3 Brain Perfusion

Introduction

The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software to be used as an advanced visualization application of CT brain perfusion images. The BP application is used to support the analysis of dynamic and/or serial CT brain images after injection of contrast. The BP application is intended to assist with the evaluation of an area of interest, and to generate qualitative and quantitative information about changes in image intensity over time. The BP application presents the results as a composite (single image that is calculated from a set of time course images at a single location) images and provides perfusion parameters maps. The following parameters related to brain perfusion are calculated: Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV), local bolus timing (Time to Peak (TTP)/Time to Maximum (Tmax)) and Mean Transit Time (MTT) and supports processing and visualization of Permeability maps.

The physician retains the ultimate responsibility for making the final diagnosis.

The BP application is launched from Philips Medical Systems' IntelliSpace Portal (ISP) environment.

Key Features

The Brain Perfusion (BP) application has the following key features:

- Supports visualization and processing of dynamic and/or serial brain CT scans with contrast agent injection.
- Displays results as composite (single image calculated from a dynamic set of images at a single location) images (tMIP images).
- Displays time-density curves reflecting the HU contrast enhancement tracked for an ROI over time.
- Supports detection of reference artery, reference vein, mirror line placement and brain mask.
- Supported option for 3D motion correction with anatomical alignment.
- Provides Perfusion maps of Cerebral Blood Volume (CBV), Mean Transit Time (MTT), Cerebral Blood Flow (CBF) and Time to Peak (TTP)/Time to maximum (Tmax).
- Provides summary maps according to default thresholds. The user may manually adjust the summary map thresholds and/or different parameters according to the physician's preference.
- Provides colored warning strips (Traffic Lights), indicating the quality of the Brain Perfusion data (acquisition).
- Supports processing and visualization of permeability maps.
- Displays pre-defined ROI templates for localized quantitative evaluation of perfusion information.

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- Supports automatic workflow – Brain Perfusion application can generate and send automatic results to defined external destination.

Intended Use/Indications for Use

The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software application intended to assist with the evaluation of an area of interest, to generate qualitative and quantitative information about changes in image intensity over time. It supports the analysis of dynamic/serial CT after injection of contrast agent, by calculating the parameters related to brain perfusion and displays the results as a composite (single image that is calculated from a set of time course images at a single location) images.

Intended User Population

The expected users of the application are trained professionals, including but not limited to physicians and medical technicians.

Limitation for Use

Rx Only

CAUTION

In the United States, Federal law restricts this device to sale, distribution and use by or on the order of a physician.

NOTICE

Depending on your Portal configuration, this application may not be available.

WARNING

When loading data into any application, verify that the image orientation shown is consistent with the image appearance. This precaution is required for data that contains incorrect orientation information and therefore, will be incorrectly presented within the application. For example: Legacy nuclear medicine volume data (SPECT or PET), reconstructed using cardiac orientations, may not encode the orientation information correctly.

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WARNING

When loading CT images into Brain Perfusion, all images which contain 16 bit data are converted to 12 bit images. This means that for rescale intercept equal to -1000, HU values above 3095 are displayed as 3095. For rescale intercept equal to -1024, HU values above 3071 are displayed as 3071.

Brain Perfusion Preprocessing

To run preprocessing, right-click on a **Series** in the **Directory** and select **Run Processing > Brain Perfusion** from the menu.

Once preprocessing is complete, a **TI-CTA** series is created (the original **Series** is retained by default). The **TI-CTA** series can be loaded into other viewing applications.

When preprocessing is selected for thin slices (typically less than 5 mm), it combines all time-points (volumes) to an approximate thickness of 5 mm and generates a new Brain Perfusion preprocessed result series. The combining process begins with the first axial slice (lowest slice position) and performs 3D registration based on the original thin- slice data. The Brain Perfusion processed result series can be launched into the brain perfusion application.

When Automatic Results Creation is configured in the Brain Perfusion application (from the Brain Perfusion batch Tab options), the Auto batch series is created based on the default settings defined by the Administrator. For detailed Automatic results creation workflow, please refer to section “Automatic Results Creation Workflow” on page 90.

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NOTICE

Preprocessing – slice thickening: Since some scans have thickness that is not a natural denominator of the predefined thickness, approximations are made. For example, for a 1.2-mm slice thickness, the system combines every 4 images to achieve a slice thickness of 4.8 mm, which is the closest slice-thickness for 5 mm (the default value).

In some cases, the application removes some slices in the time points. For example, if a 1-mm dataset contains 43 images per time point, the application starts thickening at the first image and combines every 5 images in each time point, so images [41-43] are discarded.

If more than one **Series** is selected, all **Series** will be combined into one resulting **Series**.

NOTICE

Some slices may be removed during the preprocessing procedure.

Configure Thin-slice Processing Preferences

1. Go to the **Directory**, select **Preferences**, and then select **Processing**.

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2. In order to set the processing parameters for the Brain Perfusion application, select the relevant **Protocol**, **Body Part** and other settings for which preprocessing must be run.

About the Brain-Perfusion Time-invariant CTA Series

The CT **Brain Perfusion** application includes a preprocessing option that creates the **TI-CTA** (time invariant CTA) series that may be loaded into viewing applications. The **TI-CTA** series includes tMIP images with information about the arterial, venous and collateral systems.

To create the **Series**, right-click on the desired study and select the **Brain Perfusion** preprocessing option from the menu.

Once preprocessing is complete, select the **TI-CTA** series and load it into a viewing application.

Perfusion Images

- **The original images.** These can be viewed in tMIP or Average modes.
- **CBF.** Cerebral Blood Flow.
- **TTP.** Time To Peak (Available only when using Time Arrival sensitive method).
- **CBV.** Cerebral Blood Volume.
- **MTT.** Mean Transit Time.
- Permeability (special scan protocol required).
- **Tmax.** Time to peak of deconvolution residual function (available only when using Time Arrival Insensitive method).

Summary Maps

The Brain Perfusion (BP) application provides color-coded summary maps. The default summary maps are based on the Arrival Time Sensitive method and show areas of increased MTT relative to the contra-lateral hemisphere and reduced or non-reduced absolute CBV.

The user can manually adjust the summary maps thresholds and/or different parameters according to the physician's preference.

Data Tables and Graphs

NOTICE

Before continuing, refer to the **Instructions for Use** that came with your scanner. Ensure you use the applicable protocols for the Perfusion Map functions as well as the Permeability measurements and Permeability maps.

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- Reference Vessel Statistics
- ROI Statistics
- 2D Measurements-Summary Map (Areas Statistics Table)
- 3D Measurements-Summary Map (Volume Statistics Table)
- Time and Vessel curves

NOTICE

Images from ongoing longitudinal studies that were initially processed using earlier versions of Philips Brain Perfusion application should be reprocessed in their entirety using the latest software version.

NOTICE

Before continuing, refer to the **Instructions for Use** that came with your scanner. Ensure you use the applicable protocols for the Perfusion Map functions as well as the Permeability measurements and Permeability maps.

With studies of sufficient scan duration, Permeability Analysis can be used to measure the contrast agent permeation of the blood-brain barrier.

To properly launch the **Brain Perfusion** application, you must load a **Series** with **at least 8 consecutive time points**, with a maximum of 2,080 total images.

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Brain Perfusion Scanning Protocols

NOTICE

The protocols in the following section are applicable to the Perfusion Map functions.

For the most updated scan parameters, please refer to the factory protocols for scanning. It is also recommended to consult with your local Philips application specialist.

For details about Permeability measurements and Permeability maps, see: section “Reference Permeability Scan Protocols” on page 31.

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Suggested Brain Perfusion Protocols (Brilliance scanners only)					
Brilliance Big Bore			**Brilliance 16 slice**		
	Non-Jog Mode	**Perfusion Jog Mode***		**Non-Jog Mode**	**Perfusion Jog Mode***
Thickness	6.0	6.0	Thickness	6.0	6.0
Increment	0.0	0.0	Increment	0.0	0.0
KV	90	9.0	KV	90	90
mAs	200	200	mAs	125	125
Cycle Time	2.3	–	Cycle Time	2.0	–
Cycles	30	–	Cycles	30	–
# of Jog Cycles	- -	15	# of Jog Cycles	–	15
Resolution	Standard	Standard	Resolution	Standard	Standard
Collimation	16x1.5	16x1.5	Collimation	16x1.5	16x1.5
RT	0.5	0.5	RT	0.5	0.5
FOV	250	250	FOV	250	250
Filter	UB	UB	Filter	UB	UB
WC/WW	80/40	80/40	WC/WW	80/40	80/40
Matrix	512	512	Matrix	512	512
* Perfusion Jog Mode is an available option for Philips Brilliance scanner.					

Suggested Brain Perfusion Protocols (Brilliance scanners only)					
Brilliance 40 slice			**Brilliance 64 slice**		
	Non-Jog Mode	**Perfusion Jog Mode***		**Non-Jog Mode**	**Perfusion Jog Mode***
Thickness	5.0	5.0	Thickness	5.0	5.0
Increment	0.0	0.0	Increment	0.0	0.0
KV	80	80	KV	80	80
mAs	125	125	mAs	125	125
Cycle Time	2.0	–	Cycle Time	2.0	–
Cycles	30	–	Cycles	30	–
# of Jog Cycles	- -	15	# of Jog Cycles	–	15
Resolution	Standard	Standard	Resolution	Standard	Standard

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Suggested Brain Perfusion Protocols (Brilliance scanners only)					
Brilliance 40 slice			**Brilliance 64 slice**		
Collimation	32x1.25	32x1.25	Collimation	32x1.25	32x1.25
RT	0.4	0.4	RT	0.5	0.5
FOV	250	250	FOV	250	250
Filter	UB	UB	Filter	UB	UB
WC/WW	80/40	80/40	WC/WW	80/40	80/40
Matrix	512	512	Matrix	512	512
* Perfusion Jog Mode is an available option for Philips Brilliance scanner.					

Suggested Brain Perfusion Protocols (Brilliance scanners only)					
Brilliance iCT SP			**Brilliance iCT**		
	Non-Jog Mode	**Perfusion Jog Mode***		**Non-Jog Mode**	**Perfusion Jog Mode***
Thickness	5.0	5.0	Thickness	5.0	5.0
Increment	0.0	0.0	Increment	0.0	0.0
KV	80	80	KV	80	80
mAs	125	125	mAs	125	125
Cycle Time	1.5	–	Cycle Time	1.5	–
Cycles	40	–	Cycles	40	–
# of Jog Cycles	–	15	# of Jog Cycles	–	15
Resolution	Standard	Standard	Resolution	Standard	Standard
Collimation	32x1.25	64x0.625	Collimation	64x1.25	64x1.25
RT	0.4	0.4	RT	0.4	0.4
FOV	220	220	FOV	220	220
Filter	UB	UB	Filter	UB	UB
WC/WW	80/40	80/40	WC/WW	80/40	80/40
Matrix	512	512	Matrix	512	512
* Perfusion Jog Mode is an available option for Philips Brilliance scanner.					

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NOTICE

When applying the **Summary Maps** functionality, note that there are no standard recommended threshold values for the reduced CBV and increased MTT when using scans acquired with Perfusion Jog Mode standard scan protocol in iCT/iCT SP scanners.

Reference Permeability Scan Protocols

WARNING

As with all time series, motion artifacts may affect the accuracy of permeability maps.

Patient motion should be restricted during the longer duration acquisition recommended for permeability analysis.

NOTICE

Padded hook-and-loop straps can be used for better patient fixation.

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Reference Protocols - Perfusion / Permeability Scan		
Perfusion part of scan		**Permeability part of scan**
Frames - 40 Cycle time - 1.5 s 60 s total acquisition		Frames - 5 or 6 Cycle time - 30 s 150 - 180 s
Follow the instructions for Brain Perfusion scanning in the next section, and in the Brilliance scanner Instructions for Use. For reference: the perfusion scan duration should be approximately 60 s (using the reference protocols), and should not be less than 45 s.	Allow less than <- 30 seconds -> between scans	Switch the scanner to a 30 second cycle time and start acquiring as soon as possible. Note: To identify extravasated contrast agent that has permeated the blood-brain barrier, the scan duration must be extended to include delayed phases of the passage and recirculation of contrast agent in the brain. As a reference, the total scan duration (perfusion + permeability) should be at least 210 s.
Total scan duration not less than 210 seconds. Be sure to minimize patient motion.		

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Minimizing Patient Motion

Patient motion is the main cause of unreliable perfusion and permeability maps. Permeability maps are especially sensitive to motion because the measurement is based on smaller contrast changes. Disruptive motion events (for example coughing and body motion) are more likely in a longer acquisition. Out-of-slice motion that cannot be corrected by the application may result in errors in the permeability maps.

- Motion restriction is important in perfusion and permeability analysis, particularly when low patient compliance is observed.
- Consider using fixation equipment or methods (for example, use a head holder).
- Consider using padded hook-and-loop straps to further suppress motion.
- To evaluate the presence of motion artifacts, change the rendering of tMIP images to **Average** using a viewpoint control at the bottom left corner and scroll along the time dimension to detect any residual motion.

   Use the Cine tool to scroll through the images. When activated, the Cine tool uses the Average rendering mode. The main image viewport must be active to use the Cine tool.

While scrolling along the time dimension manually, focus on easily recognizable objects to track the motion. For example: you can follow the location of the artery cursor and search for time points where the cursor has shifted away from the artery.

Review of Brain Perfusion Scanning

This section explains one possible way to perform a Brain Perfusion scan based on the Philips Brilliance scanner. For information applicable to different scanners, please refer to the Instructions for Use of the specific scanner.

NOTICE

A special scan protocol must be used to acquire a study for viewing Permeability maps and measurements.

NOTICE

Contrast flow and volume parameters may vary by institution protocols. Consult your Radiologist prior to setting up or changing any injection protocols in your department.

1. Place patient on the table.
2. Start an IV using an appropriate size IV catheter (18/20 gauge).
3. Center patient for head scan by placing the lateral laser on the EAM.

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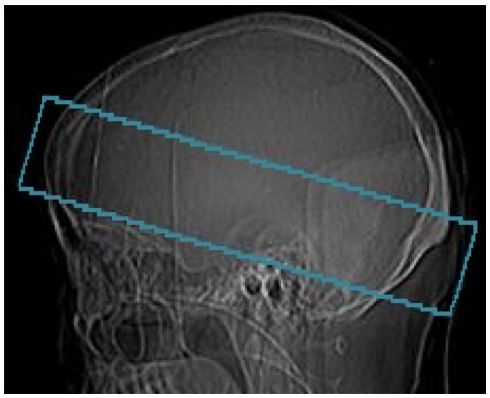
4. Perform a non-contrast study of the brain using your department's routine brain protocol.
5. Click **Plan Scan**.
6. Click **Insert Scan**.
7. From the Exam Protocol Exam Group, select **Head**.
8. From Exam Protocols, select **Brain Perfusion**.
9. Plan the desired Perfusion location.

   Refer to the illustration below of Representative Surview Plans. (Please consult with the Radiologist for exact location).

   Representative Surview plan - 64-Slice:



10. Arm the injector with Contrast. Refer to suggested Reference Contrast Protocols:
    - **For Non-Jog scans:** 40-50mL contrast, followed by 20-40mL saline.
    - **For Jog Mode scans:** 70mL contrast, followed by 45mL saline.
    - **For All scans:** injection rate of 4-6mL per second; 18-20 gauge IV placed in right antecubital vein.

NOTICE

Consult your Radiologist prior to setting up or changing any injection protocols in your department.

11. Start the Scanner and Injector at the same time.
12. End the Exam.

NOTICE

The scan will take around 45 - 60 seconds for a perfusion scan and a minimum of 210 seconds for permeability scans.

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NOTICE

A proper scanning procedure is essential for obtaining meaningful perfusion images. Special care must be taken to ensure that:

- The scan duration is sufficient to cover a pre-contrast period as well as the entire first pass of the injected contrast bolus. The pre-contrast period consists of a base line which should include at least 3 cycles. (Recommended scan minimum: 45 second scan duration; for Permeability Analysis: 210 seconds.)
- For Quantitative results, please ensure that the temporal resolution does not exceed 4.0 seconds.
- Quantitative results include the Summary maps display.
- The contrast injection is sufficiently rapid to provide reasonable enhancement in white matter while preserving a narrow bolus. See the **Reference Contrast Protocols**.
- Please verify no residual motion is present after the registration is complete by switching the rendering mode to **Average** and scrolling horizontally. Use the Cine tool to support verifying the residual motion.
- When verifying the artery and vein detection, ensure the Artery time attenuation curve (TAC) peaks before the vein TAC.
- When verifying the artery and vein detection, ensure the Artery bolus arrival time (BAT) is earlier than vein BAT.

Failure to meet the above requirements may result in the creation of unreliable perfusion images.

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WARNING

If the temporal resolution of the scans is greater than 4.0 seconds, quantitative perfusion measurements are not provided. The color maps and numeric values represent relative values only. Specifically, when applying the Summary Maps functionality note that for cases with such poor time resolution there are no recommended threshold values for Philips Brain Perfusion application for the reduced CBV and increased MTT.

- **To improve the quality of results based on Jog-mode scans, please follow the modified injection parameters procedure.**
- **When loading images into Brain Perfusion, all images which contain 16 bit data are converted into 12 bit images. This means that for rescale intercept equal to -1000, HU values above 3095 are displayed as 3095. For rescale intercept equal to -1024, HU values above 3071 are displayed as 3071.**

NOTICE

Quantitative results include the Summary maps display as well.

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WARNING

The application results should not be used as a SOLE basis for diagnosis.

WARNING

There are no recommended threshold values for Philips Brain Perfusion application for the Summary Maps calculation in conjunction with the Arrival Time Insensitive method. The default threshold values are only applicable for Brain Perfusion Application Arrival Time Sensitive method and are not transferable to other methods or to other vendors. When using the system default thresholds for the Summary Maps, after applying the Arrival Time Insensitive method, the Summary Maps results may not be optimal.

Review Adequacy of Input Data

If input data to the Brain Perfusion application is incomplete or incorrect, the resulting perfusion maps may provide inaccurate results.

Perfusion analysis requires that the scan includes the entire transit of contrast agent through tissue, from its earliest arrival to a point when the majority of the contrast agent has washed out on the venous side. Shown below is an example of a typical bolus' time attenuation curve (TAC).

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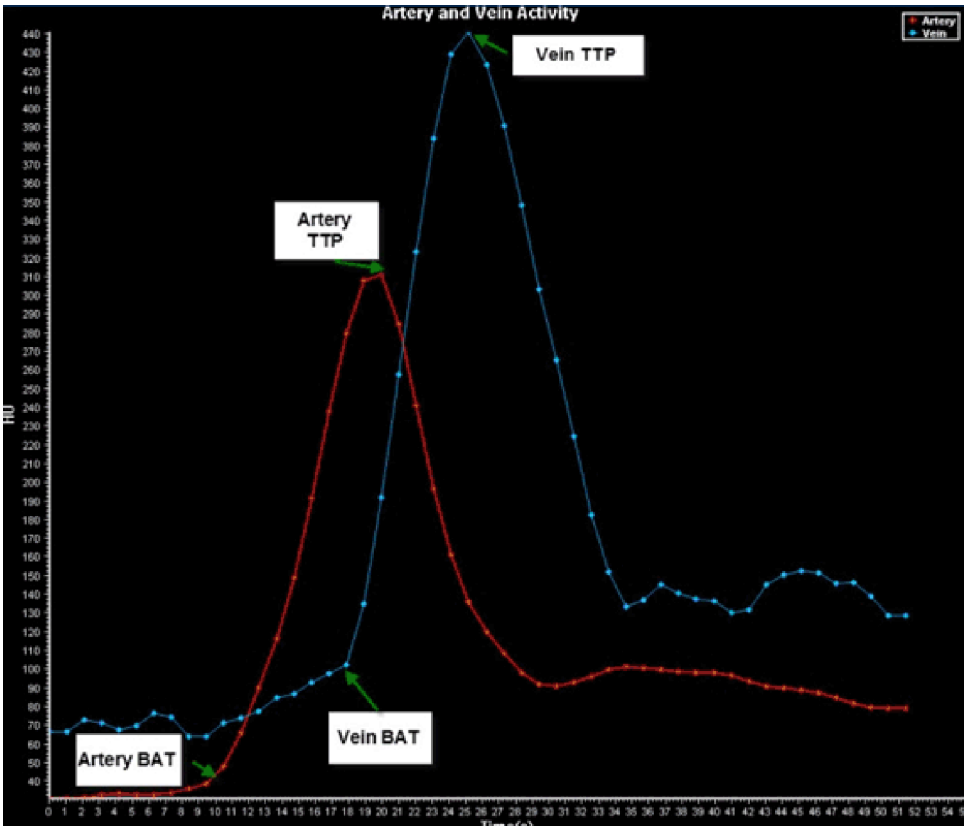

Fig. 1: Artery and Vein Activity

Therefore, one should verify that the total number of scan cycles and duration of the scan is adequate to cover the full inflow and outflow phases.

In addition, it is important to make sure that no significant patient motion occurred during the scanning. The verification should be performed after changing the rendering mode from **tMIP** to **Average** and scrolling the images (by moving the mouse in a horizontal direction from left to right) along the time domain.

- **Presence of Motion** – Cine view assists the user's review presence of motion. When activated, Cine scrolls through Average mode images from the same z location.

- **Motion Correction** – In cases where unacceptable motion has occurred, the user may remove displayed time-points to exclude specific images (up to 8 points per scan and no more than 2 consecutive time point). Additional feature "3D motion correction" can be applied by the user to perform 3D registration and anatomical alignment. After the operation of anatomical alignment, the image is adjusted in order to have the cerebral mirror as a vertical line at the center of the image.

NOTICE

In case of patient motion, the resulting perfusion may provide inaccurate results.

Brain Perfusion Input Requirements

The following are requirements for input data to the Brain Perfusion application.

Contrast Agent Injection and Timing

The duration of the scan must cover the whole uptake and outflow phase for the arterial and vein curve.

If the curves are not entirely included in the scan (i.e., if some data is missing, see below), the calculation of perfusion parameters cannot be used for diagnosis.

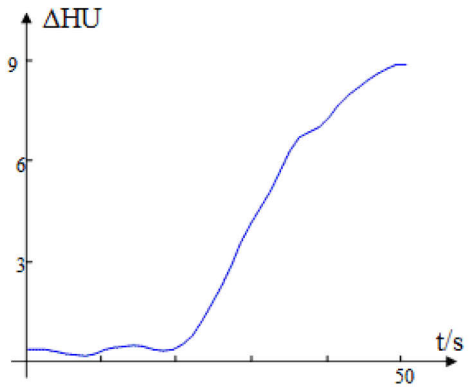

Fig. 2: Time attenuation curve with incomplete bolus (wash-out period is missing).

The perfusion analysis is also susceptible to problems during the contrast injection:

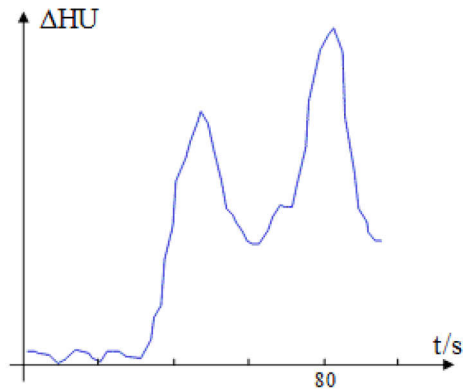

Fig. 3: Shape of the time attenuation curve due to problems during the injection.

In addition, the bolus arrival time should not be too delayed (i.e., more than 15 seconds). A delayed bolus arrival time and a normal bolus arrival time are shown in the figures below:

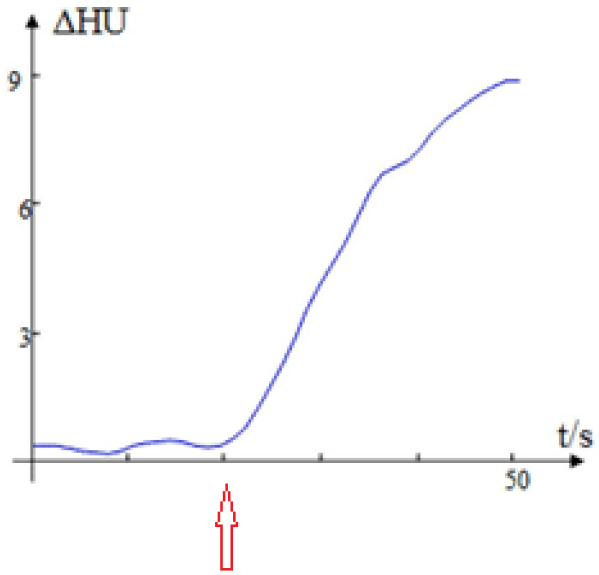

Fig. 4: The delayed bolus arrival time is identified by the red arrow.

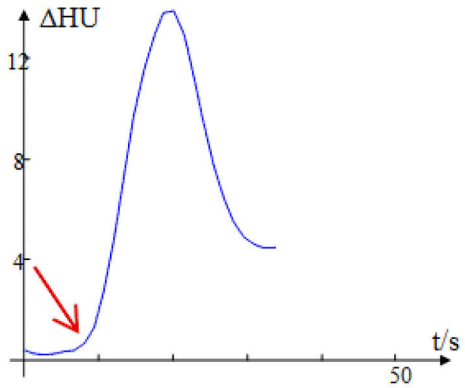

Fig. 5: The normal bolus arrival time is identified by the red arrow.

Analysis of Data

Brain Mask

Check the brain mask and verify all brain tissue is included in the mask. Adjustments of the mask can be done manually or by tuning the threshold value. See section “Vessel Definition Work Stage” on page 42 and section “Perfusion Map Work Stage” on page 57.

Vessel Selection

The perfusion maps and values are affected by the vessels selected by the user for the calculation.

- **Arterial curve.** The artery that peaks first (lowest TTP) should be selected (automatic or manual selection). Most commonly the anterior cerebral artery, or ACA, or middle cerebral artery (MCA) is selected as the reference vessel. If possible, the artery on the contralateral (non affected side) should be used.

- **Vein curve.** Verify that the vein with the highest enhancement is selected. The curve should peak later than the arterial curve and its amplitude should be higher in most cases. The vein commonly selected is the Superior Sagittal Sinus (SSS).

Remove Vessels

When using the remove vessels functionality, make sure that only vessels are removed from the cerebral mask. This can be done by comparing the resulting perfusion maps with the corresponding tMIP image. Adjustment of the threshold for vessel removal might be needed. See section “Vessel Definition Work Stage” on page 42 and section “Perfusion Map Work Stage” on page 57.

The figure below illustrates tuning the threshold of the removed vessels:

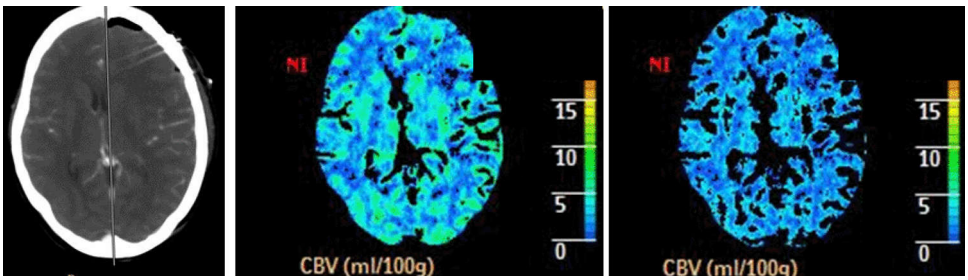

Fig. 6: (a.) original tMIP image; (b.) CBV map after removing vessels with the default value (9 ml/100 g); and (c.) CBV map after removing vessels with an incompatible threshold (too low in this case) and consequently a big portion of the cerebral mask not representing vessels was also removed.

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Merge Two Series from Same Study

The Merge function is a procedure that allows you to merge (in the time domain) two perfusion scan series from the same patient into one series.

The Merge function is initiated within the Patient Directory just before the Brain Perfusion application is launched.

Permeability Analysis

The Merge procedure is required when you want to do a Permeability Analysis calculation using two series of the same patient, which were scanned one after the other, but were acquired using different time intervals.

Note the following series characteristics that must be observed:

- the two series belong to the same study (same Study ID and FOV);
- all reconstruction parameters are the same between the two series: FOV, center x/y, filter, matrix, thickness, increment, orientation;
- the series to be merged have the same z-axis coverage; and
- the time gap between the end of the first scan and the beginning of the next is brief (ideally, less than 30 seconds).

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Merge Procedure

1. In the Patient Directory find the desired Brain Perfusion study.
2. Select 2 or more brain perfusion or permeability series (from the Series List).

   The following message displays: Loading more than 1 series is not supported. Would you like to merge the series into one?" The available responses are Merge and Close the application.
3. Click **Merge**.

Merge Outcomes

If all requirements for a successful merge are satisfied, the merge is performed.

If the time gap between the end of the first scan and the beginning of the next is more than 30 seconds, this message displays: "The time delay between the scans is higher than 30s. This may impact the analysis. Do you want to continue?" (yes, no).

Merge Output

A DICOM series is created that includes the data (pixel data) from both original series.

The resulting series is a new series which is added to the Series List, named Merged: [the series description of series 1]/[the series description of series 2].

The new series is a temporary series inside the Brain Perfusion application.

Launch Brain Perfusion

The Brain Perfusion application performs several automatic functions as it launches the study:

- Registration;
- Filtering;
- Brain mask detection;
- Reference artery detection;
- Reference vein detection;
- Mirror line placement; and
- Traffic Light check.

To properly launch the **Brain Perfusion** application, you must load a **Series** with **at least 8 consecutive time points**, with a maximum of 2,080 total images.

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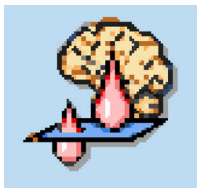
NOTICE

You can configure pre-processing to reduce loading time. If thin-slice data is present, the application will combine slices to an approximate thickness of 5 mm as part of preprocessing (see section “Brain Perfusion Preprocessing” on page 26 and section “Automatic Results Creation Workflow” on page 90).

1. From the **Directory** find and select the desired study and series.
2. Select the Brain Perfusion icon from the application icon chart.



The application processes the patient study opens in the Vessel Definition Work Stage.

NOTICE

Please verify vessels were detected correctly. See section “Brain Perfusion Reference Vessel Selection Guide” on page 79.

If Artery and Vein detection is not successful, you must manually mark the Artery and Vein.

NOTICE

If Traffic Lights found an issue with the acquisition data, before continuing see section “Using Brain Perfusion Traffic Lights” on page 85.

Minimum Scan Duration

The minimum scan duration for calculating Permeability results using the Brain Perfusion application (a Patlak analysis) is 210 seconds.

If the patient study you are launching has a shorter scan duration, the following warning message is displayed:

Scan duration is shorter than the Permeability scan duration value in the Calculation Parameters, therefore, permeability measurements are not available.

To properly launch the **Brain Perfusion** application, you must load a **Series** with **at least 8 consecutive time points**, with a maximum of 2,080 total images.

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Vessel Definition Work Stage

The Brain Perfusion application attempts to perform Vessel Definition (and mirror line generation) automatically. You must verify the correctness of the automated processes. If required, manually define vessels and adjust the mirror line.

You can always access this stage and make changes manually, if desired.

NOTICE

If Traffic Lights found an issue with the acquisition data, either the Non-Severe Warning or Severe Warning message will appear throughout the application. For example, original tMIP/ average axial view, Summary Maps and Perfusion Maps, display a red or yellow warning light (depending on the warning type). Before continuing, see section “Using Brain Perfusion Traffic Lights” on page 85.

Main Viewport

Contains a grayscale tMIP slab image. You can scroll through the slab images with the Scroll function in the **Common Tools**. It is also possible to switch to Average mode which allows scrolling along the time dimension at the same z-location.

Reference Viewports

These artery and vein Reference tables and the Activity chart (time attenuation curves) are empty until you define the blood vessels.

Image Type

A **tMIP** (temporal Maximumal Intensity Projection) image is a maximum intensity projection (across the time domain) for each z-axis location. One tMIP image is created for each z-axis slice location, and user may scroll in z direction to visualize entire volume.

Average images- The user may scroll the dynamic scan images in z direction or over time and visualize the entire volume over time.

NOTICE

Switch between the two image types with the active blue title shown in the bottom left corner of the viewport. When image type tMIP is selected, cine and scrolling along the time dimension is disabled.

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Average Image	tMIP Image

Fig. 7: Average Image

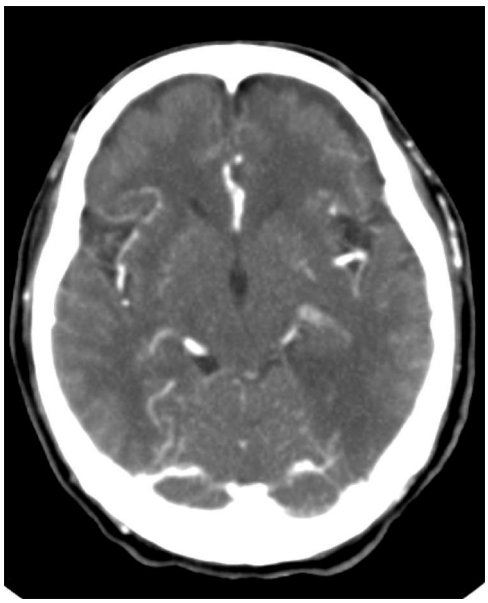

Fig. 8: tMIP Image

Artery and Vein Activity

This color-coded chart beneath the vessel definition image shows three contrast wash-in curves (arteries) and three wash-out curves (veins), with points marking each acquisition along the time axis. Arteries should enhance before the vein; this can be verified by observing that the arteries have smaller TTP than the vein.

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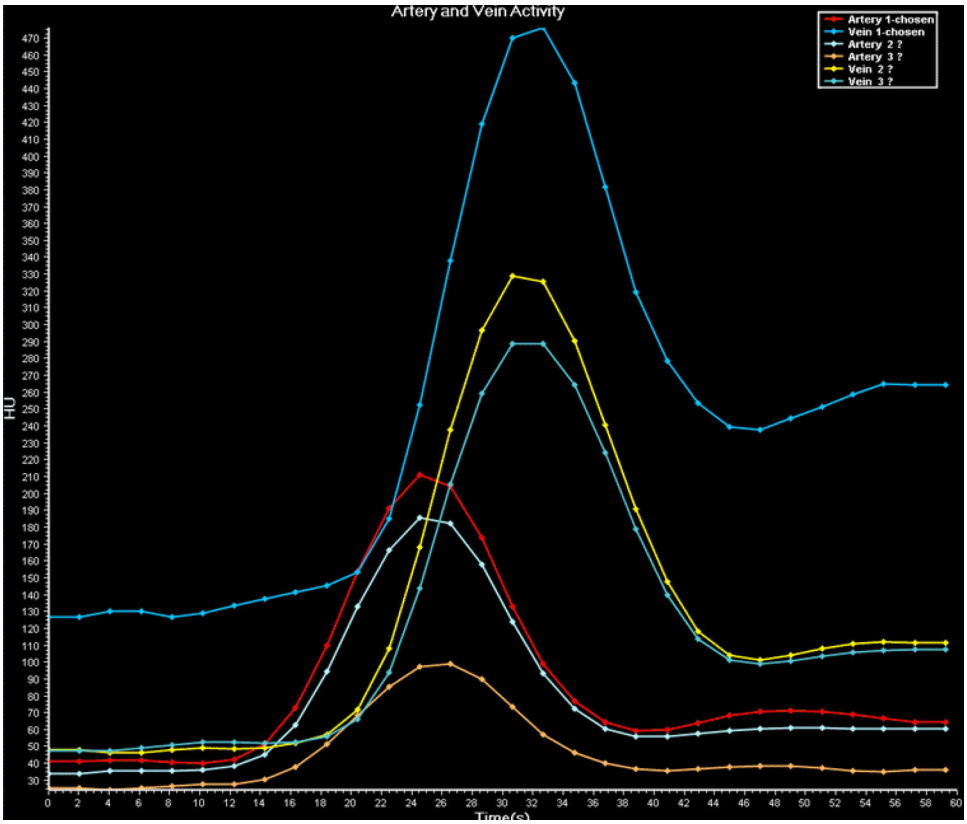


Fig. 9: Artery and Vein Activity

NOTICE

If one or more of the wash-in and wash-out curves are partial (that is, they do not show an up-slope and a down-slope), the scan is incomplete, and the data may be unreliable.

Vessel Statistics

The data table shows enhancement values and the TTP (time-to-peak) statistics for the defined arteries and vein.

NOTICE

If Traffic Lights found an issue with the acquisition data, either the Non-Severe Warning or Severe Warning message will appear throughout the application. For example, original tMIP/ average axial view, Summary Maps and Perfusion Maps, display a red or yellow warning light (depending on the warning type). Before continuing, see section “Using Brain Perfusion Traffic Lights” on page 85.

The numeric values in the vessel statistics table are calculated based on curve-fitting, and vary slightly from the raw data seen in the vessel graph.

The Enhancement is calculated as: peak enhancement value minus base line enhancement value.

The vessels are identified by ROI number and Slice number. Click on any of the vessels and the main viewport image is updated to show the slice it appears on. The vessels are color-coded so they can be correlated with the curves in the Artery and Vein Activity chart.

Time Batch

Time Batch allows creating a batch of images at the same slice position across the different time points. The Time Batch option is available only when Average rendering mode is selected.

1. Select the **Average** display mode.
2. Select Time in the Batch function tab.
3. To define the batch, click the **Start** button.
4. In the axial viewport scroll horizontally across the different times.
5. Click the **End** button when finished.

   You can skip steps 3, 4, and 5 and define all time points using the **All** button. You can limit the number of time points with the Sub-select Every option.
6. If desired, preview the batch with the **Preview** button.
7. Save the batch either from the Preview window or by using the **Save Batch As...** function in the Common Tools.
8. To create a new batch, first use the **Clear batch** button.

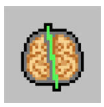
Vessel Definition Tools

Use the following tools located in the upper toolbox:

Show Mirror Line

The mirror line should divide the left and right brain hemispheres. You should inspect the line and correct it, if needed.

Detect Mirror Line



You can have Brain Perfusion try to automatically detect the mirror line by clicking the **Detect Mirror Line** button.

Edit Mirror Line Slice by Slice

Check the box to edit the mirror line slice by slice. Scroll through the images and adjust the mirror line on each slice.

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Show All Vessel Curves

Check the box to display the arteries and veins in reference graph. You can define up to 10 arteries in the Vessel Definition stage. After evaluating the artery statistics, select just one to make it “active.”

Restrict Vessel to the Cerebral Mask

When checked, the manual vessel detection range (performed by the draw functionality in artery/vein selection steps) is restricted to the cerebral mask. When checked, no vessel can be defined manually outside of cerebral mask.

Verify Mirror Line, Motion, Mask and Vessels

Typically, the following steps should be performed in the order presented.

Verify No Residual Motion Present

Use the Cine tool to scroll through the images. When activated, the **Cine** tool uses the Average rendering mode. The main image viewport must be active to use the **Cine** tool.

Correct Motion

After using the **Cine** tool, use the **Motion Correction** tools to remove time points where unacceptable motion occurred.

NOTICE

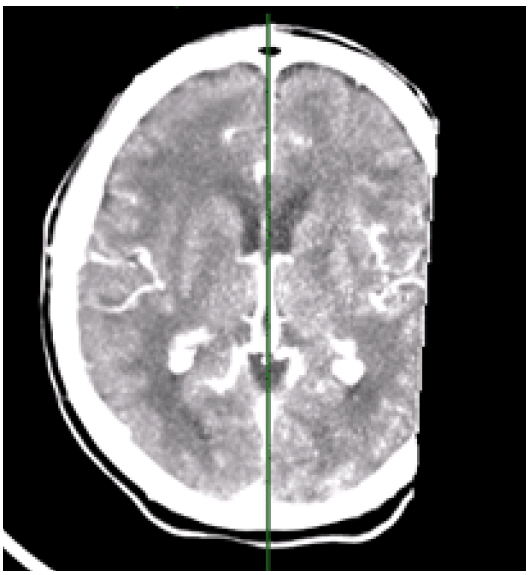
Remove undesirable motion before correcting the cerebral mask and selecting the artery and vein.

3D Motion Correction

Use the **3D Motion Correction**  button to perform 3D registration and anatomical alignment (this will reinitiate the registration and all subsequent checks: vessel detection, cerebral mask, and traffic lights).

NOTICE

The 3D registration process may modify images: the first and last slices (in terminal locations) may have black regions due to insufficient data.



Black Regions Due to Insufficient Data

Verify correctness of cerebral and perfusion maps in the central scan region. If needed, refer to original images.

In the **Perfusion Map Work Stage**, the slices with black regions in the tMIP images do not display summary maps in the contra-lateral regions to black regions, as side-by-side comparison is not available.

Before applying **Summary Maps** for a **Study**, one side of the tMIP images and **Perfusion Maps** have black regions as a result of 3D registration:

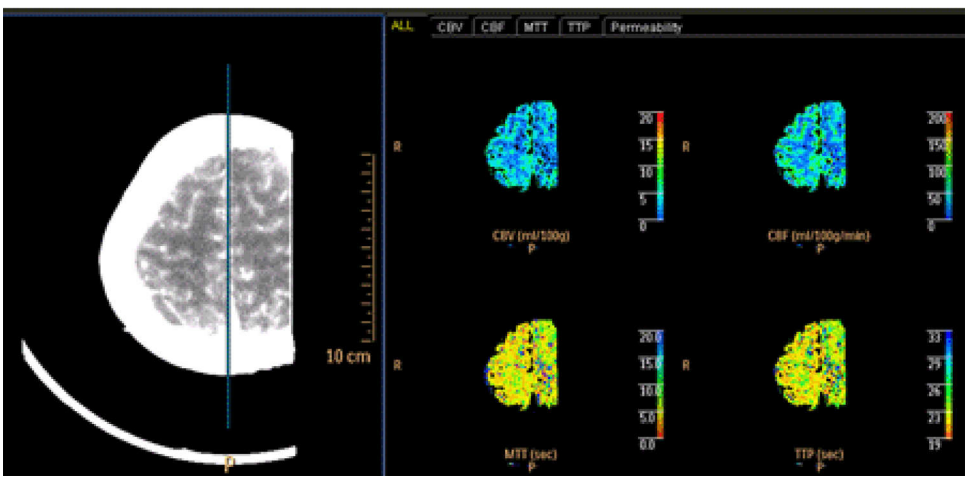
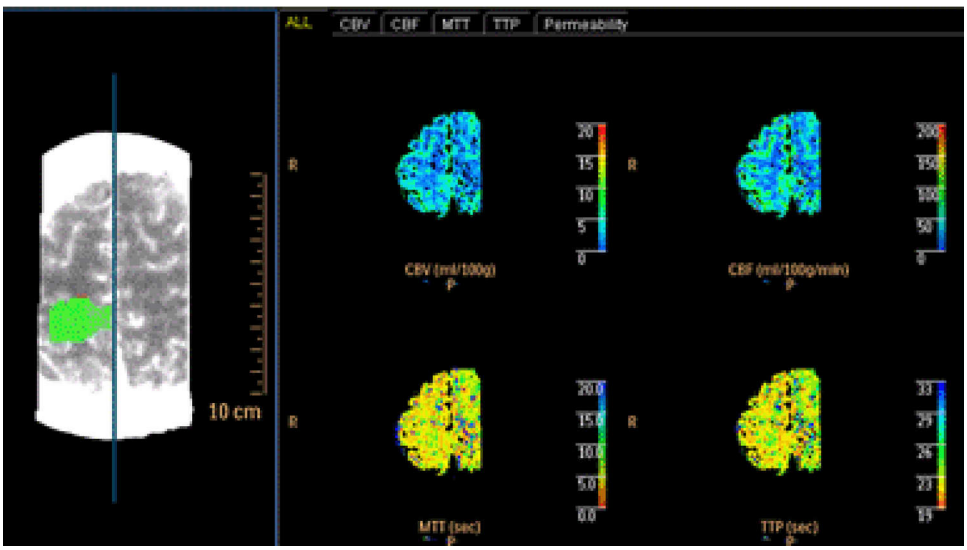


Fig. 10: tMIP Images and Perfusion Maps with Black Regions

Study After applying **Summary Maps**, the tMIP contra-lateral hemisphere includes added black regions. The **Perfusion Maps** remain intact:



The anatomical alignment is performed on a tilted scan as part of the 3D motion correction process. The cerebral midline should be a vertical line at the center of the image after successful operation of anatomical alignment. Below, the left images shows the original, tilted scan; the image on the right shows the scan after alignment, with the vertical cerebral midline.

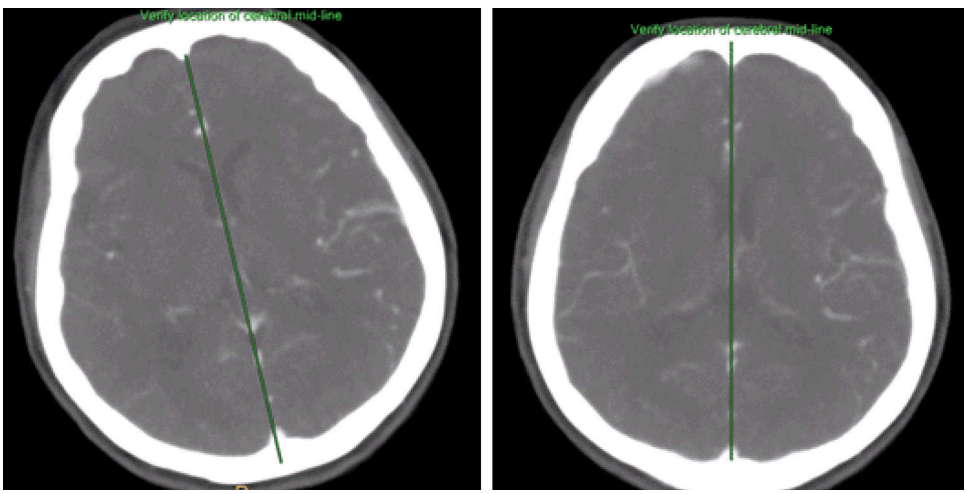


Fig. 11: A. Original Tilted Scan. B. Image After Anatomical Alignment

NOTICE

In some cases, 3D registration is successful but anatomical alignment fails. In such cases, a message appears in the status bar: **Anatomical alignment failed. Please verify patient location is correct and verify the cerebral symmetry**.

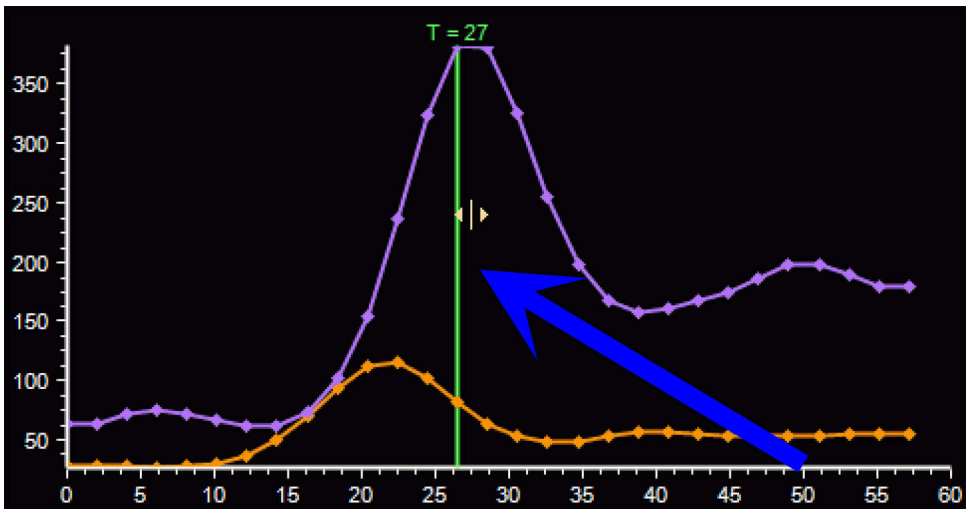
Remove Time Points

General guidelines for removing time points:

- Remove up to 8 time points from the scan.
- No more than 2 consecutive time points may be removed.
- The maximum difference between two consecutive scans must be less than 12 seconds when removing time points.

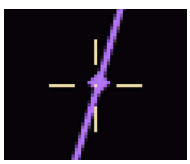
1. Click the **Remove Displayed Point**  button while in tMIP rendering mode.
2. Review the time points in the **Artery and Vein Activity** graph.
3. Scroll through the various Perfusion time points using the **Cine** tool or other methods. Pause the **Cine** tool on the time point to be removed.

   Alternately, click on a time point in the graph or grab the **Examine Line** (time-indication line) and drag it to the time point to be removed.



4. Click the **Remove Displayed Point**  button.

   Alternately, right click on the time point and select **Remove Displayed Point** from the menu.



5. Remove additional time points as necessary.
6. Use the **Bring Back Deleted Points** undo button (or select it from the right-click menu) to revert all changes.

The removed time points are marked in the artery/vein time attenuation curve with an orange dashed line.

NOTICE

After removing a time point, the title of the **Artery and Vein Activity** graph is appended with the statement: **Time points were removed**.

Verify and Edit Mirror Line

The mirror line - cerebral mid line between the hemispheres is suggested by the application. You may need to adjust the mirror line for all slices or for individual slices.

Incorrect Mirror Line	Corrected Mirror Line

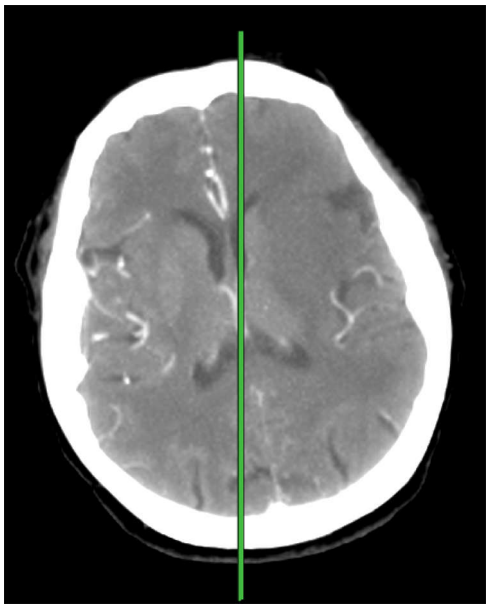
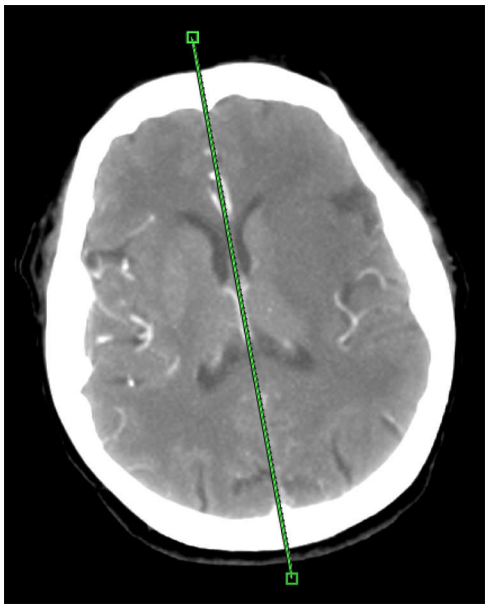
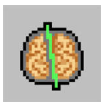

	

Fig. 12: Incorrect Mirror Line	**Fig. 13:** Corrected Mirror Line

NOTICE

If you use the **Detect Mirror Line**  feature after manually correcting the centerline, your changes will be lost and the centerline will be reverted to the auto-detected state.

Edit Mirror Line for All Slices

Editing the mirror line is applicable for all slices. Verify the correctness of the mirror line on all slices, after editing has taken place.

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1. Ensure the **Mirror Line** box is checked.
2. To move the centerline, click it and drag to the correct location.
3. To rotate, extend, or shorten the mirror line, hover over the line and click on the appropriate control point. Drag the line to the correct location.

Edit Mirror Line Slice by Slice

Editing the mirror line is applicable only for the active slice. Verify the correctness of the mirror line on all slices, after editing has taken place.

1. Ensure the **Mirror Line** box is checked.
2. Select the **Edit Mirror Line Slice by Slice** option.
3. To move the centerline for the displayed slice, click it and drag to the correct location.
4. To rotate, extend, or shorten the mirror line for the displayed slice, hover over the line and click on the appropriate control point. Drag the line to the correct location.
5. Scroll through the images and review and adjust as needed.

Verify and Edit Cerebral Mask

NOTICE

Verify the correctness of the Cerebral Mask. If needed, correct it manually using the Cerebral Mask tools.

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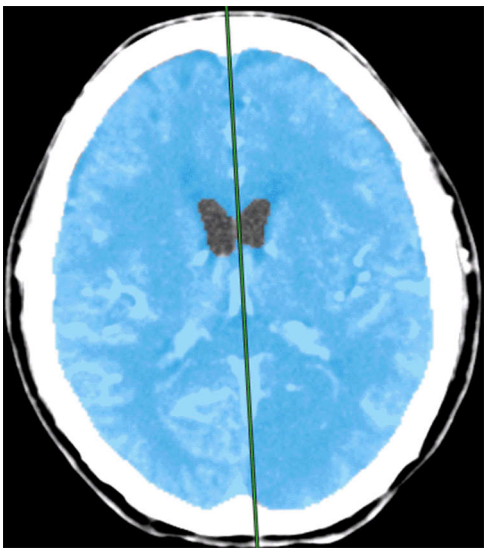
Click the **Show Mask** button to display the mask. The Cerebral Mask is an overlay that shows the volume identified as the brain by the Brain Perfusion application.

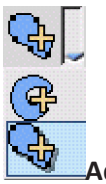


Scroll through the tMIP for the entire scan coverage to verify that the mask includes all brain tissue and excludes ventricles and the skull.

If necessary, correct the Cerebral Mask (follow the **Correct...** link to go to the **Edit Cerebral Mask** tab.

Click the **Show Mask** button in the Edit Cerebral Mask work step and scroll through the slices.

- If small corrections need to be made to the mask, these may be done by adjusting the Threshold values that define the mask.
- If old infarcts exist in the brain, they may not be included in the mask, due to low HU value. If required, lower the Threshold until the relevant area is included in the mask.

To add regions from the mask per slice, use the  **Add to mask:** feature in the **Edit Cerebral Mask** panel.

To remove regions from the mask per slice, use the  **Remove from mask:** feature in the **Edit Cerebral Mask** panel.

Each option provides two editing choices: Freehand ROI or Spline ROI, whichever is your preference.

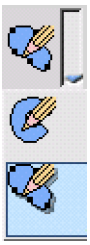
- In the freehand mode, hold down the left mouse button and trace the shape you want to add/remove from the mask by dragging the pencil pointer around the brain image until the end of the line meets the beginning.

- In the spline mode, move the pencil pointer around the perimeter of the brain, clicking wherever you want to place a line segment. Double click to end the spline drawing.

Use Thresholds to Correct Cerebral Mask

1. Raise or lower the Threshold settings until the mask correctly defines the brain volume.
2. Examine all slices to verify correct brain volume definition.
3. Click **All slices** to apply the threshold changes to all slices.

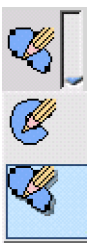
Draw New Cerebral Mask



There are two drawing choices: Freehand ROI or spline ROI, whichever is your preference. In the freehand mode, hold down the left mouse button and trace the shape of the new mask by dragging the pencil pointer around the brain image until the end of the line meets the beginning. In the spline mode, move the pencil pointer around the perimeter of the brain, clicking wherever you want to place a line segment. Double click to end the spline drawing.

1. Pick one or the other drawing mode, available from the drop-down.
2. Draw the new mask. Once the mask is drawn, it is based on threshold values that warrant what appears in the mask.
3. When done, use the left mouse click to scroll through all images; examine the green mask and verify correct definition of the brain volume.

Editing a Cerebral Mask



There are two cerebral mask editing choices: Freehand ROI or spline ROI, whichever is your preference. In the freehand mode, hold down the left mouse button and trace the shape of the new mask by dragging the pencil pointer around the brain image until the end of the line meets the beginning. In the spline mode, move the pencil pointer around the perimeter of the brain, clicking wherever you want to place a line segment. Double click to end the spline drawing.

Verify Suggested Reference Vessels

Brain Perfusion suggests reference vessels upon loading of the application. If these vessels were altered, reference vessels can be detected again by clicking the automatic function buttons.

Automatic Artery Detection	Automatic Vein Detection
	

NOTICE

Verify the correctness of the vein and artery detection and correct it manually, if required.

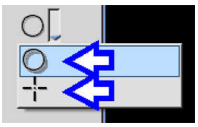
You can also manually define vessels. See section “Manually Define Vessels” on page 54.

Manually Define Vessels

You can manually define arteries and the vein in two ways:

- with the Draw ROI method, using the circular tool; or
- with the Draw Point method, using the cross hair tool.

To change tools, click the drop-down arrow and select the desired tool.



Verify and Edit Artery Selection

Brain Perfusion suggests reference artery upon loading of the application. If the vessel was altered, the artery can be detected again by clicking the automatic function button.

NOTICE

Verify the correctness of artery detection and correct it manually, if required.

If needed, you can manually define an artery.

After reviewing the study by scrolling through the slices, select the Draw method you want and by clicking its icon. The mouse pointer changes to a pencil.

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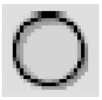
Draw Artery ROI



To use this tool, encircle the area containing the artery you want to define. To obtain correct perfusion values (perfusion maps) vessel selection is very important:

- **Arterial curve** - The artery that peaks first should be selected (automatic or manual selection). Most commonly the anterior cerebral artery (ACA), or middle cerebral artery (MCA) is selected as the reference vessel. If possible, the artery on the contra-lateral (non affected side) should be used.

The application searches for the single pixel within the ROI having the maximum enhancement, and marks it as the reference vessel with a colored cross-hair and labels it “Artery.”

Draw Artery Point

To use this tool, click the pencil pointer on a single pixel in an artery of interest. The application marks the pixel as the reference vessel with a cross-hair, assigns it a color code, and labels it “Artery.”

You can draw up to 10 arteries to find the highest HU. You can draw arteries on any and all of the slices in the study.

Each artery you define appears in the table called “Reference Artery Statistics” and is color coded. (You can double click on the table to expand it to full viewport size; double click again to reduce it.)

The artery’s enhancement curve appears in the “Artery and Vein Activity” chart, and is coded the same color as in the table.

NOTICE

After you draw an artery, the mouse cursor changes to the scroll pointer. If you want to draw another artery ROI, you must click the Draw icon again.

When the cursor is a scroll pointer, you can scroll the slices to search for another artery you want to define, and then click the Draw icon again.

There is no Undo option available, so if the marked artery is not the one you wanted, you must delete the artery (delete is a selection from the right mouse menu) and redraw the ROI.

Verify and Edit Vein Selection

Brain Perfusion suggests a reference vein upon loading of the application. If the vessel was altered, the vein can be detected again by clicking the automatic function button.

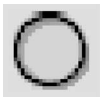
NOTICE

Verify the correctness of vein detection and correct it manually, if required.

If needed, you can manually define a vein.

To activate the Draw ROI tool, click its icon. The mouse pointer changes to a pencil.

Draw Vein ROI



To use this tool, encircle the area containing the vein you want to define.

Verify that the vein with the highest enhancement is selected. The curve should peak later than the arterial curve and its amplitude should be higher in most cases. The vein commonly selected is the Superior Sagittal Sinus (SSS).

The application searches for the single pixel within the ROI having the maximum enhancement, and marks it as the reference vessel with a blue cross-hair and labels it “Vein.”

Draw Vein Point

To use this tool, point the mouse cursor to select a single point in a vein of interest. The application marks the point as the reference vessel with a Draw Vein Point cross-hair and labels it “Vein.”

You can draw up to ten veins to find the highest HU. You can draw veins on any and all of the slices in the study.

The vein you define appears in the table called “Reference Vein Statistics” and is color coded. The veins’s blue enhancement curve appears in the “Artery and Vein Activity” chart.

NOTICE

A vein and an artery must be defined before a perfusion image can be generated.

Set Artery and Vein to Use for Calculations

All calculations performed in the Perfusion work stage are based on the artery and vein you set in the procedure below. All automatically or manually detected vessels are initially marked as **Artery?** and **Vein?** until you actively select them for calculation.

1. Hovering over a detected vessel in main viewport to show the **Use for Calculation** dialog. Or, using the right mouse button, click on the vessel (either in the table or on the image) you want to be active in the statistics table. Select **Use for Calculation**.
2. Click on the message. The color of the vessel data is changed to red, and the background is highlighted on the reference table. The selected vessel is appended with the word chosen, and the **?** (question mark) is removed from the vessel name.

3. Repeat the previous steps until both an artery and vein are selected.

When you proceed to the Perfusion Work Stage, only the active vessel is shown on the main image. See section “Perfusion Map Work Stage” on page 57.

Perfusion Map Work Stage

NOTICE

If Traffic Lights found an issue with the acquisition data, either the Non-Severe Warning or Severe Warning message will appear throughout the application. For example, original tMIP/ average axial view, Summary Maps and Perfusion Maps, display a red or yellow warning light (depending on the warning type). Before continuing, see section “Using Brain Perfusion Traffic Lights” on page 85.

NOTICE

Verify the correctness of the vein and artery detection and correct it manually, if required.

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NOTICE

If a high percentage of voxels within the cerebral mask could not be analyzed due to incompatibility to the analysis algorithms, the resulting perfusion calculations may be inaccurate.

If the system recognized a large area that cannot be analyzed, a message is displayed in the application.

A lack of suitability can stem from:

- Missing outflow phase within the tissue time attenuation curve.
- Missing inflow phase within the tissue time attenuation curve.
- High noise presence in the input images.

NOTICE

If **3D Motion Correction** was performed, the slices with black regions in the tMIP images do not display summary maps in the contra-lateral regions to black regions, as side-by-side comparison is not available. See section “Verify No Residual Motion Present” on page 46.

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Create Batch in Brain Perfusion

To create a batch in Brain perfusion, you can choose either of the following two options:

- **Whole screen for all locations:** Sends entire screen as an image, including all viewports and tables, for the entire z-coverage of the study.
- **Create a batch of a sub-set of images.** For that, please perform the following operations:

NOTICE

The **Perfusion Map** uses **TTP** for the time-arrival sensitive method and **Tmax** for the time-arrival insensitive method.

Creating a Batch

1. Choose batch content. You can select any combination (or all) of the following content types:
   - Perfusion maps (CBV, CBF, MTT, TTP, Tmax, Permeability);
   - Original image (tMIP series only);
   - ROIs on map + graph;
   - ROIs;
   - tMIP +Summary maps;
   - 2D summary map measurements;
   - 3D summary map measurements;
2. Sort batch content by:
   - **Whole screen for all locations** − Sends entire screen as an image, including all viewports and tables, for the entire z-coverage of the study.
   - **Sorted by Z-position (sort by slice)**− When the batch is created, all the content you selected is grouped together: for the first slice, then for the next slice, and so on.
   - **Sorted by map type** − When the batch is created, all selected content is grouped together by type. For example, all CBV images are shown together, then all CBF, and so on.
   - **Sorted by map type: multi series** − Same as “Sorted by map type” batch format, but each type/table/graph is saved in a separate series.
   - **Current** − The batch will only contain the selected content for the currently active slice.
   - **Comparison Overview** − When the batch is created, the defined content is displayed side by side to allow comparison between the different results types. If summary maps are defined they are displayed aside the Perfusion maps.
3. When done with your selections, click **Save batch as...** (or click on **Save Batch as...** in the Common Tools). A dialog window opens, where you can type in the batch name, the desired format (Secondary Capture, TIFF) and the destination device.

4. Click **OK** when done. The batch is saved to the destination device. As the batch is saved, a message displays the number of images and the device.

For additional information, see section “Automatic Results Creation Workflow” on page 90.

Layout of Perfusion Maps Display

The Perfusion Map Display has a number of viewports available, each providing different information.

NOTICE

The **Perfusion Map** uses **TTP** for the time-arrival sensitive method and **Tmax** for the time-arrival insensitive method.

Perfusion Maps

This viewport may display the following perfusion maps:

- Cerebral blood volume (CBV).
- Mean Transit Time (MTT).
- Cerebral Blood Flow (CBF).
- Time to Peak (TTP) - only available for Time Arrival Sensitive method.
- Tmax (only available for Time Arrival Insensitive method).

Several Color schemes that can be applied to the maps: Rainbow, Black and White, Thallium, and a-LUT.

Statistics Tables

Three statistics tables are available:

- ROI Statistics (for each slice).
- 2D measurements –Summary Map Statistics (area statistics table)
- 3D Measurements –Summary Map Statistics (volume statistics table)

NOTICE

If Traffic Lights found an issue with the acquisition data, either the Non-Severe Warning or Severe Warning message will appear throughout the application. For example, original tMIP/average axial view, Summary Maps and Perfusion Maps, display a red or yellow warning light (depending on the warning type). Before continuing, see section “Using Brain Perfusion Traffic Lights” on page 85 section “Using Brain Perfusion Traffic Lights” on page 85.

The Vessel and Tissue Curves Viewport

This viewport shows time-density curves of the selected Artery and the Vein (which you defined in the Vessel Definition stage), and the time-density curves of any Tissue ROIs (up to 10) that you draw. See section “Vessel Definition Work Stage” on page 42.

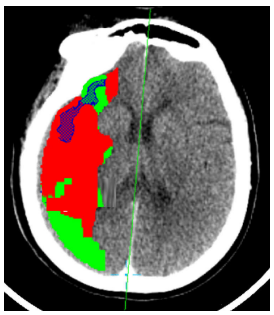
Summary Map

The Summary Map summarizes information from Perfusion Map images into a single depiction. It shows the areas with increased MTT and, within those areas, it highlights the reduced CBV versus non-reduced CBV areas. The summary maps are presented only when user manually activates them. When the user clicks on **Apply stroke Summary Map** options, it is displayed on the original tMIP or Average axial images.

View Summary Map

The Summary Map image shows (with color maps) areas of increased MTT relative to the contralateral hemisphere and reduced or non-reduced absolute CBV when factory default settings are used. (It is called the Summary Map because it summarizes information from all Perfusion Map images into a single viewport.)

COLOR CODING of the SUMMARY MAP	
GREEN and RED	Total area of increased MTT relative to the contralateral hemisphere.
GREEN	Area having increased relative MTT with non-reduced absolute cerebral blood volume.
RED	Area having increased relative MTT with reduced absolute cerebral blood volume.



View Statistics Tables

Tables contain data only if the right or left Summary Map is enabled. You can control which statistics tables are displayed from the right click menu.

NOTICE

The active table may be added to the clipboard using **Ctrl + C** or by right-clicking on the table and selecting copy. The measurements may then be pasted into common document types, including plain text, Microsoft Word, and Microsoft Excel documents.

2D & 3D Measurements-Summary Maps (Volume and Area Statistics Tables)

The 3D Measurements –Summary Map table displays the total volume.

The 2D Measurements –Summary Map/ Area Statistics table displays the calculated areas (in each slice) of the green and red overlays shown in the Summary Map.

The Refer area/volume statistics table below provides explanations about the measurements at the bottom of each column.

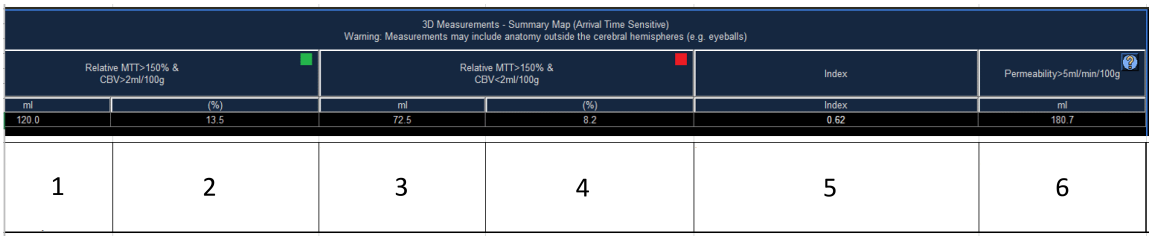


Fig. 14: Table-3D Measurements-Summary Map (Arrival Time Sensitive)

The numbers in the below table are associated with the numbers in the columns in the image above.

Item #	Description
1	The volume within the total summary map region suspected for reduced perfusion (green) for slices)
2	The % of suspected reduced perfusion volume (green) within the total cerebral volume (for all slices)
3	The volume within the summary map region that is suspected for severely reduced perfusion (red) for all slices
4	The % of suspected severely reduced perfusion volume (red) within the total cerebral volume (all slices)
5	The Green Volume/(Green + Red volumes) (for all slices)
6	The high permeability volume with the entire summary map region (for all slices)

Note: The measurements on the statistics columns (and explanations at the bottom of the column) are for illustration purpose only.

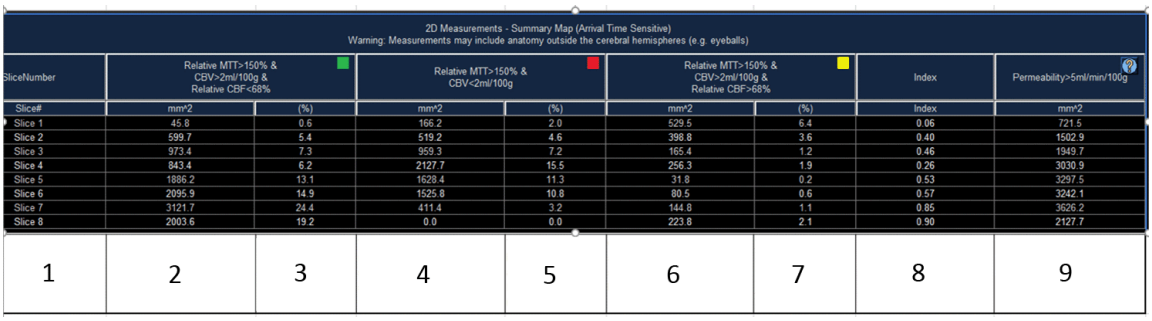


Fig. 15: Table-2D Measurements-Summary Map (Arrival Time Sensitive)

Item #	Description
1	Measurements displayed per slice
2	The area within the summary map region that is suspected for reduced perfusion (per slice)
3	The % of suspected reduced perfusion (green area) within both hemisphere areas (per slice)
4	The area within the summary map region that is suspected for severely reduced perfusion (per slice)
5	The % of suspected severely reduced perfusion area (red) within both hemispheric areas (per slice)
6	(Optional) The area within the summary map region that is suspected for slightly reduced perfusion (per slice)
7	(Optional) The % of suspected "slightly reduced “ (yellow) area within both hemispheric area s (per slice)
8	The Green area /(Green + Red + Optional Yellow)(per slice)
9	The high permeability area with the entire summary map region (per slice)

Note: The measurements on the statistics columns (and explanations at the bottom of the column) are for illustration purpose only.

ROI Statistics Table

As you draw ROIs, each is automatically assigned a unique color and number. The color is correlated to the ROI statistics in the table, and to the ROI curve graphs.

NOTICE

If you drew Tissue ROIs on more than one slice, scroll to other slices in the map images to see the ROI statistics for those slices in the table. The heading of the table identifies the slice number. The number indicates the average value within the ROI.

ROI#	the ROI number
CBV(ml/100g)	The integral of the tissue time-attenuation curve normalized by the integral of the selected vein time-attenuation curve and the hematocrit.
CBF(ml/100g/min)	The CBV divided by the MTT, per the Central volume Principle.
MTT(s)	The mean-transit-time of blood through a given brain region, measured in seconds.

TTP(s)	Time to peak enhancement at each x, y location, measured in seconds.
Tmax (s)	Time to peak enhancement of the residual function of the Singular Value Decomposition (SVD) based deconvolution, measured in seconds. (Time Arrival Insensitive method).
Permeability *	The permeability is calculated using a Patlak analysis. *

* For the Permeability analysis, the acquisition must be extended to include delayed phases of the passing and re-circulation of contrast agent in the brain to identify extravasated contrast agent that has permeated the BBB. For Patlak analysis, the time attenuation curve describing the observed amount of contrast agent in a per- fused voxel is modeled as the sum of intravascular and interstitial, extravasated contrast agent. The amount of contrast agent that has permeated through the BBB is modeled as a fraction of all contrast that has passed through the voxel since the start of the acquisition, and this fraction is interpreted as blood-to-brain transfer constant -- which is the definition of Permeability.

Perfusion Maps Tools

Use the following tools located in the upper toolbox:

Show High Permeability Areas

This check box allows you to turn off and on the areas of high permeability. Permeability measures the contrast agent permeation of the BBB (blood-brain barrier).

Show Mirror Line

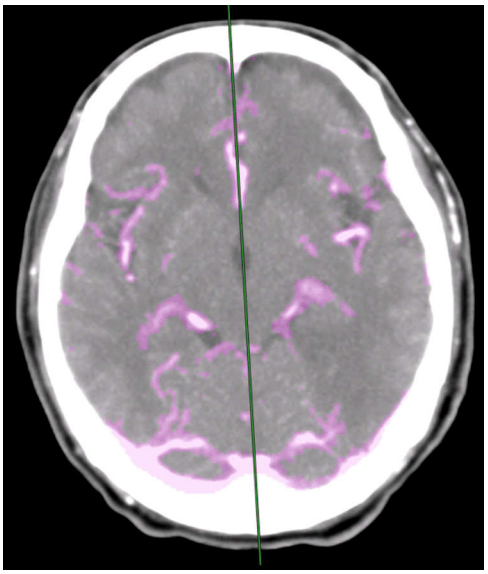
This check box allows you to turn off and on the mirror line that was created in the Vessel Definition stage. (If you want to edit the mirror line's position, see section "Vessel Definition Work Stage" on page 42.)

Show Tissue ROIs

This check box allows you to turn off and on the Tissue ROIs that you draw.

Show Vessels Segmentation

Check the box to display or hide the vessels segmentation. The purple overlay depicts areas automatically detected as **vessels**, that are removed from calculations when the **Remove Above** checkbox is checked. See section "Verify and Edit Vessel Removal" on page 72.



NOTICE

By default, the vessel segmentation overlay is disabled, if the Display Summary Maps tool is used. Check the box again to display again.

Show Invalid Voxels

Use the checkbox to display or hide the voxels that cannot be analyzed.

See **Report**, **Film**, **CT Common Processes** and **CT Common Tools** for information on using common options, tools, functions, and processes.

Key Images

Save groups of images that can be reviewed in any system supporting the defined standard. See **Instructions for Use** > **Directory** > **Key Image Notes** for more information.

Use Summary Map

NOTICE

There are no recommended threshold values for Philips Brain Perfusion application for the **Summary Maps** calculation in conjunction with poor temporal resolution cases (cycle time longer than 4 seconds). When using such data, the default thresholds that apply on densely sampled cases may not be optimal. If you wish to use the **Summary Maps** functionality in conjunction with poorly sampled data, you may adjust the thresholds manually.

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NOTICE

See also section “Apply Summary Map” on page 74.

NOTICE

The **Perfusion Map** uses **TTP** for the time-arrival sensitive method and **Tmax** for the time-arrival insensitive method.

For Arrival-time-sensitive Method Only

- The value of Increased MTT (mean transit time) affects the areas depicted as Green or Red on the Summary Map. The default factory parameter threshold for this is Increased Relative MTT at greater than 150% of contra lateral hemisphere, meaning all areas exhibiting mean transit time that increased by 50% (or more) when compared to the contra-lateral hemisphere will be shown as either Green or Red, depending on the CBV value.
- The value of Reduced CBV (cerebral blood volume) determines whether tissue identified as having a prolonged MTT will be depicted in Red or Green in the Summary Map. All tissue with a prolonged MTT and a CBV below the Reduced CBV threshold will be colored red. All tissue with a prolonged MTT and a CBV above the Reduced CBV threshold will be colored green.

NOTICE

The CBV threshold affects only tissue that has met the MTT threshold. That is, for the example given:

- Green: Relative MTT increase by 50%, CBV above 2.0 ml/100g
- Red: Relative MTT increase by 50%, CBV below 2.0 ml/100g

NOTICE

The default thresholds for the **Summary Maps**, proposed by the application, increased relative MTT at greater than 150% of the contra lateral hemisphere, and within those areas absolute non-reduced or reduced CBV of 2 ml/100g. They were calculated based on the **Arrival Time Sensitive** method. For more information on this topic please refer to the following publication: *Wintermark M, Flanders AE, Velthuis BV et al. Perfusion-CT Assessment of Infarct Core and Penumbra: Receiver Operating Characteristic Curve Analysis in 130 Patients Suspected of Acute Hemispheric Stroke. Stroke 2006; 37: 979-985*.

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NOTICE

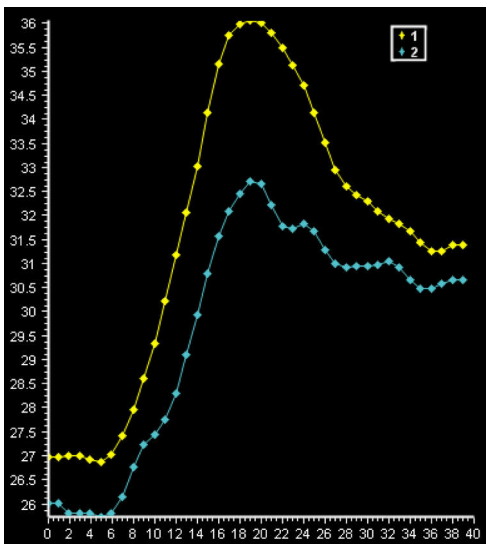
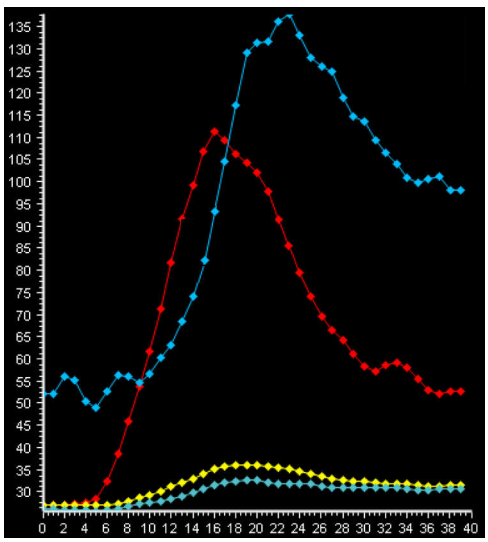
There are no recommended threshold values for Philips Brain Perfusion application for the **Summary Maps** calculation in conjunction with the **Arrival Time Insensitive** method. When using the above mentioned system default thresholds for the **Summary Maps**, after applying the **Arrival Time Insensitive** method, the **Summary Maps** results may not be optimal.

If you wish to use the **Summary Maps** functionality in conjunction with the **Arrival Time Insensitive** method, please adjust the thresholds manually. For more information on the **Arrival Time Insensitive** method refer to: *Cenic A, Nabavi DG, Craen RA, et al. Dynamic CT measurement of cerebral blood flow: a validation study. AJNR Am J Neuroradiol 1999;20:63–73*.

Show Tissue Curves

The Show Tissue ROIs function controls the display of curves in the graph viewport.

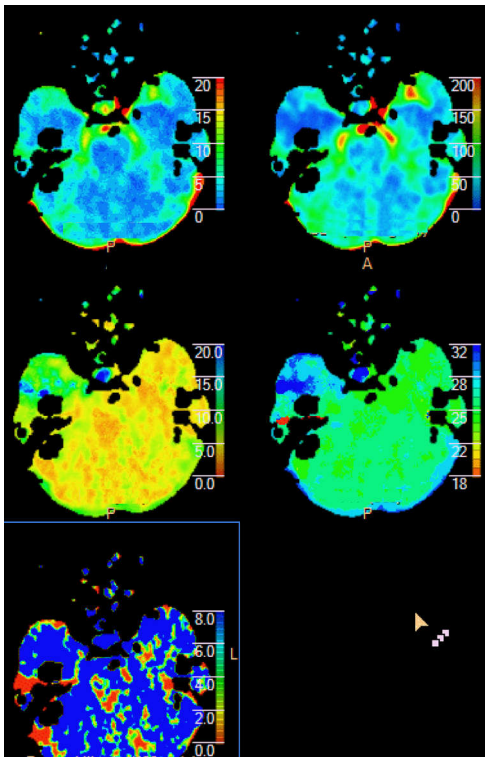
- The default curve display shows the statistics for the two user-drawn ROI curves. The two Tissue ROI curves are colored yellow and blue. (The colors were automatically assigned when the ROIs were created. You can click on a data point to see its statistics.)
- To show/hide the Artery and Vein curves, right click in the graph viewport and select **Show Artery-Vein Curve**. The red and blue Artery and Vein curves are now included in the graph viewport. The graph has been re-scaled, and the original Tissue ROI curves are smaller. (The peak of the tallest ROI may be cut off.)

Tissue ROI Curves	Artery, Vein, and Tissue ROI Curves
	

Perfusion Map Images

The viewport in the upper-right corner in the layout displays color-mapped Perfusion and Permeability images.

A Tab strip at the top of the maps viewport enables you to display all images at once or each one individually.



Cerebral Blood Volume (CBV)

CBV is defined as the total volume of flowing blood in a given volume in the brain, with units of milliliters of blood per 100 g of brain tissue. Cerebral blood volume is calculated by the ratio of two areas: area under the TAC of the tissue and the area under the TAC of the reference vein normalized by the hematocrit value. The CBV calculation is based on the partial volume effect. The color bar is scaled in milliliters/100 grams.

Mean Transit Time (MTT)

MTT is defined as the average transit time of blood through a given brain region, measured in seconds. The color bar is scaled in seconds.

MMT is computed differently for sensitive vs. insensitive.

Sensitive: MTT is extracted from the TAC of the tissue after Gaussian curve fitting. MTT is computed by summing the standard deviation of the fitted curve and the TTP and subtracting the MTT of the reference artery.

Insensitive: MTT is the first moment of the retention function.

Cerebral Blood Flow (CBF)

CBF is defined as the volume of blood moving through a given volume of brain per unit of time, with units of milliliters of blood per 100 g of brain tissue per minute. CBF is calculated by dividing the CBV by the MTT, per the Central Volume Principle. The color bar is scaled in milliliters/100 grams/minute.

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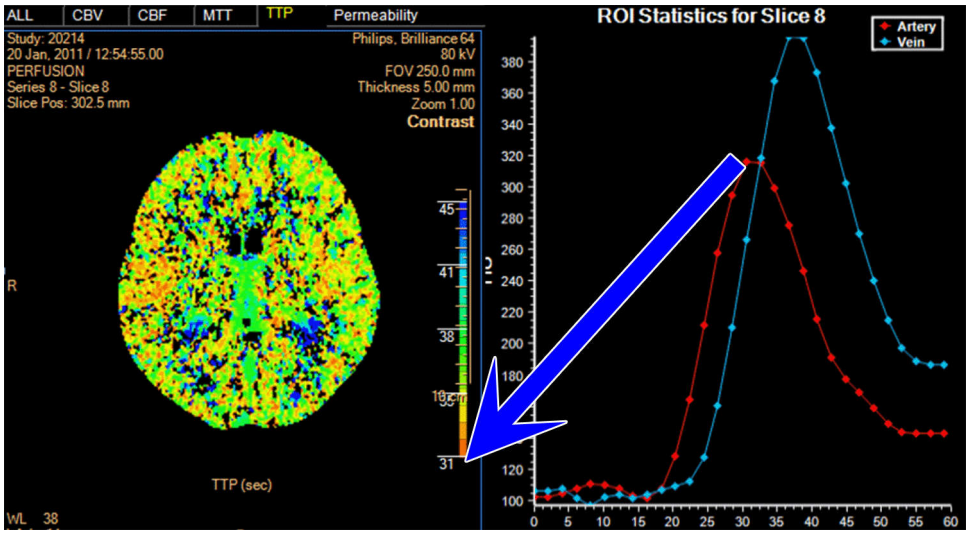
Time To Peak (TTP)

TTP displays the time it takes for the peak enhancement to be reached at each x, y location. The color bar is scaled in seconds. The lower threshold of the scale bar is set to the arterial input TTP (to accommodate for late contrast injection by default). This parameter is applicable for the Time Arrival Sensitive method.



Tmax

Tmax displays the time it takes for the peak enhancement of the residual function of the SVD-based deconvolution. The color bar is scaled in seconds.

Permeability

Areas of High Permeability are shown with a pleated blue overlay on the axial image. The Permeability perfusion map represents the ability of extravasation of a contrast agent from the intravascular space to the extravascular space [the contrast agent permeation of the BBB (blood-brain barrier)]. The default color scale displays high permeability in blue and low permeability in red yellow in the middle. The range of the scale is: [0, 8] ml/100g/min.

The amount of contrast agent that has permeated through the BBB is modeled as a fraction of all contrast that has passed through the voxel since the start of the acquisition. This fraction is interpreted as blood-to-brain transfer constant - which is defined as Permeability.

NOTICE

The **Perfusion Map** uses **TTP** for the time-arrival sensitive method and **Tmax** for the time-arrival insensitive method.

NOTICE

The Permeability analysis is only available if the scan duration is long enough.

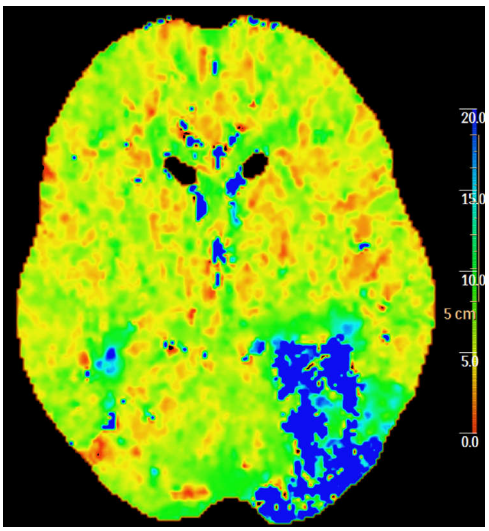
Perfusion Map Color Schemes

Various color schemes for the Perfusion Maps are available for use as needed. The choice of color map is a user preference that affects only the types and ranges of colors used to display the perfusion parameters (e.g., CBF, CBV, MTT, TTP). The values of the perfusion parameters are not changed when selecting different color maps.

- Right mouse click on a Perfusion Map image to activate a drop-down menu.
- Select “Color Schemes.” The list of available color schemes appears:
  - Rainbow black edges
  - Rainbow red/blue edges
  - Rainbow 3
  - Black and white
  - Thallium
  - a-LUT
  - Red Over Blue
  - Back to default (to set display back to default "Rainbow black edges")

Rainbow Black Edges Color Scheme

In this (the default) color scheme, perfusion data is represented as a range of colors having the same sequence as a rainbow spectrum.



Rainbow Red/Blue Edges Color Scheme

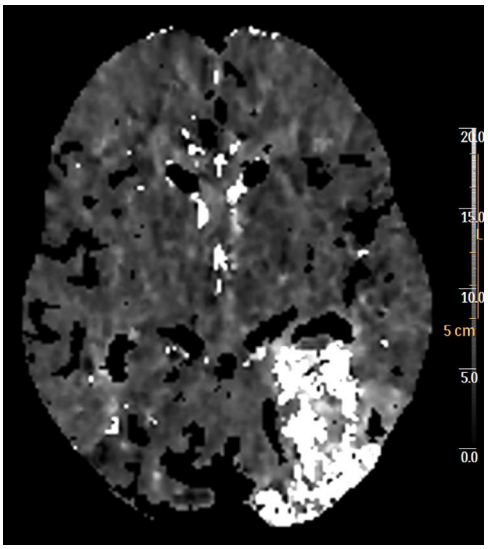
This color scheme is similar to Rainbow Black Edges Color Scheme, with this exception: Those values on the Perfusion maps that are lower than the lowest value of the scale are colored with the same color as the lowest color of the scale. (In the Rainbow color scheme, those values are colored black.)

Rainbow 3 Color Scheme

Rainbow 3 Color Scheme is similar to Rainbow Black Edges Color Scheme, with red at the bottom of the scale and blue at the top of the scale.

Black and White Color Scheme

Perfusion data is represented as a range of grayscale intensities. These maps are suitable for storage and display systems (e.g., PACS) that are incompatible with color maps.



Thallium

Perfusion data is represented by a range of colors similar to those used in conjunction with nuclear medicine perfusion scans (e.g., Thallium-201 SPECT).

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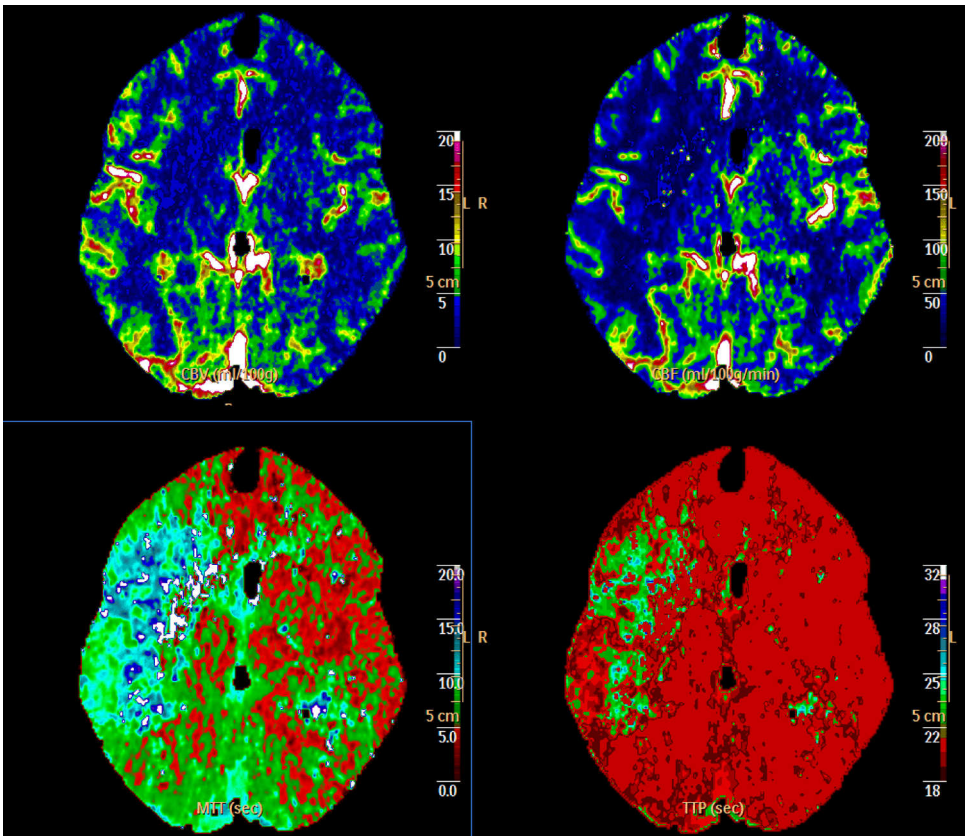
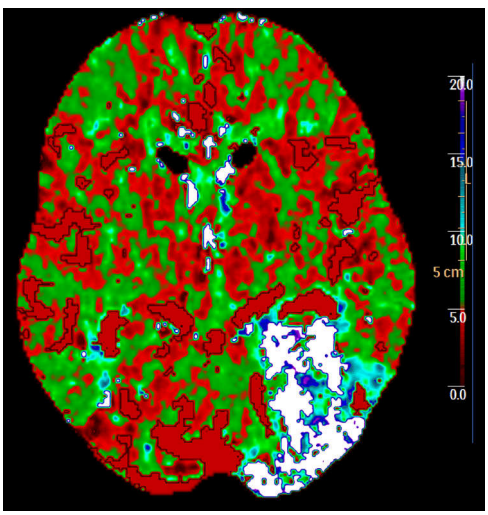


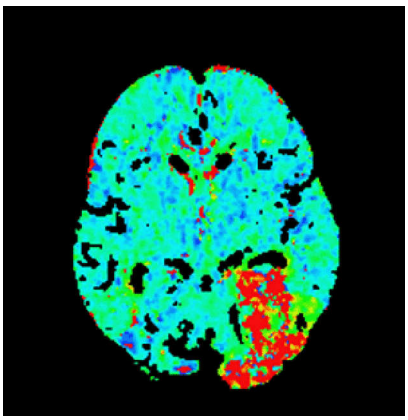
a-LUT

Perfusion parameter color maps that use the Acute Stroke Imaging Standardization Group (Japan) recommended lookup table (a-LUT).



Red Over Blue

In this color scheme, perfusion data is represented as a range of colors with a “Red over Blue Color Scheme”. It is similar to Rainbow 3 color scheme with MTT and TTP (Tmax) color scale reversed red over blue with color scheme applied on perfusion maps.



Review Perfusion Results

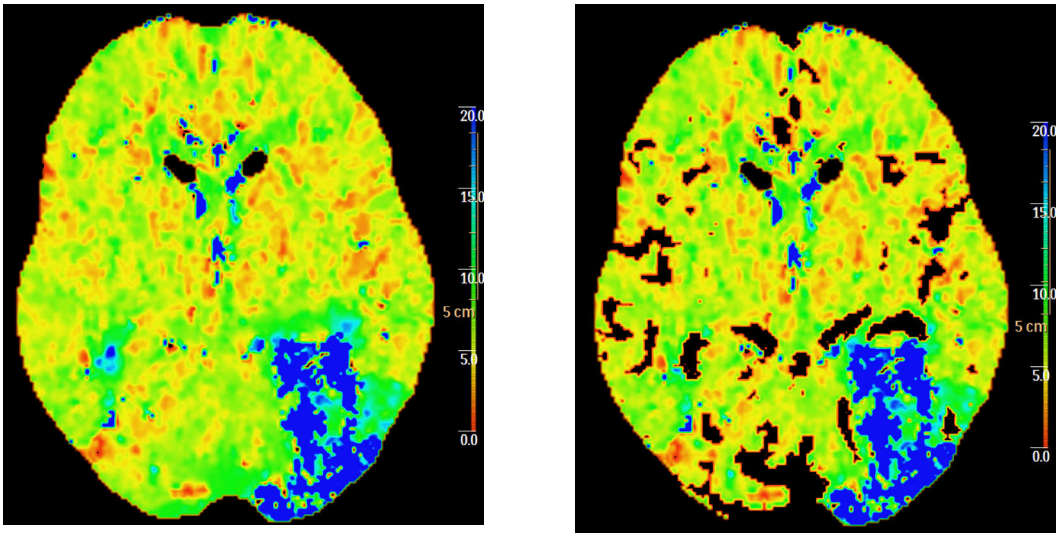
To calculate the average value of the Perfusion Maps within a region, and draw an ROI on the axial image or one of the maps.

Verify and Edit Vessel Removal

You should remove vessels after creating the perfusion maps if you plan to make quantitative ROI measurements. This removes vessel pixels from the perfusion calculation and from the CBF, MTT, TTP/Tmax, and Permeability perfusion images.

Check the **Exclude vessels from maps/ROIs** box to eliminate pixels from the calculation and from the color perfusion images. Removed pixels are colored black (zero value).

Shown below is an MTT image before (left) and after (right) the vessel removal function was activated.



Edit Vessel Threshold

The user may use the Vessel Threshold function to exclude the blood flow in larger vessels from the statistical calculation. The Vessel threshold is expressed as a pixel value in the CBV image. The default threshold value is 9. This means that any pixel in the CBV image with the value 9ml/100g and greater is not displayed on the perfusion maps or included in the ROI measurements. In cases where the temporal resolution is greater than 4.0 second, the threshold is relative.

NOTICE

Depending on the case, you may need to adjust the default value if the results are not as expected. This may be caused by too many vessels removed or too many vessels remaining after Vessel Removal.

Measure Tissue ROIs

Tissue ROIs are used for blood-flow analysis. The results are shown in the ROI Statistics Curve display and ROI Statistics table. You can draw up to 10 ROIs on both the Summary Map image and the Perfusion Map images. You can draw on all slices. Each ROI is automatically assigned a unique color and number.

Three types of ROI drawing tools are available: Ellipse, Spline, and Freehand.

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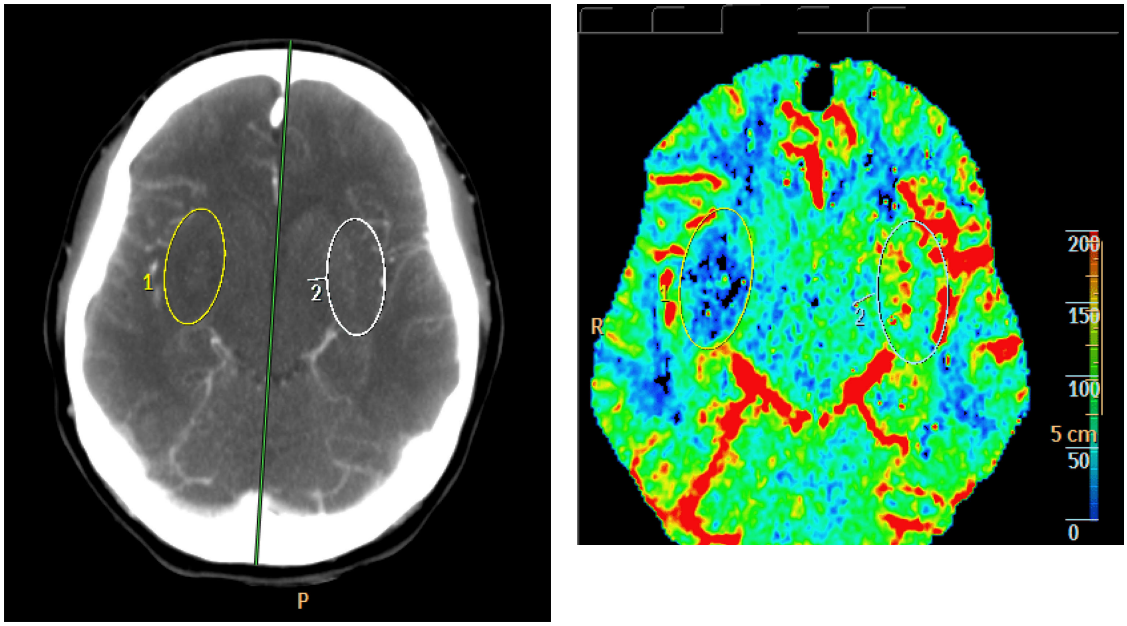


Create Contra-lateral ROI Automatically

With this feature active, any Tissue ROI drawn on one side of the mirror line automatically is mirrored the other side. Uncheck this box if you do not want mirror-image ROIs to be drawn.

Edit Tissue ROI

A Tissue ROI can be modified and deleted like any other ROI graphic. Refer to the **Common Tools** section for instructions about editing ROIs.

Place Template ROIs

When this feature is activated, Template ROIs appear in the brain periphery.

Apply Summary Map

Patient Right Hemisphere

Click the button to display the summary map on the right side (relative to the image) of the mirror line. To hide, click the button again.

Patient Left Hemisphere

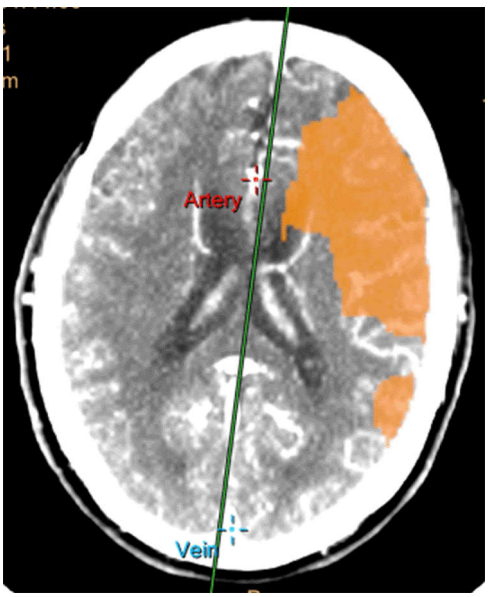
Click the button to display the summary map on the left side (relative to the image) of the mirror line. To hide, click the button again.

NOTICE

See also section “Use Summary Map” on page 64.

High Inter-scan Delay and the Time Sensitive Method

If the application identifies that the inter-scan delay is greater than 4.1 seconds but less than 4.5 seconds, the temporal resolution is not sufficient to highlight reduced CBV and non-reduced CBV within the increased MTT area. Therefore, the default Summary Maps cannot present two distinct areas. For example, there are no red/green areas when applying the summary maps. Instead, an orange overlay depicting the entire area of increased MTT is displayed, with no differentiation between reduced/non-reduced CBV. This overlay describes the full extent of area where there is a flow deficit, enabling you to determine whether there is decreased blood volume using the appropriate perfusion map. The user can manually add values/relative thresholds to be represented in the different colors of the summary maps.



NOTICE

When applying the summary maps, it is NOT possible to separate into different areas due to the low sampling rate.

High Inter-scan Delay Statistics Tables

The default Increased **Area Statistics** and **Volume Statistics** tables do not separate to different summary map (no green and red regions) regions based on CBV values, but instead show entire region of increased MTT.

Very High Inter-scan Delay and the Time Sensitive Method

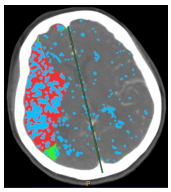
If the application identifies that the inter-scan delay is greater than 4.5 seconds, the summary map thresholds are not available by default because the delay is too long. You can only use the Perfusion Maps. You can manually insert threshold values in the **Set Calculation Settings** dialog, each time the application is used to obtain summary maps.

Invalid Voxels and the Time Sensitive Method

Under certain conditions, a high number of voxels within the left\right (screen relative) side of mirror line may not be analyzed due to incompatibility to the analysis algorithms. Such lack of suitability can stem from:

- Missing outflow phase within the tissue time attenuation curve.
- Missing inflow phase within the tissue time attenuation curve.
- High noise presence in the input images.

In such cases, a severe traffic lights warning is registered when proceeding to second stage.



In addition to the red/green summary maps, an additional blue overlay is shown, depicting all voxels which cannot be analyzed. This overlay, unlike the summary maps, is displayed on both hemispheres simultaneously.

The Invalid Voxels overlay can be removed by unchecking **Show Invalid Voxels** in the upper tool box.

Modifying Calculation Settings

To change the **Calculation Settings** parameters, click the **Edit...** link. The **Set Perfusion Parameters** window opens.

In the **Set Perfusion Maps Parameters** window, choose from a number of parameters:

- **Set Method**— Sets the calculation method. The following options are available:
  - Arrival Time Sensitive
  - Arrival Time Insensitive
- **Set Summary Maps Parameters** — Used to highlight areas with reduced perfusion.

  Please refer to section “Set Summary Maps Parameters” on page 76 for detailed information on parameters and applicable values.

Set Summary Maps Parameters

WARNING

Changing the default factory settings may change application-generated results. Please pay attention to the implications of all modifications.

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This section sets the threshold and parameters for summary maps.

Areas Suspected for Reduced Perfusion (all highlighted areas)

- This parameter defines the threshold for all of the colored regions (green, red and potentially yellow).
- Define any perfusion parameter as the basis for this area (which includes all affected regions).
- Options include: Absolute/Relative values of MTT, CBF, CBV, TTP/Tmax.
- The default factory parameter for this region is **Increased Relative MTT** at greater than 150% of contra lateral hemisphere when using the time sensitive method.

NOTICE

In most cases, it is necessary to select both *Areas suspected for reduced perfusion* and *Areas suspected for severely reduced perfusion* to visualize summary maps.

Areas Suspected for Severely Reduced Perfusion (red areas)

- This parameter defines the threshold parameters for the red regions in the map.
- Options include: Absolute/Relative values of MTT, CBF, CBV, TTP/Tmax.
- The default factory parameter for this region is **Reduced CBV** at less than 2 ml/100gr when using the arrival time sensitive method.

Areas Suspected for Slightly Reduced Perfusion (yellow areas) - Optional

- This parameter defines the threshold parameters for yellow regions in the map. This is an optional setting.
- Options include Absolute/relative values of MTT, CBF, CBV, TTP/Tmax.
- If the slightly reduced perfusion threshold is populated, the yellow regions are defined as regions that meet the slightly reduced perfusion threshold and reduced perfusion threshold, but do not meet the severely reduced perfusion threshold.
- By default, this option is not enabled and must be manually enabled by placing a checkmark in the checkbox. There is no default factory parameter set for this region.

Limitations on Input of Perfusion Parameters

- For CBV and CBF thresholds:
  - Suspected for: severely reduced perfusion < reduced perfusion < slightly reduced perfusion
- For MTT, TTP and Tmax thresholds:
  - Suspected for: severely reduced perfusion > reduced perfusion > slightly reduced perfusion

Resulting Summary Maps Table

A table of the various regions and the parameters that make up the region is displayed.

Saving Perfusion Parameters

To save the parameters as system default parameters, place a checkmark in the **Set above parameters as default** checkbox and select **OK**. Changes will be applicable for all future uses.

If the **Set above parameters as default** is not selected, changes will be applicable for the current session only.

Special Modes of Summary Maps

- In cases with a low sample rate (interscan delay between 4.1 sec and 4.5 sec,), default values cannot include absolute perfusion parameter thresholds. Users can insert manually per case and/or change the default values to any relative parameter and save as default. Example: reduced perfusion set at relative MTT > 150%, severely reduced perfusion as relative CBF lower than 30%
- In cases with a very low sample rate (interscan delay is higher than 4.5 sec.), it is not possible to use default values and the user would have to manually insert values each time the application is used.
- In cases with a low CBV (average CBV values are lower than 2.5 ml/100gr on entire brain tissue) absolute CBV values will not be shown by default for summary map threshold in case that is the user setting.

Show More Parameters

This section includes additional parameters including Permeability threshold, Minimal scan duration for permeability and Hematocrit factor.

High Permeability

Use the parameter to separate between the high and normal permeability regions within suspected reduced Perfusion areas.

Permeability Scan Duration

Set the minimum scan duration for permeability analysis. Permeability maps and measurements will not be shown by default for scans with a lower duration.

Hematocrit Factor

The hematocrit factor is the ratio of red blood cells to the total volume of blood. The factor is used to convert contrast enhancement (in HU) to CBV (in ml/100g of tissue). The default Hematocrit factor is 0.45. Do not change the default value unless you have measured the patient's factor and it is different from the default value.

Recommended: Extended Scanning Duration for Permeability Analysis

When Patlak analysis is applied to the delayed phase of an extended acquisition, it provides quantitative permeability information. However, for shorter acquisitions the analysis is strongly biased by local blood flow.

It is difficult to separate late intravascular contrast enhancement from truly extra-vascular contrast enhancement during or shortly after the first pass of predominantly intravascular contrast agent. This is because contrast agent flows in and out (especially out) much later in ischemic areas than in normally perfused regions. In such cases, residual intravascular contrast enhancement can obscure all extra-vascular contrast enhancement.

Recommended Scan Duration

The recommended duration for the delayed PCT acquisition is at least 210 seconds because acquisitions shorter than 210 seconds lead to significantly overestimated BBBP (blood-brain barrier permeability) values [Hom et. al 2009]. See also section “Brain Perfusion References” on page 99.

Brain Perfusion Reference Vessel Selection Guide

This guide includes 5 steps to be performed in both the Vessel Definition stage and the Perfusion Maps stage:

- Steps 1 through 3 are associated with the **Stage 1**.
- Steps 4 and 5 are associated with the **Stage 2**.

Stage 1: Vessel Definition

In this stage, it is crucial to verify the quality acquisition and the quality of artery and vein automatically detected by the application or manually defined by the user.

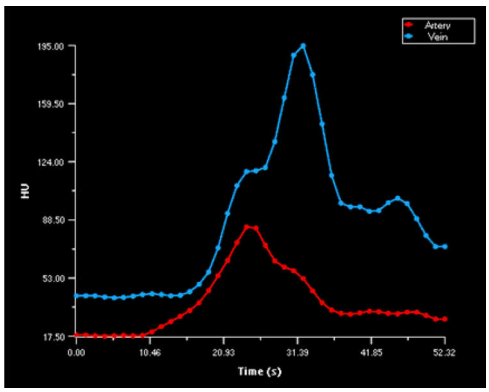
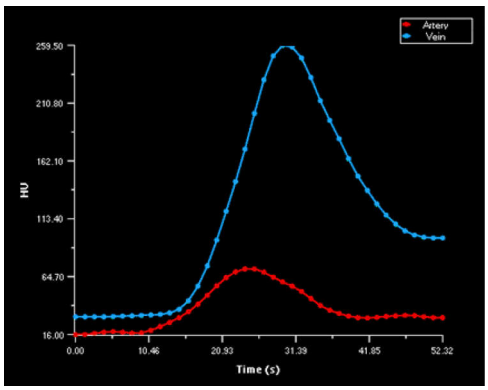
Step 1: Check Automatic Motion Correction

Verify no motion remained once registration completes. Typically, the motion correction implemented with the registration should be able to minimize the motion that was detected during the scan. However, in some cases some residual motion remains.

To detect any residual motion:

1. Switch to the **Average** rendering mode (instead of **tMIP**) using the control on the bottom left of main viewport.
2. Turn on **Cine mode**. See the **CT Common Tools** section for more information.
3. Press play and verify no motion is observed throughout scan duration.

Another way to recognize residual motion in this stage is by looking at the “artery and vein activity” graph at the bottom right viewport corner. If parts of the ascent/descent phases of either of the vessels seem highly inconsistent, it could imply that motion is still evident after the registration.

Residual Motion Effecting Vein and Artery Curve	Typical Vein and Artery Curve
	

Step 2: Verify Perfused Areas

Verify that the cerebral mask includes all the relevant perfused areas. The cerebral mask defines the area within the image that is considered as “brain” and only for this area are perfusion maps calculated. In addition, the BP application suggests potential reference vessels only from within the defined cerebral mask area. Thus, if the cerebral mask was defined incorrectly, the suitability of the suggested reference vessels may be affected.

Optimally, the cerebral mask does not include skull, brain ventricles, and eye lenses when these are present in the scan.

The recommended cerebral mask settings are as follows: lower threshold as 15 HU and upper threshold at 400 HU.

These settings can be changed by switching to **Cerebral Mask/Edit Cerebral Mask** tab and turning on the mask display. When changing the cerebral mask threshold, please note that changes can either affect all slices or only the currently active slice.

NOTICE

Verify the correctness of the cerebral mask and fix it before selecting reference vessels.

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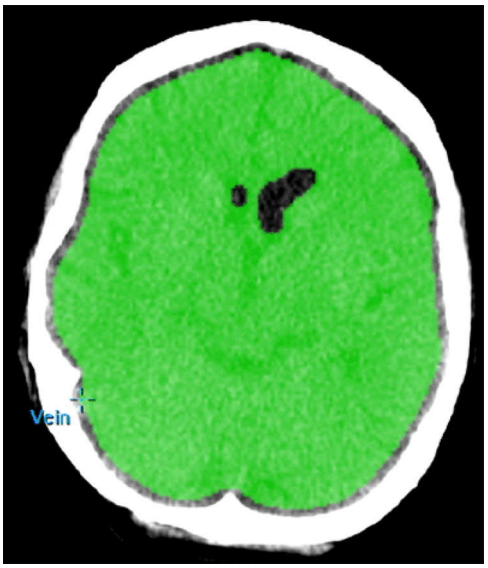
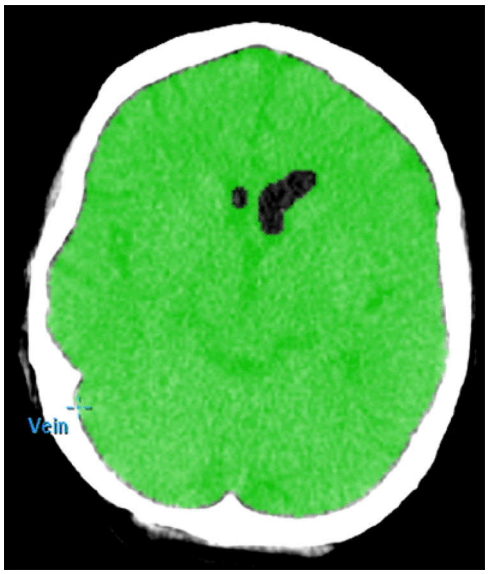
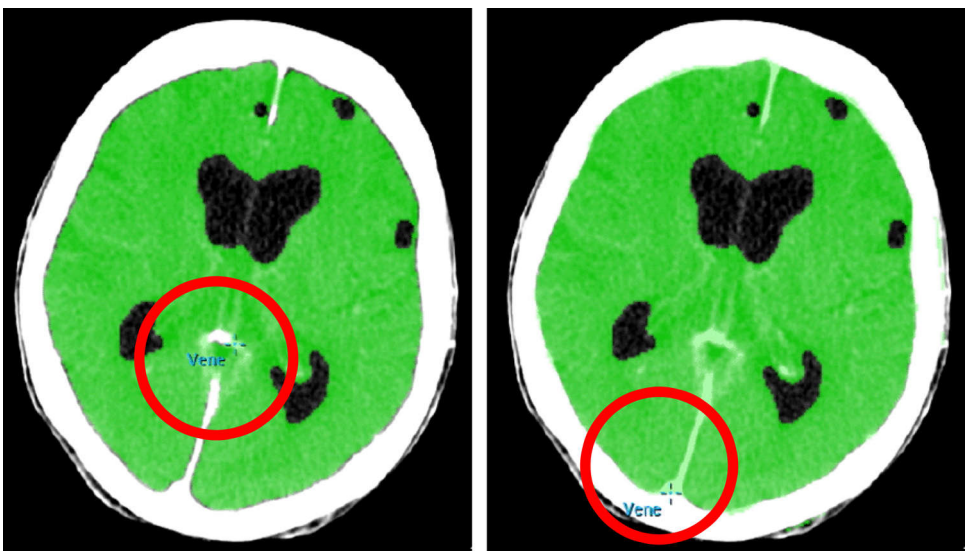
Mask Upper Threshold 100 HU and Optimal Vein Is Excluded from Cerebral Mask	Same Case (as left image) with Upper Threshold Set to 400 HU, Including Optimal Vein
	

It is advised to pay special attention in cases where a CTA scan was done prior to perfusion scan. The left image below shows the optimal vein not included in the cerebral mask due to CTA exam prior to perfusion exam. The image on the right shows the same case after manual editing: the cerebral mask optimal vein is included in the search range of reference vessels.



NOTICE

The green color will appear as blue in the application.

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Step 3: Vessel Detection

The BP application vessel detection capability suggests potential reference artery and reference vein to the user. The user may also choose to define reference vessels manually by drawing an artery or vein point, or by drawing an ROI in which the pixel with the highest enhancement value will be selected by the application to represent the vessel. It is possible to add up to ten artery and ten vein points (displayed in the time attenuation curve and reference vein statistics table), from which the user can choose the optimal reference artery and reference vein.

Whether defined manually, or suggested by the Brain Perfusion application, in order to continue to the second stage, the user must apply the "use for calculation" confirmation to the reference artery and reference vein location to be used for calculation.

NOTICE

When defining the artery for calculation, the optimal artery would be the artery which peaks first (lowest TTP).

The reference-artery detection search of the application is usually restricted to the upper part of the brain and includes ACA and MCA regions.

Incorrect artery selection could impair the analysis and affect perfusion results, especially if the chosen artery has a TTP (time to peak) and FWHM (Full Width Half Max) which are significantly different than those of the reference artery.

This information should be obtained from both the reference vessel statistics table and the vessel activity graph.

When defining the vein for calculation, the optimal vein would be the vein with the highest enhancement.

NOTICE

The enhancement is calculated as Max enhancement – baseline enhancement.

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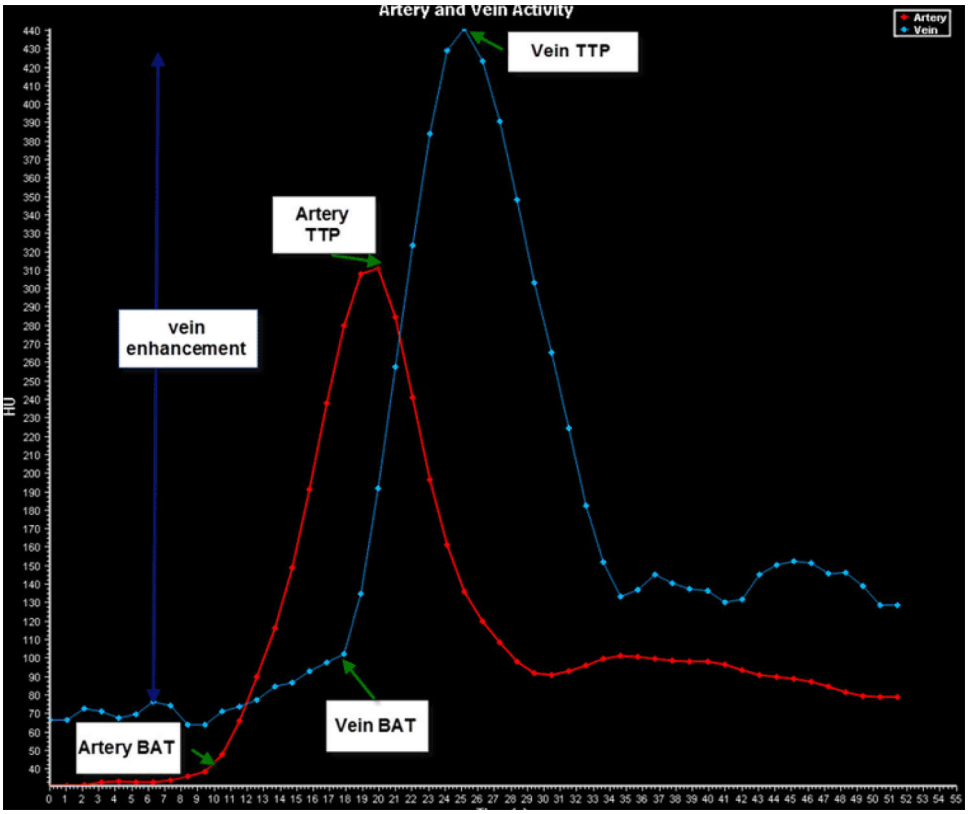


Stage 2: Perfusion Maps

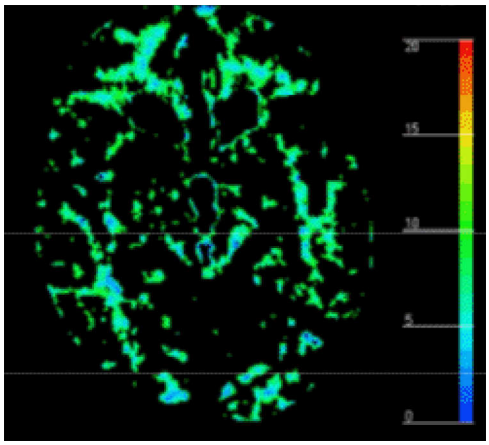
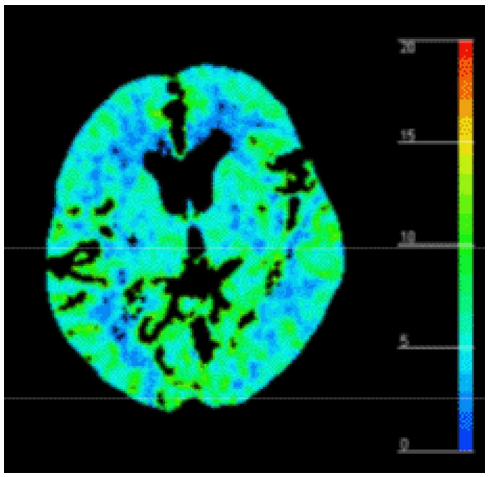
In this stage, use the remove-vessels functionality to check the resulting values and then quantify and correct errors.

Step 4: Check the Plausibility of Resulting CBV (and CBF) Values

The Remove vessels functionality can be used to check the plausibility of the resulting CBV (and CBF) values. Systematic errors in CBV assessment, resulting from the use of non-optimal reference veins, become apparent if the elimination of the vessels with the default setting (9 ml/100 g) removes more than the opacified vessels. This leads to vacancies that are larger than expected from the corresponding tMIP image. Other indications for non-optimal veins and systematic errors in CBV assessment are:

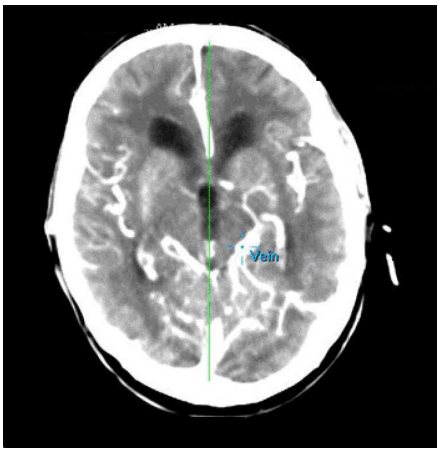
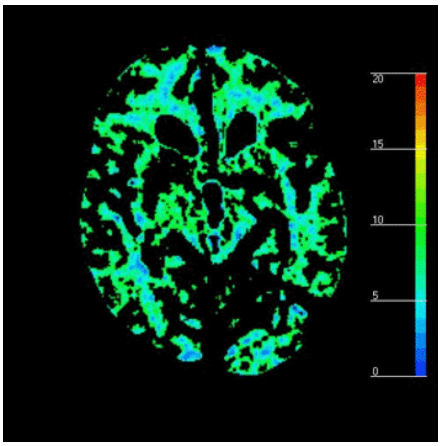
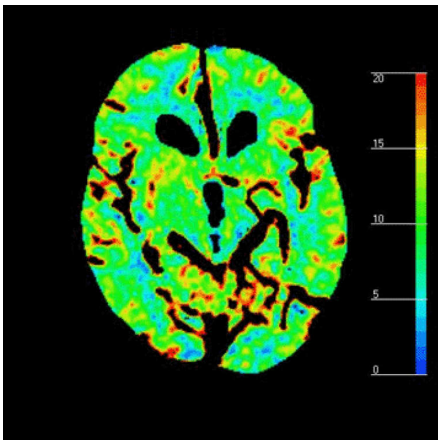
- The venous time-density curve (TDC) is only somewhat higher or even lower than the arterial curve. Normally, the venous TDC is by a factor 2 to 3 higher.
- The prevailing colors in the CBV map are green, and the vessels (red) are much broader than expected. Normal CBV values are 5-6 ml/100 g for gray matter and 2-3 ml/100 g for white matter, resulting in light-blue to light-green colors.

The corresponding images and reference vessel window for regular cases without systematic errors in CBV assessment are shown below. If at least one of these indications is found, the mask should be adjusted as described in the following section:

Large Vacancies	Only Vessels Removed
	

Step 5: Quantify and Correct Systematic Errors

If any indications for systematic errors in CBV should remain, the errors need to be quantified and corrected. This can be achieved by increasing the remove-vessels threshold until the eliminated portions in the CBV map match the vessels shown in the corresponding tMIP image.

tMIP Image	CBV Map (Threshold 9 ml/100g)	CBV Map (Threshold 21 ml/100g)
		

The ratio of the adjusted threshold to the default setting can be used as an estimate of the systematic error. For the example above, this amounts to 21/9 = 2.33. The inverse of this factor (here: 9/21 = 0.43) provides a correction factor that can be applied to the erroneous CBV and CBF values.

Using Brain Perfusion Traffic Lights

The **Traffic Lights** feature indicate the presence of many common Perfusion-Map quality issues. When you load a **Study** into the **Brain Perfusion** application, the **Traffic Lights** feature automatically checks the:

- Symmetry (brain hemispheres identified are not symmetrical)
- Contrast injection quality (amount, shape and timing, invalid voxels). These tests are based on average voxel within the cerebral mask Time Attenuation Curve and are not tested for the selected reference vessels.
- Scan sampling rate
- Residual motion after registration

If **Traffic Lights** finds any quality issues with the **Study** (acquisition) data, you will see either a **Non-severe Warning** or a **Severe Warning**. The warning will appear across the top of the viewports. Traffic light warning messages are saved along with the automatic result series. When Traffic lights are present on a perfusion study that is used for automatic result creation, the default rules discretely control the outcome of the result creation process. Automatic results are not available in the defined destinations in relevant cases; you will see an information series in such cases.

NOTICE

When Traffic Lights detects a **Non-severe Warning** and a **Severe Warning**, all warning messages will appear as part of the **Severe Warning** dialog.

Click **Learn more ...** in the header to help you:

- understand the cause of the issue;
- gather information to improve data quality; and
- propose changes to the acquisition protocol for future **Studies**.

When you have reviewed the implications of each warning, you can choose to:

- Save warnings as a table to a local or remote location. Once saved, either continue or quit the application.
- Proceed anyway. (For some cases, edits within the application can assist with some of the identified issues.)
- Close **Brain Perfusion**.

NOTICE

The **Traffic Lights** warning is included when saving, reporting, or filming images.

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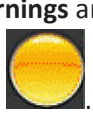
About Non-severe Warnings

Non-severe Warnings are classified as acquisitions with **mildly insufficient quality**, represented by a yellow light  .

NOTICE

If you see even one **Non-severe Warning** message (yellow light), **the resulting perfusion calculations may be inaccurate**.

If the loaded **Study** produces one or more of the following warnings, consider the implications before continuing:

Non-severe Warning	Implications
Asymmetry: The brain hemispheres in the image are not symmetric.	Visual and quantitative comparisons between hemispheres, as well as summary map calculations, have some probability of yielding incorrect results. **Recommendations**: In case of incorrect cerebral midline positioning, edit the midline within the Brain Perfusion application. In cases of head tilt, use 3D motion correction within the Brain Perfusion application. To improve future scans, position the patient's head symmetrically, without head tilt on the "couch".
The average contrast enhancement in the brain is lower than expected.	Perfusion results have some probability of yielding incorrect results. This may be due to: • Low amount of injected contrast • Low cardiac output of the patient **Recommendations:** • Adjust the perfusion maps color scale to display relevant ranges within the Brain Perfusion application. • Consider reducing the vessel's threshold in the 'Perfusion Maps' step within the Brain Perfusion application to ensure correct vessel removal. • To improve future scans, see instructions for use for recommendations of injection parameters.

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Non-severe Warning	Implications
The contrast injection outflow phase (washout) for the left/right hemisphere is incomplete.	The contrast injection outflow phase (washout) for the left/right hemisphere is incomplete. The downslope of the Time attenuation curve is incomplete. **Warning**: Perfusion results have some probability of yielding wrong results. This may be due to: • Incorrect contrast timing (e.g. the scan started too late and/or ended too early) • Patient-specific issues (e.g. low cardiac output). **Recommendations**: • Adjust the perfusion maps color scale to display relevant ranges within the Brain Perfusion application • To improve future scans, see instructions for use for recommendations of scan and injection protocols
The system has detected some residual motion after image registration.	Perfusion results have some probability of yielding incorrect results. It is recommended to use the following Motion Correction tools within the Brain Perfusion application: • Use the "3D motion correction" tool to reduce residual motion. • Use the "Remove displayed point" tool to remove time-points with high motion. • To improve future scans, make sure the patient's head is properly fixated during the scan.

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Non-severe Warning	Implications
Long interscan delay: The inter-scan delay between perfusion sampling points is higher than 4.1 seconds	The inter-scan delay between perfusion sampling points is higher than 4.1 seconds and lower than 4.5 seconds. It is not recommended to use absolute perfusion values (e.g. absolute thresholds for summary maps calculations, ROI measurements etc.). **Warning**: Perfusion results have some probability of yielding wrong results. This may be due to: • Incorrect contrast timing (e.g. the scan started too late) • Patient-specific issues (e.g.motion). **Recommendations**: • To improve future scans, see Instructions for Use for recommended scan and injection parameters.
Contrast Injection: Baseline: Shifts in the pre-bolus phase for an average pixel.	The pre-contrast arrival period (baseline) of the time attenuation curve was not detected or is too short. Warning: Perfusion results have some probability of yielding wrong results. This may be due to: • Incorrect contrast timing (e.g. the scan started too late) • Patient related issues (e.g. motion) **Recommendations**: To improve future scans, see Instructions for Use for recommended scan and contrast injection settings,

About Severe Warnings

Severe Warnings are classified as acquisitions with **inadequate quality**, represented by a red light  .

NOTICE

If you see at least one **Severe Warning** (red light), **it is not recommended to use the perfusion analysis with the loaded data**.

If the loaded **Study** produces one or more of the following warnings, it is not recommended to continue:

Severe Warning	Implications
The average contrast enhancement in the brain is significantly lower than expected.	Perfusion results have high probability of yielding wrong results . This may be due to: • Low amount of injected Contrast. • Low cardiac output of the Patient. **Recommendation**: To improve future scans-see Instructions for Use for recommendations of injection parameters.
The system has detected severe residual motion after image registration.	The presence of motion is due to patient movement during the scan. When performing subsequent scans, ensure the patient's head does not move during the scan. **Recommendations**: Use the following Motion correction tools within the Brain Perfusion application. • Use the "3D motion correction" tool to reduce residual motion. • Use the "Remove displayed point" tool to remove time-points with high motion.
Long Inter scan Delay: The inter-scan delay between perfusion sampling points is higher than 4.5 seconds.	The perfusion maps values and the summary maps have high probability of yielding wrong results. Use the recommended scan and contrast injection parameters. **Recommendation**: Do not use absolute values and summary maps.

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Severe Warning	Implications
Invalid voxel data : A high number of voxels within the brain could not be analyzed due to incompatibility with the perfusion algorithms.	Perfusion results have high probability of yielding wrong results. This may be due to : Missing inflow and/or outflow phase within the tissue time attenuation curve High noise in the images (can be due to low slice thickness, motion etc) This may be due to: • Missing outflow phase within the tissue time attenuation curve. • Missing inflow phase within the tissue time attenuation curve • High noise presence in the input images. **Recommendations**: To improve future scans, please refer to the Instructions for Use for recommended scan and contrast injection settings.
Cerebral Blood Volume (CBV) values in both hemispheres are very low. Please verify artery and vein were defined correctly.	• If absolute CBV/CBF thresholds are used for the Summary maps, they require proper adjustment. Perfusion results have high probability of yielding wrong results. • The average CBV values within both hemispheres are lower than 2.5 ml/ 100gr. • It is recommended to verify vessel detection in the “vessel detection stage”. Verify that the detected vein/artery is not located within ischemic tissue. • In addition, this could imply a very low contrast injection or multi-regional perfusion deficits. • For more information on selecting appropriate vessels, please refer to section “Brain Perfusion Reference Vessel Selection Guide” on page 79. **Recommendations**: To improve future scans, please refer to the Instructions for Use for recommended scan and contrast injection settings.

Automatic Results Creation Workflow

When Brain Perfusion data arrives to IntelliSpace Portal, the system can generate automatic Brain Perfusion results for reading on targeted devices by a user.

Automatic Results – Results Series

When automatic results are configured (by an Administrator), the following series are available on remote devices (for example PACS):

- Auto − Automatic results series will contain the map/table/graph as configured in the application by the Administrator user, displayed in the defined Batch format (detailed in “Batch format” section below). Series description will begin with “Auto”. If Summary Maps are part of automatic results, the summary maps and measurements for both right and left hemisphere are included in the results.

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- If the administrator configured automatic results, three types of series will be available in the IntelliSpace Portal local folder (under the same study as the original series):
  - **Auto** − Automatic results series – Same as described above.
  - **TI CTA series** − Can be loaded into other viewing applications. Series description will begin with TI CTA.
  - **BP Batch** − Series will only be generated if BP preprocessing was initiated on thin slices series. The series can be launched in the Brain Perfusion application. Series description will begin with BP Batch.
  - **Batch Formats** − Automatic results may be generated in the following batch formats:

    ◊ **Whole screen for all locations** − Sends entire screen as an image, including all viewports and tables, for the entire z-coverage of the study.

    ◊ **Sorted by Z-position (sort by slice)** − When the batch is created, all selected content is grouped together: for each slice, consecutive images per map type/table/graph, first for the first slice, then for the next slice, and so on.

    ◊ **Sorted by map type** − When the batch is created, all selected content is grouped together by type. For example, all CBV images are shown together, then all CBF, and so on.

    ◊ **Sorted by map type : multi series** − Same as “Sorted by map type” batch format, but each type/table/graph is saved in a separate series.

    ◊ **Current** − The batch will only contain the selected content for the currently active slice.

    ◊ **Comparison Overview** − When the batch is created, the defined content is displayed side by side to allow comparison between the different results types. If summary maps are defined they are displayed aside the Perfusion maps.

Typical Automatic Results Creation Workflow (Configurable by Administrator)

Step One - Patient Directory Preferences

1. From the Patient Directory, click Preferences.
2. Go to the Processing page.
3. Verify that the Enable Processing checkbox is checked; otherwise place a check mark.
4. Verify that the Run Processing according to the following checkbox is checked; otherwise place a check mark.
5. Click on Add. A new line appears in the table.
6. In the Algorithm column, select Brain Perfusion from the drop down menu.
7. Add the relevant DICOM tags.
8. Click on OK to save and close the window.

Step Two - Perfusion Maps Batch Tab Configuration

Identification of Brain Perfusion automatic results format and targeted send destination is based on the settings within the Brain Perfusion application.

To configure Automatic Results:

1. Navigate to the Batch tab of the 2. Perfusion Maps stage.
2. Select the batch content to be configured for automatic results.
3. Click the Configure automatic results icon.

   The Automatic results creation window opens.
4. Place a check mark in the Enable automatic results creation for all future studies check box to enable automatic results creation.
5. Review the dialog defined batch content and settings.

NOTICE

When Enable automatic results creation for all future studies is enabled, if the configured parameters are different from the factory default settings a warning is displayed. To revert to factory settings, select the Restore factory settings option.

6. (Optional)To send Results via email, place a check mark in the **Enable automatic results to be sent by Email** check box (this option is not enabled by default and must be configured by a Field Service Engineer in Portal Management Tool). For additional information, see section “Brain Perfusion Results via Email” on page 94.
7. (Optional) If Automatic results creation is already activated/the user wants to modify the defined calculation setting for the automatic results, the user can change the calculation settings within the application, and then from the dialog box click on the Copy application calculation settings button.
8. Select the following settings: the 3D motion correction and set the destination for yellow Traffic light results if needed.
9. Select the Select devices button within the Target Devices section.
10. Click Activate automatic results to proceed. A confirmation dialog opens.
11. Enter your name in the confirmation dialog and click Activate automatic results to complete automatic results configuration.

NOTICE

This change affects ALL users reviewing Brain Perfusion images.

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12. Close the IntelliSpace Portal client and reopen it to update changes. From now on, the system will identify Brain Perfusion studies arriving to IntelliSpace Portal based on this DICOM information and will apply Automatic results creation.

Automatic Results Label

An Automatic Results label is added at the middle upper location of all the images in the automatic results series, as a notification to the user that the series was created automatically.

Traffic Light Indication in Automatic Results

If data quality issues are detected by the system, a traffic light summary page is added to the results. In addition, an indication with the detected issue header is added to the top of all images in the automatic results series.

Traffic lights indicators: If severe quality issues (i.e. Red Traffic Lights) are identified in the data, automatic results series are not created. A Traffic Light summary page will be available in the remote location, containing details of the quality issues identified.

If non-severe quality issues (i.e. Yellow Traffic Lights) are identified in the data, automatic results are sent to remote location (along with the Traffic Lights information), according to the predefined settings by the administrator user. If automatic results are not generated, a Traffic Light summary page will be available in the remote location, containing details of the quality issues identified. For relevant cases, the user may review and edit the information from within the Brain Perfusion application.

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Quality Assurance Images

User's Review images are added to the Automatic results series, allowing the user to review before proceeding to the next images.

There are three types of User's Review images:

- **Reference Artery and Vein** - An image with the location of the automatically detected Artery and Vein is saved. The image contains tMIP images with the location of the detected Artery and Vein, an enlarged image of that location and the corresponding activity graph.
- **Cerebral Mask** - An image with the location of the automatically detected cerebral mask is saved in case Summary maps or ROIs are included in the batch. All tMIP slices are displayed with the with the automatically detected cerebral mask blue overlay.
- **Mirror line** - An image with the location of the automatically detected midline is saved in case Summary maps or ROIs are included in the batch. All tMIP slices are displayed with the green midline overlay.

NOTICE

Carefully review the User's Review images prior to continuing with the review of the automatically generated results. If required, do further analysis in the BP application

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Cases Excluded from Automatic Results

- If severe quality issues (i.e. Red Traffic Lights) are identified in the data, automatic results series is not created. A Traffic Light summary page will be available, containing details of the quality issues identified.(see details in the Traffic Light Indication in Automatic Results section)
- If the BP application failed to detect automatic Artery and/or Vein, automatic results are not created. A notification will be available.
- If the data is identified as invalid data for the Brain Perfusion application.

Brain Perfusion Results via Email

WARNING

Brain Perfusion emails should not be used for diagnosis.

The Brain Perfusion application can send analysis results and images to a pre-defined list of recipients as an email through preprocessing options.

The configuration of Brain Perfusion email set up is performed in Portal Management Tool (PMT) by a Field Service Engineer (FSE). Additional configuration within the application can be performed by users with Administrator privileges.

Email Creation Options

Email preferences can be sent as follows:

- Automatic email creation through Pre-processing
- Manually sent via **Send by Email** from within the application

Prerequisites

- SMTP configuration must be performed in Portal Management Tool prior to Brain Perfusion email manual email sending and BP automatic email configuration.
- The maximum allowed email size limit configured in Portal Management Tool should be more than 6MB in order to enable the BP email feature.
- The Brain Perfusion application automatically finds the maximum allowed SMTP email size for the institution and maximum email size configured in Portal Management Tool and displays it in the Automatic Results Creation dialog. The maximum email size configured in Portal Management Tool should not exceed the SMTP maximum email size value.

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Automatic Email Creation Through Pre-processing

- To run Brain Perfusion Preprocessing, right-click on a Series in the Directory and select **Run Processing** > **Brain Perfusion** from the menu.

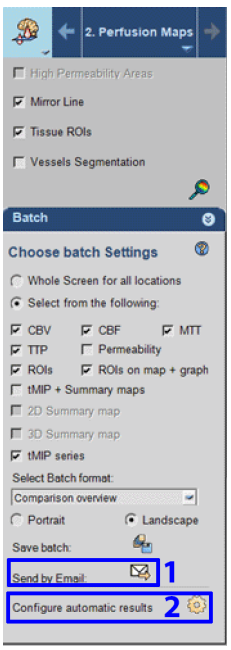
  The application initiates automatic email creation. Emails are automatically created and sent to all recipients based on the pre- defined configuration settings set in the **Automatic results creation** window within the BP application.

The email content from Automatic email creation is not editable. Administrative users can use the **Manage Mailing List** option within the Send Results by Email option to add or remove recipients.

Manual Email Creation and Configuration From the Brain Perfusion Application

Manual Sending of Email

Analysis results and images to a pre-defined list of recipients can be sent as an email by selecting the **Send by Email** option (#1) in the **Perfusion Maps** stage.



This opens the **Send Results by Email** window. This window displays the email recipients that were configured.

Administrator users can select the **Add** or **Delete** options to add or remove recipients.

Select **Send mail** to send the results. A notification appears after the email is sent successfully.

NOTICE

Brain Perfusion emails display the message “Not for diagnostic use” on all image pages of the emails.

The following contents are displayed in the message body of the email for Manual email results:

“For clinical review please use diagnostic environment. If necessary, edit in the Brain Perfusion application of IntelliSpace Portal.

Note: Image quality might be affected due to compression applied.

This email contains confidential information and is intended solely for the use of the individual or entity to whom it is addressed.

You should not disseminate, distribute or copy this email. If you have received this email by mistake delete this email from your system."

NOTICE

It is highly recommended that the recipient list includes email addresses within the organization only.

Quality Assurance Images

User Review images are added to the emails, allowing users to review before proceeding to the next images.

There are three types of User Review images:

- **Reference Artery and Vein**: An image with the location of the automatically detected artery and vein is saved. The image contains tMIP images with the location of the detected artery and vein, an enlarged image of that location and the corresponding activity graph.
- **Cerebral Mask**: An image with the location of the automatically detected cerebral mask is saved in case Summary maps or ROIs are included in the batch. All tMIP slices are displayed with the automatically detected cerebral mask blue overlay.
- **Mirror line**: An image with the location of the automatically detected midline is saved in case Summary maps or ROIs are included in the batch. All tMIP slices are displayed with the green midline overlay.

Configuration of Email for Automatic Results

- Only users with Administrator privileges can configure the BP automatic email results creation in the Perfusion Maps Stage.
- Users without administrative privileges can select this option and review the settings but cannot make changes.
- Results are sent in Comparison Overview format.

The Automatic Results Creation functionality is segregated into two tabs (**DICOM Devices** and **Emails**). The two tabs Individually define the sending of results.

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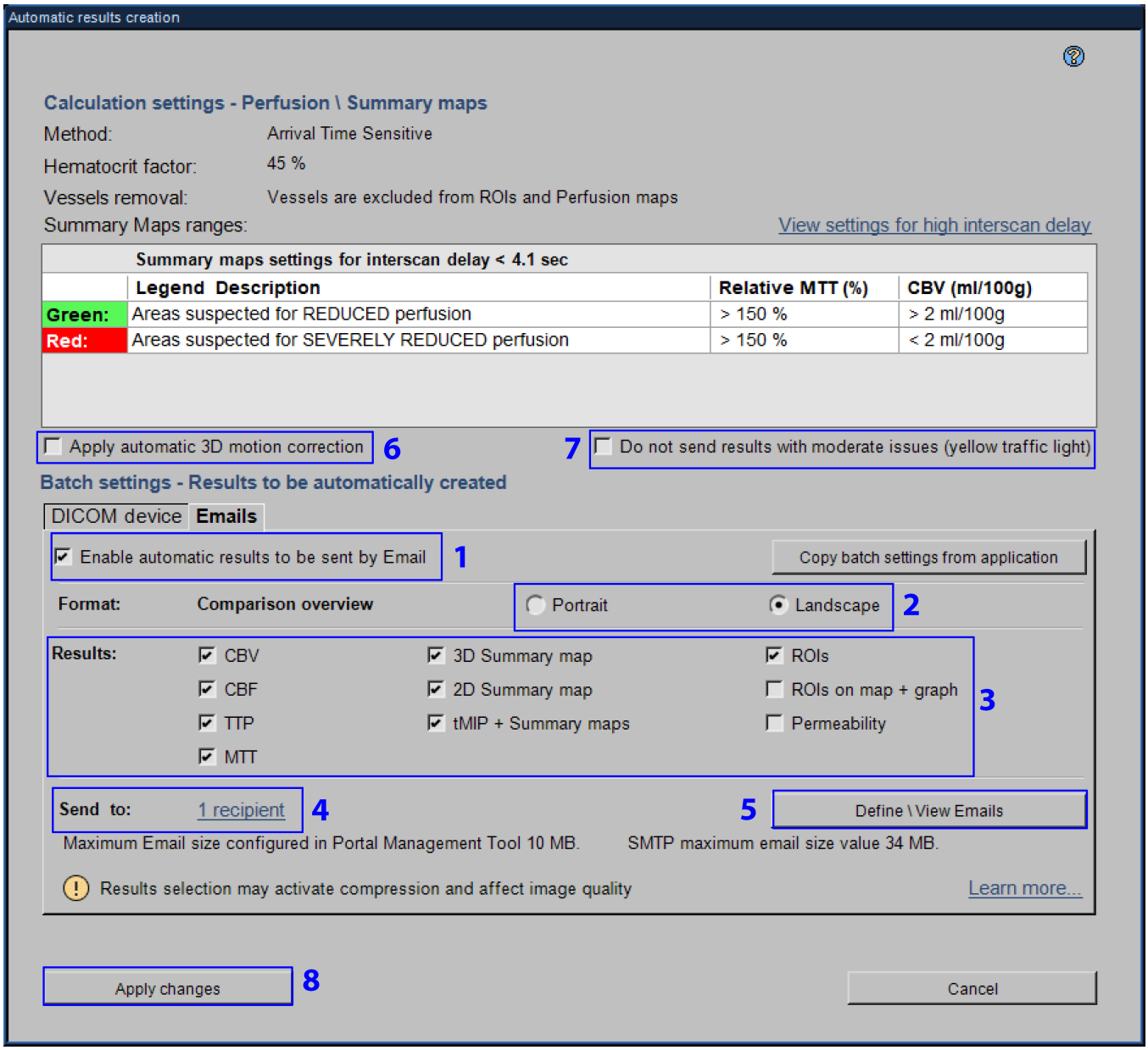

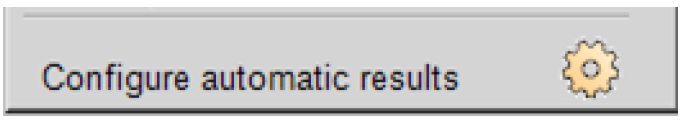

1. From the Batch tab, select the **Configure automatic results** button.

   The **Automatic Results Creation** window opens.

2. To activate emails, from the **Emails** tab, place a check mark in the **Enable automatic results to be sent by Email** (#1) check box (this option is not enabled by default).
3. Select either **Portrait** or **Landscape** email format (#2).
4. Review and select Perfusion Results options (#3).

Options include CBV, CBF ,MTT, TTP/Tmax, Permeability, ROIs, ROIs on maps +Graph , tMIP +Summary maps, 2D Summary map measurements, 3D Summary map.

The 3D Summary Map and 2D summary Map options are enabled only if the **Tmip +Summary Maps** option is selected,

5. Select **Send to:** to review the list of email recipients (#4). See above.
6. Use **Define/View emails** (#5) to configure email (Admin only). See above.
7. Enable the **Apply automatic 3D motion correction** check box (#6) to apply automatic 3D motion correction for studies with moderate image quality images (applicable for batches).
8. Enable the check box **Do not send results with moderate issues (yellow traffic light)** (#7) to exclude sending emails results for studies with moderate image equality issues (applicable for automatic batches also).

   When enabled, an email is forwarded to recipients providing details on the yellow traffic light scenario. For severe quality issues (red traffic lights) an email is forwarded to recipients providing details on the red traffic light scenario. No email results are sent automatically in this scenario.
9. Select **Apply changes** (#8).

   If there are no emails defined when applying changes, an error message appears. Click **Define /View Emails** (#5). See above.
10. Logout from IntelliSpace Portal Client in order to synchronize settings with the server (the Brain Perfusion preprocessing configuration file must be uploaded to the ISP server; this occurs upon the exiting the Client Patient Directory).

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WARNING

If ROIs or ROIs on map + graph are selected, this results in a significant increase in email size and may reduce image quality (due to compression).

NOTICE

Depending on the types of results selected for emails, the image quality and email delivery speed can be affected. Results selection may activate compression and affect image quality/ delivery speed.

Higher image quality can be achieved by increasing the email size limit.

NOTICE

Email delivery speed can be improved by removing some of the selected results or decreasing the email size limit (this may reduce image quality).

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NOTICE

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You should not disseminate, distribute or copy this email. If you have received this email by mistake delete this email from your system."

Defining and Viewing Emails

To view the currently defined email recipients, click **Send to:** (#4).

To configure email settings

1. Select **Define /View Emails** (#5) to view configuration settings.

   The **Manage Mailing List** window opens. This window enables:

   – adding, editing and deleting email addresses

   – adding an Insinuation name and uploading a logo (will appear below email content). The maximum logo size allowed is 100KB.

2. Add, edit or delete email recipients.

   The users defined in this window appear in the **Send to:** list.

3. Add an Institution name and upload an institution logo if relevant.

NOTICE

It is highly recommended that the recipient list only include email addresses within the organization

The email and images are anonymized, except displaying age and gender of the patient. The technical identifiers will be retained such as scan time, scanner name and institution name.

Brain Perfusion References

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