD alone, or a gradient of 2.8 using the median of Stiffness Index alone.

An ROC analysis was performed for all bone variables. Areas under the curve were calculated and compared at the 95% level. The results are shown in Figure 6 below.

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**Figure 6. EPIDOS ROC Results**

The data from the EPIDOS study demonstrate that the Stiffness Index can be used to predict the risk of future fracture in elderly patients (>75 years). However, no conclusions can be drawn on the basis of this study regarding patients between menopause and 75 years of age.

### BF3501 Study

BF3501 was a randomized, controlled study undertaken in the USA to collect reference data on adult Caucasian, non-Hispanic females using the Achilles+ sonometer. Five U.S. centers in four locations participated. The study had two major objectives:

1. to determine the Stiffness Index for women between 20 and 35 years of age; and
2. to collect ultrasound values on a sample of females between 40 - 79 years of age that would permit the establishment of an empirical relationship between age and Stiffness Index.

All subjects were randomly recruited utilizing public telephone listings. Qualification of each subject was determined by obtaining a medical history including prior medications, and a disease directed physical examination on subjects with known ailments. Subjects with current or historical medical conditions associated with or known to cause low bone mass were excluded. Subjects who have received medications known to alter bone metabolism were also

excluded. All subjects had their right os calcis measured, except for those cases in which the right os calcis was adversely affected due to infection or other injury. In this case, the left os calcis was measured.

## Results

Values for Stiffness Index in young adult subjects were normally distributed without significant differences in mean or standard deviation among geographic sites and were therefore pooled. The mean and standard deviation were calculated for the purpose of generating T-scores. T-scores allow comparison of a patient's results to a "young adult" reference. Values were calculated from subjects 20 to 35 years old (n=214, Stiffness Index 99.9, SD = 15.8). The standard error of the mean was - 1%.

Pooled data from all subjects (n=734, age 20-79) were used to fit a regression curve of Stiffness Index vs. age (Figure 7). This curve is used for calculation of a patient's Z-score, and percent age-matched value. The regression curve demonstrates a decline of Stiffness Index which averages -1% per year after age 50.

A linear regression of age versus Stiffness Index was calculated for the pooled data for women at ages 40 to 79 years (Table 9).

**Table 9. Regression of Stiffness Index with Age (40-79 years old)**

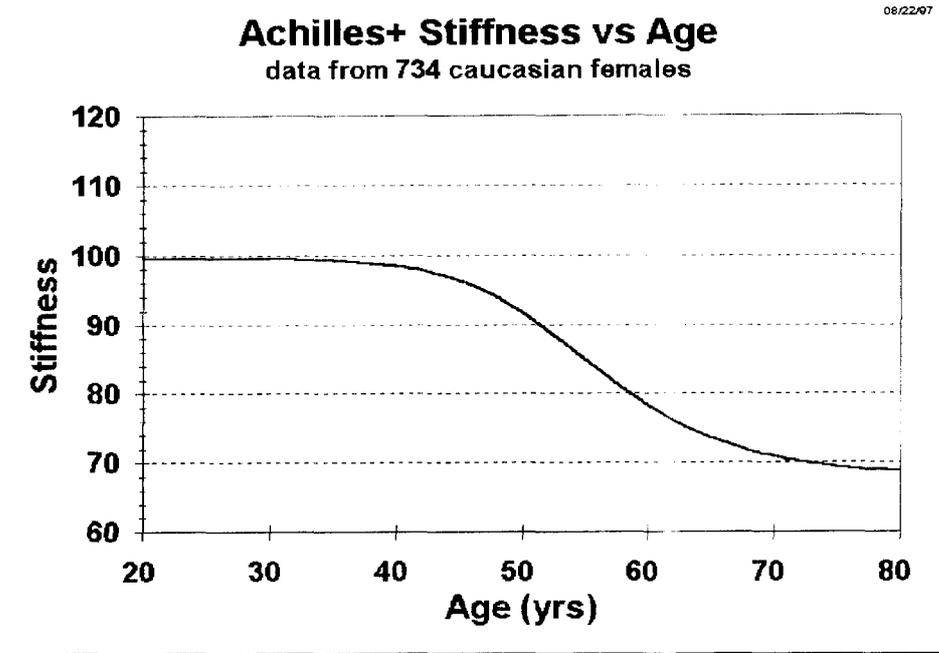
	Regression of Stiffness on Age (Age >= 40 yr.)				
	OR	NB	FL	ME	pooled
<b>slope</b>	-1.123	-1.055	-0.921	-0.942	-0.993
<b>SE slope</b>	0.167	0.143	0.133	0.100	0.112
<b>intercept</b>	146	147	133	138	141
<b>SEE</b>	14.3	17.7	14.7	14.0	15.4

Multiple regression analysis of Stiffness Index vs. age from all sites was carried out for subjects 40-79 years old. The full regression model contained terms for age, and dummy variables for slope and intercept differences among sites. Terms with coefficients significantly different than zero ( $\alpha = 0.05$ ) were included in the final model. The regression coefficient for age was 0.98 with a 95% confidence interval of -0.85 to -1.10.

As a post-hoc analysis, a curve fit was performed to select an empirical regression equation of unadjusted Stiffness Index vs age. Using values from all of the selected study subjects, the program selected the logistic dose response form as having the highest  $r^2$ . Figure 7 graphically demonstrates the equation used to calculate the decline of Stiffness Index with age.

The Stiffness Index demonstrated an age regression described by:

$$\text{Age Regression of the Stiffness Index} = 68.0 + \frac{31.6}{\left[1 + \left(\frac{\text{age}}{55.9}\right)^{10.1}\right]}$$



**Figure 7. Regression Stiffness Index vs Age**

Based on the curve described above, the age range selected for young reference values was 20 to 35 years (n=214). Young reference mean and standard deviation, along with 95% confidence intervals calculated as described above, are shown in Table 10 below:

**Table 10. Young Reference Values Age 20 - 35 Years Old (n=214)**

	value	95% confidence interval
mean	99.9	97.8 - 102.1
standard deviation	15.8	14.6 - 17.2

Summary of Additional Supporting Studies

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Nine retrospective studies [7,8,9,10,11,12,13,14,15] compare the Z-scores of axial BMD and Stiffness Index in subjects with osteoporotic fractures. Table 11 updated

HIP FRACTURE		Variable	Control	FX	Z-Score	P
Schott [16]	Stiffness		67.9	54.1	-1.0	0.0001
	Neck BMD		0.72	0.63	-0.8	0.0001
	Age		80 ± 9	83 ± 9		
	n =		86	43		
Turner et al [17]	Stiffness		74.8	64.7	-0.9	0.01
	Neck BMD		0.740	0.665	-0.7	0.01
	Age		73 ± 8	82 ± 7		
	n =		303	22		
Mautalen et al [18]	Stiffness		72.4	52.7	-1.6	0.001
	Neck BMD		0.79	0.63	-1.6	0.001
	Age		72 ± 3	74 ± 10		
	n =		29	54		
Sakata et al [19]	Stiffness		59.1	47.9	-0.9	0.0001
	Neck BMD		0.52	0.46	-0.9	0.008
	Age		78 ± 9	79 ± 9		
	n =		138	138		
Hans et al [20]	Stiffness		64.9	58.1	-0.7	0.001
	Neck BMD		0.71	0.64	-0.7	0.001
	Age		80 ± 4	82 ± 5		
	n =		5547	115		

#### SPINE FRACTURE

Yamazaki [21]	Stiffness		73.9	62.4	-2.1	0.001
	Neck BMD		0.745	0.603	-1.6	0.001
	Spine BMD		0.935	0.712	-2.1	0.001
	Age		65 ± 5	66 ± 5		
	n =		21	58		
Gonnelli et al [22]	Stiffness		86.5	69.9	-1.8	0.001
	Spine BMD		(0.851)	0.724	-1.3	0.001
	Age		58 ± 5	58 ± 6		
	n =		79	225		
Blankaert [23]	Stiffness		70.9	56.1	-1.0	0.01
	Neck BMD		0.76	0.62	-1.1	0.01
	Spine BMD		0.97	0.77	-0.9	0.01
	Age		63 ± 12	63 ± 12		
	n =		42	45		
Cepollaro [24]	Stiffness		81.2	63.9	-1.6	0.001
	Spine BMD		0.856	0.689	-1.3	0.001
	Age		58 ± 5	61 ± 6		
	n =		219	178		

**Table 11 Supporting Studies:**

**Discrimination comparison of fracture patients with age-matched controls.** with the ages of both the non-fracture controls, and the fracture subject shows and compares these Z-scores. There is little or no age difference between the fracture subjects, and the age-matched controls with no fractures a ( except in the study by Turner et al). These studies suggest that Stiffness Index provides an indicator of risk for (a) femur fracture in the elderly (>65 years), and (b) spine fracture in subjects under 65 years of age. However all of the studies listed in Table 11 are retrospective and are therefore subject to confounders. Prospective studies are the gold standard for assessment of fracture risk.

The prospective study by Thompson et al [29] demonstrates that Stiffness Index also indicates risk of fragility fracture in a younger postmenopausal population. Thompson et al examined 3180 women between the ages of 45 and 75 years over a mean follow-up of 31 months. The average age was 60.6 years at baseline. Odds ratios (OR) were calculated for all fractures traditionally considered as osteoporotic (distal, hip, vertebra, pelvis, humerus). Table 12 below summarizes the results. The odds ratio, per 1 SD decrease of age adjusted Stiffness was 1.91 (1.44-2.53 95%CI) for osteoporosis related fractures. This study is supported by several of the retrospective studies listed in Table 11 for women under 65 years.

**Table 12. Odds ratios for relative risk per 1 SD decrease in age adjusted Stiffness Thompson et al, in press, 1998**

ALL SUBJECTS		OSTEOPOROTIC FRACTURES	
Age	n	# fractures	Odds Ratio (95% CI)
60.8	3150	89	1.9 (1.4 - 2.5)

Thompson et al did not directly compare Stiffness Index to axial BMD. However, other prospective studies using axial BMD, in perimenopausal age groups, have produced comparable results. Kroger et al [26] followed 3140 women (mean age 53.4) over a two year period. The age-adjusted relative risk of any osteoporotic fracture per 1 SD decrease in spine and femur BMD were 1.67 and 1.61 respectively. Huang et al [27] followed 500 Japanese-American women (mean age of 62.9 at baseline) over 11 years. The relative risk of vertebral fracture (>20% height decrease) for 1 SD decrease in age-adjusted BMD was 1.67 for spine BMD, and 1.36 for os calcis BMD. Table 13 compares Thompson's results to prospective fracture studies using DEXA in women under 65 years of age. Figure 8 below shows the age-adjusted relative risk for major prospective fracture studies using ultrasonometry and BMD by X-ray absorptiometry. There is significant overlap of the 95% intervals of all of the studies, for a variety of sites and instruments. The two studies using Achilles+ found that Stiffness Index gave a relative risk of ~2 for a 1 SD decrease

from the normal mean, which is comparable to the relative risk for axial BMD, and somewhat better than the risk usually observed for peripheral BMD.

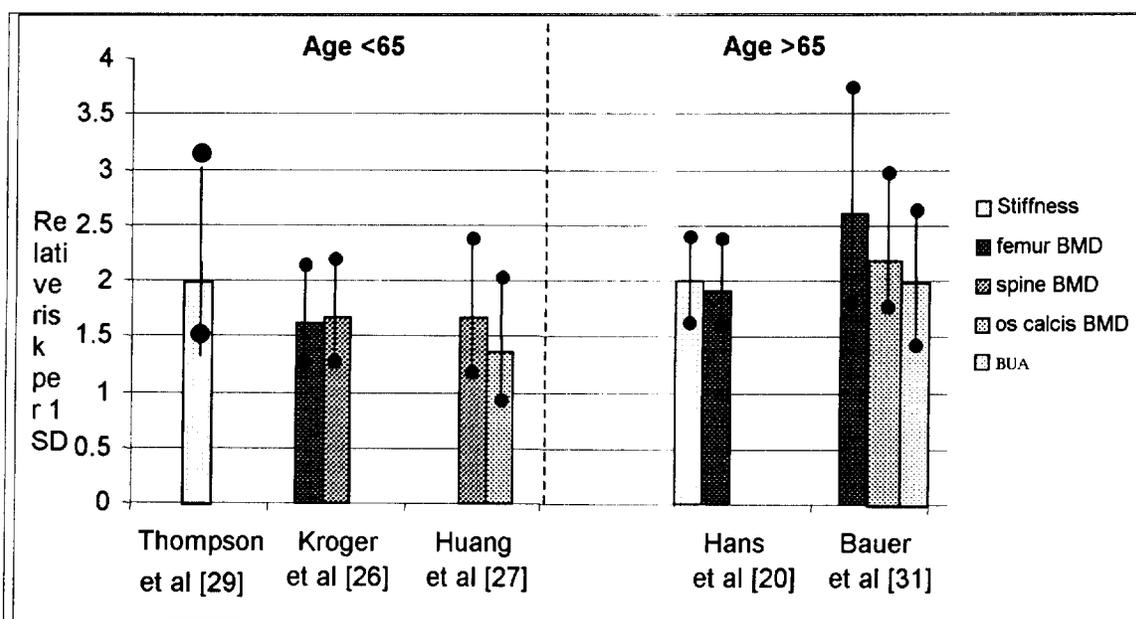
Based on the information provided by the sponsor including the prospective study by Thompson et al, FDA concluded that the Stiffness Index provides an indicator of osteoporotic fracture risk in postmenopausal women comparable to that obtained using axial BMD by X-ray absorptiometry. This conclusion has been extended to the elderly (>75 years of age) by the data provided in the EPIDOS study. Both the EPIDOS study and the Thompson study demonstrated that a Stiffness Index showing a 1 SD decrease from the mean of the value for the normal young adult population indicates a relative risk of 2 for femur fracture in the peri- and postmenopausal women. A number of retrospective studies, including FOSAMAX 349, demonstrate that the Stiffness Index is comparable to BMD as measured by X-ray absorptiometry in discrimination of subjects at risk of osteoporotic fracture.

**Table 13. Summary of prospective results in women under 65 years of age**

	Thompson [29]	Kroger [26]	Huang [27]	Stewart [28]
n	3180	3222	533	1000
Age	61 (+/- 9)	53 (+/- 3)	63 (+/- 5)	47 (+/- 1)
Average follow-up (yrs)	2.6	2.0	8.1	2.0
# osteoporotic fractures	89 <sup>a</sup>	64 <sup>a</sup>	72 <sup>b</sup>	18 <sup>c</sup>
Relative Risk (95%CI) per 1 SD	Stiffness Achilles+ 1.9 (1.4-2.5)	Spine BMD 1.7 (1.3-2.2)  Femur BMD 1.6 (1.2-2.1)	Spine BMD 1.7 (1.2-2.5)  Calcaneal BMD 1.4 (0.9-2.1)	Spine BMD 2.1 (1.2-3.8)  Femur BMD 1.4 (1.3-2.4)  BUA (UBA575) 1.4 (1.2-2.4)

<sup>a</sup> vertebral, femur, distal forearm, and humerus

<sup>b</sup> vertebral fractures, <sup>c</sup> all fractures



**Figure 8. Relative risk of fragility fracture per 1 SD in prospective studies  
All osteoporotic fractures in women <65, and femur fractures in women >65**

## **XI. CONCLUSIONS DRAWN FROM THE STUDIES**

### **A) RISK/BENEFIT ANALYSIS**

The Achilles+ is a useful clinical indicator of skeletal status, the clinical effectiveness of which compares to that of established densitometry (BMD), but without exposure to ionizing radiation. The low power level of ultrasound employed by the Achilles+ is significantly lower than the levels deemed safe and employed by medical ultrasound devices for other indications (e.g., imaging). Based on all of the evidence it is reasonable to conclude that the benefits of the Achilles+ outweigh the risk of illness or injury when it is used in accordance with the directions for use.

### **B) SAFETY**

No serious adverse reactions were reported among any subjects in the pivotal studies. This clinical experience combined with the additional clinical experience gained from the use of over 1,800 Achilles+ devices worldwide, demonstrates the safety of the Achilles+.

### **C) EFFECTIVENESS**

The studies employing the Achilles+ show that the device provides a clinical measure called Stiffness Index that indicates the risk of fracture in post-menopausal women comparable to bone mineral density measurements of the spine or hip obtained by X-ray absorptiometry. The Stiffness Index expressed as a T-score can be used by a physician in conjunction with other clinical risk factors to provide a comprehensive skeletal assessment.

## **XII. FDA Decision**

CDRH issued an approval order to Lunar for their Achilles+ on June 26, 1998. The applicant's manufacturing facility was inspected on March 20, 1998 and was found to be in compliance with the Good Manufacturing Practice Regulations (GMPs).

## **XIII. Approval Specifications**

Directions for use: See attached final labeling

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# 1

# Getting Started—Essential Prescribing Information

## Chapter 1 Contents

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Revised 7/98E

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## 1.1 Essential Prescribing Information

### 1.1.1 Device Description

The Achilles+ is a bone ultrasonometer that uses high frequency sound waves (ultrasound) to evaluate bone status in the heel (the os calcis). Achilles+ measurements are performed with the patient seated and with their foot placed into the heel bath of the Achilles+. The heel is surrounded by 100 cc of warm water: water is the optimum medium for the transmission of ultrasound. A transducer on one side of the heel bath converts an electrical signal into a sound wave which passes through water and the patient's heel. A transducer on the opposite side of the heel receives the sound wave and converts it to an electrical signal that is analyzed by the Achilles+ program. The Achilles+ measures speed of sound (SOS) and the frequency dependent attenuation of the sound waves (broadband ultrasound attenuation, BUA) and combines them to form a clinical measure called the Stiffness Index.

### 1.1.2 Indications for Use

The Achilles+ ultrasonometer measures ultrasound variables of the os calcis to provide a clinical measure called the Stiffness Index. The Stiffness Index indicates risk of osteoporotic fracture in postmenopausal women comparable to bone mineral density (BMD) as measured by X-ray absorptiometry at the spine or hip.

Stiffness Index results expressed as T-scores are used to assist physicians in the diagnosis of osteoporosis in the same way as are T-scores obtained by X-ray absorptiometry. Either the Stiffness Index T-score or X-ray absorptiometry T-score can be utilized by the physician, in conjunction with other clinical risk factors, to provide a comprehensive skeletal assessment.

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The Stiffness Index has a precision error in older women comparable to that of X-ray absorptiometry which makes it suitable for monitoring bone changes.

### **1.1.3 Contraindications**

There are no known contraindications associated with the use of the Achilles+.

### **1.1.4 Warnings**

- Do not operate the Achilles+ without first reading the Operator's Manual.
- Read the Essential Prescribing Information before prescribing the Achilles+, or interpreting results.
- The Achilles+ is not intended for measurement of patients under 20 years of age. Reference data is not available for patients who are not at least 20 years old.
- Do not use the Achilles+ for subjects with breached skin or open sores on the foot or heel area. Doing so can increase the risk of transmission of infection between patients.
- The Achilles+ is a Non-Critical Patient Contact Device. It requires low-level disinfection (reprocessing) between each patient measurement. Doing so can help prevent transmission of infection between patients. Refer to chapter 2 for reprocessing procedures.
- Make sure the computer is at least 1.5 meters (5 feet) from the patient to prevent electrical shock during PC operation. The patient must not touch the computer when their foot is positioned in the heel bath.

### **1.1.5 Precautions**

- You must complete a quality assurance (QA) procedure each week (refer to chapter 3). If the procedure fails two times, contact the LUNAR Service Department or your LUNAR distributor.
- Do not attempt any repairs. The Achilles+ contains no user-serviceable parts.
- Do not let liquids touch the computer when operating the Achilles+ with an external computer.
- Do not put any electric or battery-operated devices in the heel bath.

### **1.1.6 Adverse Events**

No adverse reactions or deaths were reported in 9,726 Achilles+ examinations performed in the pivotal clinical studies. There have been no reported adverse events associated with the use of, or operation of the Achilles+ ultrasonometer.

### **1.1.7 Clinical Studies**

There were four clinical studies performed involving 9,726 women. The clinical studies are described below.

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## Study 1: Representative Reference Data (Rosen et al<sup>4</sup>)

### Hypothesis:

Measurement of the Stiffness Index from a randomized representative sample of white women will provide a "young adult" reference, and an age regression curve for the calculation of T-scores and Z-scores.

### Methods:

Ambulatory white women, age 20 to 79 years were randomly recruited from the general population. Data were collected from four sites at different geographic locales in the US. The women were free from chronic diseases affecting bone, and not taking medications that influence bone, such as corticosteroids, anticonvulsants, and thyroxine.

### Results:

Stiffness Index results were obtained from 734 subjects. The Stiffness Index demonstrated an age regression described by:

$$\text{Age Regression of Stiffness Index} = 68 + \frac{31.6}{\left[1 + \left(\frac{\text{age}}{55.9}\right)^{10.1}\right]}$$

Stiffness Index begins to decline slightly after age 35 years, so the reference value for young adult women was taken for the group 20 to 35 years (n=214). The mean value was 99.9 with an SD of 15.8; these values are used in calculating the T-score. The standard error about the curve is 15 (figure 1-1). This value is used in calculating the Z-score.

### Conclusion:

The study provides accurate, representative reference data for the assessment of osteoporotic fracture risk.

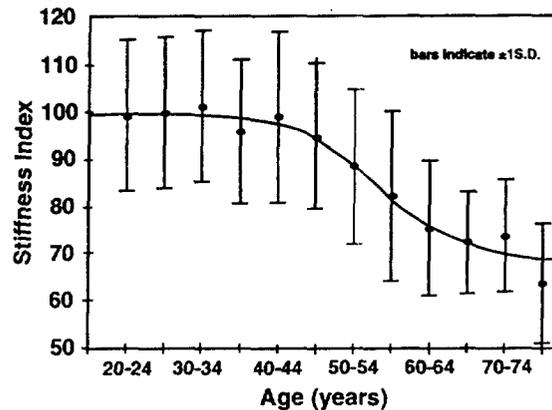


Figure 1-1. Stiffness Index Compared to age.

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Age	20-29	30-39	40-49	50-59	60-69	70-79
<i>n</i>	118	174	195	81	105	61
<i>mean</i>	99.6	98.4	97.0	86.5	73.8	69.9
<i>SD</i>	15.8	15.8	16.9	17.1	12.6	13.0

**Study 2: Indication of osteoporotic fracture of the femur in elderly women age 75-95 (Hans et al, EPIDOS<sup>1</sup>)**

*Hypothesis:*

Numerous studies have shown that a decreasing BMD as measured by X-ray absorptiometry is associated with an increased risk of osteoporotic fracture. Osteoporotic fractures of the femur are especially prevalent in the elderly. Prospective measurement of both femur BMD and the Stiffness Index in an elderly population, provides a comparison of the ability to predict the future risk of osteoporotic fracture of the femur.

*Methods:*

Ambulatory white women with no history of femur fracture, between the ages of 75 and 95 years were recruited. Single baseline measurements of femur BMD and Stiffness Index were obtained. Follow-up occurred every 4 months by way of a questionnaire. Subjects reporting fractures were subsequently interviewed.

*Results:*

Prospective results were obtained from 5,662 women (average age 81), with 115 femur fractures recorded over a mean follow-up of 2 years. The Stiffness Index showed a comparable gradient of femur fracture risk as femur BMD. An ROC analysis of these results showed no significant difference between femur BMD and the Stiffness Index (figure 1-2). The risk of femur fracture doubled for a 1 SD decrease relative to the age adjusted mean, in either Stiffness Index or femur BMD. The Stiffness Index was an independent predictor of fracture risk even after adjusting for femur BMD.

*Conclusion:*

The Stiffness Index provides an indication of risk for osteoporotic fracture of the femur in elderly women, comparable to femur BMD as measured by X-ray absorptiometry.

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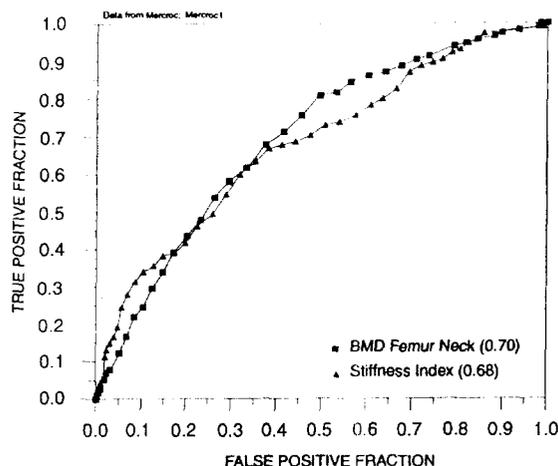


Figure 1-2. ROC curves for femur BMD and Stiffness Index from EPIDOS<sup>1</sup>

### Study 3: Indication of osteoporotic fracture risk in peri/post menopausal women age 45–75 (Thompson et al<sup>2</sup>)

*Hypothesis:*

Osteoporotic fractures in peri and post menopausal women (age 45–75) are also associated with decreased BMD at the spine or femur. Osteoporotic fracture in this population typically occur at the spine, or wrist, and less frequently at the femur, pelvis, and humerus. Prospective measurement of the Stiffness Index in a peri/post-menopausal population, will provide an indication of its ability to predict the future risk of osteoporotic fracture.

*Methods:*

Ambulatory white women, between the ages of 45 and 75 years were recruited. A single baseline measurement the Stiffness Index was obtained. Subjects were followed by means of public health records for a period of 3 years. Subsequent fractures of the wrist, spine, femur, and humerus were recorded.

*Results:*

Baseline results were obtained from 3,180 women between the ages of 46 and 75 years. The average age was 60.6 years. There were 89 osteoporotic fractures (distal forearm, femur, spine, pelvis, humerus) recorded over a mean follow up of 31 months. The relative risk of osteoporotic fracture nearly doubled (1.9) for a 1 SD decrease of the Stiffness Index relative to the age adjusted mean (table 1-1). An ROC analysis was also performed (figure 1-3). Area under the curve for the Stiffness Index was 0.66 (SD=0.031).

Table 1-1: Relative risk of osteoporotic fracture for a 1 SD decrease in age adjusted Stiffness Index (Thompson et al, in press, 1998).

ALL SUBJECTS		OSTEOPOROTIC FRACTURES	
Mean Age	n	# fractures	Relative Risk (95% CI)
60.8	3180	89	1.9 (1.4 - 2.5)

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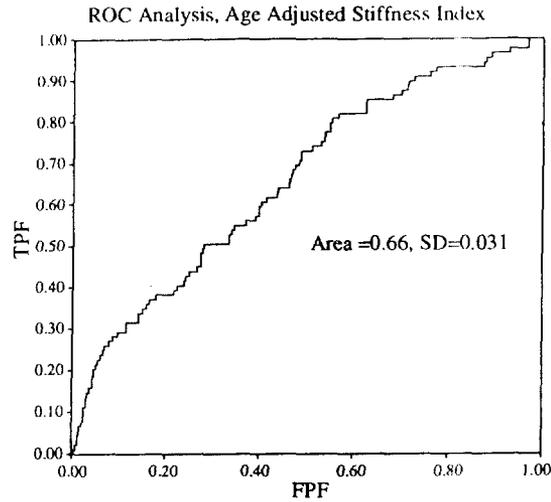


Figure 1-3. ROC analysis, age adjusted Stiffness Index  
(Thompson et al, in press, 1998)

**Conclusion:**

The prospective study by Thompson et al did not directly compare the Stiffness Index to BMD by X-ray absorptiometry. However, ROC results (area=0.66) were similar to that found in the EPIDOS study which directly compared femur BMD to the Stiffness Index (areas=0.70 and 0.68 respectively). Other prospective studies using axial BMD, in perimenopausal age groups, have also produced comparable results<sup>5-7</sup>. Figure 1-4 shows the age-adjusted odds ratios for major prospective fracture studies using ultrasonometry and BMD of the femur and spine by X-ray absorptiometry. There is significant overlap of the 95% intervals of all of the studies, for a variety of sites and instruments.

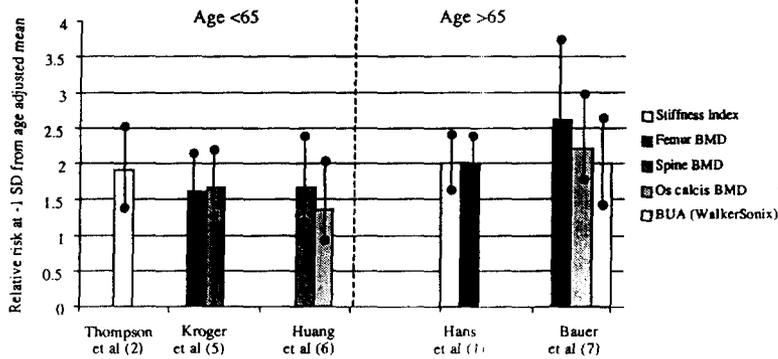


Figure 1-4. Relative risk of osteoporotic fracture for 1 SD decrease from age adjusted mean, prospective studies. All osteoporotic fractures in women <65, and femur fractures in women >65.

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#### **Study 4: Relationship of the Stiffness Index to heel BMD as measured by X-ray absorptiometry (Greenspan et al<sup>11</sup>)**

##### *Hypothesis:*

The objective of the comparative study was to examine the relationship of the Stiffness Index to heel BMD as measured by X-ray absorptiometry. The hypothesis was that the Stiffness Index would be significantly correlated to heel BMD, with a comparable short-term precision error. It was also hypothesized that the precision error of the two techniques might be significantly different in osteoporotic subjects versus young adults.

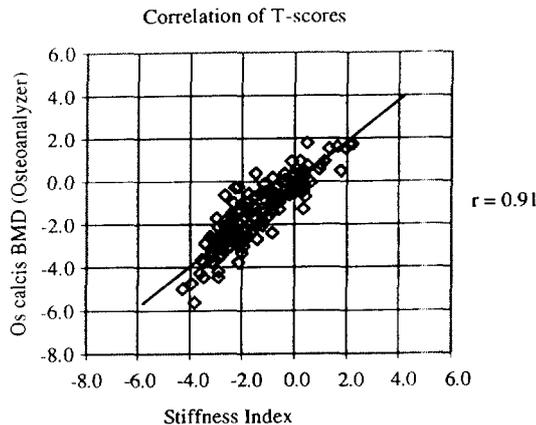
##### *Methods:*

Measurements of the Stiffness Index, calcaneal BMD, and axial BMD were obtained from 150 women, aged 24–92. The subjects were equally divided into three groups; young adult controls, osteoporotic without fractures, and osteoporotic with fractures. Osteoporotic was defined as having a BMD T-score at the femur  $< -2.5$ . Thirty of the 150 subjects received replicate ( $n=5$ ) measurements of the Stiffness Index and calcaneal BMD.

##### *Results:*

Stiffness Index results were correlated to os calcis BMD by single and dual energy X-ray absorptiometry  $r=0.91$  and  $r=0.86$  respectively. This level of correlation was similar to that of two different X-ray absorptiometers measuring the os calcis ( $r=0.93$ ). Stiffness Index predicted T-scores by X-ray absorptiometry in an individual patient with an accuracy of  $\pm 1.2$  using 95% confidence intervals. This difference was similar to that demonstrated between two different X-ray absorptiometers ( $\pm 1.0$ ) measuring os calcis BMD. The regression of Stiffness Index T-scores to those obtained by BMD was linear with a slope not statistically different from unity (figure 1-5).

The Stiffness Index demonstrated comparable standardized precision versus that obtained by X-ray absorptiometry. The precision error of the Stiffness Index was not significantly different in osteoporotic patients, versus young adult controls. The precision error of single energy X-ray absorptiometry was significantly worse in the same population. The precision error of the Stiffness Index is nominally 2%.



*Figure 1-5. Relationship of Stiffness Index and BMD using Single-Energy X-ray absorptiometry (from Greenspan, et al<sup>8</sup>)*

*Conclusion:*

T-scores by the Stiffness Index are functionally equivalent to those obtained by X-ray absorptiometry of the heel. The precision error of the Stiffness Index is comparable to the precision error of BMD by X-ray absorptiometry of the heel, making it suitable to monitor bone change.

### 1.1.8 Individualization of Treatment

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

#### T-Score and % Young Adult

The T-score represents the patient's Stiffness Index above or below a reference "Young Adult" mean and is expressed in standard deviation (SD) units. The bottom of the green region (figure 1-6) marks one standard deviation (-1 SD) below the mean Young Adult value. The yellow region represents the range from -1 to -2.5 SD. The red region represents values below -2.5 SD. Fracture risk increases continuously as the Stiffness Index values decrease. The "% Young Adult" expresses a patient's Stiffness Index value as a percentage of the "Young Adult" mean for women aged 20 to 35 years.

For example, the 70-year-old female patient plotted on the graph has a Stiffness Index value 1.9 SD below the Young Adult mean.

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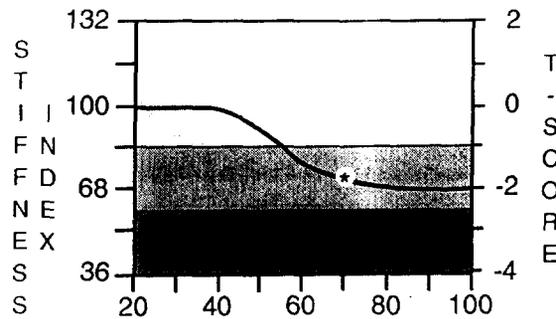


Figure 1-6. Reference graph with example:  
T-score = 1.9 and Z-score = 0.0

### Z-Score and % Age-Matched

The Z-score represents the patient's Stiffness Index above or below the expected Age-Matched value and is expressed in SD relative to the intrapopulation variation. In women, decreases in the Stiffness Index begin after age 35, but significant decreases do not occur until the perimenopausal period. The reference curve is used in calculation of the expected Stiffness Index 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 patients' Stiffness Index value as a percentage of the expected values for a reference group of the same age and sex.

For example, the Stiffness Index result plotted against Age-Matched data in figure 1-6 is 1.9 SD below the Young Adult value; however, the value falls on the Age-Matched regression line. This indicates the patient has an increased risk of fracture, but one that is typical for patients of her age. Conversely, Figure 1-7 shows a 60-year-old patient who has the same T-score (-1.9) as the 70-year-old female shown in figure 1-6, but has a Z-score of -0.3

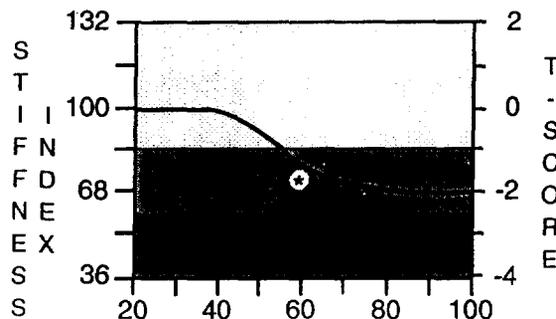


Figure 1-7. Reference graph with example:  
T-score = 1.9 and Z-score = -0.3

Stiffness Index values that are >15 below that expected at a given age (i.e. Z-score worse than -1 SD) 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 1-2. The physician should consider therapy consistent with the patient's age, physical condition, and other relevant risk factors (refer to NOF Guidelines).

Table 1-2: Causes of Secondary Osteoporosis

<b>Endocrine Disorders</b>	<b>Drug Induced (iatrogenic)</b>
hyperthyroidism	corticosteroids
hyperparathyroidism	anticonvulsants
hypogonadism	heparin (long-term use)
Cushing's syndrome	cancer drugs
growth hormone deficiency	glutethimide
juvenile diabetes	thyroid hormone
renal failure disease	LHRH, GnRH agonists
idiopathic hypercalciuria	cyclosporine
liver disease/failure	methotrexate
<b>Malignancies/Cancer</b>	lithium
multiple myeloma	<b>Heritable Disorders</b>
metastatic bone disease	Turner's Syndrome
lymphoma	Klinefelter's syndrome
<b>Diet/Malabsorption Syndromes</b>	osteogenesis imperfecta
gastrectomy	hypophosphatasia
intestinal bypass	hemolytic anemia
sprue/celiac disease	thalassemia
steatorrhea	<b>Other</b>
calcium deficiency	immobilization
vitamin D deficiency	systematic mastocytosis
vitamin C deficiency	radiation therapy
lactose intolerance	rheumatoid arthritis
anorexia	alcoholism

### Bone Ultrasonometry and Fracture Risk

T-scores for Stiffness Index 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 operational 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 of Stiffness Index, but rather there is a continuous gradient of risk. Stiffness Index values should be considered together with other risk factors (BMD, low body weight, fracture history, corticosteroid 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<sup>6</sup>. 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 Stiffness Index is somewhat independent of X-ray absorptiometry, and provides incremental information on fracture risk.

### 1.1.9 Directions for Use

Refer to the *Achilles+ Operator's Manual* for Directions for Use.

### 1.1.10 Patient Counseling Information

Supplied with the Achilles+ are 50 Patient Brochures titled "My Achilles+ Test". These brochures can be readily duplicated or can be reordered from Lunar. This brochure also references additional sources of information regarding the detection, monitoring, and treatment of metabolic bone diseases.

Each Achilles+ is also supplied with 50 informational brochures from the National Osteoporosis Foundation titled "How Strong are Bones". These brochures can be reordered by contacting the National Osteoporosis Foundation (NOF).

### 1.1.11 Detailed Device Description

The system components given in this section are required to complete a patient measurement and are applicable to Solo and PC systems.

#### Achilles+ Ultrasonometer

Refer to figure 1-8 for the components that follow:

- **Fill Bottle and Drain Bottle**—The Fill bottle (②) contains surfactant solution which helps the system measure the os calcis. Solution from the Fill bottle is pumped into the heel bath during a patient measurement. The solution is then pumped from the heel bath to the Drain bottle (①) after the measurement.
- **Storage Compartment**—Keep the system phantom in the storage compartment (③) when the phantom is not being used.
- **LCD**—Use the LCD (④), liquid crystal display, to operate the system in Solo configuration. Refer to section 1.6 for procedures to use the LCD.
- **Heel Bath**—The patient's heel is positioned in the heel bath (⑤), or "water bath," during a patient measurement.
- **Calf Support**—The calf support (⑥) helps align the heel with the transducers and keep the patient's leg stationary so the foot does not move during a patient measurement.

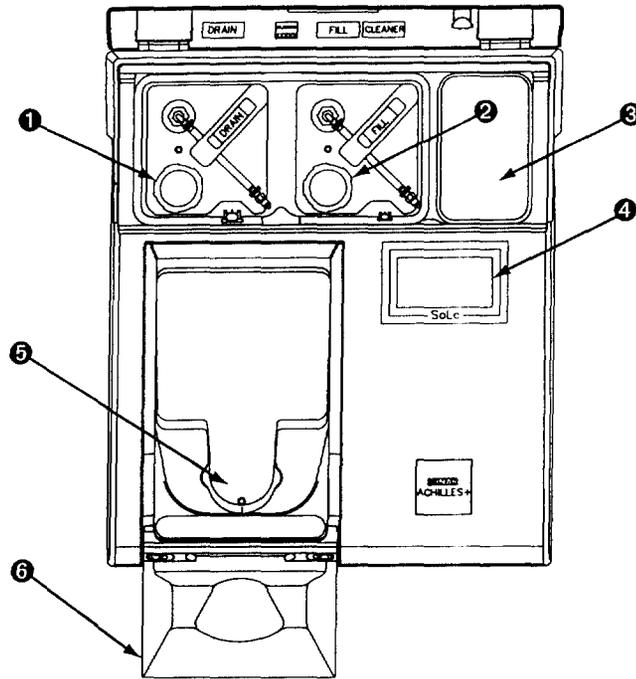


Figure 1-8. Achilles+ ultrasonometer

### Base Shim

Figure 1-9 shows the base shim assembly. The base shim (❶) is positioned in the heel bath before a patient measurement. The patient's foot is positioned on the base shim and the toe peg (❷) to keep the foot stationary and keep the heel aligned during the measurement.



**WARNING:** You must perform low level disinfection (reprocessing) between each patient measurement. Doing so will help prevent possible transmission of infection between patients (refer to chapter 2).

Because the base shim contacts the foot, low-level disinfection procedures must be completed between each patient measurement. Wipe down the base shim and toe peg with the isopropyl alcohol pads supplied with the Achilles+. Refer to chapter 2 for procedures.

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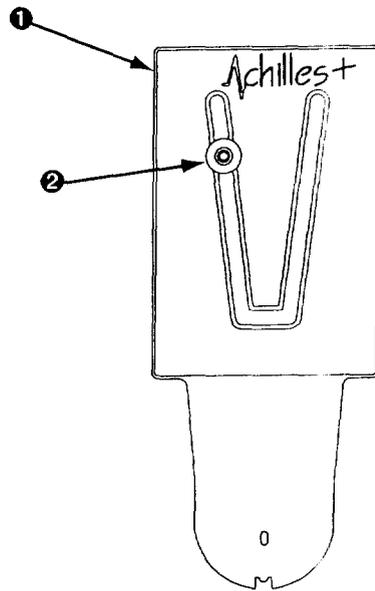


Figure 1-9. Base shim

### Power Switch

The power switch (❶ in figure 1-10) is located on the back of the Achilles+ unit and is used to turn the ultrasonometer on and off.

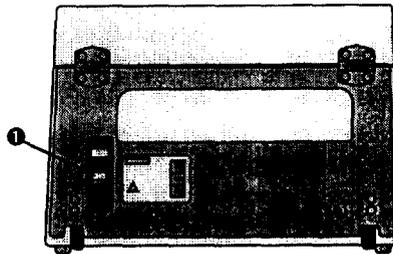


Figure 1-10. Power switch

### System Phantom

The system phantom is used to simulate the heel during Check System procedures. The phantom delivered with your Achilles+ is specific to your system. Phantoms from other systems are not valid for use with your Achilles+.

### 1.1.12 How Supplied

The Achilles+ includes initial supplies for 50 patient measurements. Additional measurements require additional surfactant solution and Isopropyl Alcohol pads. (refer to the "Fax-back Card" for re-ordering information).

CUU

### **Surfactant (LUNAR Part #4915)**

The Achilles+ includes 100 pouches of surfactant (LUNAR Part #4915). Surfactant is mixed with water in the Fill bottle and helps improve coupling of the ultrasound signal.

### **Isopropyl Pads (LUNAR Part #1268)**

The Achilles+ includes 100 isopropyl pads. These pads contain 70% isopropyl alcohol and are used to clean the patient's heel before a measurement, and to clean the system for low level disinfection after each measurement.

*NOTE: If it is necessary to purchase alcohol pads rather than ordering them from LUNAR, make sure they contain minimally 70% isopropyl alcohol.*

## **1.1.13 References**

### **Clinical Studies Using Achilles+**

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5. Kroger H, Huopio J, Hnkanen R, Tuppurainen M, Puntila E, Alhava E, Saarikoski S. (1995) Prediction of fracture risk using axial bone mineral density in a menopause population: A prospective study. *Journal of Bone Mineral Research*, 10:30-306.
6. Huang C, Ross P, Wasnich. (1998) Short term and long term fracture prediction by bone mass measurements: A prospective study. *Journal of Bone Mineral Research*, 13:107-113.
7. Bauer D, Gluer C, Cauley J, Vogt T, Ensrud K, Genant H, Black D. (1997) Broadband ultrasound attenuation predicts fractures strongly and independently of densitometry in older women. *Arch Intern Med* 157:629-634.

### **Published Practice Guidelines**

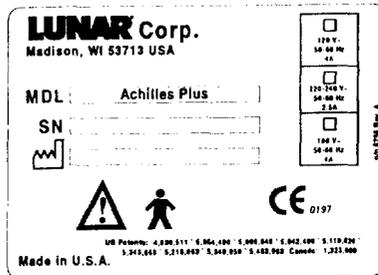
8. NOF Guidelines (1997). In press.

UK

## 1.2 Symbols and Labels

The Achilles+ labels indicate safety information and the location of Achilles+ components. These labels are fixed to the Achilles+ ultrasonometer components.

### 1.2.1 External Symbols and Labels



**System Label:** This label gives system input power requirements and compliance information.



**Safety Information:** The operator must obey the information related to this symbol for safe operation of the Achilles+. Refer to this manual for important safety information.



**CE Mark:** Indicates the Achilles+ complies with the European Council directive (93/42/EEC, Medical Device Directive, Annex II).



**Type B Equipment:** Indicates the Achilles+ has Type B protection against electrical shock. Refer to IEC-601-1 for more information about the Type B Equipment rating.



**Fuse Rating:** Indicates Achilles+ fuse rating and input voltage information.



**Drain Bottle**

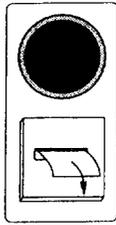


**Fill Bottle**



**Cleaner Bottle**

U/s



**Printer Feed:** Indicates the location of the printer feed button.

## 1.2.2 Internal Symbols and Labels



**Safety Ground:** Indicates electrical connections which are grounded to ensure operator and patient safety.



**Heater:** Indicates components that control the function of the Achilles+ heater.



**Drain Bottle Fuses:** Indicates the fuses for draining the Achilles+.



**Fill Bottle Fuses:** Indicates the fuses for filling the Achilles+.

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## 1.3 PC Achilles+ Components

PC systems include a computer (notebook or desktop), monitor for desktop computers, keyboard, mouse, and printer. Computer, monitor, and printer specifications follow:

### Computer

The Achilles+ computer must meet the minimum requirements that follow:

- IBM-compatible personal computer.
- An IEC 950 / EN 60950 and IEC 801-5 certified computer: 80486 CPU running at 50 Megahertz DX with a math co-processor, or Pentium CPU.
- Windows 95 operating system.

Call LUNAR Sales or your LUNAR distributor for assistance for information about compatible components.

### Monitor

The Achilles+ can support VGA and S-VGA display modes.

## Printer

The printer lets you print measurement results. The Achilles+ supports the printers that follow:

- Hewlett-Packard DeskJet 500 Series, 500C Series (color), 600C Series (color), and 800 Series.
- Hewlett-Packard LaserJet Series.
- EPSON FX-85 or compatible.
- Canon BJC-80
- NEC J180 and ESC/P (Japanese only).
- ASCII text mode.

Refer to your printer's user manual for information about your specific printer.

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## 1.4 System Installation

### 1.4.1 Reprocessing



**WARNING:** You must complete low level disinfection (reprocessing) between each patient measurement. Doing so will help prevent possible cross contamination of infection between patients (refer to chapter 2).

Low level disinfection procedures must be completed immediately after installing the Achilles+. Refer to chapter 2 for procedures.

### 1.4.2 Site Preparation

Make sure you have the items that follow to prepare your site for patient measurements:

- A chair is required for patient measurements. Use a chair that lets the patient comfortably place the foot in the Achilles+. Make sure the chair does not have wheels to prevent patient movement during a measurement.



**WARNING:** The computer must be at least 1.5 meters (5 feet) from the Achilles+ unit. Failure to do so can result in electrical shock.

- A table or desk for the computer and monitor is required for PC systems. Make sure the computer is at least 1.5 meters (5 feet) from the patient so the patient can not touch the computer.

The Achilles+ requires that you maintain the Fill and Drain bottles during system operation. Do not let fluid from these bottles spill on the computer electronics.

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### 1.4.3 Solo Configuration Installation

Connect the Achilles+ ultrasonometer into a grounded electrical outlet to install the system for Solo configuration.

*NOTE: The program saves the configuration information when disconnected for transport to a different site.*

Complete the procedures that follow to configure the software for Solo configuration. Refer to section 1.6 for procedures to use the Solo LCD.

#### Record the Date

1. Select CONFIGURE from the Main Menu. The Configure 1 menu is shown.
2. Select DATE. The Date submenu appears.
3. To set the
  - *date format*, select a format from the date menu. The change is made and the Configure 1 menu is shown.
  - *date*, select SET at the date submenu and record the current date. Select SET to save the new date and go back to the Configure menu.

#### Record the Time

1. Select TIME from the Configure 1 menu. The Time submenu appears.
2. To set the
  - *time format*, select a format from the time menu. The change is made and the Configure 1 menu is shown.
  - *time*, select SET and record the current time. Select SET to save the new time and go back to the Configure 1 menu.

#### Auto Print Option

Use the Auto Print option to record the number of results printouts automatically printed after a patient measurement. You can automatically print 1–9 copies of your results. You must select PRINT at the Results menu if you select 0.

*NOTE: Solo configuration saves up to 50 patient measurement results. You can load these results into a patient database ONLY if you have the PC Achilles+ configuration. Make sure you save the printouts for each measurement and refer to section 2.6 to load the results into the Achilles PC patient database.*

1. Select CONFIGURE from the Main menu. The Configure 1 menu is shown.
2. Select MORE. The Configure 2 menu is shown.
3. Select AUTO PRINT and select the necessary number of results printouts.
4. Select SET. The information is recorded and the Configure 2 menu is shown.

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## Print Graph Option

Use the Print Graph option to print the measurement results graph on your printouts.

1. Select CONFIGURE from the Main menu. The Configure 1 menu is shown.
2. Select MORE. The Configure 2 menu is shown.
3. Select PRINT GRAPH to turn the option on or off.

## BUA/SOS

The default for measurement results is Stiffness Index. Select BUA/SOS from the CONFIGURATION 1 menu to get BUA/SOS measurement results. Results acquired for BUA/SOS take approximately 50% longer than Stiffness Index measurements.

## 1.4.4 PC Configuration Installation

### Connect the Achilles+ to the Computer

Refer to figure 1-11 to connect the Achilles+ to the computer. Connect one end of the serial cable (❶) into the serial (COM) port on the back of the Achilles+ (❷). Connect the other end of the cable into the serial (COM1) port on the back of your computer (❸).

The Achilles+ program automatically creates a default connection to the COM serial port with the Achilles+ ultrasonometer.

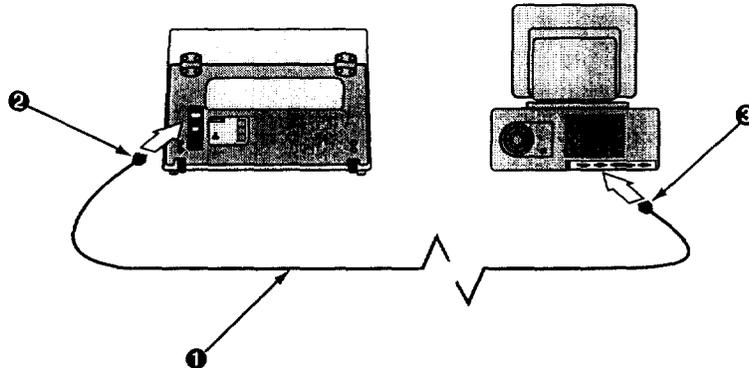


Figure 1-11. Connect the Achilles+ Ultrasonometer

### Install the Software

Complete the procedure that follows to install the Achilles+ software for the first time, or for a system upgrade.

*NOTE: Computers from LUNAR are pre-loaded with software.*

1. Insert the Achilles+ disk labeled "#1 of 2" in drive A.
2. Select Start, Run, then type A:\setup.
3. Select  to start the installation. Complete the steps as shown on the monitor.
4. To start the program, double click on the ACHPLUS icon on your desktop.

5. Select **[F4]** (Configure) then **[F4]** (Hardware) to select the printer type and to set the local time.
6. Select **[F8]** then **[Esc]** to return to the Main Menu.

### Configure the Printer for Windows 95

*NOTE: Complete the procedure that follows only if you did not purchase your printer from LUNAR. If you purchased a printer from LUNAR, the Achilles+ software is pre-configured.*

If a printer is already connected to your computer, complete the procedure that follows to make sure you can print from the Achilles+ software.

1. From the Windows 95 Taskbar, select "Start," "Settings," then "Printers." The Printers window is shown.
2. Select "File" then "Properties." The Properties window is shown and gives the settings for the installed printer.
3. Select the "Details" tab then select "Port Settings." The Configure Port window is shown.
4. Uncheck the "Spool MS-DOS Print Jobs" check box.
5. Select OK twice to go back to the Windows desktop.
6. Run the Achilles+ software. Select **[F4]** (Configure) then **[F4]** (Hardware). The Hardware Configuration screen is shown.
7. Select the necessary printer model. Select **[F8]**.

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## 1.5 Solo Operation

The LCD lets you operate the Achilles+ program for Solo operation. The LCD is a touch-sensitive screen: touch a menu option with the tip of your finger to start a specified program.

*NOTE: The word "select", as used in the Solo sections of this manual, refers to the act of touching an LCD option to start a specified program.*

### 1.5.1 The Main Menu

The Main menu (figure 1-12) is the first screen shown on the LCD. It lets you access four basic programs:

- **MEASURE**—select to complete a patient measurement. Refer to chapter 4.
- **MAINTENANCE**—select to complete maintenance and QA procedures. Refer to chapter 2 for maintenance and chapter 3 for QA procedures.
- **RESULTS**—select to view and print patient measurement results. Refer to section 4.

- **CONFIGURE**—select to configure the software for Solo operation.

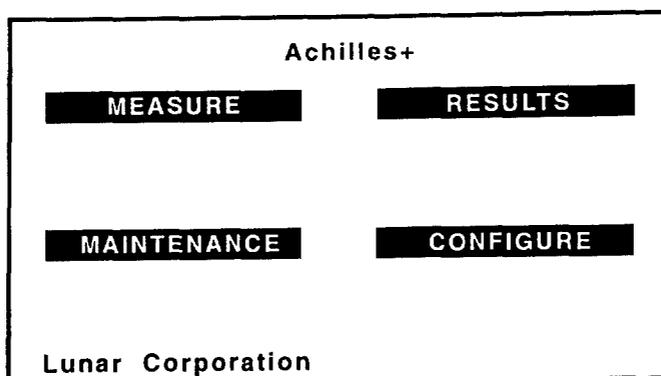


Figure 1-12. Main Menu

## 1.5.2 Menu Conventions

Review the conventions in this section before you use the LCD on the Achilles+ ultrasonometer.

### Program Title

A title is shown at the top of the LCD to indicate the program being used.

### Common Options

The LCD shows five basic options which are common to many screens:

- **BACKUP**—select to go back to the previous menu or submenu.
- **CANCEL**—select to stop a program before it starts.
- **ABORT**—select to stop a program before it is complete.
- **SET**—select to save changes you have made to current values.
- **PRINT**—select to print measurement information displayed on the LCD.

*NOTE: You can set the system to automatically print results after a patient measurement. Refer to section 1.4.3.*

### Current values

Current values show information that is recorded in the software. Values shown beneath options can be edited. Refer to section 1.5.3.

## 1.5.3 Enter/Edit Current Values

Refer to figure 1-13 to complete the procedures in this section.

### Move the Cursor

Use the arrow symbols (➔) to move the cursor (Ⓐ) within the current value. Every time you select an arrow symbol, the cursor moves one space.

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## Replace a Character

1. Use the arrow symbols to move the cursor over the necessary character.
2. Select a new character from the list (③) shown on the LCD.

*NOTE: If you replace the first character in a block of information, the first character changes and all other characters are deleted.*

## Delete a Character

1. Use the arrow symbols to move the cursor over the character to be deleted.
2. Select the solid block (④) to delete the character. The cursor moves to the next character in the current value.

*NOTE: You can use the solid block to create spaces between characters.*

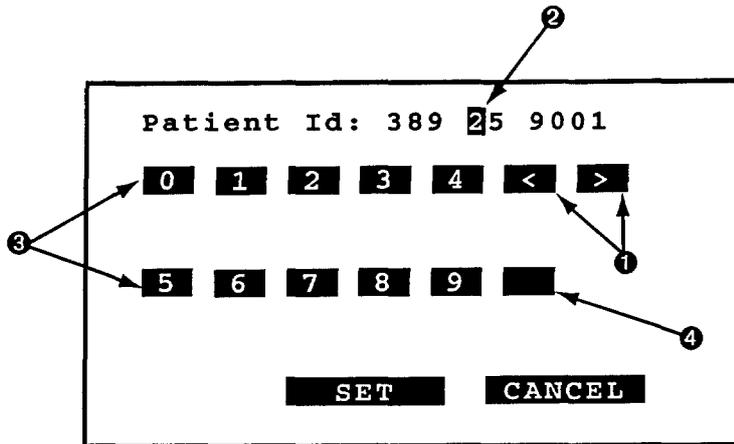


Figure 1-13. Enter/edit current values

## 1.6 PC Interface

The PC Achilles+ uses a computer, monitor, keyboard, and mouse to operate the program. The computer monitor shows options that you can select to operate a specified program. Use the mouse or the keyboard to select an option:

- **Mouse**—Use the mouse to move the cursor over the necessary option. Click on the left mouse button to select the option. Click the right mouse button to go back to the previous screen. In addition, use the mouse to select options that are shown on buttons.
- **Keyboard**—Screens during the program show options that relate to the function keys on the keyboard. To operate the program, press the function key that relates to the necessary option.

*NOTE: The word "select", as used in the PC sections of this manual, refers to the act of using the mouse or keyboard to start a specified program.*

## 1.6.1 The Main Menu

The Main menu (figure 1-14) is the first screen shown on the computer monitor. It gives options that let you access the Achilles+ programs that follow:

- F1 Measure**—select to record new patient information, find an existing patient, and begin a patient measurement. Refer to chapter 4 for procedures.
- F2 Maintenance**—select to complete QA procedures and to clean the Achilles+ ultrasonometer. Refer to chapters 2 and 3 for procedures.
- F3 Database**—select to show patient and QA results, and to archive, copy, and backup patient information. Refer to chapter 3 for procedures.
- F4 Configure**—select to record default settings for the program. You can set the reference population, language, and database location. Refer to chapter 6 for procedures.
- F5 Queue Maint**—select to configure the printing of patient results reports. Refer to chapter 7 for procedures.



Figure 1-14. Main menu

## 1.6.2 Menu Conventions

Review the conventions in this section before you use the PC Achilles+ system.

### Program Title and Active Database

The title of the current program and the active database are shown at the top each screen during the program. For example, Database Menu (Ap\_Data) is shown to indicate that you are using the Database program for the active database AP\_DATA.

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## Common Options

Use the mouse to select button options. The options that follow are common to many screens shown during the Achilles+ program.

**Tab**—Use the tab key to move the cursor to different fields shown on the screen.

Use the arrow buttons (or the **↓** **↑** keys on the keyboard) to move up and down a list one line at a time.

**PgUp PgDn**—Use the PgUp and PgDn buttons (or the PgUp PgDn keys on the keyboard) to move up and down a list one page at a time.

**HOME**—Use the HOME button (or the **Home** key on the keyboard) to go to the first line in a list of information.

**END**—Use the END button (or the **End** key on the keyboard) to go to last line of information on the screen.

**ESC BACKUP**—Use the ESC BACKUP button (or the **Esc** key on the keyboard) to go back to the previous screen.

**F10 Help**—Select this button (or **F10** on the keyboard) to access more information on options shown on the current screen.

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## 1.7 Technical Specifications

### 1.7.1 Achilles+ Ultrasonometer

- Dimensions (W x H x D): 51 x 33 x 61cm (20x 13 x 24in)
- Weight: 20kg (44lbs.)
- 230V (Part #1709)
- 120V (Part #2976)
- 100V (Part #1708)

### 1.7.2 Measurements *In Vivo*

- Stiffness Index (%Young Normal)  $\pm 2\%$
- SOS, m/sec  $\pm 4$  m/sec
- BUA, dB/MHz  $\pm 2$  dB/MHz

CC

### **1.7.3 Methods and Transducers**

- Fluid-coupled, through-transmission
- Quarter wave-matched, broadband single element
- Center frequency = 0.5 MHz

### **1.7.4 Analysis**

- Real-time, point-by-point analog/digital conversion
- Smart detection algorithm, Discrete Fourier Transform
- Simultaneous Stiffness/SOS/BUA determination

### **1.7.5 Fluid Coupling System**

- Self-contained reservoir/drain
- 20–25 measurements/fill
- Fully automated filling/draining
- Heated sampling compartment (37° C)
- Pre-measured surfactant

### **1.7.6 Output/Display**

- Stiffness Index vs. %Young Adult and %Age Matched
- SOS (m/s); BUA (dB/MHz)
- VGA graphics standard

### **1.7.7 Power**

- 100 V~, 50/60 Hz, 4A
- 120 V~, 50/60 Hz, 4A
- 220–240 V~, 50/60 Hz, 2.5A

### **1.7.8 Operating Temperature Range**

15–35° C (59–95° F)

### **1.7.9 Operating Humidity Range**

20–80%

### **1.7.10 Classification**

Type B (IEC 601)

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## 1.8 Reorder Achilles+ Supplies

To order supplies for the Achilles+ ultrasonometer, contact LUNAR Service or a LUNAR Distributor if outside the US. Use the part numbers that follow when reordering:

- Surfactant Kit [100 packets] (Part #4915)
- Alcohol Pads (Part #1268)
- Solo Printer Kit [10 paper rolls, 1 cartridge] (Part #5315)
- Achilles+ Operator's Manual (Part #1989)
- Fill Bottle Assembly (Part #2971)
- Drain Bottle Assembly (Part #2972)
- Cleaner Bottle Assembly (Part #3285)
- Patient Brochures [package of 50] (Part #6998)

In the US, contact LUNAR directly by facsimile or by email:  
support@lunarcorp.com.