VueBox® Research

Quantification Toolbox

Instructions for use

VueBox® Research v1.0

09.2024

The software described in this manual is for RESEARCH USE ONLY; not for use in diagnostic and/or clinical procedures.

The information in this manual is for instructional use only and is subject to change without notice.

Nothing in this manual shall limit or restrict in any way Bracco Suisse SA's rights to revise or otherwise change or modify the software described in this manual.

VUEBOX® RESEARCH

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FOR RESEARCH USE ONLY.
NOT FOR USE IN DIAGNOSTIC AND/OR CLINICAL PROCEDURES.

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1 INTRODUCTION

1.1 ABOUT THIS MANUAL

In this manual, examples, suggestions and warnings are included to help you to start using the VueBox® Research software application and to advise you on important items. This information is indicated using the following symbols:

The *caution symbol* indicates important information, safety precautions, or warnings.

The *stop* symbol highlights important information. You should stop and read before continuing.

The *bulb* symbol indicates a suggestion or an idea that simplifies the use of VueBox® Research. It can also refer to information available in other chapters.

1.2 DEFINITIONS

ASR	Advanced System Recognition
DVP	Dynamic Vascular Pattern
DVPP	Dynamic Vascular Pattern Parametric
FT	Fall Time
HIR	High Intensity Region
LIR	Low Intensity Region
MIP	Maximum Intensity Projection
mTT	Mean Transit Time
PA	Perfused Area
PE	Peak Enhancement
PHI	Protected Health Information
PI	Perfusion Index
PSA	Perfusion Segments Analysis
QOF	Quality Of Fit
rBV	Regional Blood Volume
ROI	Region Of Interest
rPA	Relative Perfused Area
RT	Rise Time
TSV	Tabulation-Separated Values
TTP	Time To Peak
WiAUC	Wash-in Area Under Curve
WiPI	Wash-in Perfusion Index
WiR	Wash-in Rate
WiWoAUC	Wash-in and Wash-out AUC
WoAUC	Wash-out AUC
WoR	Wash-out Rate

1.3 OVERVIEW

VueBox® Research is a software package useful for research related to the quantification of blood perfusion, based on 2D DICOM clips acquired in Dynamic Contrast Enhanced Ultrasound, in radiology applications (cardiology excluded).

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From the analysis of a time sequence of 2D contrast images, perfusion parameters are calculated, such as wash-in rate (WiR), peak enhancement (PE), rise time (RT) or area under curve during wash-in (WiAUC). Time parameters (e.g. RT) can be interpreted in absolute terms, and amplitude parameters (e.g. WiR, PE and WiAUC) in relative terms (vs. values in a reference region).
VueBox® Research can display the spatial distribution of any of these (and other) parameters, synthesizing time sequences of contrast images into single parametric images. Models are provided for the two most common modes of administration: bolus (wash-in / wash-out kinetics) and infusion (replenishment kinetics after destruction).

VueBox® Research is available in 3 application packages:

- **Tissue Perfusion:** provides time-intensity curves of ROIs and the related perfusion parameters.

- **Tissue Normalization:** is intended to identify Dynamic Vascular Patterns (DVP) within the tissue after bolus administration. Time intensity curves of ROIs are normalized with respect to a selected reference ROI. The DVP information over time is summarized in a single parametric image defined as Dynamic Vascular Pattern Parameter (DVPP).

- **Low-Intensity Signal analysis:** allows to depict Maximum Intensity Projection of a low-intensity signal in a ROI adjacent to or surrounded by a high-intensity background. This tool includes a multi-scale graph, specific perfusion quantification methods and specific quantification parameters such as Perfused Area (PA), relative Perfused Area (rPA).

An additional module, **Parameter trend tool**, can be applied to display temporal evolution of perfusion parameters across acquisitions on the same tissue, at different time points.

1.4 PATIENT POPULATION

The software described in this manual is for RESEARCH USE ONLY; not for use in diagnostic and/or clinical procedures.

VueBox® Research is suitable for evaluating medical images in a clinical research setting from any patient who was examined with CEUS except for cardiac applications.

VueBox ® Research should not be used for data from patients contraindicated for Dynamic Contrast Enhanced Ultrasound.

1.5 INTENDED USER

VueBox® Research is intended for both clinicians and researchers interested in conducting investigations related to DCE-US perfusion quantification, obtaining reliable perfusion parameter values, processing data acquired with different ultrasound platforms, documenting analyses in a report, retrieving and comparing examinations performed at different dates, and documenting work for publication purposes.

1.6 PRODUCT LIFETIME

For a given version of the product, the software and its documentation are supported for five years after the release date.

1.7 INSTALLATION AND MAINTENANCE

Bracco Suisse SA assumes no liability for problems attributable to unauthorized modifications, additions or deletions to Bracco Suisse SA software or hardware, or unauthorized installation of third party software.

As manufacturer and distributor of this product, Bracco Suisse SA is not responsible for efficacy, reliability and performance of the system, if:

- the product is not operated in accordance with the operating manual
- the product is operated outside of its operating conditions
- the product is operated outside of the specified operating environment.

The user must be satisfied with the suitability and completeness of clips acquired in a study, prior to analysis with VueBox® Research. For information about performing contrast acquisitions for reliable perfusion quantification, please refer to the operating instructions provided by the manufacturer of your ultrasound equipment as well as to Bracco's Application note "Protocol for performing reliable perfusion quantification".

The information contained in this manual is intended only for the operation of Bracco Suisse SA application software. It does not include information on echocardiograms or general ultrasound acquisition. Please refer to the operating instructions of your ultrasound equipment for further information.

1.8 MEASUREMENT

The user is responsible for a suitable choice of ROI (Region of interest), in order to include contrast-ultrasound data only. ROI should not include any overlays such as texts, labels or measurements and should be drawn on ultrasound data acquired with a contrast-specific mode only (i.e. no Fundamental B-Mode or Color Doppler overlays).

The user is responsible for determining if artifacts are present in the data to be analyzed. Artifacts can severely affect the analysis outcome and require a reacquisition. Examples of artifacts are:

- obvious discontinuity due to a jerky motion during acquisition or because the acquisition plane changed;
- excess shadowing in images;
- poorly defined anatomy or evidence of distorted anatomical representation.

In the case of a poorly reconstructed image, as determined by the above criteria (e.g. artifacts) or by the user's experience and training, measurements should not be made.
The user must ensure the accuracy of the images and measurement results. Acquisitions should be repeated if there is the slightest doubt as to the accuracy of images and measurements.

The user is responsible for a suitable length calibration. In case of incorrect usage, wrong measurement results may occur.

The user should always make sure to select the appropriate calibration according to the ultrasound system, probe and settings used. This control should be performed for each clip to be analyzed (except in case of ASR-compatible ultrasound scanners).

1.9 ASR-COMPATIBLE ULTRASOUND SCANNERS AND TRANSFER OF DATA

ASR-compatible ultrasound scanners are systems where the linearization data (required to get accurate quantification results) are directly embedded by the manufacturers in the DICOM files. Therefore, with ASR-compatible systems, manual selection of a calibration file is not required in VueBox® Research.

List of ASR-compatible ultrasound scanners, with the minimum required system version is reported on https://vuebox-research.com.

2 INSTALLATION

2.1 SYSTEM REQUIREMENTS

	Minimum	Proposed
CPU	Intel® Xeon® E5-2620 2GHz	Intel® Xeon® E5-1620 3.5 GHz
RAM	8 GB	16 GB or more
Graphics Card	Intel HD Graphics 3000 Minimum Resolution **1440x900**	Nvidia GeForce 1050 Ti 4GB GDDR5 Resolution **1920x1200 and higher**
Monitor	17''	24'' or higher
Operating System	Microsoft® Windows® 10, 32 bit	Microsoft® Windows® 10, 64 bit
Disk space	1000 MB	
Connectivity	Access to internet	

2.2 INSTALLATION OF VUEBOX® RESEARCH

The installation package of VueBox® Research includes the following mandatory prerequisites:

- Pre-requisite for Microsoft .NET Framework (Windows patch)
- Microsoft .NET Framework 4.8
- Visual C++ 2010 Runtime Libraries
- Visual C++ 2012 Runtime Libraries

During the installation procedure, you will be automatically prompted if any of these prerequisites needs to be installed.

Please perform the following steps in order to install VueBox® Research:

1. close all applications,
2. run the provided setup installation package (.exe extension)
3. accept the installation of the **prerequisites** (if not already installed),
4. select the installation folder and press **Next**,
5. follow the on-screen instructions,
6. at the end of the installation, press **Close**.

The installation is now complete. VueBox® Research can be started from the VueBox® Research folder in the start menu or more directly using the desktop shortcut.

VueBox® Research can be uninstalled through the **Uninstall** software feature from the Windows **control panel**.

2.3 ACTIVATION OF VUEBOX® RESEARCH

At first start-up, VueBox® Research launches an activation process that will validate and unlock the copy of the software application.

In this process you will be prompted to enter the following information:

- Serial number
- E-mail address

- Organization / Company name.

The activation needs to communicate these information to the activation server. This can be performed automatically through the **online activation**, or manually using the **e-mail activation**.

In the **online activation**, VueBox® Research will be activated and unlocked automatically, by simply following the on-screen instructions.

In the **e-mail activation**, an e-mail including all necessary information for the activation of VueBox® Research will be generated and you will be asked to send it to the activation server (e-mail address will be displayed). Within a few minutes, you will receive an automatic reply by e-mail including an **unlock code**. This **unlock code** will be required at the next start-up of VueBox® Research to finalize the activation process.

Please note that this activation process, either through the online or the e-mail method, needs to be performed **only once**.

2.4 SECURITY MEASURES

VueBox® Research is not intended for remote control and can only be operated via physical access to the PC where it has been installed. Authentication mechanism to the PC is provided by the Windows OS, and password policy shall be maintained by the operator.

VueBox® Research is only intended to use the Dynamic CEUS data as input, which shall be statically stored on the PC where VueBox® Research has been installed. VueBox® Research is not intended to manage the security of the data types used as input for the software.

VueBox® Research can access local drives, network drives, USB drives, and CD/DVDs if they are directly accessible as files from the computer where the software is installed. VueBox® Research does not manage the handling or security of the health data already stored within the PC and does not support other medical protocols, such as PACS, RIS, and HIS.

VueBox® Research provides output data in the form of images, PDFs and Excel sheets which are written to the local storage medium on the PC where the software is installed. VueBox® Research is also capable of generating intermediate files (identified as *.eBRI and *.BRAC) for storing analysis parameters, which are similarly written to local storage mediums. Since all output files are stored locally on the user PC, the operator is responsible for ensuring the security of the host system is maintained.

The operator is responsible for ensuring the security of the data stored on the user PC, which includes the integrity of the data used as input for VueBox® Research software. The operator is also responsible for the physical security of the PC itself, as well as for performing adequate backups of all data assets.

The operator should implement any update released for the Windows OS as soon as it becomes available. The operator should also implement any update released for VueBox® Research as soon as it becomes available.

3 FUNCTIONAL REFERENCE FOR VUEBOX® RESEARCH ANALYSES

To get instant help on working with VueBox® Research, click the "Help" menu in the top menu and select the user manual.

You will need Adobe Acrobat Reader® to display the software manual. If Adobe Acrobat Reader® is not installed on your system, please download the latest version from www.adobe.com.

3.1 USER INTERFACE

VueBox® Research is a multiple window interface software application. The possibility to process several clips in separate child windows comes in handy for the user who, for example, wants to analyze different cross-sections of a given tissue at the same time.

Another example is the case of a user who is interested to compare a given region of interest imaged in different studies. Each analysis is performed in an individual, independent child window. VueBox® Research is also multitasking, as each child window can execute processing at the same time while keeping the parent interface responsive. Furthermore, calculations that are demanding in terms of computing power, such as computing the perfusion quantification, have been optimized to benefit from multicore processors when available, a technology called parallelization.

When VueBox® Research is launched, a start page is shown.

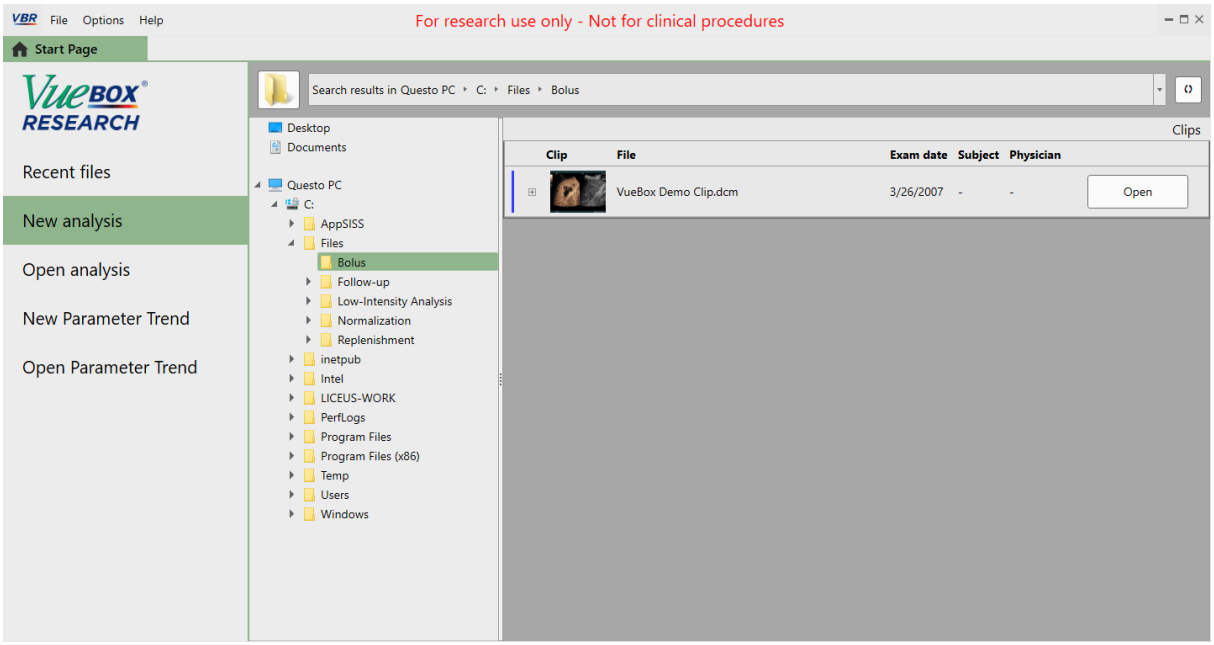


Figure 1 – VueBox® Research start page

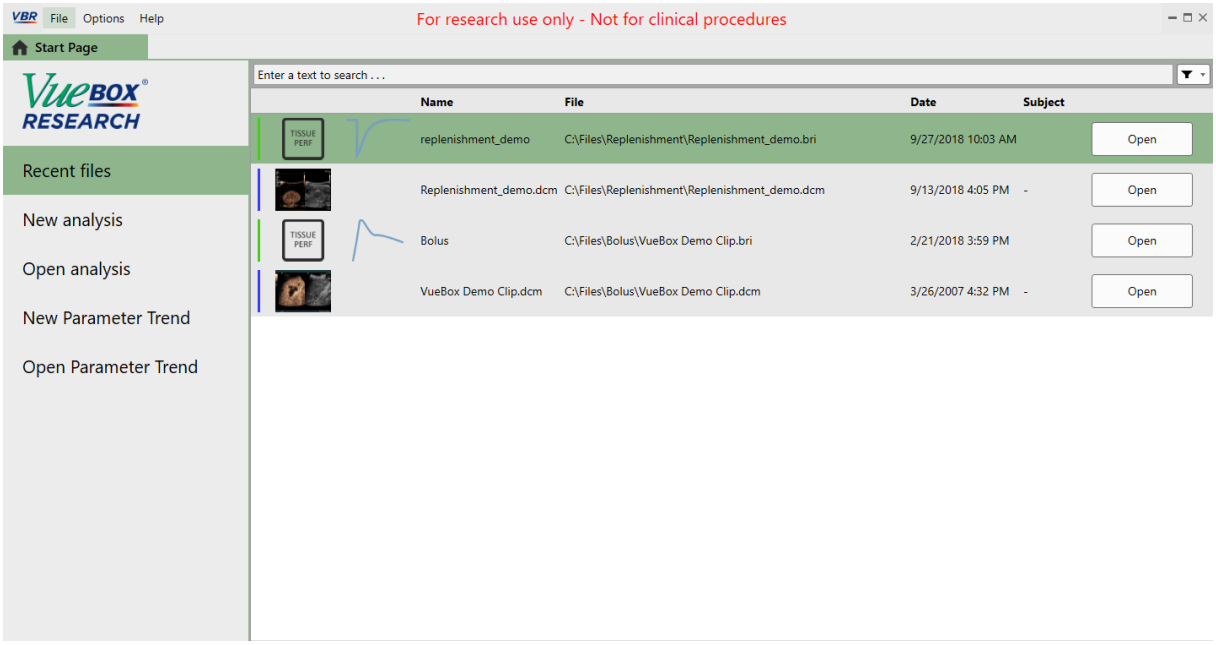


Figure 2 - List of recent clips, analyses and follow-ups accessible from the start page

From this start page, the user can start a new analysis (access the DICOM clips), as well as open an already existing VueBox® Research analyses. Recent clips, analyses and follow-ups can also be quickly re-opened from this start page (cf. Figure 2).

Additional information are displayed on the start page for each file (DICOM preview, exam date, subject name,…).
These information can be disabled from the top menu "Options -> DICOM preview -> Off". When disabled, only the file name and file path are displayed. The additional information are displayed to ease the selection of the correct file, but can also strongly increase the start page loading time in some specific cases.

The associated analyses of a clip (i.e. previously saved analysis contexts) are accessible using the "+" button (cf. Figure 3), and can be restored.

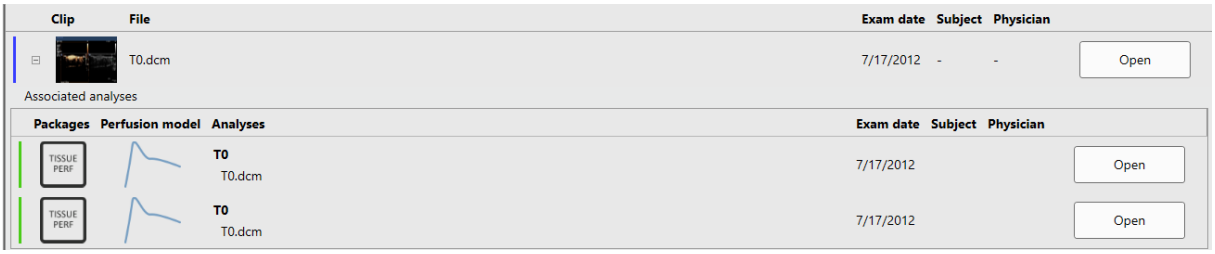


Figure 3 - Display associated analyses of a specified clip

From the start page, several clips can be opened as one concatenated clip, by selecting clips while pressing the "Ctrl" key of the keyboard. Then, if the selected clips are concatenable you can click on the button "Concatenate" (cf. Figure 4). Clips can also be concatenated later during the clip edition (cf. section 3.7.4).

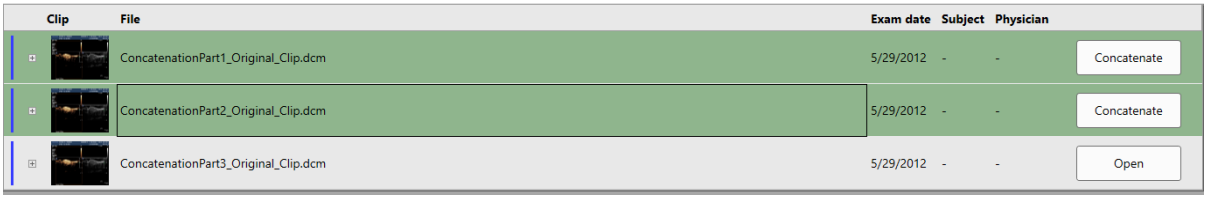


Figure 4 - Clips concatenation from the start page

If the selected clips are not concatenable (clips acquired at different times, different sources…), then VueBox® Research proposes to open them as separated clips (cf. Figure 5).

Figure 5 - Open as separated clips

Once a clip is opened, the user must select the appropriate package (e.g. Tissue Perfusion, Tissue Normalization, Low-Intensity Signal analysis), containing a set of dedicated features to be used in a specific context (cf. section 3.3).

A one-quadrant view is displayed, including the analysis settings panel, the clip editor, which are functionalities useful prior to launching the analysis process (e.g. ROI drawing, acquisition settings, etc.).

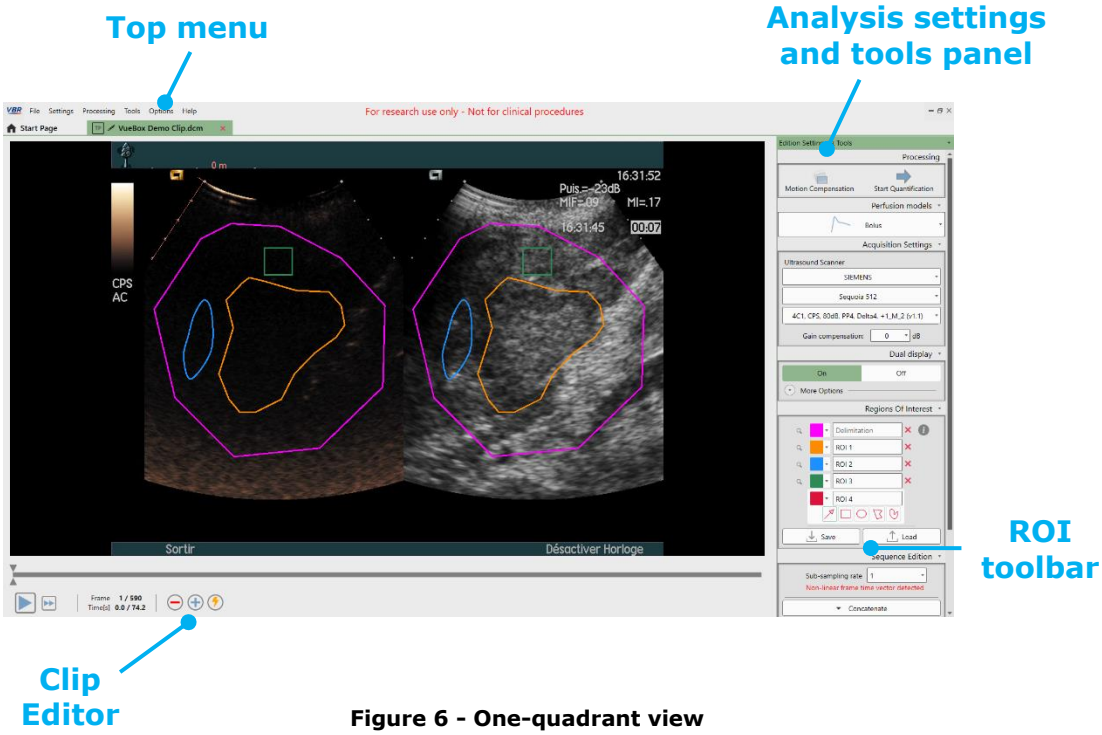


Figure 6 - One-quadrant view

Finally, when the perfusion data processing is completed, results are presented in a four-quadrant view, where time-intensity curves, parametric images, perfusion parameter values are displayed.

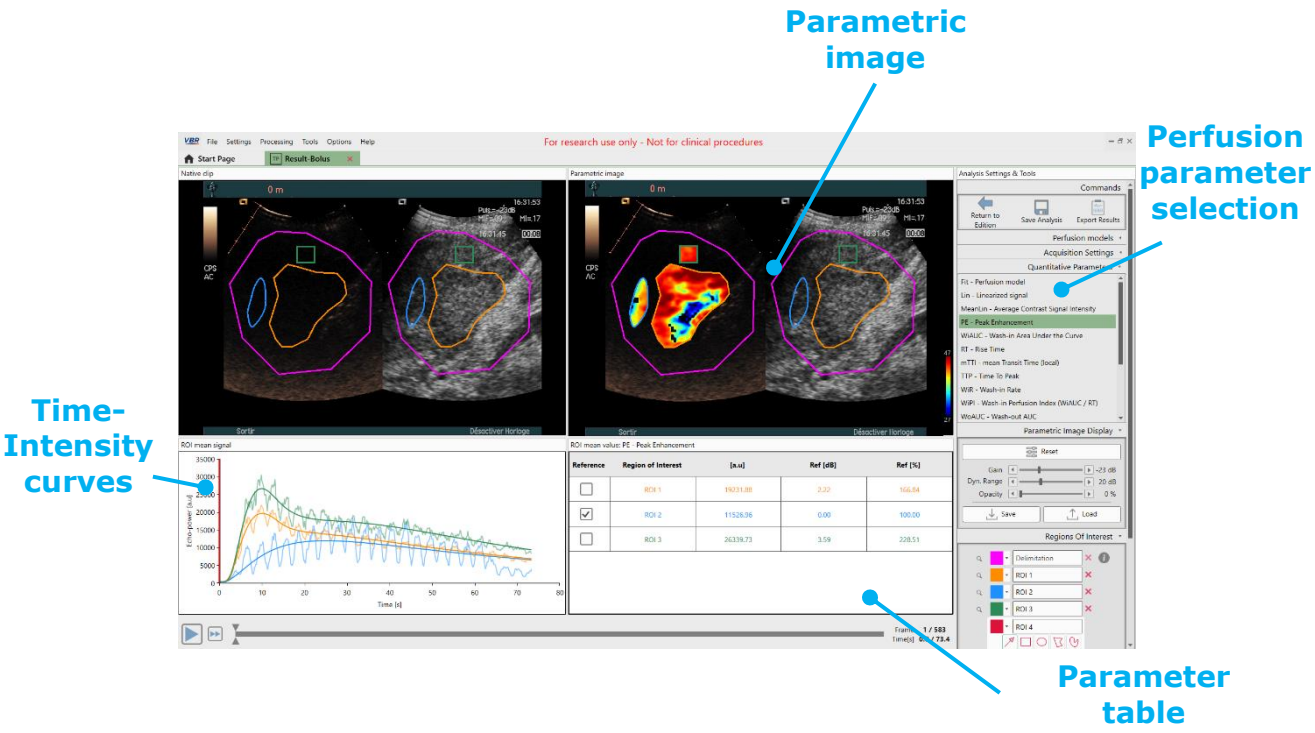


Figure 7 - Four-quadrant view

3.2 General workflow

The application workflow is easy and intuitive. It consists of the following steps:

1. Load a dataset
2. Choose an application package
3. Adjust analysis settings
4. Select perfusion model, if applicable
5. Remove unwanted images with the clip editor
6. Draw several ROI
7. Apply motion compensation if needed
8. Perform quantification
9. Visualize, save and export results

3.3 Specific application packages

3.3.1 Principle

While VueBox® Research is a general quantification toolbox, dedicated features have been developed to address specific needs.). These dedicated features are placed into "packages", which can be selected according to user needs.

In most cases, the core features of VueBox® Research (e.g. video data linearization, clip edition, ROI drawing, motion compensation, analysis context saving, result exporting, etc.) are similar in all packages.

3.3.2 Package selection

Specific application packages can be selected after opening a clip (see section 3.1) by clicking on the appropriate button.

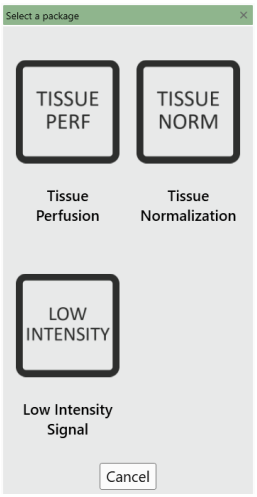


Figure 8 - Specific application package selection

The user should make sure to select the appropriate package in order to perform its analysis.

3.3.3 TISSUE PERFUSION

The Tissue Perfusion package contains generic perfusion quantification tools, including both Bolus and Replenishment perfusion models (see section 3.13.5), allowing to extract quantitative perfusion estimates through perfusion parameters.

3.3.4 TISSUE NORMALIZATION

The Tissue Normalization package contains the following specific tools:

- Bolus perfusion model
- Dynamic Vascular Pattern (see section 3.13.6)
- Dynamic Vascular Pattern Parametric (see section 3.13.7)
- Customized analysis report (see section 3.15.4)

These tools allow the enhancement of blood perfusion differences between different regions in a tissue.

This package does not include any perfusion quantification tools, as opposed to Tissue Perfusion Package.

3.3.5 LOW-INTENSITY SIGNAL ANALYSIS

This tool is designed to depict Maximum Intensity Projection of a Low-Intensity Signal in a ROI adjacent to or surrounded by a high-intensity background.

In this package, specific results are available such as:

- Perfused Area (see section Perfusion Segments Analysis 3.13.8)
- Relative Perfused Area (rPA)

3.4 SUPPORTED DATASETS

VueBox® Research supports contrast ultrasound 2D DICOM clips of systems for which linearization tables are available (also called calibration files). Other datasets such as Color Doppler clips, B-mode clips and contrast/B-mode overlay displays are not supported.

The list of compatible presets is available on https://vuebox-research.com. Bracco can only guarantee the accuracy of VueBox® Research analysis for the preset systems included in the list.

For ASR-compatible (Advanced System Recognition) ultrasound systems, linearization is performed automatically and manual selection of a calibration file is not required. More information can be found on https://vuebox-research.com.

3.5 ANALYSIS SETTINGS AND TOOLS

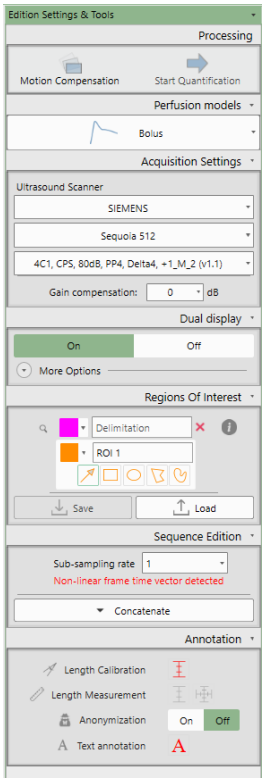


Figure 9 – Analysis settings and tools panel

The analysis settings and tools panel is displayed in any clip editor tab, when a clip is opened. From this panel, you can:

- change perfusion model (see section 3.13.5)
- specify acquisition settings and gain compensation (see section 3.6)
- manage dual display (see section 3.8.4)
- draw regions of interest (see 3.8)
- edit sequence, including sub-sampling (see section 3.7.4) and concatenation (see section 3.7.5)
- overlay text annotations (see section 3.11), enable anonymization (see section 3.10) and measure lengths (see section 3.9)
- Launch motion compensation and start quantification

3.6 ACQUISITION SETTINGS

Before processing a clip in VueBox® Research, the user has to ensure that the selected ultrasound scanner corresponds to the system and the settings used for acquisition, so as to apply the correct linearization function to the image data (cf. Figure 10).

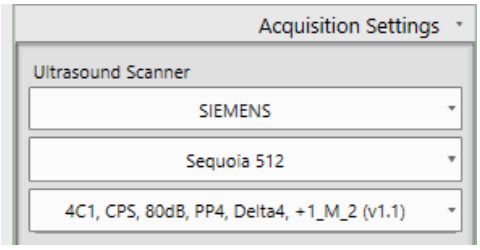


Figure 10 - Ultrasound Scanner panel

The list of scanners and settings available in this list depends on the calibration files locally stored on the user's computer. Calibration files contain the appropriate linearization function and color map correction for a given ultrasound system and specific setting (i.e. probe, dynamic range, color map, etc.). Using calibration files, VueBox® Research can convert video data extracted from DICOM clips into echo-power data, a quantity directly

proportional to the instantaneous concentration of contrast agent concentration at each location in the field of view.

Calibration files are distributed to users according to their ultrasound system(s) (e.g. Philips, Siemens, Toshiba, etc.) and can be added to VueBox® Research by a simple drag & drop into the VueBox® Research user interface.

The most common settings are available for each ultrasound system. However, new calibration files can be generated, with specific settings, upon users' request. Please contact vuebox-research@bracco.com for more information on how to obtain additional calibration files.

In case an ultrasound system is ASR-compatible (cf. section 1.9), the ultrasound scanner panel is automatically completed and cannot be changed.

It is critical to make sure that these settings are correct before continuing with the analysis.

3.6.1 GAIN COMPENSATION

The gain compensation is intended to compensate for gain variations across different examinations in order to be able to compare results of a given subject across different studies.

Gain compensation updates the linearized signal according to gain. The user can apply the compensation according to the gain (e.g.: gain = 6dB => compensation = +6dB).

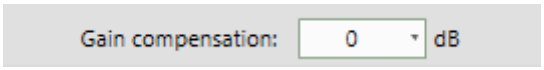


Figure 11 – Gain compensation panel

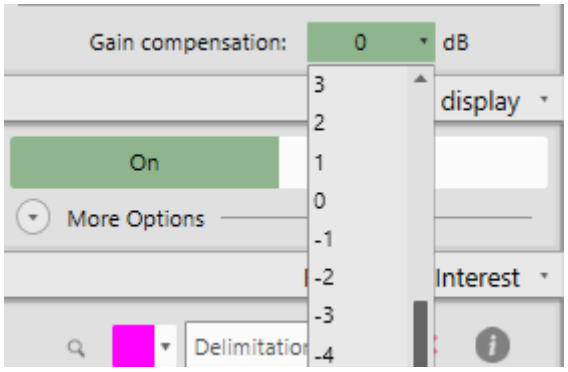


Figure 12 - Gain compensation selection

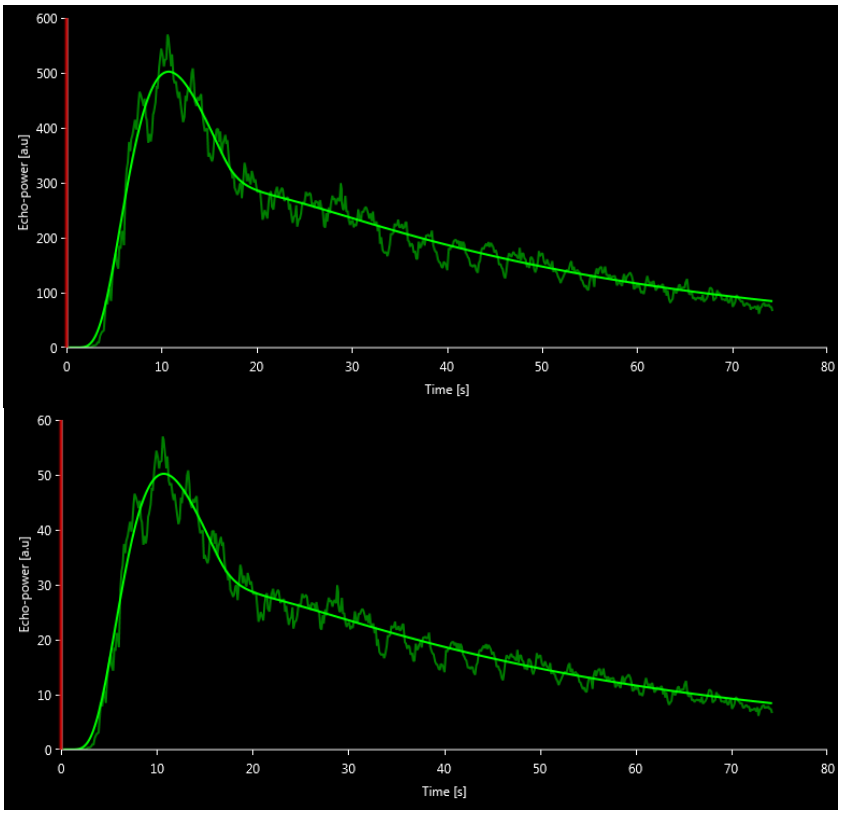


Figure 13 - Example of signals before and after gain compensation. In this case, we needed to compensate for a gain of 10 dB, meaning a compensation of +10 dB should be applied. Therefore the amplitude of the signal at the end is multiplied by 0.1 ($10^{-Gain/10}$).

3.7 CLIP EDITION

3.7.1 PRINCIPLE

The clip editor module allows you to limit the analysis to a specified time window, and also to exclude unwanted images from processing (either isolated or in ranges). The clip editor availability is described in 3.17 Tools availability.

As illustrated on the figure below, the clip editor may be used to retain, within the wash-in and wash-out phases of a bolus, only the images within a relevant time interval. If the destruction-replenishment technique is applied during the experiment, the clip editor automatically defines selectable replenishment segments by including images between two destruction events only.

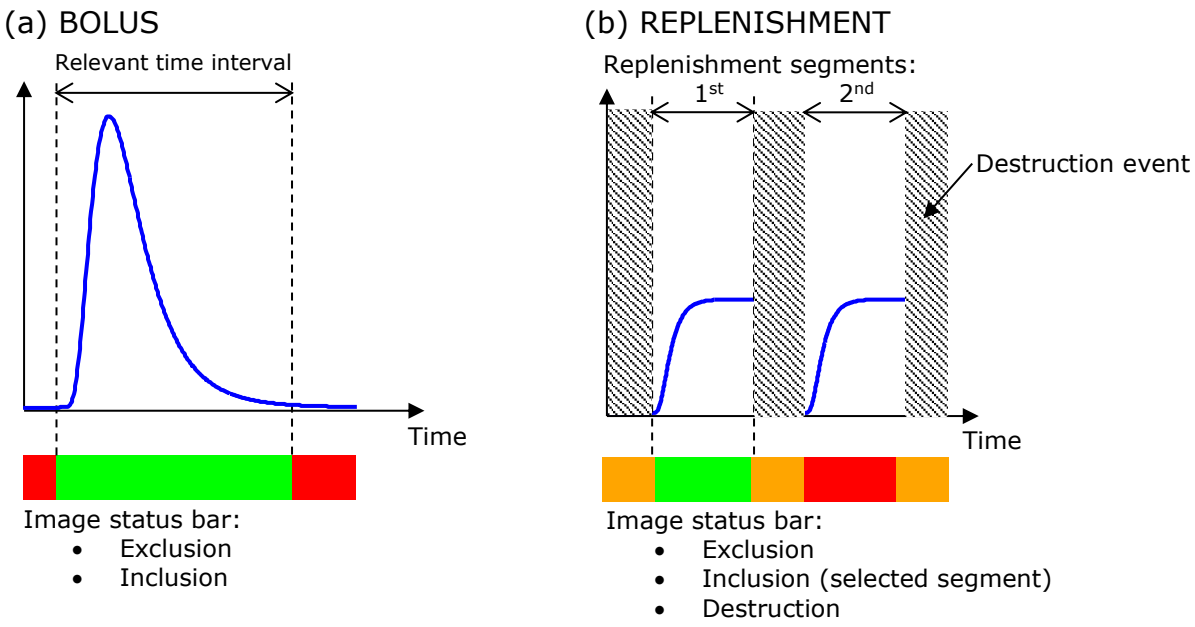


Figure 14 - Typical examples of clip edition

Using the bolus perfusion model, the user should make sure to include both wash-in and wash-out phases. Not doing so may affect the outcome of the perfusion data processing.

3.7.2 INTERFACE ELEMENTS

Figure 16 show screenshots of the interface elements in the clip editor.

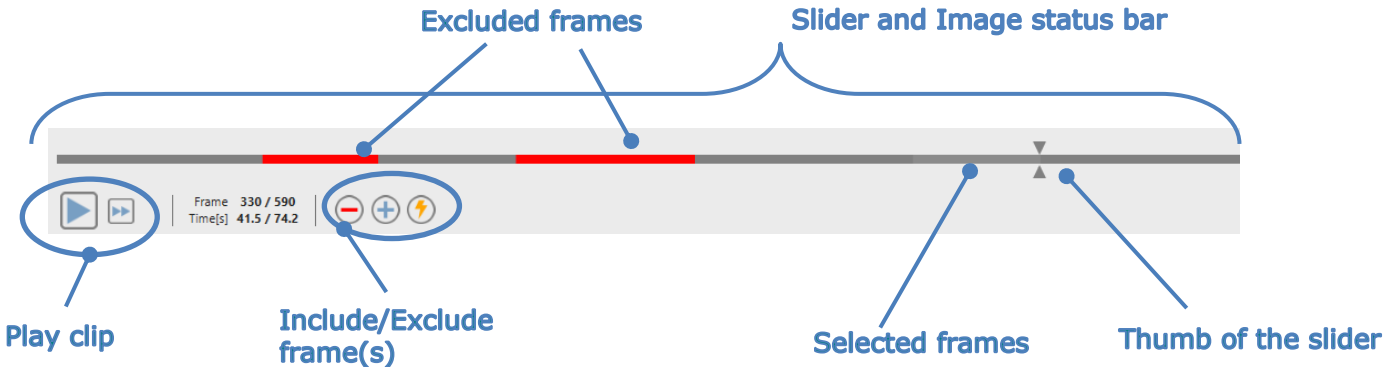


Figure 15 - User interface of the clip editor.

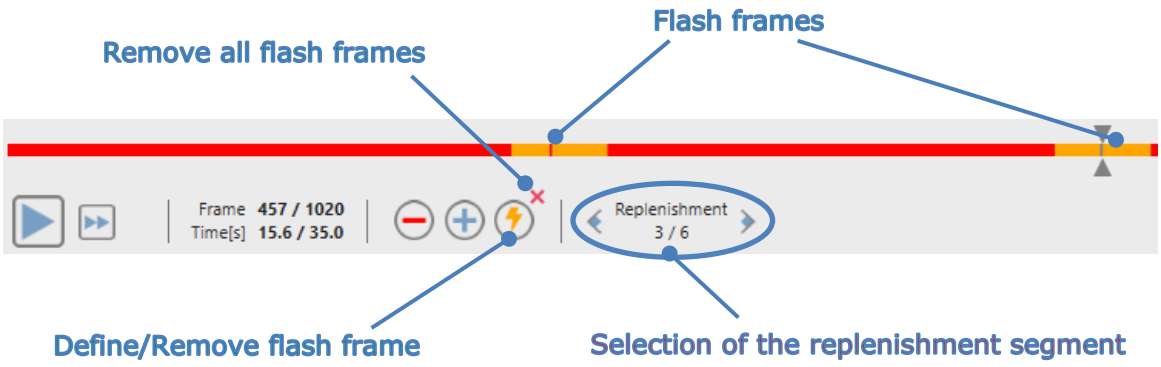


Figure 16 - Clip editor in replenishment mode.

Element	Name	Function
Image display		
Frame 457 / 1020	**Image number**	shows the order number of the currently displayed image as well as the total number of images available in the clip.
Time[s] 15.6 / 35.0	**Time indicator**	shows the time instant of the currently displayed image as well as the duration of the clip.
	Zoom In / Out	increases or decreases the image size.
	Image slider	selects the image to be displayed. If the cursor points to an excluded image, a red frame appears around it.
	Image status bar	shows excluded and included image ranges in red and gray, respectively. Destruction images are shown in orange.
	Play	runs the movie player.
	Fast play	runs the movie player in fast mode.

Clip editor

	Exclude	Excludes the selected frames (or the current frame if there is not selection).
	Include	Includes the selected frames (or the current frame if there is not selection)
	Add Flash	Marks the current image(s) as flash(es).
	**Replenishment segment selector**	selects the previous/next replenishment segment (only available if the clip includes destruction-replenishment segments).

3.7.3 WORKFLOW

EXCLUDING IMAGES

To exclude a range of images:

1. Click the **left mouse button** on the first image to be excluded and **keep it pressed**
2. Move the **Image slider** to the last image to be excluded
3. **Release** the left mouse button
4. Click the **Exclude** button (or press the "Delete" or "-" key on your keyboard)

INCLUDING IMAGES

To include a range of images:

1. Click the **left mouse button** on the first image to be excluded and **keep it pressed**
2. Move the **Image slider** to the last image to be excluded
3. **Release** the left mouse button
4. Click the **Include** button (or press the "+" key on your keyboard)

CHANGING THE RANGE OF EXCLUDED IMAGES

To change the range of excluded images:

1. Move the mouse pointer over the **Image status bar** to any border of a range of excluded images ( )
2. When the pointer's shape changes to a vertical split , drag the border to change the range of excluded images.

3.7.4 SUB SAMPLING RATE

VueBox® Research allows to define the desired **sub-sampling rate** if needed, so as to reduce the number of frames to be processed (**optional**).

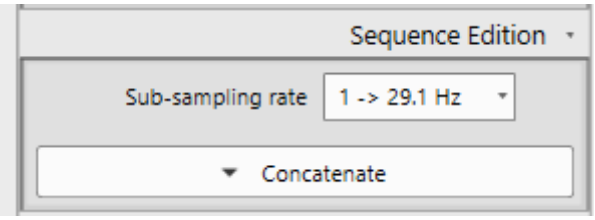


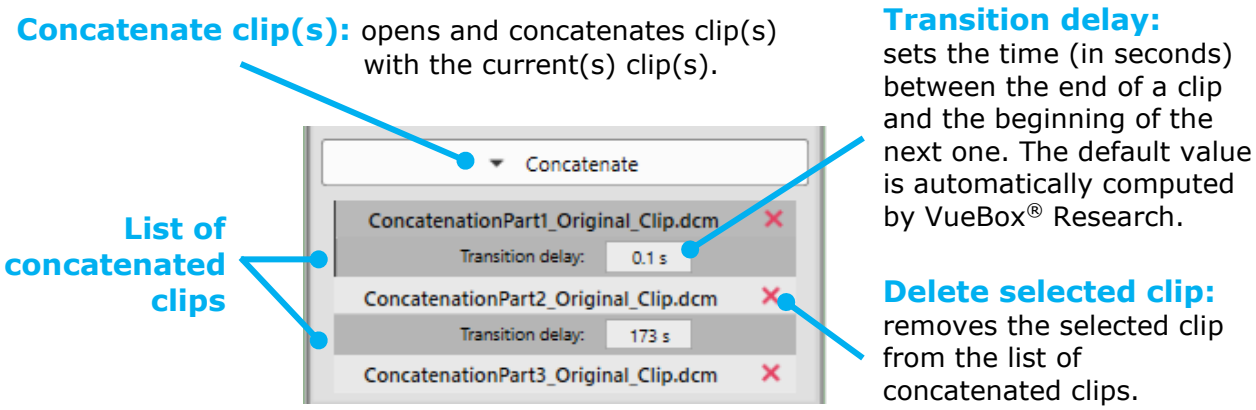
Figure 17 - Sub-sampling rate edition

The user should make sure that the clip frame rate read from the DICOM file and displayed in the video settings panel is correct before pursuing the analysis. An incorrect frame rate may result in a wrong time base and, thus, affect the computed values of perfusion parameters.

3.7.5 CLIP CONCATENATION

The clip concatenation, or combination, is the process of pooling clips together to build up a single sequence of images. Using this feature, a set of clips recorded in chronological order by an ultrasound scanner can be processed. The concatenation function is useful when the ultrasound system has a limited clip recording time per DICOM file.

Bracco recommends concatenating clips with a clip-transition delay ≤ 3 minutes.



FLASH IMAGE DETECTION

The selection of the perfusion model (i.e. Bolus or replenishment) can be performed in the clip editor. So as to reduce the risk of selecting a wrong model (e.g. the replenishment model for a bolus injection), the replenishment button becomes active only if the software has detected flash images in the clip. The flash detection is an automatic process launched every time a clip is loaded in VueBox® Research.

Figure 18 - Flash image detection

The automatic flash image detection progress can be seen in the clip editor toolbar as shown in the figure above. In some cases, this detection may not be accurate. Therefore, you may want to cancel it when the automatic detection is not accurate or fails. To cancel this flash image detection or to remove unwanted flash images:

1. If the detection is still being performed, click on the button (located at the bottom right of the flash button) to stop it.
2. If the detection is completed, click on the button (located at the top right of the flash button) to remove all flash images.

However, the "Replenishment" model will not be accessible anymore. Therefore, if you want to process destruction / replenishment clips with the replenishment model, you will need to identify flash images manually by placing the image slider at the desired location and clicking the button or pressing the "F" keyboard key on each destruction frame.

Flash image detection and/or manual definition is only available in Tissue Perfusion package.

3.8 REGIONS OF INTEREST

3.8.1 PRINCIPLE

With the help of the **ROI toolbar**, you can define up to five **Regions of Interest** on images of the clip using the mouse; a mandatory ROI named Delimitation and up to four generic ROI. The Delimitation ROI is used to delimit the processing area. It must thus exclude any non-echographic data, such as text, colorbars or image borders.

In Tissue Perfusion package, the user can select a specific ROI as reference, and all parameters of the other ROIs will be expressed as relative measurements (%) vs the reference. Note that ROI names are arbitrary and can be entered by the user.

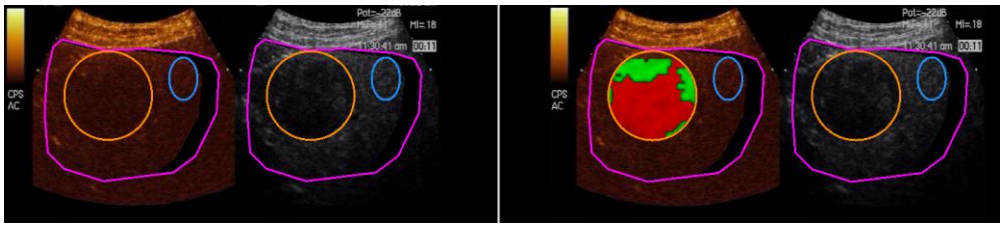


Figure 19 - Example of Regions of interest

In Tissue Normalization package, it is mandatory to create at least 2 ROIs: one for the Tissue to be analysed, and one as Reference ROI.

For the specific application package Low-Intensity Signal analysis, ROIs are not generic anymore and have a specific use.
The Low-intensity Region 1 (LIR1) must delineate an area with low intensity signal, whereas the High Intensity Region (HIR) must be positioned in the area with high contrast signal (cf. Figure 35 for an example).

Additional 2 LIRs (LIR2, LIR3) can be added at user's discretion.

3.8.2 INTERFACE ELEMENTS

The ROI tools are located in the **Regions of Interest** section of the **Analysis Settings and Tools** panel:

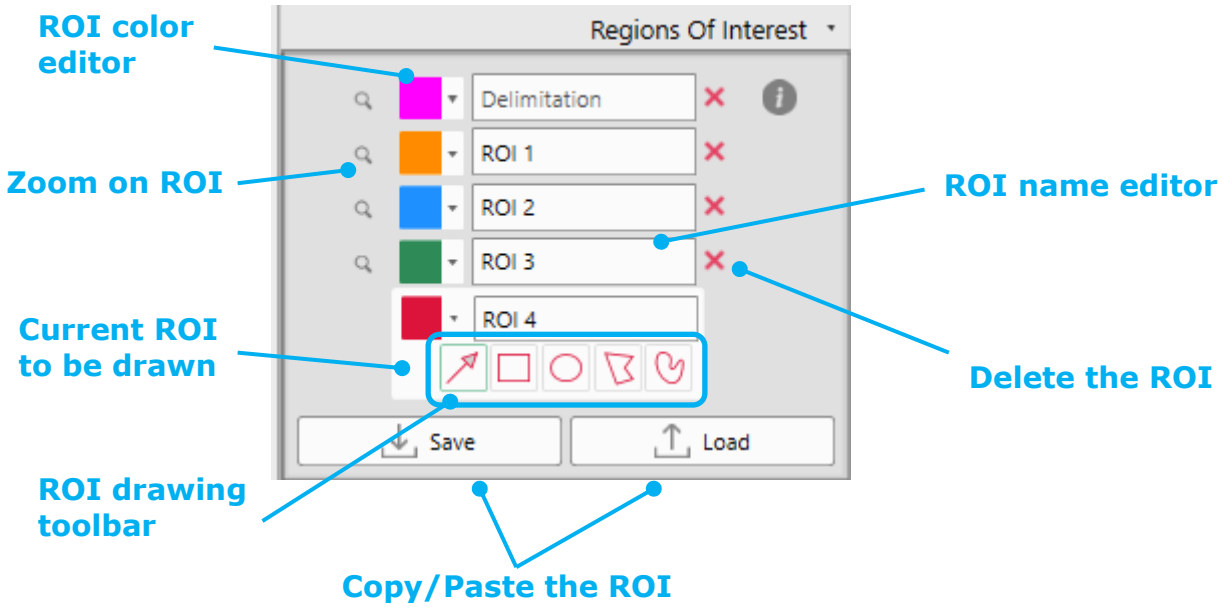


Figure 20 - Regions of Interest section

The **ROI toolbar** offers tools to draw four different shapes. The **ROI label** above the toolbar identifies the current region to be drawn.

Button	Name	Function
	Select	allows to select / modify a region of interest.
	Rectangle	draws a rectangular shape.
	Ellipse	draws an elliptical shape.
	Polygon	draws a closed polygonal shape.
	Closed curve	draws a closed curvilinear shape.

3.8.3 WORKFLOW

DRAWING A ROI

To draw a rectangular or elliptical ROI:

1. Select a shape in the ROI toolbar (or)
2. Move the mouse pointer to the wanted location in the B-mode image (left side) or the contrast image (right side)
3. Click and drag to draw the ROI.

To draw a closed polygonal or curved ROI,

1. Select a shape in the ROI toolbar ( or )
2. Move the mouse pointer to the wanted location in the B-mode image (left side) or the contrast image (right side)
3. To add anchor points, click repeatedly while moving the mouse pointer
4. Double-click at any time to close the shape.

DELETING A ROI

To delete a ROI:

- Solution 1:

  Click on the  button next to the ROI you want to remove

- Solution 2:

1. Right click in the image to set the ROI selection mode or click the  button
2. Move the mouse pointer to any border of the ROI
3. Select the ROI using the left or right mouse button
4. Press either the DELETE or BACKSPACE keys.

MOVING A ROI

To change the location of a ROI:

1. Right click in the image to set the ROI selection mode or click the  button
2. Move the mouse pointer to any border of the ROI
3. When the pointer shape changes to a double-arrow, click and drag the ROI to a new location

EDITING A ROI

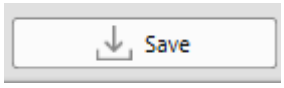
To change the location of anchor points of a ROI:

1. Right click in the image to set the ROI selection mode or click the  button
2. Move the mouse pointer to any anchor point of the ROI
3. When the pointer shape changes to a cross, click and drag the anchor point to a new location.

COPYING AND PASTING ROI

Regions of interest can be copied into a ROI library and pasted at a later time point, in any clip analysis.

To copy all the ROI currently drawn:

1. Click the 

button
2. Set a name or accept the default generated one and press the OK button

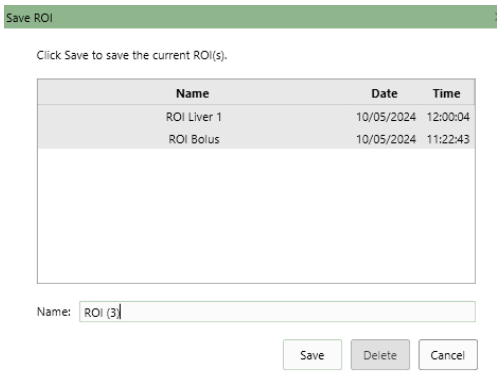
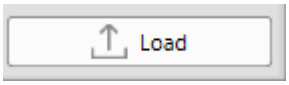


Figure 21 - Copying ROI into library

To paste ROI from the library:

1. Click the 

button
2. Select the item in the list and press the OK button

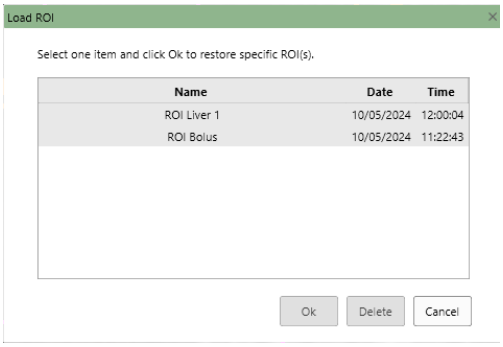


Figure 22 - Pasting ROI from library

3.8.4 DUAL DISPLAY MODE

The dual display mode takes advantage of the side by side representation available in most of DICOM clips with contrast image. Motion compensation works better with this feature activated. It also replicates all regions of interest drawn on one side to the other (see Figure 23).

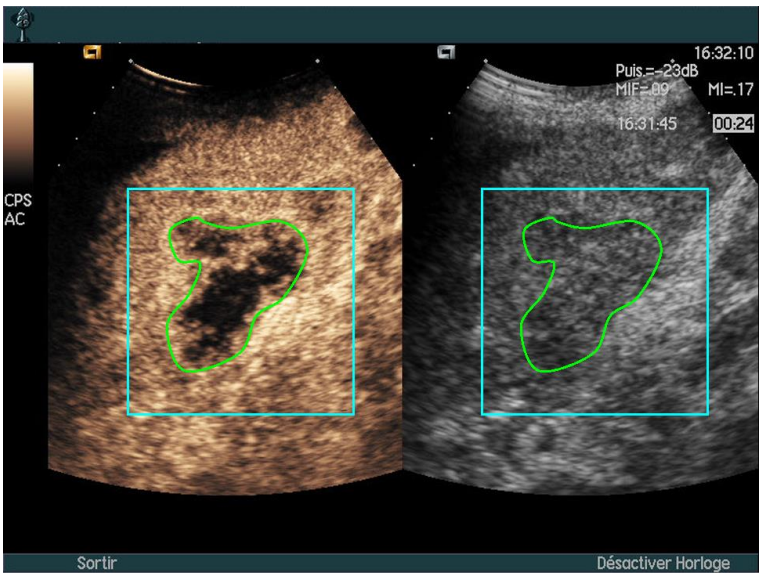


Figure 23 – Replicated ROIs on contrast and B-mode images

When possible (i.e. when all required data are present in the DICOM metadata), VueBox® Research will activate this feature automatically. This is indicated in the Dual Display section (see Figure 24).

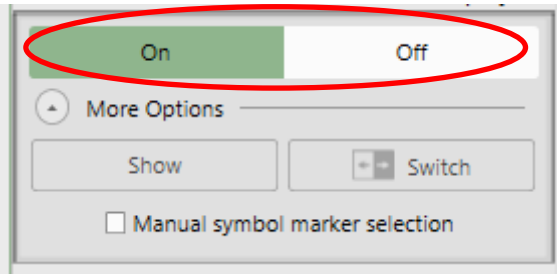


Figure 24 – Dual display Enable controls

In such case, areas for contrast and B-mode are displayed and labeled during a few seconds when a clip is being opened, as shown on Figure 25. It is also possible to display this info at any time by pressing the "Show" button on the "More Options" section. The "Switch" button allows to invert the two regions, in case the automatic dual display detection didn't detect the contrast and B-mode side properly.

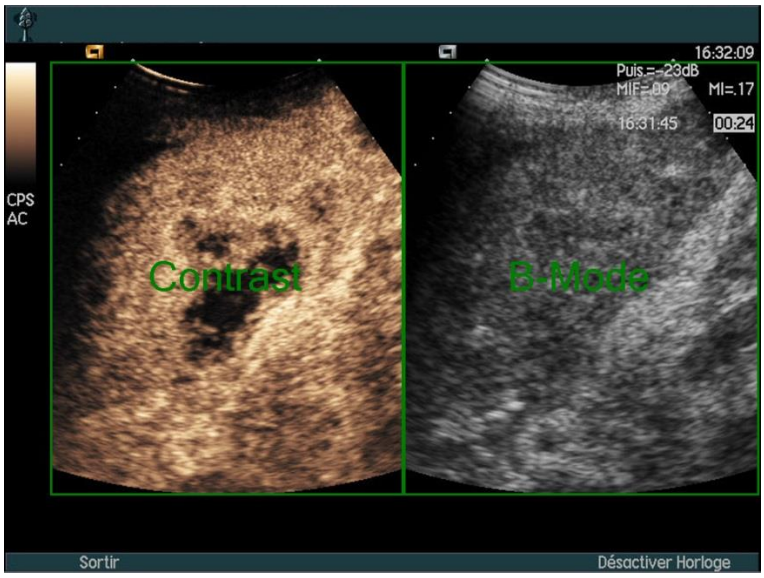


Figure 25 – Automatic contrast and B-mode area detection

If the dual display mode is not automatically activated although both contrast and B-mode images are present in the clip, it can be manually activated. It requires to define the location of the contrast symbol marker. To do so :

1. activate dual display 

2. press Ok on the message box
3. click on the probe orientation marker of the contrast image
4. control that the corresponding symbol marker is correctly located on the B-mode image, as shown on Figure 26.

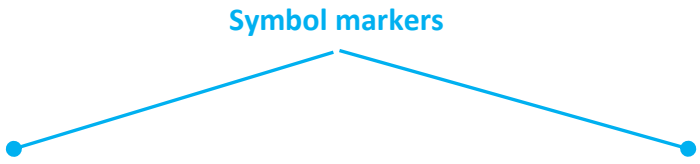


Figure 26 - Enabling Dual Display with symbol markers

If the clips do not contain symbol markers, VueBox® Research can use any other landmark to identify the location of the two images. To do so:

1. select the "Manual Symbol Marker Selection" tool on the "More Options" section
2. press Ok on the message box
3. select a recognizable landmark on contrast image
4. select the corresponding landmark on B-mode image.

The user should make sure to select the correct orientation marker (i.e. on the contrast-image side). Otherwise, all ROI may be inverted and all analysis results will be invalid.

In the manual landmarks selection mode, the user should carefully select a pair of image landmarks spaced in exactly the same way as the B-mode and contrast images. Otherwise, ROI positioning may be incorrect and this may degrade both image registration and analysis results.

Bracco recommends activating the dual display mode when available, as this feature increases the robustness of the motion compensation algorithm.

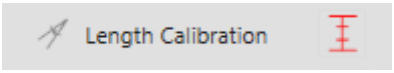
When all required data are present in the DICOM metadata, the dual display mode is automatically enabled if the clip contains both contrast and fundamental B-mode image areas.

Dual display also works with top-bottom orientation.

3.9 LENGTH CALIBRATION AND MEASUREMENT

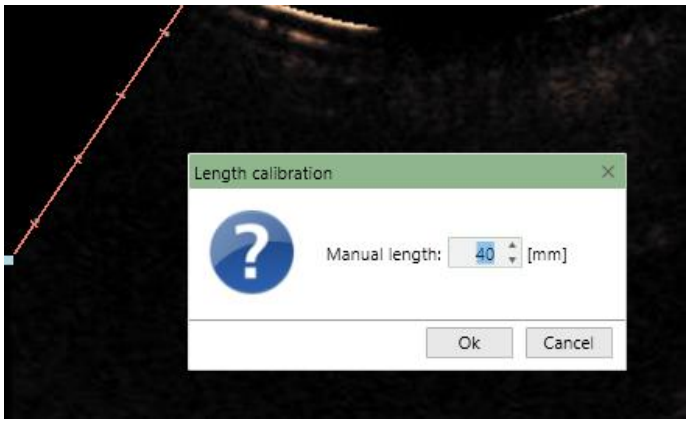
The Length Calibration tool is required for performing length and area measurements of anatomical objects in the images. It consists in identifying a known distance in any image of the clip. Once the line is drawn, the effective corresponding distance in mm needs to be entered.

The length calibration tool can be found in the "Annotations" section of the "Analysis Settings & Tools" panel, or in the "Tools" menu.



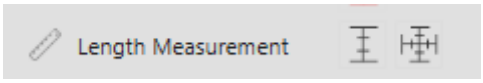
To calibrate:

1. click the length calibration button,
2. draw a line on a known distance in the image (e.g. along a calibrated depth scale),
3. in the Length calibration dialog box, type the known corresponding distance in mm.



Once the Length calibration has been defined, areas of regions of interest will be listed in cm^2, in the quantitative parameter table.

The lengths within the images can be measured with the Length measurement tool:



The first Measurement tool is called *ruler* and is used for drawing straight lines. The second one is called *cross ruler* and is able to draw a "cross", 2 lines perpendicular to each other.

To make a length measurement:

1. Select the type of ruler in the ROI toolbar (line or cross),
2. draw the ruler on the image by holding down the left mouse button and drag the line to change its length. The ruler direction, location and size can be modified with the same procedure,
3. the cross ruler follows the same principle. The user must know that the perpendicular line may be shifted by moving the mouse in the direction opposite to the first line.

The accuracy of the measurement tools was verified and the following error should be taken into account:

Error on Length (horizontal and vertical)	< 1%
Error on Area	< 1%

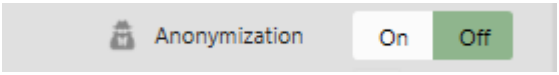
3.10 ANONYMIZATION OF CLIP

The Anonymize Clip Tool is useful for presentations, lectures or any occasions in which the user may wish to remove information embedded in the DICOM clip pixels to comply with privacy protection. This tool is available at any processing stage of VueBox® Research. The

user can move or resize the anonymization mask to hide the identification information. This mask is automatically filled with the most prominent color from the portion of the image covered.

The general workflow is as follows:

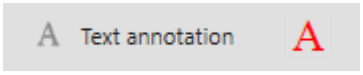
1. Click the "On" button in the Anonymization section:



2. Adjust and move the Anonymize mask (rectangular shape) to where the information to be hidden is located in the image.

Figure 27 - Anonymization mask

3.11 ANNOTATION

The Annotation Tool 

is used for labeling important parts of the image. After selecting the tool, click at a desired location for the annotation in the image. Then, the software displays a dialog box in which you may enter text. Annotations can be moved or deleted exactly like ROIs, using either the DELETE or BACKSPACE key.

3.12 MOTION COMPENSATION

3.12.1 PRINCIPLE

Motion compensation is a key tool for allowing reliable perfusion assessments. The tool availability is described in 3.17 Tools availability

Motion in a clip can be due to internal organ movements, such as breathing, or to slight probe movements. Manual alignment of individual images is extremely time-consuming and thus not proposed in VueBox® Research.

VueBox® Research provides an automatic motion correction tool to correct in-plane breathing-motion and probe movements by spatially realigning anatomical structures with respect to a user-selected reference image.

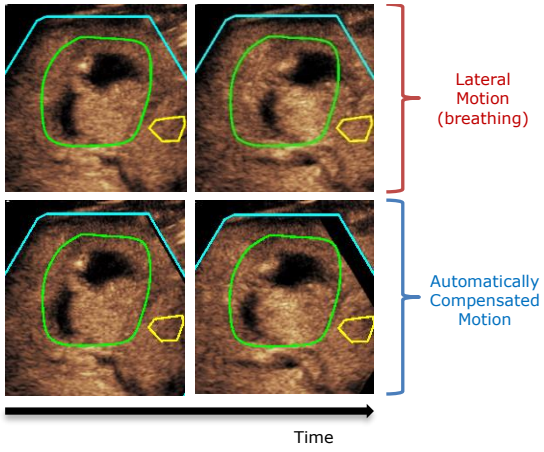


Figure 28 - Motion compensation example

3.12.2 WORKFLOW

To apply motion compensation:

1. Move the **Image slider** to choose a reference frame
2. Click the  button in the main toolbar

3. Once motion compensation is applied, the frame used as a reference is marked as blue in the clip editor ().
4. Check the accuracy of the motion compensation by scrolling through the clip using the **Image slider** (motion compensation is considered a success if the images are spatially realigned and any residual motion is deemed acceptable)
5. If the motion compensation is unsuccessful, try one of the following:
6. Select another reference image and click the  button again to re-apply **Motion compensation**.
7. Use the Clip editor to exclude any images thought to be degrading the result of motion compensation, such as out-of-plane movements, and then re-apply **Motion compensation**.

The user is responsible for checking the accuracy of the motion compensation before pursuing the clip analysis. In case of failure, incorrect results may occur.

The user should exclude any out-of-plane images using the clip editor before performing a motion compensation.
In case of input clip with poor quality or excessive motion (e.g. strong and sudden breathing), the user should remove all unwanted images.

Motion compensation is applied within the Delimitation ROI. The user should carefully draw this ROI, and check that non-echographic data (e.g. text, logo, scale, etc.) are not present within the ROI. Furthermore, in case anatomical structure is missing in images within delimitation ROI (on BMode and contrast side), user should avoid performing motion compensation.

The user should avoid performing motion compensation when the clip does not contain any motion as this may degrade slightly the analysis results.

3.13 PERFUSION DATA PROCESSING

3.13.1 PRINCIPLE

The **Perfusion data processing (or perfusion quantification)** feature represents the core of the VueBox® Research functionality. Its availability is described in section 3.17 Tools availability. It performs quantification in two steps. Video data are first converted into echo-power data, a quantity directly proportional to the instantaneous concentration of contrast agent concentration at each location in the field of view. This conversion process, called **linearization**, takes into account color or greyscale rendering, the dynamic range of log-compression used during the clip acquisition and compensates for contrast gain, as long as pixel intensity is not truncated or saturated. The echo-power data as a function of time, or **Linearized signals,** are then processed to assess blood perfusion, using a curve-fitting approach with a parametric **Perfusion model**. The parameters derived from such a model are called **Perfusion parameters** and are useful for relative estimates of local perfusion (e.g. in terms of relative blood volume or relative blood flow). In the next sections, the concepts of linearized signal, perfusion modeling and parametric imaging are explained further.

3.13.2 LINEARIZED SIGNAL

A linearized (or echo-power) signal represents echo-power data as a function of time at either the pixel level or in a region of interest. The linearized signal results from a linearization process of the video data and is proportional to the local ultrasound agent

concentration. As it is expressed in arbitrary units, only relative measurements are possible.

For instance, let's consider echo-power amplitudes at a given instant in two ROIs. If the echo-power amplitude is twice as high in the ROI A than in the ROI B, this means that the concentration of ultrasound contrast agent in ROI A is close to double that present in ROI B. The same is true at the pixel level.

3.13.3 CONTRAST ARRIVAL DETECTION

At the beginning of the perfusion quantification process, when the **Bolus model** is selected, the arrival of contrast is detected within the ROIs. The time of contrast arrival is automatically determined as the instant when the echo-power amplitude rises above the background (wash-in phase), and is represented by a red line. As shown in the **Contrast arrival detection** dialog box, this instant remains a suggestion which may be modified by dragging the red cursor line. After pressing the OK button, all images preceding the selected instant will be excluded from the analysis and the clip time origin will be updated accordingly. This instant should be shortly before contrast arrival in any region.

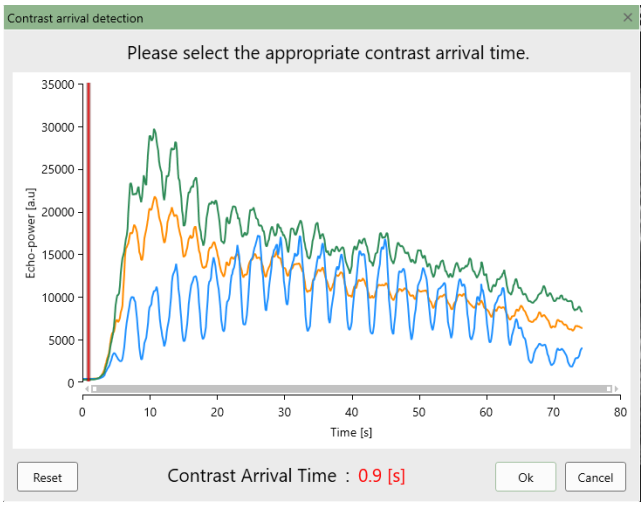


Figure 29 - Contrast arrival detection dialog box

The automatic contrast arrival detection is to be considered as a suggestion only. The user should make sure to review this suggestion before pressing OK.

3.13.4 SKIP DUPLICATE IMAGES

Duplicate images (i.e. two or more consecutive similar images) may be found when a clip was exported from the ultrasound scanner at a frame rate higher than the acquisition frame rate (e.g. 25 Hz instead of 8 or 15 Hz). In this case, duplicate images are found in the clip. In order to insure a correct analysis as well as reliable time-related parameters, the duplicate images have to be discarded. To do so, when the clip is being loaded in memory, the software compares each frame with the previous one and discards any duplicate ones. This operation is automatic and requires no user intervention.

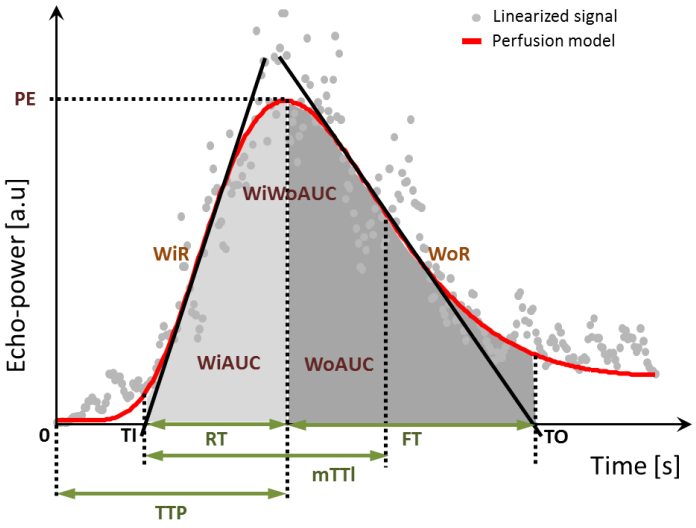
3.13.5 PERFUSION MODELS

Perfusion estimates in VueBox® Research are made by a curve fitting process that adjusts the parameters of a mathematical model function to fit the experimental linearized signal in an optimal way. In the context of ultrasound contrast imaging, the mathematical function is called **Perfusion model** and is chosen to represent either bolus kinetics or

replenishment kinetics following bubble destruction. Such models serve to estimate sets of **Perfusion parameters** for quantification purposes.

These parameters can be divided into three categories: those representing an amplitude, a time and a combination of amplitude and time. Firstly, amplitude related parameters are expressed as echo-power, in a relative way (arbitrary units). Typical amplitude parameters are the peak enhancement in a bolus kinetics, or the plateau value in a replenishment kinetics, which may be associated with relative blood volume. Secondly, time related parameters are expressed in seconds and refer to the timing of the contrast-uptake kinetics. As an example of time parameter in a bolus, the rise time (RT) measures the time that a contrast echo signal takes to go from baseline level to peak enhancement, a quantity related to blood flow velocity in a portion of tissue. Finally, amplitude and time parameters may be combined so as to produce quantities related to the blood flow (= blood volume / mean transit time) for replenishment kinetics or the wash-in rate (= peak enhancement / rise time) for bolus kinetics.

For **Bolus** kinetics, VueBox® Research provides the following parameters, illustrated in the figure hereafter:

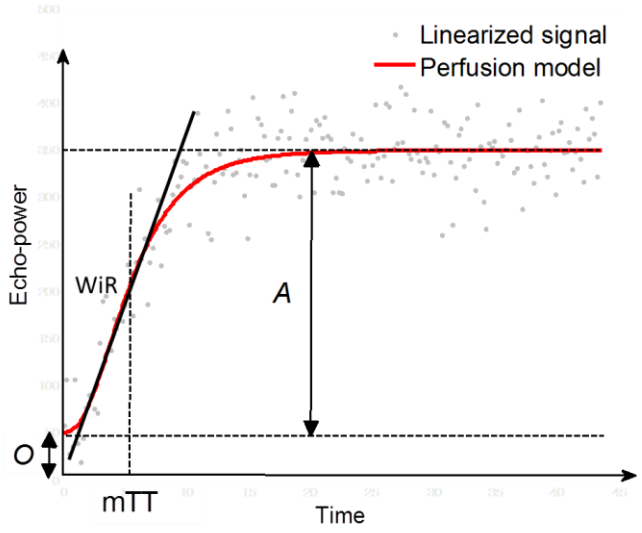


PE	Peak Enhancement	[a.u]
WiAUC	Wash-in Area Under the Curve (*AUC (TI:TTP)*)	[a.u]
RT	Rise Time (*TTP – TI*)	[s]
mTTI	mean Transit Time local (mTT – TI)	[s]
TTP	Time To Peak	[s]
WiR	Wash-in Rate (*maximum slope*)	[a.u]
WiPI	Wash-in Perfusion Index (*WiAUC / RT*)	[a.u]
WoAUC	Wash-out AUC (*AUC (TTP:TO)*)	[a.u]
WiWoAUC	Wash-in and Wash-out AUC (*WiAUC + WoAUC*)	[a.u]
FT	Fall Time (*TO – TTP*)	[s]
WoR	Wash-out Rate (*minimum slope*)	[a.u]

QOF	Quality Of Fit between the echo-power signal and *f(t)*	[%]

Where TI is the instant at which the maximum slope tangent intersects the x-axis (or offset value if present), and TO is the instant at which the minimum slope tangent intersects the x-axis (or offset value if present).

For **Replenishment** kinetics, VueBox® Research provides the following parameters, illustrated in the figure hereafter:



rBV	relative Blood Volume (A)	[a.u]
WiR	Wash-in Rate (*maximum slope*)	[a.u]
mTT	mean Transit Time	[s]
PI	Perfusion Index (*rBV / mTT*)	[a.u]
QOF	Quality Of Fit between the echo-power signal and *f(t)*	[%]

where [a.u] and [s] are arbitrary unit and second, respectively.

The selection of the perfusion model (e.g. Bolus, Replenishment) can be performed in the "Perfusion models" section in the "Analysis Settings & Tools" panel.

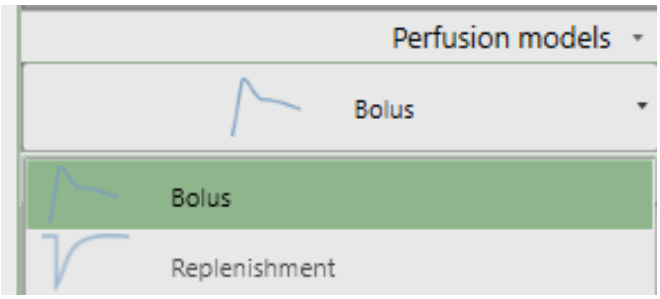


Figure 30 - Perfusion model selection

Note: the availability of perfusion models depends on the selected application package (see section 3.3).

The user must ensure that the right perfusion model was selected before performing the perfusion data processing otherwise analysis results may be incorrect.

The user must ensure that perfusion kinetics are not affected by any vessel or artifact.

In the replenishment perfusion case, the user must ensure that the plateau value is reached before considering analysis results.

3.13.6 DYNAMIC VASCULAR PATTERNS

This feature is available in the Tissue Normalization application package (see section 3.3.4).

The Dynamic Vascular Pattern (DVP) can be used to highlight how the contrast agent is being distributed in a specific area compared with the surrounding tissue. Therefore the hyper-enhanced and hypo-enhanced pixels are being displayed over the time. Hyper-enhanced areas are displayed using warm colors, whereas hypo-enhanced ones are represented with cold hues.

DVP signal is defined as the subtraction of a reference signal from pixel signals:

$$f_{DVP}(x,y,t) = [f(x,y,t) - O(x,y)] - [f_{REF}(t) - O_{REF}]$$

Where f is the instantaneous signal and O the offset associated with (x,y) pixel coordinates. On the basis of this result the software will display a curve representing the distribution of the contrast agent.

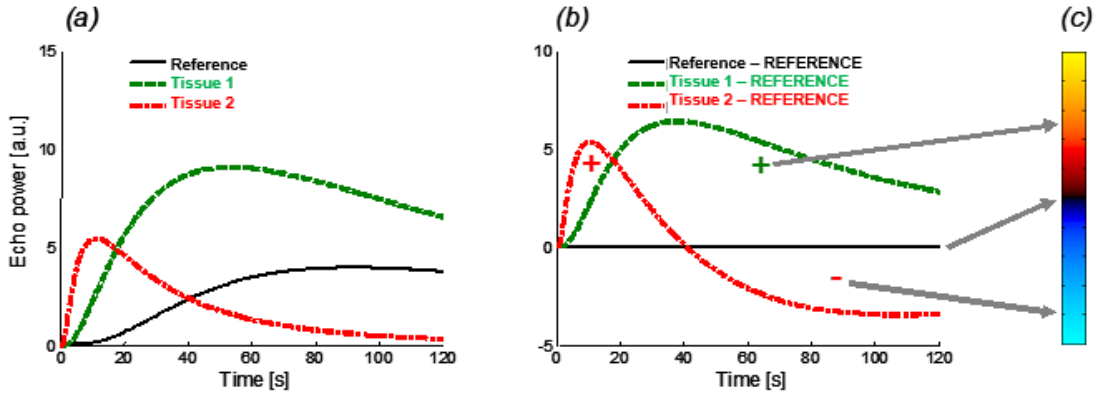


Figure 31 - DVP processing

In the above figure, (a) represents a simulation of the perfusion kinetics of Reference (black), of a "faster-washing" Tissue 1 (red) and of a "slower-washing" Tissue 2 (green), (b) is the DVP processed signals expressed as differences of echo-power signals with respect to the reference, and (c) the bipolar color map used to code Dynamic Vascular Pattern Parametric (DVPP), coding in warm and cold colors the positive and negative amplitudes, respectively, resulting from subtraction.

3.13.7 DYNAMIC VASCULAR PATTERN PARAMETRIC

This feature is available in the Tissue Normalization application package (see section 3.3.4).

In addition to the DVP feature (see section 3.13.6), the Dynamic Vascular Pattern Parametric (DVPP) maps difference signals signatures into a single image, called DVP parametric image.

Using DVP signals, a classification is performed at the pixel level where each pixel is categorized into four classes according to the polarity of its difference signal over time, namely

- unipolar positive "+"(hyper-enhanced signature),
- unipolar negative "-" (hypo-enhanced signature),
- bipolar positive "+/-" (a hyper-enhancement followed by a hypo-enhancement) and, conversely,
- bipolar negative "-/+".

A DVP parametric image is then built as a color-coded map, where pixels with red-, blue-, green-, and yellow-hue colors correspond to "+", "-" , "+/-" and "-/+" classes, respectively, with a luminance proportional to the difference signal energy.

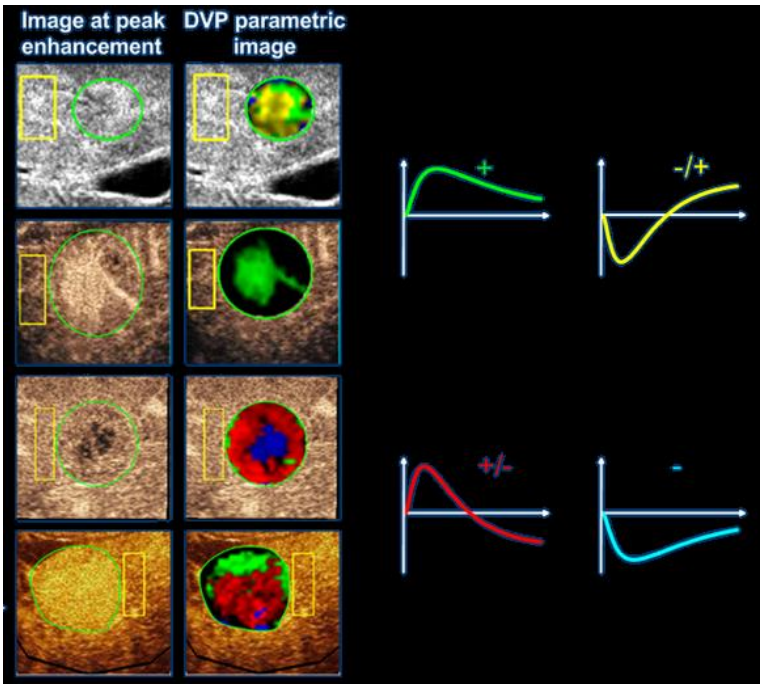


Figure 32 - Example of DVPP images

3.13.8 PERFUSION SEGMENTS ANALYSIS

This feature is available in the Low-Intensity Signal analysis application package (see section 3.3.5).

For the Low-Intensity Signal analysis application package, two ROIs must be defined: a Low-Intensity Region (LIR) and a High-Intensity Region (HIR).

Also, for this specific package, no curve fitting is applied on linearized data. The linearized data is not analyzed entirely. Indeed, only 3 time segments (1 baseline segment and 2 perfusion segments) will be analyzed.

As shown in Figure 33:

- The baseline segment is a 1 second interval selected before the contrast arrival time in the HIR.
- The perfusion segment is the concatenation of 2 segments of 2 seconds interval (the first one starts 2 seconds after the peak in the HIR, and the second one 7 seconds after the peak).

Then the quantification is performed for each individual pixel in the LIR ROI in two steps:

- A noise level detection, based on the highest intensity value of the pixel in the range of frames of the baseline segment.
- The filtering (perfused or not), based on the highest intensity value of the pixel in the range of frames corresponding to the concatenation of the two perfusion segments, and on the threshold defined after the noise level.

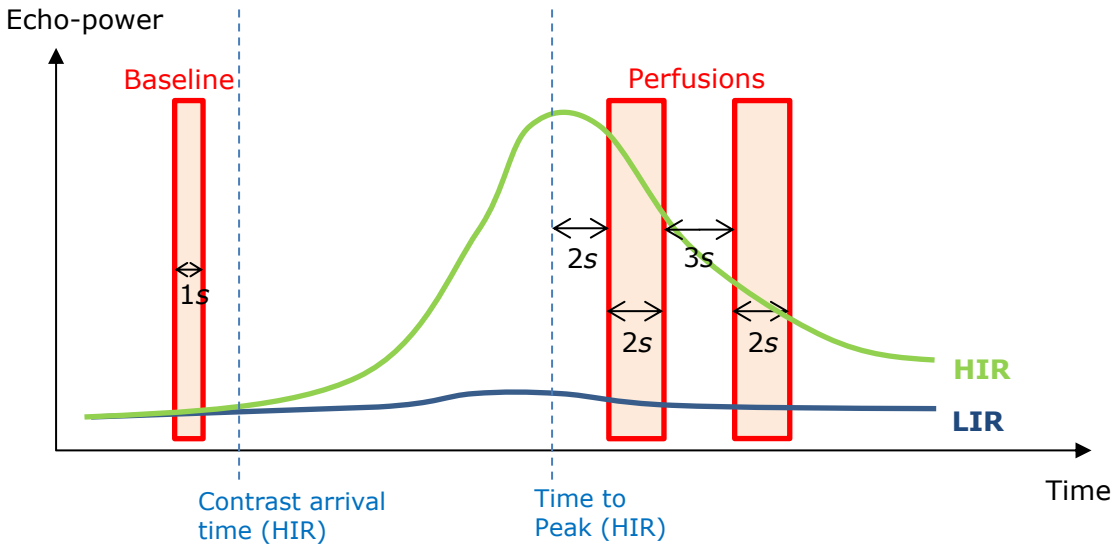


Figure 33 - Baseline and Perfused segments detection

The time segments (baseline and perfusions) are automatically detected by VueBox® Research, and displayed in the "Frame segments detection" dialog box (cf. Figure 34). The signal of each ROI is displayed in a multi-scale time/intensity graph. The left scale (in white) is dedicated to the LIR, whereas the right one is the scale associated to the HIR and is represented according to this ROI color. In this graph, the user can modify the location of each time segment independently, by a drag and drop operation. The Reset button recall the segment locations detected by VueBox® Research.

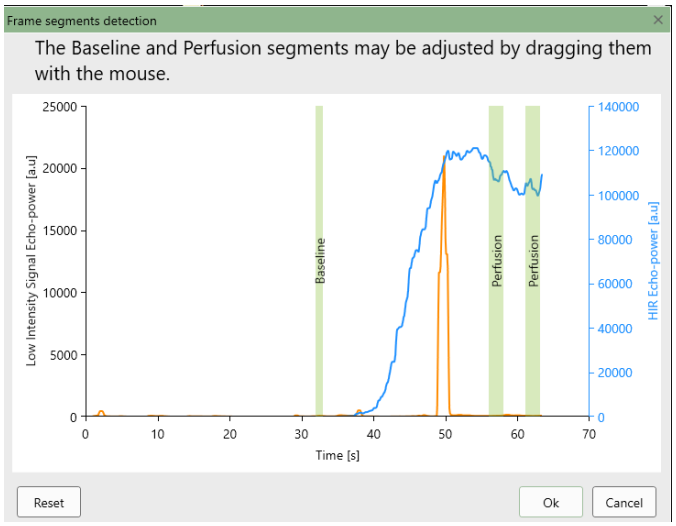


Figure 34 - Frame segments detection dialog box

Finally the following parameters are computed:

- Perfused Area (PA, PA1, PA2)
- relative Perfused Area (rPA, rPA1, rPA2)
- Mean Opacification
- Mean Opacification – Perfused Pixel only
- Mean

- Median
- Integral

PA represents the total number of pixels retained in the analysed region after the processing or the area in [mm^2] of these pixels if the length calibration has been defined. Additionally, the rPA is expressed in [%] and corresponds to percentage of retained pixels with respect to the total pixels in the LIR.

For the parameters PA and rPA, the images considered during the processing are the concatenation of the two perfusion segments. For the parameters PA1 and rPA1, only the first perfusion segment is taken into account during the processing. For PA2 and rPA2, only the second perfusion segment is taken into account during the processing.

The Mean parameter corresponds to the mean value of the linearized signal inside a ROI, the Median parameter corresponds to the median value of the linearized signal inside a ROI, and the Integral parameter corresponds to the integral value of the linearized signal inside a ROI.

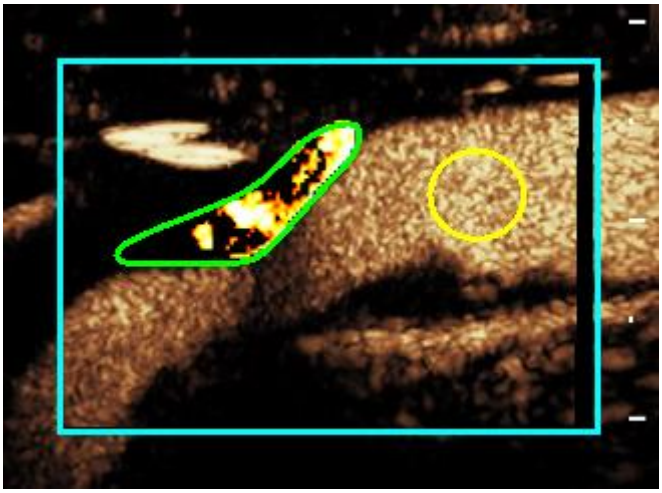


Figure 35 - Parametric image of the perfused area

Figure 35 shows the parametric image of the perfused area. In the LIR ROI, the pixels highlighted correspond to area considered as perfused.

LIR must not be contaminated by enhancement coming from the HIR. It could lead to wrong perfusion area results.

Time segments (baseline or perfusion) must contain images from the same plane (out of plane frames must not be included). It could lead to wrong perfusion area results.

During the baseline time segment (which aim is to compute the noise level in each LIR), a HIR should not be contaminated by artefacts (specular reflectors) to avoid perfusion area underestimation. Additionally, the baseline segment must be located before the contrast arrival time.

3.13.9 MEASUREMENT ACCEPTANCE CRITERIA

The accuracy of the calculated and measured parameters was verified and the following error should be taken into account:

Calculated & Measured parameters	Tolerance
$f(t)$	± 15%
$DVP(t)$	± 15%
PE	± 15%
WiAUC	± 15%
RT	± 15%
mTTl	± 15%
TTP	± 15%
WiR (Bolus)	± 15%
WiR (Replenishment)	± 15%
WiPI	± 15%
WoAUC	± 15%
WiWoAUC	± 15%
FT	± 15%
WoR	± 15%
rBV	± 15%
mTT	± 15%
rBF	± 15%
QOF	± 15%
PA	± 15%
rPA	± 15%

3.13.10 PARAMETRIC IMAGING

VueBox® Research can perform spatial rendering of any perfusion parameter, in the form of a color-rendered parametric map. This map synthesizes the time sequence of images into a single parametric image. Parametric imaging may enhance the information content of the contrast examination.

This technique may be particularly useful for making qualitative analyses in the course of a therapeutic monitoring performed on a given small-animal.

Note that in order to perform qualitative analyses on the basis of parametric images, certain recommendations must be made:

- the clips must represent the same anatomical cross-section from one exam to another;
- acquisition of contrast-ultrasound sequences must be performed using identical system settings (primarily transmit power, display settings, gain, TGC, dynamic range and post-processing);
- only parametric images of the same perfusion parameter can be compared.

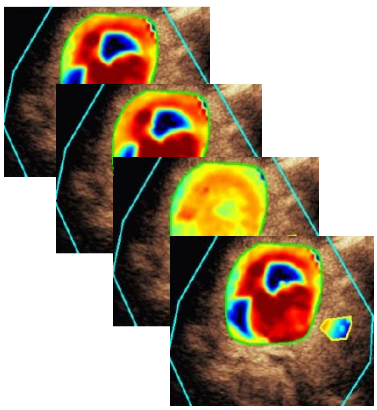


Figure 36 - Parametric images example

3.13.11 WORKFLOW

To perform **perfusion data processing**:

1. click the  button,
2. in the Bolus case only, accept, modify or ignore the automatic contrast arrival detection,
3. review the result in the result window.

3.14 RESULT WINDOW

3.14.1 INTERFACE ELEMENTS

Once the perfusion quantification processing is completed, VueBox® Research switches from the clip editing mode to the result mode. The display-layout in the result mode comprises four quadrants (Q1-Q4). The four-quadrant representation combines all results within one display, namely

- Original clip (Q1);
- Processed clip or parametric image (Q2);
- Chart displaying time intensity curves (linearized and fitted signals) in each ROI (Q3);
- Table listing the computed parameter values in each ROI (Q4).

Q1 displays the original clip and Q2 a processed clip or a parametric image, depending on the selection in the Parametric image view menu. Each parametric image has its own colormap, which is rendered in the colorbar located in the lower-right corner of Q2. For amplitude perfusion parameters, the colormap ranges from blue to red, representing low to high amplitudes, respectively. As regards time parameters, the colormap is a reversed version of the colormap used for amplitude parameters.

In Q3, the colors of the traces match those of the ROI. When a ROI is moved or modified, its corresponding signals and computed values are automatically and immediately recalculated and displayed in Q4. The ROI labels may be changed by editing the data in the left column cells (Q4).

For the specific case of the Low-Intensity Signal package, in Q3, the signal of each ROI is displayed in a multi-scale time/intensity graph (cf. Figure 34). The left scale (in white) is dedicated to the LIR(s), whereas the right one (yellow) is the scale associated to the HIR.

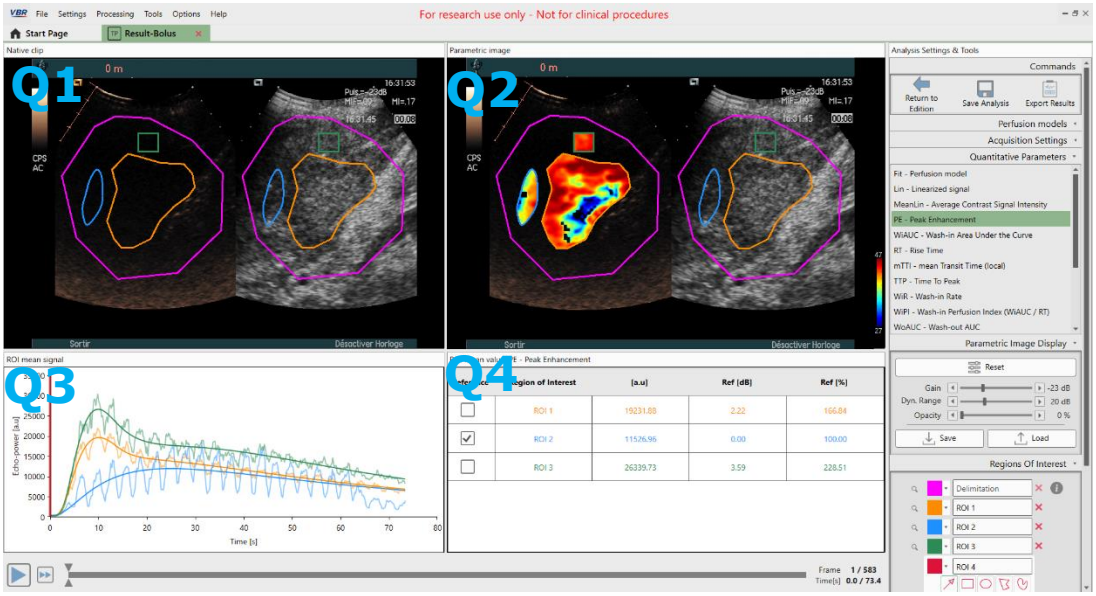
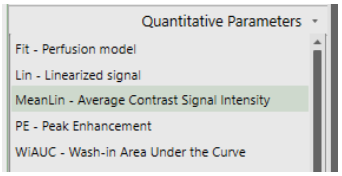


Figure 37 - User interface in result mode

Control	Name	Function
	**Quantitative Parameters**	allows the selection of parameter to be displayed.

Finally, relative measurements can be displayed in the **Q4** table by checking one of the ROI as a reference (in the Reference column). Relative values are displayed in [%] and [dB] for amplitude-related parameters and in [%] for time-related parameters.

ROI mean value: WiPI - Wash-in Perfusion Index (WiAUC / RT)

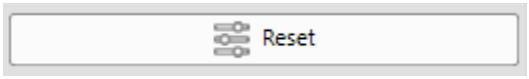
Reference	Region of Interest	[a.u]	Ref [dB]	Ref [%]
☐	ROI 1	12645.29	1.94	156.15
☑	ROI 2	8098.33	0.00	100.00
☐	ROI 3	17128.62	3.25	211.51

Figure 38 - Quantitative parameter table

When selecting DVP or DVPP parameters (i.e. in Tissue Normalization package) from the Quantitative Parameters menu, the table is replaced by a chart showing the DVP difference signals.

3.14.2 ADJUSTABLE DISPLAY PRESETS

Above Q2, sliders are provided to adjust the gain and the dynamic range (log-compression) of the processed image displayed in Q2, in a way similar to a standard ultrasound scanner.

Slider / control	Name	Function
	**Preset**	stores, restores display preset (gain and dynamic range of all parametric images).
	**Reset**	reset gain and dynamic range of all parametric images to suggested values
	**Gain**	controls the gain applied to the current processed image (Q2). (-60dB to +60dB)
	**Dynamic range**	controls the dynamic range of log-compressed applied to the current processed image (Q2). (0dB to +60dB)
	**Overlay opacity**	controls the opacity of the overlay displayed on the B-Mode side (Q2)

3.14.3 AUTO-SCALED DISPLAY PRESETS

Display presets (i.e. gain & dynamic range) for each parametric image are automatically adjusted once the perfusion quantification processing is completed using the built-in auto-scaling function. However, this adjustment is to be seen as a suggestion and may need further manual fine tuning. Below, an example of a parametric image prior and after auto-scaling is applied:

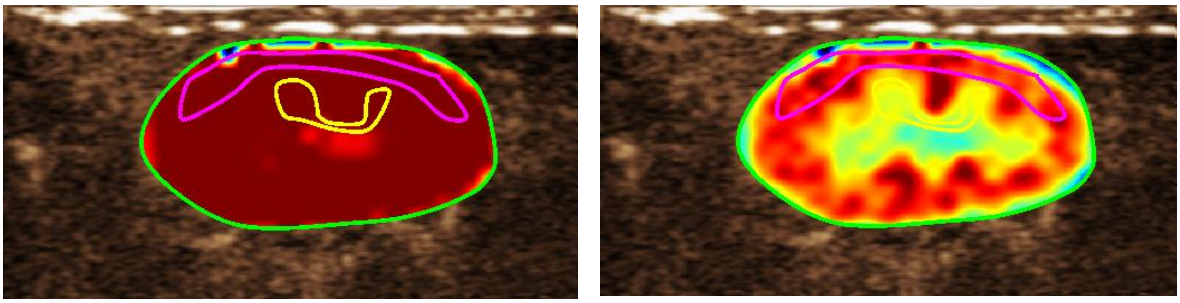


Figure 39 : Parametric image prior and after display presets auto-scaling

3.14.4 STORING / LOADING DISPLAY PRESET

Display preset can be stored into a dedicated library and loaded at a later time point.

To store the preset for all parametric images:

1. Click the 

button in the preset toolbar
2. Set a name or accept the one generated by default and press the OK button

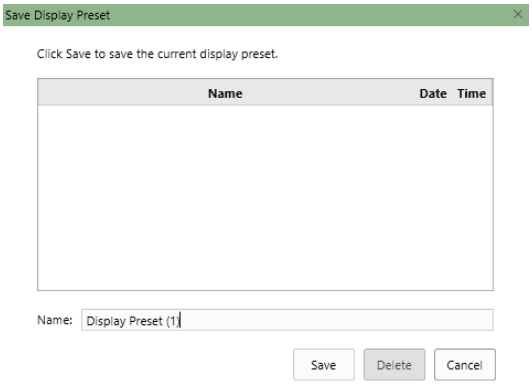
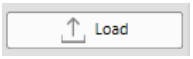


Figure 40 : Storing display presets into library

To load display presets from the library:

1. Click the 

button in the preset toolbar
2. Select the item in the list and press the OK button

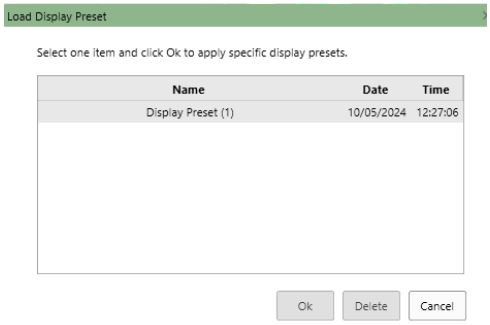


Figure 41 : Loading display presets from library

3.14.5 PARAMETRIC IMAGE OVERLAY

In Q2, the B-Mode side can also displayed the parametric image by overlay. The opacity of this overlay can be increased or decreased using the opacity slider of the display settings.

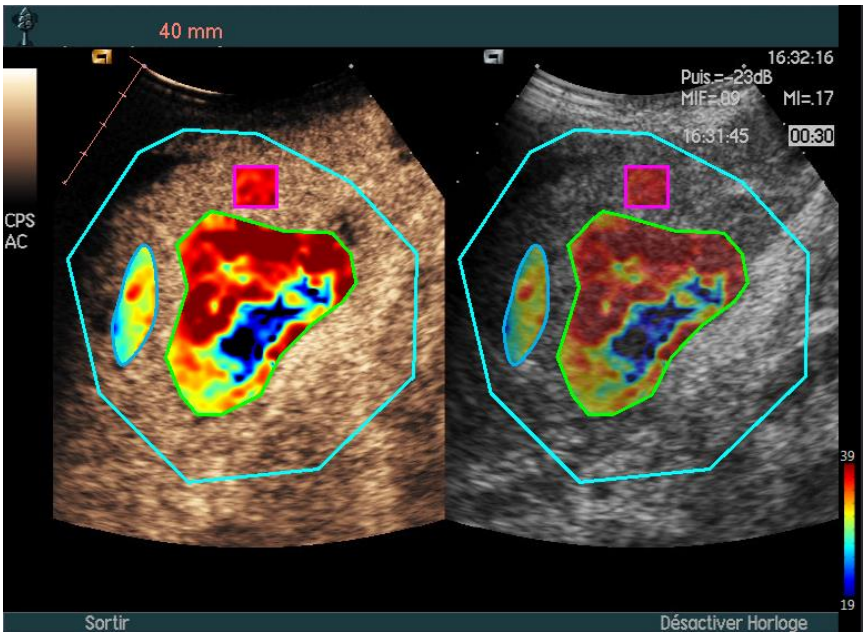


Figure 42 - An overlay is displayed on the B-Mode side in Q2

3.14.6 PERFUSION INSTANT DETECTION

This feature is only available in the Tissue normalization package (see section 3.3.4)

Most representative perfusion instants (initial, mid and last) of the DVP clip are provided by VueBox® Research as a suggestion of DVP images to be added to the study report. Once the DVP processing is performed, perfusion instants are displayed as three red vertical bars in the difference graph (Q4) as illustrated below. These instants can be easily modified by dragging the bars to the desired instants.

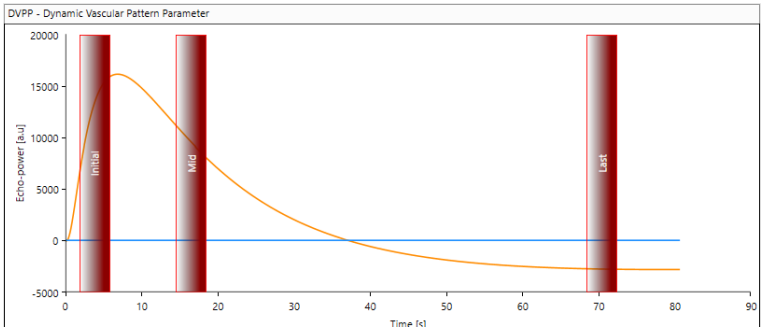


Figure 43 - DVP perfusion instants

3.14.7 ANALYSIS RESULT DATABASE

Each clip associates a result database in which the whole context of each analysis result can be stored. This enables restoration of the result at a later time by selecting the corresponding clip (previously analyzed) in the start page of VueBox® Research.

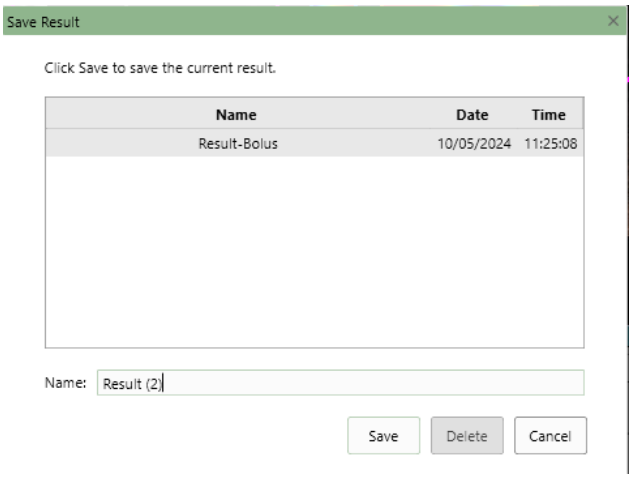


Figure 44 - Result database dialog box

The result database is automatically displayed when saving a result or loading a clip for which previous analyses exist.

SAVING AN ANALYSIS

To save the current result:

1. Click the button in the main toolbar
2. Under **Save as**, type the result name
3. Click the OK button.

Remark : the saving availability is described in section 3.17 Tools availability.
To overwrite a result:

1. Click the button in the main toolbar
2. Select a result in the list
3. Click the OK button.

To remove a result:

1. Click the button in the main toolbar
2. Select a result in the list
3. Click the DELETE button.

3.15 EXPORT ANALYSIS DATA

3.15.1 PRINCIPLE

VueBox® Research offers the possibility to export numerical, image and clip data to a user defined directory. For example, the numerical data are particularly useful for carrying out further analyses in a spreadsheet program. The image data are a set of screenshot containing both the regions of interest and parametric images. These images allow to perform qualitative comparisons between successive studies at different time points.

As a second example of qualitative analysis, the processed clips may provide a better assessment of the contrast-uptake over time. Still images or processed clips may also be useful for documentation or presentation purposes. Finally, an analysis report summarizing qualitative (i.e. still images) and quantitative (i.e. numerical data) information can be generated.

The user should always review the consistency of the exported results (i.e. images, numerical data, etc.).

3.15.2 INTERFACE ELEMENTS

Some export options may not be available in all application packages.

The figure below shows a screenshot of the interface elements in export mode.

Figure 45: User interface in export mode

Name	Function
Data	
TSV	exports a tabulated text file (XLS extension) including time intensity curves and perfusion estimates.
Images	
Full screen	exports a screenshot of the front panel (All 4 quadrants).
Ultrasound image (current)	exports the current ultrasound image with its ROIs (Quadrant 1).

Parametric images	exports all parametric images (Quadrant 2).
Time Intensity Curve	exports an image of the chart (Quadrant 3).
Clip	
Original	exports the original clip.
Parametric	exports the processed clip.
Native & Parametric	exports both the original and processed clips in a side-by-side view mode.
Video Quality	quality of the exported clip (in percent).
Frame rate	video frame rate of the exported clip (sub-sample factor).
Analysis Report	
Generate report	generates the analysis report and display the report generator dialog box.
Folder name	
Save as	indicates the folder name where the result files will be saved.

3.15.3 WORKFLOW

To export data:

1. Click the  button
2. Select a target directory in the left panel
3. Under **Data**, **Images** and **Clip** in the right panel**,** choose the type of results to export
4. Under **Option,** type a folder result name
5. Click the OK button in the main toolbar to export the results in the specified folder result name.

Remark : the export data availability is described in 3.17 Tools availability.

3.15.4 ANALYSIS REPORT

The analysis report summarizes both qualitative (i.e. still images) and quantitative (i.e. numerical data) information in a single, customizable, easy-to-read report. The report is divided into two parts: a header and a body.

The header contains the following information:

Institution-related information	Patient- and exam-related information
• Institution name • Department name	• Subject ID • Subject name

• Professor name • Phone & fax numbers	• Exam date • Contrast agent used • Indication for exam

Institution-related information are editable and are saved from one session to another. Patient- and exam-related information are automatically extracted from the DICOM dataset header, if present, and may be edited if not present.

For the specific case of the Tissue normalization package (see section 3.3.4)

The body of the report contains the following information:

- an image of the analyzed clip including ROI,
- a DVPP image,
- three images at different DVP instants,
- a chart representing the average signal within available ROI,
- a chart representing the average difference signal within available ROI (i.e. DVP signal),
- an editable comment field.

Otherwise, in all other cases:

The body of the report contains the following information:

- an image of the analyzed clip including ROI,
- a chart representing the average signal within available ROI,
- the perfusion model selected,
- a parametric image and quantitative values, in absolute and relative terms, for each perfusion parameters,
- an editable comment field.

Perfusion parameters can be dynamically added or removed from the analysis report, thus reducing or increasing the number of pages. The user selection is saved from one session to another.

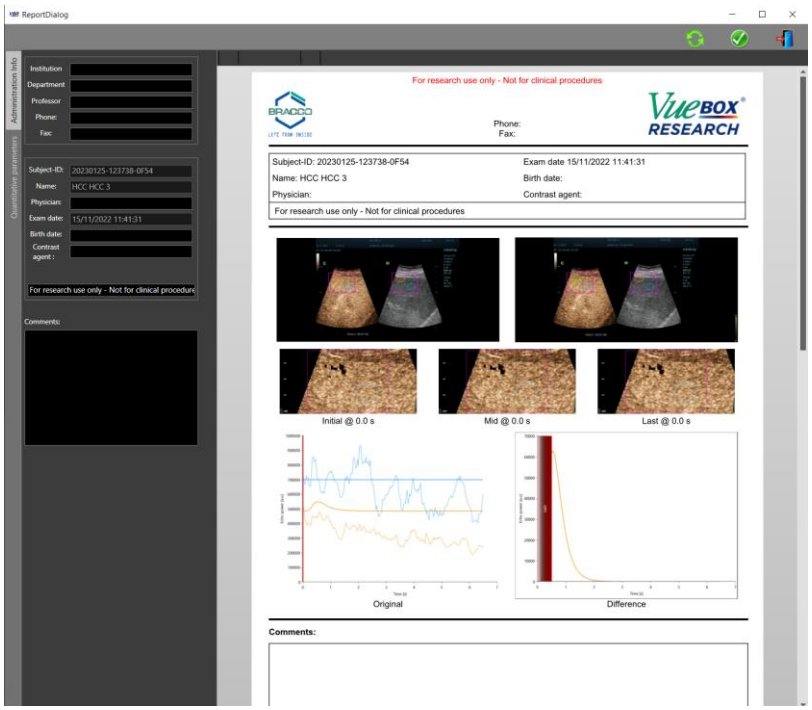


Figure 46 - Analysis report, header modification interface

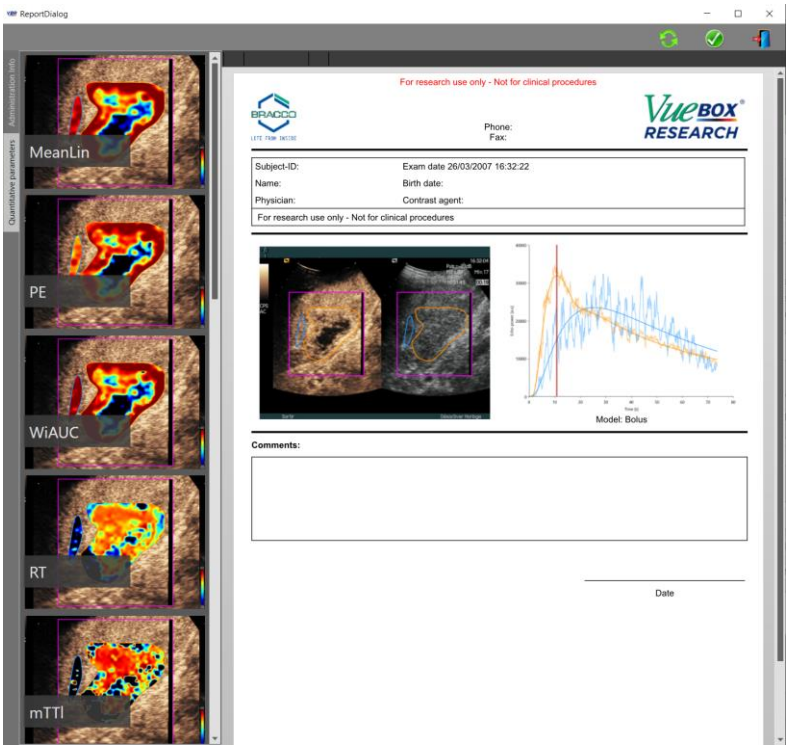


Figure 47 - Analysis report, quantitative parameter selection

Finally, the report can be saved into a finalized PDF file by pressing .

Personal Data processing

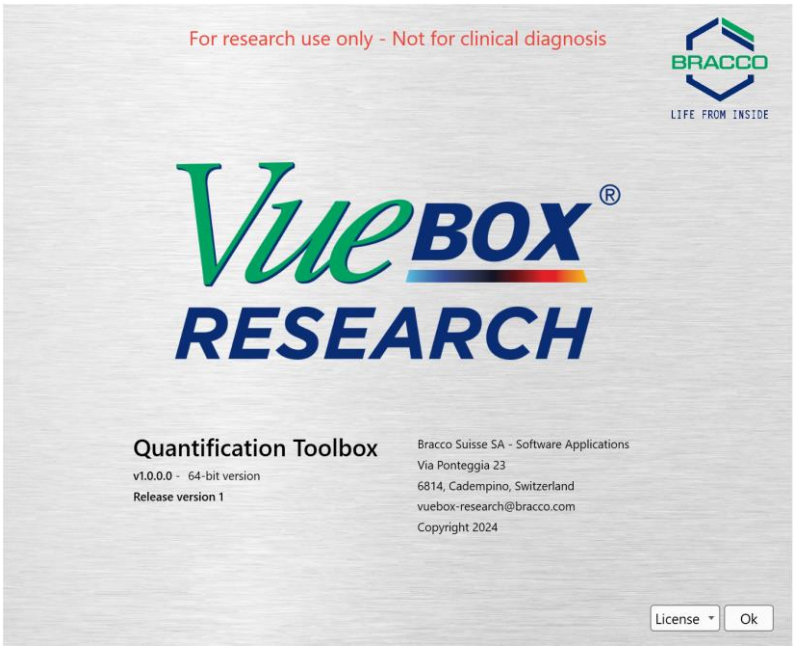
The analysis report may contain individually identifiable health information ("Protected Health Information" or "PHI") of patients. Protected Health Infromation should be handled in compliance with the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"). The processing of PHI in VueBox Research is performed under the assumption that the patient has given explicit consent to the processing activity under the authorization of the use of the software. Nevertheless, it is the responsibility of the user to comply with any applicable requirements under HIPAA and/or HITECH.

3.16 About screen / Labeling

Labeling information about the software such as version number and manufacturer can be found in the about screen.

To display the about screen:

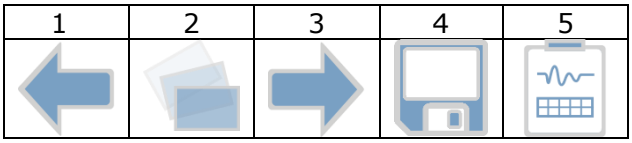
1. Click on the Options menu button in the main toolbar, then About.



3.17 Tools availability

This section describe interface elements which have specific conditions of availability.

List of elements :



		Available in mode			
Item	Function	Clip editor	Motion comp.	Result	Comments
1	Clip editor		X	X	Return to the clip editor mode.

2	Motion compensation	X	X		Apply spatial realignments on all images using a specific reference image.
3	Perfusion data processing	X	X		Perform perfusion quantification or calculate DVP according to selected package
4	Save result			X	Store a result file (analysis result context) into the result database.
5	Export data			X	Export selected data (e.g. quantification data, screenshots, movies).

4 FUNCTIONAL REFERENCES FOR THE PARAMETER TREND TOOL

4.1 PURPOSE

The purpose of the tool is to compare perfusion parameters values across different examinations of the same subject. It consists on a dashboard where graphs are displaying the evolution of the parameters.

4.2 SUPPORTED DATASETS

This tool can be launched by selecting VueBox® Research analysis files (*.eBRI files), previously obtained by performing a VueBox® Research analysis from a DICOM file.

On the start page, the user must go to the "New Parameter Trend tool" section, and select at least 2 VueBox® Research analysis files to start the comparison. An example is shown Figure 48.

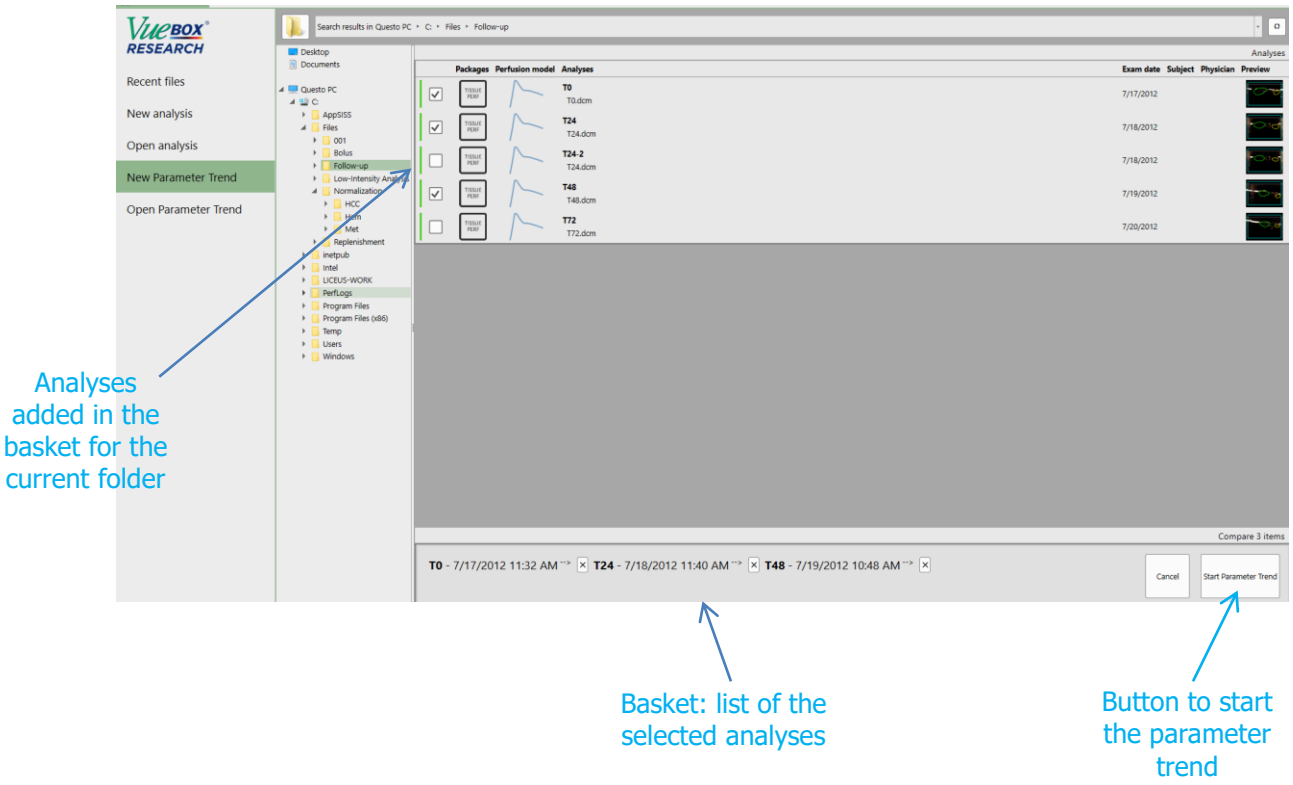


Figure 48 - Start page - Start a new parameter trend analysis

The user must select analyses from the same subject. If the DICOM tag "Patient Name" is different, VueBox® Research will display a warning before starting the tool.

The analyses selected must be generated with the same VueBox® Research application package (Tissue Perfusion or Low-intensity region analysis) and perfusion model (Bolus, Replenishment).

The examinations must have been acquired with the same ultrasound system and settings (probe, dynamic range, color map…).

When a parameter trend analysis has already been performed, it is possible to reload it from the "Open Parameter Trend analysis".

4.3 General Workflow

The application workflow consists of the following steps:

1. Select the VueBox® Research analyses to include in the parameter trend tool
2. Start the comparison
3. Add a graph for each quantification parameter you want to study
4. Optionally, add graphs to display the time intensity curves for all the analyses for one or more ROI
5. Save the analysis
6. Export the results

4.4 Display of the Dashboard

Once a Parameter Trend analysis starts, an empty dashboard is displayed, as shown Figure 49.

Figure 49 - New Parameter Trend analysis

To add a new graph, the user must click the  button. Then, the user can select if he wants to display the evolution of a quantification parameters (cf. Figure 50), or time intensity curves for a given ROI (cf. Figure 51).

An example of dashboard is displayed Figure 52.

Figure 50 - Add a graph to follow the evolution of a quantification parameter

Figure 51 - Add a graph to display all the TIC for a given ROI

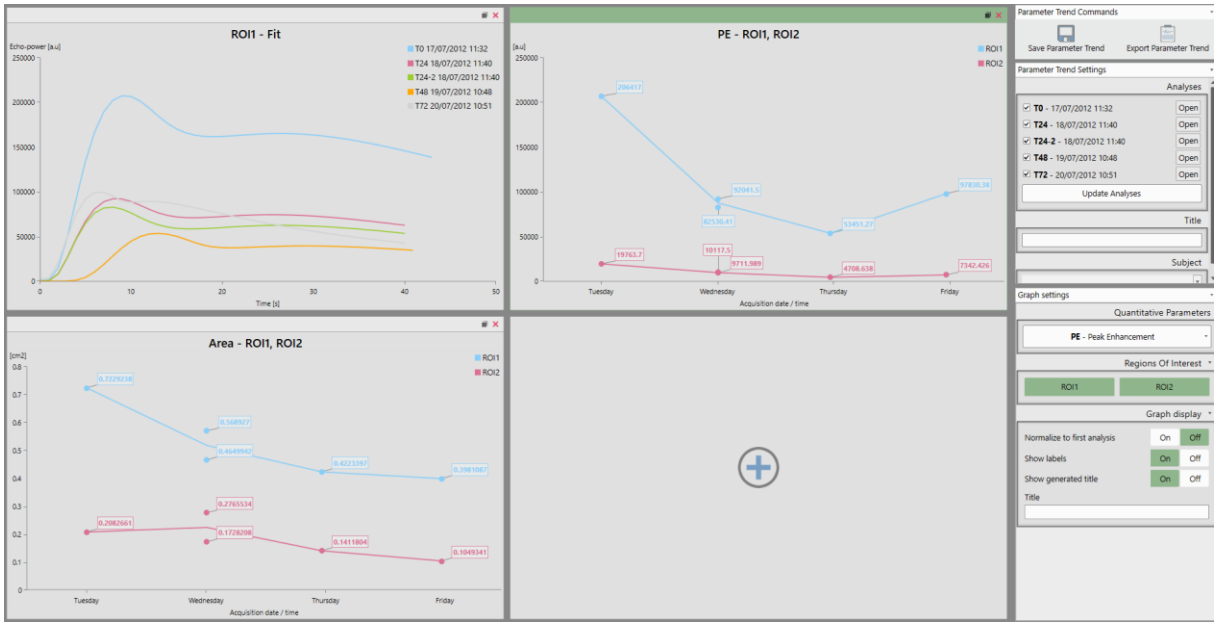


Figure 52 - Example of Dashboard

4.5 PARAMETER TREND SETTINGS

As shown Figure 53, the "Parameter Trend Settings" window allows to:

- Update the list of VueBox® Research analyses included in the parameter trend tool
- Change the title of the analysis
- See and change the ID of the subject

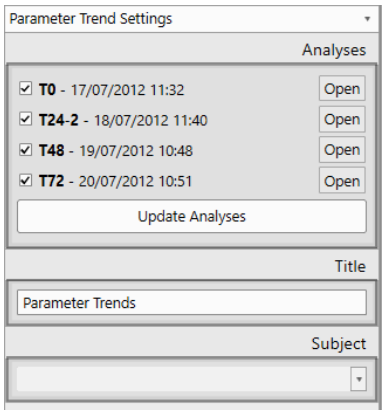


Figure 53 - Parameter Trend settings

4.5.1 OPEN A VUEBOX® RESEARCH ANALYSIS FROM THE PARAMETER TREND TOOL

VueBox® Research analyses can be reopened from the parameter trend , for example in order to be updated (modification of the ROIs, removal of images…). An "Open" button is accessible for each analysis in the Parameter Trend Settings window.

When an analysis is reopened, a new tab is created to display it. The name of the tab is "*name_of_the_parameter trend: name_of_the_analysis*", as shown Figure 54. Once the analysis was updated by the user, the parameter trend can be updated by clicking the "Update Parameter Trend" button. The original analysis is not overridden: only the parameter trend analysis is modified.

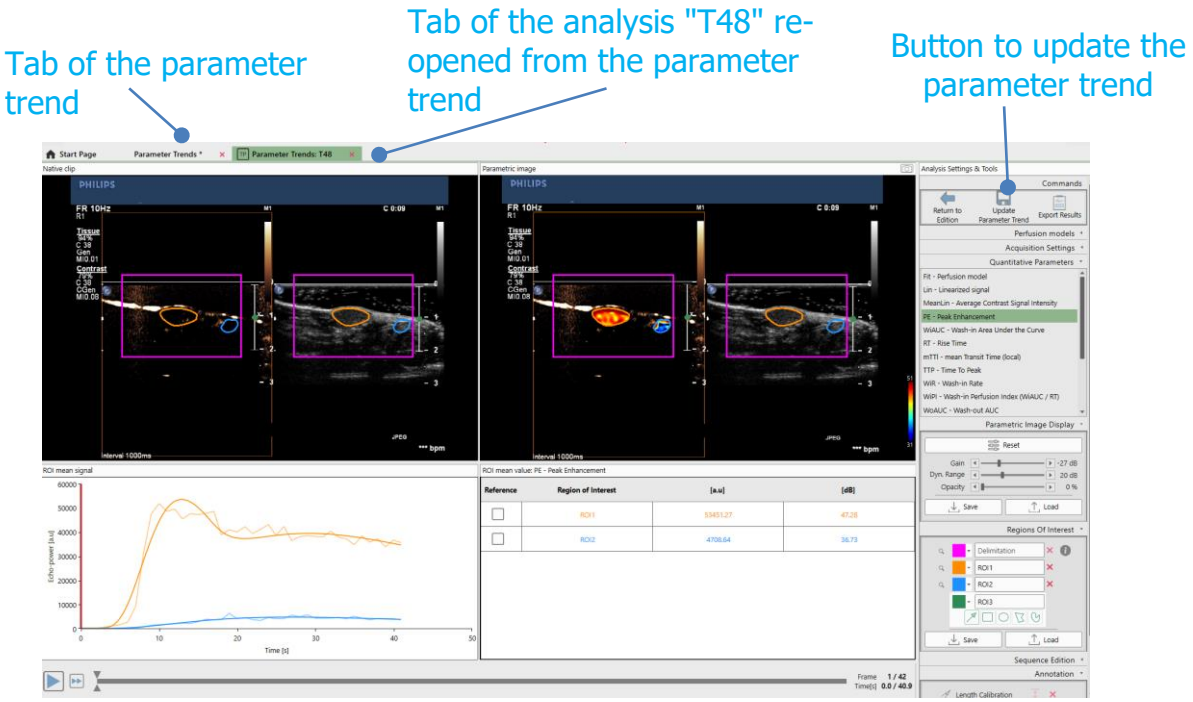


Figure 54 - Open a VueBox® Research analysis from the Parameter Trend tool

4.6 GRAPH SETTINGS

The Graph Settings panel depends on the graph which have the focus (to focus on a graph, click on it). The focused graph appears with a blue strip on top of the window, as visible in Figure 52.

4.6.1 QUANTITATIVE PARAMETER GRAPH SETTINGS

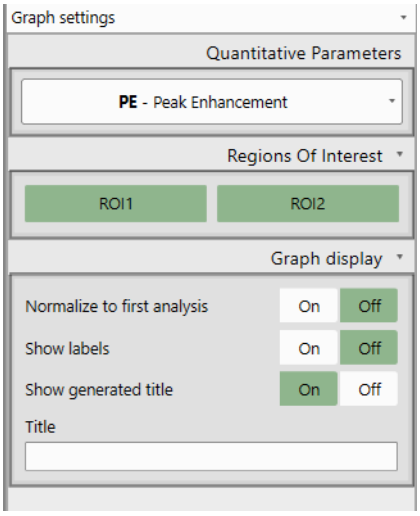


Figure 55 – Settings panel of a parameter graph

QUANTITATIVE PARAMETERS

The "Quantitative Parameters" drop down list allows to modify the parameter type of the graph, as shown in Figure 55.

REGIONS OF INTEREST

The "Region Of Interest" section contains buttons associated to each ROI. To display/hide a ROI in the graph, click on the corresponding button.

GRAPH DISPLAY

The "Graph Display" section allows to customize the display with the following possibilities:

- normalize the curve based on the first analysis
- show values as annotation on each point
- display a title by default
- prefix the default title with a customized title

4.6.2 TIC GRAPH SETTINGS

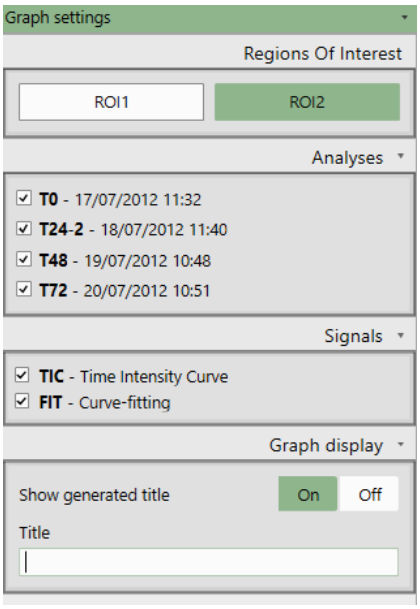


Figure 56 –Settings panel of TIC graph

REGIONS OF INTEREST

The "Region Of Interest" section contains buttons to select the ROI represented in the Graph, as shown in Figure 56.

ANALYSES

The "Analyses" section allows to select/unselect the analyses included in the graph.

SIGNALS

The "Signals" section allow to choose the type of curve. At least one of the following must be chosen :

- linearized signal of the Time Intensity Curve
- fit of the Time Intensity Curve

Both types of curves can be displayed together.

GRAPH DISPLAY

The "Graph display" section allows to customize the display with the following possibilities:

- display the default title
- prefix the default title with a customized title

4.7 LAYOUT ORGANIZATION

It is possible to switch graphs positions by drag and dropping one on another.

It is also possible to increase the size of a graph by clicking on the  icon (in the right up corner). Only one graph can be enlarged, as shown in Figure 57.

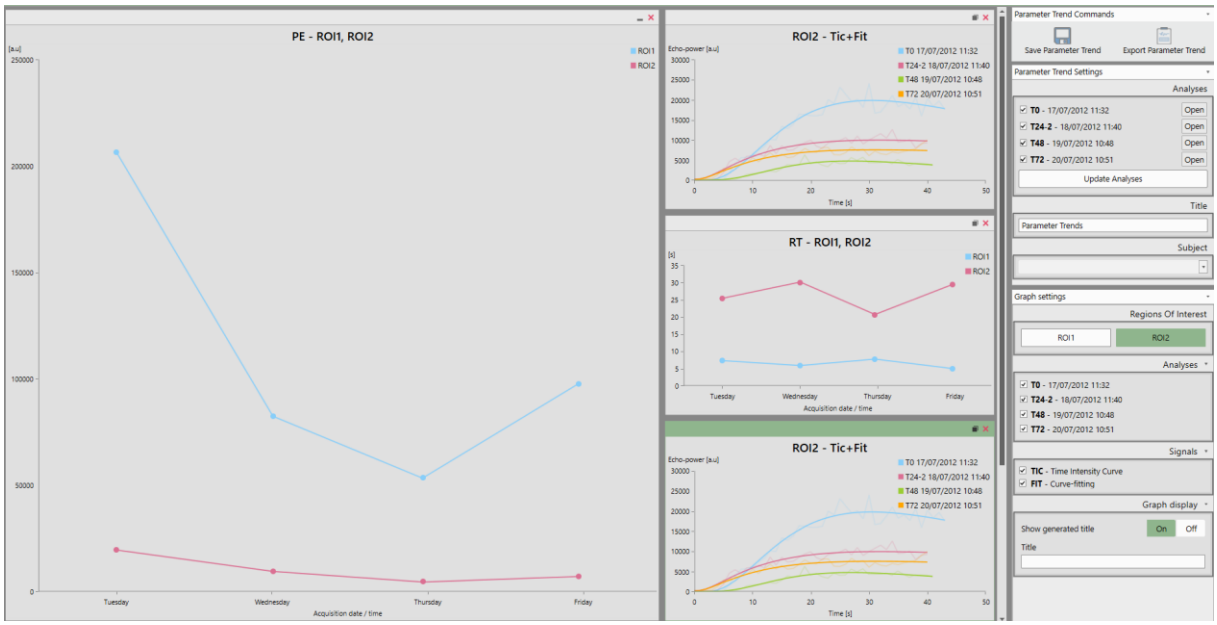


Figure 57 – Layout of the graphs

4.8 SAVE PARAMETER TREND

You can save the session with the  button. It opens a new window allowing to choose a directory.

4.9 EXPORT PARAMETER TREND DATA

You can start exporting your Parameter trend data with the  button.

It opens a new window that allows you to configure the export, as shown in Figure 58.

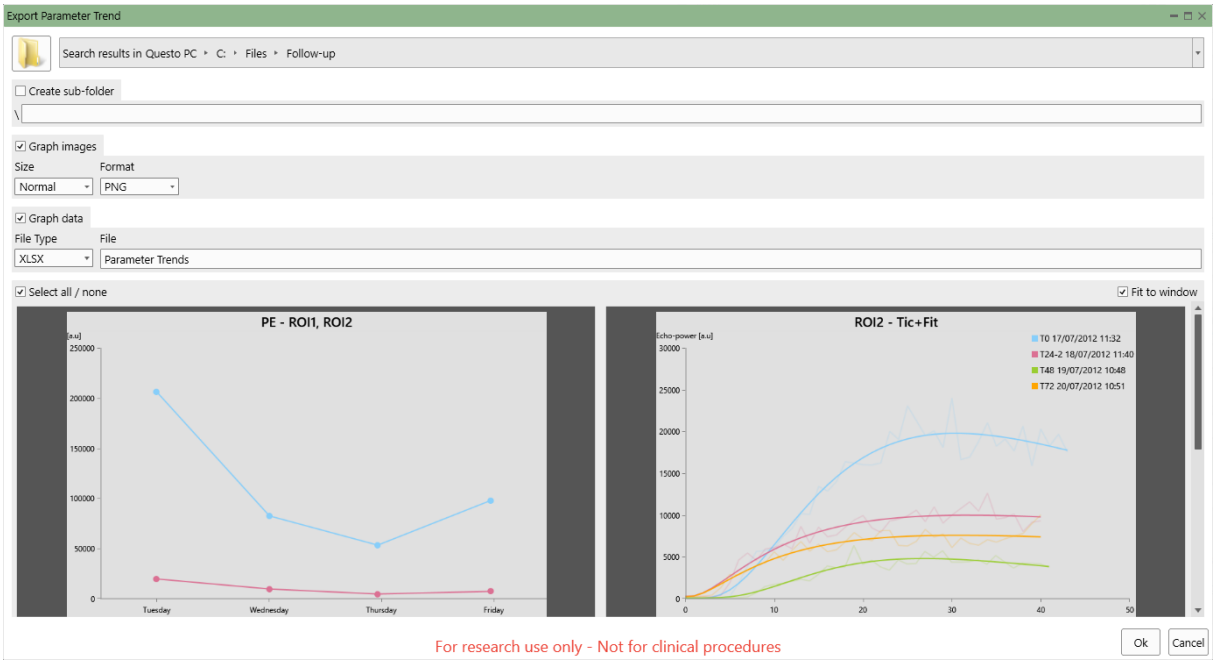


Figure 58 – Export Parameter trend window

FOLDER SELECTION

In the first section, you can select a folder where you want to create the files.

CREATE SUB-FOLDER

The "Create sub-folder" section allows to create a new folder inside the selected folder.

GRAPH IMAGES

When enabled, the "Graph Images" section allows to export each selected graph as an image.

Size specifies the pixel length and format changes the files extensions.

GRAPH DATA

When enabled, the "Graph Data" section allows to export in an Excel worksheet file (.xls or .xlsx).

The Excel file will contain the numeric values of the selected graphs and the numeric values of the Time Intensity Curve and FIT curves of all analysis.

GRAPH SELECTION

In the last section, you can select which graph you want to export by clicking on them. Selected graphs appear surrounded by yellow.

VALIDATION

After configuring all the options for the export, press 'Ok' to launch the process.

When the process is completed, a message appears on right corner of the application, as shown in Figure 59.

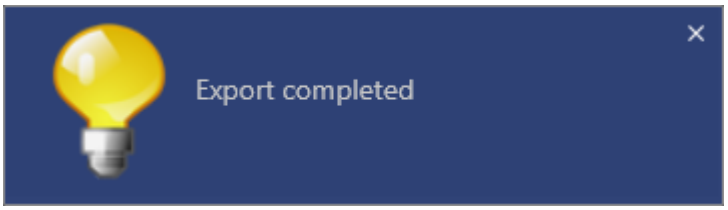


Figure 59 – Export completed message

You can click on the message to open export folder.

5 INDEX

VueBox® Research

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