Longitudinal Assessment of Transient Elastography in Cystic Fibrosis

ELASTIC CF

Manual of Operations (MOO)

Table of Contents

List of Appendices

FibroScan™

1.1 FDA Device Classification

The Food and Drug Administration (FDA) has classified the FibroScan™ device as a Class II device that does not require premarket approval for use. It is approved for pediatric and adult use. The FDA approval document is included as Appendix A.

1.2 Training

Site staff will receive study training prior to implementation of the study. Training will include review of:

- Conduct of FibroScan™ exam and measurements for FibroScan™ operators. Operators will be trained at each site to perform FibroScan™ measurements to ensure consistent and standardized acquisition of complete data. This training will be conducted by the machine's manufacturer, Echosens.
- Each trained operator will receive a training certificate from Echosens. This certificate should be filed in your site's ELASTIC Regulatory Binder and a scanned copy emailed to the DCC (Children-essentialdocs@umich.edu).
- NOTE: Operators who have been previously trained by Echosens who have a training certificate will not need to complete this training program, but will need to file a copy of their training certificate in the ELASTIC Regulatory Binder.
- For technical assistance with the FibroScan™ device, please contact:
  Chris Guay at Echosens
  Phone: (781) 790-0845
  Email: FibroScan-Help@arborresearch.org
- New FibroScan™ operators must be trained and certified by Echosens. After the initial training, Echosens will conduct annual training sessions at each site. Echosens and/or the DCC will be in touch with your site to schedule both the initial and the annual training sessions.

1.3 Communication of Results to Families

If desired by the adult subject/parent/legal guardians, the results of the FibroScan™LSM (Liver Stiffness Measurements) will be provided by an ELASTIC site investigator. These results will not be placed in the official clinical record. Guidance will be given to the family as to current understanding of the measurement results and that the clinical implications of the findings are not clear (lay explanation of FibroScan™measurement available on the ChiLDReN website in Folder: **Current Studies \ Cystic Fibrosis Liver Disease (CFLD)- ELASTIC **).

1.4 Device Description

FibroScan™ consists of a system unit and a hand-held probe. It is based on Vibration-

Controlled Transient Elastography (VCTE™) technology, and is designed to perform non-invasive measurements of liver shear wave speed and estimates of tissue stiffness. The probe containing a mechanical vibrator produces low-amplitude elastic waves that travel through the skin and intercostal space into the liver. Ultrasound is used to track the shear (elastic) wave, measure its speed and provide estimated stiffness. The results are displayed on the system unit. For detailed information about the device, please refer to Appendix B.

Figure 1: FibroScan™ 502

1.5 FibroScan™ Measurements

Operators will be trained and certified at each site to perform FibroScan™ measurements to ensure consistent and standardized acquisition of complete data. Training will take place at each site by a designated trainer from Echosens.

Four-hour fasting will be specified for this procedure. No sedation will be administered for these FibroScan™ assessments. The exam time is estimated to be 10 to 20 minutes.

The thoracic perimeter of the patient will be measured and recorded. The thoracic perimeter value will determine selection of the probe. The patient will be positioned in the dorsal decubitus position with the right arm in maximal abduction. The operator will sit on a chair on the right side of the patient facing both the patient's chest and the screen of the device. A small amount of coupling gel is applied to the right chest wall. The probe is placed on the chest wall, over the right lobe of the liver between the ribs, angled towards the middle of the parenchyma and away from the liver border. The probe is adjusted until a liver portion, free of large vascular structures, is identified. The probe is kept perpendicular to the skin and a firm

amount of pressure is applied. When all these conditions have been met and an ideal window of liver tissue is identified on the device screen, the button on the probe is pressed, without changing the probe position. The device records and displays the validity of each measurement based on standardized criteria determined by Echosens. Ten valid measurements are obtained. Repeated measurements are performed until 10 valid values are obtained. A second measurement site will then be identified that is one intercostal space superior or inferior to the initial measurement site. A otal of 2 site measurements are done. After the end of the examination the gel is removed from the patient's chest wall with a soft tissue. Gel is also removed from the probe with a soft towel and it is then disinfected with a solution containing quaternary ammonia. The report is printed and a non-identifying study ID label is applied. The report will be placed in the research binder and not in the clinical chart.

FibroScan™ is based on vibration controlled transient elastography at 50Hz. FibroScan measures 2 parameters:

1. "Liver stiffness" quantifies liver fibrosis and is measured in kPa.
2. "Controlled Attenuation Parameter (CAP)" quantifies liver steatosis and is measured in dB/m.

In addition, quality control data are collected:

- Invalid measurements and success rate
- Number and list of valid measurements
- Inter quartile range (IQR) (kPa or dB/m) of all valid measurements within the examination (reflects the dispersion of stiffness or CAP measurements)
- IQR/med. (%) indicates the IQR/median ratio and should remain as low as possible to ensure reliable results (goal < 30%)

1.6 FibroScan™LSM Exam

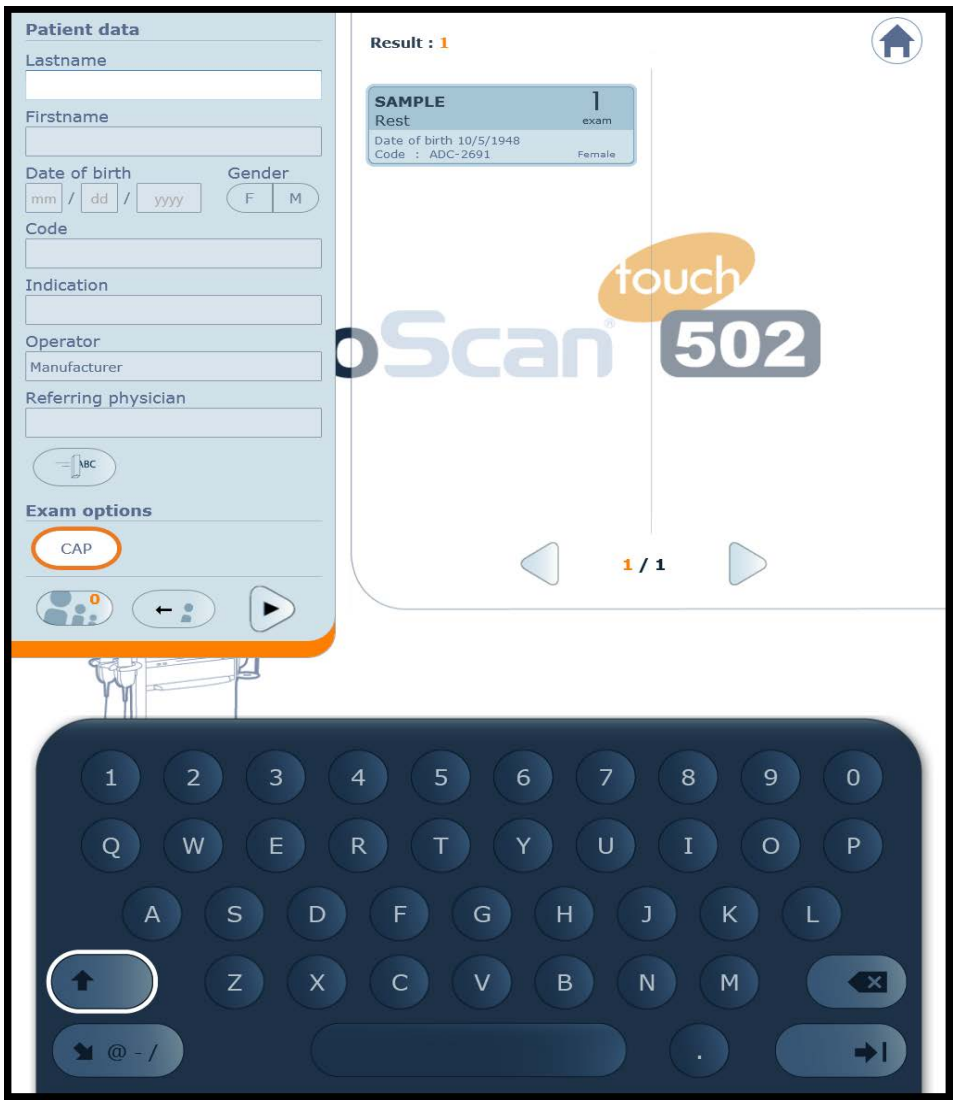
(for detailed information about the FibroScan™ machine, please refer to the manual in Appendix B).

1.7 FibroScan™Screen Preparation

The FibroScan™ screen has fields normally used for clinical care that are a permanent feature of the display. Several of these fields call for PHI entry, which will not be included in ELASTIC data. Please enter the following data into the programmed fields on the Patient data screen prior to each subject's exam:

- Lastname field = Subject ID (PUSH subject ID#)
- Firstname field = Site 1 or Site 2
- Date of Birth = leave blank
- Gender = Select M (male) or F (female)
- Code = ELASTIC
- Indication = leave blank
- Operator = DATE OF EXAM (MM/DD/YYY)
- Referring physician = leave blank

Figure 2: FibroScan™ Screen Preparation



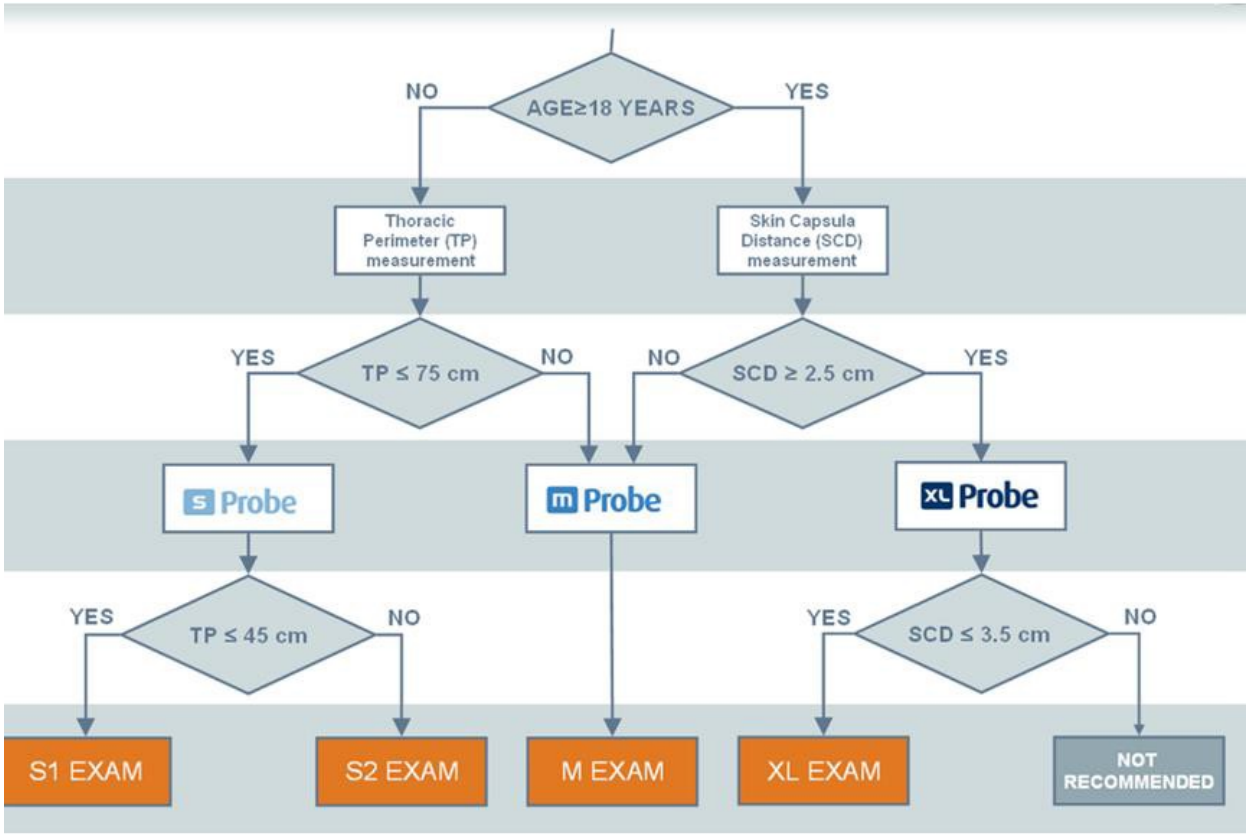
1.8 Performing the FibroScan™ Exam

- For hour fasting is required.
- No sedation will be administered for these FibroScan™ assessments.
- The exam time is estimated to be 10 to 20 minutes. The FibroScan™ machine automatically records the start and stop time of the exam and includes it in the data file for each exam
- It may be helpful to involve a Child-Life specialist to assist the subject in maintaining position during the exam
- The thoracic perimeter of the subject will be measured and recorded. The thoracic

perimeter is measured via measuring tape encircling the thorax at the level of the xiphoid process (indicate precision of measurement – i.e. to 0.1 cm

- The thoracic perimeter value will determine selection of the probe. For more information about the S probe, please refer to the S Probe Manual in Appendix C.
  - If the TP is ≤ 75cm, then the S-Probe should be utilized
  - If the TP is > 75cm, then the M-Probe should be utilized
- The type of programmed exam is also determined by the TP
  - If the TP is ≤ 45cm, then the S1 exam should be performed
  - If the TP is > 45cm, then the S2 exam should be performed
- In subjects ≥ 18 years of age, the choice of probe is determined by the Skin Capsula Distance (SCD), a measurement performed by the FibroScan™ machine, which has an automated probe recommendation tool for larger subjects. Please refer to the FibroScan™ User's Manual Section 6.5.11 (Appendix B)

Figure 3: Probe Choice Flowchart



- The subject will be positioned in the dorsal decubitus position with the right arm in maximal abduction.
- The operator will sit on a chair on the right side of the subject facing both the subject's chest and the screen of the device.
- A small amount of coupling gel is applied to the tip of the probe. (Recommended Gel: Aquasonic 100 CLEAR Ultrasound Gel, PRODUCT # 03-08, PARKER LABORATORIES, INC. 286 Eldridge Road Fairfield, NJ 07004 USA Tel: 973-

276-9500 HTTP://WWW.PARKERLABS.COM/AQUASONIC-100.ASP

- The probe is placed on the chest wall, over the right lobe of the liver between the ribs, angled towards the middle of the parenchyma and away from the liver border.
- The probe is adjusted until a liver portion, free of large vascular structures, is identified.
- The probe is kept perpendicular to the skin and a firm amount of pressure is applied.
- When all these conditions have been met and an ideal window of liver tissue is identified on the device screen, the button on the probe is pressed, without changing the probe position.
- The device records and displays the validity of each measurement based on standardized criteria determined by Echosens.
- Ten valid measurements are obtained as determined by the FibroScan™ machine's software. Repeated measurements are performed until 10 valid values are obtained. Two different site measurements are taken.
- In addition, quality control data are collected:
    - Invalid measurements and success rate
    - Number and list of valid measurements
    - Inter quartile range (IQR) (kPa or dB/m) of all valid measurements within the examination (reflects the dispersion of stiffness or CAP measurements)
    - IQR/med. (%) Indicates the IQR/median ratio and should remain as low as possible to ensure reliable results (goal < 30%)
- After the end of the examination the gel is removed from the subject's chest wall with a soft tissue.
- Gel is also removed from the probe with a soft towel and it is then disinfected with a solution containing quaternary ammonia (Recommended: Sona Ultrasound Wipes, Product: SONO4018 Advanced Ultrasound Solutions, Inc. 23865 Via Del Rio Yorba Linda, CA 92887 United States http://www.ultrasoundwipes.com/
- The report is printed
- The data will be transmitted to the DCC

1.9 Printing the Exam Report

You can either print the report directly from the FibroScan™ machine to a printer or you can export it as a PDF to an external device such as a thumb drive and print it elsewhere. The report will be placed in the subject's research binder and not in the clinical chart and serve as a source document. To view an example of LSM exam report, please see Appendix C. For detailed instructions on how to print the exam report directly or export to a thumb drive, please refer to the appropriate section of the FibroScan™ User Manual (Appendix B).

2.0 Cleaning the Machine and Probe

Apply the following recommendations to clean or disinfect the machine, probes, and accessories.

Failure to observe these recommendations may result in damage to the machine and the probes, which will then no longer be covered by the guarantee.

Recommendations

- Always wear eye protection and gloves to prevent injury.
- Observe the expiry dates of cleaning products and decontamination solutions.
- Ensure that the contact time and concentration of the cleaning product and decontamination solution are appropriate for the equipment used. Carefully apply the instructions given on the label of the cleaning product and the decontamination solution.
- Carefully read the recommendations from the Association for Professionals in Infection Control and Epidemiology (APIC) and the Food and Drug Administration (FDA), if applicable in the country.

Cleaning the machine (painted, metallic, glass, plastic surfaces and screen)

Surfaces must be cleaned in strict compliance with the following Procedure:

1. Clean using a soft cloth soaked in the recommended cleaning product.
2. If necessary, rinse using a soft cloth soaked in water.
3. Wipe the surface using a soft cloth soaked in the recommended decontamination solution.
4. If necessary, dry carefully using a soft, clean, absorbent cloth.

Precautions

Do not spray any cleaning or disinfectant product directly on the machine. Leaks may damage the system, whose guarantee would then no longer be applicable.

Do not scratch the screen.

Cleaning and Decontaminating the Probe (housing, cable and transducer)

It is not necessary to switch off the device before cleaning the probe. Surfaces must be cleaned in strict compliance with the following procedure:

1. Gently remove the gel using a soft cloth or wipe.

Figure 4: Cleaning the Probe

2. Remove all traces of bodily fluid by cleaning the surfaces using a soft cloth or wipe soaked in the recommended cleaning product (See below).
3. If necessary, rinse the cleaned surfaces using a soft cloth soaked in water.
4. Dry, if necessary, using a dry cloth.
5. Wipe the surfaces using a soft cloth or wipe soaked in the recommended decontamination solution (alcohol-free with a quaternary ammonium as the active agent).
6. Dry, if necessary, using a soft dry cloth.
7. Examine the transducer and probe cable for any damage such as cracks, breakage, or liquid leakage
    - If any damage is observed, stop using the probe and contact the DCC (cfld-dcc@umich.edu)

Precautions

- Do not submerge or soak the probe
- Apply the cleaning produce and decontamination solution to the soft cloth, not directly on the surface to be cleaned
- The probe must be cleaned after every use. Prior cleaning is not necessary to ensure

decontamination
- Do not use flexible brushes to clean the probe
- Take care not to introduce any cleaning product or decontamination solution into the probe connector

Recommended Cleaning Products

- Pure soapy water
- Detergent with neutral pH (5-8)
- Decontamination solutions using quaternary ammonium as the active agent

2.1 FibroScan™ Data Transmission to the DCC

The FibroScan™ produces two data products, a summary file stored as a table with all of the exams' data, and individual exam reports that can be exported as PDF files. On the first business day of each month, the site will send the cumulative Excel spreadsheet (shows all data from all scans done since study start) and the individual exam report PDFs from all subjects whose exam was performed since the last data transmission.

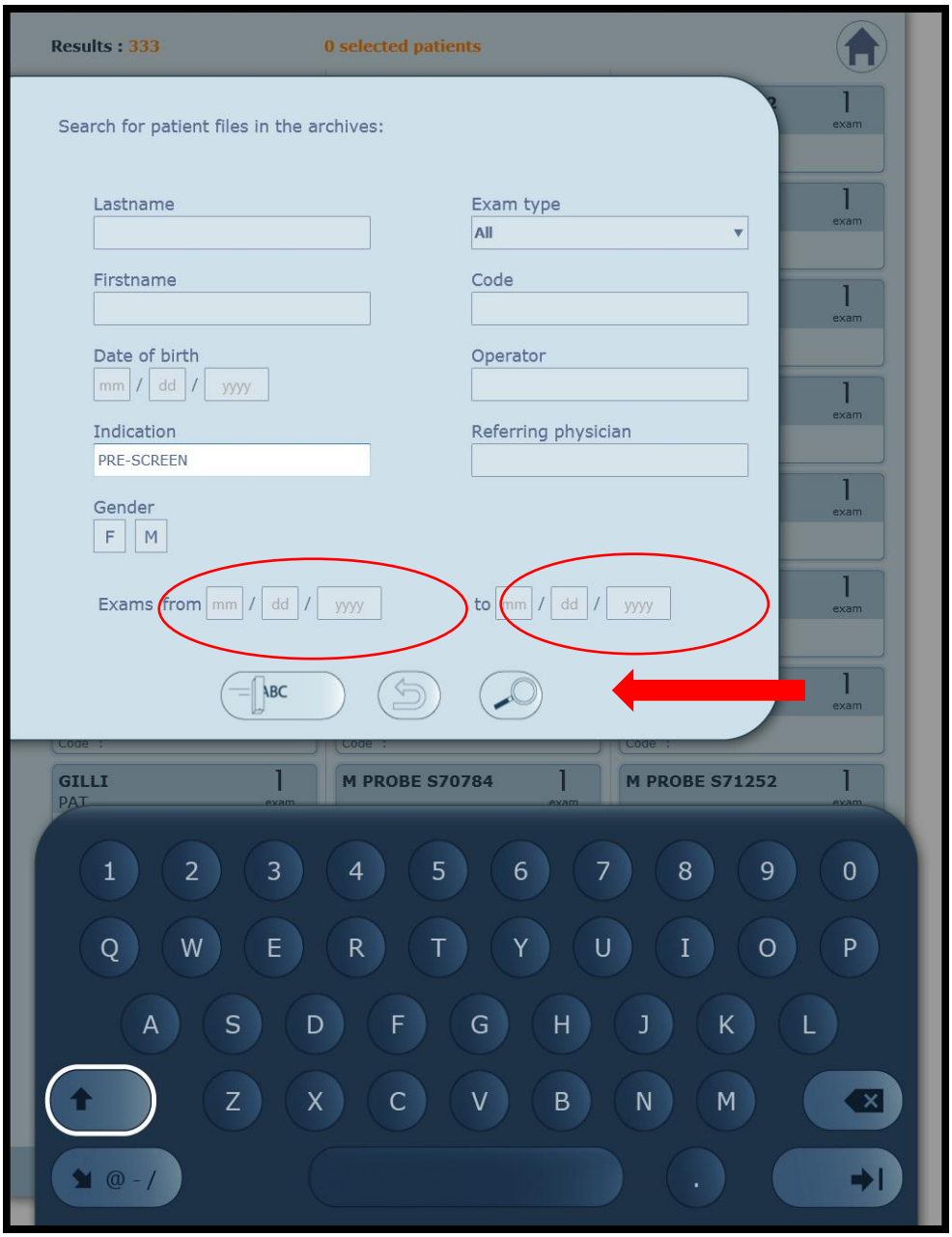
Please refer to the Users' Manual (Appendix C) for detailed instructions on how to export the files to a thumb drive. The exported files should then be transferred to a secure PC and emailed to the DCC. Please store the files in an appropriate location on your computer as a backup in case of lost data.

A summary of the export procedure for the Excel file is as follows:

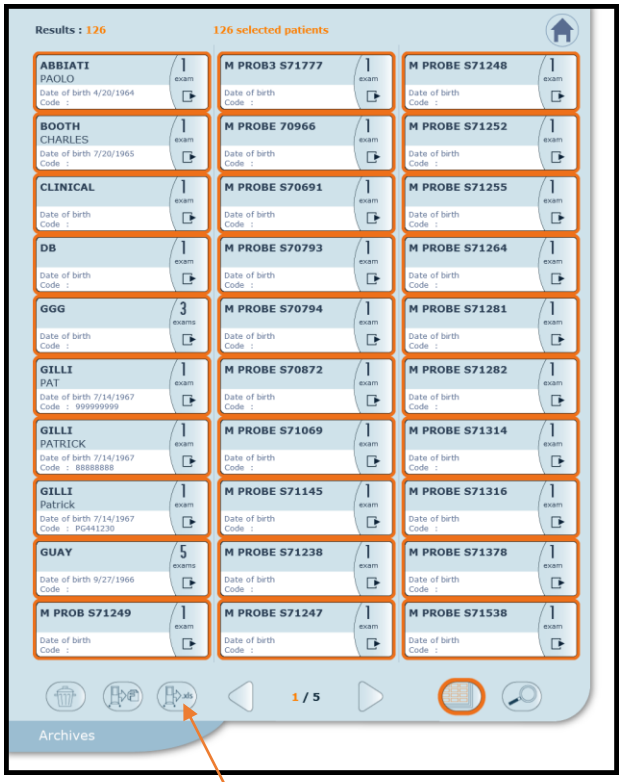
1. Insert the thumb drive into the USB port on the FibroScan™ machine
2. From the Home Screen, press the "Library" icon

3. Once in the library of exams, press the magnifying glass icon to search for exams in a designated time frame, in this case from the earliest to the latest exams.

4. A search dialog screen will appear. In the date field, enter the date of the earliest scan in the "from" field and the latest scan in the "to" field. Then press the magnifying glass to begin the search.

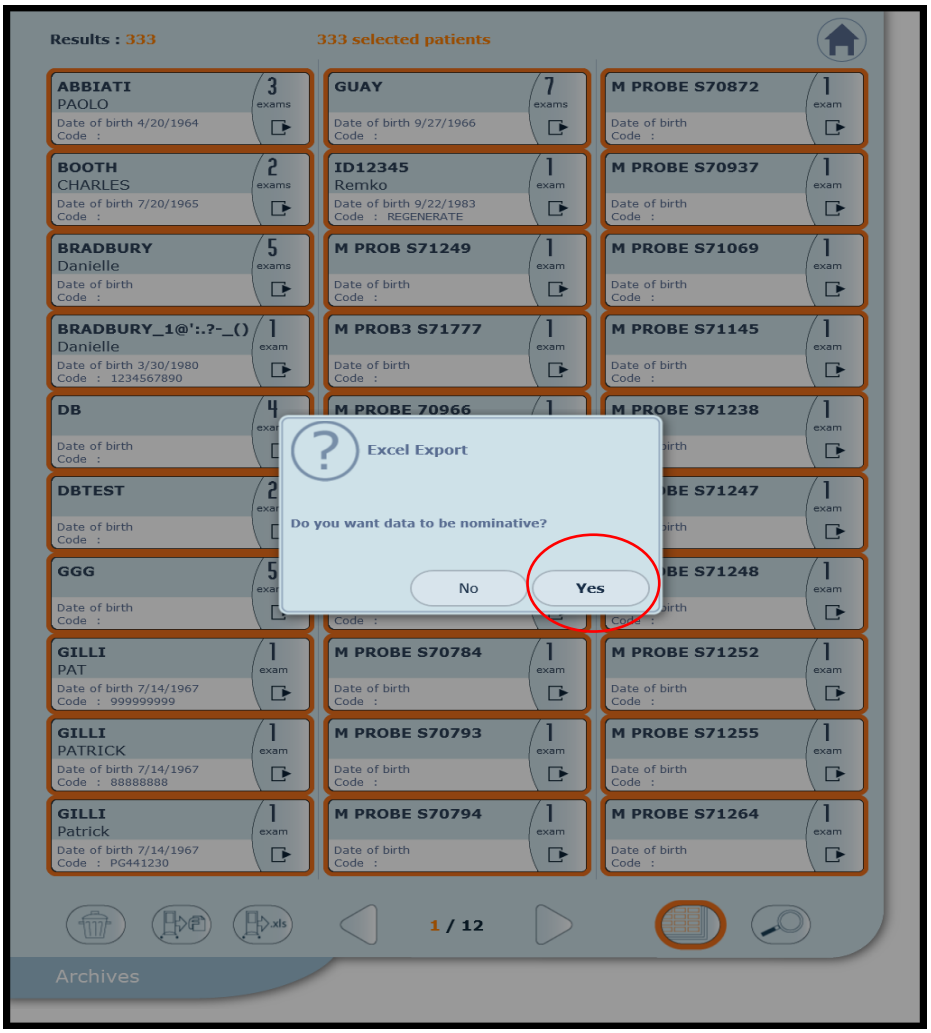


5. All exams within the designated time frame will display. Press the “Mass Selection” icon to select all exams.



6. Press the **.xls** button

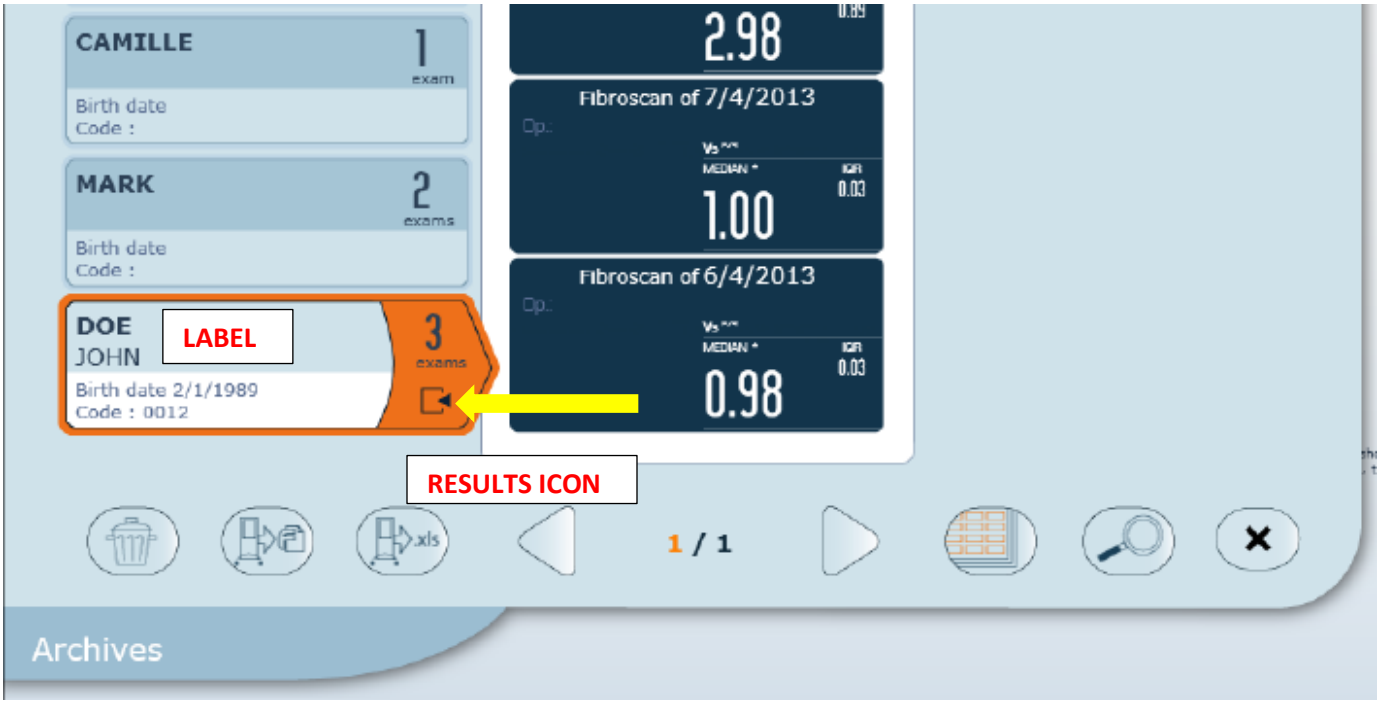
7. Press “yes” to making the report nominative (allowing the entered demographic information described in Section 7.3.5.1 above to display in the Excel file). This step is critical for accurate transmission of the data to the DCC!



8. The file will be saved on the thumb drive. The machine will name the file with the device's serial number and the date and time the Excel file was created
9. When you save it to your computer, name the file as: ELASTIC_YOURSITENUMBER_DATE.xls (e.g. ELASTIC_02_20170115.xls)

A summary of the export procedure for the individual exam PDF files is as follows:

1. Follow steps 1-4 as described above, except this time make the time frame as beginning from the last data transmission and ending with the most recent, so you're only transmitting new individual exam reports
2. Choose the first subject who was scanned since your last data transmission
3. Click the label and then click the results icon



4. A listing of exams appear for that subejct. Select the exam you want to make the pdf of. Tap the desired exam, the exam summary page will open.Click the **Export to PDF** button.

5. The file will be saved to the thumb drive.
6. Click the return button and follow steps 3-5 for each subject for whom you're saving PDF files.
7. When you save it to your computer, name each file as: ELASTIC_SITE NUMBER_YOUR SUBJECT ID NUMBER_DATE OF EXAM.pdf (e.g. ELASTIC_02P0A06_20170117.pdf).

   NOTE: ELASTIC coordinators, also participating in FORCE
   * DO NOT delete any rows in the spreadsheet (we expect the spreadsheet to be cumulative, and to include both FORCE and ELASTIC subjects). Let us (Heather) sort out what is what on our end.

   * Do not upload two files (i.e. one for FORCE, one for ELASTIC). Same reasoning.

   * Upload the file for ELASTIC (or FORCE) to the same directory as FORCE (or ELASTIC).

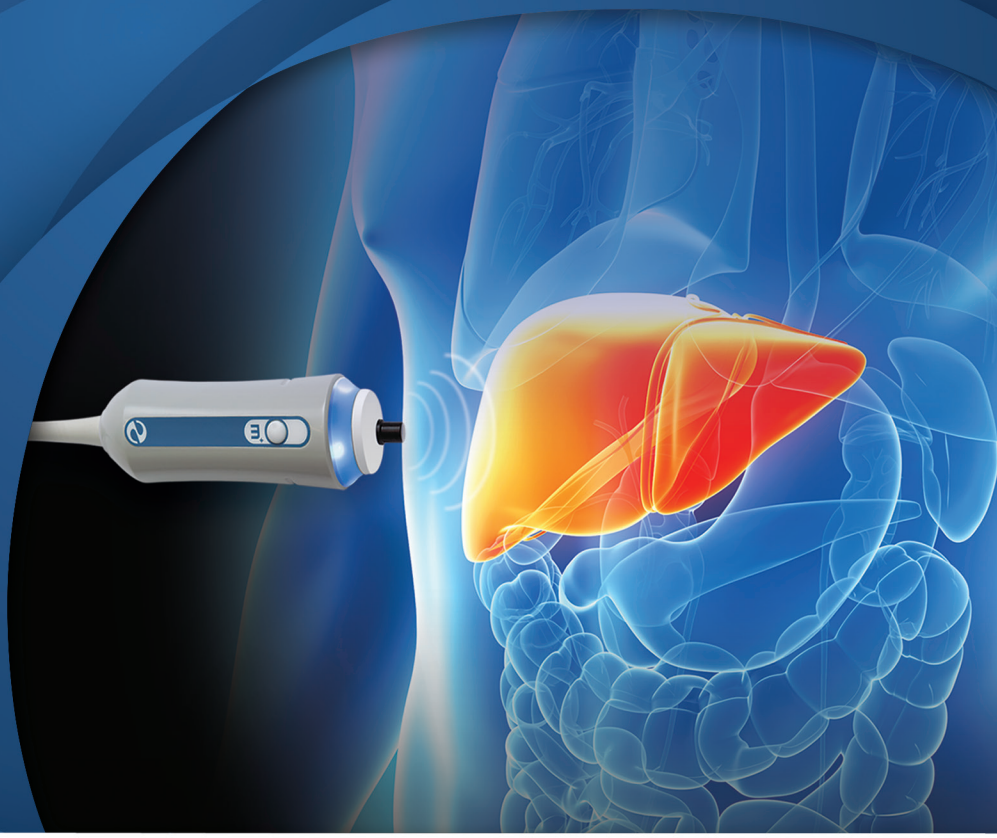
   * Upload the file just once. There will be a directory for each site, and within that a sub-directory for each month.

   * The file may be named ELASTIC in the filename, if uploaded by an ELASTIC coordinator. (If the coordinator or site also manages FORCE, it can say either FORCE or ELASTIC or both in the filename).

   * If we can't identify the subject (missing subject ID or other critical identifiable information) or if we can't identify which study (if ELASTIC or FORCE is missing from any given row in the spreadsheet), then we can't attribute it to a study and the site won't get credit for the visit.

Version 2
March 3, 2017

echosens™



FibroScan touch 502

Innovation in Liver Disease Management

Appendix A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

September 1, 2015

Echosens
% Zvi Ladin
Principal
Boston Medtech Advisors Inc.
990 Washington Street, Suite #204
DEDHAM, MA 02026

Re: K150239
Trade/Device Name: FibroScan
Regulation Number: 21 CFR 892.1560
Regulation Name: Ultrasonic Pulsed Echo Imaging System
Regulatory Class: Class II
Product Code: IYO, ITX
Dated: July 30, 2015
Received: August 3, 2015

Dear Zvi Ladin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Robert A Ochs

Robert Ochs, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K150239

Device Name

FibroScan®

Indications for Use *(Describe)*

The FibroScan® system is intended to provide 50Hz shear wave speed measurements and estimates of tissue stiffness through internal structures of the body.

FibroScan® is indicated for noninvasive measurement of shear wave speed and estimate of stiffness at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of pediatric and adult patients with liver disease.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Diagnostic Ultrasound Intended Use

System: FibroScan® 502 Touch

Intended Use: Diagnostic ultrasound imaging or fluid flow analysis of the human body as follows:

Clinical Application		Mode of Operation						
General (Track 1 Only)	Specific (Tracks 1 & 3)	B	M	PWD	CWD	Color Doppler	Combined (Specify)	Other* (Specify)
Ophthalmic	Ophthalmic							
Fetal Imaging & Other	Fetal							
	Abdominal		P					P 1, 2
	Intra-operative (Specify)							
	Intra-operative (Neuro)							
	Laparoscopic							
	Pediatric		N					N 1, 2
	Small Organ (Specify)							
	Neonatal Cephalic							
	Adult Cephalic							
	Trans-rectal							
	Trans-vaginal							
	Trans-urethral							
	Trans-esoph. (non-Card.)							
	Musculo-skeletal (**Conventional**)							
	Musculo-skeletal (**Superficial**)							
	Intravascular							
	Other (Specify)							
Cardiac	Cardiac Adult							
	Cardiac Pediatric							
	Intravascular (Cardiac)							
	Trans-esoph. (Cardiac)							
	Intra-cardiac							
	Other (Specify)							
Peripheral Vessel	Peripheral vessel							
	Other (Specify)							

N = new indication; P = previously cleared by FDA; E = added under this appendix

1. A-mode
2. Vibration Controlled Transient Elastography at 50 Hz

Diagnostic Ultrasound Intended Use

Transducer: FibroScan® M+ probe

Intended Use: Diagnostic ultrasound imaging or fluid flow analysis of the human body as follows:

Clinical Application		Mode of Operation						
General (Track 1 Only)	Specific (Tracks 1 & 3)	B	M	PWD	CWD	Color Doppler	Combined (Specify)	Other* (Specify)
Ophthalmic	Ophthalmic							
Fetal Imaging & Other	Fetal							
	Abdominal		P					P 1, 2
	Intra-operative (Specify)							
	Intra-operative (Neuro)							
	Laparoscopic							
	Pediatric		N					N 1, 2
	Small Organ (Specify)							
	Neonatal Cephalic							
	Adult Cephalic							
	Trans-rectal							
	Trans-vaginal							
	Trans-urethral							
	Trans-esoph. (non-Card.)							
	Musculo-skeletal (**Conventional**)							
	Musculo-skeletal (**Superficial**)							
	Intravascular							
	Other (Specify)							
Cardiac	Cardiac Adult							
	Cardiac Pediatric							
	Intravascular (Cardiac)							
	Trans-esoph. (Cardiac)							
	Intra-cardiac							
	Other (Specify)							
Peripheral Vessel	Peripheral vessel							
	Other (Specify)							

N = new indication; P = previously cleared by FDA; E = added under this appendix

1. A-mode
2. Vibration Controlled Transient Elastography at 50 Hz

Diagnostic Ultrasound Intended Use

Transducer: FibroScan® XL+ probe

Intended Use: Diagnostic ultrasound imaging or fluid flow analysis of the human body as follows:

Clinical Application		Mode of Operation						
General (Track 1 Only)	Specific (Tracks 1 & 3)	B	M	PWD	CWD	Color Doppler	Combined (Specify)	Other* (Specify)
Ophthalmic	Ophthalmic							
Fetal Imaging & Other	Fetal							
	Abdominal		P					P 1, 2
	Intra-operative (Specify)							
	Intra-operative (Neuro)							
	Laparoscopic							
	Pediatric							
	Small Organ (Specify)							
	Neonatal Cephalic							
	Adult Cephalic							
	Trans-rectal							
	Trans-vaginal							
	Trans-urethral							
	Trans-esoph. (non-Card.)							
	Musculo-skeletal (**Conventional**)							
	Musculo-skeletal (**Superficial**)							
	Intravascular							
	Other (Specify)							
Cardiac	Cardiac Adult							
	Cardiac Pediatric							
	Intravascular (Cardiac)							
	Trans-esoph. (Cardiac)							
	Intra-cardiac							
	Other (Specify)							
Peripheral Vessel	Peripheral vessel							
	Other (Specify)							

N = new indication; P = previously cleared by FDA; E = added under this appendix

1. A-mode
2. Vibration Controlled Transient Elastography at 50 Hz

Diagnostic Ultrasound Intended Use

Transducer: FibroScan® S+ probe

Intended Use: Diagnostic ultrasound imaging or fluid flow analysis of the human body as follows:

Clinical Application		Mode of Operation						
General (Track 1 Only)	Specific (Tracks 1 & 3)	B	M	PWD	CWD	Color Doppler	Combined (Specify)	Other* (Specify)
Ophthalmic	Ophthalmic							
Fetal Imaging & Other	Fetal							
	Abdominal							
	Intra-operative (Specify)							
	Intra-operative (Neuro)							
	Laparoscopic							
	Pediatric		N					N 1, 2
	Small Organ (Specify)							
	Neonatal Cephalic							
	Adult Cephalic							
	Trans-rectal							
	Trans-vaginal							
	Trans-urethral							
	Trans-esoph. (non-Card.)							
	Musculo-skeletal (**Conventional**)							
	Musculo-skeletal (**Superficial**)							
	Intravascular							
	Other (Specify)							
Cardiac	Cardiac Adult							
	Cardiac Pediatric							
	Intravascular (Cardiac)							
	Trans-esoph. (Cardiac)							
	Intra-cardiac							
	Other (Specify)							
Peripheral Vessel	Peripheral vessel							
	Other (Specify)							

N = new indication; P = previously cleared by FDA; E = added under this appendix

1. A-mode
2. Vibration Controlled Transient Elastography at 50 Hz

510(K) Summary
Echosens' FibroScan® System

Submitter's Name, Address, Telephone Number, Contact Persona and Date Prepared:

Manufacturer: Echosens
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Date Prepared: July 30, 2015

Name of Device and Name/Address of Sponsor

Trade/Proprietary Name: FibroScan®

Common Name: Diagnostic Ultrasound System and Accessories

Classifications:

Classification Name	Regulation	Product Code
Ultrasonic Pulsed Echo Imaging System	21 CFR §892.1560	IYO
Diagnostic Ultrasonic Transducer	21 CFR §892.1570	ITX

Manufacturing Facility: Echosens
30 Place d'Italie
75013 Paris, France
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Facsimile: +33 1 44 82 68 36

Establishment
Registration Number: 3010258456

Predicate Device
This submission claims substantial equivalence to a combination of two cleared devices:
1. FibroScan® (#K123806) manufactured by the sponsor and cleared on April 5, 2013; and
2. Aixplorer® (#K132274) manufactured by Supersonic Imagine S.A. and cleared on September 24, 2013.

Device Description

FibroScan® system consists of a system unit and a hand-held probe. It is based on Vibration-Controlled Transient Elastography (VCTE™) technology, and is designed to perform non-invasive measurements of liver shear wave speed and estimates of tissue stiffness. The probe containing a mechanical vibrator produces low-amplitude elastic waves that travel through the skin and intercostal space into the liver. Ultrasound is used to track the shear (elastic) wave, measure its speed and provide estimated stiffness. The results are displayed on the system unit.

The focus of this submission is the expansion of the indications for use for the FibroScan system by Echosens to pediatric patients. In order to address the smaller anatomic size of pediatric patients, a new probe (S+) was developed, and the indications for use of the previously cleared M+ probe were modified. The new probe uses the same principle of operation, intended use and methodology (i.e. application to patient, signal measurement, processing and display), design, materials, manufacturing and testing processes as the previously cleared M+ and XL+ probes. The device specifications are similar to those of the predicate device. The system's software was upgraded to accommodate these changes.

Recognized Consensus Standards Used

Non-clinical testing to assure compliance with acoustic output, biocompatibility as well as thermal, electrical, electromagnetic and mechanical safety were performed and have been found to conform to applicable standards. The system complies with the following standards:

- IEC 60601-2-37 Edition 2.0 2007-08: Medical Electrical Equipment - Part 2-37: Particular Requirements For The Basic Safety And Essential Performance Of Ultrasonic Medical Diagnostic And Monitoring Equipment.
- NEMA UD 2-2004 (R2009): Acoustic Output Measurement Standard For Diagnostic Ultrasound Equipment Revision 3
- AIUM MUS: Medical Ultrasound Safety, Third Edition
- IEC 62127-1 Edition 1.1 2013-02: Ultrasonics -- Hydrophones -- Part 1: Measurement And Characterization Of Medical Ultrasonic Fields Up To 40 Mhz
- IEC 62127-2 Edition 1.0 2007-08: Ultrasonics -- Hydrophones -- Part 2: Calibration For Ultrasonic Fields Up To 40 Mhz [Including: Technical Corrigendum 1:2008 And Amendment 1:2013]
- IEC 62127-03 Edition 1.1 2013-05: Ultrasonics -- Hydrophones -- Part 3: Properties Of Hydrophones For Ultrasonic Fields Up To 40 Mhz
- IEC 61161 Edition 3.0 2013-01: Ultrasonics -- Power Measurement -- Radiation Force Balances And Performance Requirements
- AAMI / ANSI ES60601-1:2005/(R)2012: Medical Electrical Equipment - Part 1: General Requirements For Basic Safety And Essential Performance (IEC 60601-1:2005, Mod)
- IEC 60601-1-2 Edition 3: 2007-03: Medical Electrical Equipment - Part 1-2: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Compatibility - Requirements And Tests

- IEC 60601-1-6 Edition 3.1 2013-10: Medical Electrical Equipment - Part 1-6: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Usability
- IEC 62366 Edition 1.1 2014-01: Medical Devices - Application Of Usability Engineering To Medical Devices
- IEC 62304 First Edition 2006-05: Medical Device Software - Software Life Cycle Processes
- ISO 14971 Second Edition 2007-03-01: Medical Devices - Application Of Risk Management To Medical Devices

Performance Data

The bias and precision of the device was documented based on tests performed on phantoms with known elasticity. The bias, i.e. the difference in the mean shear wave speed measured and the nominal shear wave of the phantom, normalized by the nominal shear wave and expressed in percent was evaluated and compared to the corresponding value reported for the predicate devices. While the Aixplorer® predicate device[1] pediatric probes reported values of bias between (-7.2%) and (43.4%), and the FibroScan® predicate devices reported values of bias between (-13.9%) and (1.3%); the range of bias values measured for the candidate device were between (-13.5%) and (3.6%). Therefore, the overall range of bias values (across all values) for the Aixplorer predicate device probes are ~50% of the nominal shear wave speed, while the corresponding range for the predicate FibroScan probes and for the candidate device probe is <20%. Hence, the candidate device has a bias value that is similar or better than that of the predicate device.

Similarly, the system's precision, i.e. the standard deviation of the independent measurements of the shear wave speed, normalized by the reference value was calculated. The range of values reported for the Aixplorer® predicate device pediatric probes were between (0%) and (3.4%), and for the FibroScan® predicate device probes were between (0%) and (3.1%), while the corresponding range for the candidate device probe was between (0.7%) and (2%). Therefore, the precision of all systems is similar – range of precision values of ~3% for the predicate device and ~2% for the candidate device.

Intended Use / Indications for Use

FibroScan® is intended to provide 50Hz shear wave speed measurements and estimates of tissue stiffness through internal structures of the body.

FibroScan® is indicated for noninvasive measurement of shear wave speed and estimate of stiffness at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of pediatric and adult patients with liver disease.

Comparison of Technological Characteristics

[1] The specific values of precision and bias for the AIXPLORER system are quoted from the 510(k) Summary of #K112255 which is the predicate for #K132274 and is stated to have a substantially equivalent non-clinical performance

The new S+ probe and the revised software are substantially equivalent to the predicate device (FibroScan® – #K123806) manufactured by the sponsor and cleared on April 5, 2013. The proposed device uses the same technology, intended use and methodology (i.e. application to patient, signal measurement, processing and display) as the FibroScan system. It is designed to accommodate the anatomy of pediatric patients.

The expansion of the Indications for Use of the FibroScan System with the new S^+ probe to include pediatric patients is substantially equivalent to the diagnostic ultrasound Indications for Use of the ShearWave™ Elastography mode of the Aixplorer (#K132274) for pediatric patients. The candidate device uses the S^+ ultrasound transducer at a center frequency of 5 MHz, which is in the range of frequencies used by the Aixplorer predicate system for pediatric applications. The analog front end and central control interface of the candidate and predicate devices have equivalent functionality.

In summary, the candidate and predicate devices are based on the same physical phenomenon, namely the effect of soft tissue elasticity on the propagation of low frequency mechanical waves in internal organs. They use ultrasound for measuring the changes in the strain field that results from the propagation of the mechanical wave, and display the shear wave speed and stiffness estimate. Therefore, the candidate and predicate devices are substantially equivalent in terms of the technology used.

Substantial Equivalence Discussion

The focus of this submission is the expansion of the indications for use for the FibroScan system by Echosens to pediatric patients. Therefore, substantial equivalence is claimed to the primary predicate device – the original FibroScan System (#K123806) in terms of the intended use, scientific principle, technological design, materials used, patient interface, data collection, processing and display. Substantial equivalence is also claimed to the secondary predicate device (AIXPLORER® #K132274), in terms of the indications for use (elastography for pediatric population), technological characteristics, signal acquisition, processing and display.

In order to address the smaller anatomic size of pediatric patients, a new probe (S+) was developed, and the indications for use of the M+ probe were modified. The center frequency of the S+ probe is well within the range of frequencies used by the predicate device (Aixplorer) for pediatric patients. The system's software was upgraded to accommodate these changes. The new probe uses the same principle of operation, design, materials, manufacturing and testing processes as the primary predicate. Therefore, the new S+ probe does not raise different questions of safety and effectiveness compared to the predicate devices.

Bench testing was performed to assure that the device meets its specifications. Measurements of the bias and precision of the device demonstrated substantial equivalence to both predicate devices.

A summary of the comparison between the candidate and predicate devices leading to the conclusion that the candidate device raises no new issues of safety or effectiveness is presented in the following table:

	FibroScan® – Pediatric Use	FibroScan®	Aixplorer®
510(k) #	K150239	K123806	K132274
Indications for Use	FibroScan® is intended to provide 50Hz shear wave speed measurements and estimates of tissue stiffness through internal structures of the body. FibroScan® is indicated for noninvasive measurement of shear wave speed and estimate of stiffness at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of pediatric and adult patients with liver disease. Prescription Use Device	FibroScan® is intended to provide 50Hz shear wave speed measurements through internal structures of the body. FibroScan® is indicated for noninvasive measurement of shear wave speed at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of patients with liver disease. Prescription Use Device	The SuperSonic Imagine AIXPLORER®) ultrasound system is indicated for use in the following applications: Abdominal, Small Organs, Musculoskeletal, Superficial Musculoskeletal, Vascular, Peripheral Vascular, GYN, Pelvic, Pediatric, Urology, Trans-rectal and Trans-vaginal. The system also provides the ability to measure anatomical structures (Abdominal, Small Organs, Musculoskeletal, Superficial Musculoskeletal, Peripheral Vascular, GYN, Pelvic, Pediatric, Urology, Transrectal and Trans-vaginal).
Clinical Application	Pediatric	Abdominal	Abdominal Pediatric Other
Ultrasound Source	Piezoelectric	Piezoelectric	Piezoelectric
Probe Frequency	Pediatric: 5 MHz (S+ Probe)	Adults: 3.5 MHz (M+ Probe) 2.5 MHz (XL+ Probe)	Pediatric: 1 – 6 MHz (SC6-1 Probe) 4 – 15 MHz (SL15-4 Probe)
Elastography Mode	Vibration-Controlled Transient™	Vibration-Controlled Transient™	ShearWave Elastography™
Bias	(-13.5%) – (3.6%)	(-13.9%) – (1.3%)	(-7.2%) – (43.4%)[2]
Precision	(0.7%) – (2.0%)	(0%) – (3.1%)	(0%) – (3.4%)[3]

[2] Pediatric probes
[3] Pediatric probes

Appendix B

Now powered by both VCTE™ & CAP™

the future of non-invasive liver diagnostics

Only FibroScan can provide the combined benefits of Vibration Controlled Transient Elastography (VCTE) and Controlled Attenuation Parameter (CAP) in a single, non-invasive test.

Worldwide Clinical Validation

Society	Region	Disease	Guidance
AASLD/IDSA[1]	USA	HCV	VCTE + Direct Biomarkers
WHO[2]	World	HCV & HBV	First Line test
EASL[3]	Europe	HCV & HBV	First Line test
NICE[4]	UK	HBV	First Line test

1. Recommendations for Testing, Managing and Treating Hepatitis C; When & In Whom to Initiate Antiviral Therapy, AASLD & IDSA Practice Guidelines; www.hcvguidelines.org
2. WHO Guidelines for Screening, Care and Treatment of Persons with Hepatitis C Infection; ISBN 978 92 4 154875 5
3. EASL Clinical Practice Guidelines : Noninvasive Tests for Evaluation of Liver Disease Severity and Prognosis; Journal of Hepatology 2015
4. Diagnosis and Management of Chronic Hepatitis B in Children, Young People & Adults; guidance.nice.org.uk/cg165

Antiviral drug stratification

ASH NAFLD HBV NASH HCV

Monitor disease progression

Monitor therapeutic response

FibroView

Review & Reporting Software

- Increase workflow efficiency by reviewing studies and generating reports at the convenience of the physician's computer
- Generate PDF reports with integrated physician interpretation commentary
- Customize report format to physician preference and disease group
- PC & MAC compatible!

Probes

- M Probe for Adult Patients
  Explored Area 25 mm - 65 mm
- XL Probe for Overweight Patients
  Explored Area 35 mm - 75 mm
- S probe for pediatric patients
  with a thoracic perimeter
  of less than 75 cm

FibroScan touch 502

Learn more by visiting **www.fibroscan502touch.com**

echosens™

ECHOSENS NORTH AMERICA • 1050 Winter Street, Waltham, MA 02451

FibroScan® 502 TOUCH

User manual

E300M010.2 – Version 2 – 11/2014

(software version C 1.5)

US

TABLE OF CONTENTS

1. PURPOSE OF THE USER MANUAL

This User Manual has no contractual value whatsoever and under no circumstances may Echosens be held responsible on the basis of the information contained in this manual.

This User Manual details, on the one hand, all of the information required for the implementation, use and maintenance of the FibroScan instrument and, on the other hand, the list of information displayed.

Thus, after carefully reading the manual, operators shall be able to:

- connect peripheral elements (mains lead, USB devices, probes) and power up the FibroScan instrument,
- configure the device,
- navigate the machine's user interface,
- perform basic maintenance.

Echosens publishes this manual "as is", without guarantees of any nature, whether explicit or implicit, including, but not limited to implicit guarantees or merchant conditions, or adaptation for specific use in view of providing simple and accurate information. Consequently, Echosens cannot accept any responsibility for the manual's incorrect interpretation. Though all efforts have been made to offer a manual that is as accurate as possible, the manual may nevertheless contain some technical inaccuracies and/or typographical errors.

Echosens cannot, under any circumstances, be held responsible for any loss of profit, loss of business, data loss, business interruption, or for any indirect, specific, accidental or consecutive damages of any type. In the event of damages arising from a defect (imperfection) or error contained in this User Manual, Echosens undertakes to send the physician, as rapidly as possible, a hard copy or electronic document containing all corrections made to this manual.

This manual is updated on a regular basis. The most recent version of this manual is available from Echosens on request. Should any major modifications be made to the manual, however, Echosens undertakes to send the physician, as rapidly as possible, a new copy of the manual in hard copy or electronic format. Note that this does not involve updating the hardware and/or software in your possession.

The product owner must keep this manual for as long as the product is used.

This manual contains a chapter for troubleshooting the most commonly encountered problems.

Any information or modification requests pertaining to this manual should be sent to: Echosens, 30 place d’Italie, 75013 PARIS France.

1.1. SYMBOLS USED IN THE MANUAL

This symbol means: ATTENTION

Warning: see the instructions before using the medical device.

Instructions preceded by this symbol may cause injuries or damage the medical device and installation if not correctly followed.

This symbol means: INFORMATION

Additional information with no impact on instrument use.

1.2. PROPERTY AND COPYRIGHT

All manuals and documents of all types are the property of the company Echosens and are protected by copyright, all rights reserved. Your right to copy this documentation is limited to legal copyright. These manuals cannot be distributed, translated or reproduced, either in whole or in part, in any manner or in any form, without prior written consent from Echosens. Hence, the reproduction, adaptation or translation of this manual without prior written consent is prohibited, within the limits provided by copyright law.

2. WARNINGS

2.1. GENERALITY

Federal law restricts this device to sale by or on the order of a physician.

2.2. ELECTRICAL SAFETY

Because the power plug allows the unit to be disconnected from the network, it must be accessible at all times.

Correct grounding operation can only be guaranteed if the system is connected to a socket compliant with safety standards.

The bases of multigrips or the extension cables must not be connected to the device.

Devices connected to the FibroScan have to comply with the IEC 60950-1 standard.

Do not connect to the system parts not specified in the user guide.

Correct earthing operation can only be guaranteed if the system is connected to a socket compliant with safety standards.

Make sure that the air vents are not obstructed, or the electronic equipment could overheat, causing irreversible damage.

Do not operate in the presence of flammable gases or anesthetics. Explosion can result.

2.3. ELECTROMAGNETIC SAFETY

The use of accessories not specified in the user guide may cause a noncompliance in terms of electromagnetic compatibility (EMC).

Avoid using the FibroScan device when placed upon or near a machine that generates electromagnetic disturbance.

2.4. USING THE DEVICE

Do not push or lean on the top of the FibroScan unit.

To avoid tipping the FibroScan when moving it, move it slowly sideways and steer it firmly by holding the decorative rods on the front and back of the unit.

To avoid tipping the FibroScan when lowering it down a step, the operator must go in front of the unit and guide it on the way down.

2.5. DELETING MEASUREMENTS

All measurements taken before the one chosen for deletion will be eliminated from the exam after confirmation.

2.6. SWITCHING OFF THE UNIT

Never switch the unit off during an exam or from configuration mode. Never switch off the main power supply when the unit is switched on. Failure to comply with these instructions could cause a malfunction of the machine and/or loss of data.

2.7. MAINTENANCE

Maintenance operations must not be performed by a third party other than a technician authorized by Echosens.

The opening or modification of the device by a person other than an authorized Echosens technician is strictly prohibited.

No CD ROMs or DVD ROMs other than those provided by Echosens should be inserted into the drive.

The probe must be calibrated periodically. Beyond the period indicated on the calibration certificate, the manufacturer no longer guarantees the performance characteristics of the probe.

2.8. CLEANING

Switch off the device and disconnect it from the power supply to prevent electric shocks.

2.9. INTERPRETING THE RESULT

Results must only be interpreted by a physician specialising in liver diseases, who is aware of the patient's pathology and clinical context.

3. MISCELLANEOUS INFORMATION

3.1. GUARANTEE

The terms of guarantee are stated in the Echosens terms of sale documents.

For any request, Echosens remains available to the physician and his/her appointees and shall, if applicable, transfer the request to a competent local representative.

3.2. LIABILITY

The information displayed on the FibroScan screen is the result of complex calculations performed by the software application built into the FibroScan. These results are then interpreted by the physician in charge. Under no circumstances, and even if Echosens had been notified, would Echosens be held responsible for the incorrect interpretation of these results; Echosens' liability being limited to making the measurements, displaying them and printing them via the FibroScan.

The data from each exam are saved on the machine's hard disk. The user is responsible for saving the data on a regular basis. Echosens cannot under any circumstances be held responsible for the partial or total loss of FibroScan data.

3.3. PRODUCT LIFE

Echosens guarantees the specification and performance characteristics of the FibroScan device for seven years, provided that all necessary precautions for use and maintenance have been taken in accordance with the recommendations of the user manuals provided.

3.4. REVERSE ENGINEERING

The software license is individual and cannot, under any circumstances, be transferred in any manner to a third party. This software cannot be distributed, reproduced, translated, disassembled, decompiled, analyzed, modified, incorporated or combined with another software application, with the exception of cases allowed by law.

Resale of the software built into the FibroScan is prohibited.

3.5. REGISTERED TRADEMARKS

Echosens and FibroScan are registered trademarks of the company Echosens.

Microsoft Excel and Windows Embedded are registered trademarks of Microsoft Corporation in the United States and other countries.

4. INDICATIONS AND PRECAUTIONS FOR USE

4.1. INTENDED USE

The FibroScan system is an active, non-implantable medical device using ultrasound.

FibroScan is intended to provide information about the 50 Hz shear wave speed through the liver.

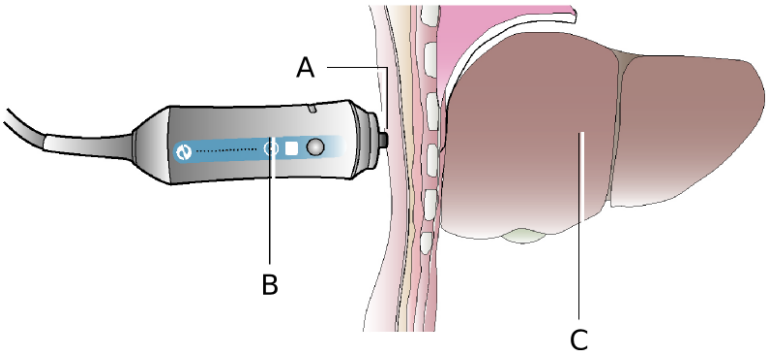
The FibroScan device is based on the Vibration-Controlled Transient Elastography principle (VCTE^{TM}).

The FibroScan probe comprises a single-element ultrasound transducer mounted on the shaft of the electrodynamic transducer. This transducer generates a transient vibration, which in turn generates an elastic shear wave. This wave propagates through the skin, the subcutaneous tissues, and then the liver. During shear wave propagation, the ultrasound transducer performs a series of ultrasound acquisitions (emission / reception) to measure the speed of shear wave propagation (Vs) in m/s. This measurement corresponds to the spatial and temporal average speed of propagation of the shear wave through the liver region of interest, which can be approximated by a cylinder with a diameter of 1 cm and a length of 4 cm (which corresponds to about 3 cm^3).

In addition, assuming that the liver is a pure elastic, linear and isotropic medium, the device converts shear wave speed Vs into equivalent stiffness E in kPa using the equation $E = 3 \times \rho \times Vs^2$ with ρ the medium density assumed to be 1000 kg/m^3. The values for shear wave speed and equivalent stiffness (or Young's modulus) are relative indexes intended only for the purpose of comparison with other measurements performed using FibroScan devices. Absolute values for these measurements may vary among measurement devices from different manufacturers.

4.2. INDICATIONS FOR USE

FibroScan is indicated for non-invasive measurement of shear wave speed at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of patients with liver disease.



How to use a probe: A: *Ultrasound transducer.* ***B:*** *Electrodynamic transducer.* ***C:*** *Liver.*

The values obtained must be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical record of the patient and the potential presence of different factors known to influence liver shear wave speed or equivalent stiffness. Based on the existing literature the following Table provides a list of parameters known to increase liver shear wave speed or equivalent stiffness.

Parameter	Reference
Liver fibrosis, cirrhosis	[1-8]
Acute hepatitis, inflammation, ALT flares	[9-12]
Portal pressure, central venous pressure	[13-15]
Extra hepatic cholestasis	[16]
Congestion (heart failure)	[17]
Meal intake	[18]
Amyloidosis	[19-21]

The intra and inter-operator agreement has been assessed in a cohort of 200 patients with chronic liver disease of various etiologies [22]. The intraclass correlation coefficient was 0.98 both within and between operators. This demonstrates that intra operator reproducibility is excellent and that changing the operator does not increase measurement variability.

[1] Friedrich-Rust, M., et al., Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. Gastroenterology, 2008. 134(4): p. 960-74.

[2] Musso, G., et al., Meta-analysis: Natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Annals of Medicine, 2011. 43(8): p. 617-49.

[3] Shaheen, et al., FibroTest and FibroScan for the Prediction of Hepatitis C-Related Fibrosis: A Systematic Review of Diagnostic Test Accuracy. American Journal of Gastroenterology, 2007: p. 1-12.

[4] Shi, K.Q., et al., Transient elastography: a meta-analysis of diagnostic accuracy in evaluation of portal hypertension in chronic liver disease. Liver Int, 2013. 33(1): p. 62-71.

[5] Smith, J.O. and R.K. Sterling, Systematic review: Non-invasive methods of fibrosis analysis in chronic hepatitis C. Alimentary Pharmacology and Therapeutics, 2009. 30(6): p. 557-76. [6] Stebbing, J., et al., A Meta-analysis of Transient Elastography for the Detection of Hepatic Fibrosis. Journal of Clinical Gastroenterology, 2010. 44(3): p. 214-9.

[7] Talwalkar, J.A., et al., Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. Clinical Gastroenterology and Hepatology 2007. 5(10): p. 1214-20.

[8] Tsochatzis, E.A., et al., Elastography for the diagnosis of severity of fibrosis in chronic liver disease: A meta-analysis of diagnostic accuracy. Journal of Hepatology, 2011. 54(4): p. 650-9.

[9] Arena, U., et al., Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology, 2008. 47(2): p. 380-4.

[10] Coco, B., et al., Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. Journal of Viral Hepatitis, 2007. 14(5): p. 360-9.

[11] Mueller, S., et al., Increased liver stiffness in alcoholic liver disease: differentiating fibrosis from steatohepatitis. World Journal of Gastroenterology, 2010. 16(8): p. 966-72.

[12] Sagir, A., et al., Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage. Hepatology, 2008. 47(2): p. 592-5.

[13] Carrión, J.A., et al., Transient elastography for diagnosis of advanced fibrosis and portal hypertension in patients with hepatitis C recurrence after liver transplantation. Liver Transplantation, 2006. 12(12): p. 1791-8.

[14] Millonig, G., et al., Liver stiffness is directly influenced by central venous pressure. Journal of Hepatology, 2010. 52(2): p. 206-10.

[15] Vizzutti, F., et al., Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. Hepatology, 2007. 45(5): p. 1290-7.

[16] Millonig, G., et al., Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. Hepatology, 2008. 28(5).

[17] Lebray, P., et al., Liver stiffness is an unreliable marker of liver fibrosis in patients with cardiac insufficiency. Hepatology, 2008. 48(6): p. 2089.

[18] Mederacke, I., et al., Food intake increases liver stiffness in patients with chronic or resolved hepatitis C virus infection. Liver International, 2009. 29(10): p. 1500-6.

[19] Janssens, E., et al., Hepatic amyloidosis increases liver stiffness measured by transient elastography. Acta Gastroenterologica Belgica, 2010. 73(1): p. 52-4.

[20] Lanzi, A., et al., Liver AL amyloidosis as a possible cause of high liver stiffness values. European Journal of Gastroenterology and Hepatology, 2010. 22(7): p. 895-7.

[21] Loustaud-Ratti, V.R., et al., Non-invasive detection of hepatic amyloidosis: FibroScan, a new tool. Amyloid, 2011. 18(1): p. 19-24.

[22] Fraquelli, M., et al., Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut, 2007. 56(7): p. 968-73.

4.3. PROBE AND EXAMINATION SELECTION CRITERIA

The recommendations for using the probes are defined by the following patient's morphological data:

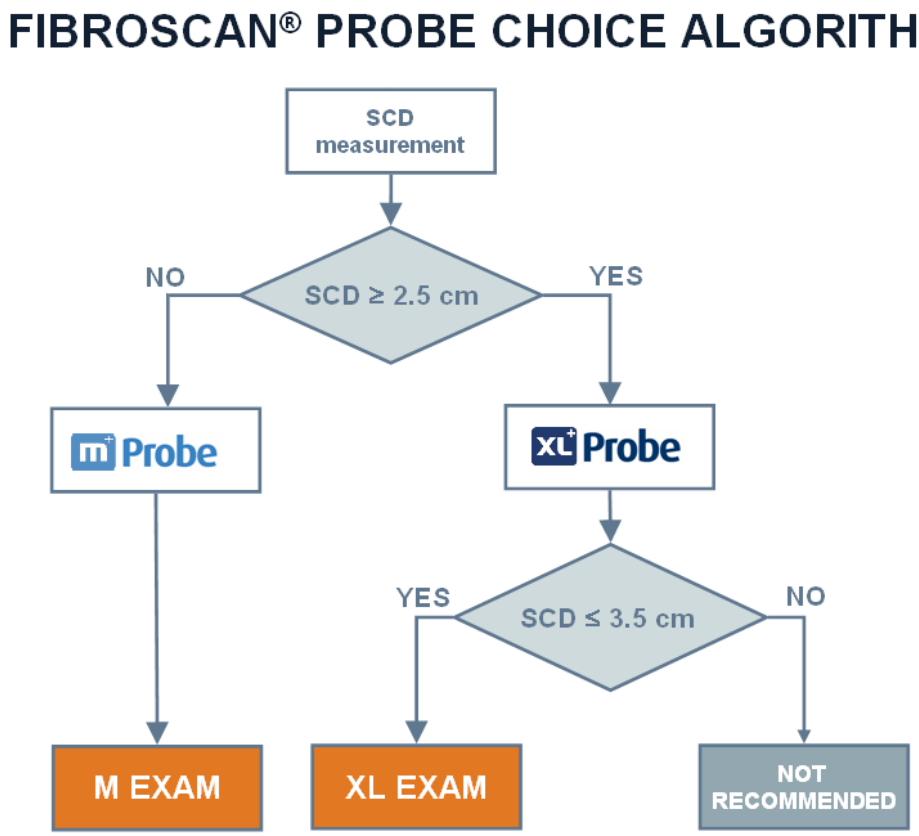
- SCD: Skin-to-Capsule Distance assessed with an ultrasound scanner or by the automatic probe selection tool.

In case of using an ultrasound scanner, SCD should be measured at the point where the shear wave speed is measured with a pressure similar to the one used with the FibroScan probe.

In case of using the automatic probe selection tool, please refer to chapter 6.5.11. Exam type selection area.

It is not recommended to use any means to compress the soft tissues merely to reduce the SCD.

Two types of examination are available. They correspond to specific measurement depths that take into account the liver's depth beneath the skin.



In all cases, Echosens recommends to perform 10 valid measurements.

4.4. PRECAUTIONS FOR USE

The following instructions must be followed in order to ensure patient safety. The FibroScan should not be used in the following situations:

- On patients of less than 18 years of age.
- On an organ other than the liver. The eyes and mucosa must absolutely be avoided.
- On patients with active implants such as pacemakers, defibrillators, pumps, etc.
- On wounds.
- On pregnant women.

Moreover, presence of ascites between the probe and the liver may prevent from obtaining measurement with the device.

The clinical personnel must follow normal safety procedures.

The FibroScan examination should be performed prudently using the principle of ALARA (As Low As Reasonably Achievable).

4.5. USER TRAINING

Only persons who have received training in the use of the FibroScan unit and who possess a user certificate are authorized to conduct an examination using FibroScan. Training is essential for correct equipment use and in order to obtain reliable and reproducible measurements.

This manual is not intended to provide user training.

4.6. ELECTRICAL SAFETY

The FibroScan is manufactured and tested in accordance with IEC electromagnetic compatibility (EMC) and electrical safety standards. It leaves the plant in full compliance with safety and performance requirements. In order to maintain this compliance and to guarantee the safe use of the medical device, the user must conform to the indications and symbols contained in this manual.

Refer to the warnings in Chapter 2 concerning electrical safety.

Prior to installation, ensure that the operating and mains voltage values match.

The electrical power lead provided must be connected to the FibroScan mains connector and to an earthed socket. Correct earthing operation can only be guaranteed if the FibroScan is connected to a socket compliant with safety standards.

Safe use is no longer guaranteed in the following main, non-exclusive cases:

- the device is visibly damaged,
- the device is inoperative,
- after prolonged storage in unfavorable conditions,
- after serious damage incurred during transport,
- in the presence of flammable or anaesthetic gases. This may cause an explosion. Do not take the device to the operating theatre.

When the safe use of the FibroScan is no longer possible, the device must be taken out of operation. Steps must be taken to prevent its inadvertent use. The medical device is entrusted to authorized technicians for inspection.

4.7. MAINTENANCE-RELATED SAFETY

For all maintenance operations, the physician and his/her appointees should contact Echosens, who will send an authorized technician.

For correct and safe use and for all maintenance operations, the personnel must conform to normal safety procedures.

5. EXTERNAL PRESENTATION

5.1. HARDWARE SUPPLIED

When opening the package, ensure the contents match the following list:

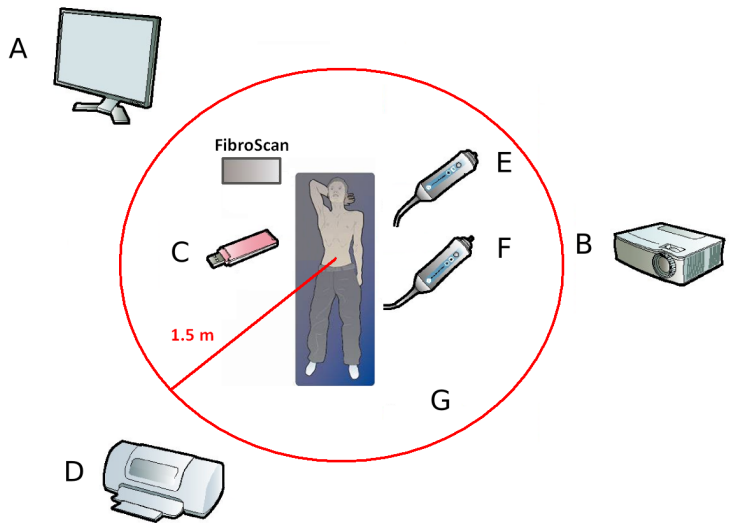
- Mounted assembly
- Mains lead US
- Case(s) fitted with probe(s)
- Sealed binder (Windows EULA license and FibroScan® manuals)
- Set of 4 fuses (type 5x20 T2.0AH 250V)

5.2. ACCESSORIES

The available accessories are:

- M^+ probe
- XL^+ probe

Set of elements that can be connected to the FibroScan unit:



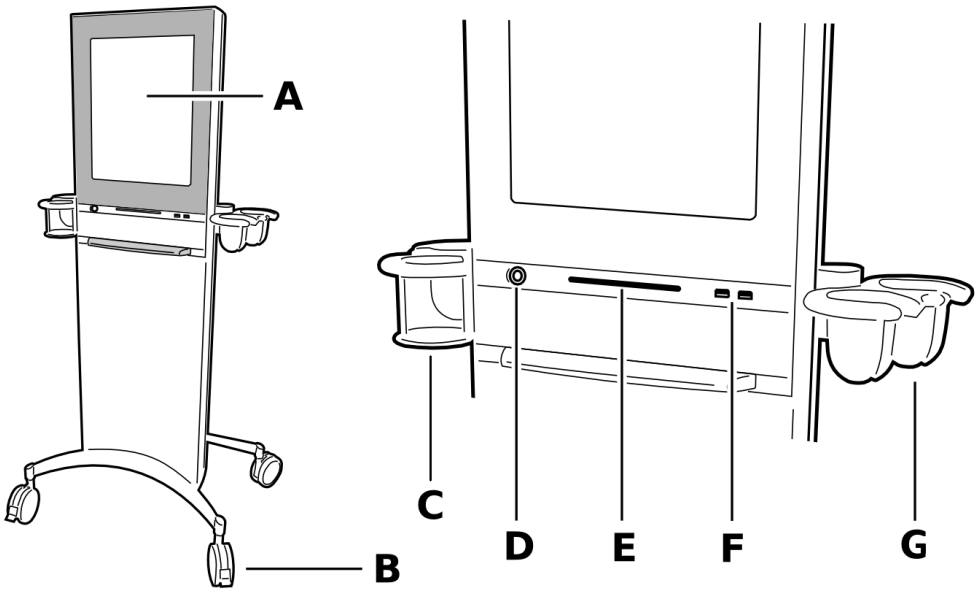
Devices not included: ***A:*** *DVI-I monitor.* ***B:*** *Overhead projector.* ***C:*** *USB storage device.* ***D:*** *USB printer.*

Accessories: ***E:*** *M^+ probe.* ***F:*** *XL^+ probe.* ***G:*** *Other accessories.*

5.3. FRONT VIEW

The FibroScan chassis encloses the electrical power supply, dedicated electronics and a computer. It also serves as support for a monitor, three probe holders and one gel holder.

The following figure presents the instrument's different user-accessible parts.



General arrangement of the FibroScan unit: A: *Touch screen.* ***B:*** *Caster with brake.* ***C:*** *Gel holder.* ***D:*** *Standby button.* ***E:*** *CD-ROM/DVD-ROM drive.* ***F:*** *Computer sockets.* ***G:*** *Probe holder.*

The standby button

This button is only active if the main switch is in the I position.

The button flashes when power is on.

Pressing this button **once** loads the application; the built-in indicator light turns green. After a few seconds, the Home window is displayed.

Pressing the button **a second time** closes the application; the built-in indicator light and monitor are both turned off. This is the usual position when the FibroScan has not been in use for a short period of time (between two patient groups for example). The FibroScan thus consumes less power.

The touch screen and the soft□are

This is a 19-inch colour LCD touch screen.

To avoid any damage to the touch screen, take care to not hang up the power cord on the top of the device.

The FibroScan is controlled by a dedicated software application.

The software is automatically loaded when the FibroScan is turned on. It performs the following functions:

- performing examinations,

- management of archived examinations.

Computer connectors

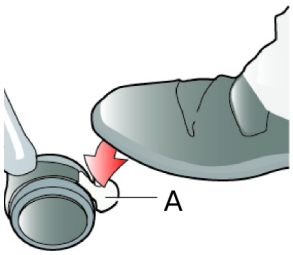
- Two USB 2.0 connectors: to connect an external hard disk for backups, a USB key, or a USB printer.

CD ROM □ DVD ROM drive

This drive lets you reinstall the software application.

Casters and brakes

The two front casters are fitted with a brake. The brake is locked by pressing the tongue. The caster is released by lifting this same tongue.



View of a caster with brake: A: *Caster brake.*

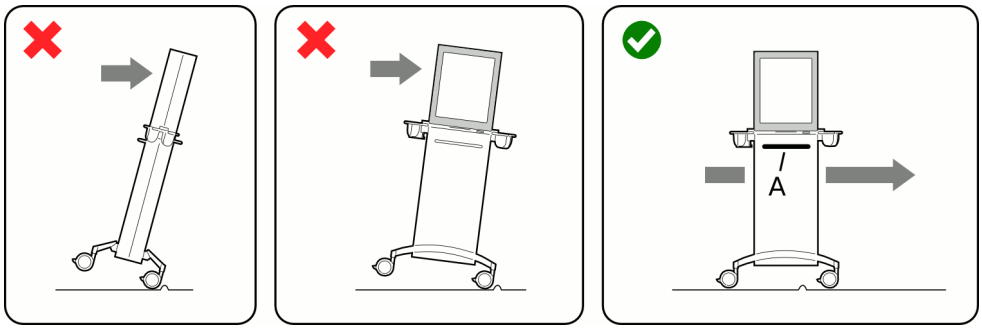
Moving the device

Always unlock the brakes before moving the device.

Do not push or lean on the top of the FibroScan unit.

To avoid tipping the FibroScan when moving it, move it slowly sideways and steer it firmly by holding the decorative rods on the front and back of the unit.

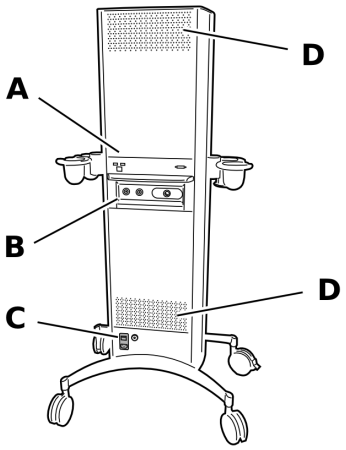
To avoid tipping the FibroScan when lowering it down a step, the operator must go in front of the unit and guide it on the way down.



Moving the device: A: *Decorative rod.*

5.4. REAR VIEW

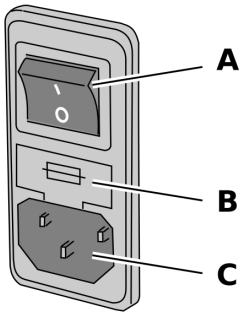
The rear part presents the instrument's user-accessible parts.



***Rear view: A:** Computer sockets. **B:** Probe sockets. **C:** Mains connector. **D:** Perforated ventilation plates.*

Mains connector

The FibroScan must be connected to a 100 V or 230 V, single phase 50-60 Hz grounded mains outlet via the power lead connected to the socket at the base of the chassis.



***View of main switch and connection socket: A:** Main switch. **B:** Location of fuses. **C:** Mains cable connection socket.*

Main s□itch

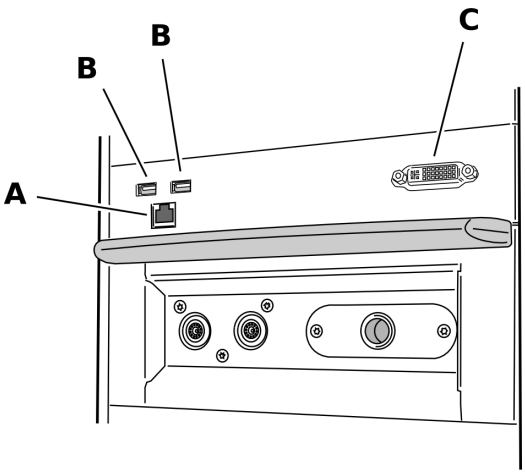
This switch has two positions:

- Position 0: no voltage is present in the internal circuits of the FibroScan; this state does not consume any electrical energy. This is the usual position when the FibroScan is no longer to be used (at the end of the day for example).
- Position 1: the AC main supply is present in the internal circuits of the FibroScan. This is the FibroScan's working position.

This switch assembly has a removable part. It provides access to the two FibroScan protection fuses.

The bottom part of the switch unit receives the mains lead plug connection outlet.

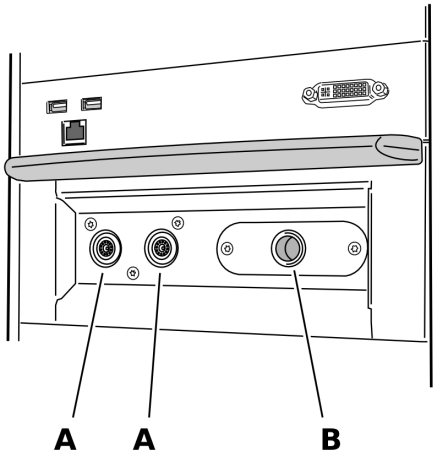
Computer connectors



***Location of data cables: A:** Ethernet. **B:** 2 USB 2.0 ports. **C:** DVI-I output.*

- Ethernet connector: used by Echosens maintenance staff.
- Two USB 2.0 connectors: to connect an external hard disk for backups, a USB key, or a USB printer.
- DVI-I output: this output is used to connect an additional monitor (e.g. an overhead projector). The maximum distance between the FibroScan and the additional monitor is approximately 1.80 meters.

Probe connectors



***Location of probe connectors: A:** Probe connectors. **B:** Location of the connector of the disconnected probe.*

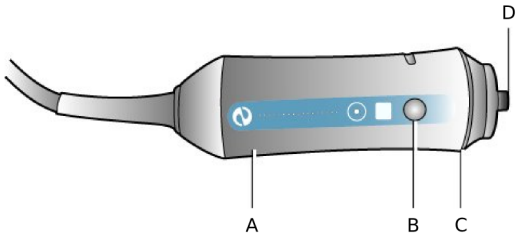
Location (B) is not operational. It protects the connector of the disconnected probe.

The probe connectors are fragile.

5.5. PROBES DESCRIPTION

Housing

The housing contains an electrodynamic transducer (vibrator), an ultrasound transducer and a measurement trigger button.



***Probe housing: A:** Electrodynamic transducer. **B:** Measurement button. **C:** Indicator light (LED). **D:** Ultrasonic transducer.*

The ultrasound transducer of the probe is a "Type B" applied part, and is the only component of the FibroScan unit in contact with the patient.

Measurement button

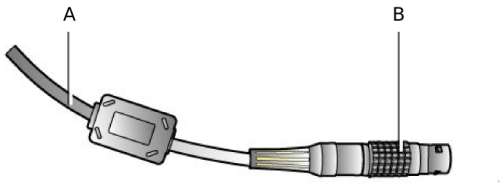
As soon as this button is pressed (if sufficient pressure is exterted on the transducer), the vibrator actuates the electrodynamic transducer, which in turn generates a shear wave (s-wave) that painlessly impacts the patient's skin. The ultrasound transducer performs a series of acquisitions (emission / reception) to measure the propagation speed of this shear wave. Acquisition lasts less than one tenth of a second.

Indicators

The indicator lights (LEDs) display a status as follows:

- On during FibroScan start-up and when standing by to launch an exam.
- Flashing lights for the probe selected when an exam starts.
- Switched off during an exam when the operator is applying an incorrect pressure to the patient’s body.
- On during an exam when the operator is applying the correct pressure to the patient's body. It is however strongly recommended that you view the pressure exerted by looking at the on-screen pressure indicator.

Lead



***Probe lead: A:** Connection cable. **B:** Connection jack.*

This 1.5 m lead connects the probe to the FibroScan by means of a multi-pin jack.

The probe transducer, the probe jack, and the FibroScan connector are fragile elements and must be handled with care.

The probe jack has a red dot that should be aligned with the red dot on the FibroScan socket before insertion.

The serial number marked on the connector identifies the probe uniquely.

6. SOFTWARE INTERFACE

When the unit is switched on, the login screen is displayed.

6.1. LOGIN SCREEN

The login window provides secure access to patient data in the machine.

To log in, select the user name, enter the corresponding password then confirm by pressing [OK].

The activation of the login window is configurable. See the Configuration section.

User name / Pass□ord

The user name and password were defined when the device was installed.

User	Pass□ord	Note
Doctor	MD	To change this password, see the Configuration section.
Biomedical Engineer	maintenance	

After having logged in, the home screen is displayed.

6.2. HOME SCREEN

The software loaded when the FibroScan unit is started up is used to:

- perform examinations,
- print the results,
- manage the archives,
- export in several formats.

Description of Home menu□

Access to FibroScan configuration. See the Configuration section.

Displayed only if auto-logon is disabled. A password will be requested before you can enter the application. See the Configuration section.

Access to the patient file archives.

Access to the exam.

The following messages can be displayed in the home window:

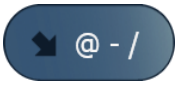
- No probe connected
- Probe out of calibration (see the Probe Calibration section)

6.3. USING THE KEYPAD

The keypad is displayed whenever an input is required.

Description of the keypad

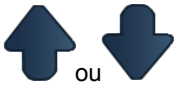
Capital.



Keyboard display to input special characters.

Deletes the previous character.

Tab. To move from one input field to another.

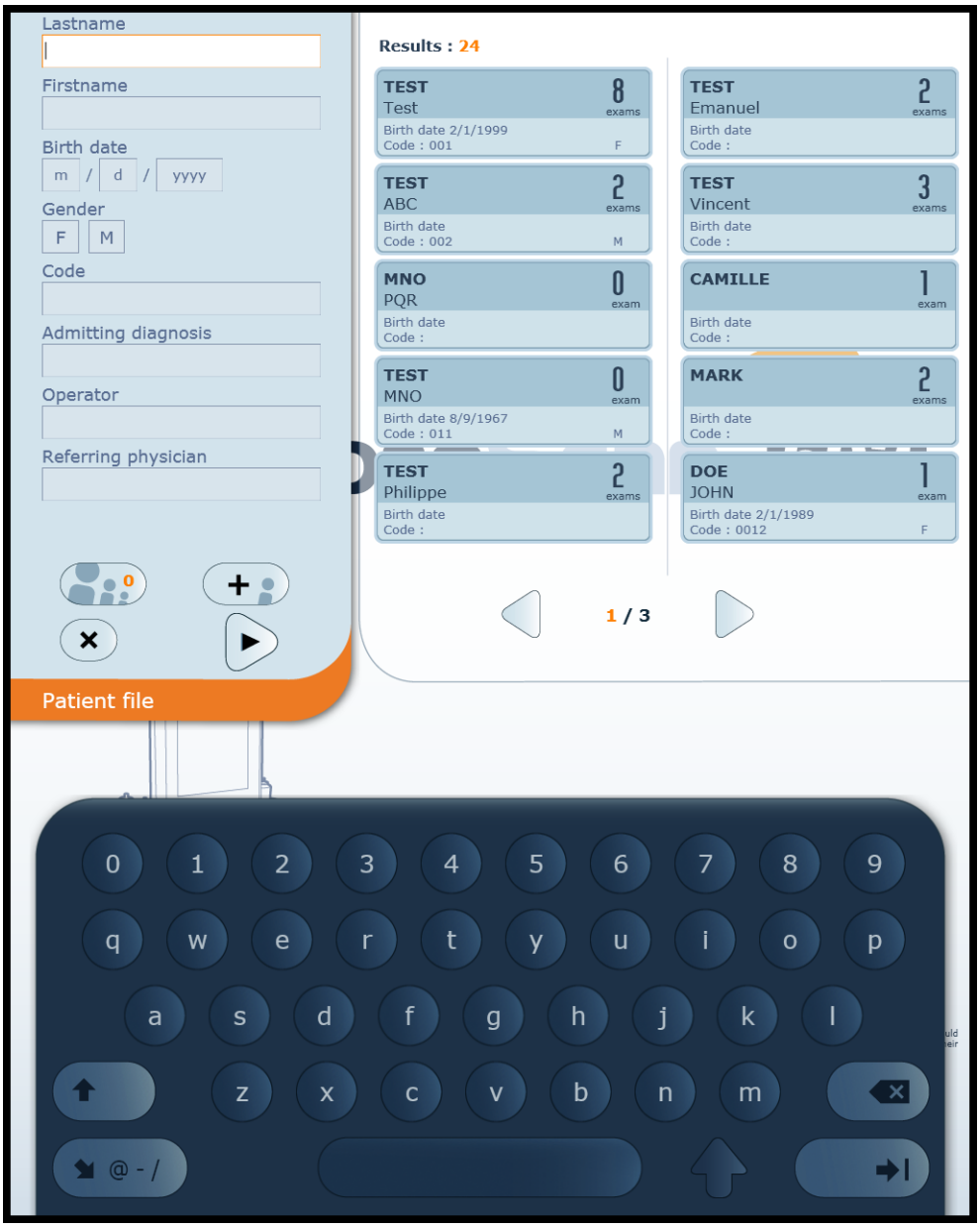


Keyboard display at the top or bottom of the screen, as selected by the user.

Special characters are accessible by pressing and holding a letter. Example:

6.4. THE PATIENT RECORD SCREEN

If the patient exists in the patient list, the data will be displayed automatically after the name is entered. Select the patient.



Complete the fields. The 'Name' or 'Code' field must be filled in to start the examination.

Displays/hides the patient waiting list.

Add the selected patient to the list of patients waiting for an exam. An examination can be performed on this patient later.

Cancels the patient entry.

Starts the examination.

After data input, if the probe is out of calibration the following message is displayed:

- Probe calibration days overdue: n. Contact your local service support.

With n the number of days.

The patient waiting list

Deletes the selected patient from the patient waiting list.

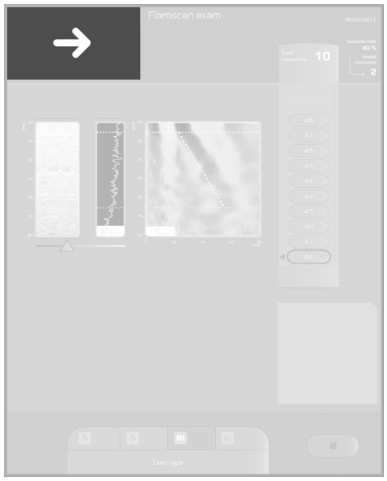
A patient file is automatically deleted from the patient waiting list if an exam with at least one valid measurement has been made, or if the patient file has been on the patient waiting list for more than three days.

6.5. ACQUISITION SCREEN

The main data displayed in an acquisition window are presented below.

The acquisition window consists of the following elements:

6.5.1. Patient data



Display/Hide patient data.

6.5.2. Ultrasound images

TM and Amplitude modes

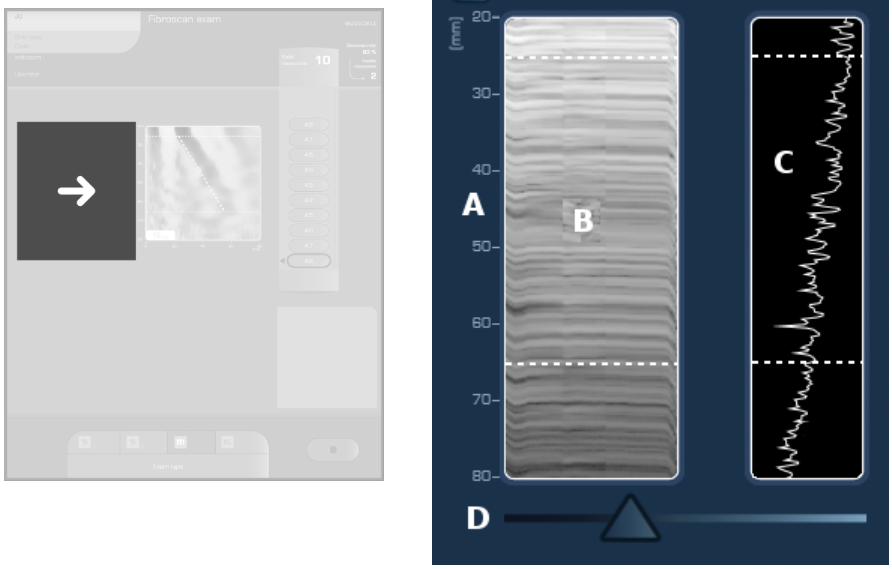


Image in TM (left) and Amplitude (right) modes: A: *Depth explored (mm).* ***B:*** *Ultrasound signal represented in TM (Time Motion) mode.* ***C:*** *Ultrasound signal represented in A (Amplitude) mode.* ***D:*** *Display gain adjustment.*

As soon as the probe makes contact with the skin, i.e. when a pressure change is detected, the ultrasound transducer begins ultrasound data acquisitions.

The system displays two ultrasound images used to locate a zone that satisfies the measurement criteria:

- One in time motion (TM) mode, two-dimensional greyscale image.
- The other in A mode (current ultrasound signal amplitude).

The gain on the display of both modes can be adjusted using the cursor under the ultrasound images.

These two modes serve to ensure that the probe is correctly positioned to perform a measurement on a sufficiently thick portion of liver, visible throughout the explored depth. Ultrasound emission/reception mode also allows the operator to ensure that the measurement will not be disrupted by the presence of large structures such as blood vessels.

Liver targeting tool

Liver targeting tool: A: *Activation button.* ***B:*** *History of the liver indicator.* ***C****: Instantaneous liver indicator.*

Liver targeting tool helps in choosing the optimal measurement point.

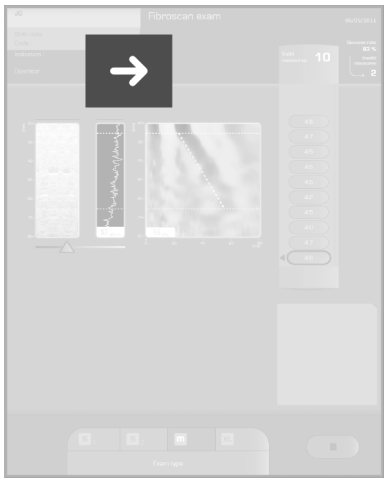
Enable/disable the liver targeting tool during examination.

When enabled, once the probe in contact with patient skin, liver targeting tool characterizes quality of ultrasonic signal in the liver with a color scale.

Color scale: Black: *Poor quality of ultrasonic signals.* ***Green:*** *Good quality of ultrasonic signals.*

The more green the indicator, the better the quality of ultrasonic signals.

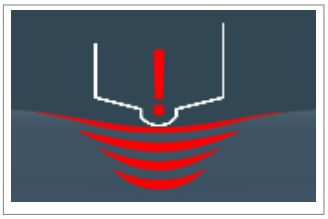
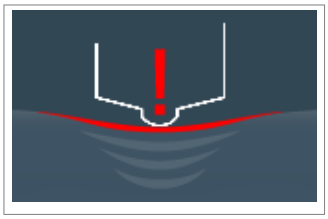
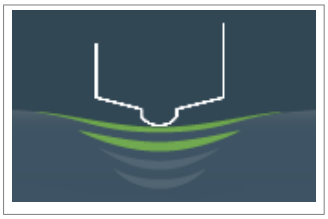
6.5.3. Pressure indicator



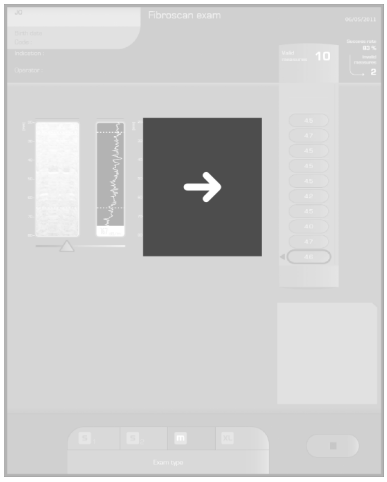
The probe contains a sensor that measures the pressure applied by the operator to the patient. The pressure level is given by:

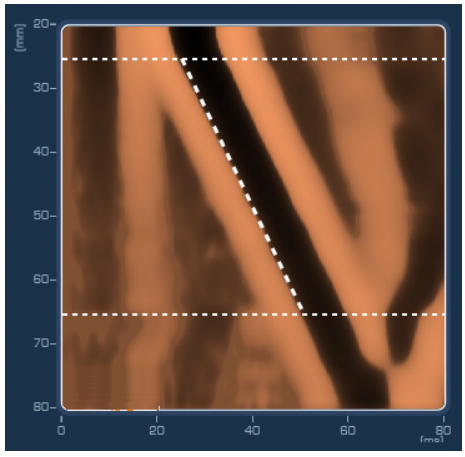
- the software: pressure indicator (green/red),
- the probe: blue LEDs.

Measurements may only be made when the pressure indicator is in the green zone.

		
Pressure to high (red).	*Pressure too low (orange).*	*Correct pressure (green).*
Probe LEDs off. Measurement impossible.	*Probe LEDs off. Measurement impossible.*	*Measurement can be carried out; the probe button is active.*

6.5.4. Shear wave propagation map





This image is displayed once the measurement is complete. It represents the levels of liver deformation generated by the propagation of the shear wave as a function of time (horizontal axis in milliseconds) and depth (vertical axis in millimetres).

The shear wave speed value is displayed if the measurement is valid.

The colour scale indicates the sign of the deformations (compression or expansion). Black areas correspond to negative deformation and pale areas to positive deformation. The black strip through the image represents deformations associated with the passage of the shear wave, which penetrates progressively deeper with time.

6.5.5. Counters: valid and invalid measurements, success rates

Valid measurements

From top to bottom: first to last measurement in m/s.

When the number of valid measurements is equal to 1, the IQR and the IQR/median ratio are undefined and therefore are not displayed.

Invalid measurements

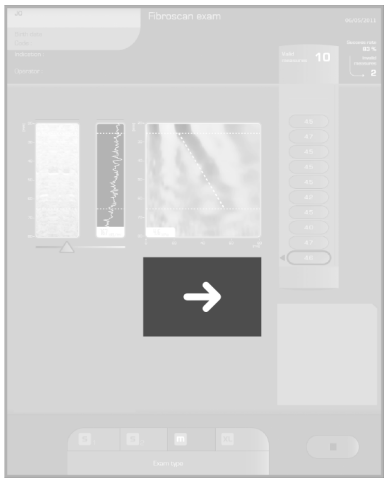
The measurement is automatically rejected by the algorithms if the pulse sent out by the transducer could not be delivered successfully and/or if the shear wave propagation maps are not satisfactory.

The message 'INVALID' is then displayed above the shear wave propagation map.

Success rate

The software calculates a % success rate. This value corresponds to the ratio of the number of valid measurements to the total number of measurements performed.

6.5.6. Shear wave speed results area



Median

Shear wave speed is expressed in meters per second (m/s). This value is the median of all valid measurements performed during the examination.

If the repeat measurement is invalid, the median is not re-computed. To obtain a reliable and representative liver shear wave speed measurement, **at least ten valid measurements should be made.**

Refer to the warning in Chapter 2 concerning interpretation of the result.

Inter□uartile range (I□R)

The interquartile range (IQR) is expressed in meters per second (m/s). It represents the interval around the median within which will fall 50% of all valid measurements. It is re-computed after each new valid measurement.

6.5.7. Stiffness results area

Median

Liver stiffness is expressed in kilopascals (kPa). This value is the median of all valid measurements performed during the examination.

Liver stiffness is calculated when shear wave speed measurement is valid.

Inter□uartile range (I□R)

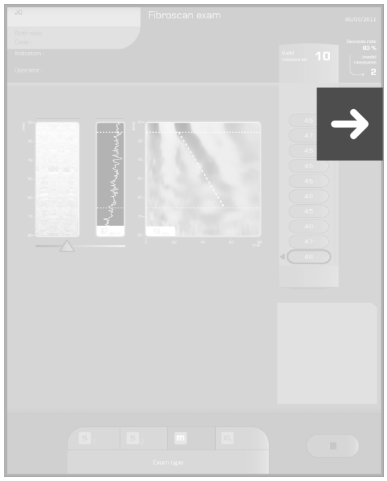
The interquartile range (IQR) is expressed in kilopascals (kPa). It represents the interval around the median within which will fall 50% of all valid measurements. It is re-computed after each new valid measurement.

I□R/med

This value, expressed as a percentage, is the ratio of the IQR to the median stiffness. It is re-computed after each new valid measurement.

6.5.8. Deleting measurements

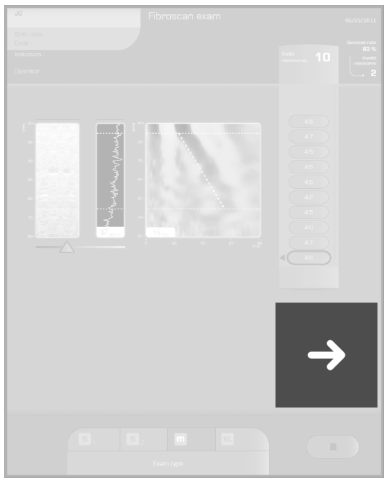
Some or all of the measurements in the current examination may be cancelled at any time during the exam. This should only be used once the optimal region of measurement (i.e. probe position) has been found and will cancel all prior measurements during that session. The patient's data, displayed in the left-hand part of the window, are saved.



Press the last measurement to be deleted and then the following button:

Refer to the warning in Chapter 2 concerning deletion of measurements.

6.5.9. Adding a comment



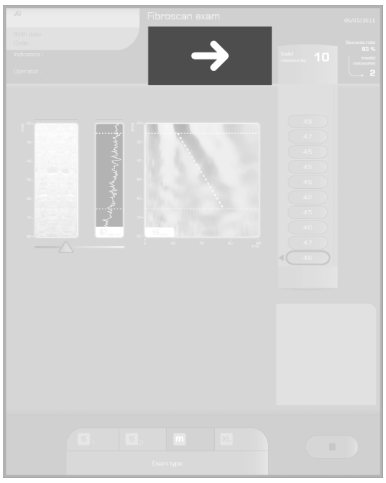
You can add comments to the current exam:

- press the ‘Comments’ field,
- enter comments using the touchpanel.

Information entered in the ‘Comments’ field will appear on the exam result printout.

The ‘Comments’ field cannot be added to or modified during an exam review.

6.5.10. Message area



The following main messages can be displayed above the shear wave propagation map.

Connect the probe.

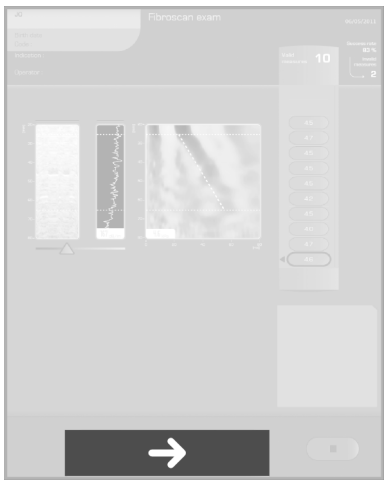
Replace the probe.

Calibrate the probe.

Electromagnetic disturbance.

6.5.11. Exam type selection area

The criteria to select the probe examination type adapted to the morphology of the patient are given in section Probe and examination selection criteria.



If only the M^+ or the XL^+ probe is connected to the device, selection of the corresponding examination is automatically made by the device software.

If both M^+ and XL^+ probes are connected, choose the exam type.

Automatic probe recommendation

The automatic probe recommendation tool is based on the SCD (skin-to-capsule distance) measurement using ultrasound signals received by the machine's probe. This feature operates in real time as soon as the probe detects ultrasound signals (probe in contact with patient skin).

The result of this tool is displayed at the bottom of the screen and may be one of the following three cases:

1. "Probe advice: in progress": the tool cannot currently measure the SCD because the probe is not correctly positioned in front of the liver and/or the ultrasound signals are of poor quality.
2. "Probe advice: M": the tool measures a SCD that justifies the use of the M^+ probe. The box containing the M exam type icon flashes.

3. "Probe advice: XL": the tool measures a SCD that justifies the use of the XL+ probe. The box containing the XL exam type icon flashes.

If the tool is able to recommend a probe (case 2 or 3), two situations are possible:

- The operator continues the exam without changing probes and, if he/she wishes, can confirm the probe choice by pressing the icon of the exam type concerned. The probe recommendation tool is then disabled until the end of the current exam.
- The probe currently in use is not the recommended probe: The operator changes the probe by applying the procedure explained in the paragraph below.

Be sure to use enough gel for this tool to function properly.

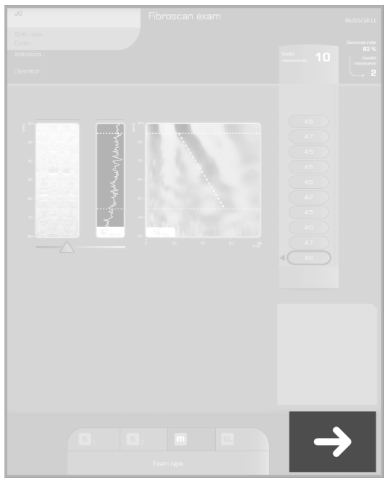
You are strongly advised to use the recommended tool, to guarantee reliable results. The decision whether or not to accept this recommendation, however, rests with the user.

Change of probe during an exam

To change the probe during an exam:

1. Select the new probe type. The following message is displayed:
   - Change of exam type. The change of exam type involves the final deletion of all measurements previously performed.
2. Click OK (warning: all the measurements done with the previous probe will be deleted). The following message is displayed:
   - The exam type has changed. Connect the appropriate probe to continue.
3. Connect the appropriate probe if necessary and resume the exam.

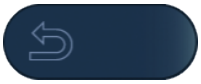
6.5.12. End of the examination



Press the button to end the exam.

The result of the examination is displayed in the examination details review screen.

Description of conte□tual buttons□



Back to the home window.

Prints the patient exam result.

Exports the patient exam result in .fibx format (a proprietary FibroScan format) to a removable USB storage device.

Exports the patient exam result in .pdf format to a removable USB storage device.

Starts a new examination.

6.6. MANAGEMENT OF PATIENT FILE ARCHIVES

To display the patient file archives, press the  button in the home screen.

File selection: [CTRL]+click to select non-consecutive files, [SHIFT]+click the first and last to select a series of files, and [CTRL]+[A] to select all files.

Deletes the selected files.

Exports the selected exam files to a .fibx file on a removable USB storage medium. You can export the last exam or all the exams for one patient.

Exports the results from all files to an .xls file on a removable USB storage medium. The .xls format export applies only to the complete set of examinations stored on the device and is therefore available only in the main Archives window.

Displays the next or previous page of archives.

Refines the advanced file search.

Selects all patient files in the window.

Closes the screen and displays the previous screen (keyboard shortcut: [Esc] key).

Excel file example

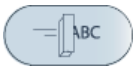
The file is generated in the root directory of the removable USB storage medium. File name integrates:

- the device serial number,
- the date and time the Excel file was created.

The Excel file comprises three data sheets (Data, SWS data and Parameters).

6.6.1. Advanced file search

Enter one or more search criteria. The list of matching files is displayed.



Deletes the input.

Closes the advanced search.

Opens the exam of the displayed patient.

6.6.2. Select and view a patient file

To view the exam summary for a patient, click the label and then  .

To view the details of an exam, click the summary of the exam.

6.6.3. Examination details review

To display the measurements, click a value in the list of valid measurements.

Description of function buttons

All those function buttons are available only in examination details review screen but not in acquisition screen.

Lets you view the previous exam or the next exam for the patient (keyboard shortcut: left or right arrow).

Back to the Archives screen.

Deletes the examination.

Prints the result of the exam.

Exports the result of the exam to a .fibx file.

Exports the result of the exam to a .pdf file.

Starts a new examination.

Displays the previous or next result of the measurements list (keyboard shortcut: up or down arrow). Displayed only in the presence of more than 12 measurements.

7. SWITCH OFF THE UNIT

7.1. BETWEEN SESSIONS

Turn the machine off by pressing the On/Off button in the bottom left-hand corner of the monitor.

7.2. AT THE END OF THE DAY

Always shut the machine down by applying the following sequence:

1. Turn the FibroScan off by pressing the On/Off button in the bottom left-hand corner of the monitor.
2. Cut the power supply by setting the main switch to **0**.

Refer to the warning in Chapter 2 concerning switching off the device.

8. CLEANING, MAINTENANCE AND REPAIRS

In the event of malfunction, only the staff of Echosens or its local representative are authorized to service FibroScan and its accessories. Any work performed by an unqualified person will terminate the guarantee.

8.1. CLEANING

Apply the following recommendations to clean or disinfect the machine, probes, and accessories.

Failure to observe these recommendations may result in damage to the machine and the probes, which will then no longer be covered by the guarantee.

Recommendations

- Always wear eye protection and gloves to prevent injury.
- Observe the expiry dates of cleaning products and decontamination solutions.
- Ensure that the contact time and concentration of the cleaning product and decontamination solution are appropriate for the equipment used. Carefully apply the instructions given on the label of the cleaning product and the decontamination solution.
- Carefully read the recommendations from the Association for Professionals in Infection Control and Epidemiology (APIC) and the Food and Drug Administration (FDA), if applicable in the country.

8.1.1. Cleaning the machine (painted, metallic, glass, or plastic surfaces and screen)

Refer to the warning in Chapter 2 concerning cleaning.

Surfaces must be cleaned in strict compliance with the following procedure:

1. clean using a soft cloth soaked in the recommended cleaning product,
2. if necessary, rinse using a soft cloth soaked in water,
3. wipe the surface using a soft cloth soaked in the recommended decontamination solution,
4. if necessary, dry carefully using a soft, clean, absorbent cloth.

Precautions

Do not spray any cleaning or disinfectant product directly on the machine. Leaks may damage the system, whose guarantee would then no longer be applicable.

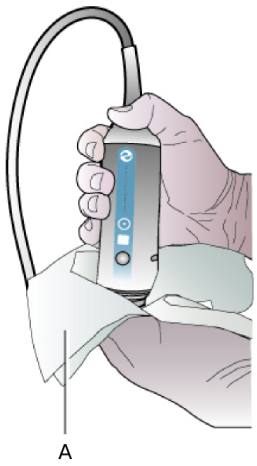
Do not scratch the screen.

8.1.2. Cleaning the probe (housing, cable and transducer)

It is not necessary to switch off the device before cleaning the probe.

Surfaces must be cleaned in strict compliance with the following procedure:

1. Gently remove the gel using a soft cloth or wipe.



Cleaning the probe: A: *Wipe.*

2. Remove all traces of bodily fluid by cleaning the surfaces using a soft cloth or wipe soaked in the recommended cleaning product.
3. If necessary, rinse the cleaned surfaces using a soft cloth soaked in water.
4. Dry, if necessary, using a dry cloth.
5. Wipe the surfaces using a soft cloth or wipe soaked in the recommended decontamination solution.
6. Dry, if necessary, using a soft dry cloth.
7. Examine the transducer and probe cable for any damage such as cracks, breakage, or liquid leakage.

If any damage is observed, stop using the probe and contact Echosens or its local representative: service@echosens.com.

Precautions

Do not submerge or soak the probe.

Apply the cleaning product and decontamination solution to the soft cloth, not directly on the surface to be cleaned.

The probe must be cleaned after every use or between patients. Prior cleaning is necessary in order to ensure effective decontamination.

Do not use a surgeon's brush to clean the probe. Even the use of flexible brushes could damage the probe.

Take care not to introduce any cleaning product or decontamination solution into the probe connector.

8.1.3. Recommended cleaning products

Echosens recommends use of the following products:

- Pure water, soapy water.

- Detergent with neutral pH (5 to 8).
- Recommended decontamination solutions (see below).

The following cleaning products are **prohibited**:

- Abrasive products (such as “Cif” and scouring powders)
- Alkaline detergents (pH > 9), bleach, etc.
- Sulphuric, acetic, nitric, hydrochloric, and oxalic acid, etc.
- Soda, potash, ammonia, etc.
- Unleaded petrol, acetone, MED, MBK, toluene, xylene, benzene, trichloroethylene, etc.
- Nail varnish solvent and remover.

8.1.4. Recommended decontamination solutions

The decontamination solutions recommended below are suitable for use on the machine and probes.

Cleaning and decontamination solution	Origin	Type	Active ingredient
105 Spray	USA	Vaporizer	Quaternary ammonium
Ascend	USA	Liquid	Quaternary ammonium
Control III	USA	Liquid	Quaternary ammonium
Coverage Spray	USA	Vaporizer	Quaternary ammonium
End-Bac II	USA	Liquid	Quaternary ammonium
PI-Spray	USA	Vaporizer	Quaternary ammonium
PI-Spray II	USA	Vaporizer	Quaternary ammonium
Thericide Plus	USA	Liquid	Quaternary ammonium
Thericide Plus	USA	Vaporizer	Quaternary ammonium
Tuffie	United Kingdom	Wipes	Quaternary ammonium
Surfanios Premium	France	Liquid	Quaternary ammonium
Aniosurf Premium	France	Liquid	Quaternary ammonium
Wip’Anios	France	Wipes	Quaternary ammonium
Wip’Anios Premium	France	Wipes	Quaternary ammonium
Surfa’Safe SH	France	Vaporizer	Quaternary ammonium
Viraclean	France	Vaporizer	Quaternary ammonium

In addition to the list of recommended decontamination solutions, any alcohol-free decontamination solutions using quaternary ammonium as an active agent can be used to decontaminate the probes.

8.2. CALIBRATING THE PROBE

The probe contains mechanical parts that may shift slightly over time.

The probe must therefore be periodically calibrated. Beyond this period, the manufacturer no longer guarantees the performance characteristics of the probe.

When an exam is opened, a window displays the expiration of the calibration of your probe. When this is displayed, contact Echosens or its local representative to arrange calibration: service@echosens.com.

During the exam, the message "Calibrate the probe" is displayed in the message zone.

At the end of an exam, the message "Uncalibrated probe!" is displayed on the printed exam report.

8.3. TROUBLESHOOTING

Events	Solutions
The probe is no longer calibrated.	Contact Echosens or its local representative: service@echosens.com.
The standby pushbutton is inoperative. When pressed, the device is not turning on.	Check that the device is connected to a correctly powered mains socket (test another electrical device connected to the same socket) and that the main switch is in the I position. Have the main switch's fuses checked by the maintenance department.
The standby pushbutton is on, but the software is not booting.	Turn the device off, then on again.

In the event of a failure or malfunction, please contact Echosens or its local representative: service@echosens.com.

9. CONFIGURING THE FIBROSCAN

9.1. ENTERING CONFIGURATION MODE

To enter Configuration mode, press  in the Home screen.

A screen then asks for an identifier and password.

The available passwords and identifiers are in ascending order of the features to which they give access (note: respect the case):

Doctor level

User: Doctors

Password by default: Password by default: MD (this password can be modified in General tab)

The Doctor has access to the General, Log file, Institution, System, Service, Exam Files, and Admin tabs.

Biomedical Engineer level

User: Biomedical Engineer

Password: maintenance

The Biomedical Engineer has access to the General, Log File, Institution, System, Printer, Network, Connect, Service, Exam Files and Admin tabs.

9.2. GENERAL TAB

This tab is used to configure the date and time, language and the autologon.

9.2.1. For Doctor

Date/Time

Press [Change] and then enter the system date and time, and then press [OK] to save the data.

Internationali□ation

From each list, select the language, date format, and decimal separator normally used in the country concerned.

Click [OK] to confirm the input and save the new data.

9.2.2. For Biomedical Engineer

Lets you enable or disable an authentication to start the system. Automatic login is enabled by default. The system will not ask for the password before launching the FibroScan application.

To disable automatic login, press [Disabled]. The default password is MD. To change it, enter the new password in the 'password' field. Confirm by pressing [OK].

To enable automatic login, press [Enabled].

9.3. LOG FILE TAB

This tab lets you view and back up log files.

The log file tracks system activity and gives the operator a history of the events that occurred during use of the FibroScan software.

[EXPORT] Exports the log file for back-up.

From any login identifier, save the Log file by pressing the [Export] button after connecting a back-up device (usually a USB key connected to one of the unit's USB ports). The file is exported to the root and its name integrates:

- the device serial number,
- the date and time the file was created.

The key may not be recognized immediately after insertion. In that case, press [Export] again if an error message is displayed.

9.4. INSTITUTION TAB

This tab lets you input the institution contact details.

Automatic login

Institution information

The entered details will be displayed on the printed report.

Logo

Press [Change] then insert the institution logo. Logo is displayed on the exam report.

Report

Press [Enabled] to display the last 10 shear wave propagation maps of the examination on the report.

9.5. SYSTEM TAB

This tab displays information about the system and the software.

9.6. PRINTER TAB

This tab lets you input the number of copies of the report printed automatically after the end of the examination.

Number of automatic printings

Enter a digit corresponding to the number of reports to print at the end of each examination.

The digit 0 is input by default.

[Add printer] Lets you add a printer. Follow the on-screen instructions.

[Update] Lets you refresh the set-up printer list.

9.7. NETWORK TAB

This tab is used to configure the network parameters.

This operation must be performed only by personnel trained in network management.

IP Address

The IP address can be configured statically or dynamically via the DHCP protocol. To configure the IP address statically, click [Manual] and complete the "IP Address", "Mask" and "Gateway" fields.

9.8. CONNECT TAB

This tab is used to enable/disable the connectivity of the machine.

The IT department will provide user support for the configuration of these parameters.

9.9. SERVICE TAB

This tab gives access to the troubleshooting options.

9.9.1. For Doctor

[Eject CD] To eject the CD from the drive.

9.9.2. For Biomedical Engineer

[Launch Program] To execute an ECHOSENS-certified program present on a USB medium.

	A removable USB device must be connected.
[Probes memory]	Displays the characteristics of the probes connected to the machine.
[Touch Screen Calib.]	Touch screen calibration utility.

9.10. EXAM FILES TAB

This tab is used to export and archive exam files.

9.10.1. For Doctor

Archiving/Deleting exam files

Lets you archive exams on a removable USB device or delete the exams from a selected period. The files are saved in a folder named "backup".

Erased exams are permanently deleted from the hard disk if the ‘Erase from disk’ function is enabled (the ‘Yes’ option is selected).

9.10.2. For Biomedical Engineer

Automatic USB export

Lets you enable automatic export of exams in .fibx format to a USB key at the end of each exam. The files are stored in the root directory of the storage device.

A removable USB device must be connected!

9.11. ADMIN TAB

This tab is used to enable or disable the available software options.

9.11.1. For Biomedical Engineer

Liver targeting tool.

Lets you enable or disable the liver targeting tool.

Automatic Probe Selection

Enables or disables automatic probe recommendation.

9.12. SOFTWARE UPDATE

Software updates may only be applied by qualified personnel.

10. SYMBOLS ON THE DEVICE

10.1. CONNECTORS

	DVI-I output
	Ethernet connector RJ45
	USB connector
	Elastometry probe connection
	Location for the connector of the unconnected probe.

10.2. WARNINGS

	General safety symbol. The associated symbols must be read carefully.
	Support not intended to be used as FibroScan probe holder

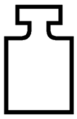
Do not block the vents

(WARNING: This symbol does not appear on machines manufactured before 2013)

WARNING: only Echosens-approved maintenance personnel are authorized to open and modify the FibroScan unit.

Refer to the user manual to ensure operator and patient safety.

(WARNING: This symbol does not appear on machines manufactured before 2013).



Weight of machine with accessories

(WARNING: This symbol does not appear on machines manufactured before 2013).

Do not push or lean on the top of the FibroScan unit.

To avoid tipping the FibroScan when moving it, move it slowly sideways and steer it firmly by holding the decorative rods on the front and back of the unit.

To avoid tipping the FibroScan when lowering it down a step, the operator must go in front of the unit and guide it on the way down.

(WARNING: This symbol does not appear on machines manufactured before 2013).

10.3. MARKING AND ELECTRICAL SAFETY

CE marking and notified body identification number

Certificate affixed on 21th July 2011

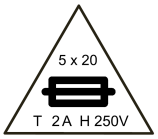
Scrapping the battery

The FibroScan uses a 'button cell' battery. This is a long-life battery and it may never need replacing.

In the event of replacement, however, do not discard the old battery with ordinary household waste. Contact your local waste processing department for the address of the nearest battery disposal location.

Scrapping the FibroScan and its probe(s)

To reduce the risk of pollution by electrical and electronic waste, and within the framework of European Directive 2011/65/EC, the FibroScan unit and its probe(s) must not be discarded with ordinary household waste. Contact your local electrical and electronic waste processing service for instructions.

	Equipotential terminal
	Protective earth (ground)
	Alternating current
	2-A accessible time-delay fuses
	Applied part type B
	Standby pushbutton
	Main switch

10.4. NOTE

The serial number marked on the device identifies the FibroScan uniquely.

11. TECHNICAL CHARACTERISTICS

11.1. CHARACTERISTICS OF THE DEVICE

Manufacturer	Echosens 30 place d'Italie 75013 PARIS – France
Model	FibroScan 502 TOUCH
MDD Classification	Class IIa according to directive 93/42/EC
Electrical classification	Class I, type B Group I class A relative to CISPR 11
IP code	IPX0: the instrument without probe is not protected against liquids.
Operating mode	Continuous operation
Mechanical Index	MI < 1.0 for all operation mode.
Thermal Index	TI < 1.0

11.1.1. Computer properties

Operating system	Windows Embedded
Hard drive	Minimum 250 Gb

11.1.2. Metrological performance

NB: the quantities measured are shear wave speed written as 'Vs' and stiffness written as 'E'.

Shear wave speed	Mini: 0.7 m/s Maxi: 5.0 m/s

		Shear □ave speed Vs (m/s)□			
		M+		**XL+**	
Vs (m/s)	**Phantom number**	**Bias (□)**	**Accuracy (□)**	**Bias (□)**	**Accuracy (□)**
Zone 1 1.14	1 2	0.7 − 4.7	0.6 0.8	1.3 − 3.9	0.0 0.0
Zone 2 1.79	1 2	− 11.3 − 11.5	0.9 0.9	− 12.4 − 13.9	1.4 1.4
Zone 3 2.77	1 2	− 4.3 − 3.1	0.9 1.9	− 11.0 − 9.2	3.1 2.2

* Values obtained with CIRS phantoms E-1493-1 (1) and E-1493-2 (2)

Stiffness	Mini: 1.5 kPa Maxi: 75 kPa

		Stiffness E (kPa)□			
		M+		XL+	
E (kPa)	Phantom number	Bias (□)	Accuracy (□)	Bias (□)	Accuracy (□)
Zone 1 3.9	1 2	1.3 − 9.2	1.3 1.5	2.6 − 7.7	0.0 0.0
Zone 2 9.6	1 2	− 21.3 − 21.6	1.7 1.7	− 23.1 − 25.7	2.8 2.8
Zone 3 23.3	1 2	− 8.3 − 5.9	1.8 3.8	− 20.5 − 17.3	6.3 4.4

* Values obtained with CIRS phantoms E-1493-1 (1) and E-1493-2 (2)

11.1.3. Electrical characteristics

Power supply	100-240 V ~ 50–60 Hz
Apparent power	70-75 V·A
Fuse	2 x type 5x20 T2,0AH 250V

11.1.4. Mechanical properties

Dimensions	1350 mm x 680 mm x 610 mm (H x L x P)
Weight	41 kg (without probe)

11.1.5. Environmental properties

Operating temperature	+ 10 °C to + 40 °C (+ 50 °F to + 104 °F)
Operating humidity	30 % to 75 % relative humidity, non-condensed
Maximum operating altitude	3000 m
Operating atmospheric pressure	700 hPa to 1060 hPa
Storage temperature	− 20 °C to + 70 °C (− 4 °F to + 158 °F)
Storage humidity	10 % to 85 % relative humidity, non-condensed
Maximum altitude for storage and transportation	5000 m
Storage and transportation atmospheric pressure	540 hPa to 1060 hPa

11.1.6. Further information

Cables provided	1 x mains lead (length 2 m) 1 x probe cable (length 1.5 m)

11.2. CONSUMABLES

Not applicable.

12. REGULATIONS

Electromagnetic interference (EMI) is a signal or emission, conveyed through open space or through electrical or signal conductors, which may severely disrupt radio navigation or other safety services, or seriously and frequently damage, obstruct or interrupt an authorized radio communication service. These communication services include, but are not limited to, commercial AM/FM radio services, television, cellular telephone services, radio detection, air traffic control, radio paging and GSM systems. These authorized services, along with unwilling disrupters, such as digital equipment, including computer systems, contribute to the electromagnetic environment.

Electromagnetic compatibility is the ability of the elements of an electronic device to interact correctly with the electronic environment. Although this computer system has been designed to conform to the restrictions of the EMI regulatory body, there is no guarantee concerning interference that may occur in a specific installation. Should the device generate interference with radio communication services (this may be determined by turning the device off and on), users are encouraged to attempt to correct this phenomenon by adopting one or all of the following measures:

- Change the orientation of the reception aerial.
- Reposition the computer relative to the receiver.
- Move the computer away from the receiver.
- Connect the computer to a different power socket such that the computer and receiver are on different branch circuits.

12.1. ELECTROMAGNETIC EMISSIONS

The FibroScan 502 TOUCH is designed for use in the electromagnetic environment defined below. FibroScan 502 TOUCH customers or users must ensure that it is indeed used in such an environment.

Emission test	Compliance	Electromagnetic Environment - Recommendations
RF CISPR11 emissions	Group 1	The FibroScan 502 TOUCH uses RF energy for its internal functions only. Consequently, its RF emissions are very low and unlikely to cause any interference with nearby electronic equipment.
RF CISPR11 emissions	Class A	The FibroScan 502 TOUCH may be used on all nonresidential premises and premises not directly connected to the public low-voltage energy grid used to supply residential buildings.
Harmonic emissions EN 61000-3-2	Class A	
Voltage fluctuations/ Oscillating emissions EN 61000-3-3	Applicable	

NOTE: The use of cables and/or accessories not specified in the user guide may increase the device's emissions.

12.2. ELECTROMAGNETIC IMMUNITY (1)

The FibroScan 502 TOUCH is designed for use in the electromagnetic environment defined below. FibroScan 502 TOUCH customers or users must ensure that it is indeed used in such an environment.

Immunity test	IEC 60601 test level	Compliance	Electromagnetic Environment - Recommendations
Electrostatic Discharge IEC 61000-4-2	± 6 kV contact ± 8 kV air	± 6 kV on contact ± 8 kV through l'air	Floors should be wooden, concrete or ceramic. If the floor is covered with a synthetic material, the relative humidity must be at least 30%.
Spike/Burst IEC 61000-4-4	± 2 kV supply ± 1 kV input/output	± 2 kV supply ± 1 kV input/output	The quality of the electrical network must be that of a typical commercial or hospital environment.
Voltage shocks EN 61000-4-5	Differential mode ± 1 kV Common mode ± 2 kV	Differential mode ± 1 kV Common mode ± 2 kV	The quality of the main supply must be that of a typical commercial or hospital environment.
Voltage drops, short interruptions and supply inlet voltage variation IEC 61000-4-11	< 5 % U_T [1], for 10 ms. 40 % U_T, for 100 ms. 70 % U_T, for 500 ms. < 5 % U_T, for 5 s.	<5 % U_T, for 10 ms. 40 % U_T, for 100 ms. 70 % U_T, for 500 ms. < 5 % U_T, for 5 s.	The quality of the electrical network must be that of a typical commercial or hospital environment. If the FibroScan502 TOUCH user requires continuous operation during mains power cuts, the FibroScan 502 TOUCH should be connected to an uninterruptible power supply or battery.
Magnetic field immunity at supply frequency (50-60 Hz) IEC 61000-4-8	3 A/m	3 A/m	Supply frequency magnetic fields must be those of a typical commercial or hospital environment.

12.3. ELECTROMAGNETIC IMMUNITY (2)

The FibroScan 502 TOUCH is designed for use in the electromagnetic environment defined below. FibroScan 502 TOUCH customers or users must ensure that it is indeed used in such an environment.

Immunity test	IEC 60601 Test level	Compliance	Electromagnetic Environment - Recommendations
			Portable and mobile RF communication devices must be kept away from the FibroScan 502 TOUCH (including its cables), at a greater distance than the recommended value calculated using the applicable equation at the emitter frequency.

1. U_T: network power supply voltage measured before the test

Immunity test	IEC 60601 Test level	Compliance	Electromagnetic Environment - Recommendations
			Recommended separation distance
Conducted RF IEC 61000-4-6	3 Vrms 150 kHz to 270 kHz	3 V	d = 1.17 $\sqrt{P}$
	0,1 Vrms 270 kHz to 11 MHz	0,1 V	d = 35 $\sqrt{P}$
	3 Vrms 11 MHz to 80 MHz	3 V	d = 1.17 $\sqrt{P}$
Radiated RF IEC 61000-4-3	3 V/m 80 MHz to 2.5 GHz	3 V/m	d = 1.17 $\sqrt{P}$ 80 Mhz to 800 MHz
			d = 2.33 $\sqrt{P}$ 800 MHz to 2.5 GHz
			where P is the maximum emitter power in watts (W), as specified by the emitter manufacturer, and d is the recommended separation distance in meters (m). The strength of the EM fields of fixed emitters as determined by an electromagnetic survey of the site [2] must be below the compliance level in each of the frequency bands [3]. Interference may occur in the vicinity of devices bearing the following symbol: 

NB 1: at 80 MHz and 800 MHz, the upper frequency band is applicable.

NB 2: these recommendations may not be applicable in all cases. Electromagnetic propagation is affected by absorption and reflection caused by structures, objects and individuals.

NB 3: the use of cables and/or accessories not specified in the user guide may reduce the device's immunity.

NB 4: in case of electromagnetic disturbances, FibroScan 502 TOUCH displays a message (see the Message area section) and no measurement can be performed.

12.4. RECOMMENDED SEPARATION DISTANCES

(between portable or mobile RF communication devices and the FibroScan 502 TOUCH)

2. The strength of EM fields for fixed emitters such as commercial AM/FM radio broadcasting services, television, cell phone services, radio detection, air traffic control, radio paging receivers and GSM services cannot be accurately predicted. To assess the EM environment caused by fixed emitters, a site EM study must be conducted. If the strength of the fields measured at the location where the FibroScan 502 TOUCH is used exceeds the above-mentioned compliance levels, correct operation of the FibroScan 502 TOUCH must be checked. If any abnormal performance is observed, additional measurements may be necessary, e.g. reorienting or moving the FibroScan 502 TOUCH.

3. Beyond the 150 kHz – 80 MHz band, the strength of the EM field must be less than 3 V/m.

The FibroScan 502 TOUCH is designed for use in an electromagnetic environment in which RF disturbance is controlled. FibroScan 502 TOUCH customers or users may prevent interference by maintaining at least a minimum distance between portable or mobile (transmitter) RF communication devices and the FibroScan 502 TOUCH, as recommended below according to the transmitter's maximum power.

Ma□imum transmitter emission po□er (W)	**Separation distance according to transmitter fre□uency (m)**				
	150 kH□to 270 kH□	**270 kH□to 11 MH□**	**11 MH□to 80 MH□**	**80 MH□to 800 MH□**	**800 MH□to 2.5 GH□**
	d □1.17 $\sqrt{P}$	**d □35 $\sqrt{P}$**	**d □1.17 $\sqrt{P}$**	**d □1.17 $\sqrt{P}$**	**d □2.33 $\sqrt{P}$**
0.01	0.12	3.50	0.12	0.12	0.23
0.1	0.37	11.01	0.37	0.37	0.74
1	1.17	35.00	1.17	1.17	2.33
10	3.70	110.70	3.70	3.70	7.37
100	11.70	350.00	11.70	11.70	23.30

For emitters whose maximum power is not listed above, the recommended separation distance d can be estimated using the applicable equation at the transmitter's frequency, where P is the maximum transmitter power in watts (W) as specified by the transmitter manufacturer.

NB 1: at 80 MHz and 800 MHz, the upper frequency band is applicable.

NB 2: These recommendations may not be applicable in all cases. Electromagnetic propagation is affected by absorption and reflection caused by structures, objects and individuals.

INDEX

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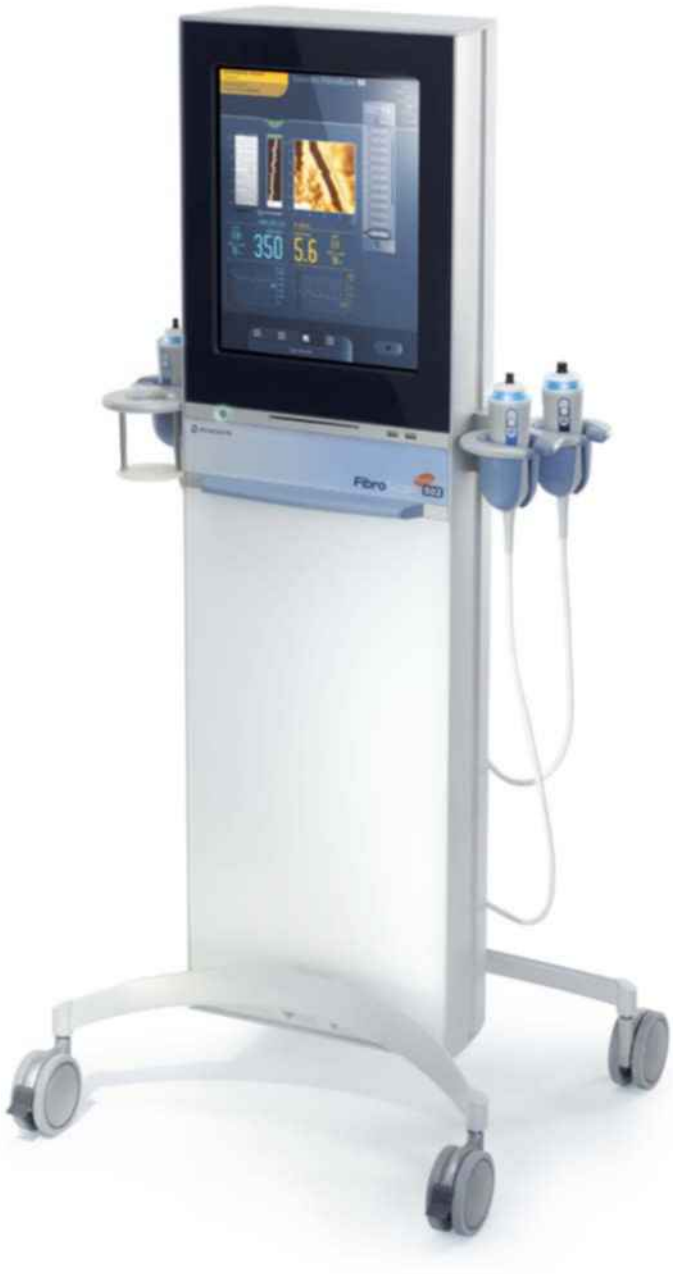
E-mail: info@echosens.com



FibroScan touch 502

POWERED BY VCTE™

INNOVATION *in liver disease management*

echosens™

Discover FibroScan®, the state of the art technology that will improve your liver diagnosis.

This unique, accurate and efficient device brings you extra clinical confidence to support your patient management.

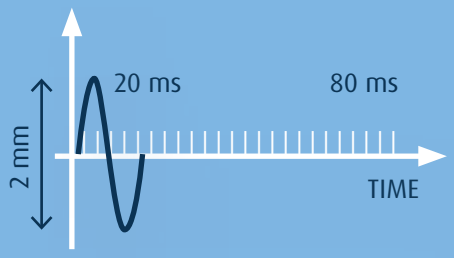
FibroScan touch 502

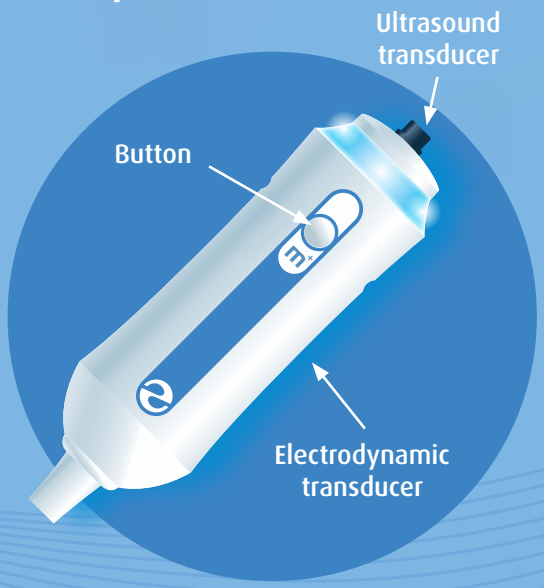
Sharing INNOVATIVE technology

Based on patented Vibration-Controlled Transient Elastography (VCTE™), FibroScan® 502 Touch provides multiple controls for reliable, accurate and reproducible assessment of liver tissue stiffness: CONTROLLED VIBRATION, CONTROLLED ENERGY, CONTROLLED ALGORITHM.

POWERED BY VCTE™

CONTROLLED VIBRATION





- → This custom-designed ergonomic transducer generates a controlled vibration which induces a mechanical shear wave with consistent frequency and energy
- → Static force is monitored in real time to prevent wave distortions
- → Shear wave center frequency is 50Hz

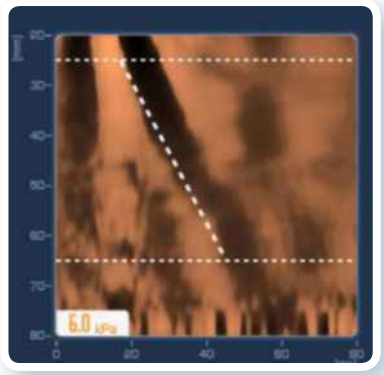
CONTROLLED ENERGY

- → Propagation of the mechanical shear wave through the skin and liver tissues is measured using low energy 3.5 MHz ultrasound
- → Large explored volume of 3 cm^3 (at least 100 times more than a biopsy)
- → Depth of measurement from 15 to 75 mm depending on probe

CONTROLLED ALGORITHM

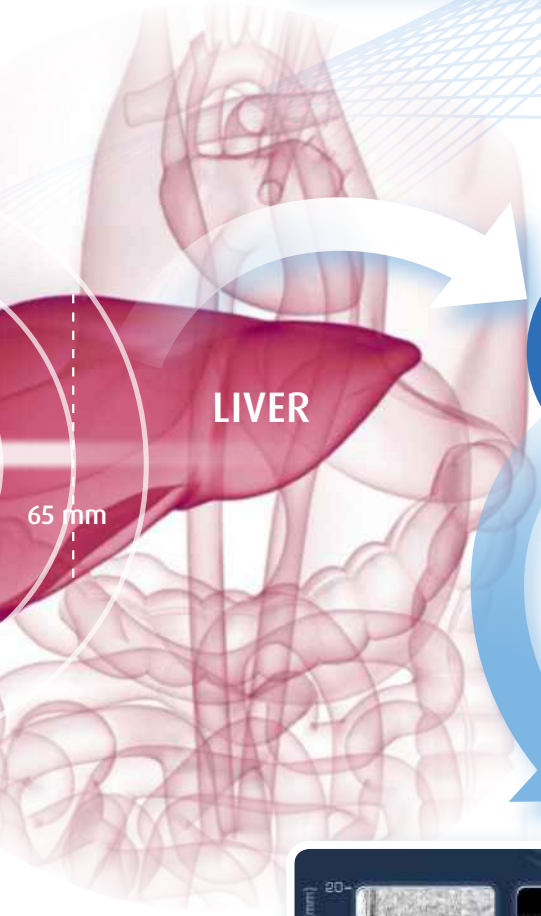
- → VCTE guidance process ensures the operator obtains measurements of the liver
- → A sophisticated algorithm computes liver stiffness and ultrasound attenuation
- → A quality controlled calculation is performed automatically, the algorithm selects the valid measurements

Stiffness (E)



- Stiffness is computed from the ELASTOGRAM
- The Elastogram is a GRAPHIC REPRESENTATION of the shear wave propagation as a function of time and depth
- The Young's Modulus (E) is expressed in KILOPASCAL (kPa)

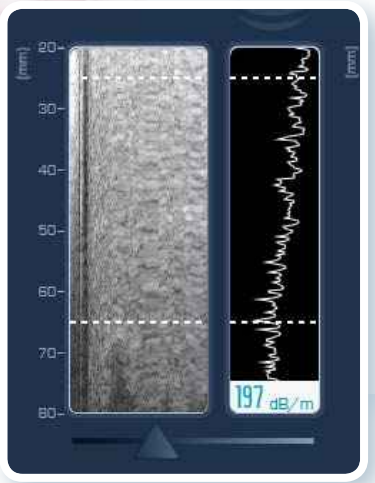
FIBROSIS[1-22]



3 CM³

- ***At least 100 TIMES LARGER than with a liver biopsy***
- ***Steatosis and stiffness are simultaneously measured IN THE SAME LIVER VOLUME***
- ***Stiffness & CAP results are the MEDIAN of 10 valid measurements***

Controlled Attenuation Parameter (CAP™)



- CAP is computed from the ULTRASOUND acquired for stiffness measurement
- CAP IS ONLY CALCULATED if the stiffness acquisition is VALID
- CAP is expressed in DECIBEL PER METER (dB/m)

STEATOSIS[23-27]

FibroScan touch 502

Sharing INNOVATIVE features: CAP

CONTROLLED ATTENUATION PARAMETER

NON INVASIVE ASSESSMENT AND QUANTIFICATION OF LIVER STEATOSIS

CAP is a measure of the ultrasound attenuation which corresponds to the decrease in amplitude of ultrasound waves as they propagate through the liver.

CAP is powered by a sophisticated guidance process based on VCTE:

- → **Steatosis and stiffness are simultaneously measured in the same liver volume**
- → Liver steatosis is calculated only if liver stiffness measurement is valid

- → Gain (ultrasound amplitude)
- → Ultrasound frequency
- → Area of measurement

ARE CONTROLLED AND PREDEFINED

- → CAP is measured at 3.5 MHz and is expressed in decibel per meter (dB/m)
- → CAP is measured with the M probe at depth between 25 and 65 mm for adult patients with a thoracic perimeter > 75 cm and a skin capsula distance < 2.5 cm
- → CAP is measured with the XL probe at depth between 35 and 75 mm for adult patients with a skin capsula distance between 2.5 cm and 3.5 cm.

CAP measurement

Like liver stiffness measurement with the FibroScan® 502 Touch, CAP measurement:

- → IS NON INVASIVE
- → IS IMMEDIATE: does not lengthen the FibroScan® examination
- → can be performed by an operator without any ultrasound imaging skills

CAP is a tool for non invasive assessment and QUANTIFICATION OF STEATOSIS enhancing the spectrum of non invasive methods for the examination and follow-up of patients with liver disease.

CAP is a non invasive physical quantitative parameter ***AVAILABLE*** *with the*

FibroScan touch 502

Sharing CLINICAL DATA

LITERATURE OVERVIEW

FibroScan® procedures are easy to put into routine practice for all chronic liver diseases.

- → ***To date, more than 900 peer reviewed original articles have demonstrated the usefulness of liver stiffness measurement with the FibroScan®***
- → ***As a stand-alone tool or as an adjunct to liver biopsy, FibroScan® allows accurate decisions as part of your patient management strategy***
- → ***From mass screening to follow-up of post transplanted patients and prognostic value, liver stiffness measured by FibroScan® has a wide range of use***

Liver stiffness

FIBROSCAN® HAS BEEN STUDIED IN DIFFERENT CLINICAL SETTINGS

- → Tertiary units
- → Mass screening [18]
- → Street-based outreach for drug users [19]
- → Paediatrics [20, 21]
- → Tropical medicine [22]

CHRONIC HEPATITIS C (HCV)

In chronic viral hepatitis C, the diagnosis accuracy of liver stiffness measurement is good to excellent. According to the first pivotal study [1], the AUROC* were:

- → **0.79 for the diagnosis of significant fibrosis**
- → **0.91 for the diagnosis of advanced fibrosis**
- → **0.97 for the diagnosis of cirrhosis**

Overall, the diagnosis accuracy depends on the quality of the liver biopsies used as the reference and the distribution of patients into the different stages of fibrosis.

CHRONIC HEPATITIS B (HBV)

The diagnosis accuracy of FibroScan® to assess fibrosis has been shown to be similar in patients with chronic hepatitis B compared to patients with chronic hepatitis C [2]. However, necro-inflammatory activity has also been shown to significantly affect liver stiffness in this etiology [3].

HIV-HCV CO-INFECTION

The presence of HIV co-infection with HCV, does not impair the diagnosis accuracy of FibroScan® [4].

ALCOHOLIC LIVER DISEASE (ALD)

Liver stiffness measured by FibroScan® can be used to assess liver fibrosis in patients with alcoholic liver disease with diagnosis accuracies similar to those obtained in chronic viral hepatitis [5].

Moreover, the FibroScan® procedure is very well accepted by patients with alcohol dependence or abuse and therefore appears as a first choice tool to detect advance fibrosis or cirrhosis at-risk population with a better accuracy than simple biological evidence [6].

NON ALCOHOLIC FATTY LIVER DISEASE (NALFD)

A recent meta-analysis [7] based on 6 different studies has shown that liver stiffness measured with FibroScan® is good to detect :

- → significant liver fibrosis with a **mean AUROC* of 0.84 (95% CI**: 0.79-0.90)**
- → excellent to detect cirrhosis with a **mean AUROC of 0.94 (0.86-0.99).**

* AUROC: area under Receiver Operator Characteristics curve
** 95% CI : 95% confidence interval

Moreover, the availability of the XL probe dedicated to overweight patients with a skin-to-liver capsula distance greater than 2.5 cm will allow assessment of a large portion of the patients that could not previously benefit from the FibroScan® procedure [8].

BILIARY DISEASE

Liver stiffness has also been shown to be of clinical use to detect fibrosis and cirrhosis in patients with primary biliary cirrhosis and primary sclerosing cholangitis [9].

Controlled Attenuation Parameter (CAP)

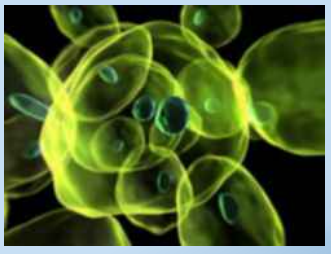
In addition to measuring liver stiffness, FibroScan® 502 Touch now allows you to also assess the Controlled Attenuation Parameter (CAP) which has been developed for the detection of liver steatosis. Several publications and communications support this new feature of the FibroScan® 502 Touch.

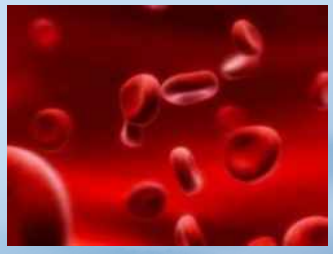
→ A proof of concept publication on the CAP™ technology [23]

→ In a cohort of 115 patients with various chronic liver diseases, the AUROC* of CAP to assess steatosis were:

- 0.91 for steatosis superior or equal to 11%
- 0.94 for steatosis superior or equal to 34%
- 0.89 for steatosis superior or equal to 67%

→ Several communications in international hepatology meetings (AASLD, EASL, APASL) [24-27]





FibroScan® 502 Touch, with its dedicated probes, is a diagnostic aid measuring liver stiffness and Controlled Attenuation Parameter.

These values must be interpreted by a medical doctor specialized in liver disease taking into account the complete medical record of the patient, presence of identified confounding factors and the quality of the measurement procedure (number of valid measurements, dispersion,...).

FibroScan® is of use THROUGHOUT THE COURSE of chronic liver disease

Fortuitous diagnosis or screening

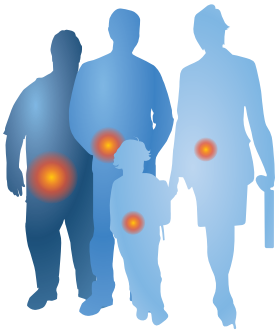
Follow-up | TREATMENT

Diagnosis by initial symptoms

TREATMENT

Diagnosis by complications

TREATMENT



Asymptomatic patient | Symptomatic patient

Follow-up of UNTREATED patients

Follow-up of TREATED PATIENTS (adaptation of treatments) [11]

COMPLICATION RISKS assessment, prognosis [13, 14, 28]

Little or no fibrosis | Significant fibrosis | Cirrhosis

MASS SCREENING (occupational medicine, Health Screening Centre, etc.) [18, 19]

DECISION for initiation of treatment [1-9]

Decision to start SPECIFIC CIRRHOSIS follow-up, prognosis [10, 12]

POST-TRANSPLANTATION follow-up [15, 16]

Your patients will be asking you:
"Can I have a FibroScan® exam?"

FibroScan touch 502

Sharing POWERFUL practice

AN INNOVATIVE DESIGN WHICH IMPROVES PRODUCTIVITY

To date, thousands **FibroScan®** devices have been installed worldwide. FibroScan® is used to aid diagnosis in 1.5 million men, women and children every year.

New Software

TACTILE INTERFACE WITH A NEW DESIGN

- → Optimized ergonomy & data workflow
- → User-friendly interface
- → Easy to use

PATIENT DATA MANAGEMENT

- → Organized by patients
- → Multi-criteria search (last name, first name, date...)

NETWORK CONNECTION

- → Easy data export
- → Push data to shared network directories

Smart Tools

AUTOMATED PROBE SELECTION

- → An indicator to recommend the probe best suited to the patient's morphology

LIVER TARGETING TOOL

- → An indicator to target optimal measurement areas

FIBROSCAN® REPORTS

- → Generate and edit multilingual reports
- → Personalize reports with hospital logo, address...
- → Print examination history

FibroScan® 502 Touch expert tools

Non invasive liver stiffness measurement
Innovative steatosis quantification

Hardware

TOUCH SCREEN

- → Optimal comfort & image quality in all situation
- → High contrast & brightness
- → Wide viewing angle

ADVANCED CONNECTIVITY OPTIONS

- → Save & export data to removable drive (USB key...) or network (FibroView).

2 PROBE CONNECTORS

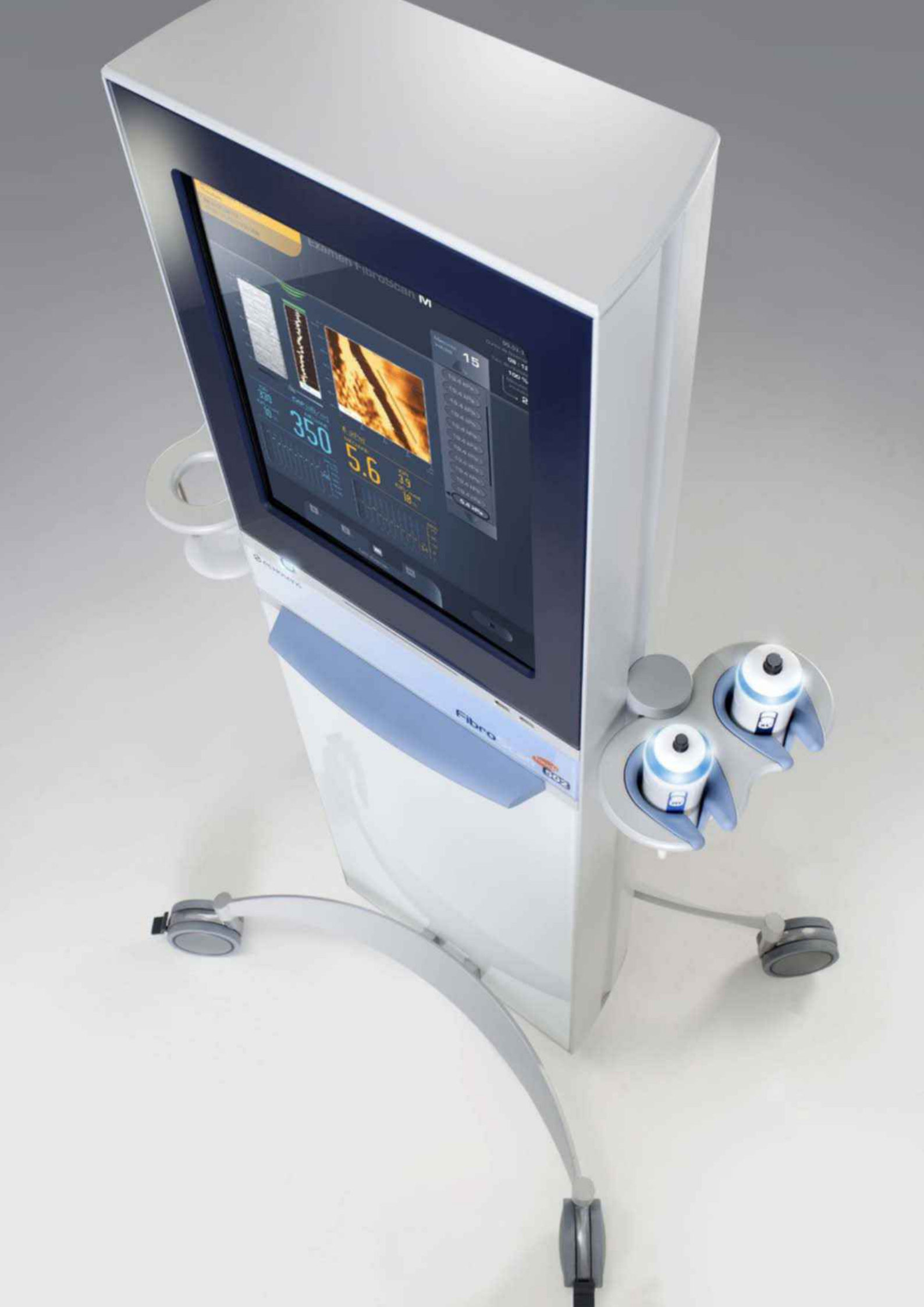
- → Connect two probes simultaneously

FRONT AND REAR HANDLES

- → Easy to move and manipulate

ADVANCED ELECTRONIC FOR FAST AND EFFECTIVE EXAMINATION

- → High speed elastrometry engine


M
15
350
5.6
Fibro

Probes

THREE DIFFERENT ERGONOMIC PROBES ENABLE YOU TO ADDRESS A FULL RANGE OF CLINICAL AND MORPHOLOGICAL NEEDS

Each patient is different. Echosens has designed its probes to ensure efficient diagnosis in all circumstances.

PAEDIATRIC PROBE

- → Transducer specifically designed for being placed into narrow intercostal space
- → A higher ultrasound frequency, 5 MHz, enabling measurements adapted for chest perimeter from 45 to 75 cm
- → Depth of measurement are adapted from 15 to 50 mm depending on children's morphology

ADULT PROBE

- → The M probe is designed for the general population. It is used for the majority of adults with a thoracic perimeter of more than 75 cm
- → Ultrasound frequency is 3.5 MHz
- → Liver stiffness measurements take place between 25 and 65 mm under the skin

PROBE FOR OVERWEIGHT PATIENTS

- → A more sensitive ultrasound sensor at the frequency of 2.5 MHz has been designed to enhance deeper signal penetration through tissues over a 35 to 75 mm depth
- → XL probe must be used on patient with a skin capsula distance (SCD) greater than 2.5 cm. Automated probe selection will recommend the probe best suited to the patient's morphology

RECOMMENDATIONS FOR USE

- → Training: Echosens or its representative must certify the operator to ensure the proper use of the device and all its features
- → Examination procedures provide better reproducibility and accuracy with 10 valid stiffness measurements at the same measurement point

Sharing SERVICE solutions

DISTRIBUTION, TRAINING AND AFTER-SALES SERVICE

Distribution

OUR DISTRIBUTOR NETWORK IN YOUR COUNTRY IS YOUR DIRECT CONTACT

Echosens has an exclusive distribution network that provides sales, training and after-sales support.

We will also provide direct support in countries we serve directly.

For more information, contact our sales team:
distribution@echosens.com or you local distributor

Training

HOW TO ACHIEVE BEST PRACTICE

After on site training, you will be certified to use FibroScan®. The training is mandatory in order to obtain accurate and reliable measurements. Nurses can use the equipment but only physicians can interpret the results in light of the patient's history.

Dedicated training includes:

- → A custom-designed theory session aimed at understanding indications and criteria for use of the device and individual probes
- → A practical session to teach in good examination practice

For more information, contact our training team:
training@echosens.com

Accessing technology know-how after you acquire your FibroScan®

After-sales service

LOCAL SUPPORT IS AVAILABLE

Distributors are in charge of ensuring the after-sales service of all Echosens products. Our specially trained and certified engineers will take care of your device. We ensure fast and efficient answers that will keep your device up and running*.

ACCESSORIES AND SUPPLIES

To enhance your productivity, the Echosens Service Centre or your local distributor will support you with calibration, repairs, parts and maintenance services.

→ ***FibroScan® probes need to be calibrated every year to maintain proper performance.***

SERVICE CONTRACT

Service contracts with local support.

It can range from probe maintenance alone to an all-inclusive contract.
You're free to choose.

For more information, contact our team after-sales service:
service@echosens.com

* After acceptance of an estimate or under a service contract

Sharing EXPERTISE & INNOVATION

ABOUT ECHOSENS

Echosens is actively expanding its global presence. We are supported by a team of medical experts who have helped to transform our core technology*, VCTE, into the first commercially available product with Transient Elastography: FibroScan®.

OUR MISSION

Offer to our customers technological and ergonomic solutions in hepatology to improve patient quality of life based on:

- A robust portfolio of patents
- A totally non-invasive solution

OUR PARTNERS

Echosens establishes many medical and scientific partnerships around the world (Germany, China, USA, United Kingdom...).

In France, we develop strong links with the universities as:

- Université Rabelais de Tours
- Centre d'investigation Clinique – Innovation Technologie, CHRU de Tours, Hôpital Bretonneau
- Institut Pierre et Marie Curie, Paris
- Telecom ParisTech
- INSERM

OUR COMMITMENT

Our commitment to quality is shown by:

- ISO 13485 certification since 2005
- CE mark since 2003

* Echosens owns 17 patents in the domain of transient elastography.

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FS502T072015 - Revision date [07/15] - FibroScan® 502 Touch is a class IIa medical device according to Directive EC/93/42 and is manufactured by Echosens. Assessment of its conformity with the essential requirements of the Directive EC/93/42 is established by the LNE-G-MED (n°0459) - France. FibroScan® is indicated for the noninvasive measurement of liver stiffness (E) and controlled attenuation parameter (CAP) in humans.

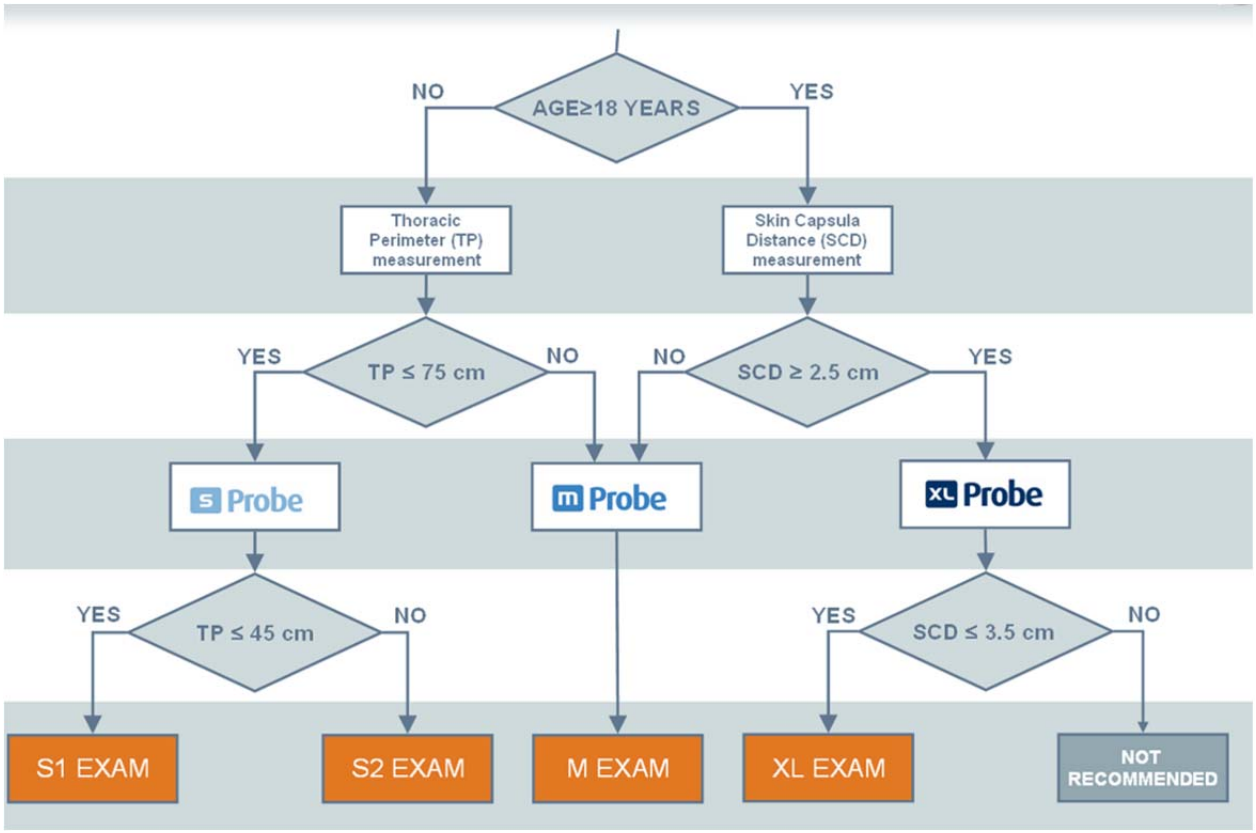
It is expressly recommended to carefully read the guidance within the users' guide and labeling of the device. FibroScan® examination must only be performed by operators certified by the manufacturer or its accredited local representative. The values obtained with FibroScan® must be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical record of the patient. In France, liver stiffness measurement by FibroScan® is reimbursed by national Social Security medical insurance, in some circumstances and under certain conditions: see terms on the ameli.fr website.

FibroScan® and its probes (M+ and XL+) is a class II medical device according to the Code of Federal regulation (21 CFR Sections 892.1560 and 892.1570). The FibroScan® system is intended to provide 50Hz shear wave speed measurements through internal structure of the body. FibroScan® is indicated for noninvasive measurement of shear wave speed at 50Hz in the liver. The shear wave speed may be used as an aid to clinical management of patients with liver disease.

FLASH THIS CODE

echosens™

WWW.ECHOSENS.COM - CONTACT@ECHOSENS.COM



The recommendations for using the probes are defined by the following patient's morphological data:

- TP: Thoracic Perimeter measured at the xiphoid using a tape measure.
- SCD: Skin-to-Capsule Distance assessed with an ultrasound scanner or by the
- automatic probe selection tool.

Fibroscan Users Manual S+ Probe, Section 4.3, pg. 11

FibroScan®

S+ Probe

User manual

E117M010.3 – Version 3 – 06/2015

en-US

TABLE OF CONTENTS

1. PURPOSE OF THE USER MANUAL

This User Manual has no contractual value whatsoever and under no circumstances may Echosens be held responsible on the basis of the information contained in this manual.

The present user manual details all of the information required for the implementation, use and maintenance of the probe designed to be connected to the FibroScan. Interpretation of the displayed data is covered in the FibroScan user manual.

Thus, after carefully reading the manual, operators shall be able to:

- connect the probe to the FibroScan,
- use the probe in accordance with technical and clinical requirements,
- carry out the maintenance work of the probe.

Echosens publishes this manual "as is", without guarantees of any nature, whether explicit or implicit, including, but not limited to implicit guarantees or merchant conditions, or adaptation for specific use in view of providing simple and accurate information. Consequently, Echosens cannot accept any responsibility for the manual's incorrect interpretation. Though all efforts have been made to offer a manual that is as accurate as possible, the manual may nevertheless contain some technical inaccuracies and/or typographical errors.

Echosens cannot, under any circumstances, be held responsible for any loss of profit, loss of business, data loss, business interruption, or for any indirect, specific, accidental or consecutive damages of any type. In the event of damages arising from a defect (imperfection) or error contained in this User Manual, Echosens undertakes to send the physician, as rapidly as possible, a hard copy or electronic document containing all corrections made to this manual.

This manual is updated on a regular basis. The most recent version of this manual is available from Echosens on request. Should any major modifications be made to the manual, however, Echosens undertakes to send the physician, as rapidly as possible, a new copy of the manual in hard copy or electronic format. Note that this does not involve updating the hardware and/or software in your possession.

The product owner must keep this manual for as long as the product is used.

This manual contains a chapter for troubleshooting the most commonly encountered problems.

Any information or modification requests pertaining to this manual should be sent to: Echosens, 30 place d’Italie, 75013 PARIS France.

1.1. SYMBOLS USED IN THE MANUAL

This symbol means: ATTENTION

Warning: see the instructions before using the medical device.

Instructions preceded by this symbol may cause injuries or damage the medical device and installation if not correctly followed.

This symbol means: INFORMATION

Additional information with no impact on instrument use.

1.2. PROPERTY AND COPYRIGHT

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2. WARNINGS

2.1. GENERALITY

Caution: Federal law restricts this device to sale by or on the order of a physician.

2.2. HANDLING THE PROBE

The probe is a fragile electromechanical device that must be handled with care and kept away from liquids. Between two examinations, it should be placed on its holder on the FibroScan. In the event of prolonged non-use, the probe should be stored in its case.

2.3. MAINTENANCE

Maintenance operations must not be performed by a third party other than a technician authorized by Echosens.

The probe must be calibrated periodically. Beyond the period indicated on the calibration certificate, the manufacturer no longer guarantees the performance characteristics of the probe.

3. MISCELLANEOUS INFORMATION

3.1. GUARANTEE

The terms of guarantee are stated in the Echosens terms of sale documents.

For any request, Echosens remains available to the physician and his/her appointees and shall, if applicable, transfer the request to a competent local representative.

3.2. REGISTERED TRADEMARKS

Echosens and FibroScan are registered trademarks of the company Echosens.

4. INDICATIONS AND PRECAUTIONS FOR USE

4.1. INTENDED USE

The FibroScan system is an active, non-implantable medical device using ultrasound. This device is designed to be used in a doctor's office.

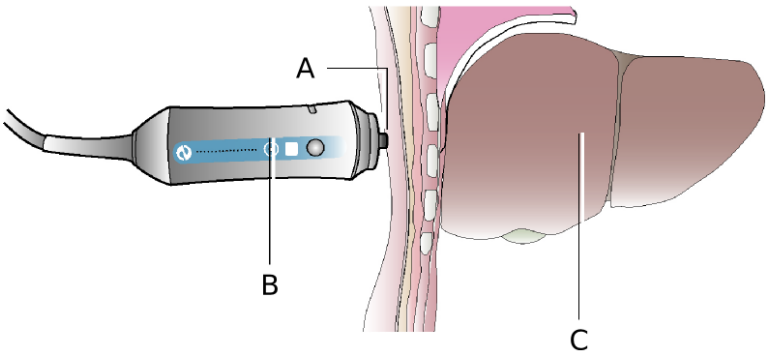
The FibroScan system is intended to provide 50 Hz shear wave speed measurements and estimates of tissue stiffness through internal structures of the body.

The FibroScan probe comprises a single-element ultrasound transducer mounted on the shaft of the electrodynamic transducer. This transducer generates a transient vibration, which in turn generates an elastic shear wave. This wave propagates through the skin, the subcutaneous tissues, and then the liver. During shear wave propagation, the ultrasound transducer performs a series of ultrasound acquisitions (emission / reception) to measure the speed of shear wave propagation (Vs) in m/s. This measurement corresponds to the spatial and temporal average speed of propagation of the shear wave through the liver region of interest, which can be approximated by a cylinder with a diameter of 1 cm and a length of 4 cm (which corresponds to about 3 cm^3).

In addition, assuming that the liver is a pure elastic, linear and isotropic medium, the device converts shear wave speed Vs into equivalent stiffness E in kPa using the equation $E = 3 \times \rho \times Vs^2$ with ρ the medium density assumed to be 1000 kg/m^3. The values for shear wave speed and equivalent stiffness (or Young's modulus) are relative indexes intended only for the purpose of comparison with other measurements performed using FibroScan devices. Absolute values for these measurements may vary among measurement devices from different manufacturers.

4.2. INDICATIONS FOR USE

FibroScan is indicated for non-invasive measurement of shear wave speed and estimate of stiffness at 50 Hz in the liver. The shear wave speed may be used as an aid to clinical management of pediatric and adult patients with liver disease.



How to use a probe: A: *Ultrasound transducer.* ***B:*** *Electrodynamic transducer.* ***C:*** *Liver.*

The values obtained must be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical record of the patient and the potential presence of different factors known to influence liver shear wave speed or equivalent stiffness. Based on the existing literature the following Table provides a list of parameters known to increase liver shear wave speed or equivalent stiffness.

Parameter	Reference
Liver fibrosis, cirrhosis	[1-9]
Acute hepatitis, inflammation, ALT flares	[10-13]
Portal pressure, central venous pressure	[14-16]
Extra hepatic cholestasis	[17]
Congestion (heart failure)	[18]
Meal intake	[19]
Amyloidosis	[20-22]

The intra and inter-operator agreement has been assessed in a cohort of 200 adult patients with chronic liver disease of various etiologies [23]. The intraclass correlation coefficient was 0.98 both within and between operators. Moreover, in a cohort of 31 NASH children, a 0.96 inter-operator intra class correlation coefficient was found [24]. This demonstrates that intra operator reproducibility is excellent and that changing the operator does not increase measurement variability both in adults and children.

[1] Friedrich-Rust, M., et al., Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. Gastroenterology, 2008. 134(4): p. 960-74.

[2] Musso, G., et al., Meta-analysis: Natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Annals of Medicine, 2011. 43(8): p. 617-49.

[3] Shaheen, et al., FibroTest and FibroScan for the Prediction of Hepatitis C-Related Fibrosis: A Systematic Review of Diagnostic Test Accuracy. American Journal of Gastroenterology, 2007: p. 1-12.

[4] Shi, K.Q., et al., Transient elastography: a meta-analysis of diagnostic accuracy in evaluation of portal hypertension in chronic liver disease. Liver Int, 2013. 33(1): p. 62-71.

[5] Smith, J.O. and R.K. Sterling, Systematic review: Non-invasive methods of fibrosis analysis in chronic hepatitis C. Alimentary Pharmacology and Therapeutics, 2009. 30(6): p. 557-76.

[6] Stebbing, J., et al., A Meta-analysis of Transient Elastography for the Detection of Hepatic Fibrosis. Journal of Clinical Gastroenterology, 2010. 44(3): p. 214-9.

[7] Talwalkar, J.A., et al., Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. Clinical Gastroenterology and Hepatology 2007. 5(10): p. 1214-20.

[8] Tsochatzis, E.A., et al., Elastography for the diagnosis of severity of fibrosis in chronic liver disease: A meta-analysis of diagnostic accuracy. Journal of Hepatology, 2011. 54(4): p. 650-9.

[9] Lee, C.K., et al., Serum Biomarkers and Transient Elastography as Predictors of Advanced Liver Fibrosis in a United States Cohort: The Boston Children's Hospital Experience. The Journal of pediatrics, 2013. 163(4): p. 1058-64.

[10] Arena, U., et al., Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology, 2008. 47(2): p. 380-4.

[11] Coco, B., et al., Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. Journal of Viral Hepatitis, 2007. 14(5): p. 360-9.

[12] Mueller, S., et al., Increased liver stiffness in alcoholic liver disease: differentiating fibrosis from steatohepatitis. World Journal of Gastroenterology, 2010. 16(8): p. 966-72.

[13] Sagir, A., et al., Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage. Hepatology, 2008. 47(2): p. 592-5.

[14] Carrión, J.A., et al., Transient elastography for diagnosis of advanced fibrosis and portal hypertension in patients with hepatitis C recurrence after liver transplantation. Liver Transplantation, 2006. 12(12): p. 1791-8.

[15] Millonig, G., et al., Liver stiffness is directly influenced by central venous pressure. Journal of Hepatology, 2010. 52(2): p. 206-10.

[16] Vizzutti, F., et al., Liver stiffness measurement predicts severe portal hypertension in patients with HCV-related cirrhosis. Hepatology, 2007. 45(5): p. 1290-7.

[17] Millonig, G., et al., Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. Hepatology, 2008. 28(5).

[18] Lebray, P., et al., Liver stiffness is an unreliable marker of liver fibrosis in patients with cardiac insufficiency. Hepatology, 2008. 48(6): p. 2089.

[19] Mederacke, I., et al., Food intake increases liver stiffness in patients with chronic or resolved hepatitis C virus infection. Liver International, 2009. 29(10): p. 1500-6.

[20] Janssens, E., et al., Hepatic amyloidosis increases liver stiffness measured by transient elastography. Acta Gastroenterologica Belgica, 2010. 73(1): p. 52-4.

[21] Lanzi, A., et al., Liver AL amyloidosis as a possible cause of high liver stiffness values. European Journal of Gastroenterology and Hepatology, 2010. 22(7): p. 895-7.

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[23] Fraquelli, M., et al., Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut, 2007. 56(7): p. 968-73.

[24] Nobili, V., et al., Accuracy and reproducibility of transient elastography for the diagnosis of fibrosis in pediatric nonalcoholic steatohepatitis. Hepatology, 2008. 48(2): p. 442-8.

4.3. PROBE AND EXAMINATION SELECTION CRITERIA

The recommendations for using the probes are defined by the following patient's morphological data:

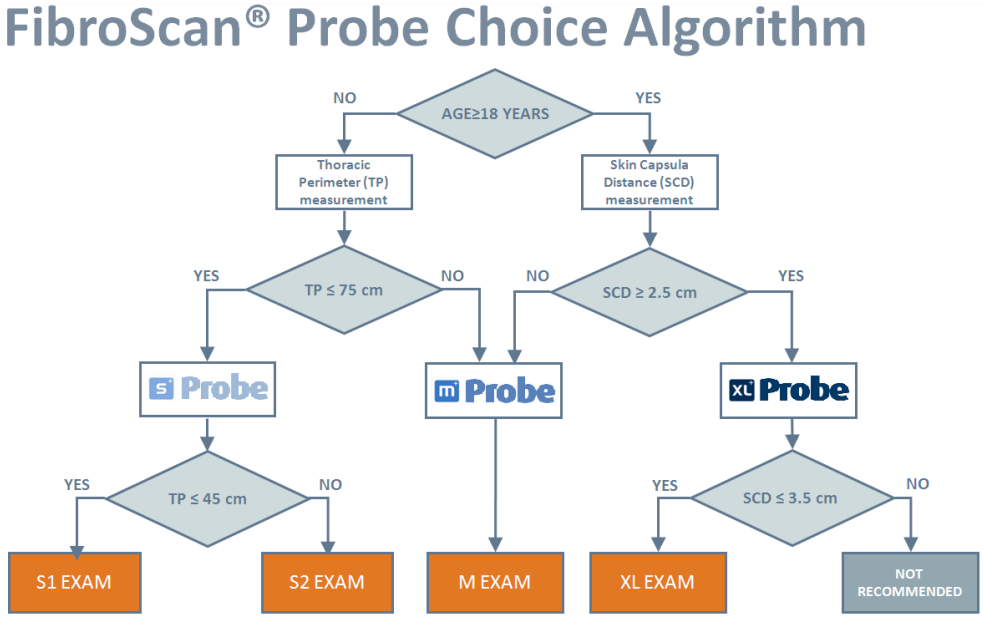
- TP: Thoracic Perimeter measured at the xiphoid using a tape measure.
- SCD: Skin-to-Capsule Distance assessed with an ultrasound scanner or by the automatic probe selection tool.

In case of using an ultrasound scanner, SCD should be measured at the point where the shear wave speed is measured with a pressure similar to the one used with the FibroScan probe.

In case of using the automatic probe selection tool, please refer to FibroScan 502 Touch User manual (chapter 6.5.11. Exam type selection area).

It is not recommended to use any means to compress the soft tissues merely to reduce the SCD.

Four types of examination are available: S1, S2, M and XL. They correspond to specific measurement depths that take into account the liver's depth beneath the skin.



In all cases, Echosens recommends to perform 10 valid FibroScan measurements.

4.4. PRECAUTIONS FOR USE

The following instructions must be followed in order to ensure patient safety. Thus, the present probe designed for the FibroScan should not be used in the following situations:

- On patients above 18 years old.
- On patients with a thoracic perimeter of more than 75 cm.
- On an organ other than the liver. The eyes and mucosa must absolutely be avoided.
- On patients with active implants such as pacemakers, defibrillators, pumps, etc.
- On wounds.
- On pregnant women.

Moreover, presence of ascites between the probe and the liver may prevent from obtaining measurement with the device.

The clinical personnel must follow normal safety procedures.

The FibroScan examination should be performed prudently using the principle of ALARA (As Low As Reasonably Achievable).

4.5. USER TRAINING

Only persons who have received training in the use of the FibroScan unit and who possess a user certificate are authorized to conduct an examination using FibroScan. Training is essential for correct equipment use and in order to obtain reliable and reproducible measurements.

This manual is not intended to provide user training.

4.6. ELECTRICAL SAFETY

The probe, designed for the FibroScan, has been manufactured and tested in accordance with IEC electromagnetic compatibility (EMC) and electrical safety standards. It leaves the factory in full compliance with safety and performance requirements. In order to maintain this compliance and to guarantee the safe use of the medical device, the user must conform to the indications and symbols contained in this manual.

Safe use is no longer guaranteed in the following main, non-exclusive cases:

- the probe is visibly damaged,
- the probe does not work,
- after prolonged storage in unfavorable conditions,
- after serious damage incurred during transport.

When safe use of the probe is no longer possible, the probe must be taken out of operation. Steps must be taken to avoid its inadvertent use. The probe should be handed to authorized technicians for inspection.

4.7. MAINTENANCE-RELATED SAFETY

For all maintenance operations, the physician and his/her appointees should contact Echosens, who will send an authorized technician.

For correct and safe use and for all maintenance operations, the personnel must conform to normal safety procedures.

5. EXTERNAL PRESENTATION

5.1. HARDWARE SUPPLIED

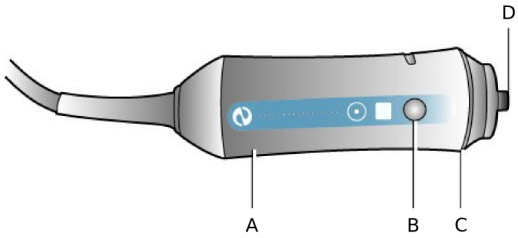
When opening the package, ensure the contents match the following list:

- Probe and case
- User Manual

5.2. PROBE DESCRIPTION

Housing

The housing contains an electrodynamic transducer (vibrator), an ultrasound transducer and a measurement trigger button.



***Probe housing: A:** Electrodynamic transducer. **B:** Measurement button. **C:** Indicator light (LED). **D:** Ultrasonic transducer.*

The ultrasound transducer of the probe is a "Type B" applied part, and is the only component of the FibroScan unit in contact with the patient.

Measurement button

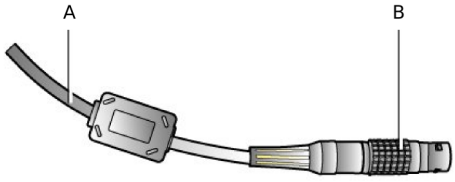
As soon as this button is pressed (if sufficient pressure is exterted on the transducer), the vibrator actuates the electrodynamic transducer, which in turn generates a shear wave (s-wave) that painlessly impacts the patient's skin. The ultrasound transducer performs a series of acquisitions (emission / reception) to measure the propagation speed of this shear wave. Acquisition lasts less than one tenth of a second.

Indicators

The indicator lights (LEDs) display a status as follows:

- On during FibroScan start-up and when standing by to launch an exam.
- Flashing lights for the probe selected when an exam starts.
- Switched off during an exam when the operator is applying an incorrect pressure to the patient's body.
- On during an exam when the operator is applying the correct pressure to the patient's body. It is however strongly recommended that you view the pressure exerted by looking at the on-screen pressure indicator.

Lead



Probe lead: A: *Connection cable.* ***B:*** *Connection jack.*

This 1.5 m lead connects the probe to the FibroScan by means of a multi-pin jack.

The probe transducer, the probe jack, and the FibroScan connector are fragile elements and must be handled with care.

The probe jack has a red dot that should be aligned with the red dot on the FibroScan socket before insertion.

The serial number marked on the connector identifies the probe uniquely.

6. USE DURING AN EXAMINATION

6.1. USER RECOMMANDATIONS

The following recommendations must be followed during the different phases of an examination.

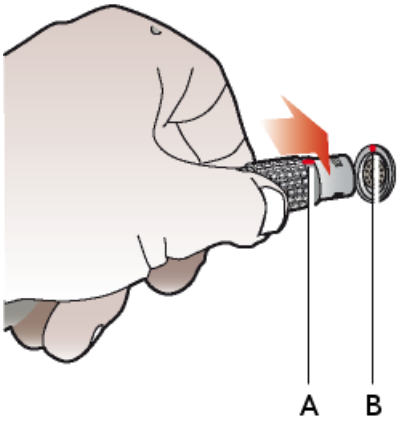
- Hold the probe perpendicular to the patient's skin during the measurements.
- Avoid probe impacts.
- Do not immerse the probe.
- Avoid any liquid projections on the medical device.
- Clean and decontaminate the probe with a suitable product (see paragraph Cleaning, maintenance and repairs).
- Place the probe after use in one of the holders or in its case.

6.2. CONNECTING / DISCONNECTING THE PROBE

- Location of the probe connector: user manual.
- To insert the probe jack: align the probe lead jack's red dot with the socket's red dot and insert the jack.

Both the jack and socket are fragile elements. Handle with care.

To connect the probe lead, insert the jack after aligning the red dots.

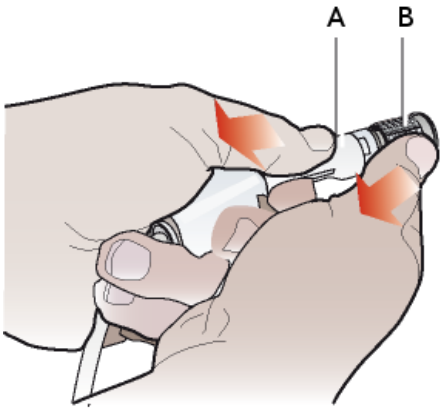


Connecting the probe: A: *Red dot on probe socket.* ***B:*** *Red dot on probe jack.*

- To disconnect the probe jack: first pull the jack's splined sleeve back to unlock it, then pull the whole jack back.

When starting an exam, be sure to follow the instruction in this message: “Do not unplug the probe until the end of the exam.”

A probe may be disconnected for replacement with another probe between two examinations. If the probe is disconnected during an examination, this examination is automatically closed.



Disconnecting the probe: A: *Socket.* ***B:*** *Splined sleeve.*

6.3. HANDLING THE PROBE

Refer to the warnings in Chapter 2 concerning the handling of the probe.

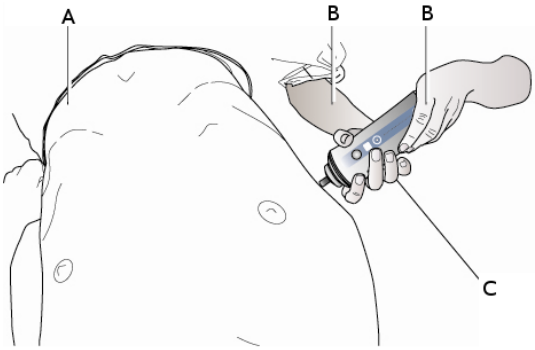
6.3.1. Probe resting position

When the probe is not in use, it must be positioned on the probe holder, as shown.

Probe resting position.

6.3.2. Gripping the probe

Hold the probe as shown. During measurements, continuously make sure that the probe is maintained perpendicular to the skin surface of the patient.



***Gripping the probe: A:** Patient. **B:** Operator. **C:** Probe.*

6.4. END OF EXAMINATION

Once the examination is complete, proceed as follows:

1. Click on the button below to deactivate the probe.
2. Remove any excess gel in holding the probe, head pointing downwards.
3. Disinfect the probe with a suitable product indicated in paragraph Cleaning, maintenance and repairs.
4. Place the probe, head pointing up, onto the FibroScan probe holder.
5. If the device is no longer required:
   - Press the on/off button next to the monitor of the FibroScan.
   - Set the main switch to the 0 position.
   - Disconnect the probe as indicated in paragraph Connecting / disconnecting the probe.
   - Store the probe in its case.

7. CLEANING, MAINTENANCE AND REPAIRS

In the event of malfunction, only the staff of Echosens or its local representative are authorized to service FibroScan and its accessories. Any work performed by an unqualified person will terminate the guarantee.

7.1. CLEANING

Apply the following recommendations to clean or disinfect the probe.

Failure to observe these recommendations may result in damage to the probe, which will then no longer be covered by the guarantee.

Recommendations

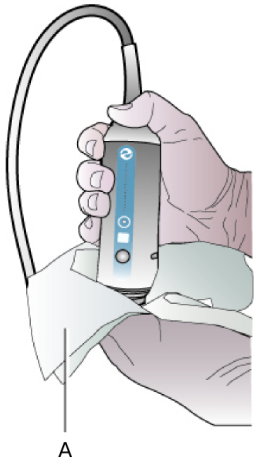
- Always wear eye protection and gloves to prevent injury.
- Observe the expiry dates of cleaning products and decontamination solutions.
- Ensure that the contact time and concentration of the cleaning product and decontamination solution are appropriate for the equipment used. Carefully apply the instructions given on the label of the cleaning product and the decontamination solution.
- Carefully read the recommendations from the Association for Professionals in Infection Control and Epidemiology (APIC) and the Food and Drug Administration (FDA), if applicable in the country.

7.1.1. Cleaning the probe (housing, cable and transducer)

It is not necessary to switch off the device before cleaning the probe.

Surfaces must be cleaned in strict compliance with the following procedure:

1. Gently remove the gel using a soft cloth or wipe.



Cleaning the probe: A: *Wipe.*

2. Remove all traces of bodily fluid by cleaning the surfaces using a soft cloth or wipe soaked in the recommended cleaning product.
3. If necessary, rinse the cleaned surfaces using a soft cloth soaked in water.
4. Dry, if necessary, using a dry cloth.
5. Wipe the surfaces using a soft cloth or wipe soaked in the recommended decontamination solution.
6. Dry, if necessary, using a soft dry cloth.
7. Examine the transducer and probe cable for any damage such as cracks, breakage, or liquid leakage.

If any damage is observed, stop using the probe and contact Echosens or its local representative: service@echosens.com.

Precautions

Do not submerge or soak the probe.

Apply the cleaning product and decontamination solution to the soft cloth, not directly on the surface to be cleaned.

The probe must be cleaned after every use or between patients. Prior cleaning is necessary in order to ensure effective decontamination.

Do not use a surgeon’s brush to clean the probe. Even the use of flexible brushes could damage the probe.

Take care not to introduce any cleaning product or decontamination solution into the probe connector.

7.1.2. Recommended cleaning products

Echosens recommends use of the following products:

- Pure water, soapy water.
- Detergent with neutral pH (5 to 8).
- Recommended decontamination solutions (see below).

The following cleaning products are **prohibited**:

- Abrasive products (such as “Cif” and scouring powders)
- Alkaline detergents (pH > 9), bleach, etc.

- Sulphuric, acetic, nitric, hydrochloric, and oxalic acid, etc.
- Soda, potash, ammonia, etc.
- Unleaded petrol, acetone, MED, MBK, toluene, xylene, benzene, trichloroethylene, etc.
- Nail varnish solvent and remover.

7.1.3. Recommended decontamination solutions

The decontamination solutions recommended below are suitable for use on the machine and probes.

Cleaning and decontamination solution	Origin	Type	Active ingredient
105 Spray	USA	Vaporizer	Quaternary ammonium
Ascend	USA	Liquid	Quaternary ammonium
Control III	USA	Liquid	Quaternary ammonium
Coverage Spray	USA	Vaporizer	Quaternary ammonium
End-Bac II	USA	Liquid	Quaternary ammonium
PI-Spray	USA	Vaporizer	Quaternary ammonium
PI-Spray II	USA	Vaporizer	Quaternary ammonium
Thericide Plus	USA	Liquid	Quaternary ammonium
Thericide Plus	USA	Vaporizer	Quaternary ammonium
Tristel Wipes System	United Kingdom	Wipes	Chlorine dioxide
Tuffie	United Kingdom	Wipes	Quaternary ammonium
Surfanios Premium	France	Liquid	Quaternary ammonium
Aniosurf Premium	France	Liquid	Quaternary ammonium
Wip'Anios	France	Wipes	Quaternary ammonium
Wip'Anios Premium	France	Wipes	Quaternary ammonium
Surfa'Safe SH	France	Vaporizer	Quaternary ammonium
Viraclean	France	Vaporizer	Quaternary ammonium

In addition to the list of recommended decontamination solutions, any alcohol-free decontamination solutions using quaternary ammonium as an active agent can be used to decontaminate the probes.

7.2. CALIBRATING THE PROBE

The probe contains mechanical parts that may shift slightly over time.

The probe must therefore be periodically calibrated. Beyond this period, the manufacturer no longer guarantees the performance characteristics of the probe.

As soon as the deadline is reached, an icon is displayed in the information window during the examination.

The user then has one month to send the probe to Echosens for calibration.

Despite the presence of the icon, the operator can perform examinations as usual. We strongly recommend, however, sending the probe for calibration as rapidly as possible.

Calibration icon.

7.3. TROUBLESHOOTING

Events	Solutions
The probe is no longer calibrated.	Contact Echosens or its local representative: service@echosens.com.
"Hardware error" message.	Check that the probe is correctly connected.
"Vibration error" message.	Incorrect transducer movement.

In the event of a failure or malfunction, please contact Echosens or its local representative: service@echosens.com.

8. TECHNICAL CHARACTERISTICS

Manufacturer	Echosens 30 place d'Italie 75013 PARIS – France
Model	Type S+
IP Code	IPX1: the probe, excluding connectors, is protected from vertically falling drops of water.
Mechanical Index	MI < 1.0 for all operation mode.

8.1. ULTRASOUND TRANSDUCER

Central frequency: 5 MHz

Measurement depth: S1 exam: 15 mm to 40 mm
S2 exam: 20 mm to 50 mm

Acoustic output: The acoustical outputs are maximal during the transient elastography sequence which is a mixed between M mode and Elastography acquisition mode.

Acoustic Output			**MI**	**$I_{SPTA.3}$ (mW/cm²)**	**$I_{SPPA.3}$ (W/cm²)**
Pre-amendments					
Global Maximum Value (95 % T.L. for 99 % of measurements values)			0.31	11.9	24.3
Associated acoustic parameter (Maximum values)	$p_{r.3}$ (MPa)		0.66 (± 8 %)		
	W_o (mW)			0.29 (± 23 %)	0.29 (± 23 %)
	f_c (MHz)		5.9 (± 3 %)	5.9 (± 3 %)	5.9 (± 3 %)
	z_{sp} (cm)		2.08 (± 5 %)	2.08 (± 5 %)	2.08 (± 5 %)
	Beam dimensions	x_{-6} (cm)		0.34 (± 6 %)	0.34 (± 6 %)
		y_{-6} (cm)		0.26 (± 6 %)	0.26 (± 6 %)
	PD (µsec)		0.31		0.31
	PRF (Hz)		500		500
	EBD	Az. (cm)		0.47 (± 6 %)	
		Ele. (cm)		0.46 (± 6 %)	
Operating control conditions	Control 1	NPL ultrasound beam calibrator	NPL ultrasound beam calibrator	NPL ultrasound beam calibrator	

8.2. ELECTRICAL CHARACTERISTICS

EMI	See the FibroScan user manual.

8.3. MECHANICAL CHARACTERISTICS

Dimensions	158 mm x 52 mm (L x diameter)
Weight	500 grams

8.4. ENVIRONMENTAL PROPERTIES

Operating temperature	+ 10 °C to + 40 °C (+ 50 °F to + 104 °F)
Operating humidity	30 % to 75 % relative humidity, non-condensed
Storage temperature	− 20 °C to + 70 °C (− 4 °F to + 158 °F)
Storage humidity	10 % to 85 % relative humidity, non-condensed

INDEX

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Appendix C

FibroScan touch 502

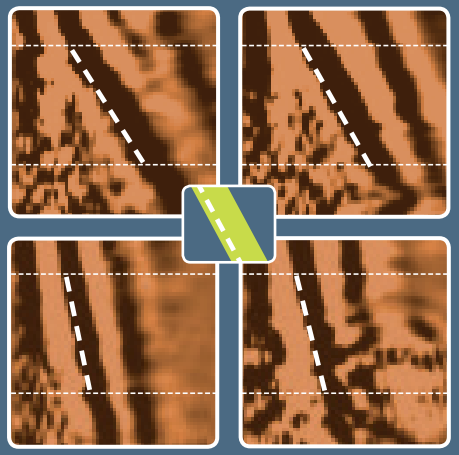
REMINDER SHEET

How to make **a reliable measurement?**

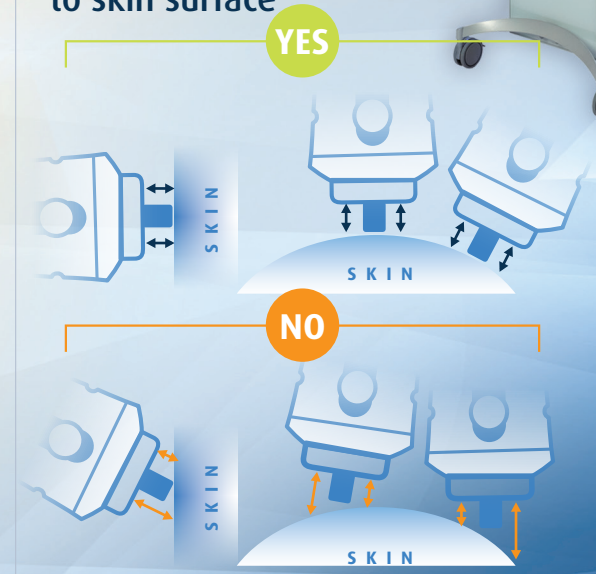
- Operator position: ***facing screen***

YES

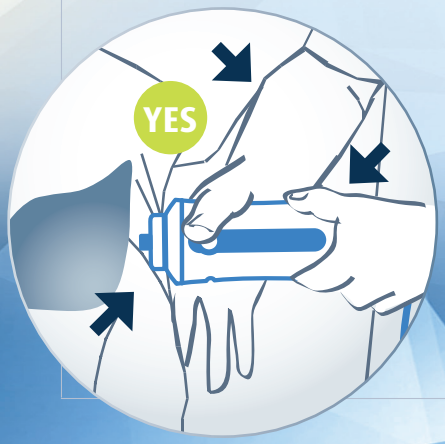
FOUR EXAMPLES OF SATISFACTORY ELASTOGRAMS



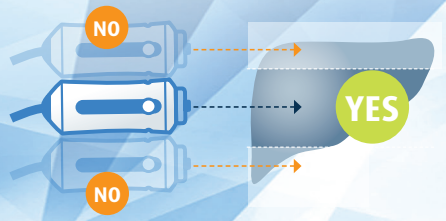
- Probe ***perpendicular*** to skin surface



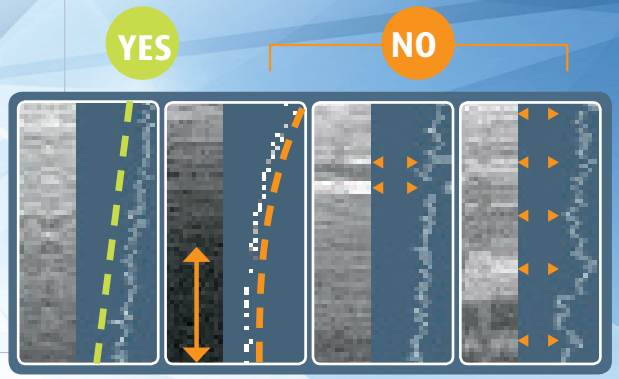
- ***Three-point*** probe control



- Measurement zone at a ***distance from edges of liver***



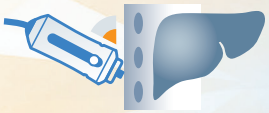
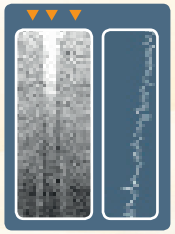
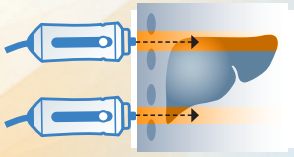
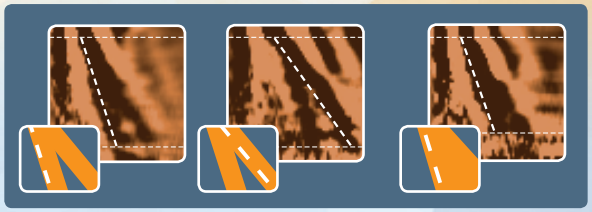
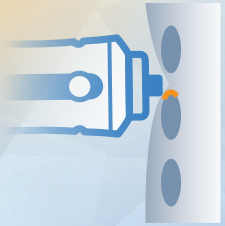
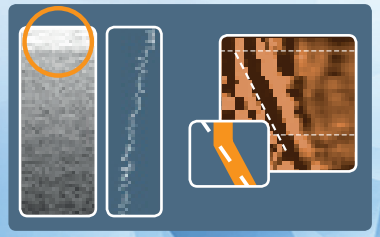
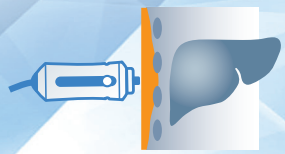
- ***Homogenous*** parenchyma



FibroScan touch 502

REMINDER SHEET

How to explain an **overestimated result?**

OBSERVATIONS	CAUSES	SOLUTIONS
No particular observation: Overestimation of liver stiffness is sometimes undetectable on the screen	 The probe **is not perpendicular** to the skin surface	Always check that the probe is **perpendicular on all axes** before starting the measurement
 TM displays, **in alternation**, liver parenchyma and other tissues (for example during breathing)	 The measurement region is **too close to the edges** of the liver	Make sure that the measurement point is at a sufficient distance from the edges of the liver: **at least 60mm of visible parenchyma** on TM and A modes, without interpolation of other tissues
A waves (double) **E waves** (enlarged) 	 The transducer is in **contact with a rib**	Move the probe to a point where **the intercostal space is wider** Check that the probe **is not pressing against a rib** **Widen the patient's intercostal space** with maximum abduction of the right arm, the legs outstretched and breathing in deeply
 TM mode is **saturated** AND/OR the elastogram is **angulated**	 The layer of adipose tissue is **too thick** at the measurement point	Locate a measurement point where **the adipose layer is not as thick** **Compress the subcutaneous tissue** with the finger

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