QUIPU

Cardiovascular Suite

Cardiovascular Suite 4.0 User Manual

Document number: TEC0002EN Rev. 13
November 26th, 2019

Table of Contents

Cardiovascular Suite

Cardiovascular Suite 4.0 User Manual

Document number: TEC0002EN Rev.13

November 26th, 2019

Cardiovascular Suite is a software for the estimation of early markers of cardiovascular risk. In particular, the software is composed of two main modules of measurement: 1) the FMD-Studio for the measurement of Flow-Mediated Dilatation (FMD) of the brachial artery 2) the Carotid-Studio for measuring the Intima-Media Thickness (IMT) and the diameter of the carotid artery that, when combined with an estimate of pressure, provides parameters of arterial elasticity. The device is based on an algorithm that identifies the edges of the arterial vessel by analysing sequences of ultrasound images of the longitudinal section of the vessel itself. The system is able to process video files previously recorded or directly in real-time the video output of an ultrasound system.

According to the description and the intended use, which are showed in the subsequent chapters, and in accordance with the rules of application of chapter 1.4 of Annex IX of the Directive 93/42/EEC and subsequent amended and the provisions of Chapter III of Annex IX of Directive 93/42/EEC and subsequent amendments, Cardiovascular Suite software is within the medical devices of Class IIa according to rule 10.

CE 0476 The product is in compliance with the legal requirements of 93/42/EEC and subsequent amendments and supplements (Directive 2007/47/EC) for medical devices.

The labelling is available on the login screen of the software.

For USA only: Cardiovascular Suite is not FDA approved and can be utilised for investigational use only.

1 Recommendations

CAUTION : This manual describes the instructions for proper use of the device software Cardiovascular Suite. Please read carefully the advices in this document.

The software must be used by trained and qualified personnel, such as laboratory technicians, nurses, physicians and / or sonographers, who have experience in acquisition and analysis of vascular ultrasound images. It is recommended that the user be aware of the meaning of the parameters measured and returned as a result from the device. It is recommended that the operator does not have serious problems with vision and hearing. It is required knowledge of the mother tongue or, for those countries that allow it, of the English language.

A visual impaired due to particular weather conditions, a visually impaired user, a not optimized brightness and/or not optimized resolution of the monitor may affect the correct interpretation of the results provided.

The analysis performed by the device can be applied to any person over the age of 36 months. It is not recommended to use the system for analysis of people with a distorted anatomy of the examined arterial segment.

It is recommended that the device is used according to the international guidelines for estimating carotid intima-media thickness (IMT), arterial elasticity and flow-mediated dilation (FMD).

The software is installed on a computer and it can be used in conjunction with an ultrasound device and a video converter. For the correct operation it is advisable to pay attention to environmental influences that may alter the operation of these devices. For details, refer to the instructions provided by individual producers.

The software is licensed by a USB dongle key. Use the USB dongle key in an environment with the following conditions of temperature and humidity: operating temperature: +5 ... +55 ° C (+41 ... +131 ° F), humidity: 5 ... 95% We recommend that you do not expose the USB dongle key to solvents and flammable media. It is recommended to protect the USB dongle key by physical damages.

2 Installation

Cardiovascular Suite can be installed on Apple computer or on Microsoft Windows computer. Please see the minimum System requirements of the computer for a correct execution of Cardiovascular Suite.

The software installer can be downloaded from the Quipu web site www.quipu.eu

Please follow the correct instruction for the installation of the software on Apple computers and on Microsoft Windows computer respectively.

Once installed, Cardiovascular Suite requires the activation of a License. The license is contained inside a Quipu License Key, which is a USB dongle key. The Quipu License Key must be plugged into the computer where the software is running. Please follow the instruction for Activating a license.

You can ask for a 14-days Evaluation license.

2.1 System requirements

2.1.1 Minimum Requirements

2.1.1.1 APPLE COMPUTER

- Apple Mac Computer with: Intel Core i5 2.3 GHz, 4GB RAM, 1GB free Hard Disk space*, 1280x800 monitor resolution.
- Mac OS X 10.11 - 10.14

2.1.1.2 MICROSOFT WINDOWS COMPUTER

- Intel Core i5 2.3 GHz, 4GB RAM, 1GB free Hard Disk space*, 1024x768 monitor resolution.
- Microsoft Windows 7 64 bit, Windows 8.1 64 bit, Windows 10 64 bit

* 250GB free Hard Disk space is suggested for the Archive

> ⚠ **CAUTION: the computer must be a Medical Grade Computer in compliance with EN 60601-1 standards for electrical isolation and safety or a common CE marked personal computers (89/366/EEC) connected to power supply via Medical Grade Isolation Transformers that meet IEC 60601-1 standards for electrical leakage.**

2.1.2 Optional video capture devices for on-line analysis:

- Epiphan - AV.io HD hardware video capture (to connect your computer to DVI, VGA or HDMI video outputs)
- Magewell USB capture AIO (to connect your computer to DVI, VGA, HDMI, S-video and C-video outputs)

2.2 Software installation

Cardiovascular Suite can be installed on Apple computer or on Microsoft Windows computer.

> **CAUTION: Failure / incomplete / incorrect installation makes it not possible to use the software.**

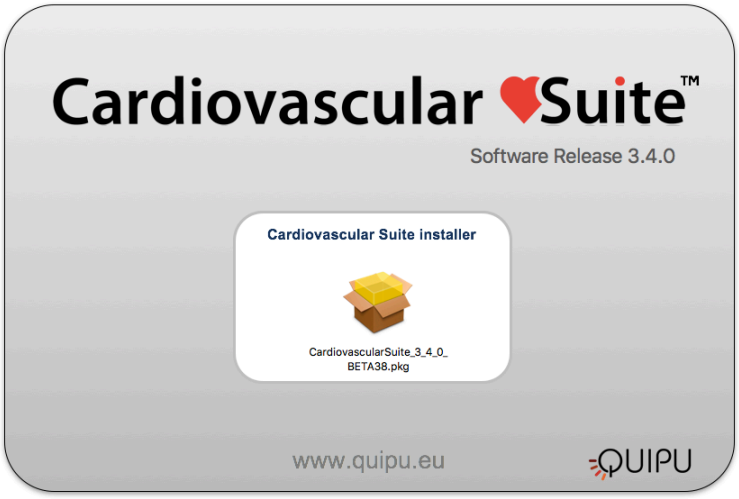
> **CAUTION: It is recommended to perform regular backups of the system. The non-operation of the backup could result in permanent data loss.**

2.2.1 Apple computers

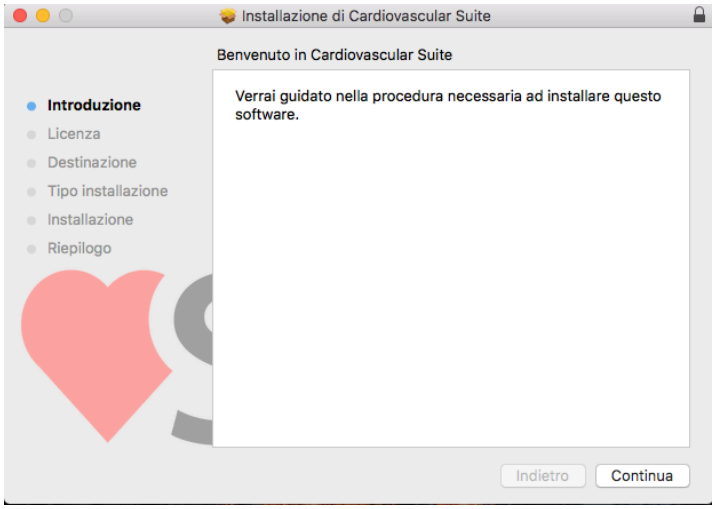
The software installation follows the usual procedure of installing software on Apple computers.

For information or support please contact Quipu support team at support@quipu.eu.

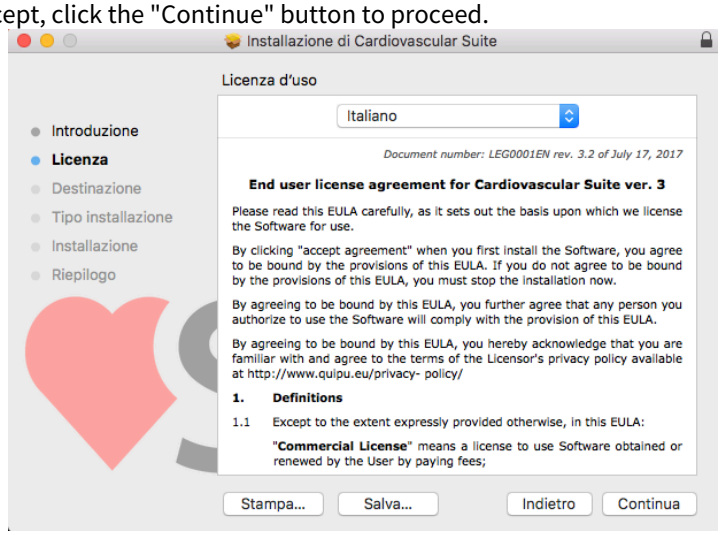
1. Mount the Cardiovascular Suite Disk Image File (*.dmg file) on your desktop. This file contains the Cardiovascular Suite Installer. Double click on the Cardiovascular Suite Installer to start installation.



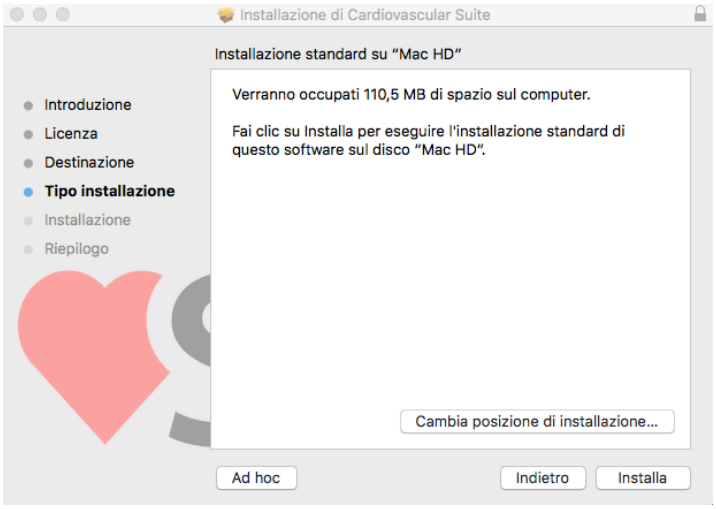
2. A Welcome message is displayed, please click the "Continue" button to proceed.



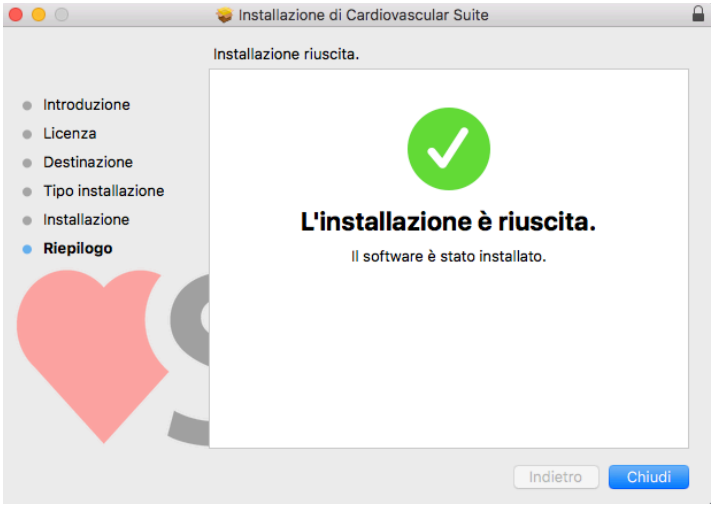
3. Read the License Agreement. If you don't accept the license agreement, please close the Cardiovascular Suite setup. If you accept, click the "Continue" button to proceed.



4. Confirm the installation location. In most cases, you can use the proposed installation location. Click the "Install" button to start installation. Cardiovascular Suite will be installed.



5. A message will confirm that the installation was successful.

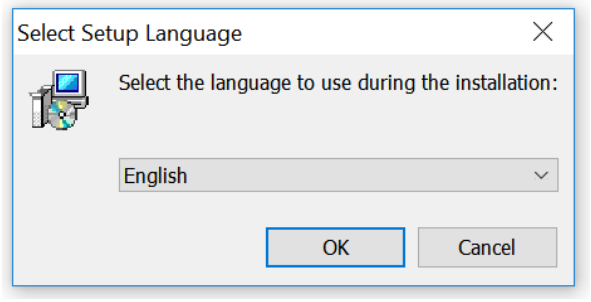


2.2.2 Microsoft Windows computer

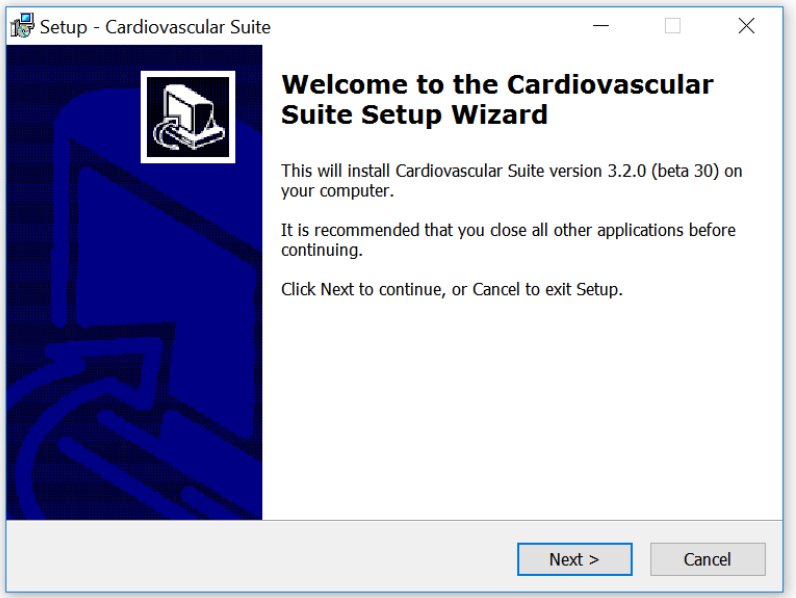
The software installation follows the usual procedure of installing software on Microsoft Windows.

For information or support please contact Quipu support team at support@quipu.eu.

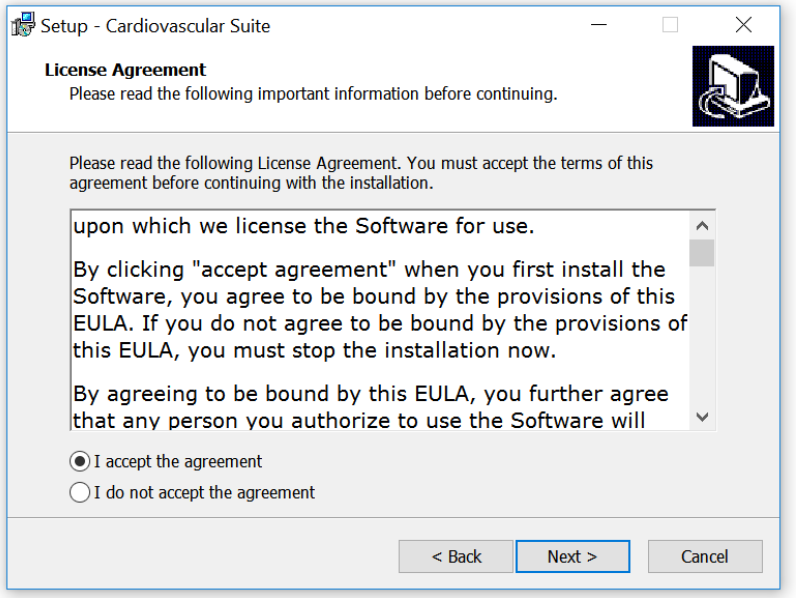
1. Select the language that will be used during the installation.



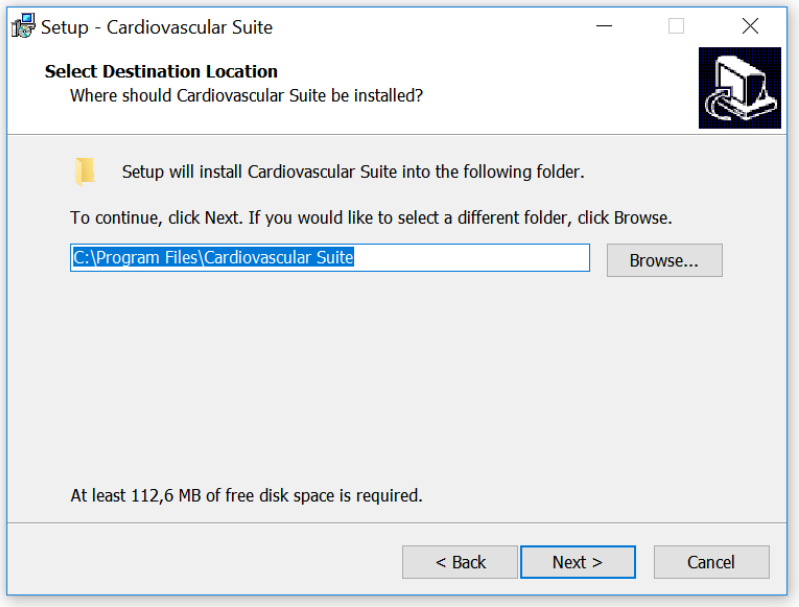
2. A Welcome message is displayed, please click the "Next" button to proceed.



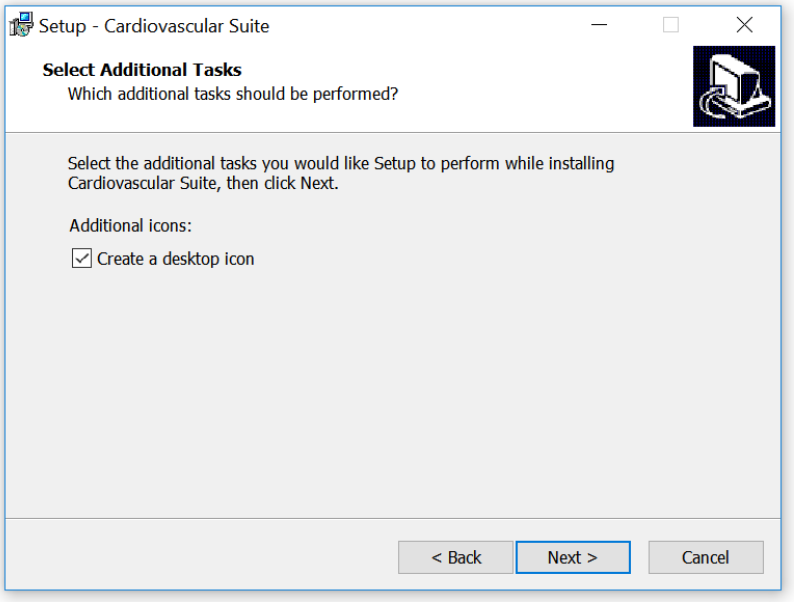
3. Read the License Agreement. If you don't accept the license agreement, please close the Cardiovascular Suite setup. If you accept, click the "Next" button to proceed.



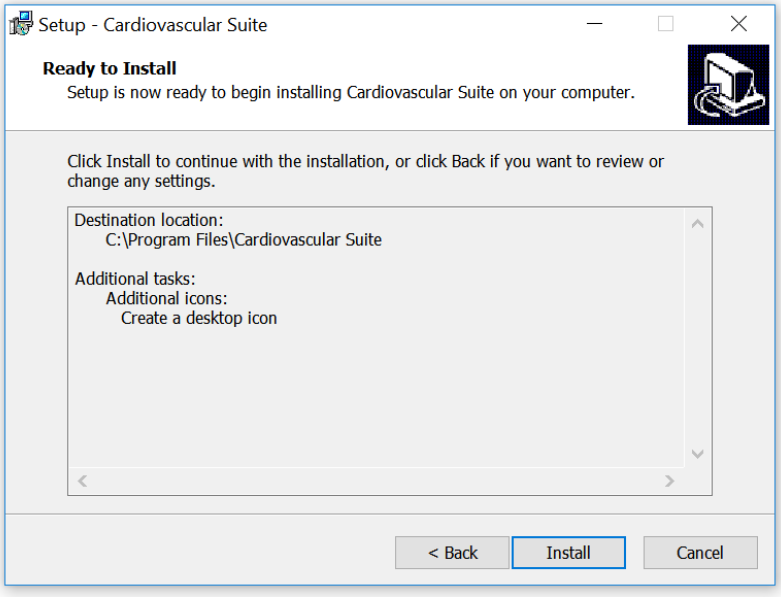
4. Select the installation folder. In most cases, you can use the proposed installation folder. Click the "Next" button to proceed.



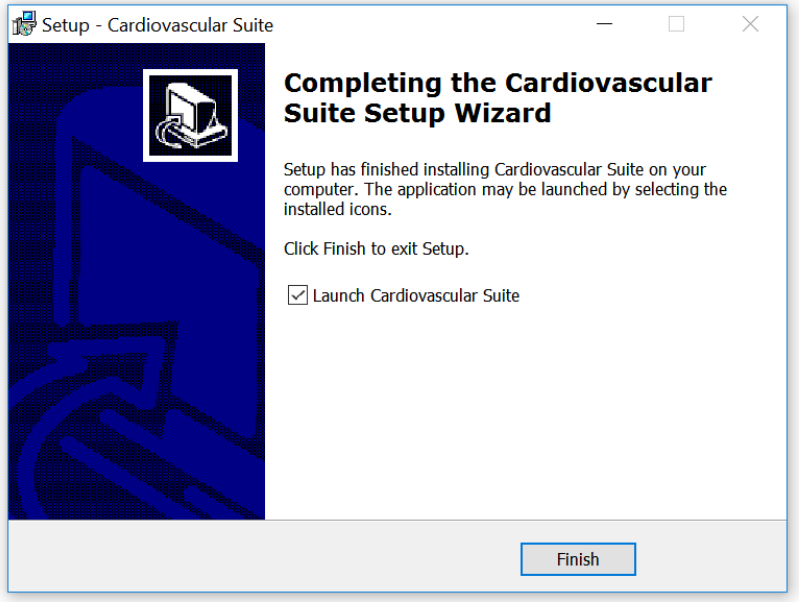
5. Select whether you want to create a Desktop Icon. Click the "Next" button to proceed.



6. Review the installation setting. Click the "Install" button to start installation. Cardiovascular Suite will be installed.



7. When the installation is completed, please click the "Finish" button.



2.3 License

Cardiovascular Suite is licensed under the EULA.

Cardiovascular Suite has independent licenses for FMD Studio and Carotid Studio. You can choose between two types of license:

- **Perpetual License:** it is a license that never expires. With the Perpetual License you are entitled to run all the minor updates of the application. For example, if you have a perpetual license for FMD Studio ver. 3, you

will be entitled to run FMD Studio ver. 4.0, 4.1, 4.2 and so on, but you will not be entitled to run FMD Studio ver. 5.0

- **Time License:** it is a time limited license. With this license, you are entitled to run any version of the application within the expiry day. After the expiry date, it is no longer possible to run the application or modify the stored data.

Cardiovascular Suite is licensed by the Quipu License Key, which is a USB dongle key.

Quipu License Key

When you receive the Quipu License Key, it will contain a not activated license. Please follow the instruction for Activating a license.

Once activated, your license will be stored inside your Quipu License Key.

> ⚠ **CAUTION : The Quipu License Key contains your license. Store it in a safe place in order to avoid loss and / or theft.**

The Quipu License Key must be plugged into the computer where the software is running. If you unplug the Quipu License Key while Cardiovascular Suite is running, the software will stop working.

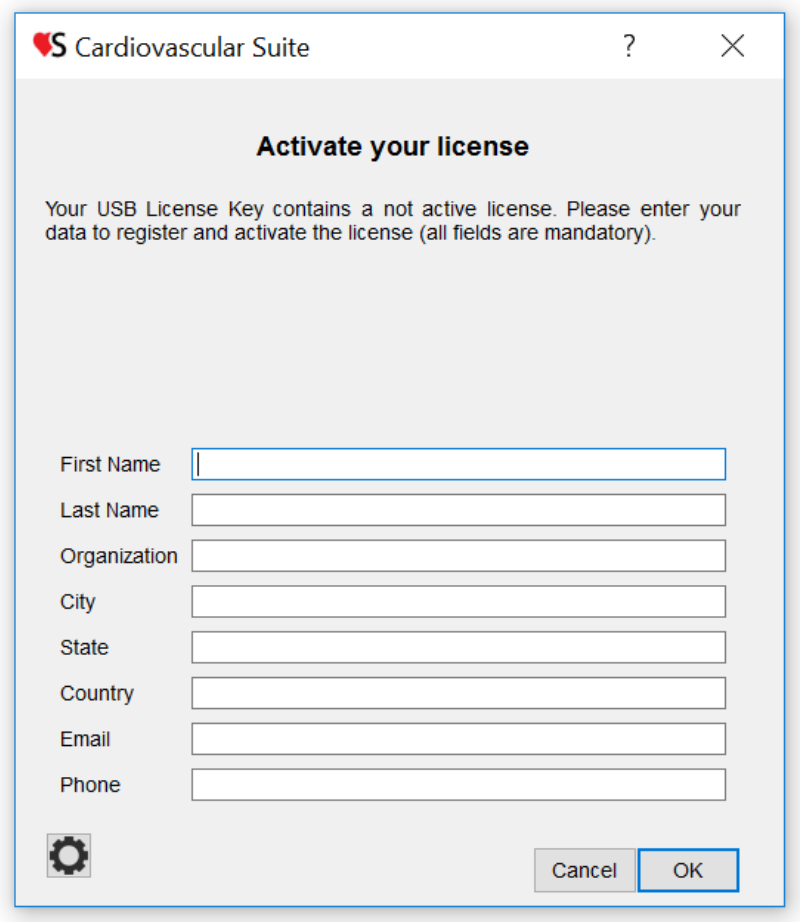
You license will work only on the computer where the Quipu License Key is used for the first time (i.e. it will be locked to this computer). If you want to replace your computer, please contact the Quipu support team (support@quipu.eu) for instructions on how to move your license to the new computer. You are allowed to move your license in a new computer three times in a year.

> ⚠ **CAUTION : The Quipu License Key will work only on the computer where it is used for the first time.**

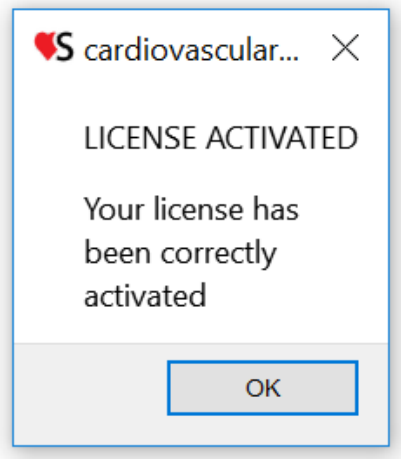
2.4 Activating a license

Plug the Quipu License Key into your computer and run Cardiovascular Suite.

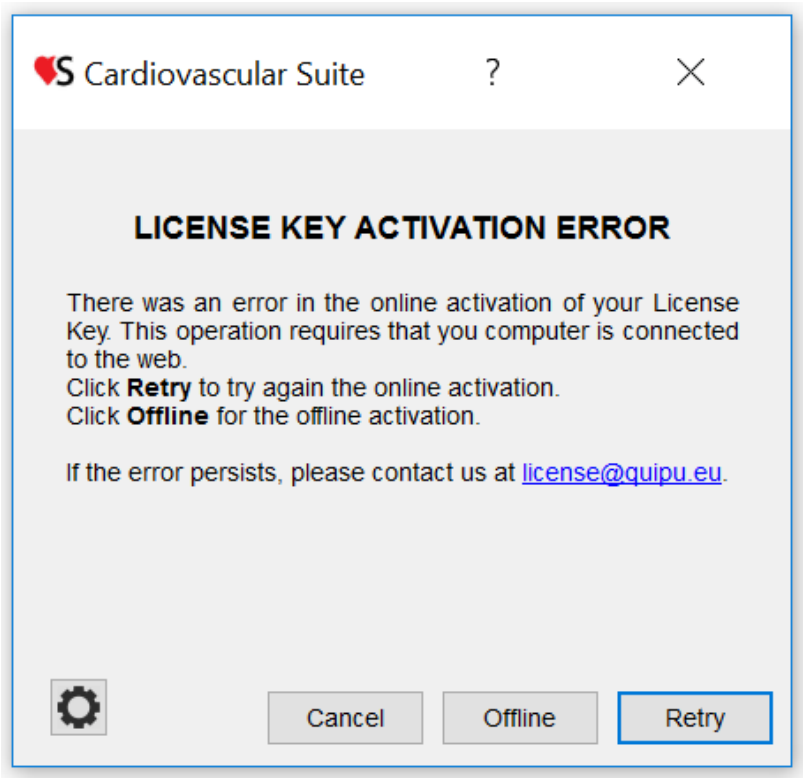
The following form is shown. Please enter your data to register and activate the license (all fields are mandatory). Then, click on the OK button.



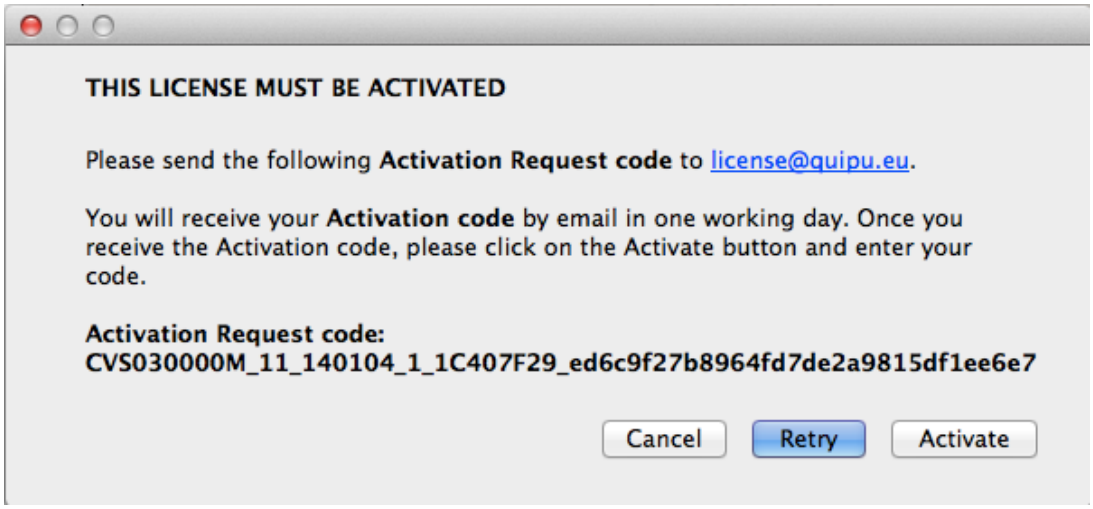
After a few seconds, a confirmation message will appear. CLick on the OK button and Cardiovascular Suite will start automatically.



If activation failed, proceed with offline activation by clicking the Offline button.



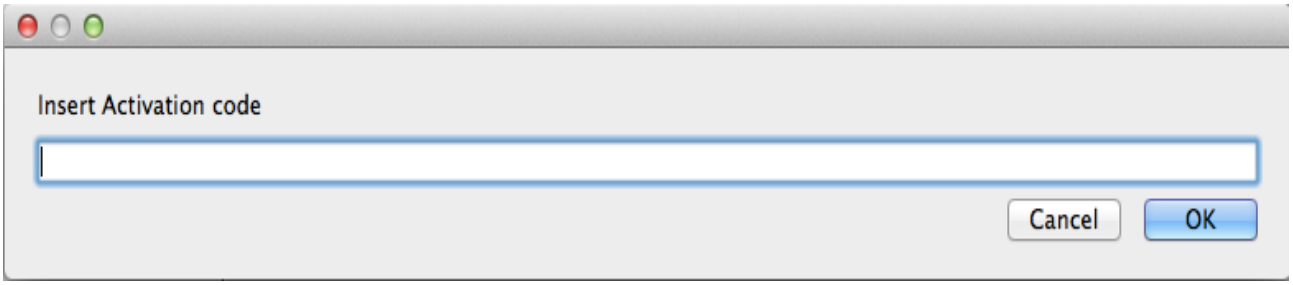
The following message will be shown:



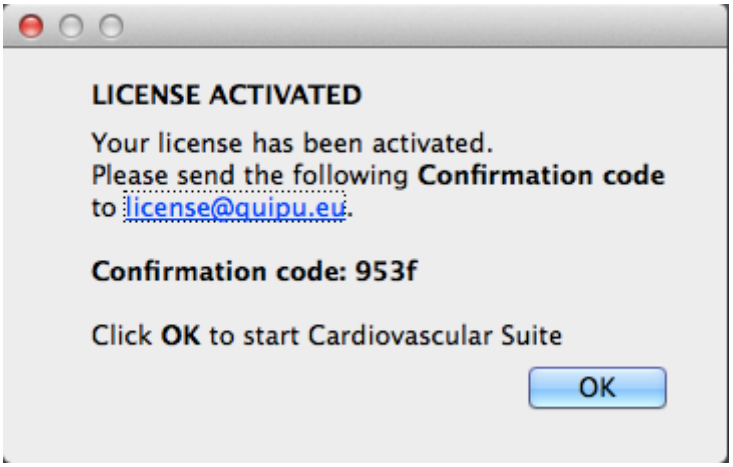
Click on the license@quipu.eu; if you have a mail application on your computer, it will generate a pre-compiled email with your data (Name, Organization, City, Country) and the **Activation request code** that is displayed on the message. Otherwise, please send an email to license@quipu.eu containing your data (Name, Organization, City, Country) and the **Activation request code** that is displayed on the message.

Within a working day, you will receive an email with the **Activation Code**.

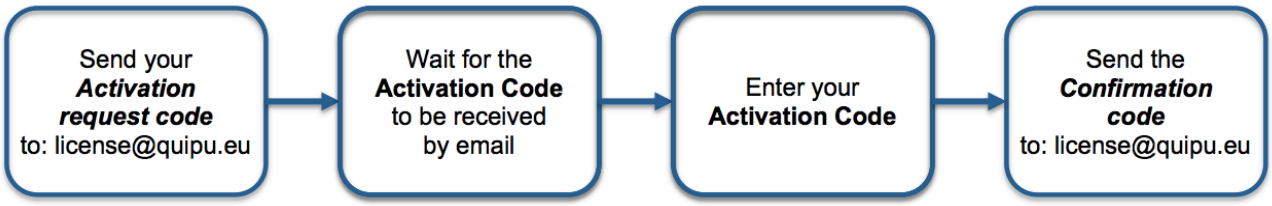
You can now click on the Activate button. The following message is shown:



Enter your Activation code and click OK. A confirmation message is shown.



Please send the Confirmation Code to Quipu by email, then click OK to start Cardiovascular Suite.



Offline Activation steps

2.5 Evaluation license

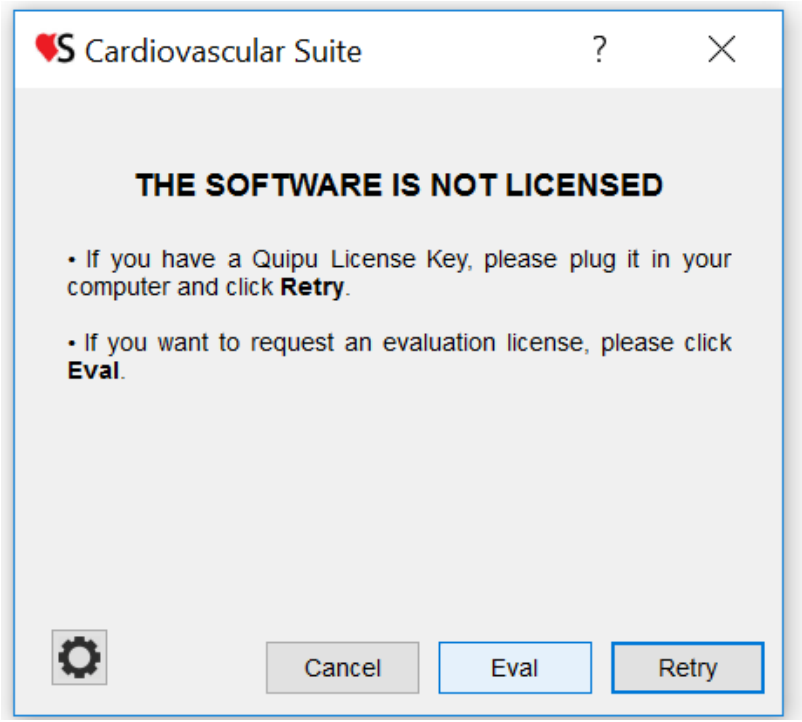
You can evaluate Cardiovascular Suite by a 14 days evaluation license.

With this license, you are entitled to use cardiovascular Suite **only for EVALUATION PURPOSES**. If you wish to use the software for any other purpose, you must purchase a commercial license. If you do not purchase a commercial license, at the end of the 14 days your content will no longer be available to you.

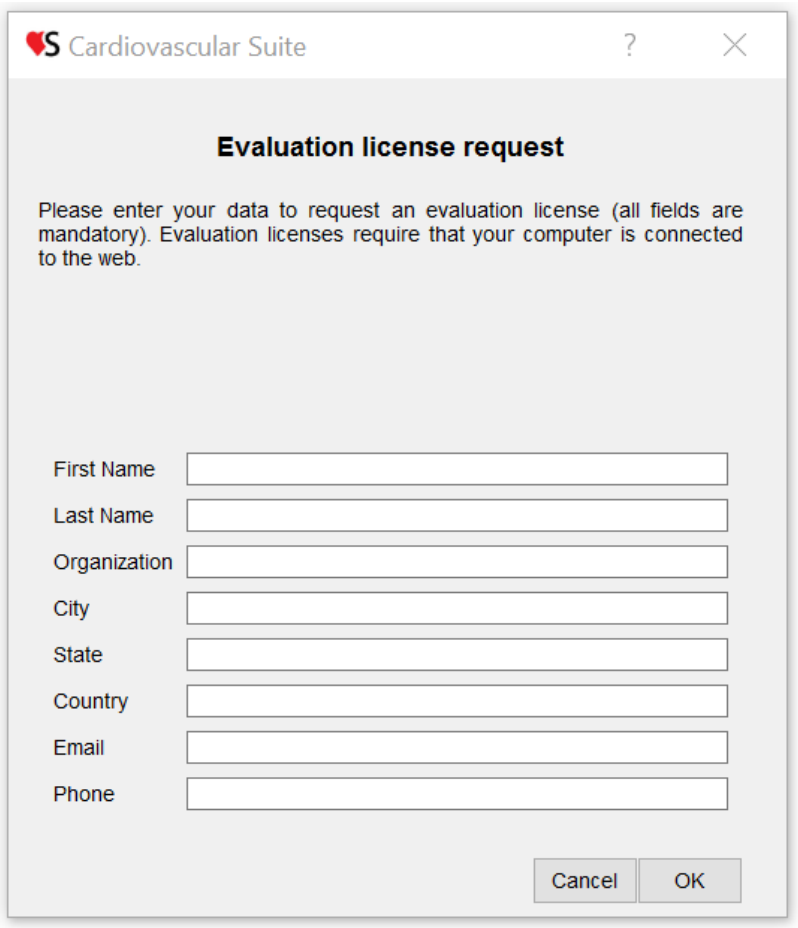
You cannot use/publish/distribute data generated by the Cardiovascular Suite in the evaluation period unless you purchase a commercial license.

⚠ **Please, note that an Internet connection is needed to obtain and use the Evaluation License.**

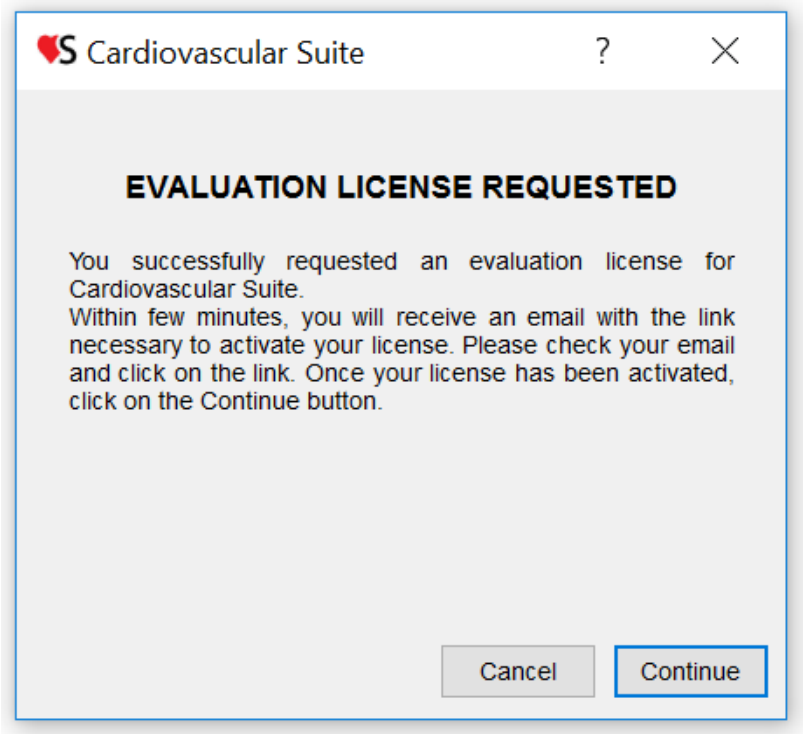
After downloading and installing the software, run Cardiovascular Suite. The following message is displayed:



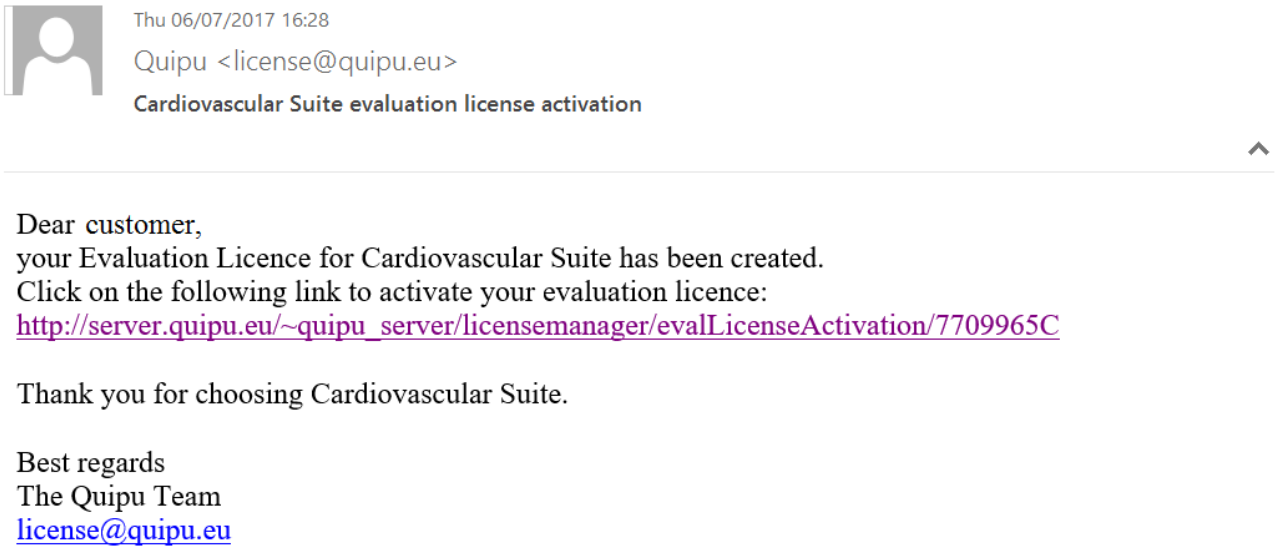
Click on the Eval button to request a fully functional 14-days Evaluation License. The following form is shown:



Please, enter your data to request an Evaluation License (all fields are mandatory). Then, click on the OK button. Please wait and after a few second the following confirmation message will be shown:



Within few minutes, you will receive an email with the **Activation link**.



Click on the **Activation link**. Your web browser will open the following web page and your license will be activated:

Your license has been activated correctly. You can now evaluate Cardiovascular Suite

If you still have Cardiovascular Suite open with the "Evaluation License Requested" message, please click on the Continue button. Otherwise run again Cardiovascular Suite. Now, the software starts and the Login window is displayed.

If the Evaluation Licence Request failed or errors occurred, please contact our technical support by mail or Skype message (support@quipu.eu)

2.6 Using video clips for offline analysis

Video clips recorded on the ultrasound imaging device can be moved on the computer using a digital medium (flash pen drive, hard disk, CD ROM). Video files can be in DICOM 3 or in all the most common video formats (AVI, MOV, MP4). Note that the B-mode window must to have a minimal resolution of 480x480 pixels.

For more information on supported video formats, please contact support@quipu.eu

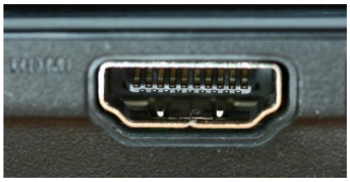
2.7 Connecting your computer to the ultrasound system

You need a video capture device to connect the computer with the ultrasound system and perform real-time analysis. Quipu recommends two USB devices: the Epiphan AV.io HD or the Magewell USB Capture AIO.

If your ultrasound machine has a VGA, DVI or HDMI output (see next figure for reference), you can directly connect your ultrasound machine to the computer by using either the Epiphan AV.io HD or the Magewell USB Capture AIO video capture device. (See more...)

VGA

DVI

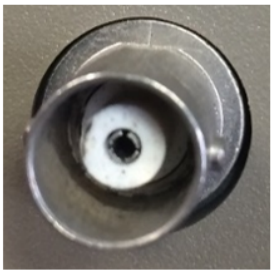


HDMI

If your ultrasound machine has a "legacy" video standard (S-Video or C-Video) output (see next figure for reference), you can directly connect your ultrasound machine to the computer by using the Magewell USB Capture AIO. If you want to use the Epiphan AV.io HD, you must first convert the video output to VGA, and then to acquire the VGA by the Epiphan AV.io HD. For the first video conversion, you can use any high-quality S-Video to VGA or C-Video to VGA converter. We suggest to use the Lindy Video to VGA Converter. (See more...)

S-Video

C-Video (RCA)



C-Video (BNC)

	Epiphan AV.io HD	Magewell USB Capture AIO
VGA	Directly supported	Directly supported
DVI	Directly supported	Directly supported
HDMI	Directly supported	Directly supported
S-Video	Conversion to VGA is required	Directly supported
C-Video	Conversion to VGA is required	Directly supported

NOTE: Please, verify with the ultrasound machine technician that the video output of your ultrasound machine is active.

Note also that the B-mode window must have a minimal resolution of 480x480 pixels.

For information on the availability and the standard of the video output, please contact the manufacturer of the ultrasound system.

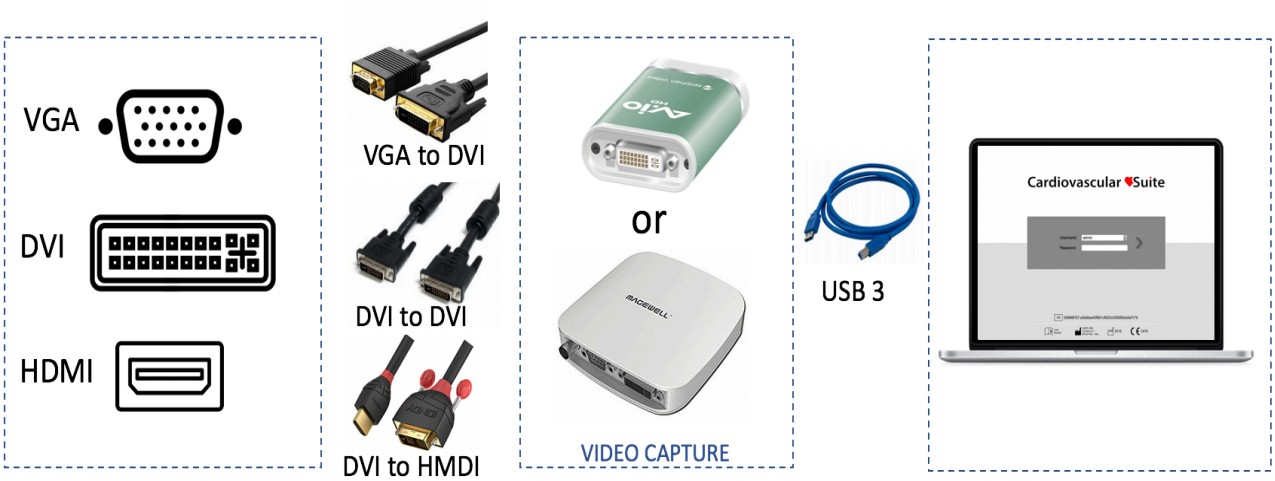
For additional technical information on how to connect the computer to the ultrasound apparatus and on the compatible video standards, please contact us at support@quipu.eu

> ⚠ **CAUTION: The ultrasound scanner must be in accordance with the European Medical Device Directive 93/42/EEC.**

> ⚠ **CAUTION: If the video converter is used with an AC/DC power adapter, it must be a medical grade power adapter according to IEC 60601-1, 3rd Edition.**

2.7.1 Using VGA/DVI/HDMI output

You can directly connect your ultrasound machine to the computer by using either the Epiphan AV.io HD or the Magewell USB Capture AIO video capture device.



Detail of the connections based on the output video format:

- **VGA video output**: use a VGA-to-DVI cable to connect your ultrasound machine to the Epiphan AV.io HD or the Magewell USB Capture AIO; then use the USB 3.0 cable to connect the video capture device to your computer.
- **DVI video output**: use a DVI cable to connect your machine to the Epiphan AV.io HD or the Magewell USB Capture AIO; then use the USB 3.0 cable for connecting the video capture device to your computer.
- **HDMI video output**: use an HDMI to DVI cable to connect your ultrasound machine to the Epiphan AV.io HD or the Magewell USB Capture AIO; then use the USB 3.0 cable to connect the video capture device to your computer.

See more About Epiphan AV.io HD or About Magewell AIO.

2.7.2 Using "legacy" video standard output

Magewell USB Capture AIO

You can directly connect your ultrasound machine to the computer by using the Magewell USB Capture AIO video capture device.

Detail of the connections based on the output video format:

- **S-Video output**: use an S-Video cable to connect your ultrasound machine to the Magewell USB Capture AIO.
- **C-Video (RCA) output**: use an RCA cable to connect your ultrasound machine to the Magewell USB Capture AIO.
- **C-Video (BNC) output**: use a BNC-to-RCA adapter and then an RCA cable to connect your ultrasound machine to the Magewell USB Capture AIO.

Use the USB USB 3.0 cable to connect the video capture device to your computer. See more about About Magewell USB Capture AIO.

2.7.2.1 Epiphan Av.io HD

You must first convert the video output to VGA by the Lindy Video to VGA Converter, and then to acquire the VGA by the Epiphan AV.io HD.

Detail of the connections based on the output video format:

1. First, connect your apparatus video output to the Lindy Video to VGA Converter.
    - **S-Video output**: use an S-Video cable to connect your ultrasound machine to the Lindy Video to VGA Converter.

- **C-Video (RCA) output**: use an RCA cable to connect your ultrasound machine to the Lindy Video to VGA Converter.
- **C-Video (BNC) output**: use a BNC-to-RCA adapter and then an RCA cable to connect your ultrasound machine to the Lindy Video to VGA Converter.

2. Once you have connected your apparatus to the Lindy Video to VGA Converter, you have to connect it to your computer by the Epiphan AV.io HD. You have to use the DVI-to-VGA cable to connect the Video Converter to the Epiphan AV.io HD. Then, use the USB 3.0 cable to connect the video capture device to your computer.

See more About Epiphan AV.io HD.

See more About Lindy Video to VGA Converter.

2.7.3 About Magewell USB Capture AIO

The USB Capture AIO is a USB2.0/USB3.0 video capture device from Nanjing Magewell Electronics Co., Ltd, China.

The device can be used to connect your computer to DVI, VGA, HDMI, S-Video and Composite video outputs coming from the ultrasound system. See Connecting your computer to the ultrasound system for more details.

There's no software to install to use USB Capture AIO; simply connect the cables and go. It works on Microsoft Windows computers and Apple Mac OS X computers.

USB Capture AIO video converter

Once you have connected your ultrasound apparatus to the USB Capture AIO, connect your computer to the video converter via the USB cable. The red LED (PWR) shows that the device is powered on. The green LED (ACT) shows the status of the device.

GREEN LED (ACT)	STATUS
Pulsing slowly	Idle
ON	Input signal connected
OFF	Input signal unconnected
Double blinks	Memory failed or FPGA configuration failed

The USB Capture AIO supports resolution up to 2048x2160. Performance may be limited by your computer features.

The Magewell USB Capture AIO supports both USB 3.0 and USB 2.0.

CAUTION: the video converter must be connected directly to a USB port on your computer. Do not use hubs or the USB socket on the external keyboard. Use USB 3.0 to maximize performances.

CAUTION: verify that the video output type and resolution of the ultrasound scanner are compatible with this video converter.

2.7.4 About Epiphan AV.io HD

The AV.io HD is a USB2.0/USB3.0 video capture device from Epiphan Systems Inc. Canada.

The device can be used to connect your computer to DVI, VGA or HDMI video outputs coming from the ultrasound system (or coming from a Video Converter if you use "legacy" standard video output). See Connecting your computer to the ultrasound system for more details.

There's no software to install to use the AV.io HD; simply connect the cables and go. It works on Microsoft Windows computers and Apple Mac OS X computers.

AV.io HD video capture

1. Once you have connected your ultrasound apparatus to the AV.io HD, connect your computer to the video converter via the USB cable. The lighting of the **red** LED indicates that the device initializing.
2. After a few seconds, the LED turns **blue or green** to indicate proper connection between computers and video converter.
3. Connect the video converter to the ultrasound device via the VGA, DVI or HDMI cable.
4. The LED will be **blue or green** until you start capturing a video signal.
5. LED will be **blinking green** or **blinking blue** during the acquisition of a video signal.

LED COLOR	STATUS
OFF	Video converter not connected to the computer
Solid red	AV.io HD initializing
Blinking red	Adjustment to VGA input in progress
Solid green or blue	USB connection active
Blinking green or blue	Video and/or audio transferring successfully

The Epiphan AV.io HD supports resolution from 640x360 up to 1920x1200. Performance may be limited by your computer features.

The Epiphan AV.io HD supports both USB 3.0 and USB 2.0.

CAUTION: the video converter must be connected directly to a USB port on your computer. Do not use hubs or the USB socket on the external keyboard. Use USB 3.0 to maximize performances.

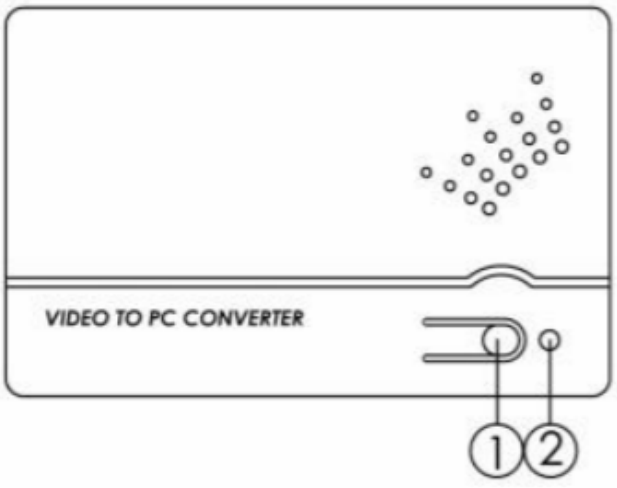
CAUTION: the AV.io HD must be updated with the last firmware from Epiphan System Inc.

CAUTION: verify that the video output type and resolution of the ultrasound scanner are compatible with this video converter.

2.7.5 About Lindy Video to VGA Converter

The Video to VGA Converter from Lindy (Germany) will allow you to convert your S-Video or Composite Video output to a VGA.

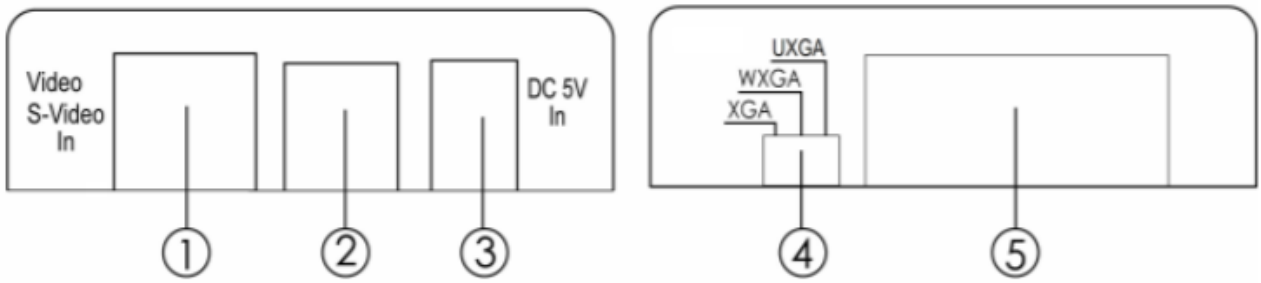
Lindy Video to VGA converter



Top Panel

1. The Input selection switch toggles between Composite and S-Video input
2. The LED indicator shows which input signal is selected

LED COLOR	INPUT
Green	Composite input signal
Red	S-Video input signal



Front & Rear Panel

1. S-Video input
2. Composite video input
3. DC power supply input
4. Output resolution selection switch (we suggest to use XGA):
    - XGA 1024x768
    - SXGA 1280x1024
    - UXGA 1600x1200
5. VGA output

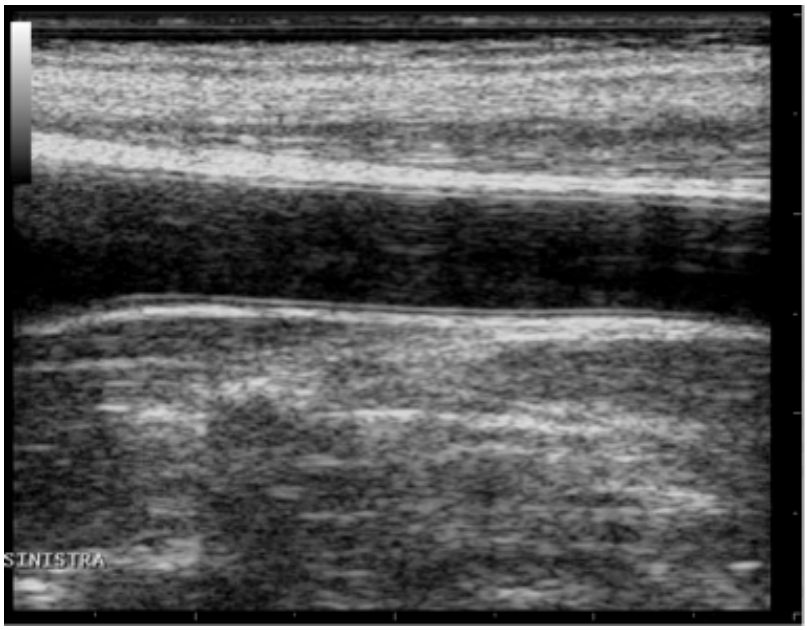
2.8 How to set up the ultrasound system

Cardiovascular Suite is based on image processing of a B-mode ultrasound scans. The quality of the results can depend on the quality of the ultrasound image supplied to the system.

We recommend the use of a **vascular probe** with a frequency between 7 MHz and 15 MHz. The general settings of the ultrasound system must be those suggested by the manufacturer of the apparatus. It is important, however, exclude any noise reduction filters that could degrade the performance of the edge detection algorithm. In particular, it is important to exclude any time filters that cause a smoothing effect on the images in motion. These filters may have different designations (the most common name is **persistence**) depending on the model of ultrasound equipment. Please contact the manufacturer of ultrasound apparatus for information on how to exclude this type of filter.

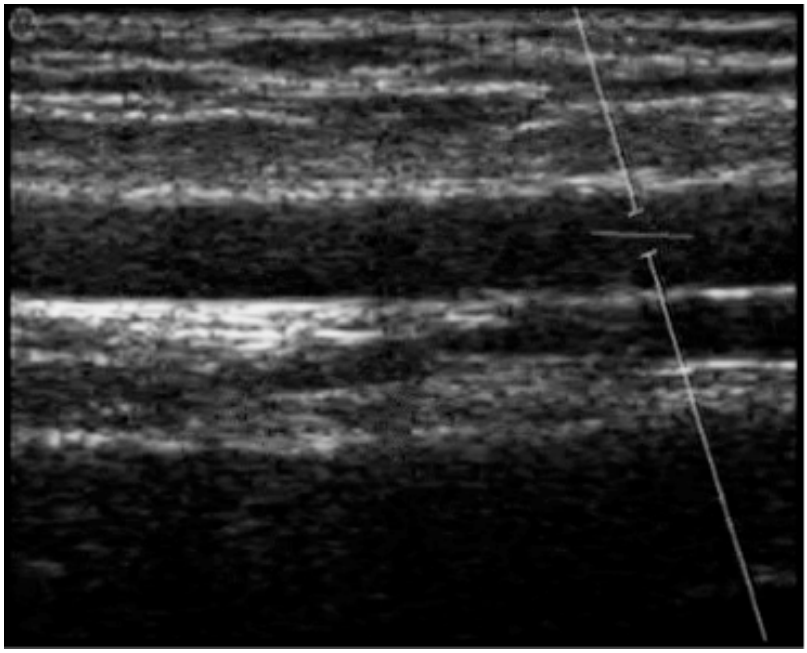
> ⚠ **CAUTION: Exclude any noise reduction filter (especially temporal filters).**

The artery should be viewed in longitudinal section and should be as horizontal as possible to the image. For Carotid Studio we recommend an image depth of 3-4 cm.



Example of carotid artery image

For FMD Studio we recommend an image depth of 2-3 cm. It is suggested also to choose a projection so that the vein is not visible (this normally appears immediately above the brachial artery). The algorithm for automatic tracking of the edges of the vessel could recognize the edge of the vein instead of the artery.

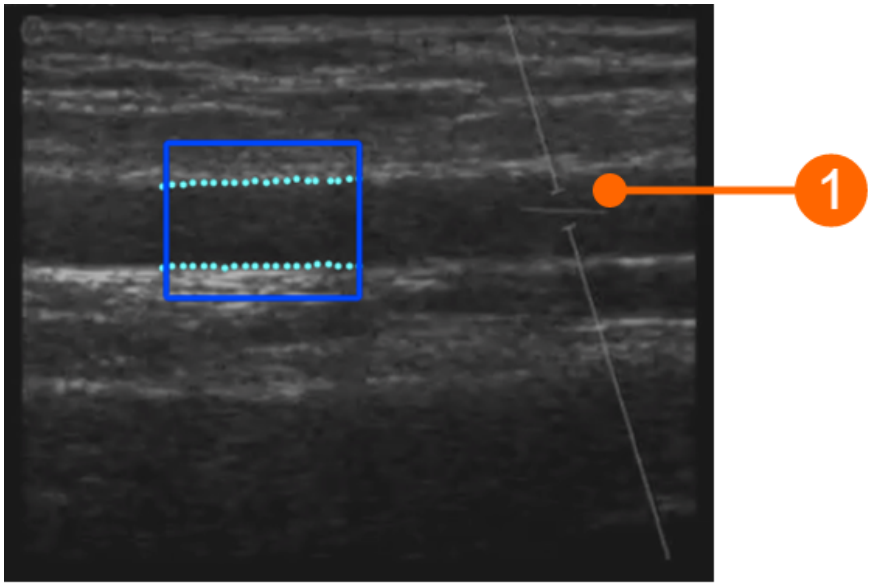


Example of brachial artery image

2.8.1 How to set up the ultrasound system in Duplex Mode (FMD Studio)

The ultrasound system must be in Duplex mode (simultaneous acquisition of B-mode and Doppler) for the determination of both vessel diameter and shear rate.

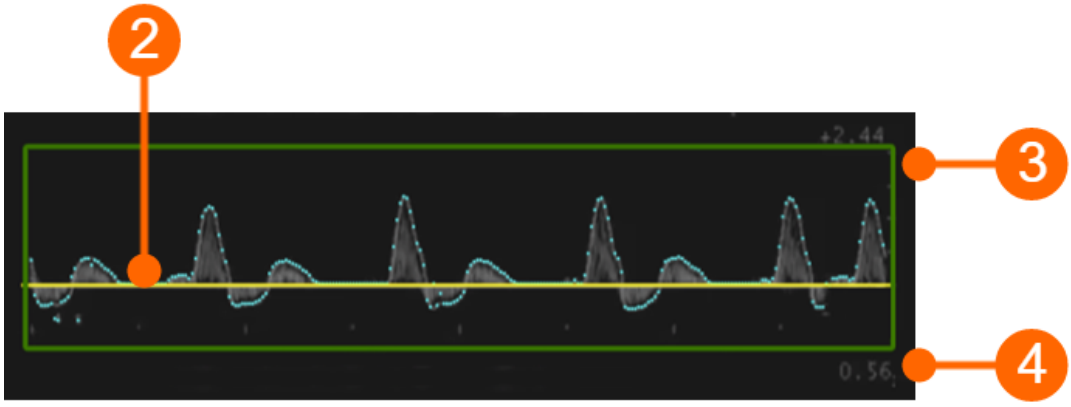
The angle between the Doppler beam and the vessel orientation should be ≤60 degrees. The sample volume should be as wide as possible but without encompassing the vessel walls and allowing for a slight margin for error in case of movement. Pay attention that the cursor of the doppler sample volume **(1)** is not into the ROI where the diameter is computed. It is recommended that the sample volume is 5 - 15 mm apart from the ROI.



CAUTION: pay attention that nothing but the ultrasound image is into the ROI. Please note that the processing can be affected by annotations or any other graphical object that is superimposed to the image. In particular, pay attention that the cursor of the doppler sample volume is not into the ROI.

The scale of the Doppler flow profile should be set correctly on the ultrasound system. The vertical scale must be large enough to include the velocity profile during all the examination (in FMD measurements, greater velocity values are in reactive iperemia). For the horizontal scale, we suggest a value of 3-4 seconds. Please note that the time average is computed over all the extend of the horizontal scale.

The Doppler Flow ROI must cover all the extent of the Doppler flow profile. The zero flow axis **(2)** must be included in the ROI: it will be automatically recognized and plotted in yellow. The vertical axis **(3)** must be external to the ROI. Please also ensure that any annotation **(4)** is outside the ROI since it could affect the flow analysis.



CAUTION: the processing can be affected by annotations or any other graphical object that is superimposed to the image into the Doppler Flow ROI.

Please remember that the tool for the calculation of the shear rate must be re-calibrated every time you change the size or scale of the Doppler flow profile. This calibration is present in Settings - FMD Studio. It is recommended that the size or scale of the Doppler trace will be no longer changed once you have decided how to set up the ultrasound system.

2.9 Extraordinary maintenance

There are no updates of parts of the software. In case of correction of "bugs", the user is alerted via e-mail and the software must be re-installed in the usual manner described in the Software installation instruction.

3 Login

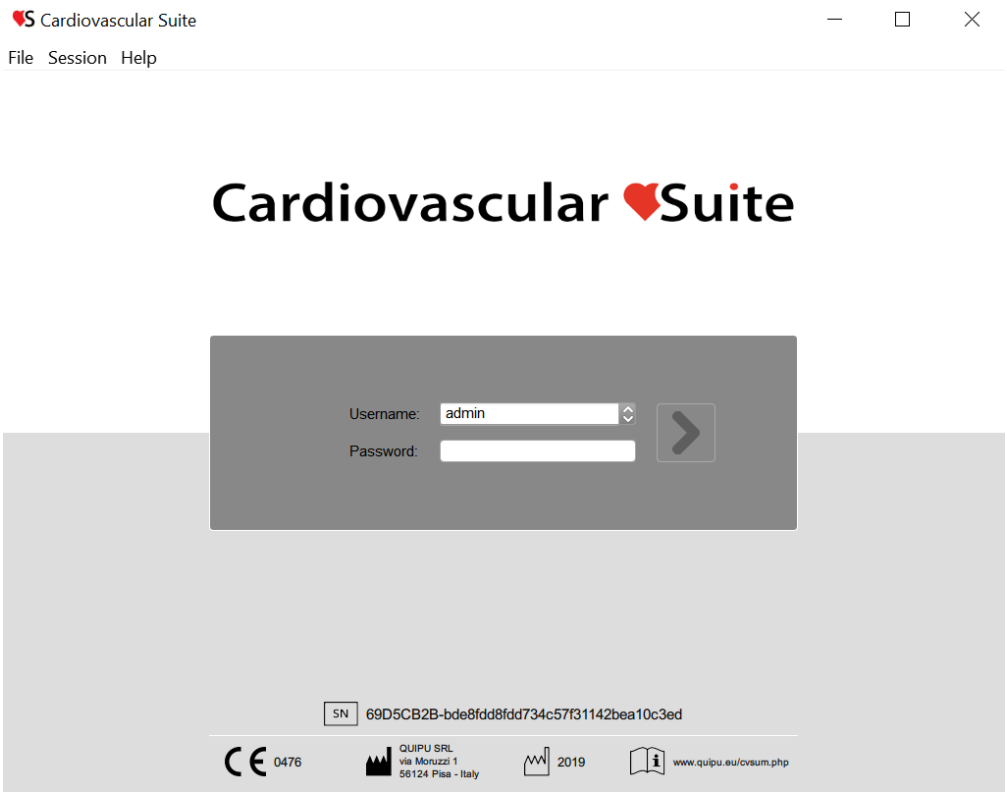
When you run Cardiovascular Suite, you are asked to login with a Username and Password. Please enter your Username and Password, then click on the Login  button to access the software.

When you first install Cardiovascular Suite, the default user account is:

Username: admin

Password: admin

You can modify this user account and add other user accounts in the Users management section.



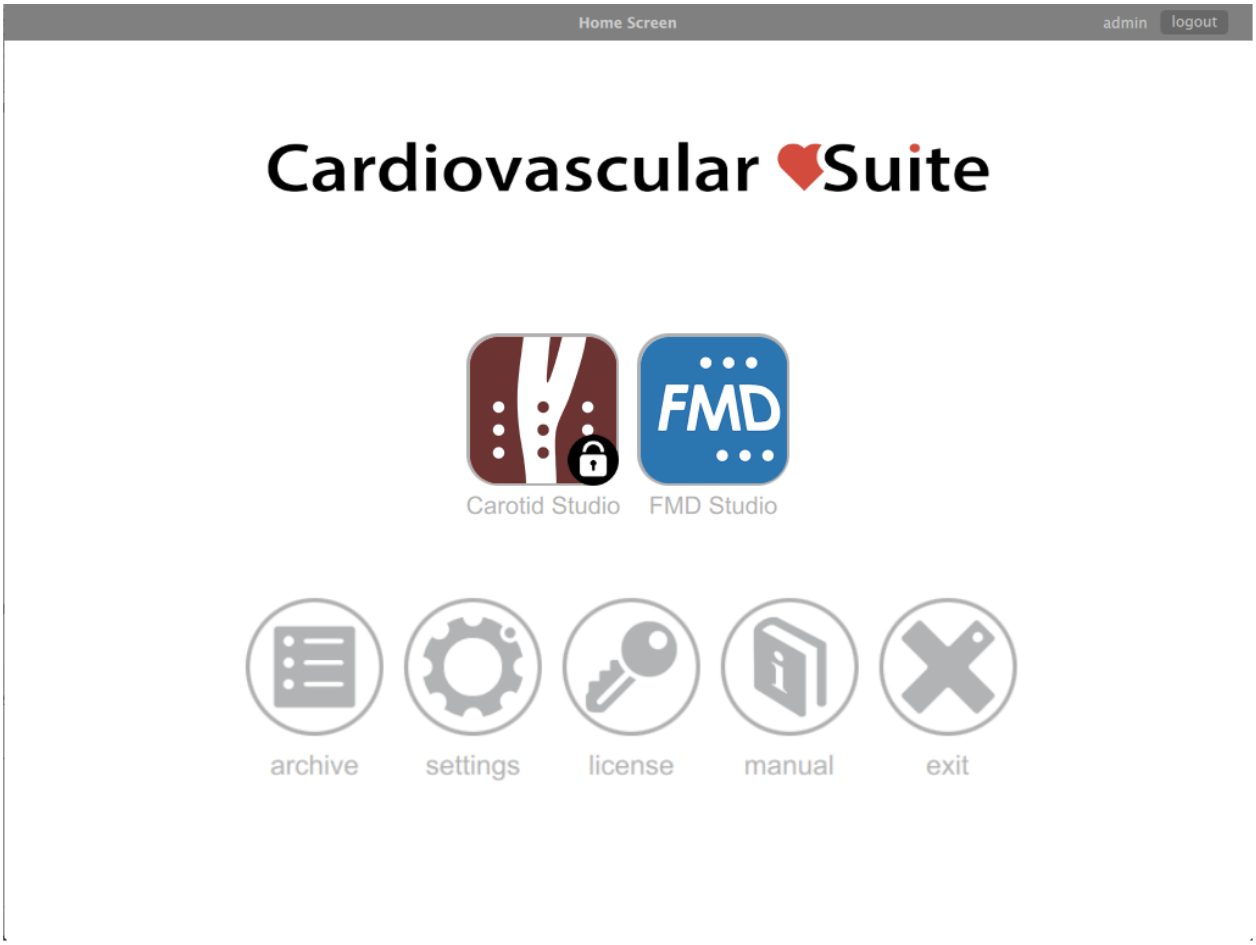
Login window

In the lower part of the Login window, the labelling of the device is shown.

In particular, on the right of the 

symbol you can find the Serial Number of your software.

4 Home screen



Home screen

The Home Screen contains the main controls of the software.

The Carotid Studio and the FMD Studio buttons start a new study with Carotid Studio and FMD Studio respectively.

If a lock icon  is present inside the button, this means that you don't have a valid license for this application.

The buttons in the lower part of the the Home Scree are:

- **archive**: opens the Archive window.

- **settings**: opens Settings window.
- **license**: opens the License manager window.
- **manual**: opens this User Manual in an external browser.
- **exit**: quit Cardiovascular Suite.

On the top right of the Home Screen, you can find the name of the logged user and the logout button.

5 Operators

The **operator** is the person who uses Cardiovascular Suite. When the software starts, the operator must login with its user account (username and password).

Two classes of operator are available in Cardiovascular Suite:

1. **Users**. They have full access to the software.
2. **Read-only users**. These users can only read the archive and the documents.

An operator is characterized also by a **status** that can be **active** or **disabled.** If an operator has been disabled, he/she cannot access to the software.

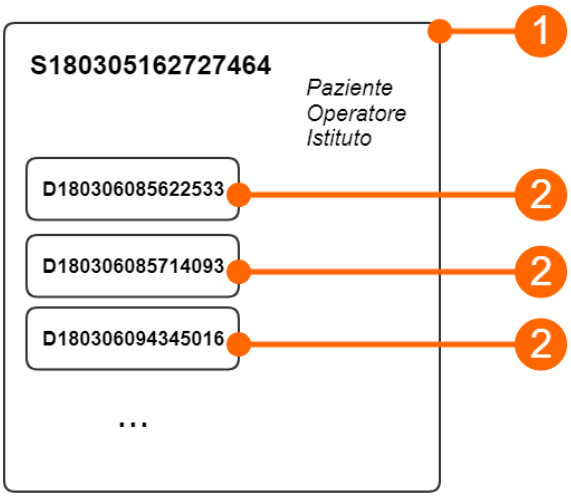
See Operators management for more details.

6 Archive

The Archive contains:

- the studies and their documents;
- the patients;
- the operators;
- the institutes;
- the protocols;
- the tags.

6.1 STUDIES AND DOCUMENTS



The study **(1)** contains the results generated by a Software Application. These results are organized into documents **(2)**. Each documents contains the results of the analysis and can contain videos and/or images.

Each study has a unique study identification number (study ID), which is a string starting with the letter "S" and followed by 15 numeric digits.

Analogously, each document has a unique study identification number (document ID), which is a string starting with the letter "D" and followed by 15 numeric digits.

6.2 PATIENTS

The patient is the person who undergo the examination.

The archive can contain the following patient data:

- Patient ID
- First name
- Middle name
- Last Name
- Sex (it can be: "Unspecified", "Female" or "Male")
- Birth date (it can be set or "unspecified")
- Address (Street, number, City, ZIP, State/Region, Country)
- Telephone
- E-mail

You can enter the data of the patients. The only mandatory field is the patient ID. If you don't enter patient ID, a random value will be automatically proposed, which is a string starting with the letter "P" and followed by 15 numeric digits.

6.3 OPERATORS

The operator is the person who make the examination.

The archive can contain the following operator data:

- First name
- Middle name
- Last Name
- Birth date (it can be set or "unspecified")
- Telephone
- E-mail

You can also set a picture of the operator.

6.4 INSTITUTES

The institute is the organization where the examination is performed.

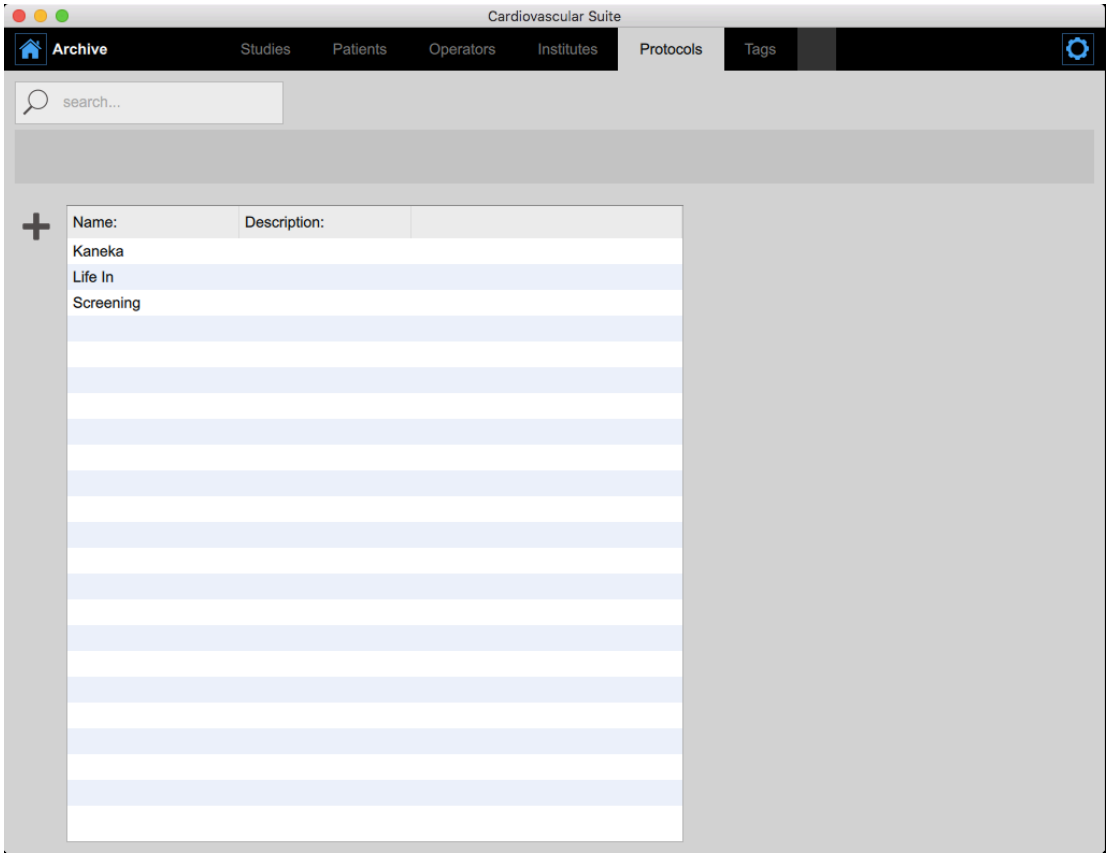
The archive can contain the following institute data:

- Name
- Address (Street, number, City, ZIP, State/Region, Country)
- Telephone
- Fax
- E-mail

You can also set a picture of the institute.

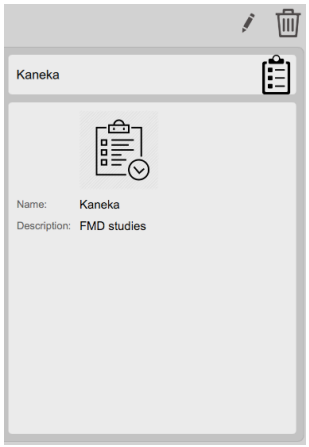
6.5 PROTOCOLS

The archive can contain information about protocols, to which each study may be associated.



Each protocol can be described through:

- Name
- Description (facultative)

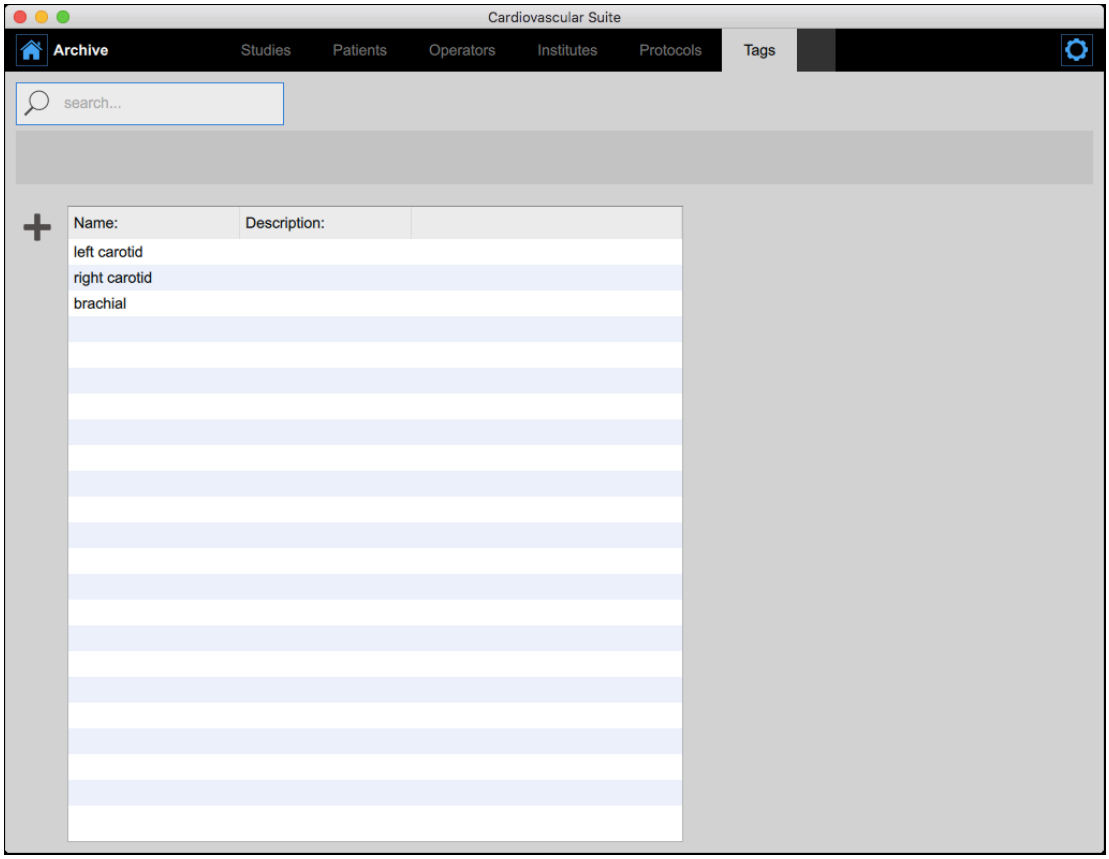


The protocol can be modified and more information can be added:

It is possible to delete the protocol with Delete button. With the Save button you can save the information about the protocol. The Restore button restores the previous information before the change. With the Back button it is possible to close the window in which changes are made. At the top of the screen there is the search space to search for protocols in the list.

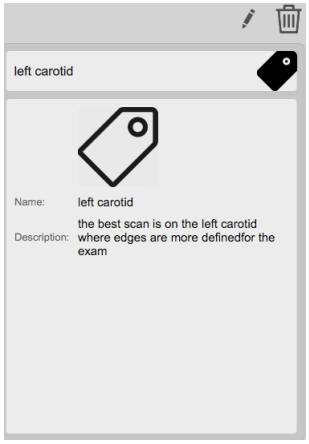
6.6 TAGS

Tags are labels that can be associated with documents of the Archive.

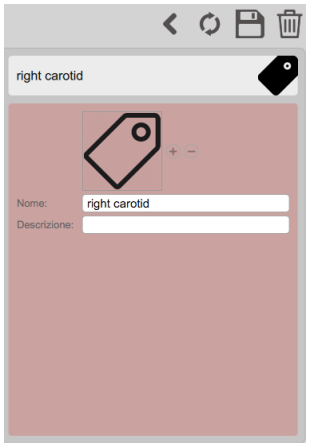


Each tag can be described through:

- Name
- Description (facultative)



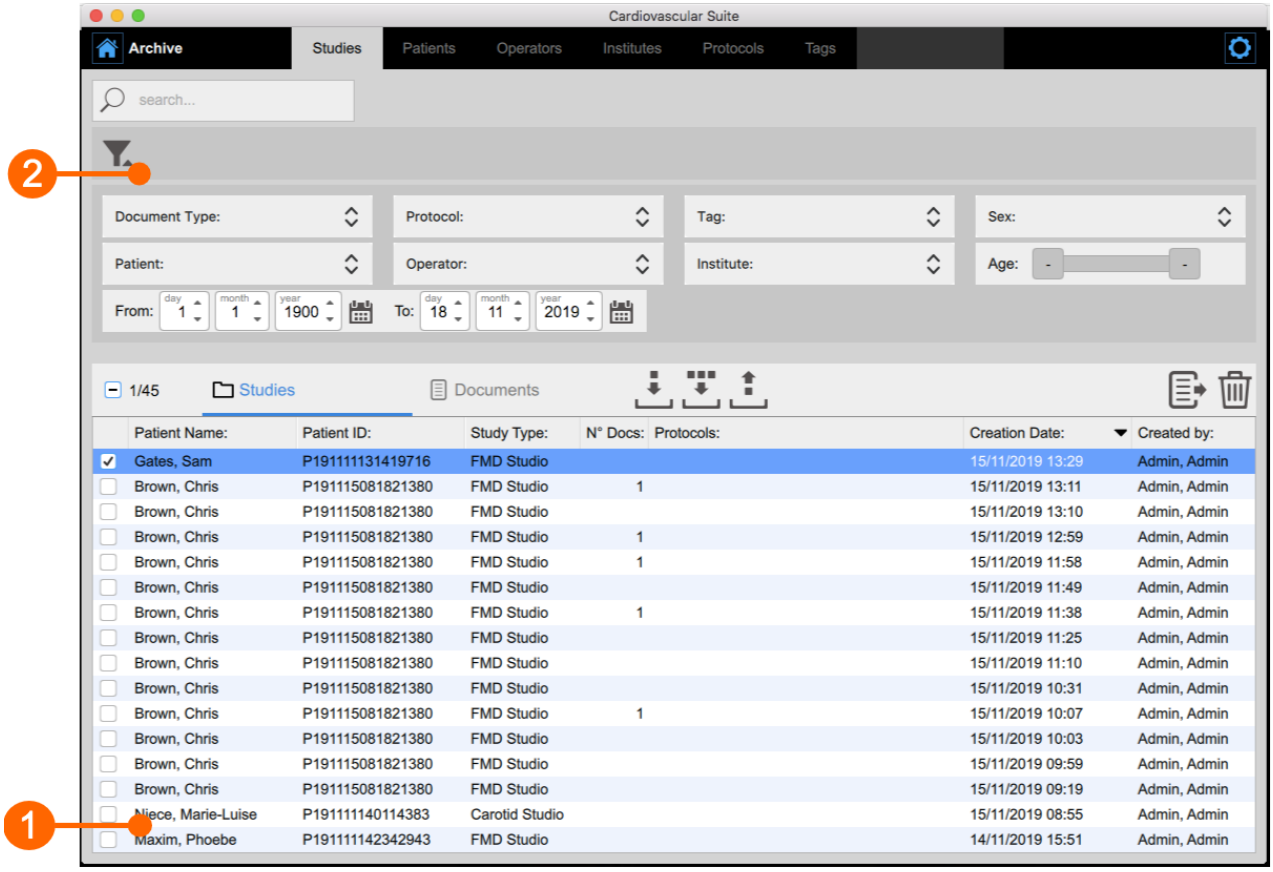
The tag can be modified and more information can be added:

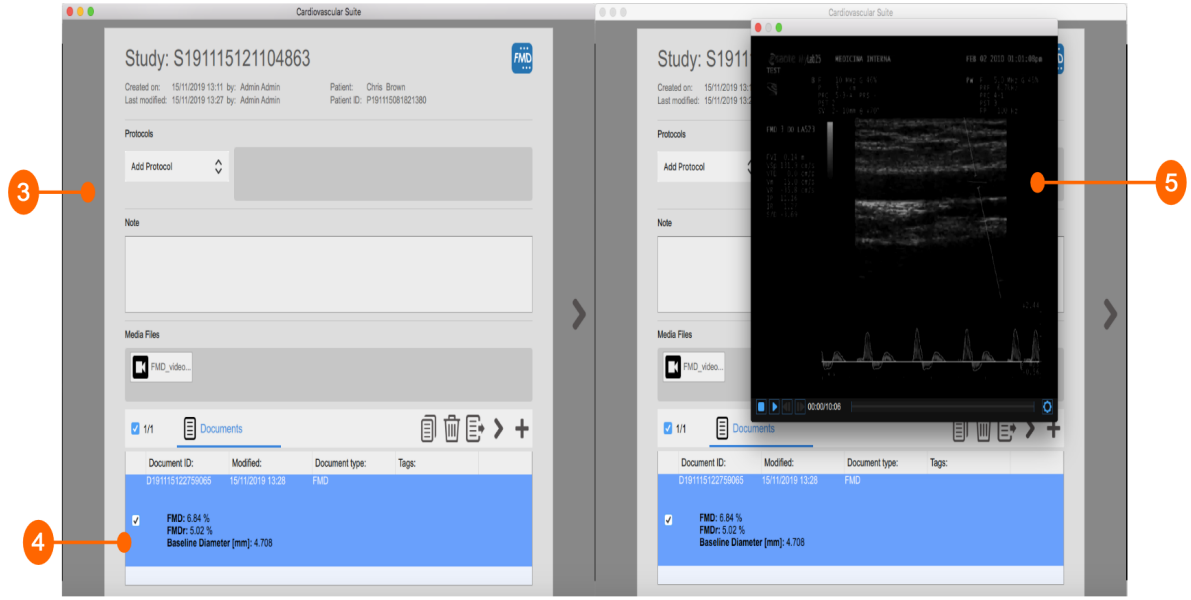


It is possible to delete the tag with Delete button. With the Save button you can save the information about the tag. The Restore button restores the previous information before the change. With the Back button it is possible to close the window in which changes are made. At the top of the screen there is the search space to search for tags in the list.

6.7 Studies management

Allows you to manage studies and documents.



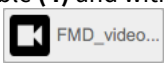


The study list is given in the table **(1)**. In the frame **(2)** you can add and remove filters to the study list. The following filter can be used:

- Document type
- Patient
- Operator
- Institute
- Operator
- Sex
- Age
- Tag
- Protocol

In addition, you can filter the studies by patient by going to the Patients management panel and double clicking on the patient.

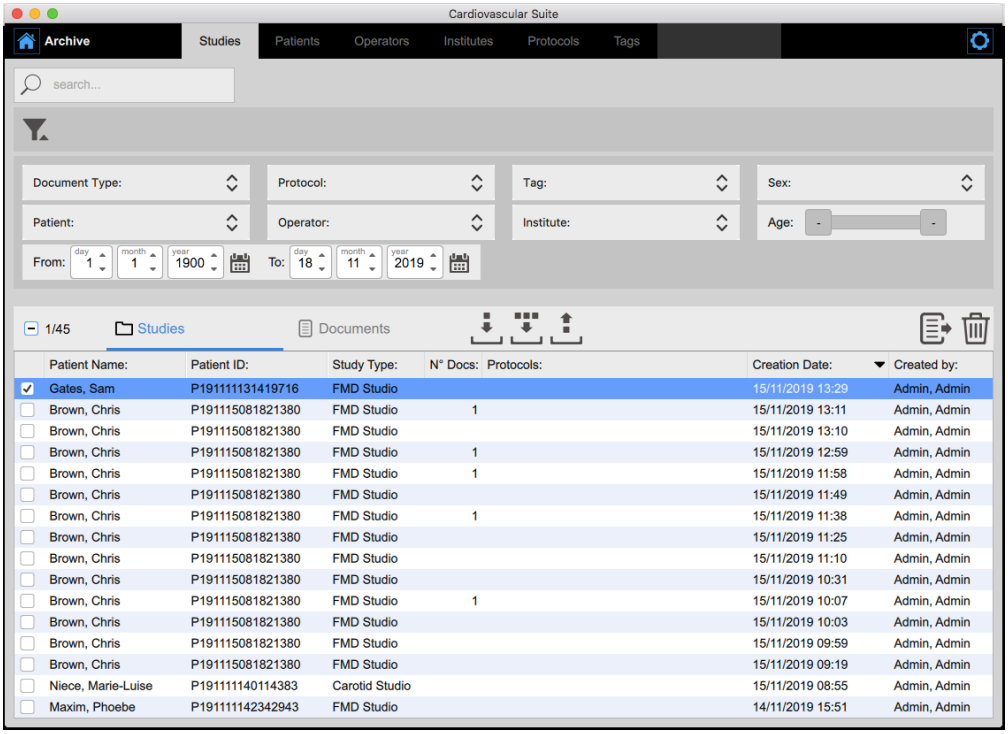
Once you select one of the studies, the study details are shown in the frame **(3)**. The first value in this frame is the study identification number (study ID).

The documents included in the selected study are shown in the table **(4)** and with a single click on an item the document preview is shown **(5)**. In particular, clicking on the icon 

the video clip is opened.

6.7.1 Management of Studies Table

The Archive is structured with several panels: Studies, Patients, Operators, Institutes, Protocols and Tags. In the Studies section you can find two different panels: Studies and Documents. The list of the studies is shown in Studies panel, and the management of the studies is described here:



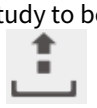
6.7.1.1 Import a study:

- Click on the Import Study  button that is placed on the top of the Studies Table **(1)**.
- Select the folder that contains the study to be imported, then press Open.

6.7.1.2 Import more than one study:

- Click on the Multiple Import Study  button that is placed on the top of the Studies Table **(1)**.
- Select the folder that contains the studies to be imported, then select the studied and press Open.

6.7.1.3 Export a study:

- In table **(1)**, click on the study to be exported.
- Click on the Export Study  button that is placed on the left of the Studies Table **(1)**.
- Select the destination path where you want to save your exported study, then press Save.

6.7.1.4 Delete a study:

- In table **(1)**, click on the study to be deleted.
- Click on the Delete Study  button that is placed above the Studies Table, on the right **(1)**.

6.7.1.5 Multiple selection:

In Studies Table multi-select feature is available. You can select more than one study and perform export and delete operation on selected studies.

In table **(1)**, select the studies through the check-box. The label over the table shows how many studies are selected from the available ones.

After you have selected studies you can export them (clicking on multiple Export  button, placed on the left of the Studies Table) or delete them (clicking on multiple Delete  button, placed above the Studies Table, on the right) **(1)**.

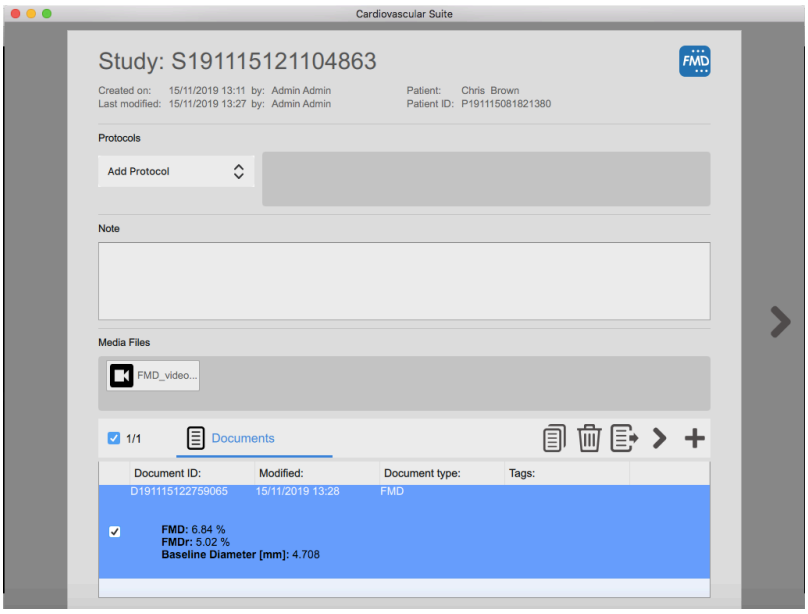
6.7.1.6 Advanced export:

It is possible to export documents of selected study/studies as CSV, TSV or PDF file.

- In table **(1)**, click on the study/studies to be exported

- Click on the Export Documents  button that is placed on the top of Studies Table **(1)**. A drop-down menu appears:
  - *Export Document Results*: it exports a TSV/CSV file containing information about the study, the document and the computed results. You can export also a PDF report of the document.
  - *Export Document Data*: it exports a TSV/CSV file containing the results of the study and the instantaneous data.
- Select the destination path where you want to save your exported documents, then press Save.

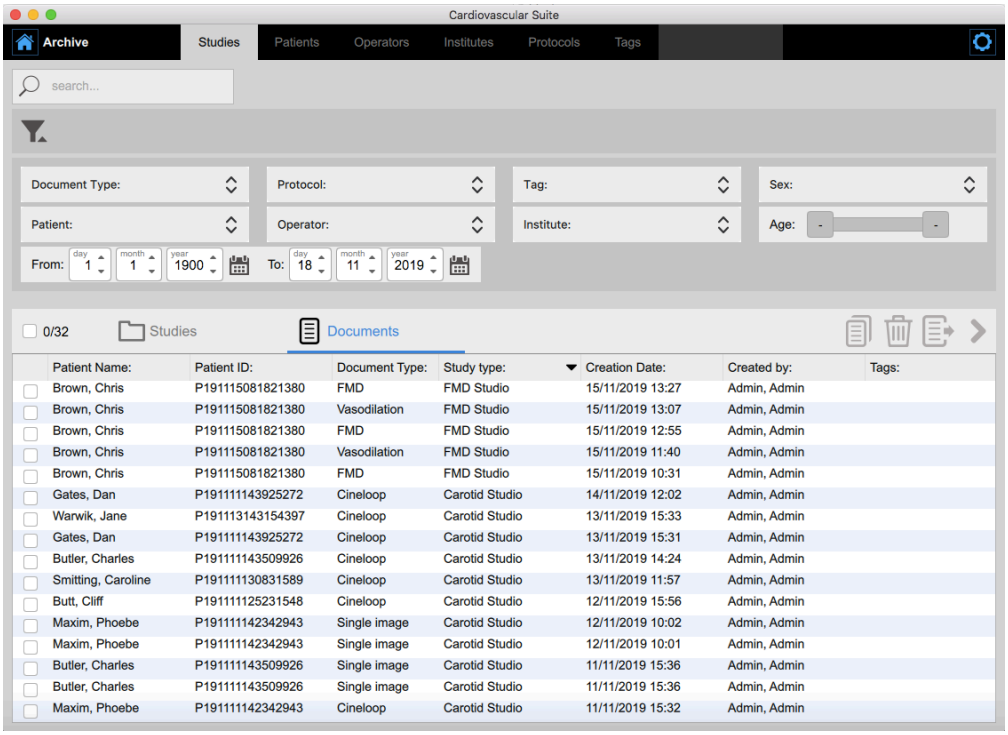
Clicking on a study, a Study View window is opened, containing information about the study.



Here, you have access to media file related to that study, the relative documents and there are information on the study (Study ID, Creation, Patient, Patient ID). It is also possible to create a new document related to that study, with the button "Create new document for the current study"  . You can duplicate the document with the Duplicate  button.

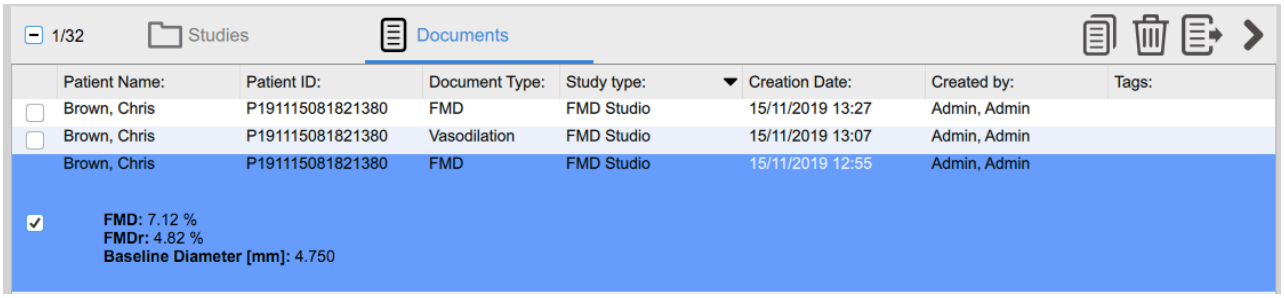
6.7.2 Management of Documents Table

To perform any operation on a document, you have to select first a study in Document table. In the Studies section you can find two different panels: Studies and Documents. The list of the documents is shown in Documents panel:



6.7.2.1 Document preview:

Once you have selected a document in Document Table, the list of documents appears (if at least one document exists).



Clicking on a document, it is possible to see some information about the document itself. A short preview of the document with the values (if calculated) of the characteristic parameters for that document type is available.

With a single click on a document it will be possible to show its preview, that is made up by:

- Image: by default it is empty and the user can set one of the frames of the video clip as image preview. In order to do this, open an existing document (or at the end of the analysis, during the review) and perform a right click on the video player once the desired frame is displayed. Then, click on the menu item "Set this image as preview"
- Text: it shows a short preview of the document with the values (if calculated) of the characteristic parameters for that study type.

6.7.2.2 Open a document:

- Click on the document to be open.
- Click on the Go  button in document preview and the document will open in the application that created it or,
- Double click on the document to be open.
- The document will open in the application that created it

6.7.2.3 Duplicate a document:

- In table, click on the document to be duplicated.
- Click on the Duplicate Document  button in the document preview.

6.7.2.4 Delete a document:

- In table, click on the document to be deleted.
- Click on the Delete Document  button in the document preview.

6.7.2.5 Export a document:

- In table, click on the document to be exported (PDF report).
- Click on the Export Document  button in the document preview.

6.7.2.6 Create a new document:

It is possible to create a new document starting form Studied table, clicking on a study and having access to the related documents:

- Click on the Create New Document  button that is inside the document whose video/image source is to be re-analysed.
- The application that created the document will open. You can analyse again the data and create a new document.

6.7.2.7 Multiple selection:

In Documents Table multi-select feature is available. You can select more than one document and perform export and delete operation on selected documents.

In table, select the documents through the check-box. The label over the table shows how many documents are selected from the available ones.

After you have selected documents you can export them (clicking on multiple Export  button) or delete them (clicking on multiple Delete  button).

6.7.2.8 Advanced export:

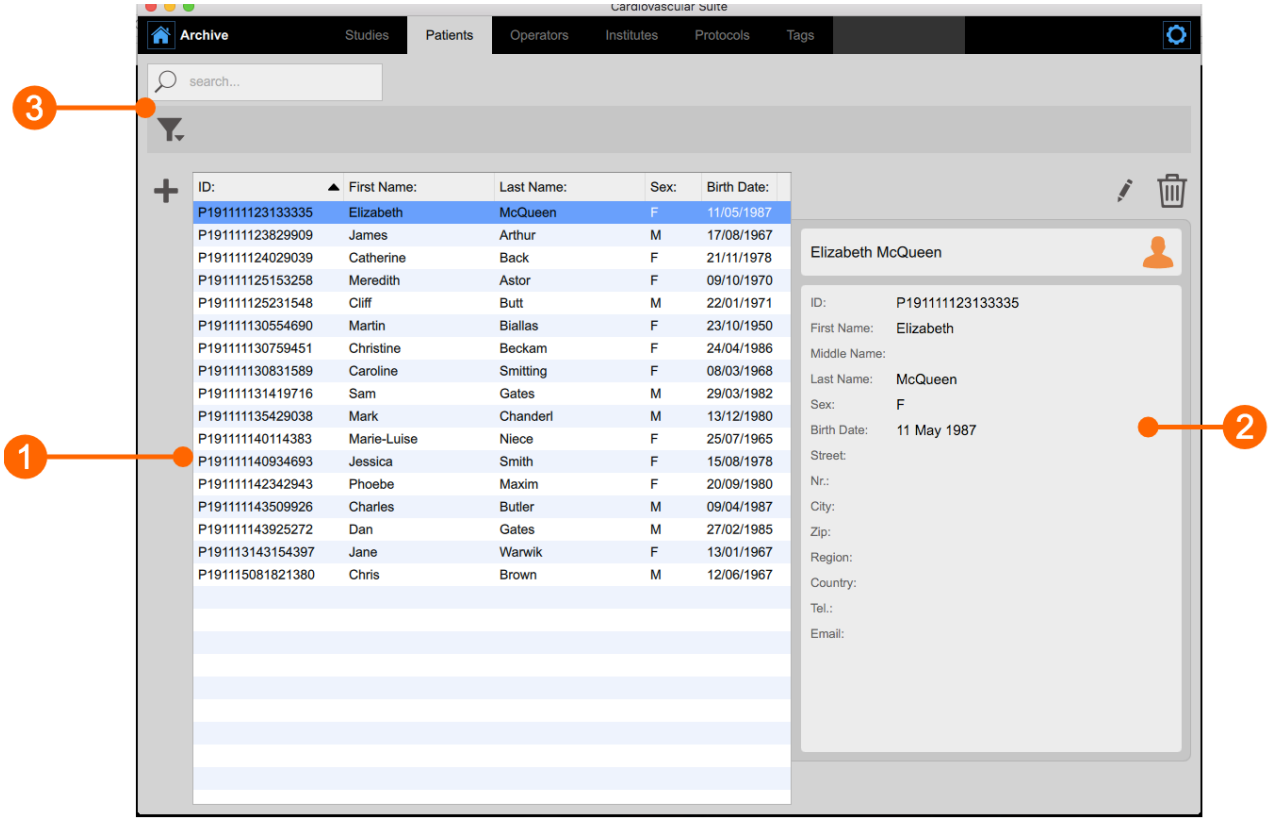
It is possible to export documents of selected study/studies as CSV, TSV or PDF file.

- In table, click on the study/studies to be exported
- Click on the Export Documents  button that is placed on the top of Documents Table. A drop-down menu appears:
- *Export Document Results*: it exports a TSV/CSV file containing information about the study, the document and the computed results. You can export also a PDF report of the document.
- *Export Document Data*: it exports a TSV/CSV file containing the results of the study and the instantaneous data.
- *Export Aggregated Results*: it is also possible to export aggregated results of different study documents in a single CSV or TSV file (please note that selected studies should all be of the same type, e.g. Carotid, FMD or Vasodilation).

- Select the destination path where you want to save your exported documents, then press Save.

6.8 Patients management

Allows you to manage patients.

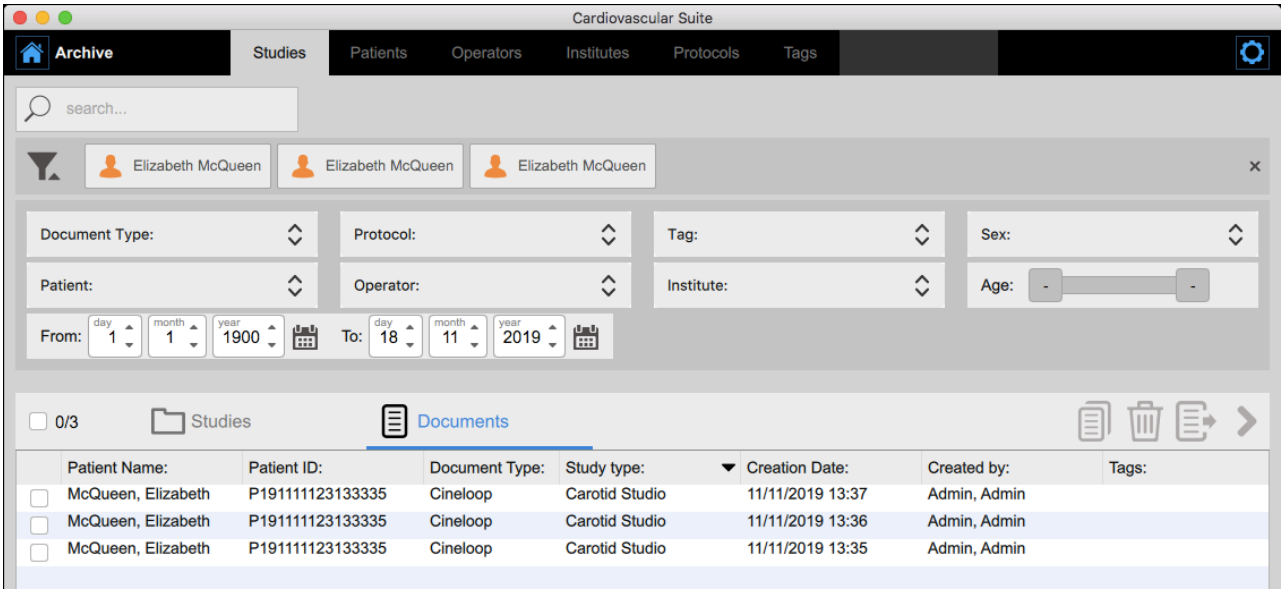


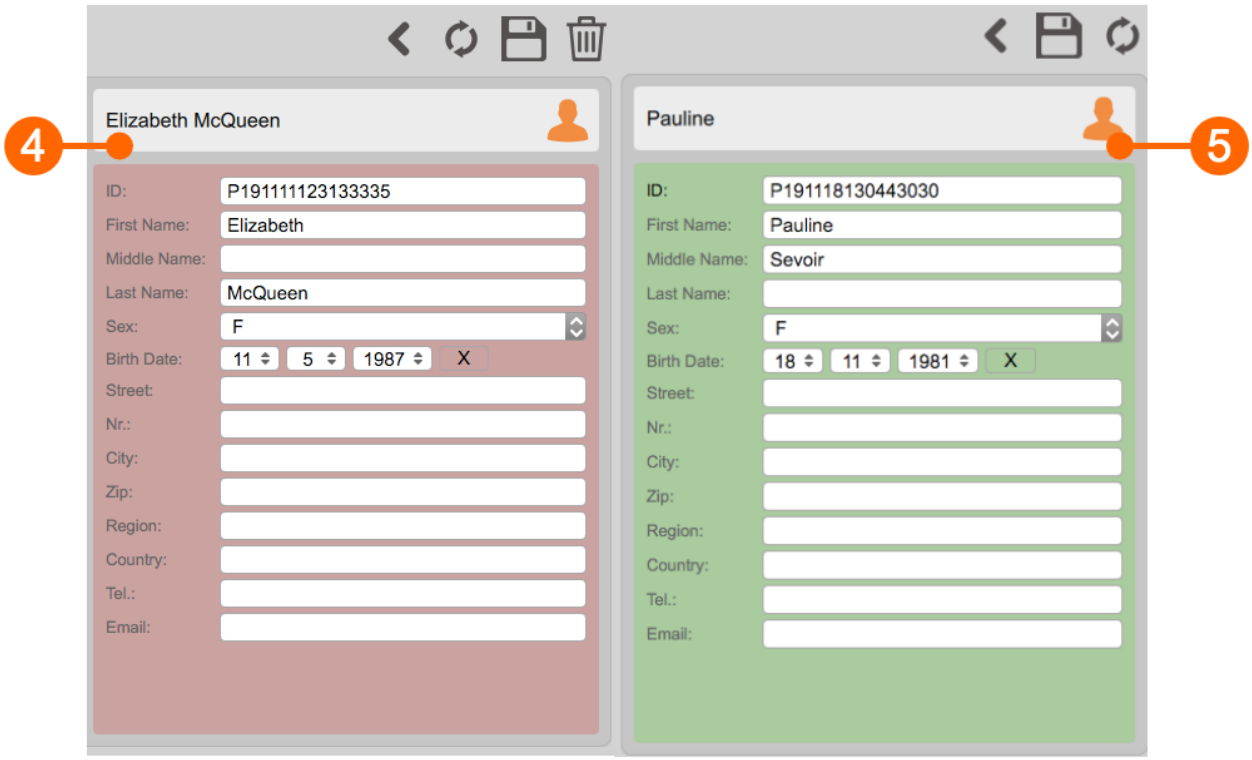
The patient list is given in table **(1)**. Once you select one of patients, detailed information are shown in the frame **(2)**.

In the frame **(3)** you can add and remove filters to the patient list. The following filter can be used:

- Sex
- Age

With a double click on a patient, the list of the study related to that patient is shown in the Studies management window:





New Patient and Edit Patient frames

6.8.1 Add a new patient:

- Click on the Add New Patient  button.
- In the new patient frame **(5)**, enter the patient data. The only mandatory field is the patient ID and the software automatically creates a new one.
- Click on the Save button to save the patient data.

6.8.2 Modify a patient:

- Select the patient to be modified.
- Click on the Edit  button.
- Modify the patient data in the frame **(4)**.
- Click on the Save  button to save the data.
- You can use the Restore  button to restore data.

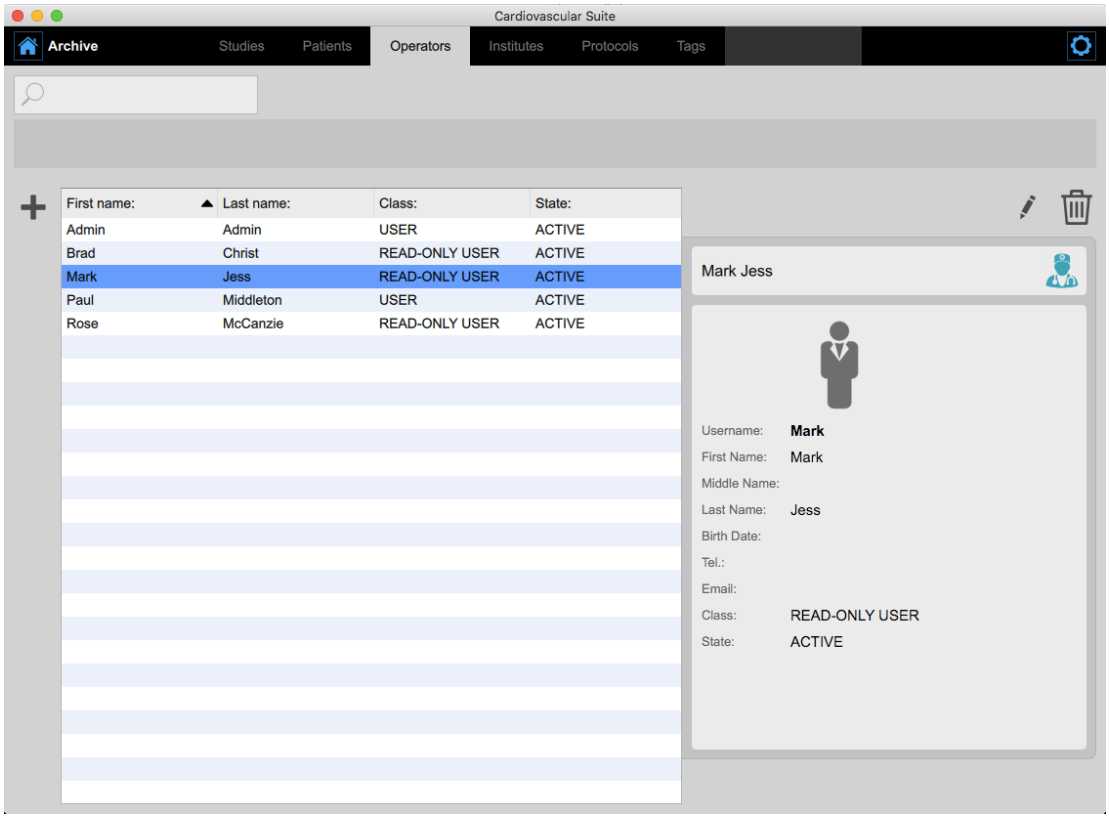
6.8.3 Delete a patient:

- Select the patient to be deleted.
- Click on the Delete  button.
- Confirm deletion with the OK button.

NOTE: you cannot delete a patient with related studies.

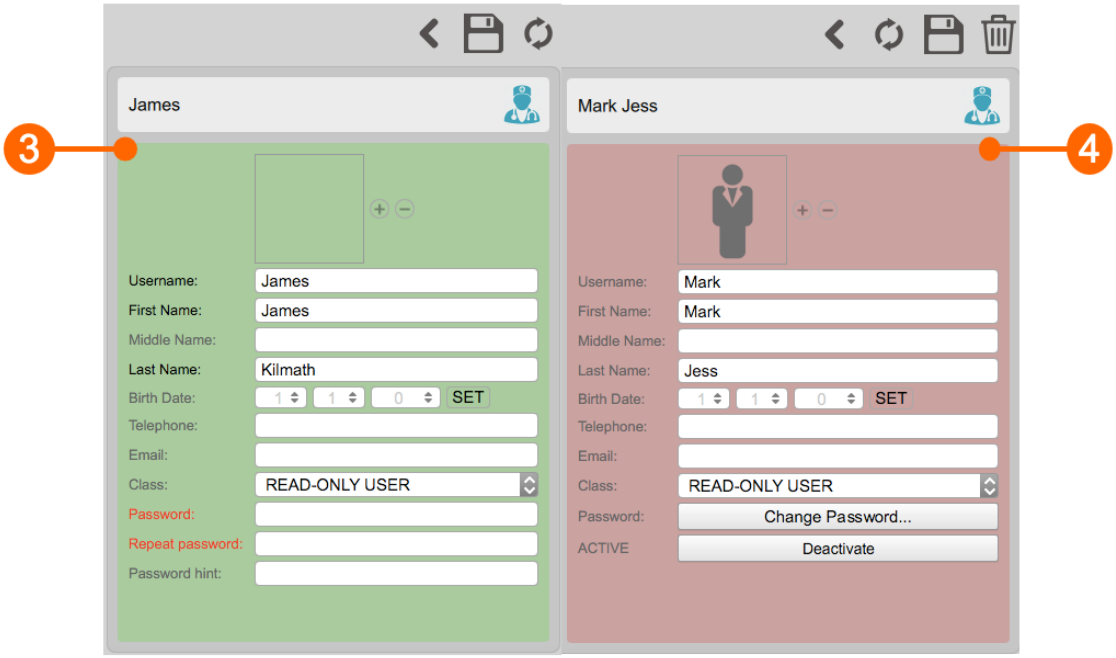
6.9 Operators management

Allows you to manage operators.



The operators list is given in the table above. Once you select one of the operators, detailed information are shown in the frame **(2)**.

You can double click on the operator in table **(1)** to show the studies performed by this operator in the Studies management window.



New Operator and Edit Operator frames

6.9.1 Add a new operator:

- Click on the Add New Operator button.
- In the new operator frame **(3)**, enter the operator data. Labels of mandatory fields (First Name, Last Name) are red.
- Click on the Save button to save the operator data.

6.9.2 Modify an operator:

- Select the operator to be modified.
- Click on the Edit button.
- Modify the operator data in the frame **(4)**.
- Click on the Save button to save the data.
- You can use the Restore button to restore data.

6.9.3 Delete an operator:

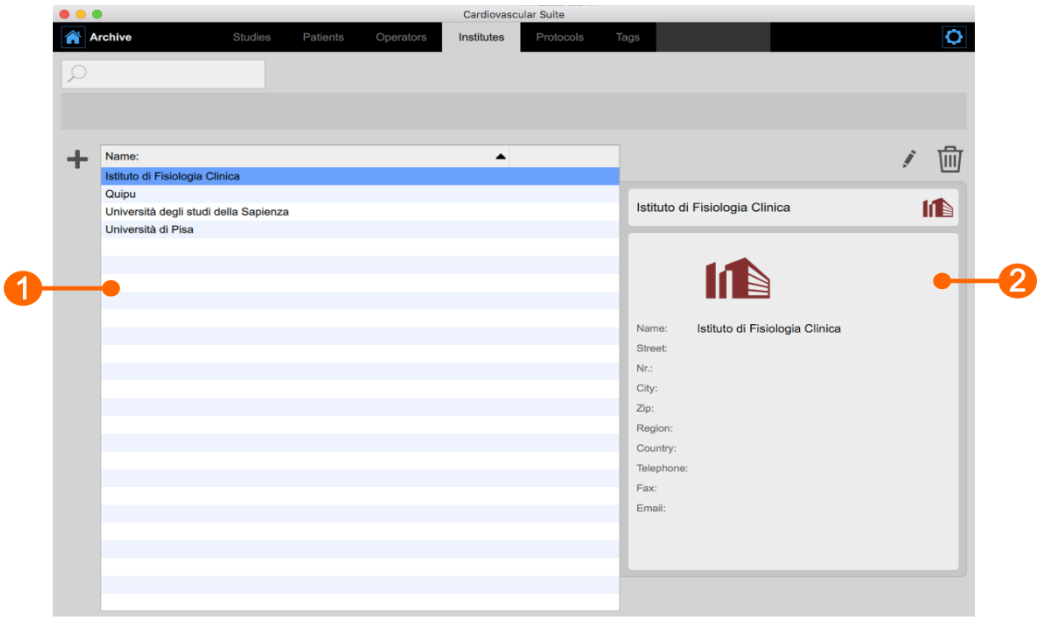
- Select the operator to be deleted.
- Click on the Delete button.

- Confirm deletion with the OK button.

NOTE: you cannot delete an operator with related studies.

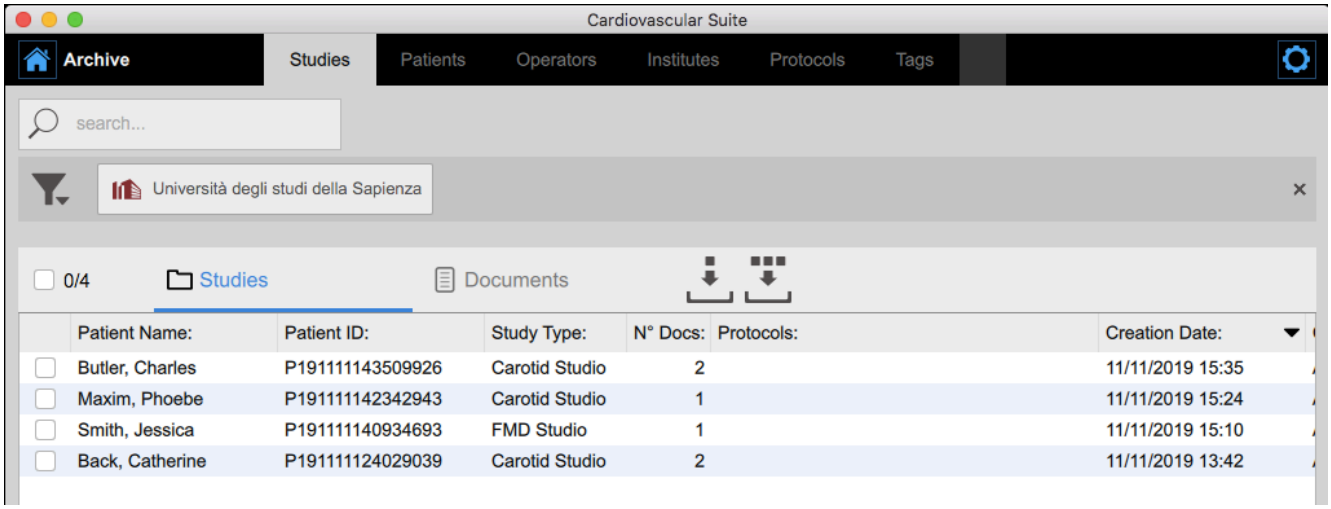
6.10 Institutes management

Allows you to manage institutes.



The institutes list is given in table **(1)**. Once you select one of the institutes, detailed information are shown in the frame **(2)**.

You can double click on the institute in table **(1)** to show the studies performed within this institute in the Studies management window.



New Institute and Edit Institute frames

6.10.1 Add a new institute:

- Click on the Add New Institute  button.

- In the new institute frame **(3)**, enter the institute data. The mandatory field (Name) is in red.
- Click on the Save button to save the institute data.

6.10.2 Modify an institute:

- Select the institute to be modified.
- Click on the Edit  button.
- Modify the institute data in the frame **(4)**.
- Click on the Save  button to save the data.
- You can use the Restore  button to restore data.

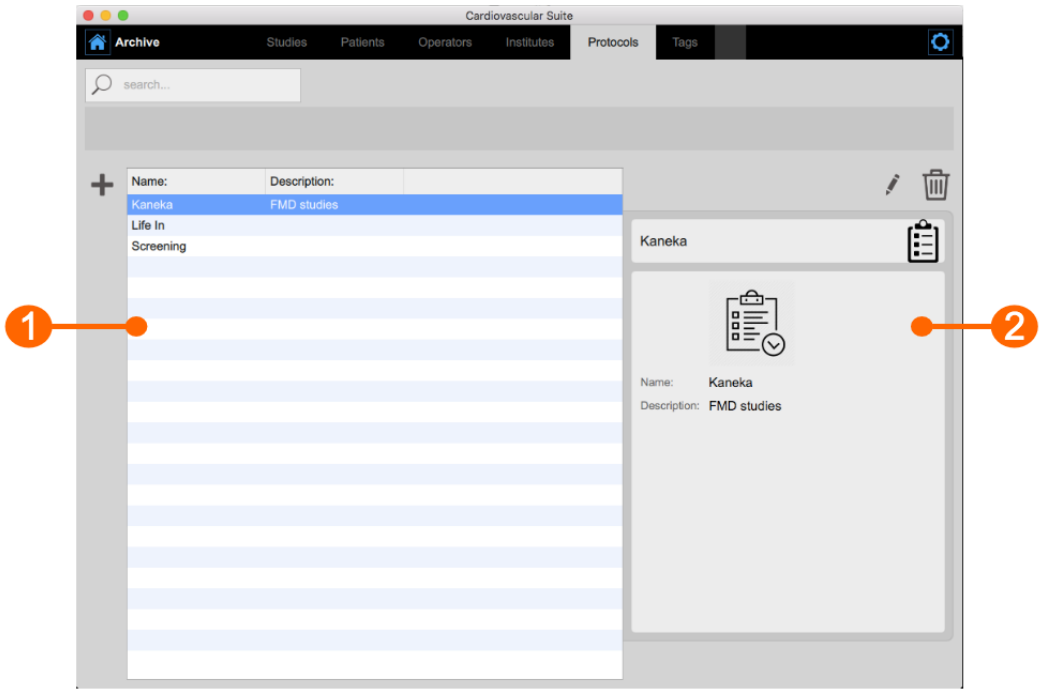
6.10.3 Delete an institute:

- Select the institute to be deleted.
- Click on the Delete  button.
- Confirm deletion with the OK button.

NOTE: you cannot delete an institute with related studies.

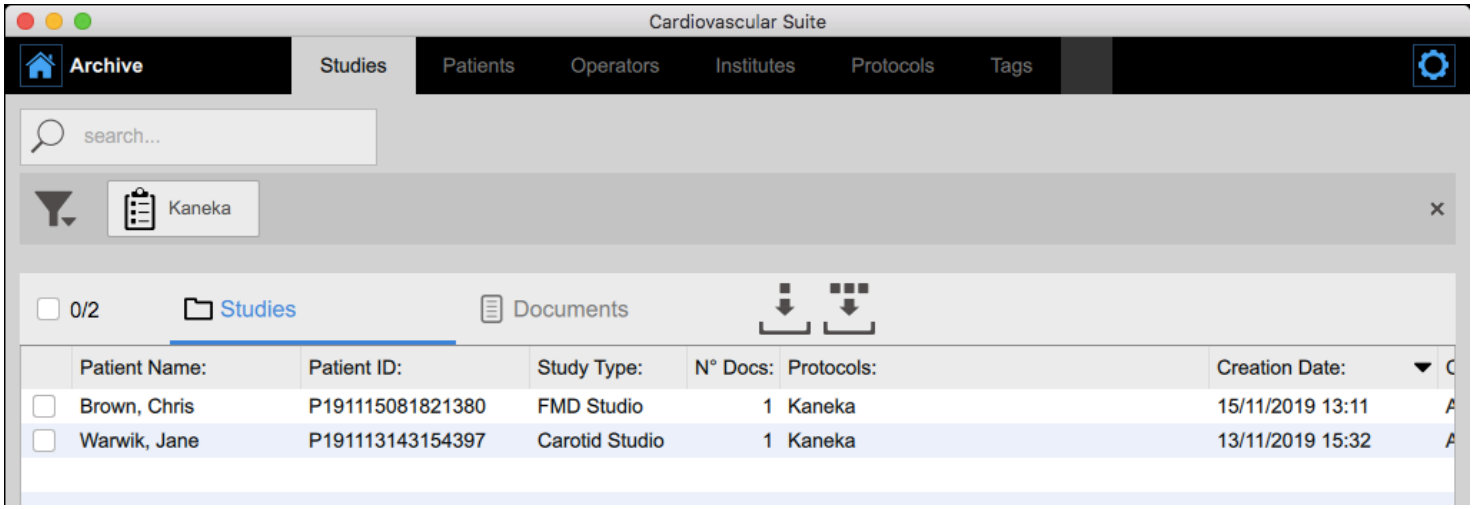
6.11 Protocols management

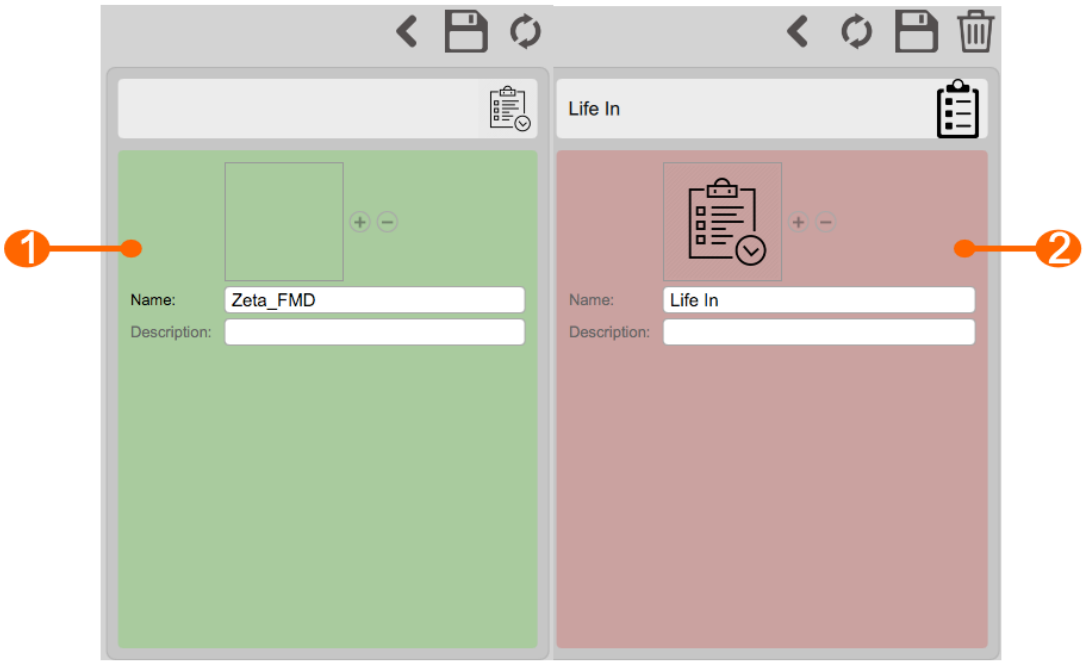
Allows you to manage protocols.



The protocols list is given in table **(1)**. Once you select one of the protocols, detailed information are shown in the frame **(2)**.

You can double click on the protocol in table **(1)** to show the studies performed within this protocol in the Studies management window.





6.11.1 Add a new protocol:

- Click on the Add New Protocol  button.
- In the new protocol frame **(3)**, enter the protocol data. The mandatory field (Name) is in red.
- Click on the Save button to save the protocol data.

6.11.2 Modify an protocol:

- Select the protocol to be modified.
- Click on the Edit  button.
- Modify the protocol data in the frame **(4)**.
- Click on the Save  button to save the data.
- You can use the Restore  button to restore data.

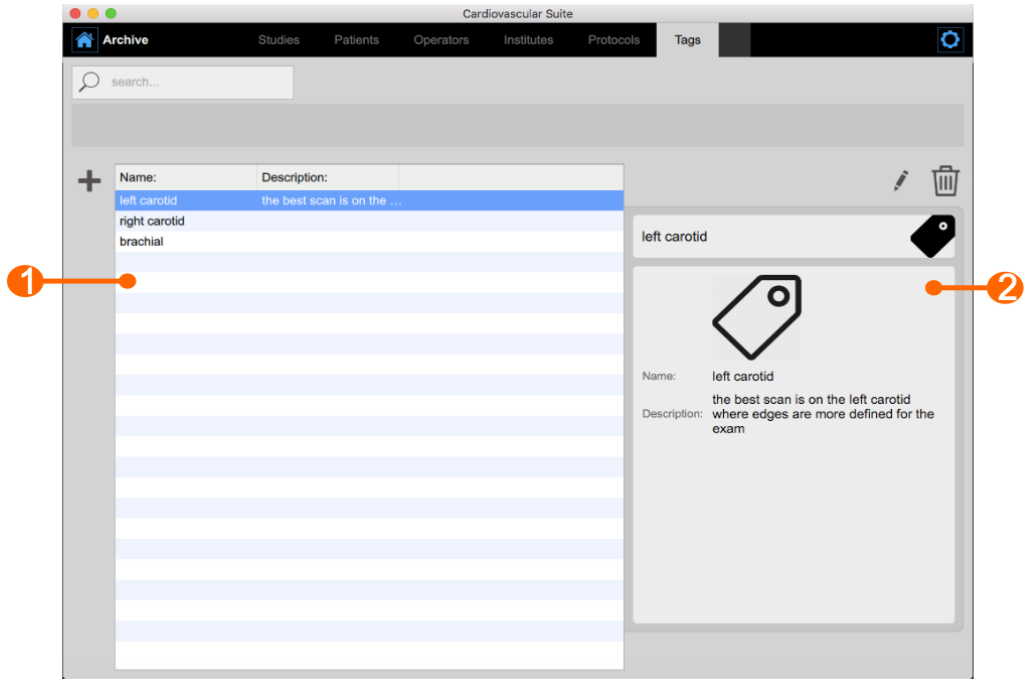
6.11.3 Delete an protocol:

- Select the protocol to be deleted.
- Click on the Delete  button.
- Confirm deletion with the OK button.

NOTE: you cannot delete a protocol with related studies.

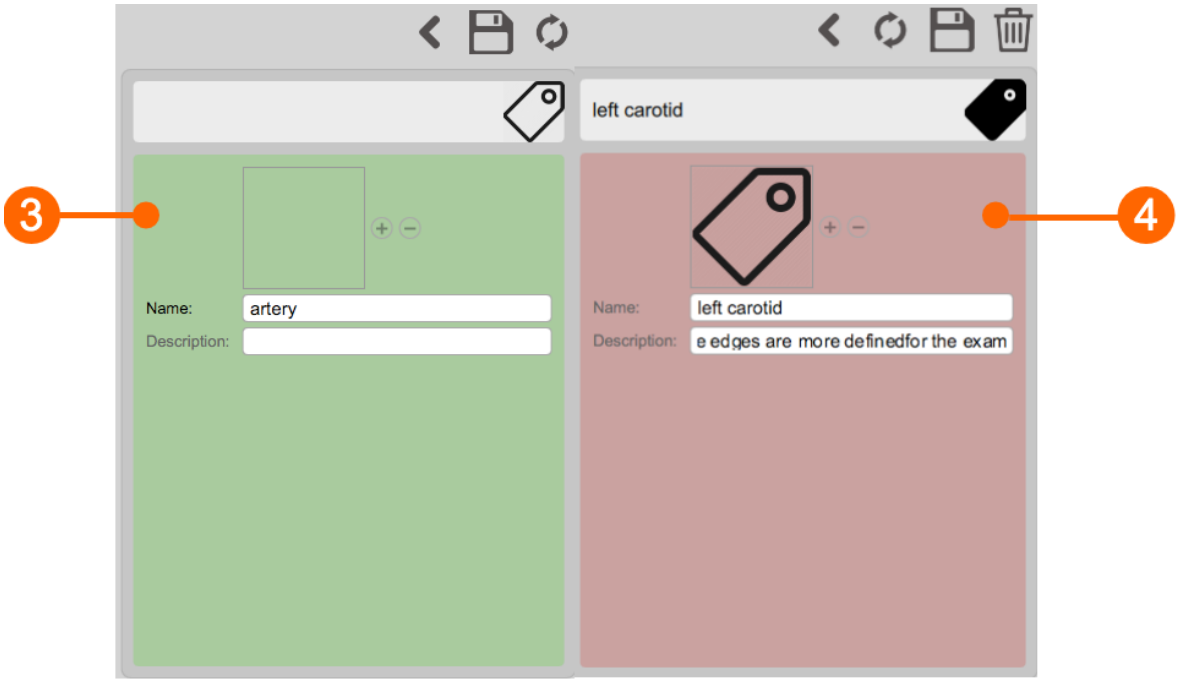
6.12 Tags management

Allows you to manage tags.



The tags list is given in table **(1)**. Once you select one of the tag, detailed information are shown in the frame **(2)**.

You can double click on the tag in table **(1)** to show the studies performed within this tag in the Studies management window.



New Tag and Edit Tag frames

6.12.1 Add a new tag:

- Click on the Add New Tag  button.
- In the new institute frame **(3)**, enter the tag data. The mandatory field (Name) is in red.
- Click on the Save button to save the tag data.

6.12.2 Modify an tag:

- Select the tag to be modified.
- Click on the Edit  button.
- Modify the tag data in the frame **(4)**.
- Click on the Save  button to save the data.
- You can use the Restore  button to restore data.

6.12.3 Delete an tag:

- Select the tag to be deleted.
- Click on the Delete  button.
- Confirm deletion with the OK button.

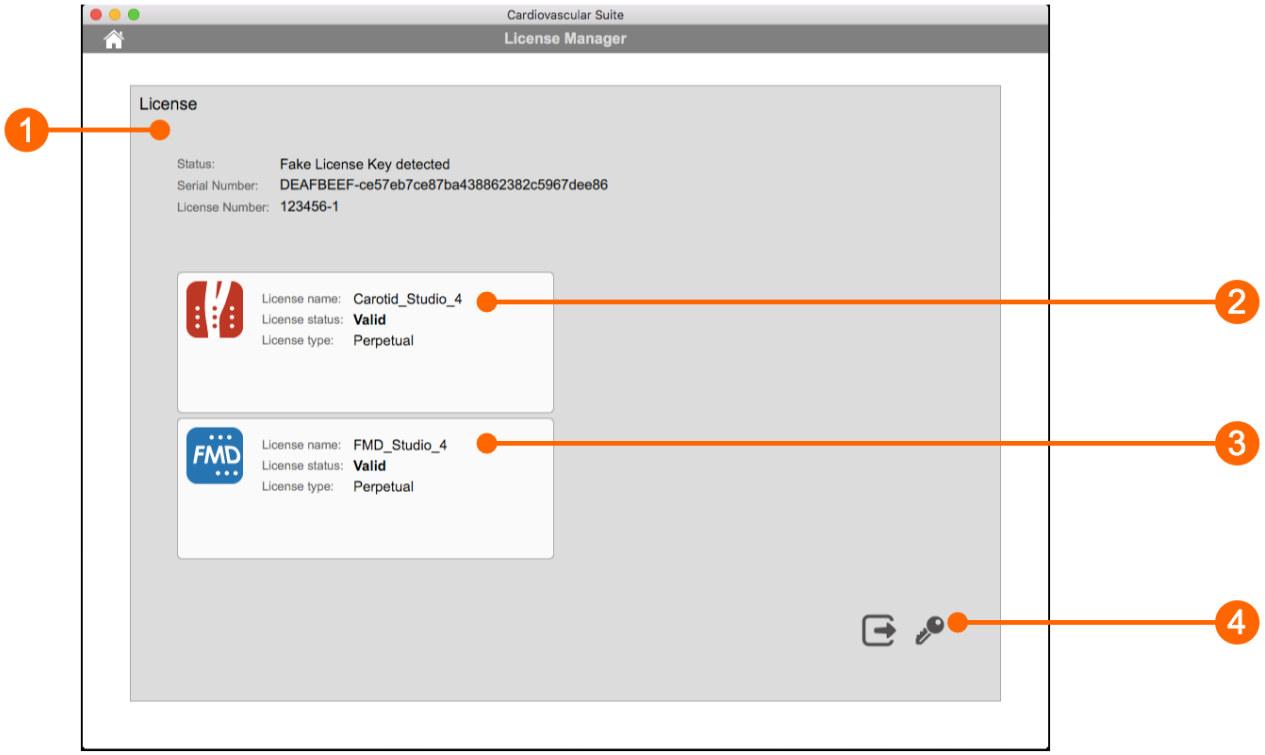
NOTE: you cannot delete a tag with related studies.

7 Settings

In the cardiovascular Suite settings, you can access the Carotid Studio settings and the FMD Studio settings.

8 License manager

The license managers shows the status of your license and can be used to make updates to the license.



The section **(1)** shows some "general" license data:

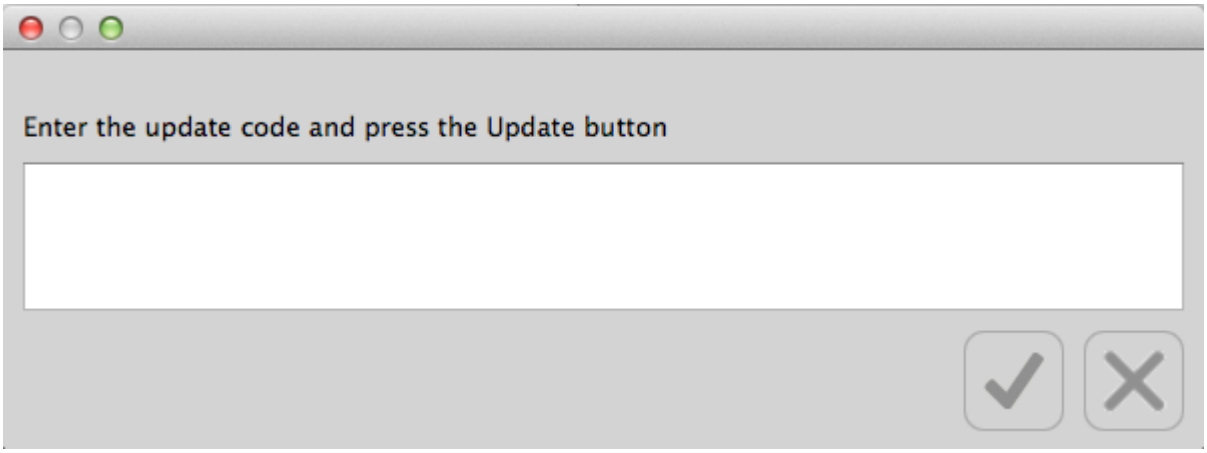
Status: shows whether a USB License Key or a temporary License Key has been detected.

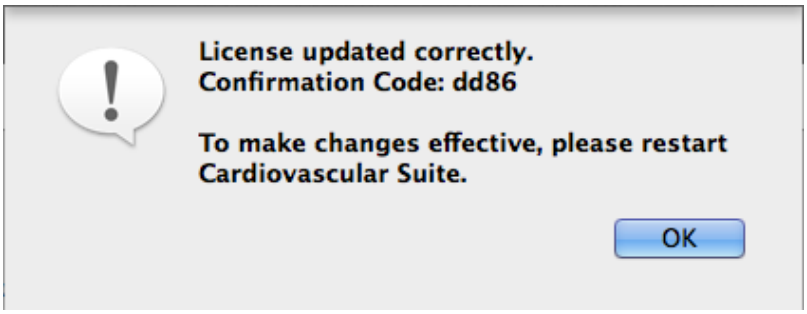
Serial Number: shows the serial number of Cardiovascular Suite.

License Number: shows the number of your License Key.

In the white frames **(2)** and **(3)** the data of the applications licenses are shown. Here you can see if your license is Valid or Not Valid, if it is Perpetual, Time or Evaluation and the expiry date (for time and evaluation only).

The buttons **(4)** can be used to enter the code that updates your license (Update Code) and to save your license data in a file that can be read by the Quipu support team. For more information, please contact support@quipu.eu





8.1 Update a license

- Click on the Update License button.
- Enter the Update Code provided by Quipu.
- Confirm with the Update button.
- A confirmation message will shown the Confirmation Code. You must restart Cardiovascular Suite to make changes effective.

8.2 Export license data

Click on the Export License Data button to export the data of your license in a file that can be read by the Quipu support team. This can be useful when you encounter a problem with your license and you need support.

9 Carotid Studio

Carotid Studio is a software for the measurement of the Intima Media Thickness (IMT) and of stiffness parameters of the carotid artery.

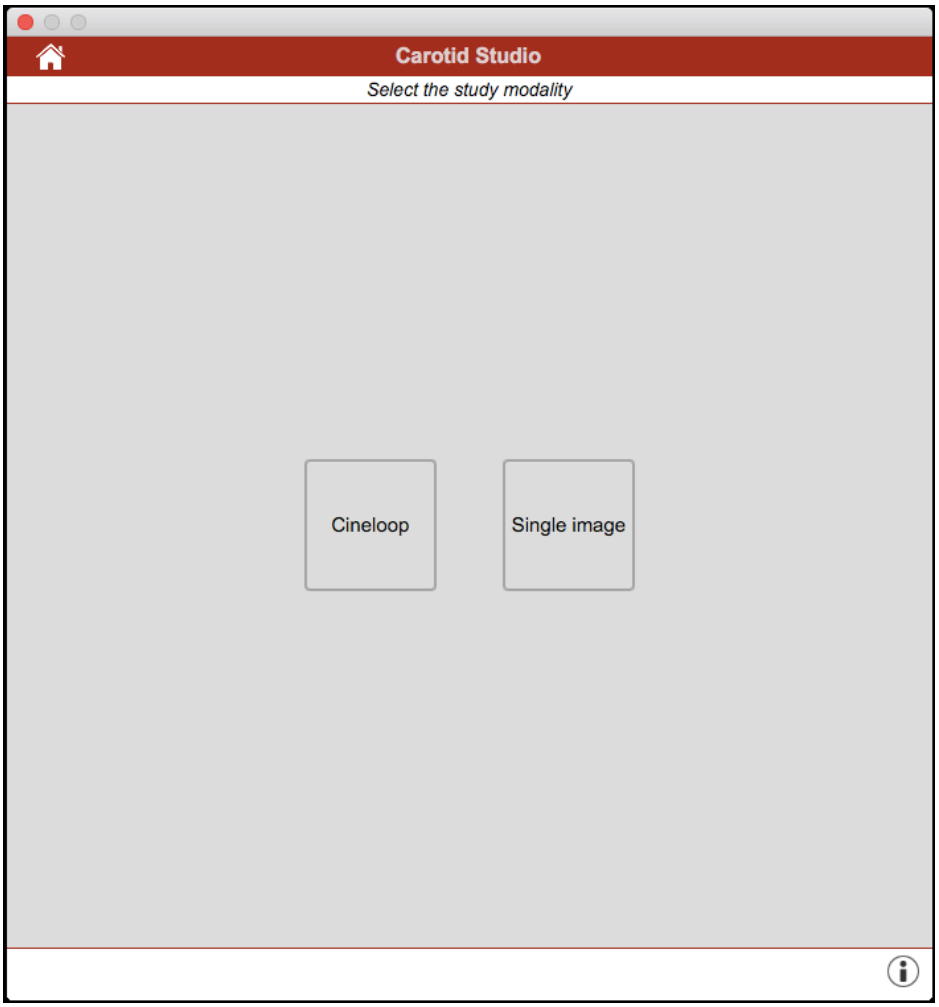
Click on the Carotid Studio  icon to Create a new study with Carotid Studio.

9.1 Create a new study

When you start Carotid Studio, a procedure guides you in the creation of a new study. The steps are:

1. Select the study modality
2. Select the source
3. Select the patient
4. Select the operator
5. Select the institute
6. Review

9.1.1 Select the study modality



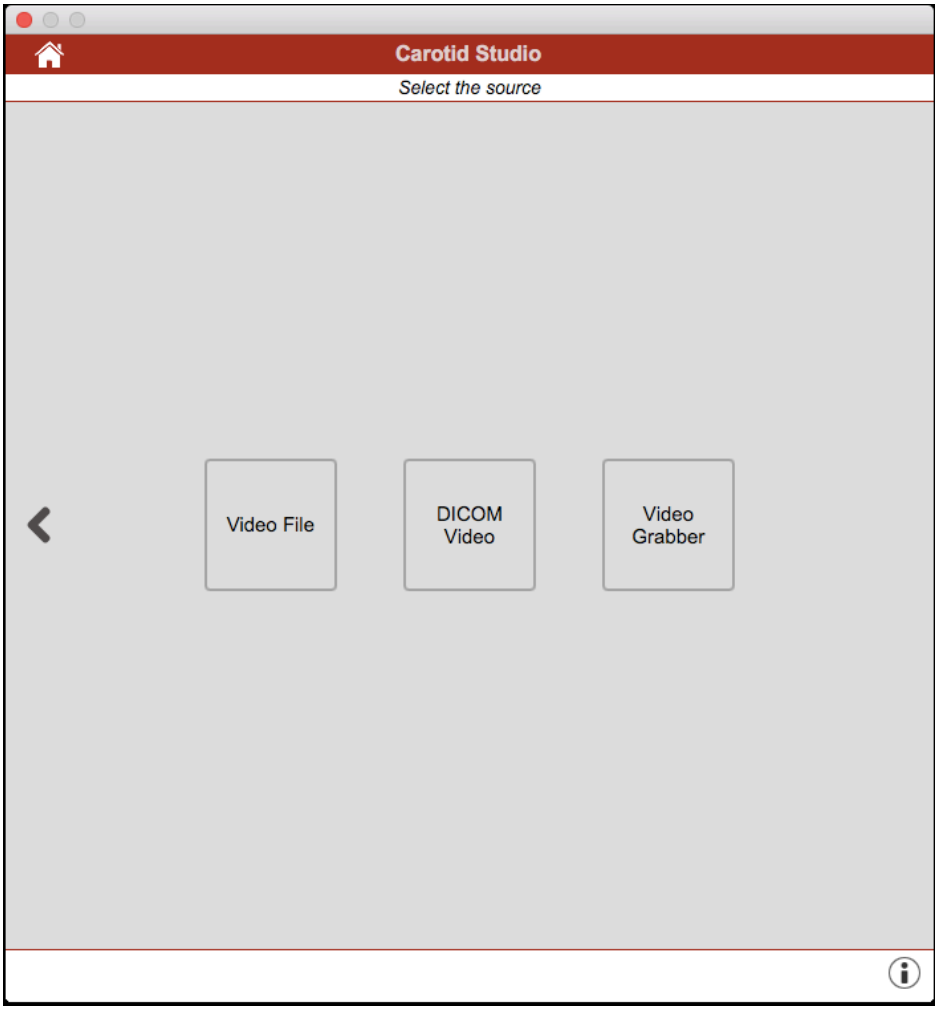
Select the study modality

In this tab, you can select the study modality.

Carotid Studio allows to analyse through "Cineloop" modality (loading a video clip) and "Single Image" modality (processing a single frame coming from a video or loaded as image).

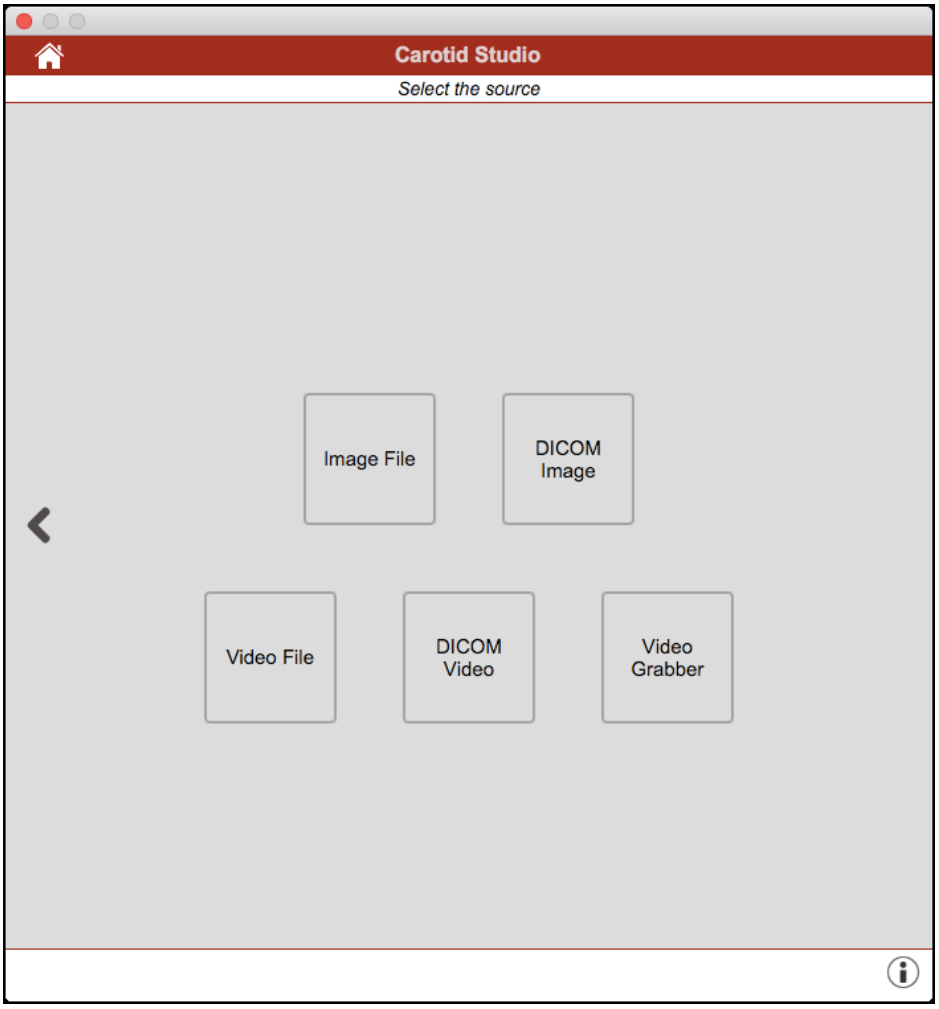
9.1.2 Select the source

Depending on the selected modality, there are several sources you can choose.



Select the source in Cineloop modality

In this tab, you can select the study video source after selecting the modality "Cineloop". With this modality, Carotid Studio processes video sources and can work in two video modalities: "Offline" (processing a Video File or a DICOM File) and "Online" (processing a video coming from a video frame grabber).

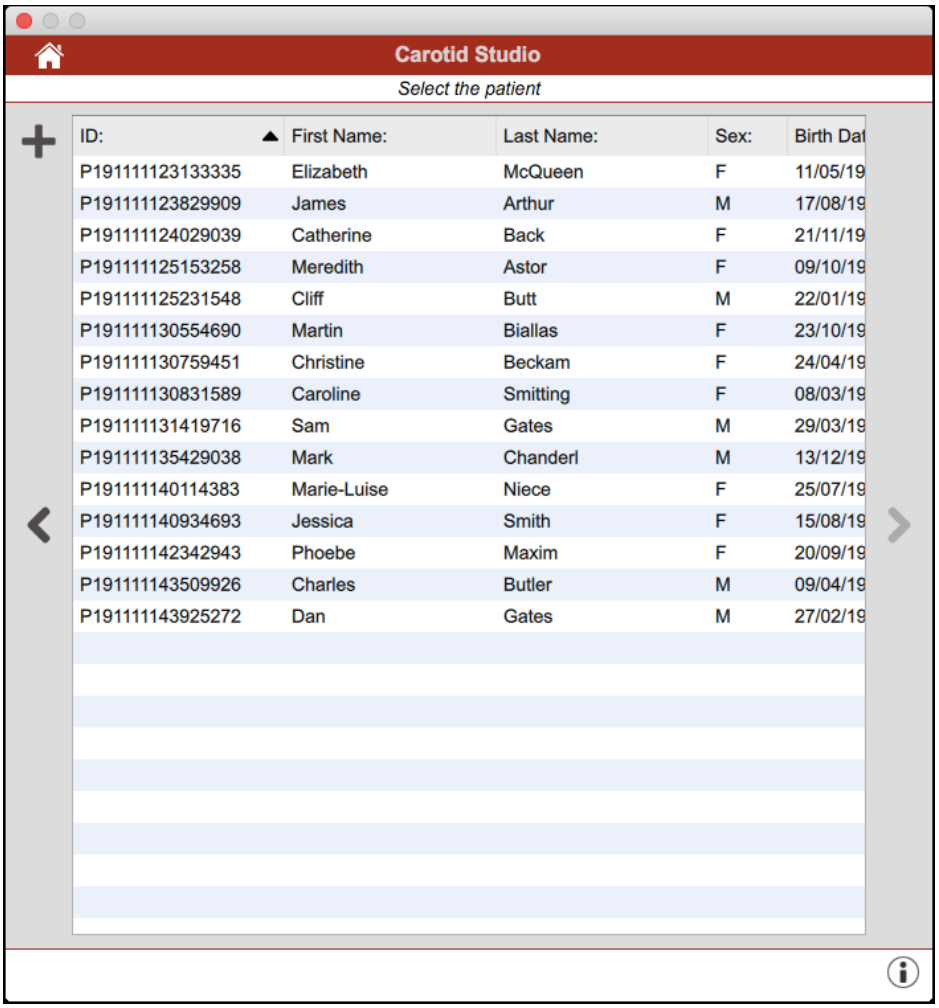


Select the source in Single Image modality

In this tab, you can select the study video source after selecting the modality "Single Image". With this modality, Carotid Studio processes the following video sources:

- Image File
- DICOM Image
- Video file
- DICOM Video
- Video Grabber

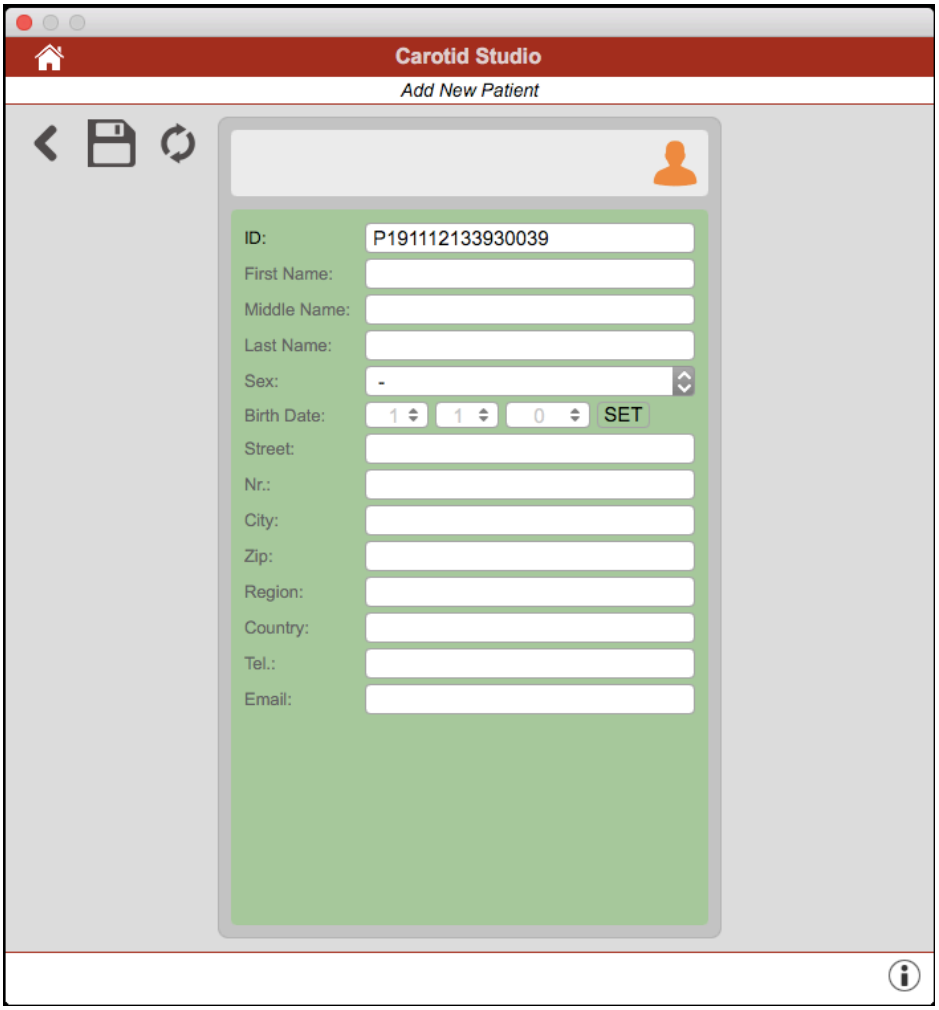
9.1.3 Select the patient



Select the patient

In this tab, you can select the patient among the ones already present in the Archive. Select the patient and click on the Next button (you can simply double-click on the patient to proceed).

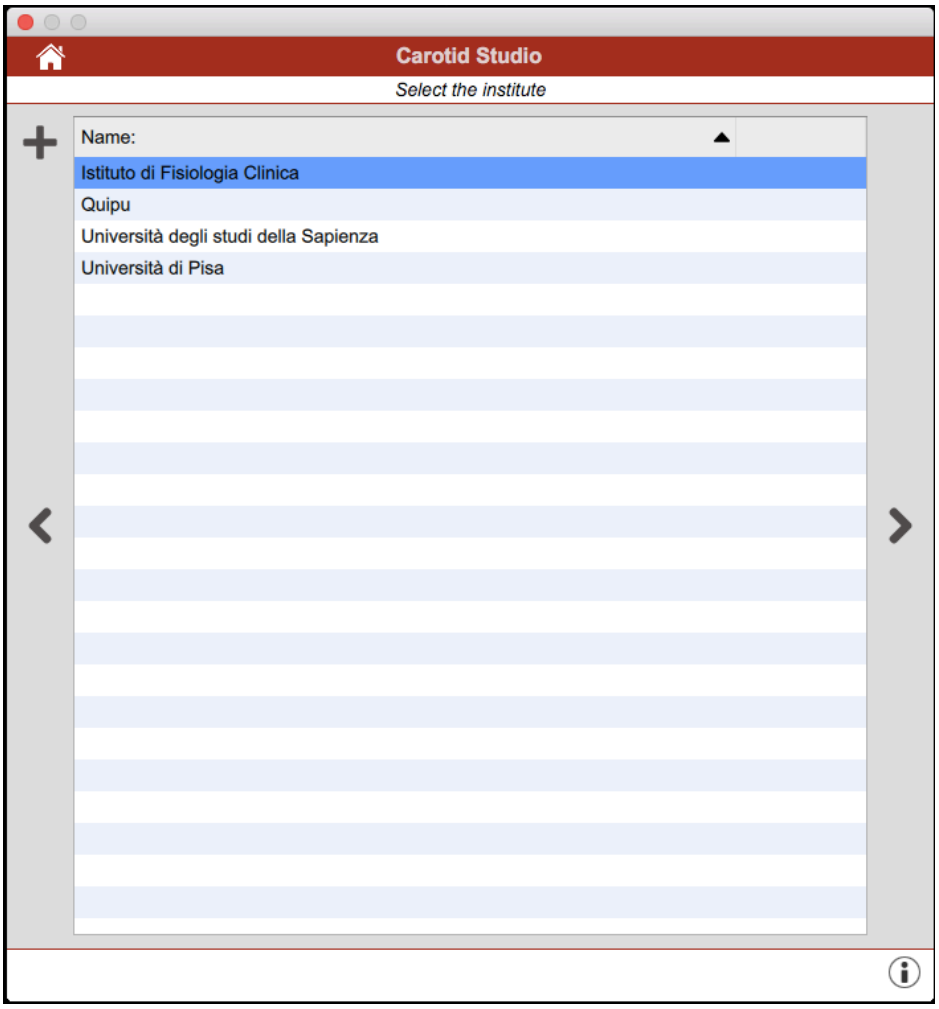
If you want to create a new patient, click of the Add New Patient button. In the Add new patient frame, enter the patient data. The only mandatory field is the patient ID (a random value is automatically proposed). Click on the Save button to save the patient data.



Add a new patient

NOTE: If it is the first time you create a study, after selecting the patient you will also need to select the operator and the institute. If you have already created at least one study, the software remembers the operator and the institute used for the previous study and after selecting the patient shows you automatically the final Review (wher e you can still make changes before starting the new study).

9.1.4 Select the institute



Select the institute

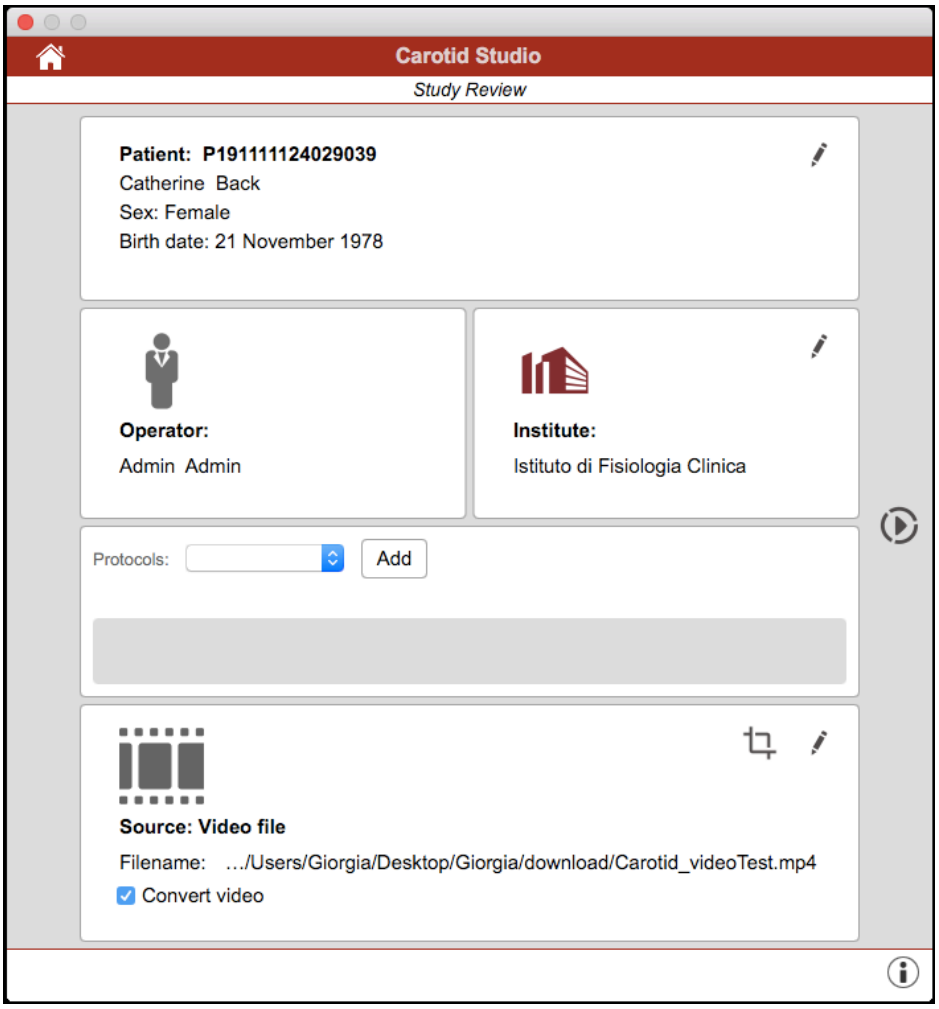
In this tab, you can select the institute among the ones already present in the Archive. Select the institute and click on the Next button (you can simply double-click on the institute to proceed).

If you want to create a new institute, click of the Add New Institute button. In the Add new institute frame, enter the institute data. The mandatory field (Name) is in red until you have filled in the Name blank. Click on the Save button to save the institute data.

Add a new institute

NOTE: If it is the first time you create a study, after selecting the patient you will also need to select the operator and the institute. If you have already created at least one study, the software remembers the operator and the institute used for the previous study and after selecting the patient shows you automatically the final Review (wher e you can still make changes before starting the new study).

9.1.5 Review



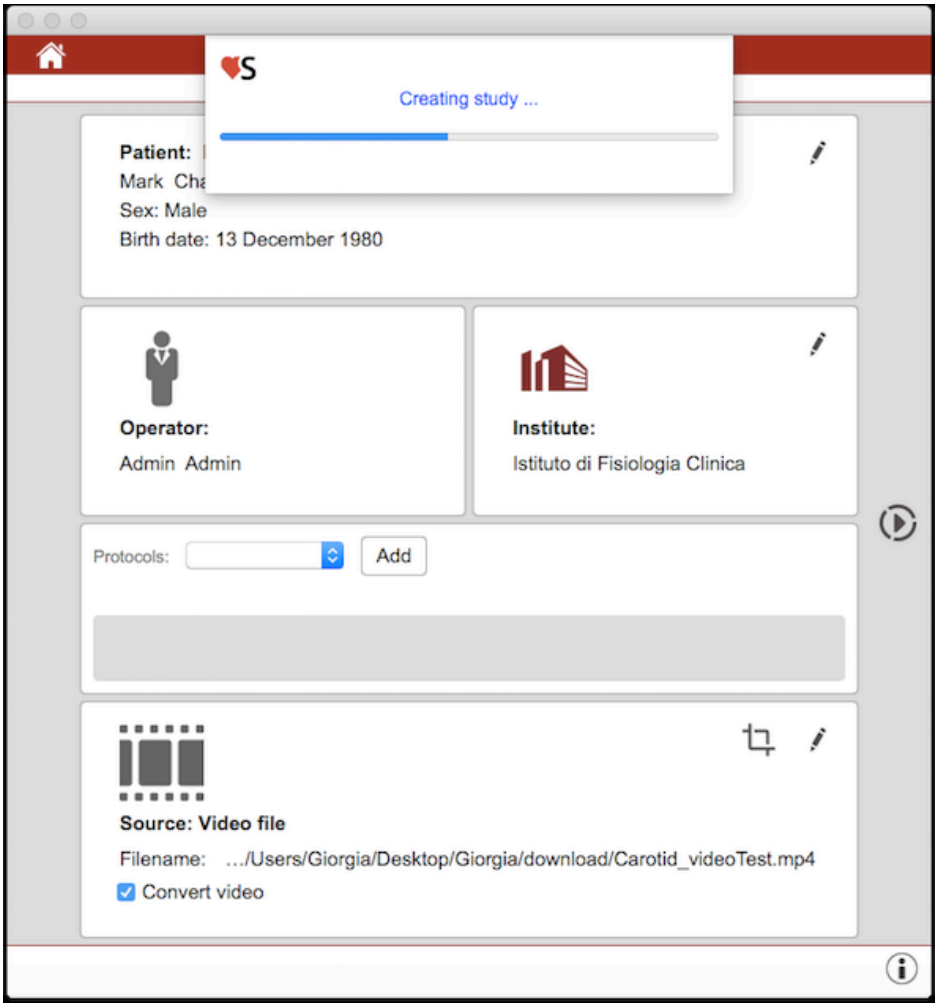
Study Review

In this tab you can review your selection (you can also change Patient and Institute clicking on the Edit button).

It is possible also to change the selected source for this study clicking on the Edit button.

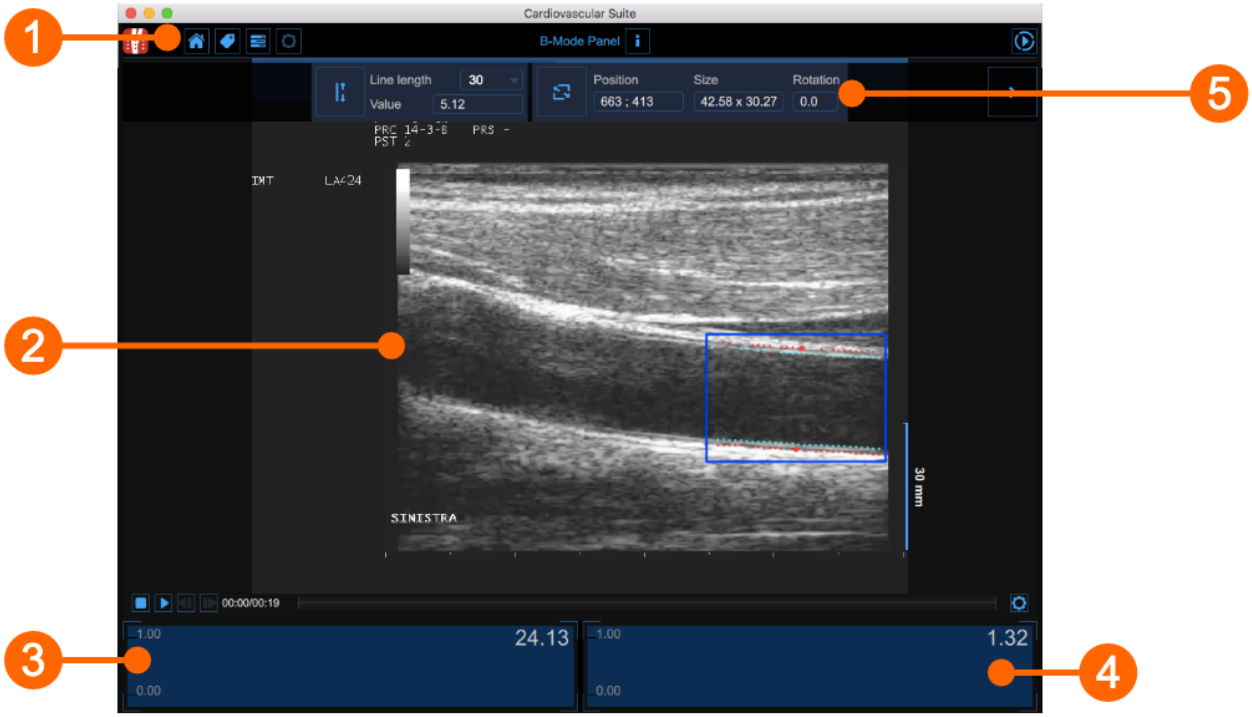
In addition, if you have chosen a video file as source, it is possible to convert the video file to be optimised for the analysis with Carotid Studio. This operation may take few minutes. You can also crop the images by clicking the Crop button in the source panel.

Click on the Start the Study button to proceed. A progress bar, as shown in the following picture, will show you the progression of the study creation.



Progression of the study creation

9.2 Carotid cineloop analysis



The Analysis window contains the following components:

1. Top bar
2. Video window
3. Diameter chart
4. IMT chart
5. Setup panel

9.2.1 Top bar

The top bar contains some essential information for the navigation. Several icons are displayed.

The Carotid Studio button  shows information about the study and about Cardiovascular Suite. Regarding the studio, the number identification (ID) is displayed together with information about patient and the institute. Information about the software such as version and type of license are shown in the upper part of the windows, as figure 1 shows.

Fig.1: Carotid Studio Analysis information windows

The home button  closes the Carotid Studio application and returns to the home screen of Cardiovascular Suite.

The Tags Management button  opens a windows shown in figure 2 that allows to manage tags that can be associated to documents. Tags are labels that confers information to documents. Tags can be managed through a panel in the Archive. In this windows it is possible to add some tags in the tag list.

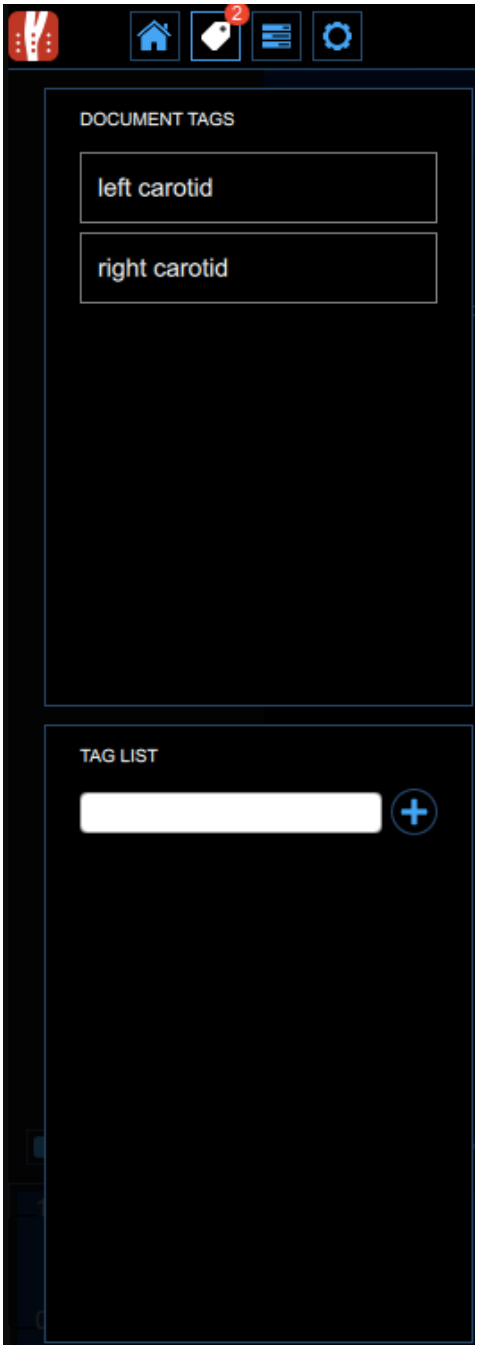


Fig.2: Tags Management windows

The preset management button  opens the preset management windows (Figure 3) that allows to manage settings. In particular, it allows to remember settings of calibration and ROI and to reuse them for following studies.

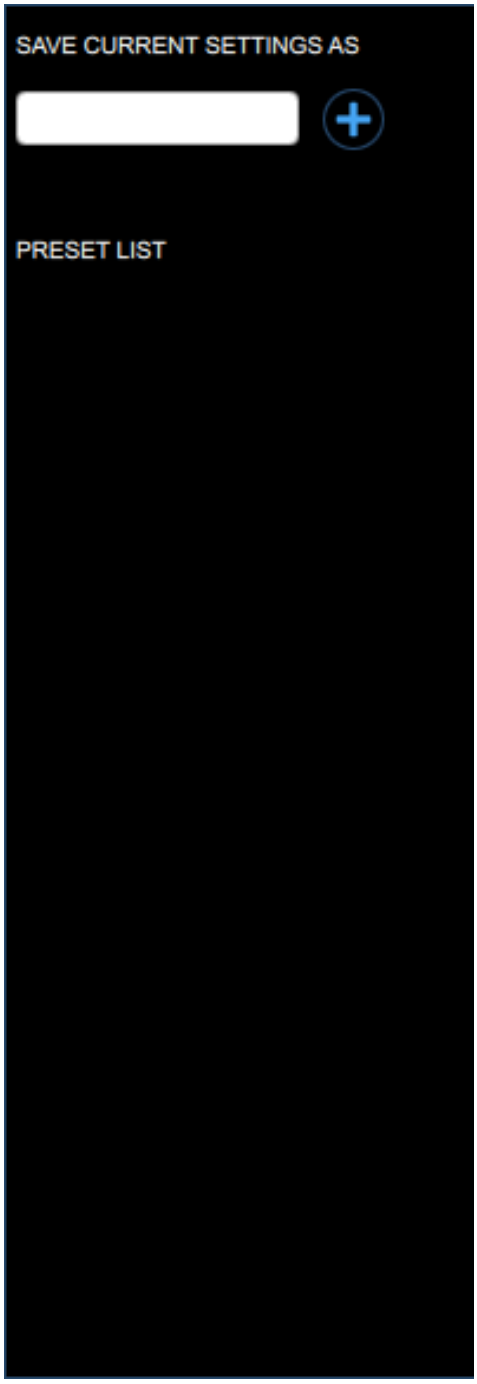
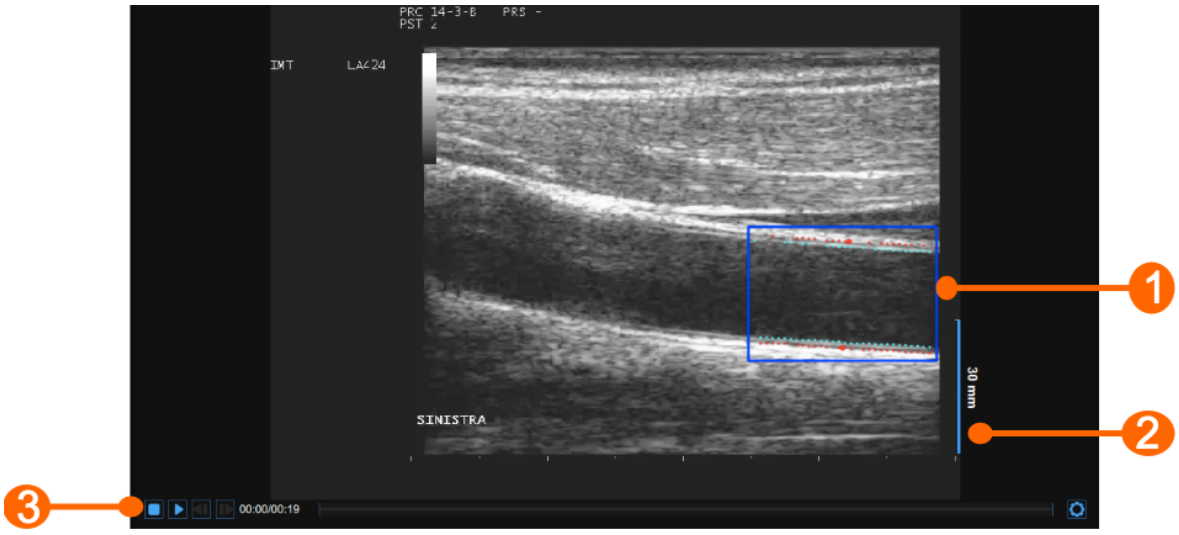


Fig.3: Preset Management windows

The setup button  permits to display the setup panel to see settings.

On the right other icons are shown. In particular, with the button Save  it is possible to save documents of the study. With the Clear Chart button  it is possible to delete data in the Diameter and IMT charts. The button Stop and Review  allows to proceed and see the final report of the study. The button is only activated if you save at least one document from the study.

9.2.2 Video window



The video window shows the video signal from your ultrasound system. A ROI **(1)** can be traced in the video windows, where both the IMT and the diameter are computed.

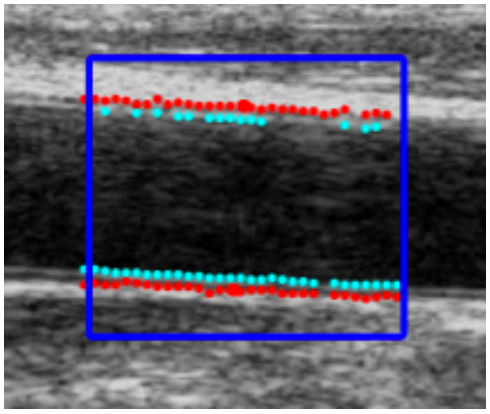
The windows contains also the calibration line for the B-mode image **(2)** once this has been calibrated (see Calibrate the B-Mode image).

The video controls bar **(3)** is located at the bottom of the window. The bar has different controls according to the video modality: Video control bar - online or Video control bar - offline.

9.2.2.1 ROI

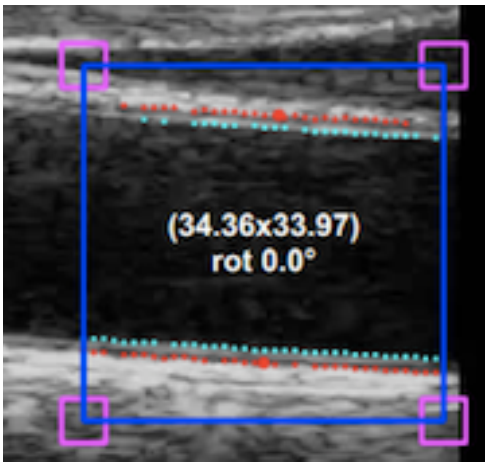
The Region of Interest (ROI) is the portion of the image where both the diameter and the IMT are calculated. The points of the Lumen-Intima interface and the Media-Adventitia interface are displayed within the ROI in cyan and red color respectively.

The ROI can be moved, resized and/or rotated. Each time you change the position, size and/or inclination of the ROI, the analysis is re-initialized.



Draw a new ROI:

- Click on the Set ROI  button in the Setup panel(the button remains active).
- Click inside the video window and drag until the ROI is complete (the size of the ROI is shown in the Setup panel and graphically within the ROI).



- When you release the mouse, the analysis is initialized.

Modify the ROI:

- Click on one of the sides or one of the corners of the ROI.
- Drag to change the size of the the ROI.

NOTE: an alternative, you can modify the size of the ROI by typing the value in the Setup panel.

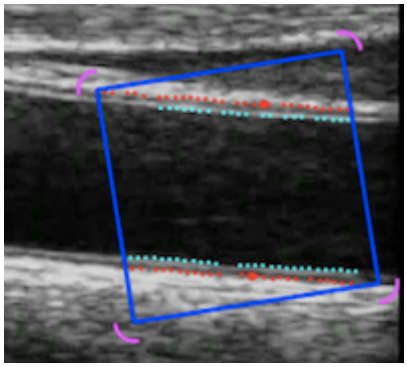
Move the ROI:

- Click and hold inside the ROI.
- Drag the ROI to the location of interest.

NOTE: as an alternative, you can modify the position of the ROI by typing the value in the Setup panel.

Rotate the ROI:

- Click on the upper side of the ROI and use the special cursor that indicates a rotation
- Hold inside the ROI, drag the rectangle by rotating it to the desired angle



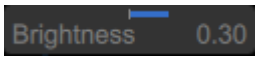
NOTE: as an alternative, you can modify the position of the ROI by typing the value in the Setup panel

9.2.2.2 Video control bar - online

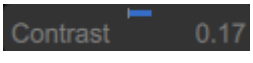
The video control bar is at the bottom of the Video window and contains controls to manage the recording of a movie and the brightness and contrast adjustment.

Adjust the image

Click on the Setting  button on the right of the video control bar. The Brightness and Contrast sliders will appear.

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the recording of a movie

Click on the Record/Pause  buttons to record / pause the recording of the movie.

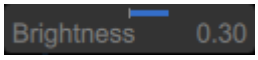
While recording, a blinking red icon  is shown.

9.2.2.3 Video control bar - offline

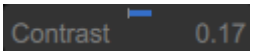
The video control bar is at the bottom of the Video window and contains controls to manage the playback of a movie and the brightness and contrast adjustment.

Adjust the image

Click on the Setting  button on the right of the video control bar. The Brightness and Contrast sliders will appear.

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the playback of a movie

Click on the Play/Pause  buttons to play/pause the movie.

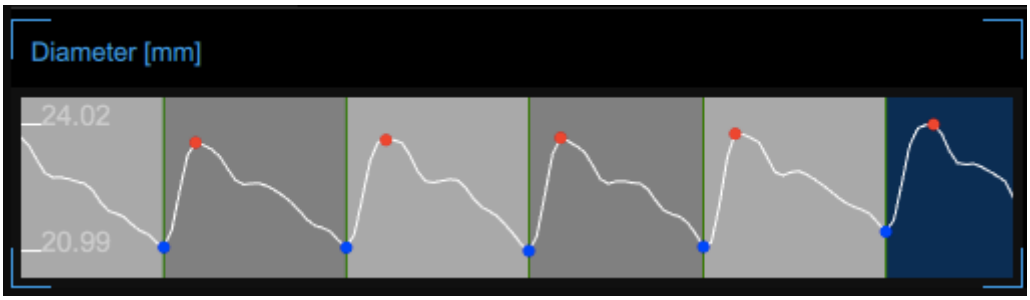
Click on the Step forward  button to advance an image.

Click on the Step backward  button to go back an image.

Click on the Stop  button to stop and return to the beginning of the movie.

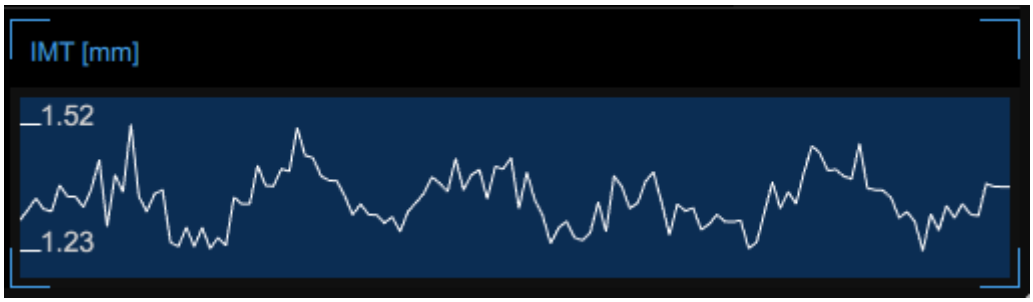
Drag the time slider  to move to any point of the movie.

9.2.3 Diameter chart



The chart shows the trend of the diameter during the examination. During the analysis, Carotid Studio recognizes the heart cycles that are shown in dark and light gray alternatively. The red points in the chart are the systolic diameters and the blue points are the diastolic diameters.

9.2.4 IMT chart



The chart shows the trend of the IMT during the examination.

9.2.5 Setup panel

The Setup Panel must be used to Set the Recording Data Length, to Calibrate the B-Mode image, to set the ROI ,to set the *sensitivity* of the algorithm and to set systolic and diastolic pressure.

|

9.2.5.1 Calibration

The Set Calibration  button is used to Calibrate the B-Mode image.

The drop-down menu **(1)** shows the length of the line used for the calibration.

The numeric display **(2)** shows the calibration value.

NOTE: if you click in the value field, you are allowed to manually enter the calibration value in the editable field (if you already know the value). The click the Save button to enter the values.

9.2.5.2 ROI

The Set ROI  button is used to set the ROI.

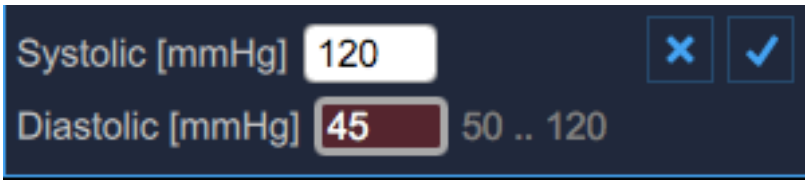
The numeric display **(3)** shows the top-left position, in pixels, of the ROI (top-left corner).

The numeric display **(4)** shows the size (width x height), in pixels, of the ROI.

NOTE: if you click in the value field, you are allowed to manually enter the ROI position and size values in the editable fields (if you already know the values). The click the Save button to enter the values.

9.2.5.3 Blood Pressure

The numeric displays **(7)** show the values of systolic and diastolic blood pressure. If you click in the value field, you are allowed to manually enter the values of systolic and diastolic blood pressure. The click the Save button to enter the values.



If present, these values will be used to compute the stiffness parameters. For this purpose, the local carotid pressure should be used: in this case the carotid waveform is obtained by tonometer or similar device and it is generally calibrated by brachial measurement (sphygmomanometer) assuming that mean and diastolic values are constant along the arterial tree.

Notes: Since the tonometry is not always available, it is possible to use the brachial blood pressure (also the reference values for carotid stiffness works* included this approach). In this case, you should pay attention to the amplification phenomenon from central to peripheral vessel, in particular in young subjects.

***"Reference values for local arterial stiffness. Part A: Carotid artery",** Engelen L, Bossuyt J, Ferreira I et al., *J Hypertens.* 2015 Oct;33(10):1981-96

"Expert consensus document on arterial stiffness: methodological issues and clinical applications.", S. Laurent, J. Cockcroft, L. Van Bortel et al., *Eur Heart J.* 2006 Nov;27(21):2588-605

9.2.5.4 Sensitivity

The slider **(5)** sets the sensitivity of the algorithm. Adjust this value in order to have a better detection of the intima-media border and the media-adventitia border.

9.2.5.5 Recording Data Length

The drop-down menu **(6)** shows the time length of the diameter and IMT data recording.

9.2.5.6 Rotation

The numeric displays **(8)** show the degree of rotation of the ROI.

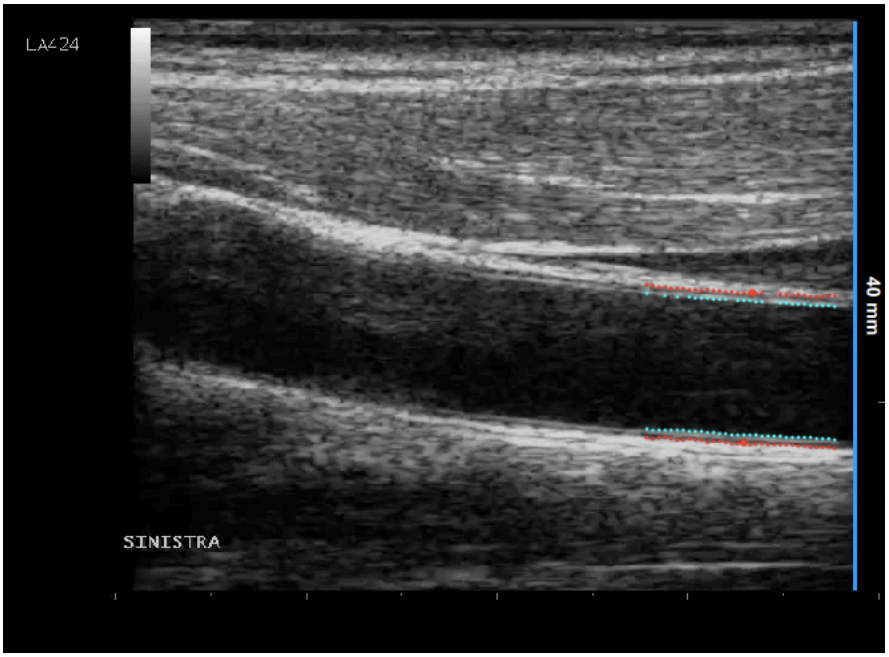
NOTE: if you click in the value field, you are allowed to manually enter the degree value of rotation.

Once you have calibrated the B-Mode image and set the ROI, click on the Next  button to proceed.

9.2.6 Calibrate the B-Mode image

The calibration of the images must be done before starting a new examination because it is necessary to provide information about the size of the image generated by ultrasound system. The calibration factor changes depending on the settings of your ultrasound machine. You should check the calibration at each new examination.

CAUTION: the lack of calibration can generate a software malfunction.



9.2.6.1 Calibrate the B-Mode image

- Locate, in ultrasound image, a range of known distance (40 mm. in the example of figure).
- In the Setup panel, select from the drop-down menu, the distance specified above.
- In the Setup panel, click on the Set B-Mode Calibration  button (button remains active).
- Draw a line on the image corresponding to the known distance: click on one end and drag the mouse to the other extreme (press the Shift key or Ctrl+Shift keys on your keyboard if you want the line to be not vertical or horizontal).

NOTE: you can directly type the calibration value in the "calib" field of the Setup panel (if you already known the value).

9.3 Carotid single image analysis

The Single Image Analysis window contains the following components:

1. Top bar
2. Video window
3. Data panel
4. Setup panel

With this modality, Carotid Studio processes image files and video sources. If you load a video or if you have chosen video grabber, you can select a single image to be analysed.

9.3.1 Top bar

The top bar contains some essential information for the navigation. Several icons are displayed.

The Carotid Studio button  shows information about the study and about Cardiovascular Suite. Regarding the studio, the number identification (ID) is displayed together with information about patient and the institute. Information about the software such as version and type of license are shown in the upper part of the windows, as figure 1 shows.

Fig.1: Carotid Studio Single Image Analysis information windows

The home button  closes the Carotid Studio application and returns to the home screen of Cardiovascular Suite.

The Tags Management button  opens a windows shown in figure 2 that allows to manage tags that can be associated to documents. Tags are labels that confers information to documents. Tags can be managed through a panel in the Archive. In this windows it is possible to add some tags in the tag list.

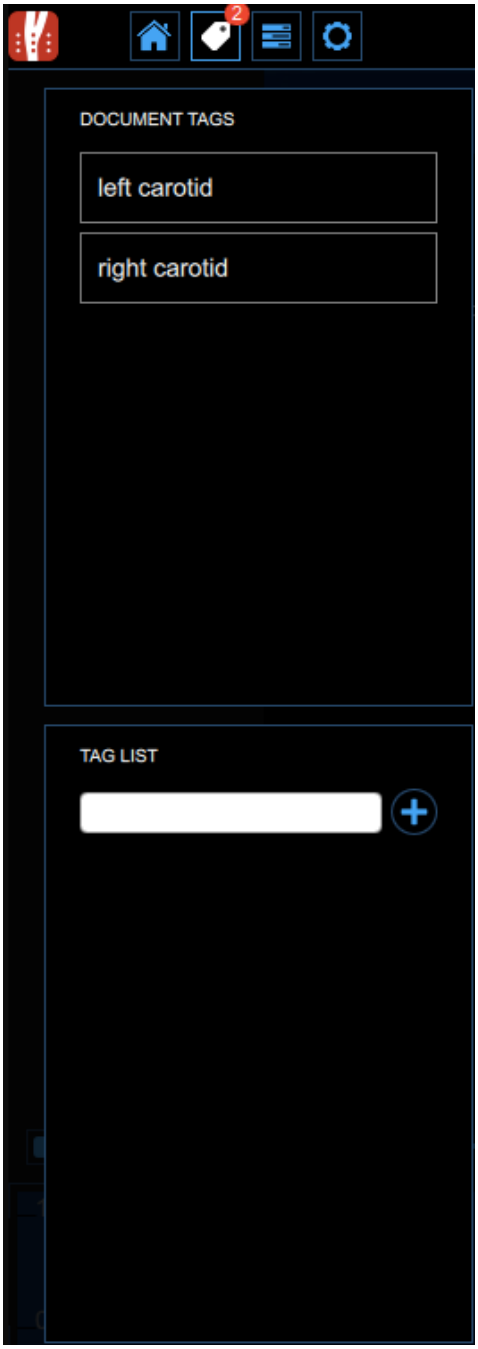


Fig.2: Tags Management window

The preset management button  opens the preset management windows (Figure 3) that allows to manage settings. In particular, it allows to remember settings of calibration and ROI and to reuse them for following studies.

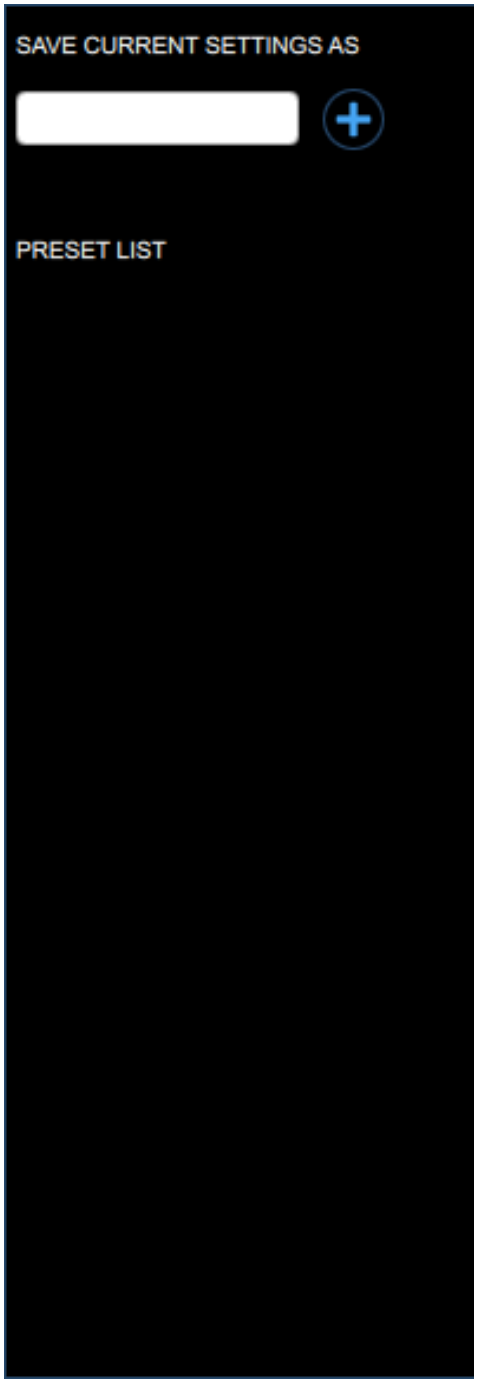


Fig.3: Preset Management window

The setup button  permits to display the setup panel to see settings.

On the right other icons are shown. In particular, with the button Save  it is possible to save documents of the study. With the Clear Chart button  it is possible to delete data in the Diameter and IMT charts. The button Stop and Review  allows to proceed and see the final report of the study. The button is only activated if you save at least one document from the study.

9.3.2 Video window

The video window shows the video signal from your ultrasound system. A ROI **(1)** can be traced in the video windows, where both the IMT and the diameter are computed.

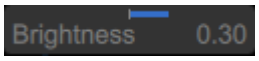
The windows contains also the calibration line for the B-mode image **(2)** once this has been calibrated (see Calibrate the B-Mode image).

The video controls bar **(3)** is located at the bottom of the window. The bar has different controls according to the video modality: Video control bar - online or Video control bar - offline.

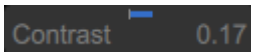
9.3.2.1 Video control bar- online

The video control bar is at the bottom of the Video window and contains controls to manage the recording of a movie and the brightness and contrast adjustment.

Adjust the image

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the recording of a movie

Click on the Record/Pause  buttons to record / pause the recording of the movie.

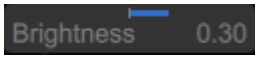
While recording, a blinking red icon  is shown.

9.3.2.2 Video bar - offline

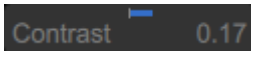
The video control bar is at the bottom of the Video window and contains controls to manage the playback of a movie and the brightness and contrast adjustment.

Adjust the image

Click on the Setting  button on the right of the video control bar. The Brightness and Contrast sliders will appear.

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the playback of a movie

Click on the Play/Pause  buttons to play/pause the movie.

Click on the Step forward  button to advance an image.

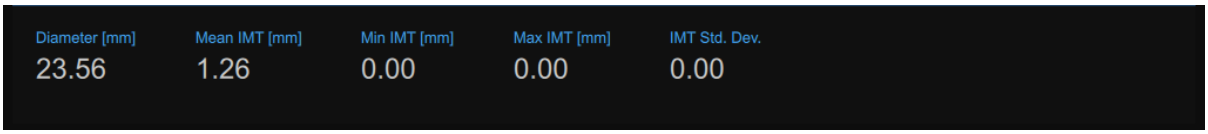
Click on the Step backward  button to go back an image.

Click on the Stop  button to stop and return to the beginning of the movie.

Drag the time slider

to move to any point of the movie.

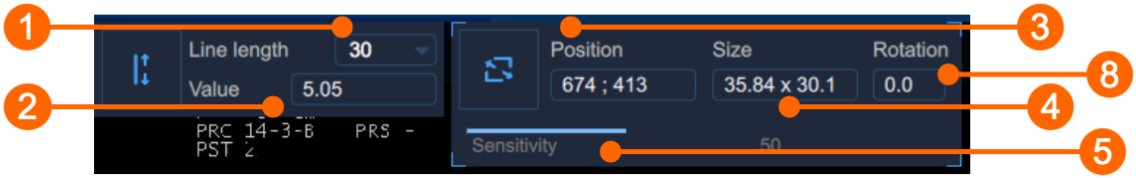
9.3.3 Data panel



This panel shows a set of parameters that are computed by the software during the analysis. In particular:

- Diameter: value of the diameter of the vessel in the image
- Mean IMT: Intima Media Thickness. It is computed as an average value of the IMT data present in the ROI
- Min IMT: minimum value of Intima Media Thickness
- Max IMT: maximum value of Intima Media Thickness
- IMT Std Dev: Standard Deviation of Intima Media Thickness values

9.3.4 Setup panel



The Setup Panel must be used to Set the Recording Data Length, to Calibrate the B-Mode image, to set the ROI ,to set the *sensitivity* of the algorithm and to set systolic and diastolic pressure.

9.3.4.1 Calibration

The Set Calibration  button is used to Calibrate the B-Mode image.

The drop-down menu **(1)** shows the length of the line used for the calibration.

The numeric display **(2)** shows the calibration value.

NOTE: if you click in the value field, you are allowed to manually enter the calibration value in the editable field (if you already know the value). The click the Save button to enter the values.

9.3.4.2 ROI

The Set ROI  button is used to set the ROI.

The numeric display **(3)** shows the top-left position, in pixels, of the ROI (top-left corner).

The numeric display **(4)** shows the size (width x height), in pixels, of the ROI.

NOTE: if you click in the value field, you are allowed to manually enter the ROI position and size values in the editable fields (if you already know the values). The click the Save button to enter the values.

9.3.4.3 Sensitivity

The slider **(5)** sets the sensitivity of the algorithm. Adjust this value in order to have a better detection of the intima-media border and the media-adventitia border.

9.3.4.4 Rotation

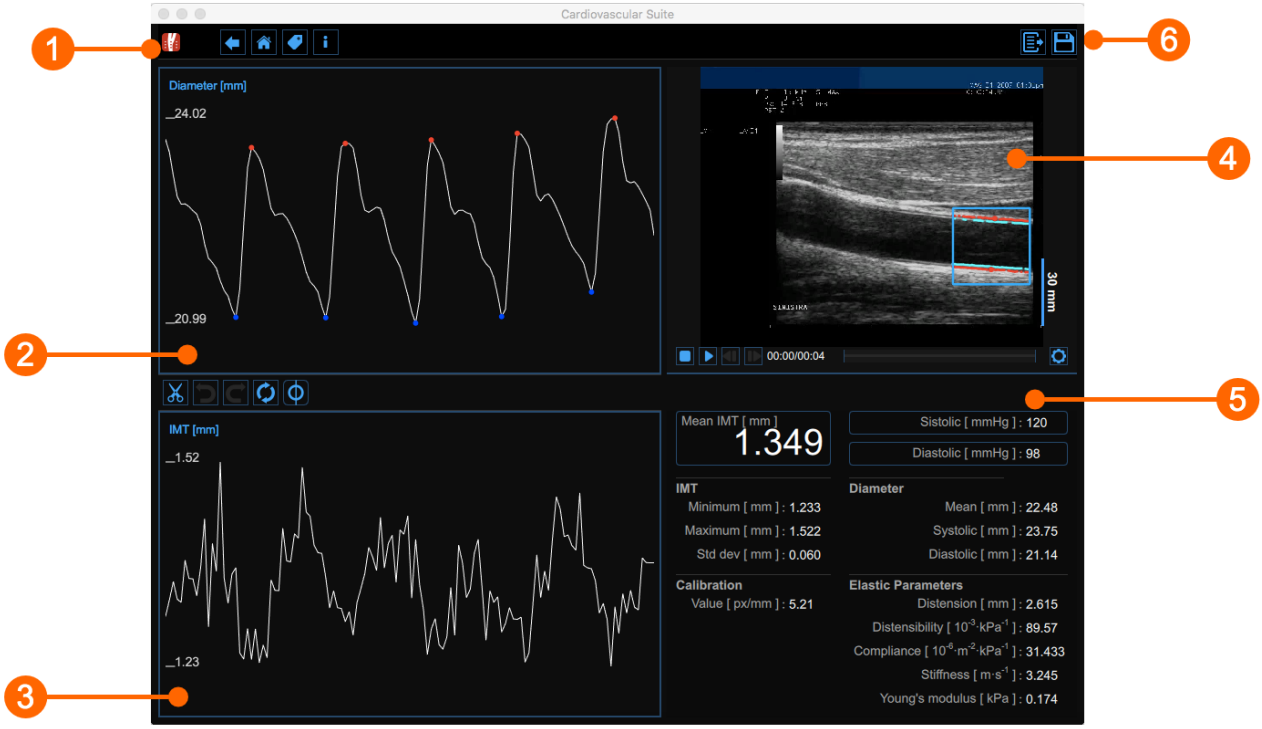
The numeric displays **(8)** show the degree of rotation of the ROI.

NOTE: if you click in the value field, you are allowed to manually enter the degree value of rotation.

Once you set calibration ROI and rotation if needed, the computed parameters appear in the Data panel.

With the Save  button it is possible to save the document.

9.4 Carotid cineloop review



The Review window shows the result of the analysis and allows you to remove piece of data that are considered to be "outliers".

The Review window contains the following components:

1. Top bar
2. Diameter chart
3. IMT chart
4. Video window

5. Results and info panel
6. Export and save

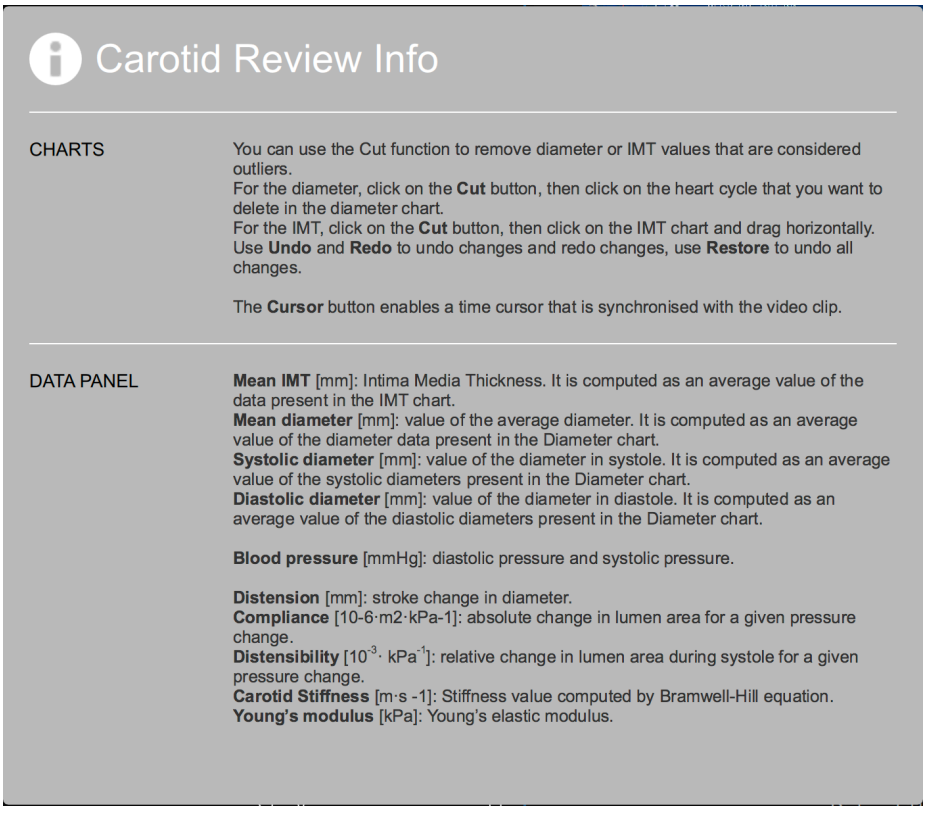
9.4.1 Top bar

The top bar contains some essential information for the navigation.

The back button  closes the Review Window and comes back to the Archive.

The home button  closes the Review Window and returns to the home screen of Cardiovascular Suite.

The Info  button shows information about the review:



Carotid Review Info

CHARTS

You can use the Cut function to remove diameter or IMT values that are considered outliers.
For the diameter, click on the **Cut** button, then click on the heart cycle that you want to delete in the diameter chart.
For the IMT, click on the **Cut** button, then click on the IMT chart and drag horizontally.
Use **Undo** and **Redo** to undo changes and redo changes, use **Restore** to undo all changes.

The **Cursor** button enables a time cursor that is synchronised with the video clip.

DATA PANEL

Mean IMT [mm]: Intima Media Thickness. It is computed as an average value of the data present in the IMT chart.
Mean diameter [mm]: value of the average diameter. It is computed as an average value of the diameter data present in the Diameter chart.
Systolic diameter [mm]: value of the diameter in systole. It is computed as an average value of the systolic diameters present in the Diameter chart.
Diastolic diameter [mm]: value of the diameter in diastole. It is computed as an average value of the diastolic diameters present in the Diameter chart.

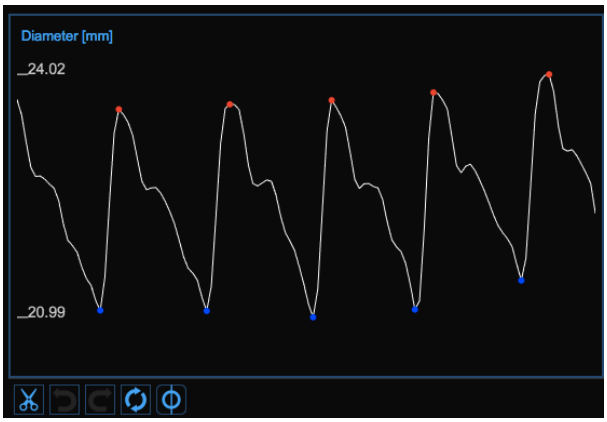
Blood pressure [mmHg]: diastolic pressure and systolic pressure.

Distension [mm]: stroke change in diameter.
Compliance [10-6·m2·kPa-1]: absolute change in lumen area for a given pressure change.
Distensibility [$10^{-3}\cdot$ kPa^{-1}]: relative change in lumen area during systole for a given pressure change.
Carotid Stiffness [m·s -1]: Stiffness value computed by Bramwell-Hill equation.
Young's modulus [kPa]: Young's elastic modulus.

The Export  button allows to export data and to save them in PDF, CVS or TSV format.

the Save  button saves the current document.

9.4.2 Diameter chart



The chart shows the trend of the diameter.

The buttons on the bottom can be used for editing the chart and removing the outliers.

9.4.2.1 Remove the outliers

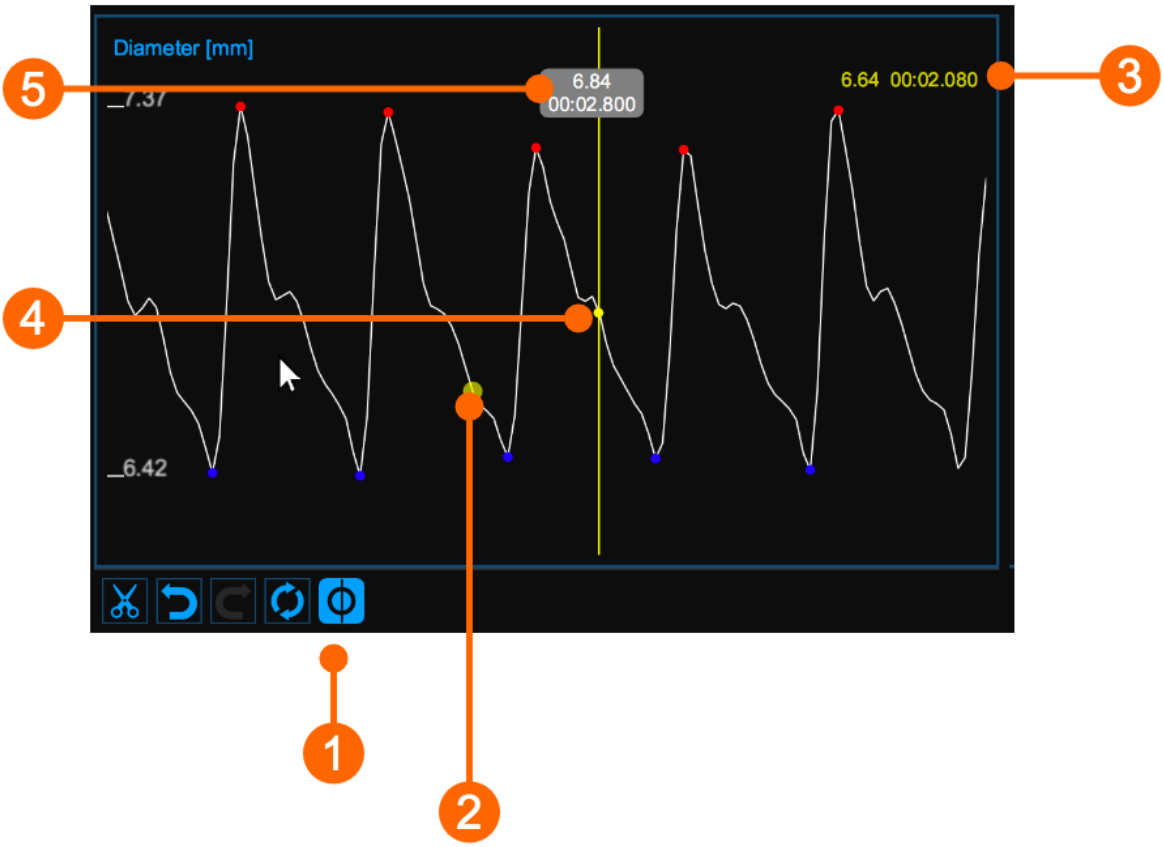
- Click on the Cut button. The heart cycle will be highlighted in the diameter chart.
- Click on the cardiac cycles you want to remove.
- Once you have removed the outliers, the data on the Results panel will be automatically updated.

You can use the undo and redo buttons to cancel and restore your changes. The restore button cancels all your changes and restore original data.

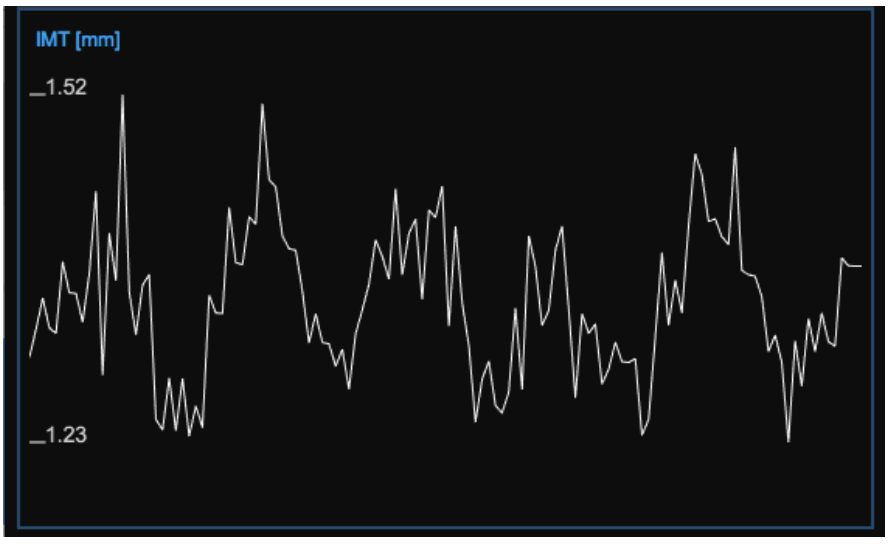
Note: Click on the Save button in the Export and save area to save your changes to the document.

9.4.2.2 Graph cursors

As shown in the following figure, the Cursor button **(1)** activates a cursor **(2)** on the Diameter chart that shows the current time position on the graph according to the images shown in the Video window. The coordinates (diameter value in millimeters and time value in the format *minutes:seconds.milliseconds*) of the cursor are dynamically updated and shown in **(3)**. When the Cursor button is active, it is also possible to know the coordinates of an exact point in the graph; it is only needed to hover over the chart and a second cursor **(4)** is displayed. It follows the mouse movements and the exact coordinates of the point are shown in the label **(5)** (diameter value is expressed in millimeters and the time value has the format *minutes:seconds.milliseconds*).



9.4.3 IMT chart



The chart shows the trend of the IMT.

The buttons at the bottom of the Diameter chart can be used for editing the chart and removing the outliers.

9.4.3.1 Remove the outliers

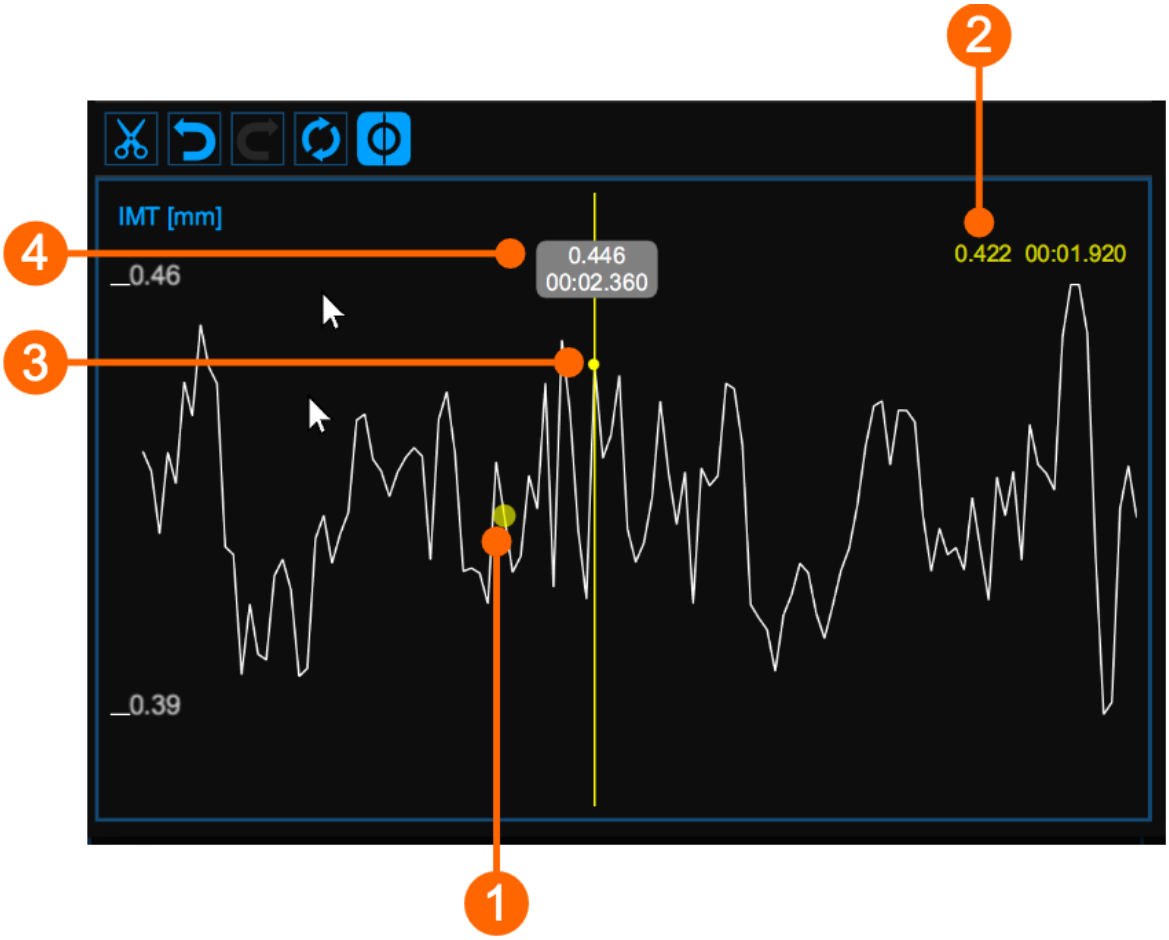
- Click on the Cut  button.
- In the IMT chart, click on one of the two extremes of the range to be deleted.
- Drag the mouse horizontally to the other extreme of the range to be deleted.
- Once you have removed the outliers, the data on the Results panel will be automatically updated.

You can use the undo  and redo  buttons to cancel and restore your changes. The restore  button cancels all your changes and restore original data.

Note: Click on the Save  button in the Export and save area to save your changes to the document.

9.4.3.2 Graph cursors

As shown in the following figure, the Cursor  button at the bottom of the Diameter chart activates a cursor **(1)** on the IMT chart that shows the current time position on the graph according to the images shown in the V ideo window. The coordinates (IMT value in millimeters and time value in the format *minutes:seconds.milliseconds*) of the cursor are dynamically updated and shown in **(2)**. When the Cursor button is active, it is also possible to know the coordinates of an exact point in the graph; it is only needed to hover over the chart and a second cursor **(3)** is displayed. It follows the mouse movements and the exact coordinates of the point are shown in the label **(4)** (IMT value is expressed in millimeters and the time value has the format *minutes:seconds.milliseconds*).

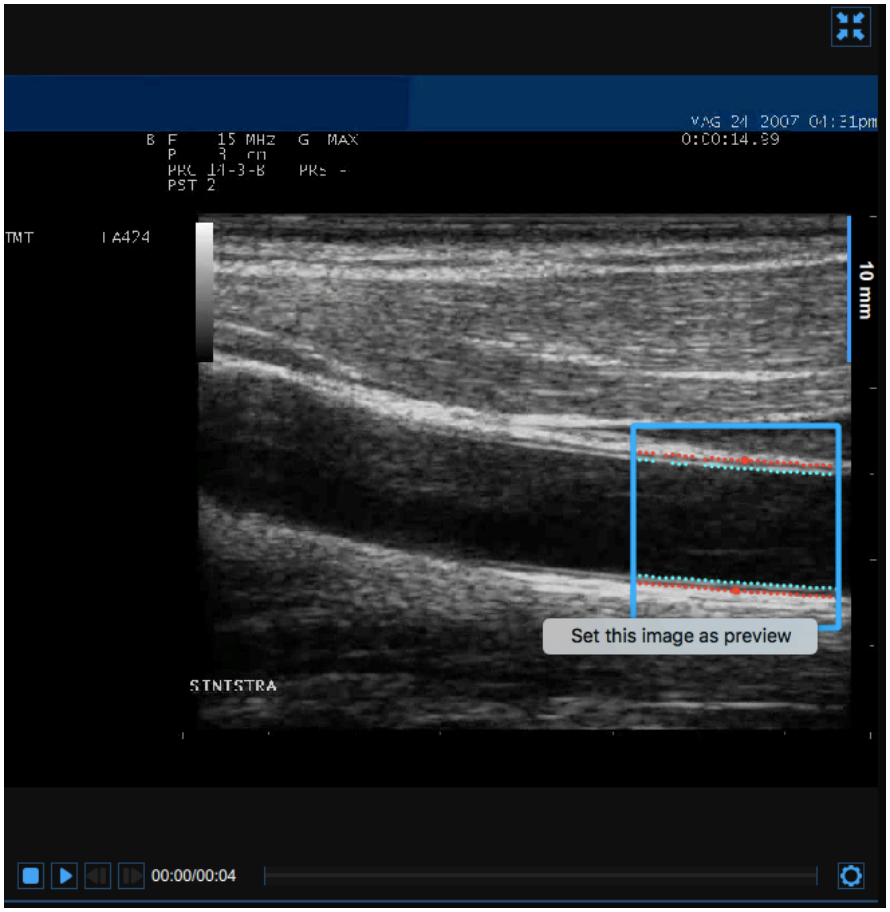


9.4.4 Video window

The video window shows the video signal from your ultrasound system. The points of the Lumen-Intima interface and the Media-Adventitia interface are displayed within the ROI in cyan color.

The Video control bar is located at the bottom of the window.

If you want to expand the video window, you have to click on the Enlarge  button.

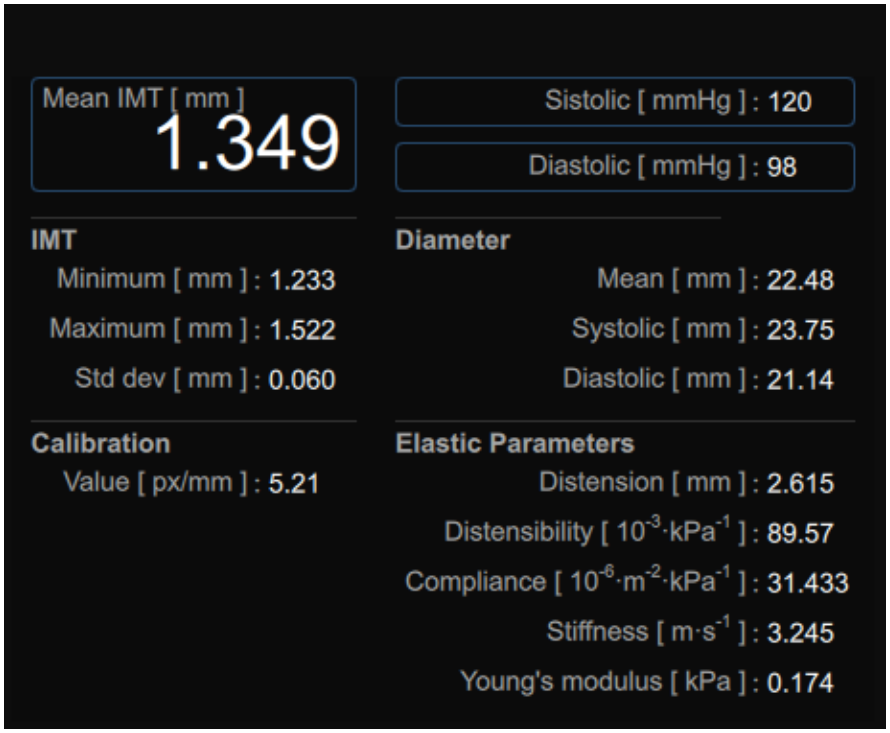


NOTE: if you perform right click on the video window and click on "Set this image as preview" the current frame will be saved and displayed in the Documents Table as document preview (see Studies management)

9.4.5 Results and info panel

This panel consists of two tab-sheets: Results panel and Other info panel.

9.4.5.1 Results panel



The panel shows the results of the analysis. The following data are displayed:

- ***Mean IMT [mm]***: Intima Media Thickness. It is computed as an average value of the data present in the IMT chart.
- ***Mean diameter [mm]***: value of the average diameter. It is computed as an average value of the diameter data present in the Diameter chart.
- ***Systolic diameter [mm]***: value of the diameter in systole. It is computed as an average value of the systolic diameters present in the Diameter chart.
- ***Diastolic diameter [mm]***: value of the diameter in diastole. It is computed as an average value of the diastolic diameters present in the Diameter chart.
- ***Blood pressure [mmHg]***: diastolic pressure and systolic pressure.
- ***Distension [mm]***: stroke change in diameter.

$$Distension = \Delta D = D_s - D_d$$

- ***Compliance [10^{-6}·m^2·kPa^{-1}]***: absolute change in lumen area for a given pressure change.

$$Compliance = \frac{\Delta A}{\Delta P} = \frac{\pi}{4} \cdot \frac{D_s^2 - D_d^2}{P_s - P_d}$$

- ***Distensibility [10^{-3}· kPa^{-1}]***: relative change in lumen area during systole for a given pressure change.

$$Distensibility = \frac{1}{A_d} \cdot \frac{\Delta A}{\Delta P} = \frac{1}{D_d^2} \cdot \frac{D_s^2 - D_d^2}{P_s - P_d}$$

- ***Carotid Stiffness [m·s^{-1}]***: Stiffness value computed by Bramwell-Hill equation.

$$Stiffness = \frac{1}{\sqrt{\rho \cdot Distensibility}} = \sqrt{\frac{A_d \cdot \Delta P}{\rho \cdot \Delta A}} = \sqrt{\frac{D_d^2 \cdot (P_s - P_d)}{\rho \cdot (D_s^2 - D_d^2)}}$$

- ***Young's elastic modulus [kPa]***:

$$Young's\ Modulus = \frac{3}{Distensibility} \cdot \left(1 + \frac{A_d}{WCSA}\right)$$

where:

D_e = External Diameter (between the media-adventitia interfaces) measured in diastole.

D_i = Internal Diameter (between the lumen-intima interfaces) measured in diastole.

D_s = Systolic Diameter (external).

D_d = Diastolic Diameter (external), $D_d = D_e$

WCSA = Wall Cross Section Area.

$$WCSA = \frac{\pi}{4} \cdot (D_e^2 - D_i^2)$$

ΔA = Stroke change in lumen area.

$$\Delta A = \frac{\pi}{4} \cdot (D_s^2 - D_d^2)$$

A_d = Diastolic Area.

$$A_d = \frac{\pi}{4} \cdot D_d^2$$

P_s = Systolic Pressure.

P_d = Diastolic Pressure.

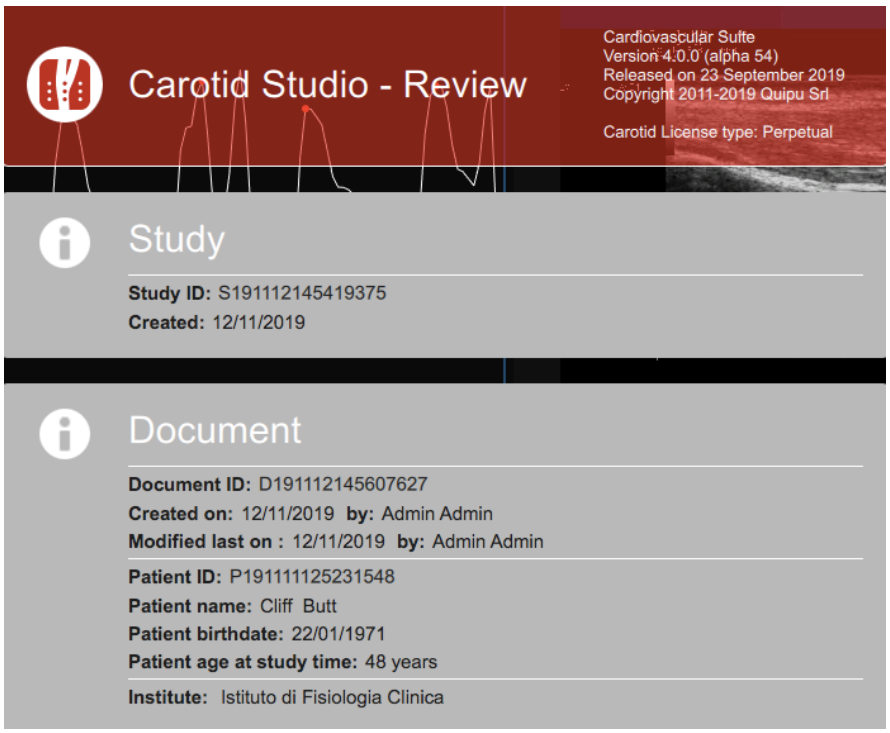
$\Delta P = P^s - P^d$

ρ = Blood density: is assumed to be constant and equal to 1.06 g/cm^3.

These data can be exported in the Document Data. Please see Export and save.

9.4.5.2 Other info panel

Clicking on the icon  a window containing information about the study will appear.



The panel shows the information about the study, the document, the patient, the operator and the institute.

9.4.6 Export and save

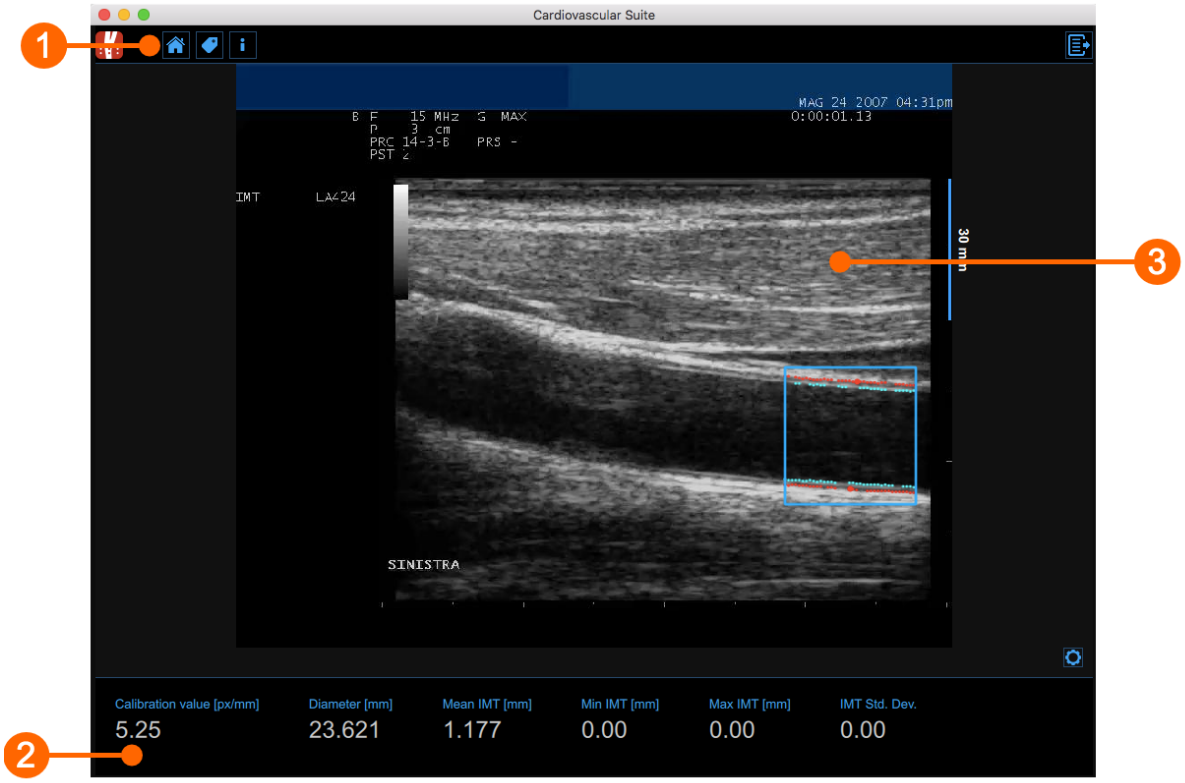
The Save  button is used to save your changes to the document, once you have edited the data.

The Export  button is used to export the Document Results and the Document Data.

The **Document Results** contains all the results of the analysis and all the information about the study, the document and the patient.

The **Document Data** contains all the Document Results, a list of the Diameter and the IMT values computed at each frame.

9.5 Carotid single image Review



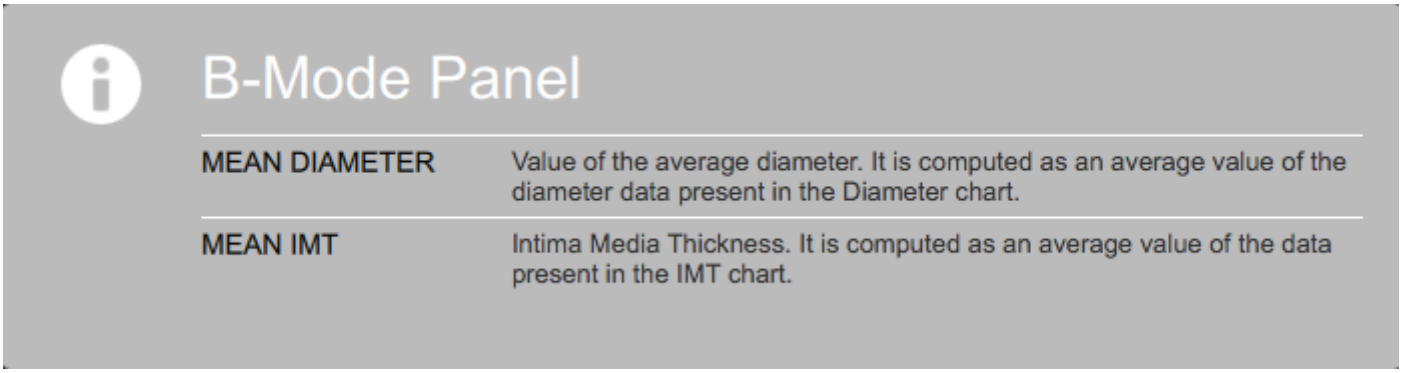
1. Top bar
2. Results panel
3. Video Window

9.5.1 Top bar

The top bar contains some essential information for the navigation.

The home button  closes the Carotid Studio application and returns to the home screen of Cardiovascular Suite.

The Info  button shows information about the review:

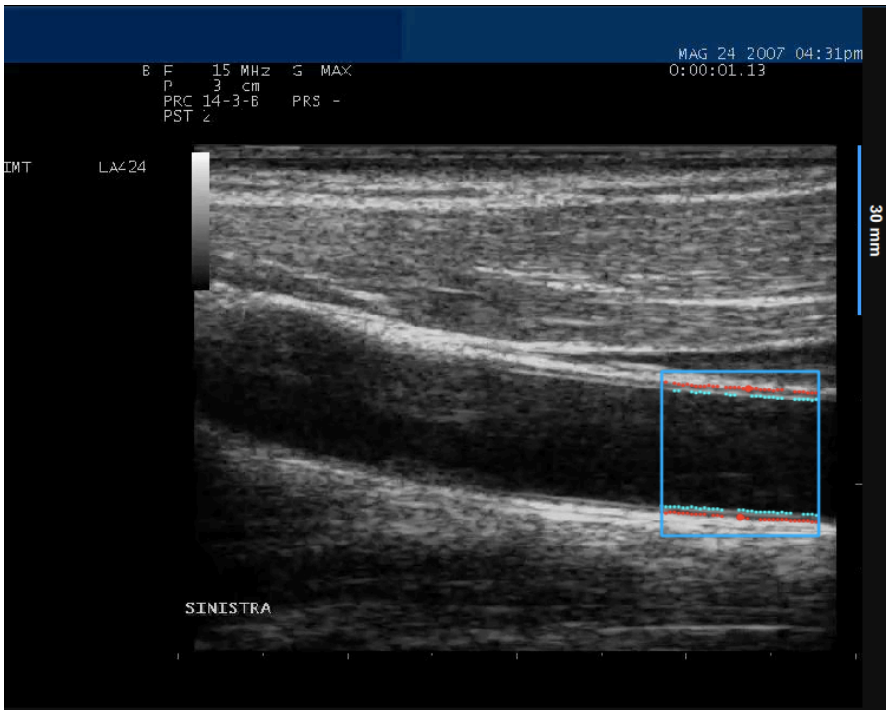


The Export  button allows to export data and to save them in PDF, CVS or TSV format.

9.5.2 Results panel

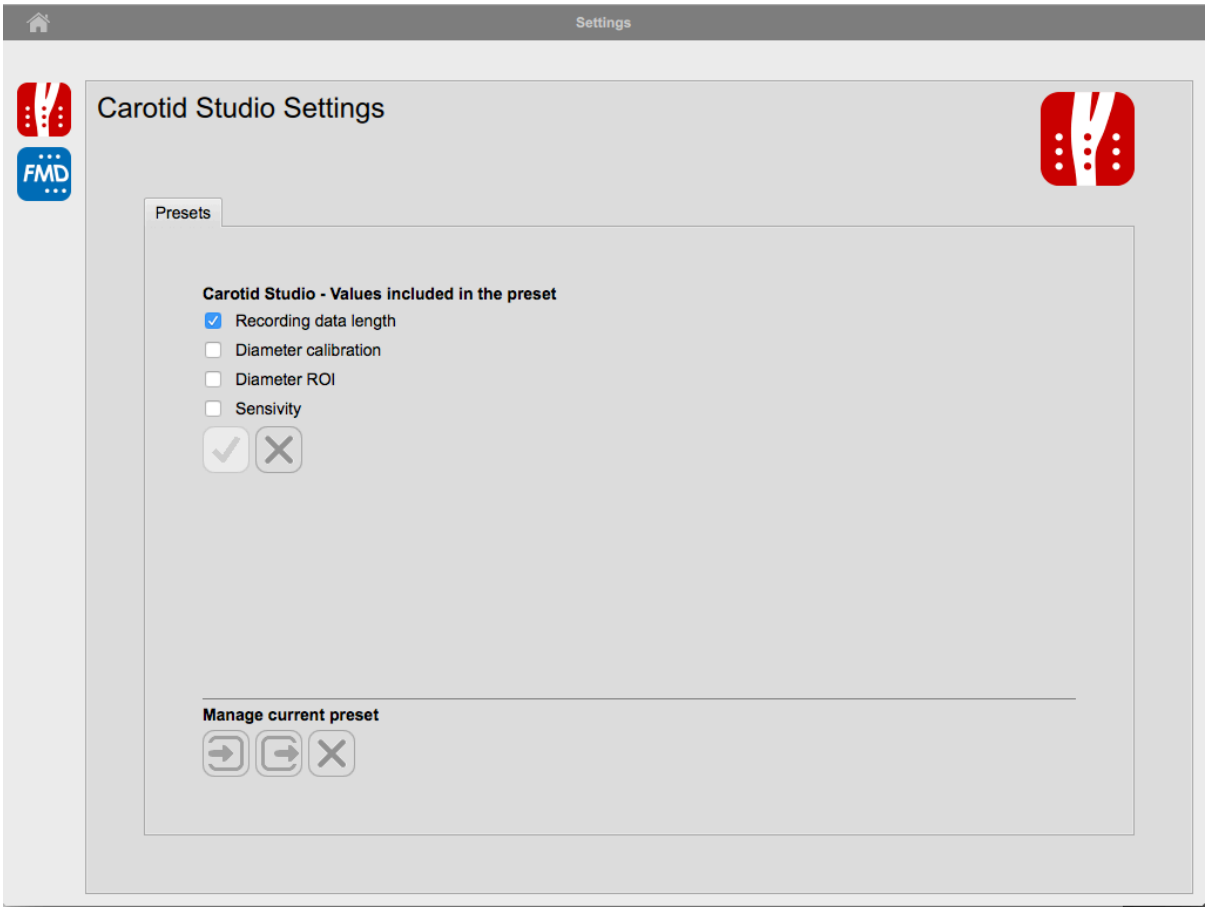
The results panel contains the result of the analysis.

9.5.3 Video Window



The video window shows the video signal from your ultrasound system. The points of the Lumen-Intima interface and the Media-Adventitia interface are displayed within the ROI in cyan color.

9.6 Carotid Studio settings



Carotid Studio can remember the values that you enter in the Setup panel. You can decide whether or not to remember the current values by the special thick box in the Analysis panel. If you check this tick box, Carotid Studio will create a preset that is used every time you start a new analysis.

In the Carotid Studio Settings, you can decide which values are included in the preset. The values are:

- Recording data length
- Diameter calibration
- Diameter ROI
- Sensitivity

Select/deselect the values that you want to include/not include in the preset, then click on the Apply button.

Click on the Reset to Default button to restore the default selection.

In the lower part of the windows, you can manage the current preset.

- Click on the Export button to save the current preset as a new file.

- Click on the Import  button to import a preset from a file.
- Click on the Reset  button to cancel the current preset and to restore the default preset.

10 FMD Studio

FMD Studio is a software for the measurement of the Flow-Mediated Dilatation (FMD) or other general Vasodilations of the brachial artery.

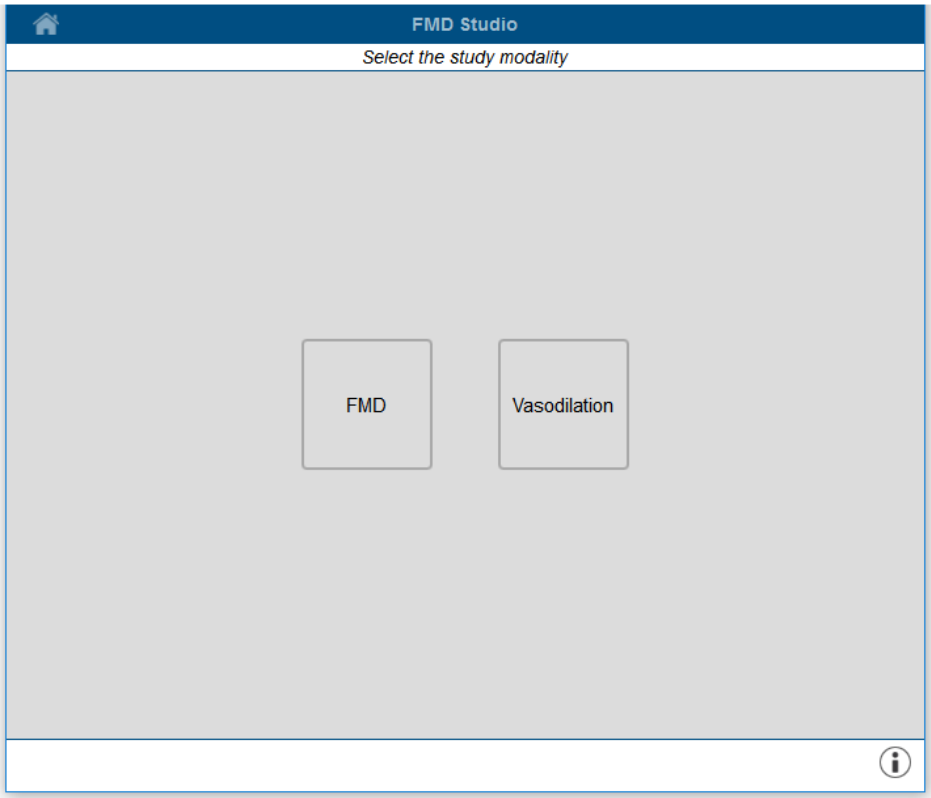
Click on the FMD Studio  icon to Create a new study with FMD Studio.

10.1 Create a new study

When you start FMD Studio, a procedure guides you in the creation of a new study. The steps are:

1. Select the study modality
2. Select the source
3. Select the patient
4. Select the institute
5. Review

10.1.1 Select the study modality



In this tab, you can select the study modality.

FMD Studio can work in two modalities: "FMD" and "Vasodilation". The two modalities differ in how the timeline of the examination is organized.

In **FMD modality**, the timeline is divided into three parts:

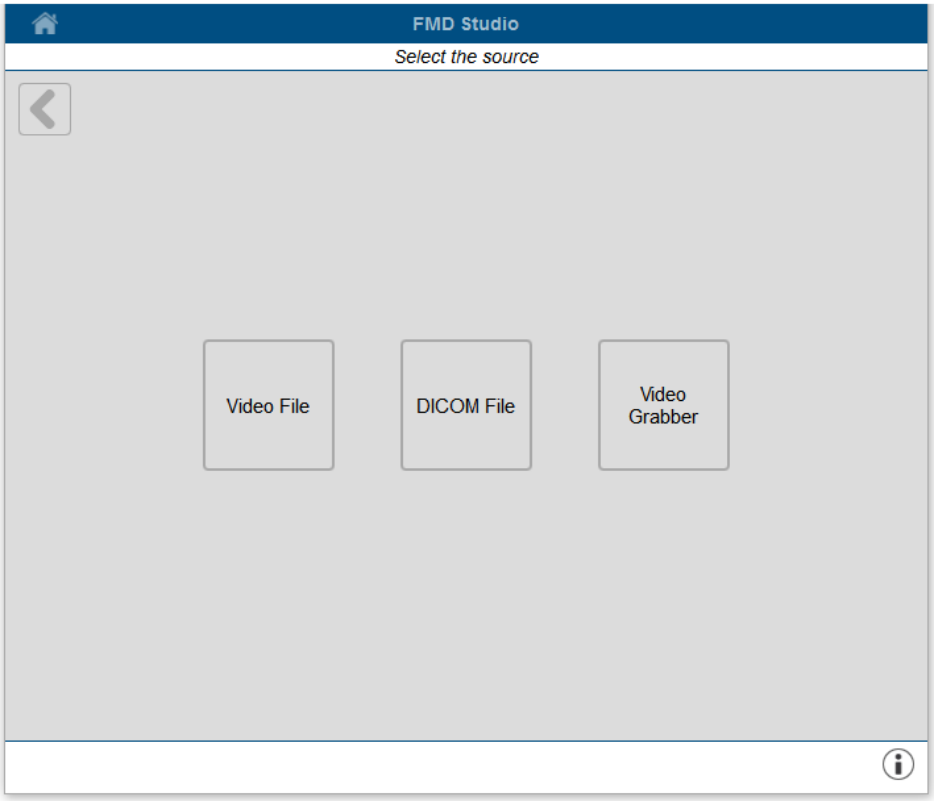
1. Baseline, where the software computes the baseline diameter and the shear-rate diameter.
2. Ischemia, which is not used for the analysis.
3. Vasodilation, where the software computes the maximum diameter, the recovery diameter, the maximum shear-rate and the area under the curve of the shear-rate.

In **Vasodilation modality**, the timeline is divided into two parts:

1. Baseline, where the software computes the baseline diameter and the shear-rate diameter.
2. Vasodilation, where the software computes the maximum diameter, the maximum shear-rate and the area under the curve of the shear-rate.

The time length of the timeline parts can be set in the Time panel.

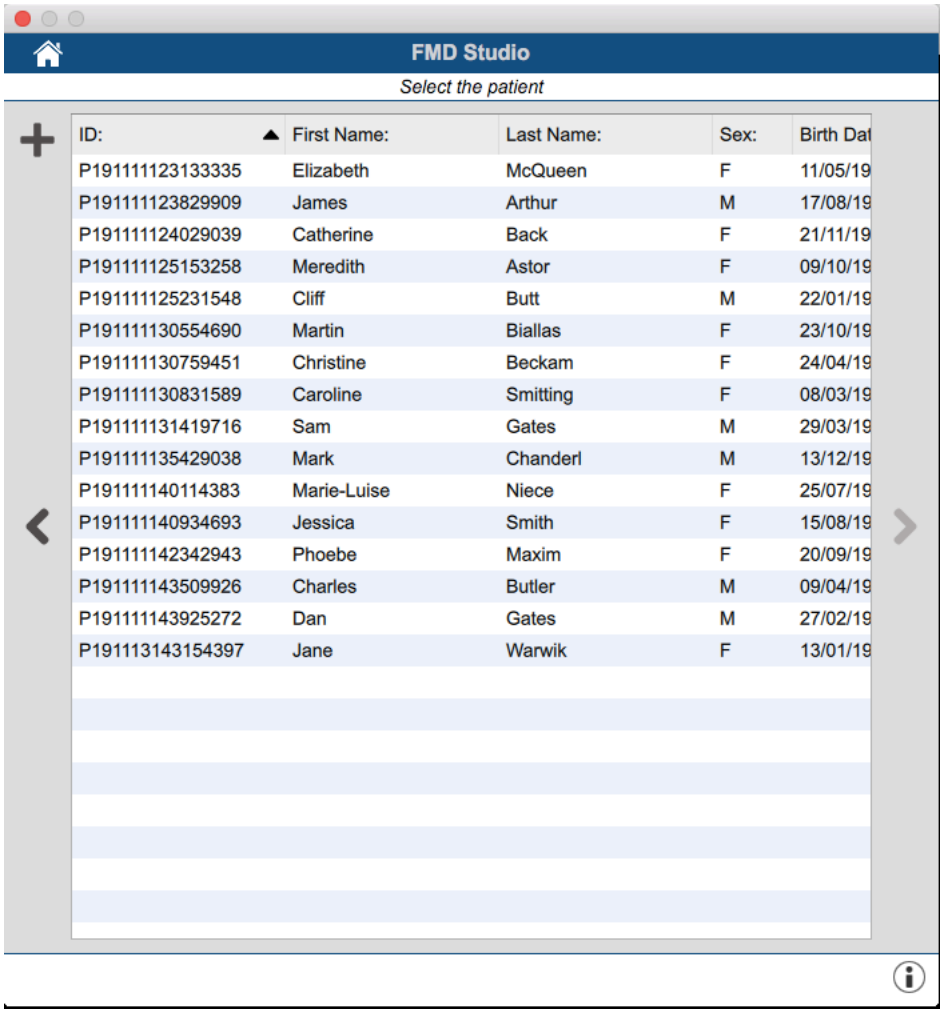
10.1.2 Select the source



In this tab, you can select the study video source.

FMD Studio processes video sources and can work in two video modalities: "Offline" (processing a Video File or a DICOM File) and "Online" (processing a video coming from a video frame grabber).

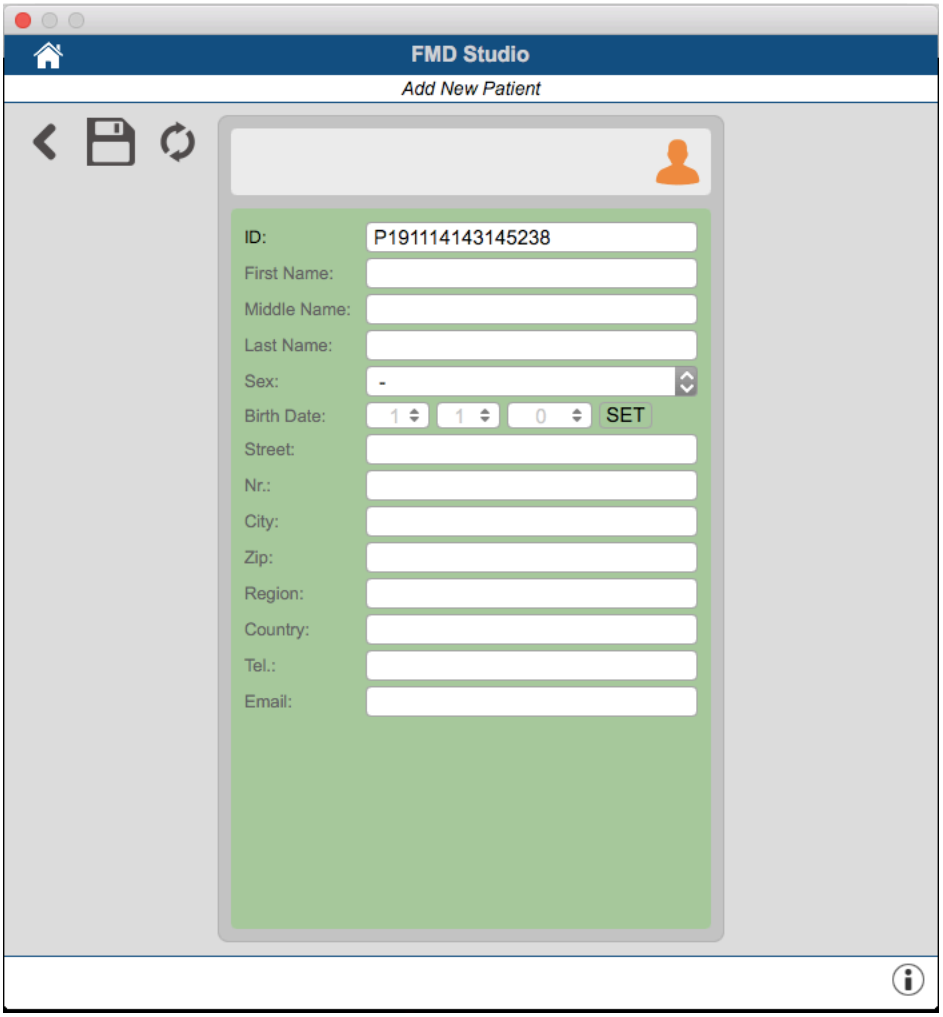
10.1.3 Select the patient



Select the patient

In this tab, you can select the patient among the ones already present in the Archive. Select the patient and click on the Next button (you can simply double-click on the patient to proceed).

If you want to create a new patient, click of the Add New Patient button. In the Add new patient frame, enter the patient data. The only mandatory field is the patient ID. If you don't enter patient ID a random value is automatically proposed. Click on the Save button to save the patient data.

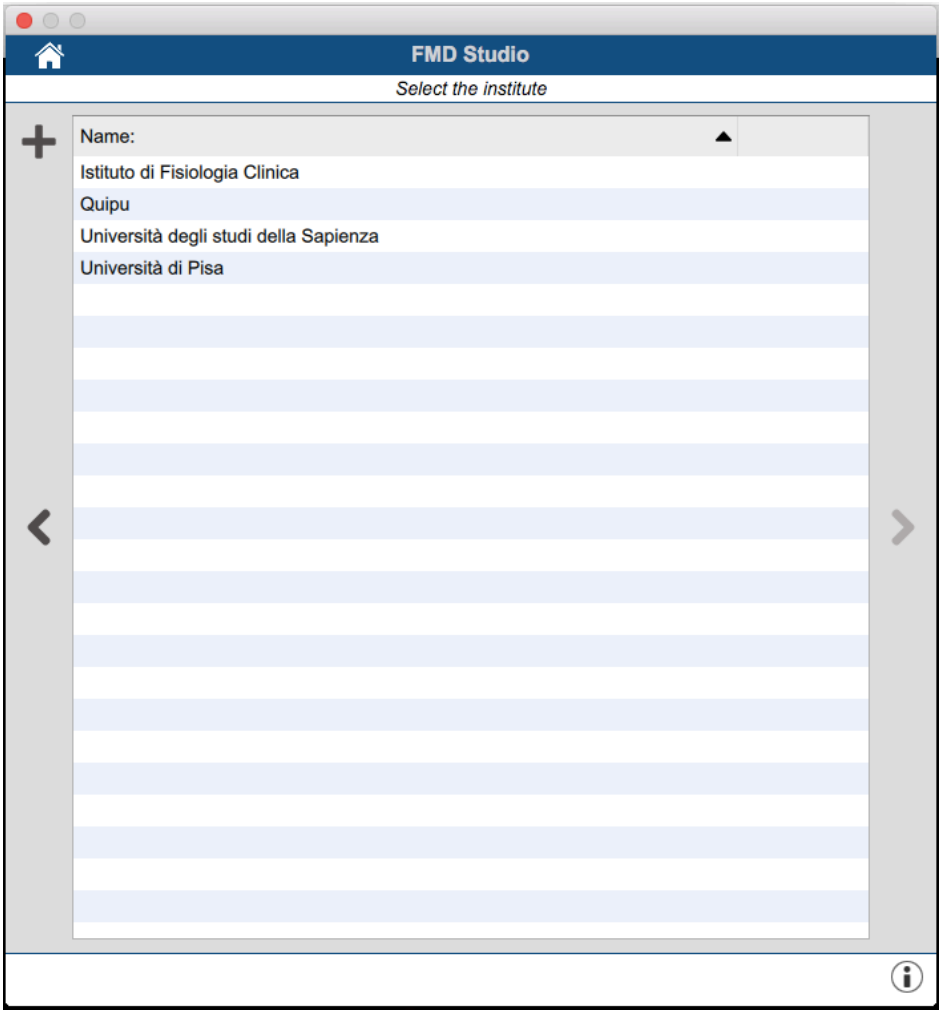


Add a new patient

NOTE: If it is the first time you create a study, after selecting the patient you will also need to select the institute. If you have already created at least one study, the software remembers the institute used for the previous study and after selecting the patient shows you automatically the final Review (where you can still make changes before starting the new study).

10.1.4 Select the operator

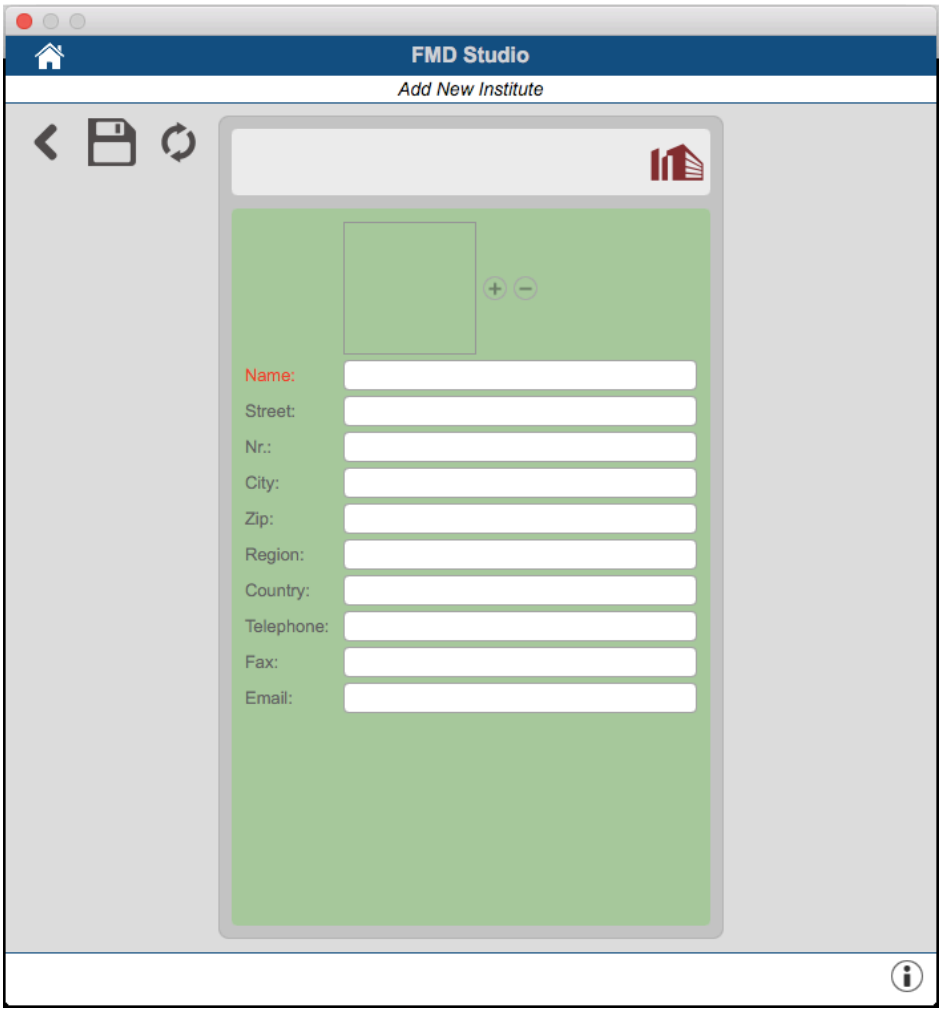
10.1.5 Select the institute



Select the institute

In this tab, you can select the institute among the ones already present in the Archive. Select the institute and click on the Next button (you can simply double-click on the institute to proceed).

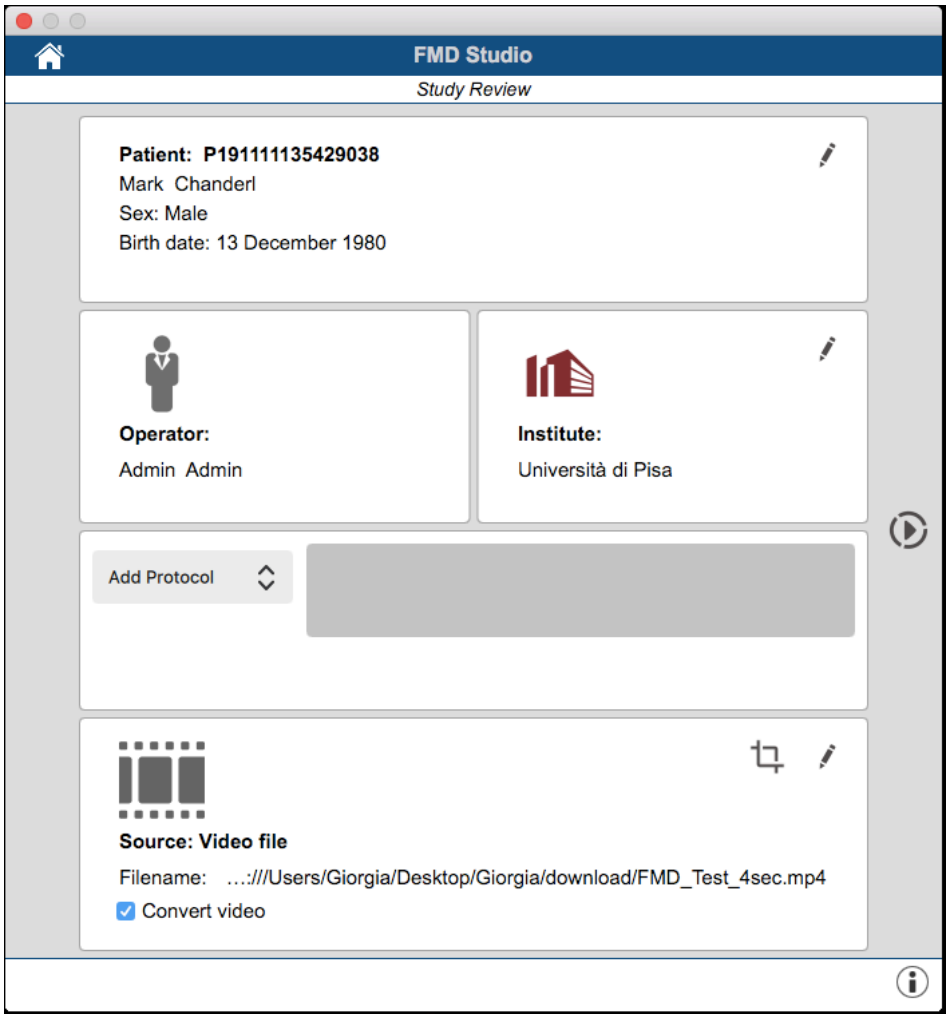
If you want to create a new institute, click of the Add New Institute button. In the Add new institute frame, enter the institute data. The mandatory field (Name) is in red until you have filled in the Name blank. Click on the Save button to save the institute data.



Add a new institute

NOTE: If it is the first time you create a study, after selecting the patient you will also need to select the institute. If you have already created at least one study, the software remembers the institute used for the previous study and after selecting the patient shows you automatically the final Review (where you can still make changes before starting the new study).

10.1.6 Review

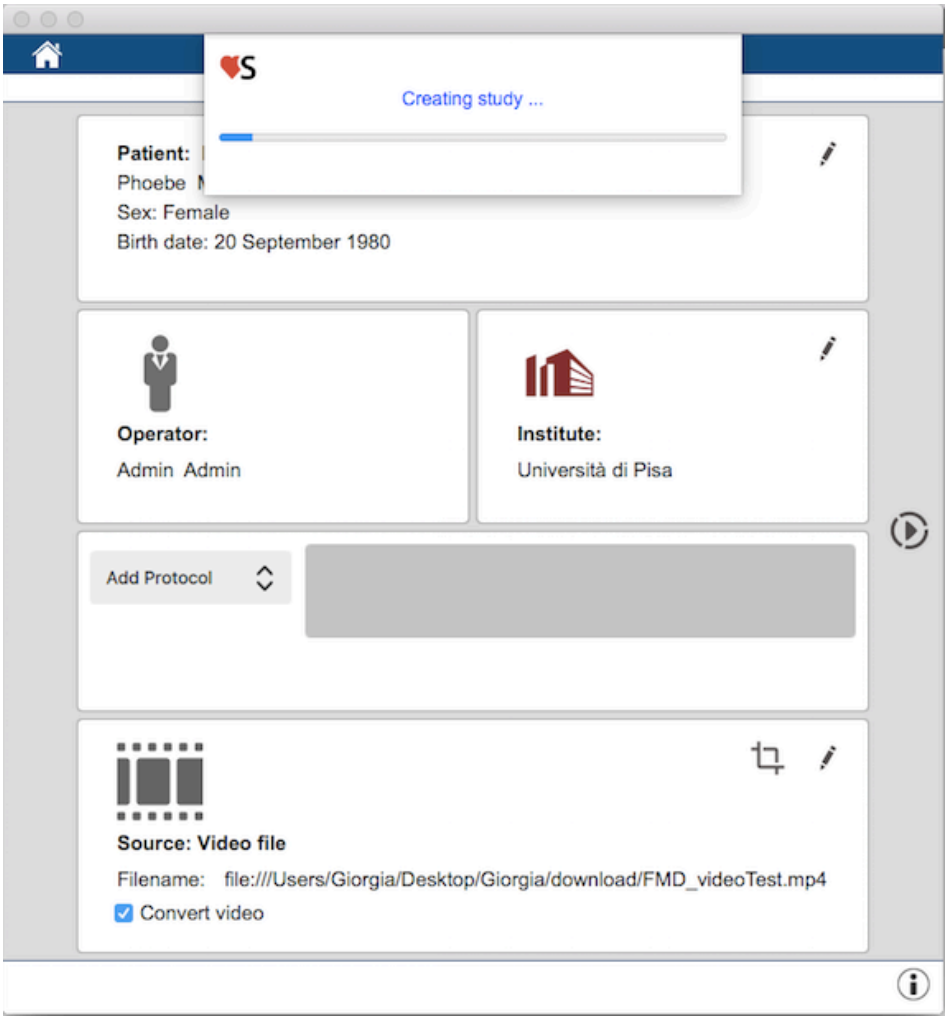


In this tab you can review your selection (you can also change Patient and Institute clicking on the corresponding Edit button).

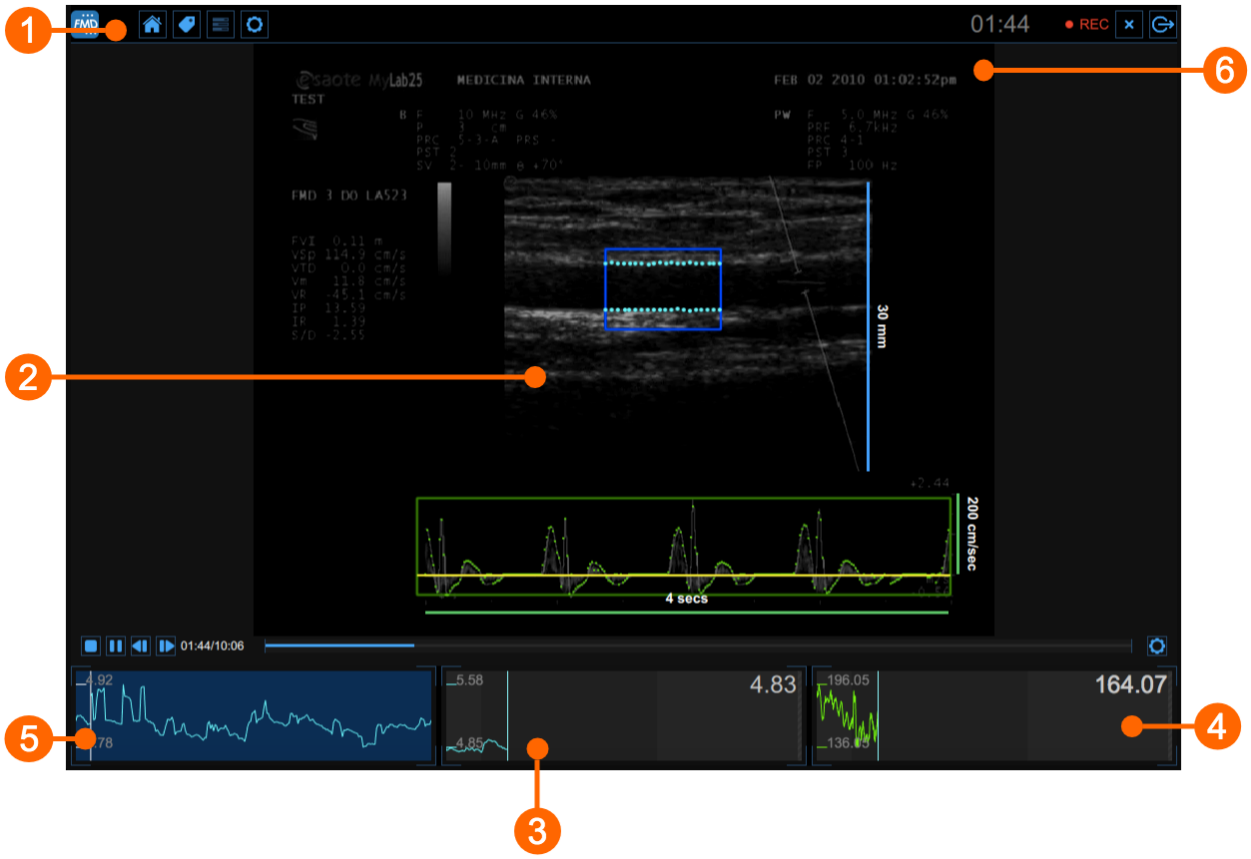
It is possible also to change the selected source for this study clicking on the Edit button.

In addition, if you have chosen a video file as source, it is possible to convert the video file to be optimized for the analysis with Carotid Studio. This operation may take few minutes. You can also crop the images by clicking the Crop button in the source panel.

Click on the Start the Study button to proceed. A progress bar, as shown in the following picture, will show you the progression of the study creation.



10.2 Analysis



The Analysis window contains the following components:

1. Top bar
2. Video window
3. Mean diameter chart
4. Shear rate chart
5. Instantaneous diameter chart
6. Setup panels

10.2.1 Top bar

The top bar contains some essential information for the navigation. Several icons are displayed.

The FMD Studio button  shows a panel holding some information about the study and about Cardiovascular Suite. Regarding the studio, the number identification (ID) is displayed together with information about patient and the institute. Information about the software such as version and type of license are shown in the upper part of the panel, as figure 1 shows.

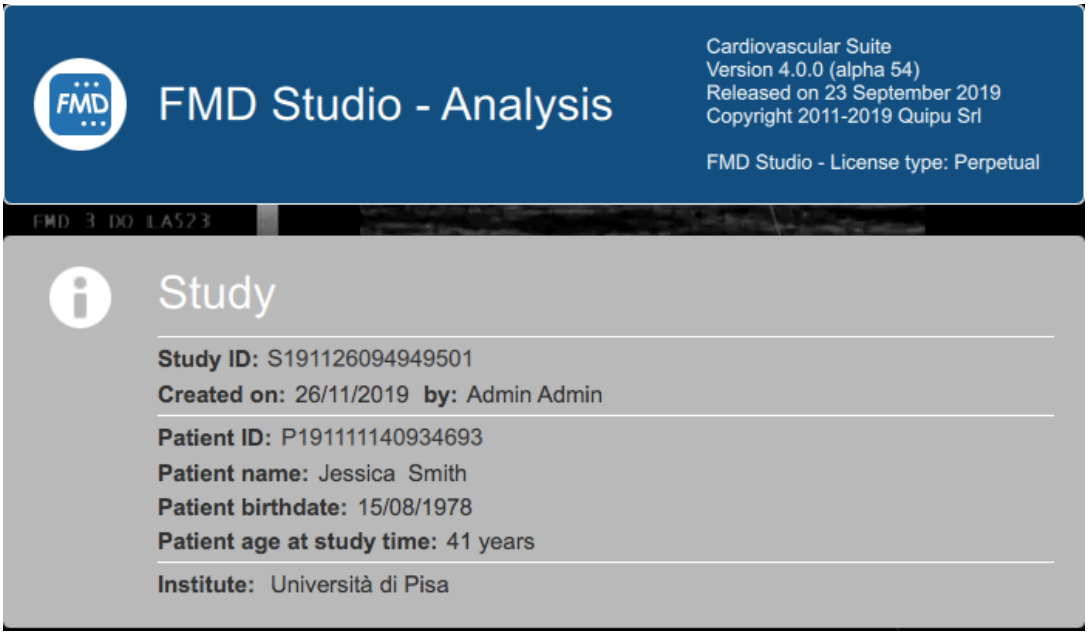


Fig.1: FMD Studio Analysis panel

The home button  closes the FMD Studio application and returns to the home screen of Cardiovascular Suite.

The Tags Management button  opens a panel shown in figure 2 that allows to manage tags that can be associated to documents. Tags are labels that confer information to documents. Tags can be managed through the Tags management into the Archive. In this panel it is possible to add an existing tag to the document or create a new one.

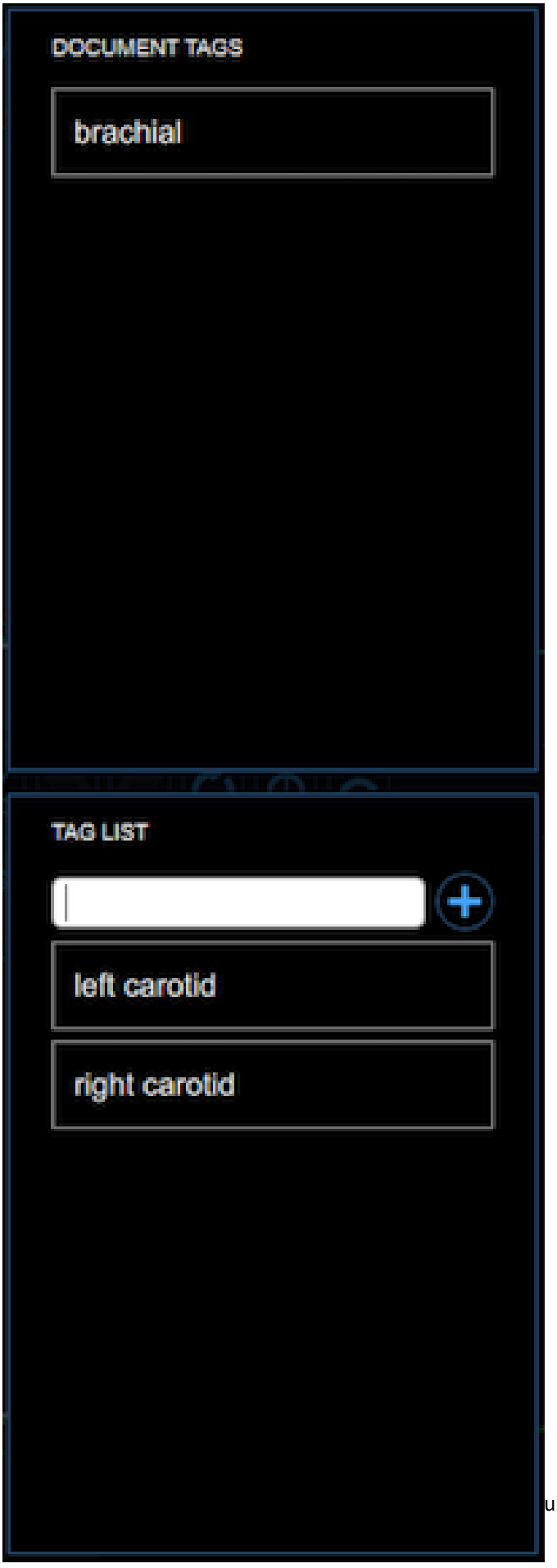


Fig.2: Tags Management panel

The preset management button  opens the preset management panel (Figure 3) that allows to manage settings. In particular, it allows to remember settings of calibration and ROI and to reuse them for following studies.

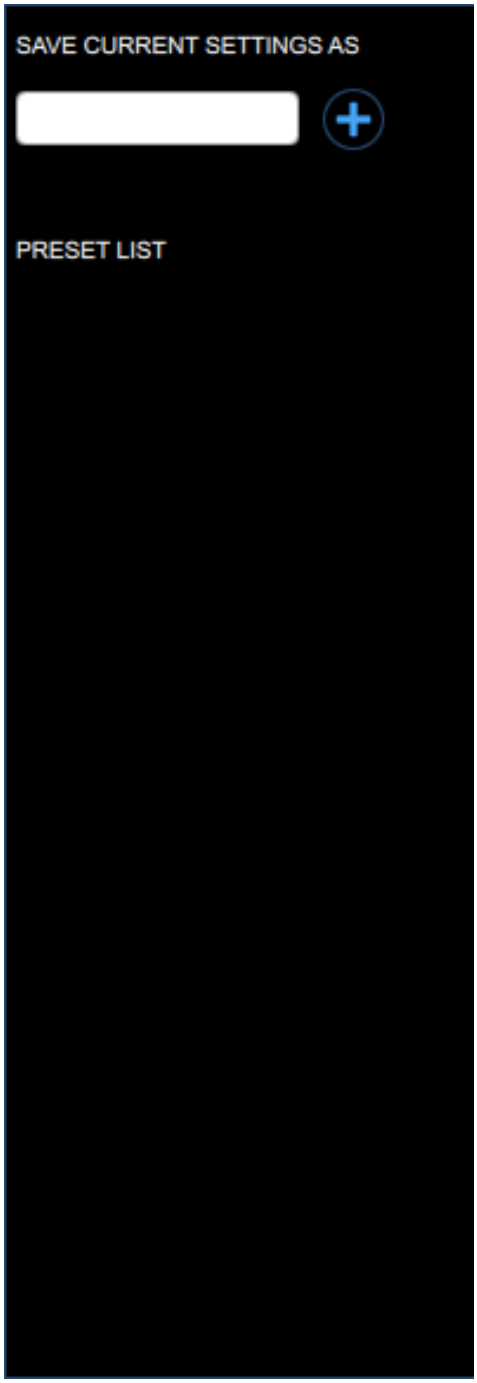


Fig.3: Preset Management panel

The "Info" button shows information about active controls (calibration lines, ROI, etc.).

The "Start Exam" button starts the examination.

Once the exam is started, the computed data are recorded and displayed in the Mean diameter chart , the Instantaneous diameter chart and the Shear rate chart. These charts will contain the final result of the analysis.

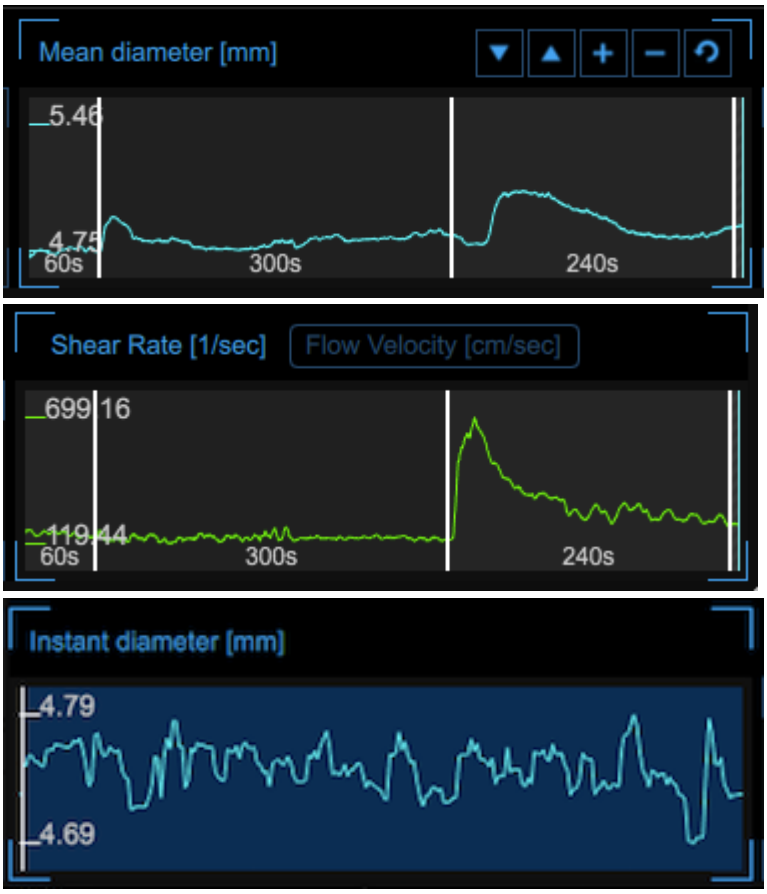


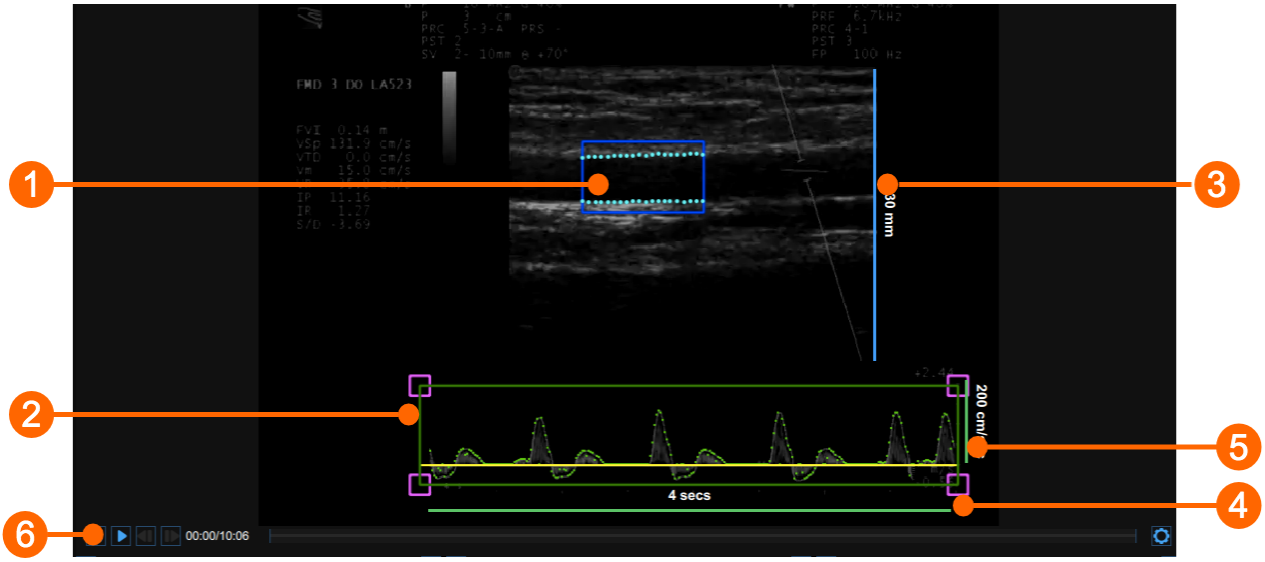
Fig. 4: Mean diameter, Shear rate and Instantaneous diameter charts

The functioning is different according to the video modality:

- **Offline analysis**
  The time is the current position in the movie time-line and the two charts are populated accordingly.
  During the exam, you can use the Video control bar to pause and start again the data recording, and to move to any point of the movie time-line.
- **Online analysis**
  The time starts from 00:00 when you press the "Start Exam" button and the two charts are populated starting from the left origin.
  During the exam, the video is recorded. You can pause and start again both the data recording and the video recording by using the Video control bar.

On the right other icons are shown. In particular, with the Cancel the analysis button  it is possible to stop the analysis and start again. The button Stop and Review  allows to proceed and see the final report of the study.

10.2.2 Video window



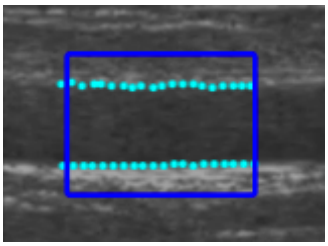
The video window shows the video signal from your ultrasound system. Two ROIs can be present in the window: the diameter ROI in blue **(1)** and the Doppler flow ROI in green **(2)**.

The window contains also the calibration lines for the B-mode image **(3)** and for the Doppler flow **(4)(5)**, once these have been calibrated (see Calibrate the B-Mode image and Calibrate the Doppler flow).

The video controls bar **(6)** is located at the bottom of the window. The bar has different controls according to the video modality: Video control bar - online or Video control bar - offline.

10.2.2.1 Diameter ROI

The Diameter Region of Interest (ROI) is the portion of the image where the diameter is calculated. The edges of the vessel obtained by the algorithm of edge detection are displayed within the ROI. The ROI can be moved and/or resized. Each time you change the position and/or size of the ROI, the contours of the vessel are re-initialized.



Draw a new Diameter ROI:

- Click on the Set B-Mode ROI  button in the B-Mode panel (the button remains active).
- Click inside the video window and drag until the Diameter ROI is complete (the size of the ROI is shown in the B-Mode panel).
- When you release the mouse, the contours are initialized.

Modify the Diameter ROI

- Click on one of the sides or one of the corners of the Diameter ROI.
- Drag to change the size of the the Diameter ROI.

NOTE: as an alternative, you can modify the size of the Diameter ROI by typing the value in the B-Mode panel.

Move the Diameter ROI

- Click and hold inside the Diameter ROI.
- Drag the Diameter ROI to the location of interest.

NOTE: as an alternative, you can modify the position of the Diameter ROI by typing the value in the B-Mode panel.

Re-initialize the edge detection algorithm

- Click on the Diameter ROI.

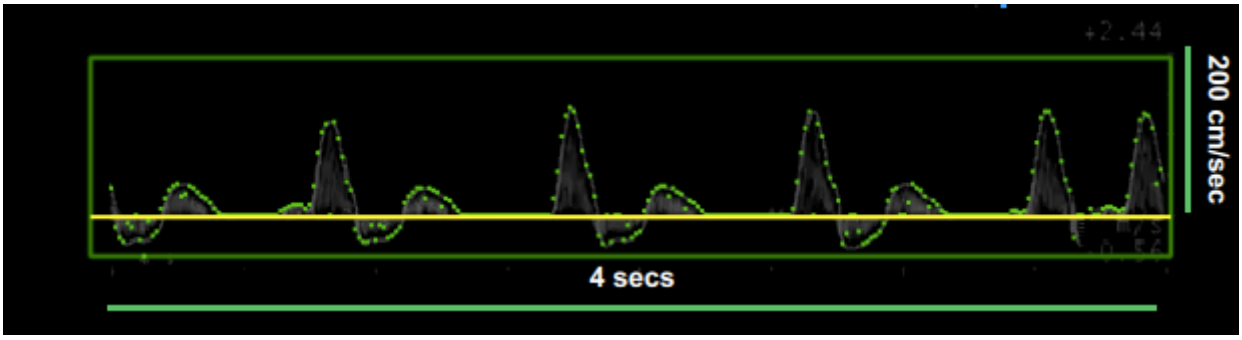
10.2.2.2 Doppler flow ROI

The Doppler Flow Region of Interest (ROI) is the portion of the image that includes the Doppler Flow waveform.

The algorithm for the Doppler Flow analysis, automatically locate the zero line, which is displayed in yellow, and the waveform, which is displayed in green.

The Doppler Flow ROI can be moved or resized. Each time you change the position and/or size of the ROI, the algorithm is re-initialized and the zero line is re-localized.

For more information on ultrasound setting for Doppler analysis, please see How to set up the ultrasound system in Duplex Mode (FMD Studio)



Draw a new Doppler Flow ROI

- Click on the Set Doppler Flow ROI  button in the Doppler panel (the button remains active).
- Click inside the video window and drag until the Doppler Flow ROI is complete (the size of ROI is shown in the Doppler panel).
- When you release the mouse, the algorithm for the Doppler Flow analysis is initialized.

Modify the Doppler Flow ROI

- Click on one of the corners of the Doppler Flow ROI.
- Drag to change the size of the the Doppler Flow ROI (the size of ROI is shown in the Doppler panel).

NOTE: as an alternative, you can modify the size of the Doppler Flow ROI by typing the value in the Doppler panel.

Move the Doppler Flow ROI

- Click and hold inside the Diameter ROI.
- Drag the Doppler Flow ROI to the location of interest.

NOTE: as an alternative, you can modify the position of the Doppler Flow ROI by typing the value in the Doppler panel.

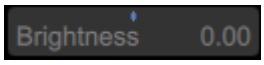
Re-initialize the algorithm for the Doppler Flow analysis

- Click into the Doppler Flow ROI.

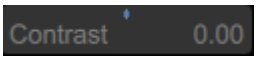
10.2.2.3 Video control bar - online

The video control bar is at the bottom of the Video window and contains controls to manage the recording of a movie and the brightness and contrast adjustment.

Adjust the image

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the recording of a movie

Click on the Record/Pause  buttons to record / pause the recording of the movie.

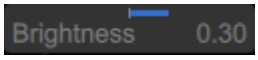
While recording, a blinking red icon  is shown.

10.2.2.4 Video control bar - offline

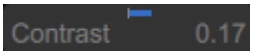
The video control bar is at the bottom of the Video window and contains controls to manage the playback of a movie and the brightness and contrast adjustment.

Adjust the image

Click on the Setting  button on the right of the video control bar. The Brightness and Contrast sliders will appear.

Drag the brightness slider 

to adjust the brightness of the image.

Drag the contrast slider 

to adjust the contrast of the image.

Control the playback of a movie

Click on the Play/Pause  buttons to play/pause the movie.

Click on the Step forward  button to advance an image.

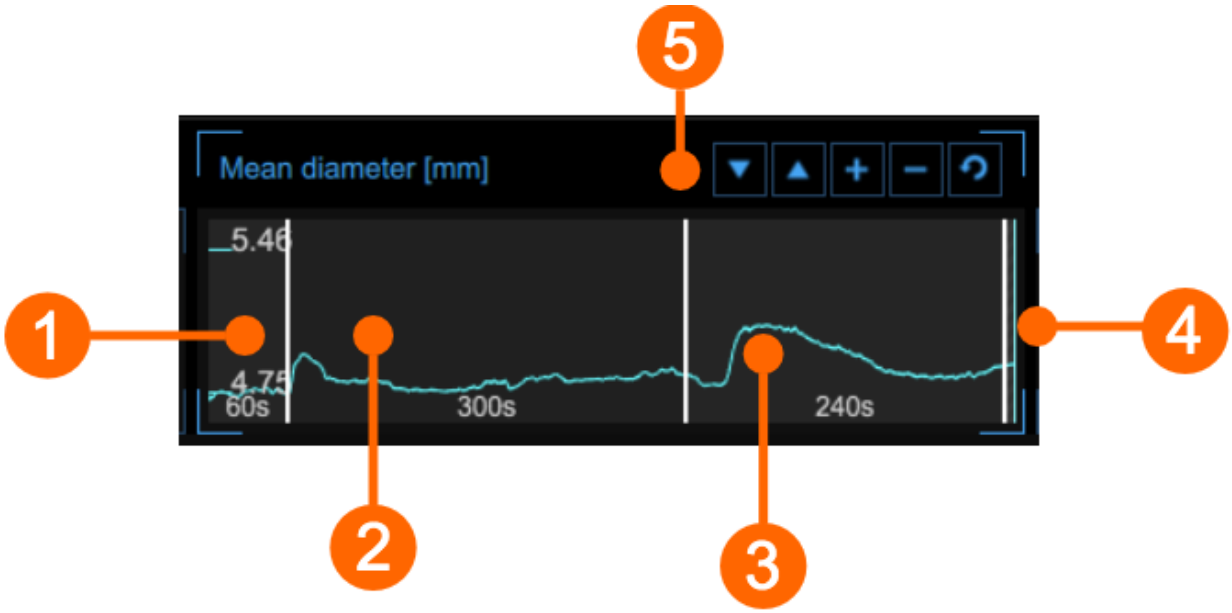
Click on the Step backward  button to go back an image.

Click on the Stop  button to stop and return to the beginning of the movie.

Drag the time slider

to move to any point of the movie.

10.2.3 Mean diameter chart

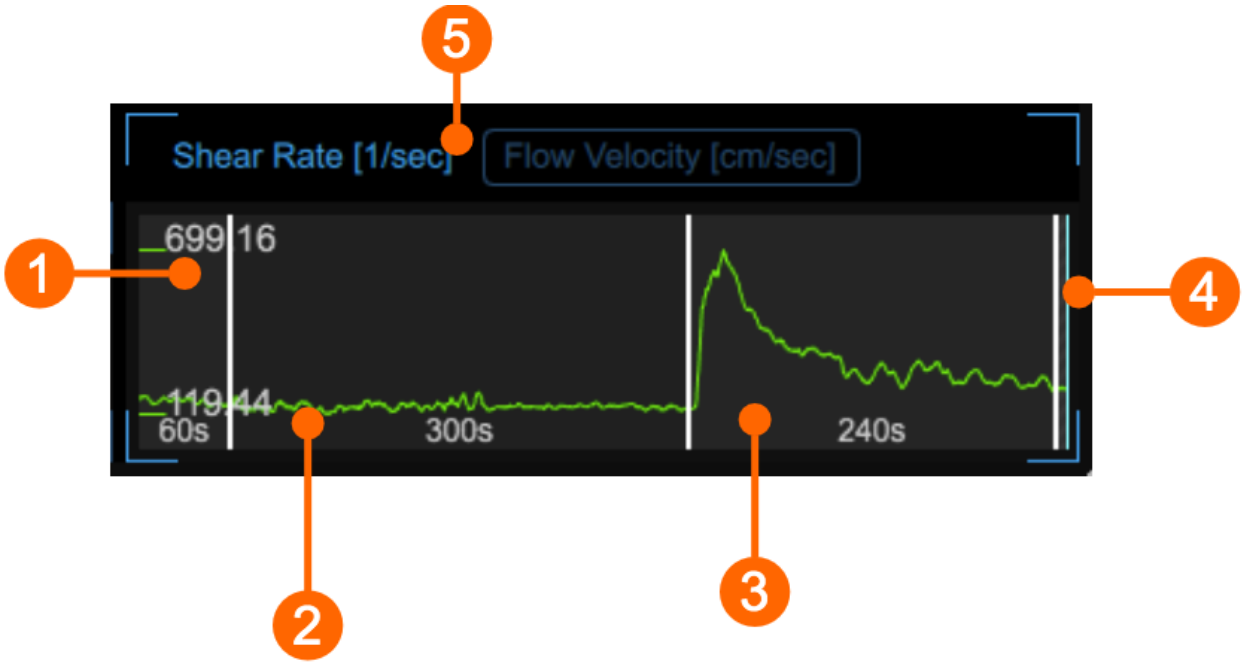


The chart shows the trend of the mean diameter during the examination. The chart is divided into three or two parts, according to the Studio modality. You have basal **(1)**, ischemia **(2)** and vasodilation **(3)** in FMD; ischemia is missing in "Vasodilation". In offline mode, a fourth part **(4)** may be present if the time length of the video is greater than the sum of the basal + (ischemia) + vasodilation.

The time length of the three (two) parts is set in the Time panel.

Using the buttons at the top right **(5)** you can move up  or down  the chart, enlarge  or reduce  the vertical scale or restore  the default view.

10.2.4 Shear rate chart

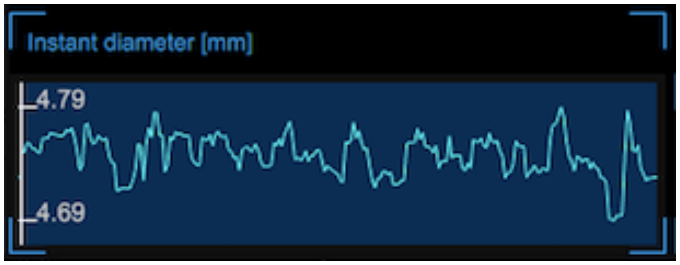


The graph shows the trend of the time averaged positive Shear Rate or the time averaged positive Flow Velocity during the examination. You can switch between the two view by the selector **(5)**.

The chart is divided into parts in a similar manner to the Mean diameter chart.

NOTE: the chart is enabled if the Doppler analysis has been enabled in the Doppler panel.

10.2.5 Instantaneous diameter chart



This chart shows the diameter changes within the cardiac cycle. The correct form of this chart is an index of measurement quality. The chart will automatically scale.

10.2.6 Setup panels

The Setup contains three panels with the commands to operate FMD Studio Analysis.

1. Time panel
2. B-Mode panel

3. Doppler panel

You can move among the panels by using the Next button and the Previous button. The Next button is enable only if you have set all the mandatory data in the panel.

After the Doppler Panel, you can start the analysis.

10.2.6.1 Time panel

In the Time Panel, you can choose the time length **(1)** of baseline, ischemia and vasodilation (ischemia is present only in "FMD" modality).

Once the time length have been set, click on the Next button to proceed.

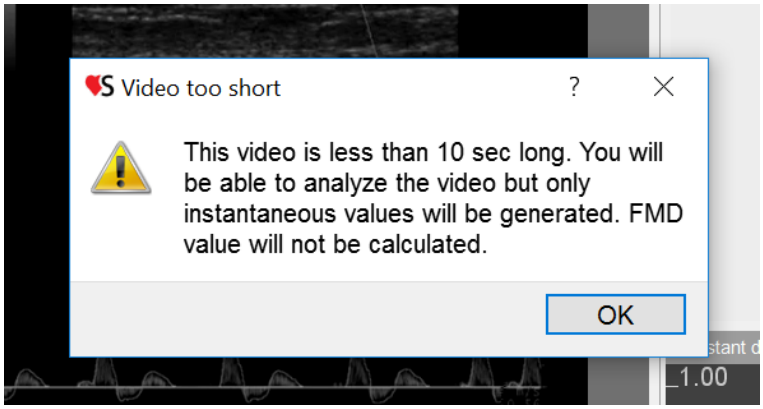
Timeline management

User can set and modify the time length entering values into the Text Fields **(1)** but also dragging one of the vertical cursors in graphs, as shown in the following picture:

FMD Studio allows the users to manage the timeline in a flexible way able to meet their clinical and/or research needs. There are constraints on the timeline in terms of minimum and maximum allowed values for each interval (you can not set values outside the allowed range and, if the video modality is "Offline analysis", the sum of the intervals cannot be grater than the time length of the video file under examination). There are also suggested minimum values: if the user decides to ignore this advice, the analysis will be performed anyway but there will be a yellow alert icon ( ) next to the values that may not be reliable in that configuration. In the following table allowed and suggested values are shown:

Timeline constraints (in seconds)			
	Baseline	*Ischemia*	*Vasodilation*
FMD	5* - 180	0 - 420	5** - 1200
Vasodilation	5* - 300	-	5 - 1500
* we suggest a basal period of at least 20 sec. ** we suggest a vasodilation period of at least 120 sec.			

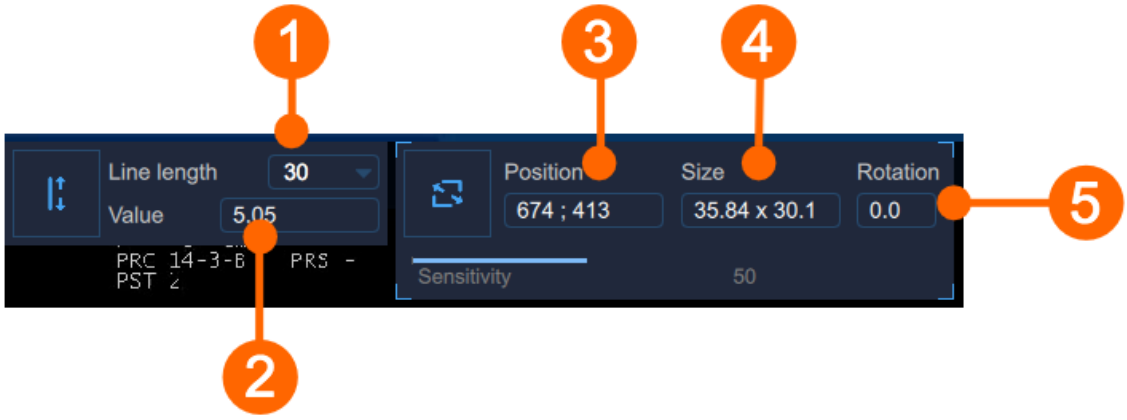
If the user uploads a video clip (for offline analysis) with a lower duration than the minimum allowed values (it means 10 seconds; 5 for baseline and 5 for vasodilation) an error message will appear: "This video is less than 10 sec long. You will be able to analyse the video but only instantaneous values will be generated. FMD value will not be calculated."



In this configuration user cannot set the timeline and characteristics parameters (i.e. FMD, FMDr, baseline diameter,...) will not be computed but only instantaneous values will be generated.

You can hover over the yellow icon ( ) or the red one ( ) and an informative message about the warning or error situation will be displayed.

10.2.6.2 B-Mode panel



The B-Mode Panel must be used to Calibrate the B-Mode image and to set the Diameter ROI.

Calibration

The Set B-Mode Calibration  button is used to Calibrate the B-Mode image.

The drop down menu **(1)** shows the length of the line used for the calibration.

The numeric display **(2)** shows the calibration value.

NOTE: if you click in the value field, you are allowed to manually enter the calibration value in the editable field (if you already know the value). The click the Save button to enter the values.

ROI

The Set B-Mode ROI  button is used to set the Diameter ROI.

The numeric display **(3)** shows the top-left position, in pixels, of the Diameter ROI (top-left corner).

The numeric display **(4)** shows the size (width x height), in pixels, of the Diameter ROI.

NOTE: if you click in the value field, you are allowed to manually enter the ROI position and size values in the editable fields (if you already know the values). The click the Save button to enter the values.

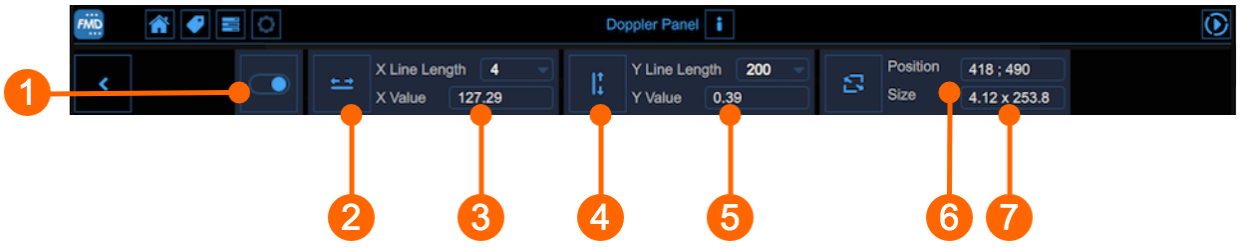
Rotation

The numeric displays **(5)** show the degree of rotation of the ROI.

NOTE: if you click in the value field, you are allowed to manually enter the degree value of rotation.

Once you have calibrated the B-Mode image and set the Diameter ROI, click on the Next button to proceed.

10.2.6.3 Doppler panel



The Doppler Panel must be used to Calibrate the Doppler flow and to set the Doppler flow ROI.

The switch **(1)** enables and disables the Doppler Flow analysis.

Calibration

The Set Doppler X-Calibration button is used to Calibrate the x-axis of the Doppler Flow.

The drop down menu **(2)** shows the length of the line used for the calibration.

The numeric display **(3)** shows the x-calibration value.

The Set Doppler Y-Calibration button is used to Calibrate the y-axis of the Doppler Flow.

The drop down menu **(4)** shows the length of the line used for the calibration.

The numeric display **(5)** shows the y-calibration value.

ROI

The Set Doppler Flow ROI  button is used to set the Doppler flow ROI.

The numeric display **(6)** shows the top-left position, in pixels, of the Doppler flow ROI (top-left corner).

The numeric display **(7)** shows the size (width x height), in pixels, of the Doppler flow ROI.

The analysis of the negative value is enabled by checking the "Compute negative values" **(8)** tick box.

The sensitivity of the Doppler Flow analysis algorithm is set by the slider **(9)**.

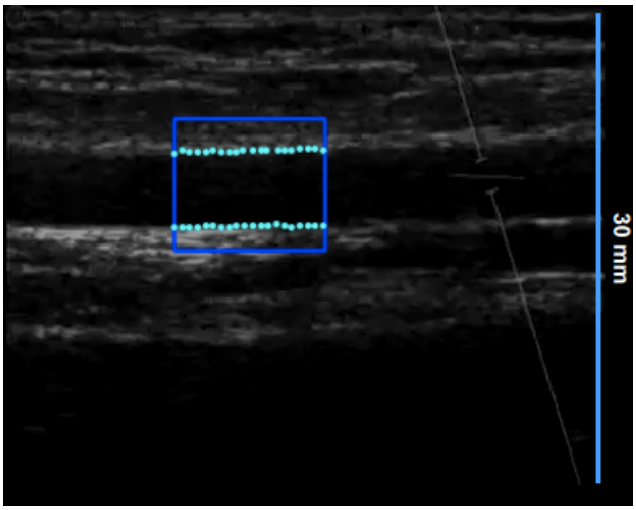
Once you have calibrated the B-Mode image and set the Diameter ROI, click on the Next  button to proceed.

10.2.7 Analysis panel

10.2.8 Calibrate the B-Mode image

The calibration of the images must be done before starting a new examination because it is necessary to provide information about the size of the image generated by ultrasound system. The calibration factor changes depending on the settings of your ultrasound machine. You should check the calibration at each new examination.

> ⚠ **CAUTION: the lack of calibration can generate a software malfunction.**



10.2.8.1 Calibrate the B-Mode image

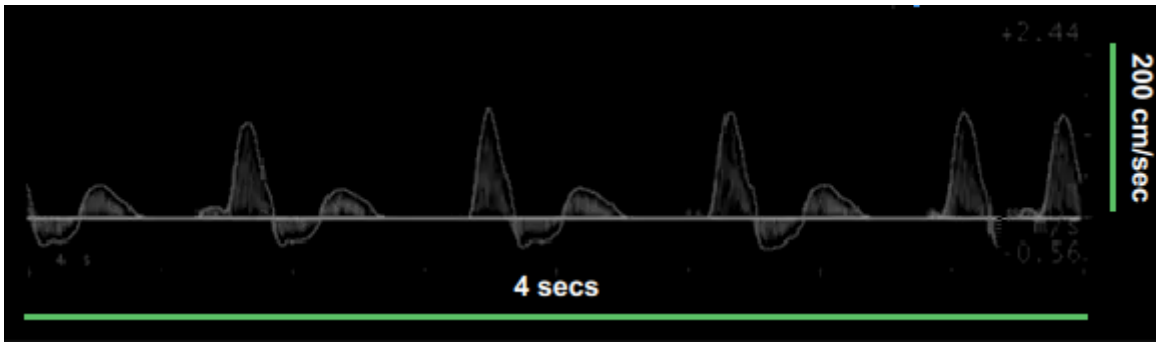
- Locate, in ultrasound image, a range of known distance (30 mm. in the example of figure).
- In the B-Mode panel, select from the drop-down menu, the distance specified above.
- In the B-Mode panel, click on the Set B-Mode Calibration  button (button remains active).
- Draw a line on the image corresponding to the known distance: click on one end and drag the mouse to the other extreme (press the Shift key or Ctrl+Shift keys on your keyboard if you want the line to be not vertical or horizontal).

NOTE: you can directly type the calibration value in the "calib" field of the B-Mode panel (if you already know the value).

10.2.9 Calibrate the Doppler flow

The calibration of the Doppler Flow analysis must be done before starting a new examination because it is necessary to provide information about the size of the Doppler waveform generated by ultrasound system. The calibration factor changes depending on the settings of your ultrasound machine. You should check the calibration at each new examination.

CAUTION: the lack of calibration can generate a software malfunction.



10.2.9.1 Calibrate the Doppler Flow

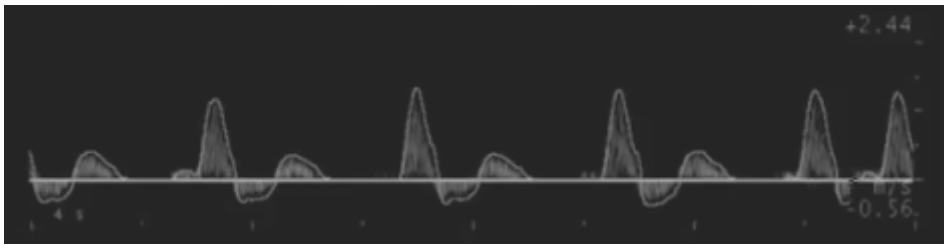
- Locate, on the x axis of the Doppler flow profile, a known time length (1 sec in the example in figure).
- In the Doppler panel, select from the "x-line length" drop-down menu, the time length specified above.
- In the Doppler panel, click on the Set Doppler X-Calibration  button (button remains active).
- Draw a line on the image corresponding to the known distance: click on one end and drag the mouse to the other extreme (press the Shift key on your keyboard if you want the line to be not horizontal).
- Locate, on the y axis of the Doppler flow profile, a known flow velocity value (200 cm/sec in the example in figure).
- In the Doppler panel, select from the "y-line length" drop-down menu, the flow velocity value specified above.
- In the Doppler panel, click on the Set Doppler Y-Calibration  button (button remains active).

- Draw a line on the image corresponding to the known distance: click on one end and drag the mouse to the other extreme (press the Shift key on your keyboard if you want the line to be not vertical).

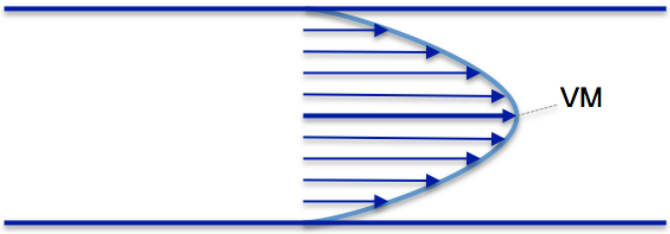
NOTE: you can directly type the calibration values in the "x-calib" and "y-calib" fields of the Doppler panel (if you already know the values).

10.2.10 Doppler flow analysis

FMD Studio computes the envelope of the Doppler flow velocity waveform over the time interval defined by the Doppler flow ROI. The result is used to compute the Time Average Wall Shear Rate.



We assume the velocity profile to be parabolic and we assume that the Doppler flow velocity waveform provides the maximum value (VM) of the velocity profile (i.e. the maximum spatial velocity). In fact, the analysis is based only on the Doppler flow envelope because the video image data does not give information on the velocity profile of the vessel.



Velocity Profile in a vessel

With this assumptions, the Shear Rate (SR) can be computed as:

$$SR = \frac{4 \cdot V}{d}$$

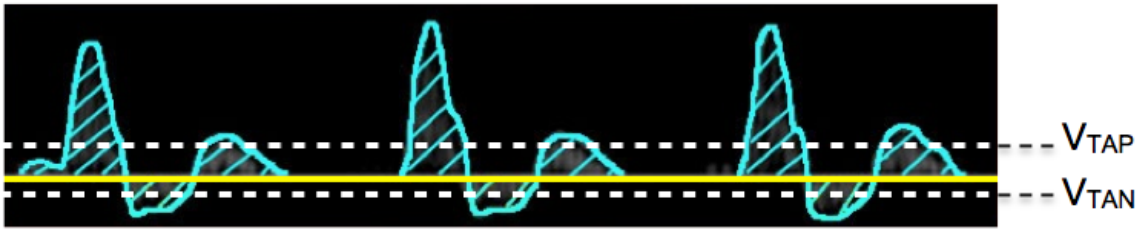
where d is the diameter of the vessel.

FMD Studio computes two values for velocity:

V_{TAP} : time averaged of the positive values of V.

V_{TAN} : time averaged of the negative values of V.

Both the averages are computed over the Doppler flow ROI.



These two values are used to compute the Shear Rate as:

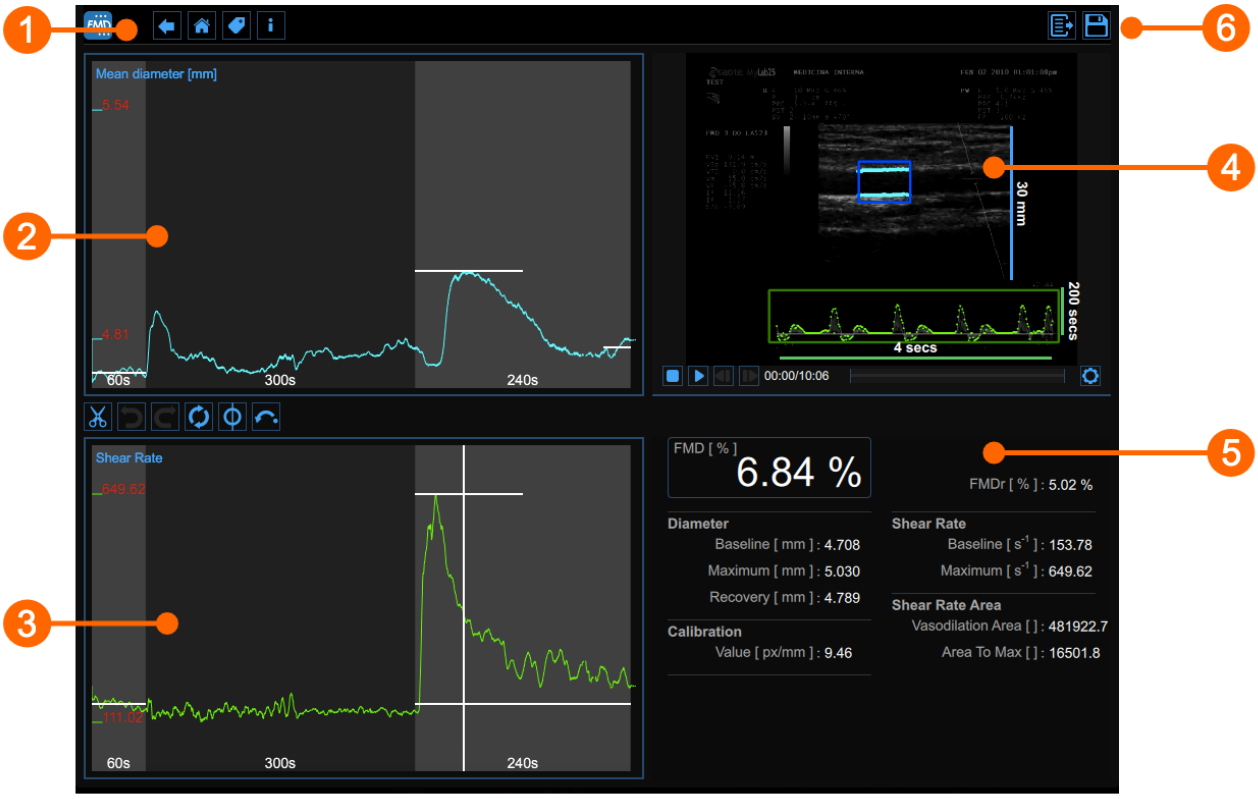
SR_{TAP} : Time Average Positive wall Shear Rate.

SR_{TAN} : Time Average Negative wall Shear Rate.

You can choose that FMD Studio will compute only the positive value or both the positive and the negative values (please see the Doppler panel).

NOTE: the possibility of computing both the positive and the negative flow velocity may depend on the settings of the ultrasound system.

10.3 Review



The Review window shows the result of the analysis and allows you to remove piece of data that are considered to be "outliers". This can happen, for example, if in a short time interval the patient did move and the brachial artery was not correctly displayed. In the Review window you can review both the images and the result of the analysis and decide to remove the data that were generated in this time interval.

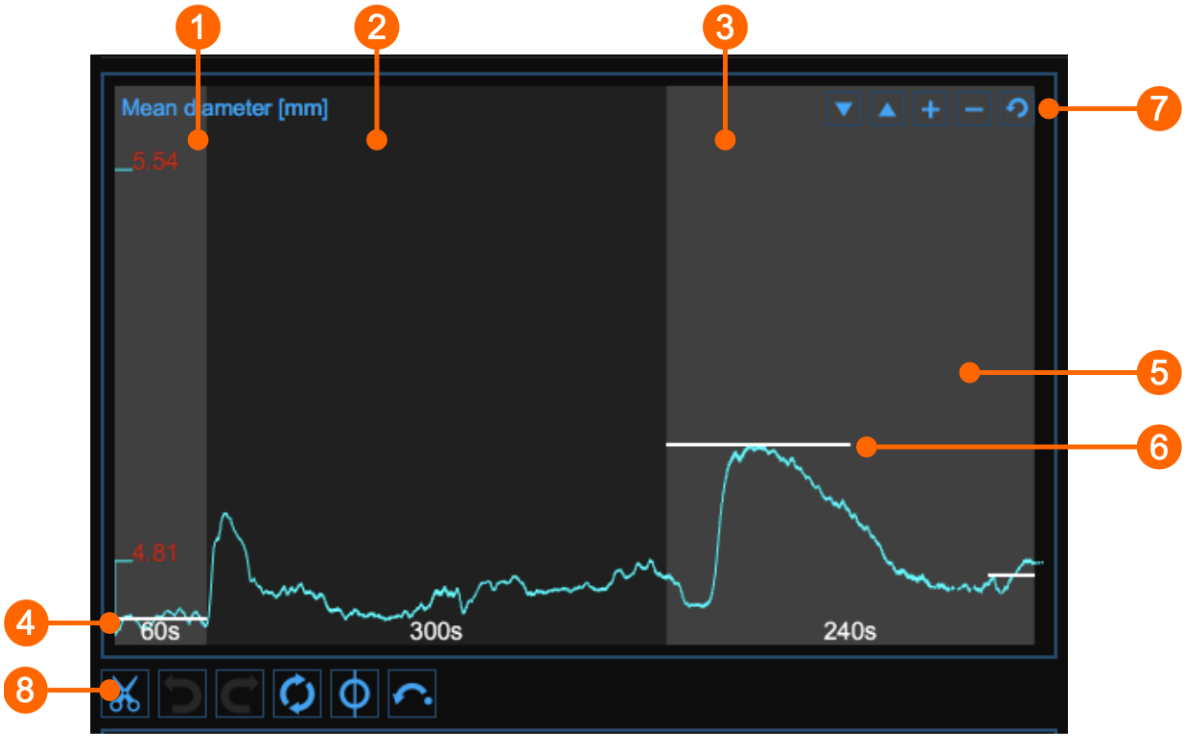
The Review window contains the following components:

1. Top bar
2. Mean diameter chart
3. Shear rate chart
4. Video window
5. Results and info panel
6. Export and save

10.3.1 Top bar

The top bar contains some essential information for the navigation. In the centre, the studio modality ("FMD" or "Vasodilation") is displayed. The document identification number is displayed on the right. The home button closes the FMD Studio application and returns to the home screen of Cardiovascular Suite. The back button closes the Carotid Studio application and comes back to the Archive.

10.3.2 Mean diameter chart



The chart shows the trend of the mean diameter during the examination. The chart is divided into three or two parts, according to the Studio modality. You have basal **(1)**, ischemia **(2)** and vasodilation **(3)** in FMD; ischemia is missing in "Vasodilation".

In the chart, three cursors are present (two cursors in "Vasodilation" study mode): the first one **(4)** is places at the baseline diameter value; the second one **(5)** is placed at the maximum diameter value in vasodilation; the third one **(6)** is places at the post baseline (this cursors is absent in "Vasodilation" study mode). Cardiovascular Suite places the cursors at the position automatically computed at the end of the analysis. You can manually reposition these values if you see that some outliers have affected the automatic analysis.

These values are shown in the Results panel.

Using the buttons at the top right **(7)** you can move up or down the chart, enlarge or reduce the vertical scale or restore the default view.

The buttons under the chart **(8)** can be used for editing the chart and removing the outliers.

10.3.2.1 Remove the outliers

- Click on the Cut  button.
- In the Mean diameter chart, click on one of the two extremes of the range to be deleted.
- Drag the mouse horizontally to the other extreme of the range to be deleted (see next paragraph for removal constraints).
- Once you have removed the outliers, click on the recompute  button if you want to reanalyse the data on the edited chart.

You can use the undo  and redo  buttons to cancel and restore your changes. The restore  button cancels all your changes and restore original data.

Note: Click on the Save  button in the Export and save are to save your changes to the document.

10.3.2.2 Graph cursors

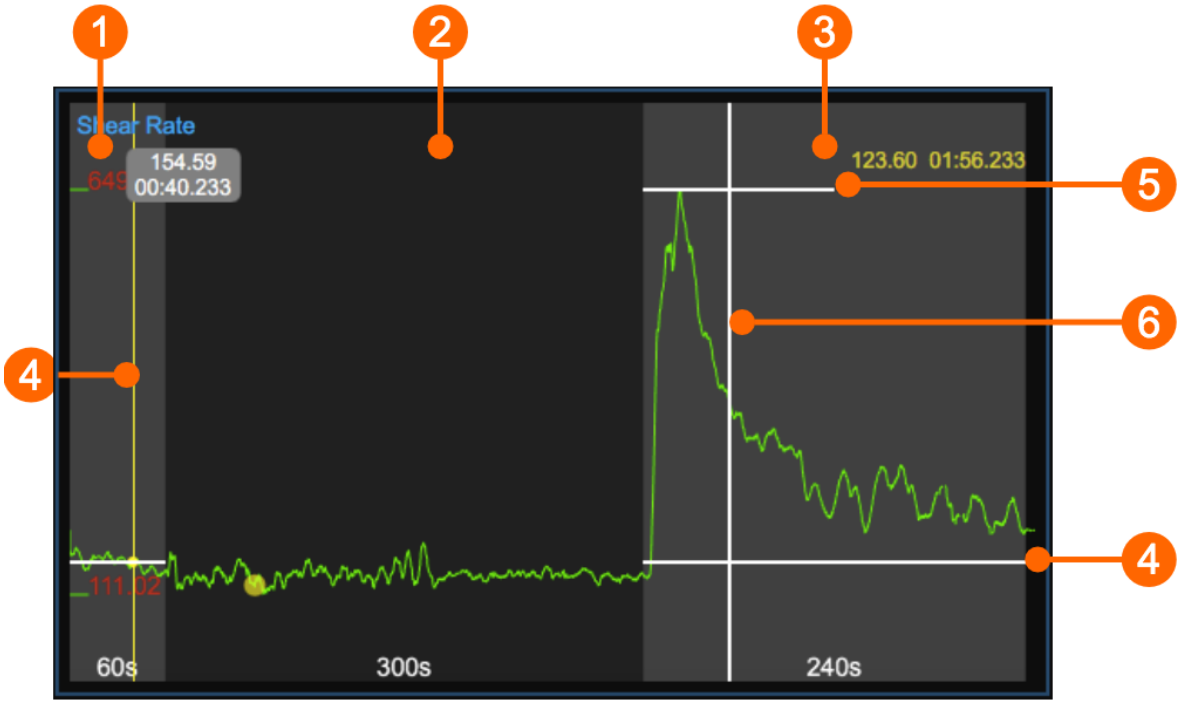
As shown in the following figure, the Cursor  button **(1)** activates a cursor **(2)** on the Mean Diameter chart that shows the current time position on the graph according to the images shown in the Video window. The coordinates (diameter value in millimeters and time value in the format *minutes:seconds.milliseconds*) of the cursor are dynamically updated and shown in **(3)**. When the Cursor button is active, it is also possible to know the coordinates of an exact point in the graph; it is only needed to hover over the chart and a second cursor **(4)** is displayed. It follows the mouse movements and the exact coordinates of the point are shown in the label **(5)** (diameter value is expressed in millimeters and the time value has the format *minutes:seconds.milliseconds*).

10.3.2.3 Alerts

In FMD Studio Review you can cut and delete data from the mean diameter chart. Please, note that timeline constraints are already valid (see ***Timeline management*** paragraph in Time panel).

After data removal, if there are intervals with a duration lower than the suggested value or than the allowed value, a yellow ( ) or red ( ), respectively, alert icon will appear next to the parameters that can be affected by the too short time interval. In addition, if the intervals do not meet the minimum duration allowed value some parameters will not be calculated. You can hover over the icons and an informative message about the warning or error situation will be displayed.

10.3.3 Shear rate chart



The chart shows the trend of the time averaged positive Shear Rate during the examination. The chart is divided into three or two parts, according to the Studio modality. You have basal **(1)**, ischemia **(2)** and vasodilation **(3)** in FMD; ischemia is missing in "Vasodilation".

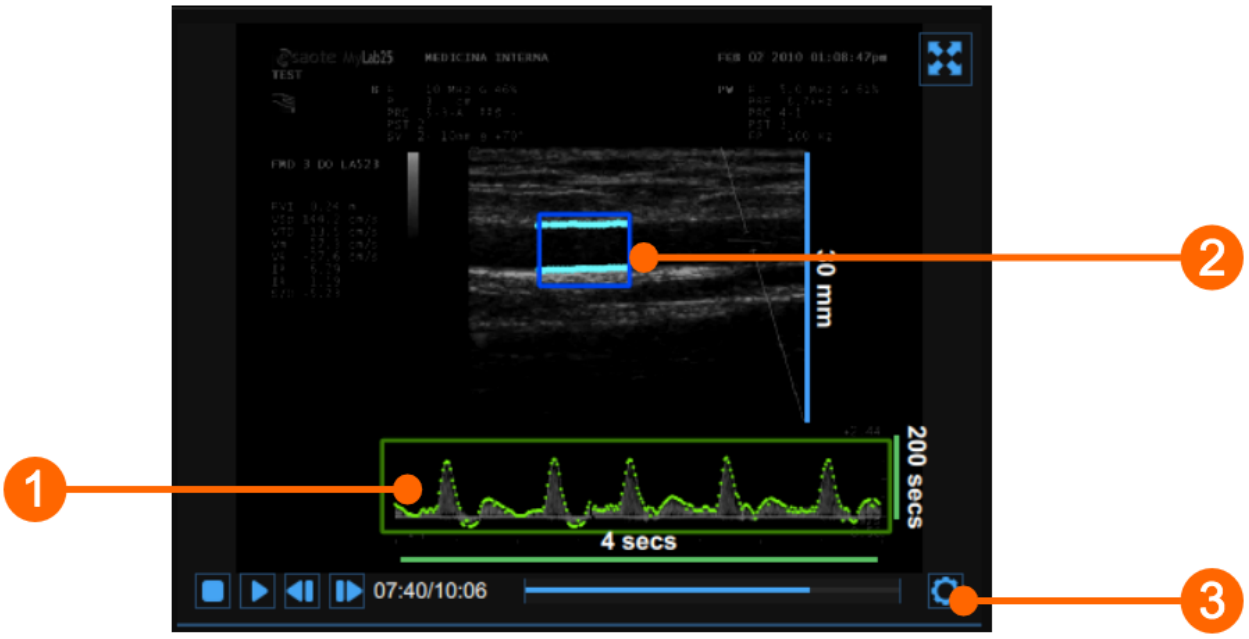
In the chart, three cursors are present (two cursors in "Vasodilation" study mode): the first one **(4)** is placed at the baseline value and it is reported also in the Vasodilation interval **(4)**; the second **(5)** one is placed at the maximum value in vasodilation; the third one **(6)** is placed at the time value corresponding to the maximum value of the diameter in the Mean diameter chart (this cursors is absent in "Vasodilation" study mode). Cardiovascular Suite places the cursors at the position automatically computed at the end of the analysis. You can manually reposition these values if you see that some outliers have affected the automatic analysis.

These values are shown in the Results panel.

10.3.3.1 Graph cursors

As shown in the following figure, the Cursor  button at the bottom of the Mean diameter chart activates a cursor **(1)** on the Shear Rate chart that shows the current time position on the graph according to the images shown in the Video window. The coordinates (shear rate value in s^{-1} and time value in the format *minutes:seconds.milliseconds*) of the cursor are dynamically updated and shown in **(2)**. When the Cursor button is active, it is also possible to know the coordinates of an exact point in the graph; it is only needed to hover over the chart and a second cursor **(3)** is displayed. It follows the mouse movements and the exact coordinates of the point are shown in the label **(4)** (shear rate value is expressed in $s^{-1}$and the time value has the format *minutes:seconds.milliseconds*).

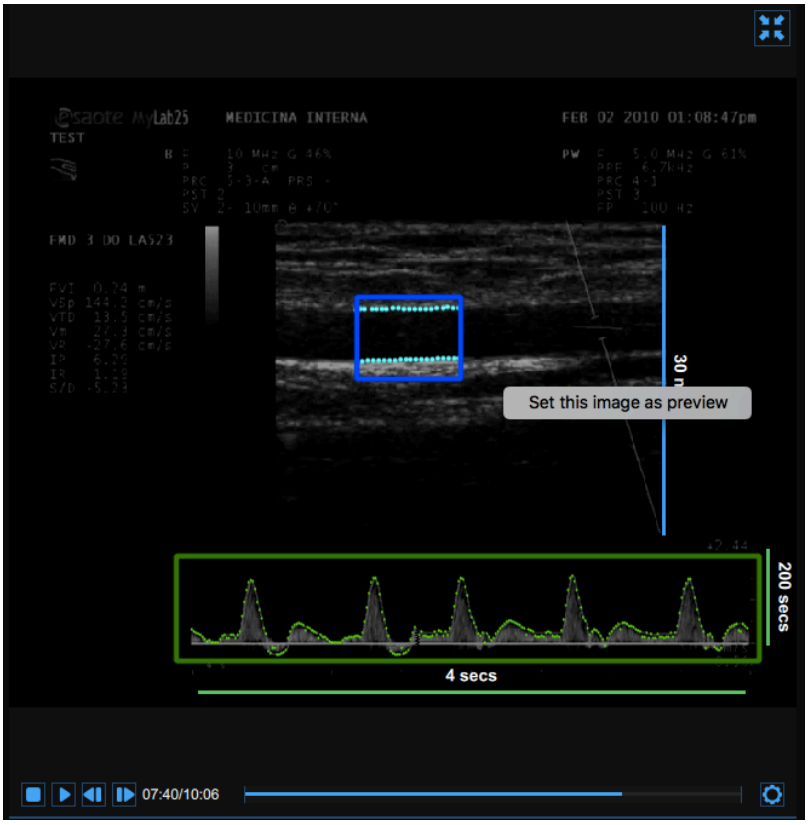
10.3.4 Video window



The video window shows the video signal from your ultrasound system. Two ROIs can be present in the window: the diameter ROI in blue **(1)** and the Doppler flow ROI in green **(2)**.

The Video control bar **(3)** is located at the bottom of the window.

If you want to expand the video window, you have to click on the Enlarge  button.

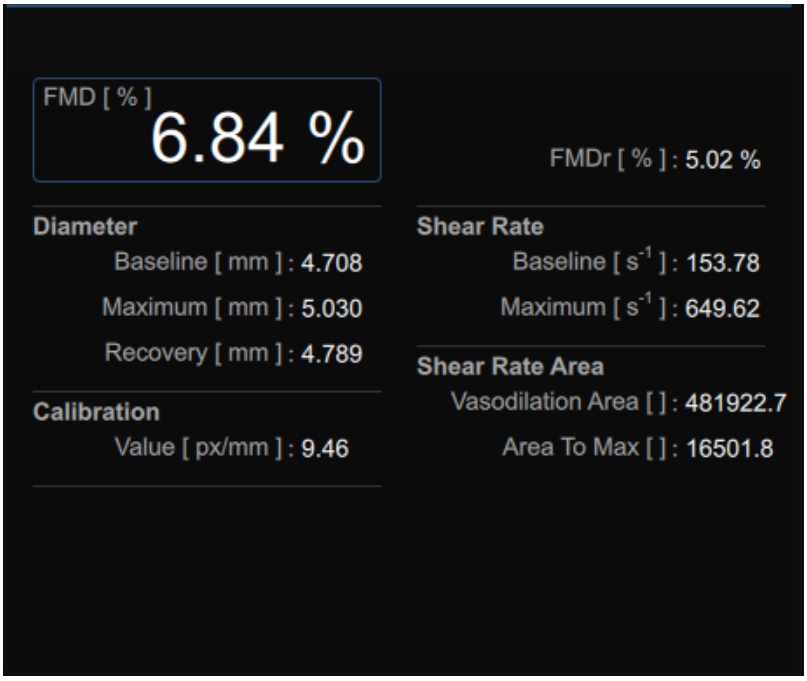


NOTE: if you perform right click on the video window and click on "Set this image as preview" the current frame will be saved and displayed in the Documents Table as document preview (see Studies management)

10.3.5 Results and info panel

This panel shows Results.

10.3.5.1 Results panel



The panel shows the results of the analysis. The following data are displayed:

- ***Baseline Diameter [mm]***: mean of the diameter values in the "Baseline" time interval.
- ***Maximum Diameter [mm]***: maximum diameter value in the "Vasodilation" time interval.
- ***Recovery Diameter [mm]***: mean of the last 30 seconds of diameter values available in the "Vasodilation" time interval.
- ***Baseline Shear Rate [s^{-1}]***: mean of the shear rate values in the Baseline time interval.
- ***Maximum Shear Rate[s^{-1}]***: maximum of the shear rate values in the Vasodilation time interval.
- ***Area [dimensionless]***: area under the curve of the shear rate in the Vasodilation time interval, calculated with reference to the baseline shear rate value (Figure 1).
- ***Area to Max [dimensionless]***: area under the curve of the shear rate in the time interval that begins with the Vasodilation and ends at the time of the Maximum Diameter, calculated with reference to the baseline shear rate value (Figure 2).
- ***FMD [%]: Flow Mediated Dilation***

$$FMD = \frac{Maximum\ Diameter - Baseline\ Diameter}{Baseline\ Diameter}$$

- ***FMDr [%]: Flow Mediated Dilation with respect to the Recovery Diameter***

$$FMD_r = \frac{Maximum\ Diameter - Recovery\ Diameter}{Recovery\ Diameter}$$

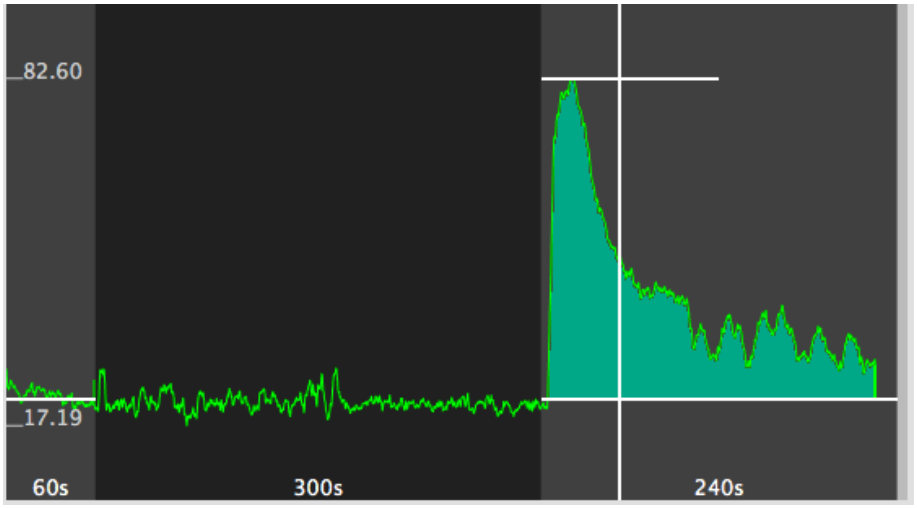


Figure 1: Area

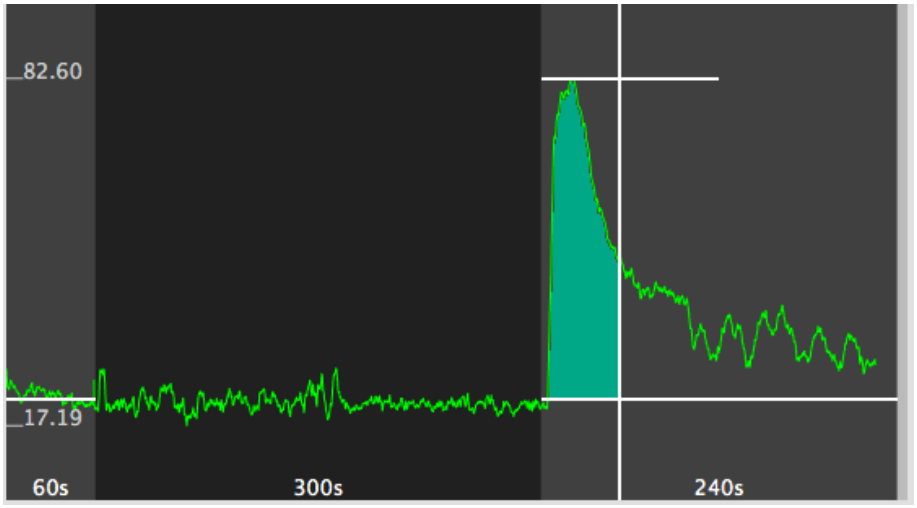


Figure 2: Area to Max

These data can be exported in the Document Data. Please see Export and save.

In addition, there is also the Calibration value in px/mm.

10.3.5.2 Other info panel

Clicking on the icon  a window containing information about the study will appear.

The panel shows the information about the study, the document, the patient, the operator and the institute.

10.3.6 Export and save

The Save  button is used to save your changes to the document, once you have edited the data.

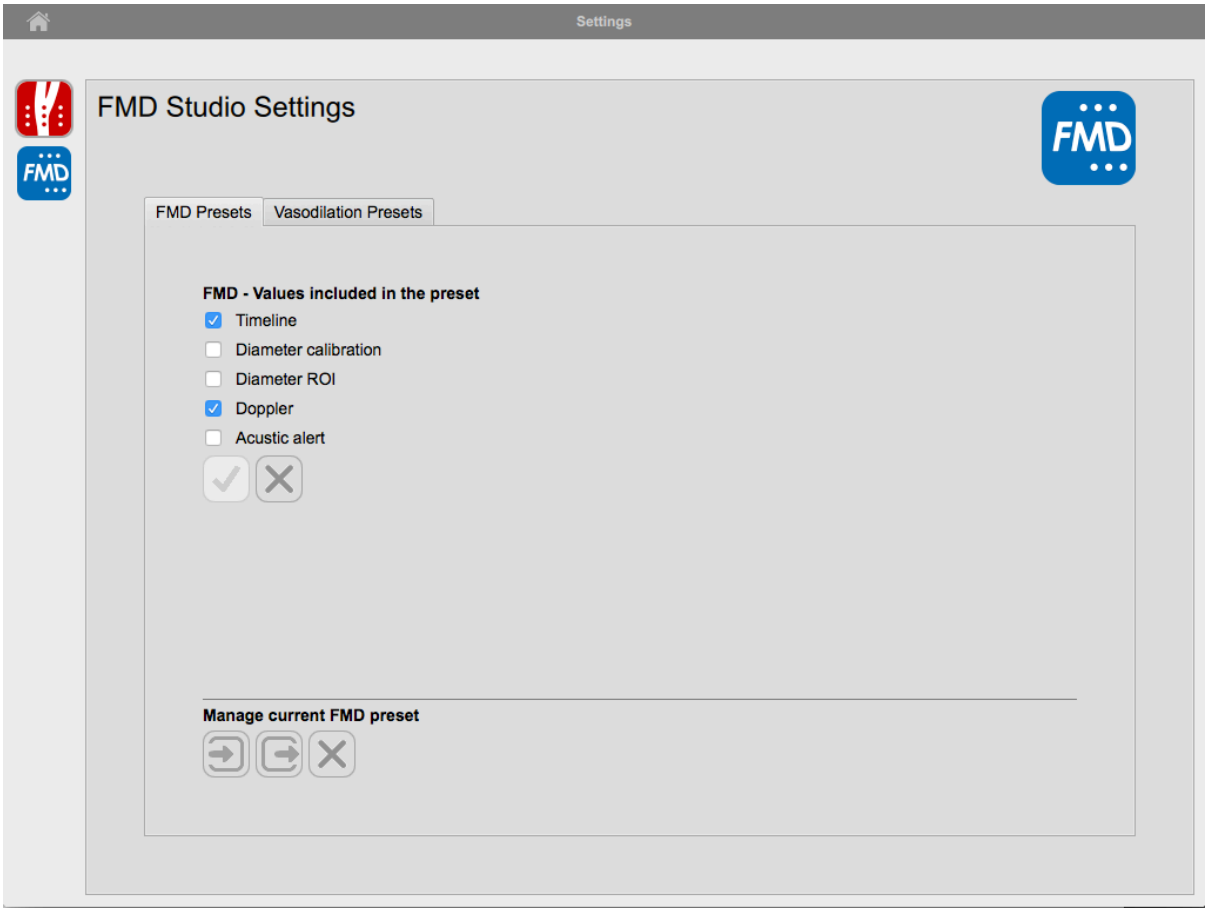
The Export  button is used to export your data. You can export the Document Results and the Document Data.

The **Document Results** contains all the results of the analysis and all the information about the study, the document and the patient.

The **Document Data** contains all the Document Results, a list of the Mean Diameter, the Shear Rate and the Doppler Velocity (one value per second) and the Diameter and the Doppler Velocity values computed at each frame.

NOTE: Only the diameter values are actual instantaneous values because they are computed on the single images. The Doppler Velocity **is actually a Time averaged value**. In fact, despite it is calculated on the single image, it is computed in the time interval defined by the Doppler flow ROI. For more info, please see Doppler flow analysis.

10.4 FMD Studio settings



FMD Studio can remember the values that you enter in the Setup panels. You can decide whether or not to remember the current values by the special thick box in the Analysis panel. If you check this tick box, FMD Studio will create a preset that is used every time you start a new analysis.

In the FMD Studio Settings, you can decide which values are included in the preset. The values are:

- Timeline (baseline, ischemia, vasodilation)
- Diameter calibration
- Diameter ROI
- Doppler settings
- Acoustic alert

The options are available for FMD and Vasodilation modes.

Select/deselect the values that you want to include/not include in the preset, then click on the Apply button.

Click on the Reset to Default button to restore the default selection.

In the lower part of the windows, you can manage the current preset.

- Click on the Export button to save the current preset as a new file.
- Click on the Import button to import a preset from a file.

- Click on the Reset  button to cancel the current preset and to restore the default preset.

11 Warnings

WARNING

This software may provide incorrect results in the following cases: i) if the images acquired by the operator are not of sufficient quality, they have been acquired through a machine or an ultrasound probe not adequate or by an operator who is not sufficiently experienced; ii) if the user does not perform the basic operations required, such as calibration and proper tracking of initial contours.

Essential requirement for a correct analysis is the operation of the device. In case of a fault i) close and reopen the application software, or ii) restart the computer where the software is installed and open the application again iii) contact your dealer for assistance.

Any malfunction of the device, however, does not affect the state of health of the patient.

The user has the responsibility to check the accuracy of the external ultrasound images to avoid the possibility of generating an incorrect diagnosis.

The software device must be used in an environment that allows optimal visibility of the screen. The ambient noise level must be below the 35 dB.

The software device has a limited life span, estimated at 5 years.

12 References

Gemignani V, Faita F, Ghiadoni L, Poggianti E, Demi M.

“A system for real-time measurement of the brachial artery diameter in B-mode ultrasound images.”

IEEE Trans Med Imaging. 2007 Mar;26(3):393-404.

Gemignani V, Bianchini E, Faita F, Giannarelli C, Plantinga Y, Ghiadoni L, Demi M.

“Ultrasound measurement of the brachial artery flow-mediated dilation without ECG gating”

Ultrasound Med Biol. 2008 Mar;34(3):385-91. Epub 2007 Oct 26.

Faita F, Gemignani V, Bianchini E, Giannarelli C, Ghiadoni L, Demi M.

“Real-time measurement system for evaluation of the carotid intima-media thickness with a robust edge operator.”

J Ultrasound Med. 2008 Sep;27(9):1353-61

Bianchini E, Bozec E, Gemignani V, Faita F, Giannarelli C, Ghiadoni L, Demi M, Boutouyrie P, Laurent S.

“Assessment of carotid stiffness and intima-media thickness from ultrasound data: comparison between two methods.”

J Ultrasound Med. 2010 Aug;29(8):1169-75.

Faita F, Masi S, Loukogeorgakis S, Gemignani V, Okorie M, Bianchini E, Charakida M, Demi M, Ghiadoni L, Deanfield JE.

“Comparison of two automatic methods for the assessment of brachial artery flow-mediated dilation.”

J Hypertens. 2011 Jan;29(1):85-90.

Ghiadoni L, Faita F, Salvetti M, Cordiano C, Biggi A, Puato M, Di Monaco A, De Siati L, Volpe M, Ambrosio G, Gemignani V, Muiesan M, Taddei S, Lanza GA, Cosentino F.

“Assessment of Flow-Mediated Dilation Reproducibility: a Nationwide Multicenter Study".

J Hypertens. 2012 Jul;30(7):1399-405

Charakida M, Masi S, Lüscher TF, Kastelein JJ, Deanfield JE.

“Assessment of atherosclerosis: the role of flow-mediated dilatation.”

Eur Heart J. 2010 Dec;31(23):2854-61. Epub 2010 Sep 23.

Yeboah J, Crouse JR, Hsu FC, Burke GL, Herrington DM.

“Brachial flow-mediated dilation predicts incident cardiovascular events in older adults: the Cardiovascular Health Study.”

Circulation. 2007 May 8;115(18):2390-7. Epub 2007 Apr 23.

O'Leary DH, Bots ML.

“Imaging of atherosclerosis: carotid intima-media thickness.”

Eur Heart J. 2010 Jul;31(14):1682-9. Epub 2010 Jun 11.

Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA, Asmar R, Reneman RS, Hoeks AP, Breteler MM, Witteman JC.

“Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study.”

Circulation. 2006 Feb 7;113(5):657-63.

13 Contacts

13.1 Quipu S.r.l.

13.1.1 *Address:*

13.1.2 via Moruzzi 1

13.1.3 I-56124 Pisa Italy

13.1.4 *Telephone:*

13.1.5 (+39) 050 315 2612

13.1.6 *Web:*

www.quipu.eu

info@quipu.eu

14 Notes

14.1 Trademarks

Cardiovascular Suite, FMD Studio and Carotid Studio are trademarks of Quipu srl.

Mac, OS X and macOS are registered trademarks of Apple Inc.

Microsoft and Windows are either registered trademarks or trademarks of Microsoft Corporation in the United States and/or other countries.

AV.io HD is a trademark of Epiphan Systems Inc.

Magewell is a trademark of Nanjing Magewell Electronics Co.

HDMI is a trademark of HDMI Licensing LLC.

14.2 EULA

End user license agreement for Cardiovascular Suite

Document number: LEG0001EN rev. 4 of May 8, 2018

Please read this EULA carefully, as it sets out the basis upon which we license the Software for use.

By clicking "accept agreement" when you first install the Software, you agree to be bound by the provisions of this EULA. If you do not agree to be bound by the provisions of this EULA, you must stop the installation now.

By agreeing to be bound by this EULA, you further agree that any person you authorize to use the Software will comply with the provision of this EULA.

By agreeing to be bound by this EULA, you hereby acknowledge that you are familiar with and agree to the terms of the Licensor's privacy policy available at http://www.quipu.eu/privacy-policy/

14.2.1 Definitions

1.1 Except to the extent expressly provided otherwise, in this EULA:

"**Commercial License**" means a license to use Software obtained or renewed by the User by paying fees;

"**Documentation**" means the documentation for the Software produced by the Licensor and delivered or made available by the Licensor to the User;

"**EULA**" means this end user license agreement, including any amendments to this end user license agreement from time to time;

"**Effective Date**" means the date upon which the User gives the User's express consent to this EULA, following the issue of this EULA by the Licensor;

"Expiry Date" means such date as may be the ending of the usage of the Software.

"Evaluation License" means a 14 days license according to this EULA, limited only for evaluation of the Software purposes, in accordance with Clause 5.

"**Force Majeure Event**" means an event, or a series of related events, that is outside the reasonable control of the party affected (including failures of the internet or any public telecommunications network, hacker attacks, denial of service attacks, virus or other malicious Software attacks or infections, power failures,

industrial disputes affecting any third party, changes to the law, disasters, explosions, fires, floods, riots, terrorist attacks and wars);

"**Intellectual Property Rights**" means all intellectual property rights wherever in the world, whether registrable or unregistrable, registered or unregistered, including any application or right of application for such rights (and these "intellectual property rights" include copyright and related rights, database rights, confidential information, trade secrets, know-how, business names, trade names, trade marks, service marks, passing off rights, unfair competition rights, patents, petty patents, utility models, semi-conductor topography rights and rights in designs);

"**Licensor**" means Quipu s.r.l., a company incorporated in Italy (registration number 01995110507) having its registered office at via Moruzzi 1 I-56124 Pisa – Italy;

"**License Key**" means a piece of hardware (USB dongle) provided by the Licensor, which must be plugged into a USB port of the computer where the Software is installed and allows the Software to run.

"**Perpetual License**" means a license with no specified term or expiration.

"**Software**" means the Software Cardiovascular Suite.

"**Software Defect**" means a defect, error or bug in the Software having an adverse effect on the appearance, operation, functionality or performance of the Software, but excluding any defect, error or bug caused by or arising as a result of:

- any act or omission of the User;
- any use of the Software contrary to the Documentation by the User or any person authorized by the User to use the Software;
- a failure of the User to perform or observe any of its obligations in this EULA; and/or
- an incompatibility between the Software and any other system, network, application, program, hardware or Software not specified as compatible in the Software Specification;

"**Software Specification**" means the specification for the Software set out in the Documentation;

"**Source Code**" means the Software code in human-readable form or any part of the Software code in human-readable form, including code compiled to create the Software or decompiled from the Software, but excluding interpreted code comprised in the Software;

"**Term**" means the term of this EULA, commencing in accordance with Clause 2.1 and ending in accordance with Clause 2.2;

"**Time License**" means a time limited license that is granted until the expiry date.

"**Update**" means a hotfix, patch or minor version update to the Software;

"**Upgrade**" means a major version upgrade of the Software;

"**User**" means the person to whom the Licensor grants a right to use the Software under this EULA;

14.2.2 Term

2.1 This EULA shall come into force upon the Effective Date.

2.2 This EULA shall continue in force:

- indefinitely, for Perpetual Licenses; or
- until the expiry date, for Time Licenses; or
- 14 days, for Evaluation Licenses;

subject to termination in accordance with Clause 12.

14.2.3 License

3.1 The Licensor hereby grants to the User from the date of supply of the Software to the User until the end of the Term a worldwide, non-exclusive license to:

- install a single instance of the Software;
- use a single instance of the Software in accordance with the Documentation; and
- create, store and maintain up to 5 back-up copies of the Software,

subject to the limitations and prohibitions set out and referred to in this Clause 3.

3.2 The User may not sub-license and must not purport to sub-license any rights granted under Clause 3.1 without the prior written consent of the Licensor.

3.3 Save to the extent expressly permitted by this EULA or required by applicable law on a non-excludable basis, any license granted under this Clause 3 shall be subject to the following prohibitions:

- the User must not sell, resell, rent, lease, loan, supply, publish, distribute or redistribute the Software;
- the User must not alter, edit or adapt the Software; and
- the User must not decompile, de-obfuscate or reverse engineer, or attempt to decompile, de-obfuscate or reverse engineer, the Software;

14.2.4 Restrictions of use of the License Key

4.1 The Software will run under a commercial license only if the License Key is plugged into the computer where the Software is installed; if the License Key is disconnected, the Software will stop working;

4.2 The License Key will work only on the computer where it is used for the first time (i.e. it will be locked to this computer);

4.3 The License Key can be unlocked by the Licensor, so to be locked again to a new computer, maximum three times a year.

14.2.5 Restrictions of the Evaluation License

5.1 Under the Evaluation License, the User agrees to use the Software only for evaluation purposes.

5.2 The User cannot use/publish/distribute data generated by the Software in the period of time when the Evaluation License is in force, unless the User purchases a Commercial License.

14.2.6 Updates and upgrades

6.1 Licensor may, in its sole discretion, provide Updates (hotfix, patch or minor version update) of the Software; the User is entitled to receive and run Updates of the Software during the Term;

6.2 Licensor may, in its sole discretion, provide Upgrades (major version upgrade) of the Software; in order to be entitled to receive and run Upgrades of the Software, the User must subscribe a separate upgrade agreement;

14.2.7 Source Code

7.1 Nothing in this EULA shall give to the User or any other person any right to access or use the Source Code or constitute any license of the Source Code.

14.2.8 No assignment of Intellectual Property Rights

8.1 Nothing in this EULA shall operate to assign or transfer any Intellectual Property Rights from the Licensor to the User, or from the User to the Licensor.

14.2.9 Warranties

9.1 The Licensor warrants to the User that it has the legal right and authority to enter into this EULA and to perform its obligations under the EULA.

9.2 The User warrants to the Licensor that it has the legal right and authority to enter into this EULA and to perform its obligations under the EULA.

9.3 All of the parties' warranties and representations in respect of the subject matter of this EULA are expressly set out in this EULA. To the maximum extent permitted by applicable law, no other warranties or representations concerning the subject matter of this EULA will be implied into the EULA or any related contract.

14.2.10 Acknowledgements and warranty limitations

10.1 The User acknowledges that complex Software is never wholly free from defects, errors and bugs; and subject to the other provisions of this EULA, the Licensor gives no warranty or representation that the Software will be wholly free from defects, errors and bugs.

10.2 The User acknowledges that complex Software is never entirely free from security vulnerabilities; and subject to the other provisions of this EULA, the Licensor gives no warranty or representation that the Software will be entirely secure.

10.3 The User acknowledges that the Software is only designed to be compatible with that Software specified as compatible in the Software Specification; and the Licensor does not warrant or represent that the Software will be compatible with any other Software.

10.4 The User acknowledges that the Licensor will not provide any legal, financial, accountancy or taxation advice under this EULA or in relation to the Software; and, except to the extent expressly provided otherwise in this EULA, the Licensor does not warrant or represent that the Software or the use of the Software by the User will not give rise to any legal liability on the part of the User or any other person.

10.5 The User acknowledges that is fully responsible of protecting the License Key against loss and damage; in case of malfunction, the User will be entitled to obtain a replacement License Key only if the original defective License Key is returned to the Licensor by a trackable courier service; when the malfunction of the License Key is due by the User, the User will be charged of a cost of 80 EUR plus shipping cost for the replacement.

14.2.11 Limitations and exclusions of liability

11.1 Nothing in this EULA will:

- limit or exclude any liability for death or personal injury resulting from negligence;
- limit or exclude any liability for fraud or fraudulent misrepresentation;
- limit any liabilities in any way that is not permitted under applicable law; or
- exclude any liabilities that may not be excluded under applicable law,

and, if a party is a consumer, that party's statutory rights will not be excluded or limited by the EULA, except to the extent permitted by law.

11.2 The limitations and exclusions of liability set out in this Clause 11 and elsewhere in this EULA:

1. are subject to Clauses 11.1 and 14.6; and
2. govern all liabilities arising under the EULA or relating to the subject matter of the EULA, including liabilities arising in contract, in tort (including negligence) and for breach of statutory duty, except to the extent expressly provided otherwise in the EULA.

11.3 The Licensor will not be liable to the User in respect of any losses arising out of a Force Majeure Event.

11.4 The Licensor will not be liable to the User in respect of any loss of profits or anticipated savings.

11.5 The Licensor will not be liable to the User in respect of any loss of revenue or income.

11.6 The Licensor will not be liable to the User in respect of any loss of business, contracts or opportunities.

11.7 The Licensor will not be liable to the User in respect of any loss or corruption of any data, database or Software.

11.8 The Licensor will not be liable to the User in respect of any special, indirect or consequential loss or damage.

11.9 The liability of the Licensor to the User under this EULA in respect of any event or series of related events shall not exceed the greater of:

- *1 EUR*; and
- the total amount paid and payable by the User to the Licensor under the EULA in the 12 months period preceding the commencement of the event or events.

11.10 The aggregate liability of the Licensor to the User under this EULA shall not exceed the greater of:

- *1 EUR*; and
- the total amount paid and payable by the User to the Licensor under the EULA.

14.2.12 Termination

12.1 Either party may terminate this EULA immediately by giving written notice of termination to the other party if the other party commits any breach of the EULA.

12.2 Either party may terminate this EULA immediately by giving written notice of termination to the other party if:

- the other party:

1. is dissolved;
2. ceases to conduct all (or substantially all) of its business;
3. is or becomes unable to pay its debts as they fall due;
4. is or becomes insolvent or is declared insolvent; or
5. convenes a meeting or makes or proposes to make any arrangement or composition with its creditors;

- an administrator, administrative receiver, liquidator, receiver, trustee, manager or similar is appointed over any of the assets of the other party;
- an order is made for the winding up of the other party, or the other party passes a resolution for its winding up (other than for the purpose of a solvent company reorganization where the resulting entity will assume all the obligations of the other party under the EULA);
- if that other party is an individual:

1. that other party dies;
2. as a result of illness or incapacity, that other party becomes incapable of managing his or her own affairs; or
3. that other party is the subject of a bankruptcy petition or order.

12.3 The Licensor may terminate this EULA immediately by giving written notice to the User if:

- any amount due to be paid by the User to the Licensor under the EULA is unpaid by the due date and remains unpaid upon the date that that written notice of termination is given; and

- the Licensor has given to the User at least 30 days' written notice, following the failure to pay, of its intention to terminate the EULA in accordance with this Clause 12.

14.2.13 Effects of termination

13.1 Upon the termination of this EULA, all of the provisions of this EULA shall cease to have effect, save that the following provisions of this EULA shall survive and continue to have effect (in accordance with their express terms or otherwise indefinitely): Clauses 1, 3.1, 11, 13, 14, 15.

13.2 The termination of this EULA shall not affect the accrued rights of either party.

13.3 For the avoidance of doubt, the licenses of the Software in this EULA shall terminate upon the termination of this EULA; and, accordingly, the User must immediately cease to use the Software upon the termination of this EULA.

13.4 Within 10 Business Days following the termination of this EULA, the User must:

- return to the Licensor or dispose of as the Licensor may instruct all media in its possession or control containing the Software; and
- irrevocably delete from all computer systems in its possession or control all copies of the Software.

14.2.14 General

14.1 No breach of any provision of this EULA shall be waived except with the express written consent of the party not in breach.

14.2 If any provision of this EULA is determined by any court or other competent authority to be unlawful and/or unenforceable, the other provisions of the EULA will continue in effect. If any unlawful and/or unenforceable provision would be lawful or enforceable if part of it were deleted, that part will be deemed to be deleted, and the rest of the provision will continue in effect (unless that would contradict the clear intention of the parties, in which case the entirety of the relevant provision will be deemed to be deleted).

14.3 This EULA may not be varied except by a written document signed by or on behalf of each of the parties.

14.4 Neither party may without the prior written consent of the other party assign, transfer, charge, license or otherwise deal in or dispose of any contractual rights or obligations under this EULA.

14.5 This EULA is made for the benefit of the parties, and is not intended to benefit any third party or be enforceable by any third party. The rights of the parties to terminate, rescind, or agree any amendment, waiver, variation or settlement under or relating to this EULA are not subject to the consent of any third party.

14.6 Nothing in this EULA shall exclude or limit any liability of a party for fraud or fraudulent misrepresentation, or any other liability of a party that may not be excluded or limited under applicable law.

14.7 Subject to Clauses 11.1 and 14.6, this EULA shall constitute the entire agreement between the parties in relation to the subject matter of this EULA, and shall supersede all previous agreements, arrangements and understandings between the parties in respect of that subject matter.

14.8 This EULA shall be governed by and construed in accordance with Italian law.

14.9 The courts of justice of Pisa - Italy shall have exclusive jurisdiction to adjudicate any dispute arising under or in connection with this EULA.

14.2.15 Interpretation

15.1 In this EULA, a reference to a statute or statutory provision includes a reference to:

- that statute or statutory provision as modified, consolidated and/or re-enacted from time to time; and
- any subordinate legislation made under that statute or statutory provision.

15.2 The Clause headings do not affect the interpretation of this EULA.

15.3 In this EULA, general words shall not be given a restrictive interpretation by reason of being preceded or followed by words indicating a particular class of acts, matters or things.

14.2.16 Privacy Policy

16.1 By agreeing to be bound by this EULA, you hereby acknowledge that you are familiar with and agree to the terms of the Licensor's Privacy Policy available at http://www.quipu.eu/privacy-policy/.

16.2 This document is not the official document of Privacy Policy of the Licensor. For further information, please see the Privacy Policy in the footer of the Licensor's website.

16.3 The Licensor collects User information to communicate with User about the Licensor's products, services and promotions. Personal data are also collected by the Licensor for the Software evaluation license and the Software activation license. The Licensor does not sell or rent User's personal information to third parties. The Licensor does, however, share User's information with third parties that provide services on Licensor's behalf or with whom the Licensor has partnered to offer a particular product or service.

16.4 Personal data collected are also needed for the Licensor to guarantee traceability of the medical device.

16.5 If the Licensor privacy policy changes, the Licensor shall post an updated version on Licensor's website. The policy revision date will be posted at the top of the page.

16.6 It is important to inform you that you are the only owner and responsible of data collected by your instance of the Software. These data may include personal data of the analyzed subjects that shall be managed according to the GDPR regulation https://gdpr-info.eu/.

14.3 Privacy policy

Privacy policy

Document number: LEG0003EN rev. 4 of May 25, 2018

Quipu s.r.l. is committed to safeguarding the privacy of our customers and website visitors; this policy sets out how we will treat your personal information.

Our website uses cookies. By using our website and agreeing to this policy, you consent to our use of cookies in accordance with the terms of this policy.

14.3.1 1. What information do we collect?

We may collect, store and use the following kinds of personal information:

1. information that you provide to us when you purchase one of our products (including Name, Company, Address, Email, Phone number);
2. information relating to any transactions carried out between you and us, including information relating to any purchases you make of our goods or services;

3. information that you provide to us for the purpose of using our free trial software (including Name, Company, Address, Email, Phone number, City, State, Country);
4. information that you provide to us for the purpose of get an evaluation license (including First Name, Last Name, Company, Address, Email, Phone number, City, State, Country);
5. information that you provide to us for the purpose of activate license (including First Name, Last Name, Company, Address, Email, Phone number, City, State, Country);
6. information about your computer and about your visits to and use of our website (including your IP address, geographical location, browser type and version, operating system, referral source, length of visit, page views, website navigation);
7. information that you provide to us when you visit the "Contact us" section on the website to have further information (including Name, Email and Phone number)
8. any other information that you choose to send to us;

Before you disclose to us the personal information of another person, you must obtain that person's consent to both the disclosure and the processing of that personal information in accordance with the terms of this privacy policy.

14.3.2 2. Why we collect your personal data

We ask you to share your personal data with us for purposes that include, but are not limited to:

- Activating or registering licenses for QUIPU's product or enabling functionalities;
- Receiving information about QUIPU's product and services;
- Participating in QUIPU online communities, including our social media channels/pages and blogs;
- Helping us to improve the product and services, and allowing QUIPU to keep you informed of new versions of the software;
- Resolving consumer and/or product and services issues;
- Managing customer relationships;
- Facilitating information access;
- Enhancing communications;
- Traceability of medical device;

We generally process your personal data only for those purposes that we have communicated to you. If we use it for other (closely related) purposes, additional data protection measures will be implemented if required by law.

14.3.3 3. Definitions for personal data processing

User
The individual using this Application, which must coincide with or be authorized by the Data Subject, to whom the Personal Data refer.
Data Subject
The legal or natural person to whom the Personal Data refers.
Data Processor (or **Data Supervisor**)
The natural person, legal person, public administration or any other body, association or organization authorized by the Data Controller to process the Personal Data in compliance with this privacy policy.
Data Controller (or Owner)
The natural person, legal person, public administration or any other body, association or organization with the right, also jointly with another Data Controller, to make decisions regarding the purposes, and the methods of processing of Personal Data and the means used, including the security measures concerning the operation and use of this Application. The Data Controller, unless otherwise specified, is the Owner of this Application.

Referring Person of Personal Data Processing

The natural person that the CEO of the Company nominates as a person who acts as an Internal Referring Person for processing personal data. This person is nominated after a verification of his/her competencies and abilities in Personal Data Processing and related legal issues.

This Application
The hardware or software tool by which the Personal Data of the User is collected.
Legal information
Notice to European Users: this privacy statement has been prepared in fulfillment of the obligations under Art. 10 of EC Directive n. 95/46/EC, and under the provisions of Directive 2002/58/EC, as revised by Directive 2009/136/EC, on the subject of Cookies. It has also been prepared in fulfillment of the obligations of the General Data Protection Regulation (GDPR) (EU) 2016/679.
This privacy policy relates solely to this Application.

14.3.4 4. Contact data

Data controller's personal data:

- Name: Vincenzo Gemignani
- Address: Via Verdi 3/b, Torre del Lago (LU)
- Email: gemignani@quipu.eu
- PEC: vincenzo.gemignani@pec.it
- Phone number: 0039/050-3152612

Referring Person of Personal Data Processing's personal data:

- Name: Elisabetta Bianchini
- Address: via Nottolini 466, San Concordio (LU)
- Email: bianchini@quipu.eu
- PEC: elisabettabianchini@pec.it
- Phone number: 0039/050-3152630

14.3.5 5. Methods of processing

The Data Controller processes the Data of Users in a proper manner and shall take appropriate security measures to prevent unauthorized access, disclosure, modification, or unauthorized destruction of the Data.The Data processing is carried out using computers and/or IT enabled tools, following organizational procedures and modes strictly related to the purposes indicated. In addition to the Data Controller, in some cases, the Data may be accessible to certain types of persons in charge, involved with the operation of the site (administration, sales, marketing, legal, system administration) or external parties (such as third party technical service providers, mail carriers, hosting providers, IT companies, communications agencies) appointed, if necessary, as Data Processors by the Owner. The updated list of these parties may be requested from the Data Controller at any time.

14.3.6 6. Place

Personal data are processed at the Data Controller’s operating offices and in any other places where the parties involved with the processing are located. For further information, please contact the Data Controller at privacy@quipu.eu.

14.3.7 7. Retention time

Personal data are kept for the time necessary to provide the service requested by the User, or stated by the purposes outlined in this document, and the User can always request that the Data Controller suspend or remove the data, sending an email at privacy@quipu.eu.

14.3.8 8. Cookies

A cookie is a file containing an identifier (a string of letters and numbers) that is sent by a web server to a web browser and is stored by the browser. The identifier is then sent back to the server each time the browser requests a page from the server. This enables the web server to identify and track the web browser.

We may use both "session" cookies and "persistent" cookies on the website. Session cookies will be deleted from your computer when you close your browser. Persistent cookies will remain stored on your computer until deleted, or until they reach a specified expiry date.

While browsing our website you may also receive cookies from third parties such as those used for Google Analytics, a web analysis service supplied by Google, Inc. ("Google"). We use Google Analytics to analyze the use of our website. Google Analytics generates statistical and other information about website use by means of cookies, which are stored on users' computers. The information generated relating to our website is used to create reports about the use of the website. Google will store this information. Google's privacy policy is available at: http://www.google.com/privacypolicy.html.

Most browsers allow you to reject all cookies, whilst some browsers allow you to reject just third party cookies. For example, in Internet Explorer (version 9) you can refuse all cookies by clicking "Tools", "Internet options", "Privacy", and selecting "Block All Cookies" using the sliding selector. Blocking all cookies will, however, have a negative impact upon the usability of many websites.

There are a number of different ways of managing cookies; please refer to the instruction manual or help screen of your browser to determine how to control and adjust settings. Users may change the predefined configuration and disable cookies (block them permanently) by setting the highest level of protection.

Below are the paths to follow to manage cookies on the following browsers:

Explorer:
https://support.microsoft.com/en-gb/help/17442/windows-internet-explorer-delete-manage-cookies

Safari:
https://support.apple.com/kb/PH21411?viewlocale=en_US&locale=en_US

Chrome:
https://support.google.com/chrome/answer/95647?hl=it-IT&hlrm=fr&hlrm=en

Firefox:
http://support.mozilla.org/it-IT/kb/enable-and-disable-cookies-website-preferences

How to disable third party services' cookies:

Google Analytics services:

http://www.google.it/analytics/learn/privacy.html
https://tools.google.com/dlpage/gaoptout

Third party cookies are not controlled directly by the Data Controller, and so if you wish to revoke your consent to use of these cookies you must contact the third parties' internet sites or go to the website www.youronlinechoices.com to obtain information on how to delete or manage cookies on the basis of the browser you use and to manage your preferences regarding third-party profiling cookies.

In accordance with section 122 paragraph two of Legislative Decree 196/2003 and following simplified methods for notification and acquisition of consent to use of cookies published in Gazzetta Ufficiale no. 126 on June 3 2014 and the corresponding register of measures no. 229 dated May 8 2014, at the foot of each page of QUIPU website it is possible to find the link to cookies in the Privacy Policy document.

14.3.9 9. Using your personal information

Personal information submitted to us will be used for the purposes specified in this privacy policy or in relevant parts of the website.

We may use your personal information to:

1. send you e-mail invitation in product usability surveys;
2. keep you posted on last products' updates;
3. send statements and invoices to you, and collect payments from you;
4. send you general commercial communications;
5. send you email notifications which you have specifically requested;
6. administer the website;
7. improve your browsing experience by personalizing our website;
8. enable your use of the services available on our website;
9. send you goods purchased via the website, and supply to you services purchased via the website;
10. deal with enquiries and complaints made by or about you relating to our website;
11. keep the website secure and prevent fraud;
12. set up your free trial software license;
13. set up your license activation;

We will not, without your express consent, provide your personal information to any third parties for the purpose of direct marketing.

14.3.10 10. Duration of Data Processing

The duration of data processing is balanced with the scope of the processing itself. It is limited to the services required by the customers. You can request for restriction or suspension of the processing by sending an email at privacy@quipu.eu.

14.3.11 11. Obligatoriness of personal data provision

Your consent to processing of personal data is mandatory for the Company for the reasons listed in section 2, especially for the traceability of the medical device sold by the Company. If you do not agree with this consent, it will not be possible to download Company's product or activate any evaluation/activation license.

14.3.12 12. How to propose requests for Personal Data

If you desire to modify, get access, ask for erasure or rectification, or any other request related to your personal data provided, it is necessary to send an email to privacy@quipu.eu specifying your request. The Data protection Officer or the controller will perform your request and reply to your mail.

14.3.13 13. Disclosures

We may disclose your personal information to any of our employees, officers, agents, suppliers or subcontractors insofar as reasonably necessary for the purposes set out in this privacy policy.

In addition, we may disclose your personal information:

1. to the extent that we are required to do so by law;
2. in connection with any ongoing or prospective legal proceedings;
3. in order to establish, exercise or defend our legal rights (including providing information to others for the purposes of fraud prevention and reducing credit risk);

Except as provided in this privacy policy, we will not provide your information to third parties.

14.3.14 14. International data transfer

Information that we collect may be stored and processed in and transferred between any of the countries in which we operate in order to enable us to use the information in accordance with this privacy policy.

Information which you provide may be transferred to countries (including the United States and Canada) which do not have data protection laws equivalent to those in force in the European Economic Area.

You expressly agree to such transfers of personal information.

14.3.15 15. Security of your personal information

We will take reasonable technical and organizational precautions to prevent the loss, misuse or alteration of your personal information.

We will store all the personal information you provide on our secure (password- and firewall-protected) servers.

All electronic transactions entered into via the website will be protected by encryption technology.

You acknowledge that the transmission of information over the internet is inherently insecure, and we cannot guarantee the security of data sent over the internet.

QUIPU's activities include also ultrasound images analysis for third parties. Images provided by the customer to Quipu should be in an anonymous form. Quipu, if required by the customer, can provide a cryptographic process to ensure data security.

14.3.16 16. Personal data breach

In case of a personal data breach, QUIPU carries out specific actions in accordance with Regulation (EU) 2016/679 (General Data Protection Regulation). QUIPU shall without undue delay and, where feasible, not later than 72 hours after having become aware of it, notify the personal data breach to the supervisory authority competent in accordance with Article 55 of GDPR, unless the personal data breach is unlikely to result in a risk to the rights and freedoms of natural persons. Where the notification to the supervisory authority is not made within 72 hours, it shall be accompanied by reasons for the delay.

Article 32 of GDPR indicates that QUIPU shall implement appropriate technical and organizational measures to ensure a level of security appropriate to the risk.

14.3.17 17. Policy amendments

We may update this privacy policy from time to time by posting a new version on our website. You should check this page occasionally to ensure you are happy with any changes.

14.3.18 18. Your rights

A data subject shall have the right to obtain confirmation as to whether or not personal data concerning him exist and to know their content and origin, to check their accuracy and to request integration or updating, or rectification (section 7 of Legislative Decree no. 196/2003) or objection to data processing, as stated in Article 21 of GDPR. Your rights are listed here:

- Article 12: Transparent information, communication and modalities for the exercise of the rights of the data subject
- Article 13: Information to be provided where personal data are collected from the data subject
- Article 14: Information to be provided where personal data have not been obtained from the data subject
- Article 15: Right of access by the data subject
- Article 16: Right to rectification
- Article 17: Right to erasure ('right to be forgotten')
- Article 18: Right to restriction of processing
- Article 19: Notification obligation regarding rectification or erasure of personal data or restriction of processing
- Article 20: Right to data portability
- Article 21: Right to object
- Article 22: Automated individual decision-making, including profiling

Under the same section, data subjects are entitled to request erasure, anonymization or blocking of data that have been processed unlawfully, and in all cases to object to their treatment on legitimate grounds.

Requests in this regard should be sent to the Data Controller, sending an email at privacy@quipu.eu.

We may withhold such personal information to the extent permitted by law.

You can expressly agree to our use of your personal information for marketing purposes; you can opt out of the use of your personal information for marketing purposes by sending an email to us at privacy@quipu.eu.

14.3.19 19. Third party websites

The website contains links to other websites. We are not responsible for the privacy policies or practices of third party websites.

We may provide only your email address to third party websites in order to set up a survey about our services and products. The email address will be used only to send the invitation to our surveys. Every kind of sensitive information given to the survey provider are treated as an aggregate variable so both Quipu and any eventual third part involved in surveys don't retain anything except of what explained in section Cookies.

It is in count that joining any kind of survey powered by a third part you accept also the private policy of the third part.

We are not responsible of the eventual wrongs belonging to the third part.

14.3.20 20. Updating information

Please let us know if the personal information which we hold about you needs to be corrected or updated. You can send an email to privacy@quipu.eu specifying your request.

14.3.21 21. Changes to this Privacy Policy

The Data Controller reserves the right to make changes to this privacy policy at any time by giving notice to its Users on the website. It is strongly recommended to check this page often, referring to the date of the last modification listed at the bottom. If a User objects to any of the changes to the Policy, the User must cease using this Application and can request that the Data Controller removes the Personal Data. Unless stated otherwise, the then-current privacy policy applies to all Personal Data the Data Controller has about Users.

14.3.22 22. Contacts

If you have any questions about this privacy policy or our treatment of your personal information, please write to us by email to privacy@quipu.eu or by post to Quipu s.r.l., via Moruzzi 1, Pisa I-56124, Italy.

14.3.23 23. Data controller

The data controller responsible in respect of the information collected on this website is Vincenzo Gemignani, Via Verdi 3/b, Torre del Lago (LU), Italy.

14.4 Opensource

This page contains Third Party Software Notices and/or Additional Terms and Conditions for licensed third party software components included within Cardiovascular Suite software products.

14.4.1 The Qt Toolkit Copyright © The Qt Company Ltd. and other contributors

Qt is available under the GNU Lesser General Public License version 3.

The Qt Toolkit is Copyright (C) 2018 The Qt Company Ltd. and other contributors.
Contact: https://www.qt.io/licensing/

14.4.2 FFMpeg Copyright © Fabrice Bellard and FFMpeg Team

Modified sources: https://github.com/Quipusrl/FFmpeg

FFmpeg is free software; you can redistribute it and/or modify it under the terms of the GNU Lesser General Public License as published by the Free Software Foundation; either version 2.1 of the License, or (at your option) any later version.
FFmpeg is distributed in the hope that it will be useful, but WITHOUT ANY WARRANTY; without even the implied warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE. See the GNU Lesser General Public License for more details.

You should have received a copy of the GNU Lesser General Public License along with FFmpeg; if not, write to the Free Software Foundation, Inc., 51 Franklin Street, Fifth Floor, Boston, MA 02110-1301 USA

14.4.3 QtAV Copyright © Wang Bin

Modified sources: https://github.com/Quipusrl/QtAV

QtAV is free software; you can redistribute it and/or modify it under the terms of the GNU Lesser General Public License as published by the Free Software Foundation; either version 2.1 of the License, or (at your option) any later version.
QtAV is distributed in the hope that it will be useful, but WITHOUT ANY WARRANTY; without even the implied warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE. See the GNU Lesser General Public License for more details.
You should have received a copy of the GNU Lesser General Public License along with QtAV; if not, write to the Free Software Foundation, Inc., 51 Franklin Street, Fifth Floor, Boston, MA 02110-1301 USA

14.5 LGPL 2.1

GNU LESSER GENERAL PUBLIC LICENSE

Version 2.1, February 1999

Copyright (C) 1991, 1999 Free Software Foundation, Inc.
51 Franklin Street, Fifth Floor, Boston, MA 02110-1301 USA

Everyone is permitted to copy and distribute verbatim copies of this license document, but changing it is not allowed.

[This is the first released version of the Lesser GPL. It also counts as the successor of the GNU Library Public License, version 2, hence the version number 2.1.]

Preamble

The licenses for most software are designed to take away your freedom to share and change it. By contrast, the GNU General Public Licenses are intended to guarantee your freedom to share and change free software--to make sure the software is free for all its users.

This license, the Lesser General Public License, applies to some specially designated software packages--typically libraries--of the Free Software Foundation and other authors who decide to use it. You can use it too, but we suggest you first think carefully about whether this license or the ordinary General Public License is the better strategy to use in any particular case, based on the explanations below.

When we speak of free software, we are referring to freedom of use, not price. Our General Public Licenses are designed to make sure that you have the freedom to distribute copies of free software (and charge for this service if you wish); that you receive source code or can get it if you want it; that you can change the software and use pieces of it in new free programs; and that you are informed that you can do these things.

To protect your rights, we need to make restrictions that forbid distributors to deny you these rights or to ask you to surrender these rights. These restrictions translate to certain responsibilities for you if you distribute copies of the library or if you modify it.

For example, if you distribute copies of the library, whether gratis or for a fee, you must give the recipients all the rights that we gave you. You must make sure that they, too, receive or can get the source code. If you link other

code with the library, you must provide complete object files to the recipients, so that they can relink them with the library after making changes to the library and recompiling it. And you must show them these terms so they know their rights.

We protect your rights with a two-step method: (1) we copyright the library, and (2) we offer you this license, which gives you legal permission to copy, distribute and/or modify the library.

To protect each distributor, we want to make it very clear that there is no warranty for the free library. Also, if the library is modified by someone else and passed on, the recipients should know that what they have is not the original version, so that the original author's reputation will not be affected by problems that might be introduced by others.

Finally, software patents pose a constant threat to the existence of any free program. We wish to make sure that a company cannot effectively restrict the users of a free program by obtaining a restrictive license from a patent holder. Therefore, we insist that any patent license obtained for a version of the library must be consistent with the full freedom of use specified in this license.

Most GNU software, including some libraries, is covered by the ordinary GNU General Public License. This license, the GNU Lesser General Public License, applies to certain designated libraries, and is quite different from the ordinary General Public License. We use this license for certain libraries in order to permit linking those libraries into non-free programs.

When a program is linked with a library, whether statically or using a shared library, the combination of the two is legally speaking a combined work, a derivative of the original library. The ordinary General Public License therefore permits such linking only if the entire combination fits its criteria of freedom. The Lesser General Public License permits more lax criteria for linking other code with the library.

We call this license the "Lesser" General Public License because it does Less to protect the user's freedom than the ordinary General Public License. It also provides other free software developers Less of an advantage over competing non-free programs. These disadvantages are the reason we use the ordinary General Public License for many libraries. However, the Lesser license provides advantages in certain special circumstances.

For example, on rare occasions, there may be a special need to encourage the widest possible use of a certain library, so that it becomes a de-facto standard. To achieve this, non-free programs must be allowed to use the library. A more frequent case is that a free library does the same job as widely used non-free libraries. In this case, there is little to gain by limiting the free library to free software only, so we use the Lesser General Public License.

In other cases, permission to use a particular library in non-free programs enables a greater number of people to use a large body of free software. For example, permission to use the GNU C Library in non-free programs enables many more people to use the whole GNU operating system, as well as its variant, the GNU/Linux operating system.

Although the Lesser General Public License is Less protective of the users' freedom, it does ensure that the user of a program that is linked with the Library has the freedom and the wherewithal to run that program using a modified version of the Library.

The precise terms and conditions for copying, distribution and modification follow. Pay close attention to the difference between a "work based on the library" and a "work that uses the library". The former contains code derived from the library, whereas the latter must be combined with the library in order to run.

TERMS AND CONDITIONS FOR COPYING, DISTRIBUTION AND MODIFICATION

0. This License Agreement applies to any software library or other program which contains a notice placed by the copyright holder or other authorized party saying it may be distributed under the terms of this Lesser General Public License (also called "this License"). Each licensee is addressed as "you".

A "library" means a collection of software functions and/or data prepared so as to be conveniently linked with application programs (which use some of those functions and data) to form executables.

The "Library", below, refers to any such software library or work which has been distributed under these terms. A "work based on the Library" means either the Library or any derivative work under copyright law: that is to say, a

work containing the Library or a portion of it, either verbatim or with modifications and/or translated straightforwardly into another language. (Hereinafter, translation is included without limitation in the term "modification".)

"Source code" for a work means the preferred form of the work for making modifications to it. For a library, complete source code means all the source code for all modules it contains, plus any associated interface definition files, plus the scripts used to control compilation and installation of the library.

Activities other than copying, distribution and modification are not covered by this License; they are outside its scope. The act of running a program using the Library is not restricted, and output from such a program is covered only if its contents constitute a work based on the Library (independent of the use of the Library in a tool for writing it). Whether that is true depends on what the Library does and what the program that uses the Library does.

1. You may copy and distribute verbatim copies of the Library's complete source code as you receive it, in any medium, provided that you conspicuously and appropriately publish on each copy an appropriate copyright notice and disclaimer of warranty; keep intact all the notices that refer to this License and to the absence of any warranty; and distribute a copy of this License along with the Library.

You may charge a fee for the physical act of transferring a copy, and you may at your option offer warranty protection in exchange for a fee.

2. You may modify your copy or copies of the Library or any portion of it, thus forming a work based on the Library, and copy and distribute such modifications or work under the terms of Section 1 above, provided that you also meet all of these conditions:

- **a)** The modified work must itself be a software library.
- **b)** You must cause the files modified to carry prominent notices stating that you changed the files and the date of any change.
- **c)** You must cause the whole of the work to be licensed at no charge to all third parties under the terms of this License.
- **d)** If a facility in the modified Library refers to a function or a table of data to be supplied by an application program that uses the facility, other than as an argument passed when the facility is invoked, then you must make a good faith effort to ensure that, in the event an application does not supply such function or table, the facility still operates, and performs whatever part of its purpose remains meaningful.

(For example, a function in a library to compute square roots has a purpose that is entirely well-defined independent of the application. Therefore, Subsection 2d requires that any application-supplied function or table used by this function must be optional: if the application does not supply it, the square root function must still compute square roots.)

These requirements apply to the modified work as a whole. If identifiable sections of that work are not derived from the Library, and can be reasonably considered independent and separate works in themselves, then this License, and its terms, do not apply to those sections when you distribute them as separate works. But when you distribute the same sections as part of a whole which is a work based on the Library, the distribution of the whole must be on the terms of this License, whose permissions for other licensees extend to the entire whole, and thus to each and every part regardless of who wrote it.

Thus, it is not the intent of this section to claim rights or contest your rights to work written entirely by you; rather, the intent is to exercise the right to control the distribution of derivative or collective works based on the Library.

In addition, mere aggregation of another work not based on the Library with the Library (or with a work based on the Library) on a volume of a storage or distribution medium does not bring the other work under the scope of this License.

3. You may opt to apply the terms of the ordinary GNU General Public License instead of this License to a given copy of the Library. To do this, you must alter all the notices that refer to this License, so that they refer to the ordinary GNU General Public License, version 2, instead of to this License. (If a newer version than version 2 of the ordinary

GNU General Public License has appeared, then you can specify that version instead if you wish.) Do not make any other change in these notices.

Once this change is made in a given copy, it is irreversible for that copy, so the ordinary GNU General Public License applies to all subsequent copies and derivative works made from that copy.

This option is useful when you wish to copy part of the code of the Library into a program that is not a library.

4. You may copy and distribute the Library (or a portion or derivative of it, under Section 2) in object code or executable form under the terms of Sections 1 and 2 above provided that you accompany it with the complete corresponding machine-readable source code, which must be distributed under the terms of Sections 1 and 2 above on a medium customarily used for software interchange.

If distribution of object code is made by offering access to copy from a designated place, then offering equivalent access to copy the source code from the same place satisfies the requirement to distribute the source code, even though third parties are not compelled to copy the source along with the object code.

5. A program that contains no derivative of any portion of the Library, but is designed to work with the Library by being compiled or linked with it, is called a "work that uses the Library". Such a work, in isolation, is not a derivative work of the Library, and therefore falls outside the scope of this License.

However, linking a "work that uses the Library" with the Library creates an executable that is a derivative of the Library (because it contains portions of the Library), rather than a "work that uses the library". The executable is therefore covered by this License. Section 6 states terms for distribution of such executables.

When a "work that uses the Library" uses material from a header file that is part of the Library, the object code for the work may be a derivative work of the Library even though the source code is not. Whether this is true is especially significant if the work can be linked without the Library, or if the work is itself a library. The threshold for this to be true is not precisely defined by law.

If such an object file uses only numerical parameters, data structure layouts and accessors, and small macros and small inline functions (ten lines or less in length), then the use of the object file is unrestricted, regardless of whether it is legally a derivative work. (Executables containing this object code plus portions of the Library will still fall under Section 6.)

Otherwise, if the work is a derivative of the Library, you may distribute the object code for the work under the terms of Section 6. Any executables containing that work also fall under Section 6, whether or not they are linked directly with the Library itself.

6. As an exception to the Sections above, you may also combine or link a "work that uses the Library" with the Library to produce a work containing portions of the Library, and distribute that work under terms of your choice, provided that the terms permit modification of the work for the customer's own use and reverse engineering for debugging such modifications.

You must give prominent notice with each copy of the work that the Library is used in it and that the Library and its use are covered by this License. You must supply a copy of this License. If the work during execution displays copyright notices, you must include the copyright notice for the Library among them, as well as a reference directing the user to the copy of this License. Also, you must do one of these things:

- **a)** Accompany the work with the complete corresponding machine-readable source code for the Library including whatever changes were used in the work (which must be distributed under Sections 1 and 2 above); and, if the work is an executable linked with the Library, with the complete machine-readable "work that uses the Library", as object code and/or source code, so that the user can modify the Library and then relink to produce a modified executable containing the modified Library. (It is understood that the user who changes the contents of definitions files in the Library will not necessarily be able to recompile the application to use the modified definitions.)

- **b)** Use a suitable shared library mechanism for linking with the Library. A suitable mechanism is one that (1) uses at run time a copy of the library already present on the user's computer system, rather than copying library

functions into the executable, and (2) will operate properly with a modified version of the library, if the user installs one, as long as the modified version is interface-compatible with the version that the work was made with.

- **c)** Accompany the work with a written offer, valid for at least three years, to give the same user the materials specified in Subsection 6a, above, for a charge no more than the cost of performing this distribution.
- **d)** If distribution of the work is made by offering access to copy from a designated place, offer equivalent access to copy the above specified materials from the same place.
- **e)** Verify that the user has already received a copy of these materials or that you have already sent this user a copy.

For an executable, the required form of the "work that uses the Library" must include any data and utility programs needed for reproducing the executable from it. However, as a special exception, the materials to be distributed need not include anything that is normally distributed (in either source or binary form) with the major components (compiler, kernel, and so on) of the operating system on which the executable runs, unless that component itself accompanies the executable.

It may happen that this requirement contradicts the license restrictions of other proprietary libraries that do not normally accompany the operating system. Such a contradiction means you cannot use both them and the Library together in an executable that you distribute.

7. You may place library facilities that are a work based on the Library side-by-side in a single library together with other library facilities not covered by this License, and distribute such a combined library, provided that the separate distribution of the work based on the Library and of the other library facilities is otherwise permitted, and provided that you do these two things:

- **a)** Accompany the combined library with a copy of the same work based on the Library, uncombined with any other library facilities. This must be distributed under the terms of the Sections above.
- **b)** Give prominent notice with the combined library of the fact that part of it is a work based on the Library, and explaining where to find the accompanying uncombined form of the same work.

8. You may not copy, modify, sublicense, link with, or distribute the Library except as expressly provided under this License. Any attempt otherwise to copy, modify, sublicense, link with, or distribute the Library is void, and will automatically terminate your rights under this License. However, parties who have received copies, or rights, from you under this License will not have their licenses terminated so long as such parties remain in full compliance.

9. You are not required to accept this License, since you have not signed it. However, nothing else grants you permission to modify or distribute the Library or its derivative works. These actions are prohibited by law if you do not accept this License. Therefore, by modifying or distributing the Library (or any work based on the Library), you indicate your acceptance of this License to do so, and all its terms and conditions for copying, distributing or modifying the Library or works based on it.

10. Each time you redistribute the Library (or any work based on the Library), the recipient automatically receives a license from the original licensor to copy, distribute, link with or modify the Library subject to these terms and conditions. You may not impose any further restrictions on the recipients' exercise of the rights granted herein. You are not responsible for enforcing compliance by third parties with this License.

11. If, as a consequence of a court judgment or allegation of patent infringement or for any other reason (not limited to patent issues), conditions are imposed on you (whether by court order, agreement or otherwise) that contradict the conditions of this License, they do not excuse you from the conditions of this License. If you cannot distribute so as to satisfy simultaneously your obligations under this License and any other pertinent obligations, then as a consequence you may not distribute the Library at all. For example, if a patent license would not permit royalty-free redistribution of the Library by all those who receive copies directly or indirectly through you, then the only way you could satisfy both it and this License would be to refrain entirely from distribution of the Library.

If any portion of this section is held invalid or unenforceable under any particular circumstance, the balance of the section is intended to apply, and the section as a whole is intended to apply in other circumstances.

It is not the purpose of this section to induce you to infringe any patents or other property right claims or to contest validity of any such claims; this section has the sole purpose of protecting the integrity of the free software distribution system which is implemented by public license practices. Many people have made generous contributions to the wide range of software distributed through that system in reliance on consistent application of that system; it is up to the author/donor to decide if he or she is willing to distribute software through any other system and a licensee cannot impose that choice.

This section is intended to make thoroughly clear what is believed to be a consequence of the rest of this License.

12. If the distribution and/or use of the Library is restricted in certain countries either by patents or by copyrighted interfaces, the original copyright holder who places the Library under this License may add an explicit geographical distribution limitation excluding those countries, so that distribution is permitted only in or among countries not thus excluded. In such case, this License incorporates the limitation as if written in the body of this License.

13. The Free Software Foundation may publish revised and/or new versions of the Lesser General Public License from time to time. Such new versions will be similar in spirit to the present version, but may differ in detail to address new problems or concerns.

Each version is given a distinguishing version number. If the Library specifies a version number of this License which applies to it and "any later version", you have the option of following the terms and conditions either of that version or of any later version published by the Free Software Foundation. If the Library does not specify a license version number, you may choose any version ever published by the Free Software Foundation.

14. If you wish to incorporate parts of the Library into other free programs whose distribution conditions are incompatible with these, write to the author to ask for permission. For software which is copyrighted by the Free Software Foundation, write to the Free Software Foundation; we sometimes make exceptions for this. Our decision will be guided by the two goals of preserving the free status of all derivatives of our free software and of promoting the sharing and reuse of software generally.

NO WARRANTY

15. BECAUSE THE LIBRARY IS LICENSED FREE OF CHARGE, THERE IS NO WARRANTY FOR THE LIBRARY, TO THE EXTENT PERMITTED BY APPLICABLE LAW. EXCEPT WHEN OTHERWISE STATED IN WRITING THE COPYRIGHT HOLDERS AND/OR OTHER PARTIES PROVIDE THE LIBRARY "AS IS" WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. THE ENTIRE RISK AS TO THE QUALITY AND PERFORMANCE OF THE LIBRARY IS WITH YOU. SHOULD THE LIBRARY PROVE DEFECTIVE, YOU ASSUME THE COST OF ALL NECESSARY SERVICING, REPAIR OR CORRECTION.

16. IN NO EVENT UNLESS REQUIRED BY APPLICABLE LAW OR AGREED TO IN WRITING WILL ANY COPYRIGHT HOLDER, OR ANY OTHER PARTY WHO MAY MODIFY AND/OR REDISTRIBUTE THE LIBRARY AS PERMITTED ABOVE, BE LIABLE TO YOU FOR DAMAGES, INCLUDING ANY GENERAL, SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES ARISING OUT OF THE USE OR INABILITY TO USE THE LIBRARY (INCLUDING BUT NOT LIMITED TO LOSS OF DATA OR DATA BEING RENDERED INACCURATE OR LOSSES SUSTAINED BY YOU OR THIRD PARTIES OR A FAILURE OF THE LIBRARY TO OPERATE WITH ANY OTHER SOFTWARE), EVEN IF SUCH HOLDER OR OTHER PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

END OF TERMS AND CONDITIONS

How to Apply These Terms to Your New Libraries

If you develop a new library, and you want it to be of the greatest possible use to the public, we recommend making it free software that everyone can redistribute and change. You can do so by permitting redistribution under these terms (or, alternatively, under the terms of the ordinary General Public License).

To apply these terms, attach the following notices to the library. It is safest to attach them to the start of each source file to most effectively convey the exclusion of warranty; and each file should have at least the "copyright" line and a pointer to where the full notice is found.

one line to give the library's name and an idea of what it does.
Copyright (C) year name of author

This library is free software; you can redistribute it and/or modify it under the terms of the GNU Lesser General Public License as published by the Free Software Foundation; either version 2.1 of the License, or (at your option) any later version.

This library is distributed in the hope that it will be useful, but WITHOUT ANY WARRANTY; without even the implied warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE. See the GNU Lesser General Public License for more details.

You should have received a copy of the GNU Lesser General Public License along with this library; if not, write to the Free Software Foundation, Inc., 51 Franklin Street, Fifth Floor, Boston, MA 02110-1301 USA

Also add information on how to contact you by electronic and paper mail.

You should also get your employer (if you work as a programmer) or your school, if any, to sign a "copyright disclaimer" for the library, if necessary. Here is a sample; alter the names:

Yoyodyne, Inc., hereby disclaims all copyright interest in
the library `Frob' (a library for tweaking knobs) written
by James Random Hacker.

signature of Ty Coon, 1 April 1990
Ty Coon, President of Vice

That's all there is to it!

14.6 LGPL 3

14.6.1 GNU LESSER GENERAL PUBLIC LICENSE

Version 3, 29 June 2007

Copyright © 2007 Free Software Foundation, Inc. <https://fsf.org/>

Everyone is permitted to copy and distribute verbatim copies of this license document, but changing it is not allowed.

This version of the GNU Lesser General Public License incorporates the terms and conditions of version 3 of the GNU General Public License, supplemented by the additional permissions listed below.

14.6.1.1 0. Additional Definitions.

As used herein, “this License” refers to version 3 of the GNU Lesser General Public License, and the “GNU GPL” refers to version 3 of the GNU General Public License.

“The Library” refers to a covered work governed by this License, other than an Application or a Combined Work as defined below.

An “Application” is any work that makes use of an interface provided by the Library, but which is not otherwise based on the Library. Defining a subclass of a class defined by the Library is deemed a mode of using an interface provided by the Library.

A “Combined Work” is a work produced by combining or linking an Application with the Library. The particular version of the Library with which the Combined Work was made is also called the “Linked Version”.

The “Minimal Corresponding Source” for a Combined Work means the Corresponding Source for the Combined Work, excluding any source code for portions of the Combined Work that, considered in isolation, are based on the Application, and not on the Linked Version.

The “Corresponding Application Code” for a Combined Work means the object code and/or source code for the Application, including any data and utility programs needed for reproducing the Combined Work from the Application, but excluding the System Libraries of the Combined Work.

14.6.1.2 1. Exception to Section 3 of the GNU GPL.

You may convey a covered work under sections 3 and 4 of this License without being bound by section 3 of the GNU GPL.

14.6.1.3 2. Conveying Modified Versions.

If you modify a copy of the Library, and, in your modifications, a facility refers to a function or data to be supplied by an Application that uses the facility (other than as an argument passed when the facility is invoked), then you may convey a copy of the modified version:

- a) under this License, provided that you make a good faith effort to ensure that, in the event an Application does not supply the function or data, the facility still operates, and performs whatever part of its purpose remains meaningful, or
- b) under the GNU GPL, with none of the additional permissions of this License applicable to that copy.

14.6.1.4 3. Object Code Incorporating Material from Library Header Files.

The object code form of an Application may incorporate material from a header file that is part of the Library. You may convey such object code under terms of your choice, provided that, if the incorporated material is not limited to numerical parameters, data structure layouts and accessors, or small macros, inline functions and templates (ten or fewer lines in length), you do both of the following:

- a) Give prominent notice with each copy of the object code that the Library is used in it and that the Library and its use are covered by this License.
- b) Accompany the object code with a copy of the GNU GPL and this license document.

14.6.1.5 4. Combined Works.

You may convey a Combined Work under terms of your choice that, taken together, effectively do not restrict modification of the portions of the Library contained in the Combined Work and reverse engineering for debugging such modifications, if you also do each of the following:

- a) Give prominent notice with each copy of the Combined Work that the Library is used in it and that the Library and its use are covered by this License.
- b) Accompany the Combined Work with a copy of the GNU GPL and this license document.
- c) For a Combined Work that displays copyright notices during execution, include the copyright notice for the Library among these notices, as well as a reference directing the user to the copies of the GNU GPL and this license document.
- d) Do one of the following:
    - 0) Convey the Minimal Corresponding Source under the terms of this License, and the Corresponding Application Code in a form suitable for, and under terms that permit, the user to recombine or relink

the Application with a modified version of the Linked Version to produce a modified Combined Work, in the manner specified by section 6 of the GNU GPL for conveying Corresponding Source.
    - 1) Use a suitable shared library mechanism for linking with the Library. A suitable mechanism is one that (a) uses at run time a copy of the Library already present on the user's computer system, and (b) will operate properly with a modified version of the Library that is interface-compatible with the Linked Version.
- e) Provide Installation Information, but only if you would otherwise be required to provide such information under section 6 of the GNU GPL, and only to the extent that such information is necessary to install and execute a modified version of the Combined Work produced by recombining or relinking the Application with a modified version of the Linked Version. (If you use option 4d0, the Installation Information must accompany the Minimal Corresponding Source and Corresponding Application Code. If you use option 4d1, you must provide the Installation Information in the manner specified by section 6 of the GNU GPL for conveying Corresponding Source.)

14.6.1.6 5. Combined Libraries.

You may place library facilities that are a work based on the Library side by side in a single library together with other library facilities that are not Applications and are not covered by this License, and convey such a combined library under terms of your choice, if you do both of the following:

- a) Accompany the combined library with a copy of the same work based on the Library, uncombined with any other library facilities, conveyed under the terms of this License.
- b) Give prominent notice with the combined library that part of it is a work based on the Library, and explaining where to find the accompanying uncombined form of the same work.

14.6.1.7 6. Revised Versions of the GNU Lesser General Public License.

The Free Software Foundation may publish revised and/or new versions of the GNU Lesser General Public License from time to time. Such new versions will be similar in spirit to the present version, but may differ in detail to address new problems or concerns.

Each version is given a distinguishing version number. If the Library as you received it specifies that a certain numbered version of the GNU Lesser General Public License “or any later version” applies to it, you have the option of following the terms and conditions either of that published version or of any later version published by the Free Software Foundation. If the Library as you received it does not specify a version number of the GNU Lesser General Public License, you may choose any version of the GNU Lesser General Public License ever published by the Free Software Foundation.

If the Library as you received it specifies that a proxy can decide whether future versions of the GNU Lesser General Public License shall apply, that proxy's public statement of acceptance of any version is permanent authorization for you to choose that version for the Library.

14.7 Decommissioning and disposal

The user can safely decommission and dispose the Cardiovascular Suite and the license key. In particular, the software can be uninstalled following the usual procedure of uninstalling software on Apple computers or Windows computer. The license key must be disposed according to the local regulation regarding the waste management.