

SISCOM

Subtraction Ictal SPECT Co-Registered to MRI

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Introduction

SISCOM (Subtraction Ictal SPECT CO-registered to MRI) is a research application which allows ictal and interictal SPECT images to be combined with MRI images. This application allows fusion of the functional information from the SPECT scans with the structural detail of the MRI, an important synergistic visualization which allows direct functional to structural correlation and analysis. SISCOM has been a part of the Analyze visualization and analysis software package since 1996 and is used by researchers around the world. The implementation of SISCOM in Analyze 15.0 allows for a more intuitive workflow involving the following steps:

- Determine thresholds for both the ictal and interictal SPECT images to segment cortical voxels for registration and analysis.
- Register the ictal and interictal SPECT volume images.
- Segment the brain from the ictal and co-registered interictal images and create a combined mask for the cortical structure.
- Normalize and subtract the ictal and interictal SPECT images.
- Determine the statistical regions of hyperperfusion and hypoperfusion from the subtraction SPECT image.
- Segment the cortical anatomy from the 3D T1-weighted MRI.
- Register the SPECT volume images to the MRI volume.
- Apply the SPECT/MRI registration transform to the hyper- and hypoperfusion maps.
- Fuse the functional maps with the MRI to directly correlate function to structure.
- Review the 3D SISCOM volume image to examine areas of relevance in both hyperperfusion and hypoperfusion.
- Generate a new full color, secondary capture DICOM volume for the 3D SISCOM volume image.

The majority of these steps are automated and require minimal user intervention.

Required SISCOM Image Data

SISCOM requires three data sets: an ictal SPECT image, an interictal SPECT image and an MRI image of the same region. Examples of such scans can be downloaded from <https://analyzedirect.com/data>. These example image files include:

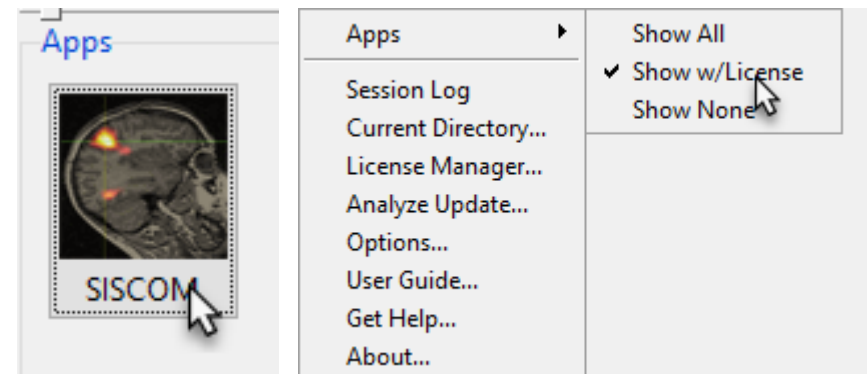
- **SISCOM_Ictal_SPECT:** An ictal SPECT volume image. The volume is 64 x 64 x 45, acquired coronally, and has an isotropic voxel resolution of 4.1 x 4.1 x 4.1 mm³. A colormap is associated with this volume image.
- **SISCOM_Interictal_SPECT:** An interictal SPECT volume image. This volume is 64 x 64 x 45, acquired coronally, and has an isotropic voxel resolution of 4.1 x 4.1 x 4.1 mm³. A colormap is also associated with this volume image.
- **SISCOM_MRI:** An isotropic MRI volume image. This volume is 256 x 256 x 231, acquired coronally, and has an isotropic voxel resolution of 0.859 x 0.859 x 0.859 mm³.

For the remainder of this guide, we will refer to these data sets. To follow along, download the files from <https://analyzedirect.com/data/> and load into the Analyze workspace using the Input/Output module.

Accessing SISCOM

SISCOM is accessed from the Analyze Apps area in the lower right-hand corner of the main Analyze window. If SISCOM does not show in the Apps area it can be enabled by right-clicking in the module selection area and then selecting the Apps > Show All menu option.

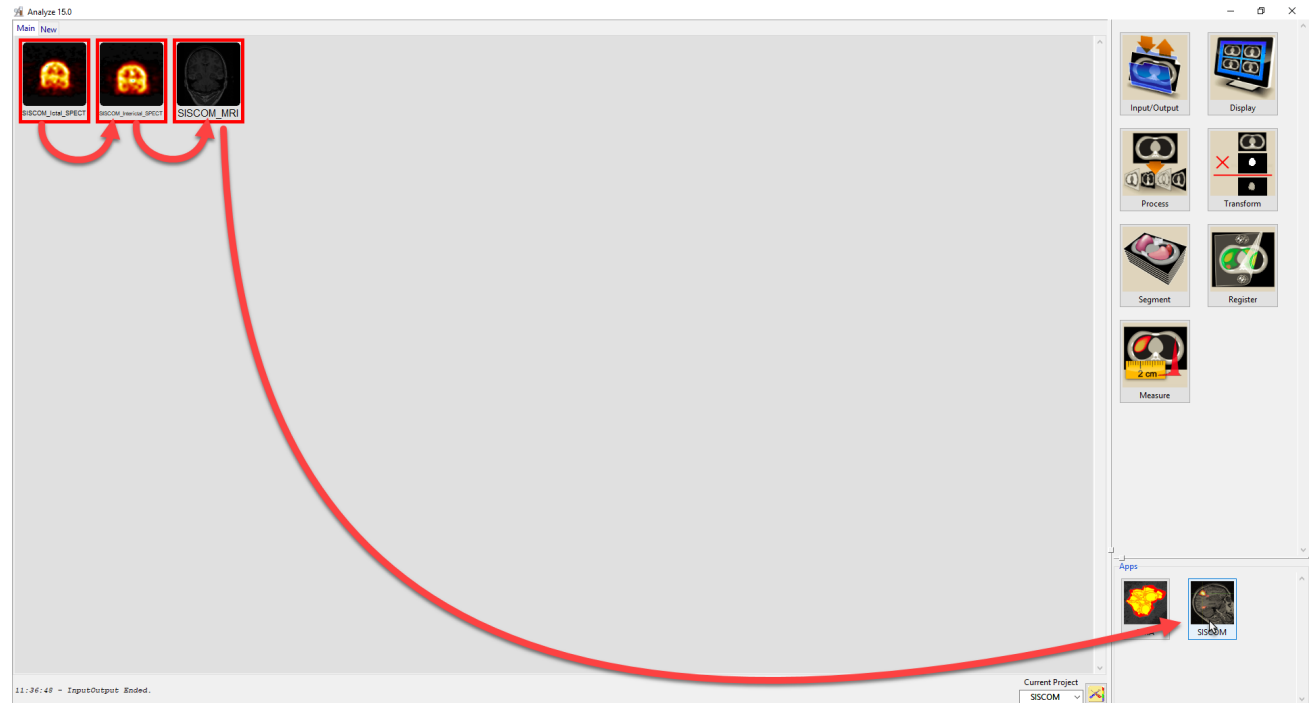
Please note that SISCOM is accessible to all Analyze users and requires a modification to the Analyze license to run. If your Analyze license has not yet been modified for SISCOM access, a validation error will be returned. Please follow the instruction on the message or contact support@analyzedirect.com for more information about accessing SISCOM.



Loading Data into SISCOM

As mentioned, SISCOM requires three input volumes; An ictal SPECT, an interictal SPECT, and an MRI. This is also the order in which the data must be loaded into SISCOM, as when the module is opened, the first selection is expected to be the ictal SPECT volume input, the second selection the interictal SPECT volume input, and the third the MRI volume image input.

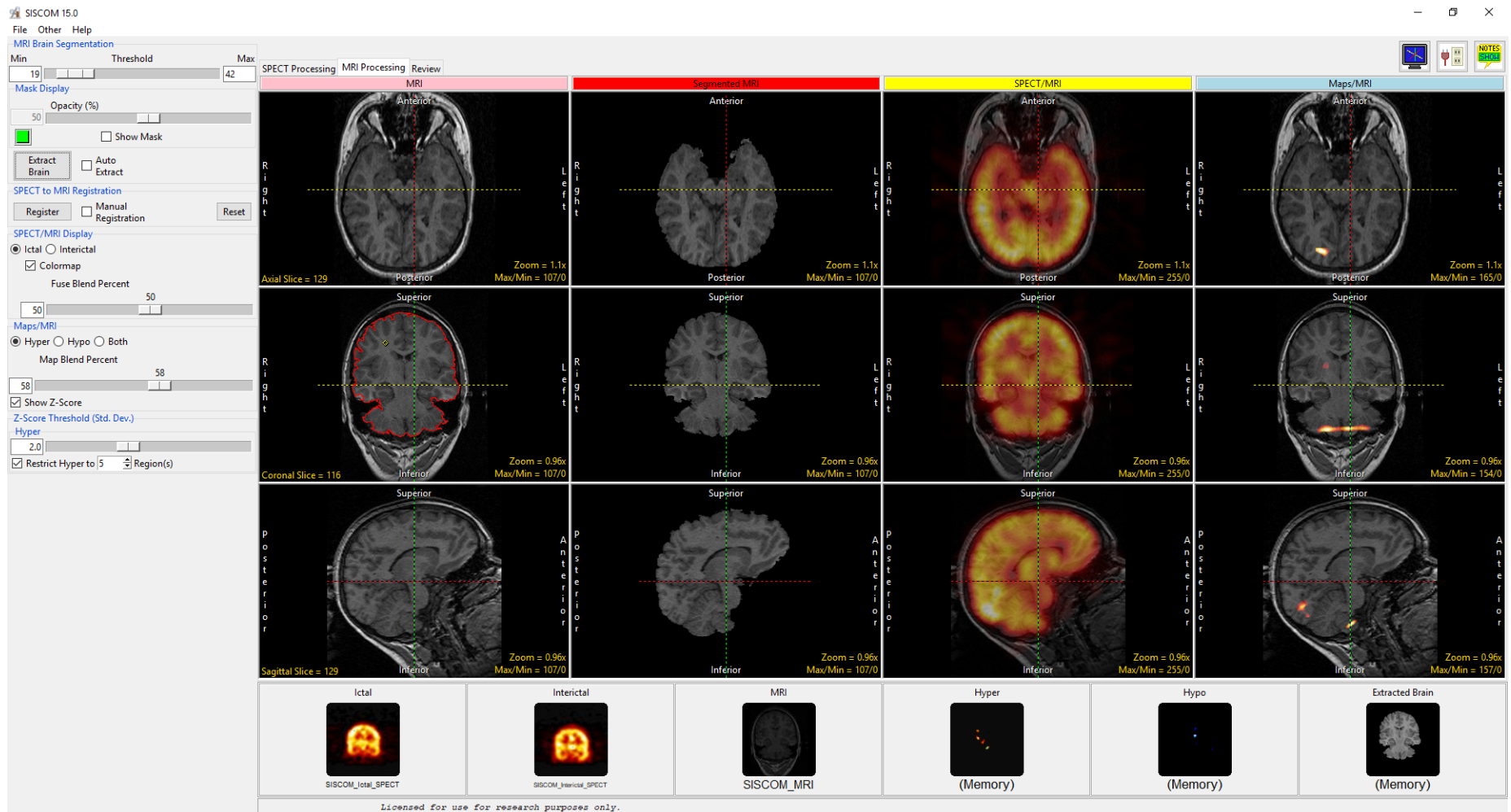
In the Analyze workspace, select the ictal SPECT volume image with the left mouse button. Then select the Interictal SPECT volume image using the middle mouse button (or Shift > left mouse button if no middle button is available). Then select the MRI volume image using the middle mouse button, this will result in all three of the input volume images being selected. Having selected the images in the correct order, click on the SISCOM icon to open SISCOM.



SISCOM Module Interface

The SISCOM module interface provides access to all functions and tools required to process image data for SISCOM analysis, including: 1) Menu, 2) Display tools, and 3) SISCOM processing tabs and tools.

Each of these functional areas will be described in the following pages.





Menu

The SISCOM menu provides access to the File, Other, and Help menus.

File

The File menu allows users to access the Input/Output ports and Exit function.

Input/Output ports: Displays a Volume area at the bottom of the SISCOM module window. This area facilitates the dragging and dropping of image data into the module. The area also displays the volumes created during the SISCOM process. **Right clicking** on any of the input ports in the Input/Output Ports provide several additional options for unloading data and exporting volumes and registration matrix files. These are now described:

- **Ictal:** Right clicking on the Ictal port provides the following options:
 - **Unload Ictal:** Unloads the current ictal input volume.
 - **Export Registered Ictal:** Saves the registered ictal data set to the workspace.
 - **Export Matrix:** Allows users to save the following registration transformation matrix files.
 - Ictal > Interictal:** Save the Ictal to Interictal matrix file.
 - Interictal > Ictal:** Save the Interictal to Ictal matrix file.
- **Interictal:** Right clicking on the Interictal port provides the following options:
 - **Unload Interictal:** Unloads the current interictal input volume.
 - **Export Registered Interictal:** Saves the registered interictal data set to the workspace.
 - **Export Matrix:** Allows users to save the following registration transformation matrix files.
 - Interictal > Ictal:** Save the Interictal to Ictal matrix file.
 - Interictal > MRI:** Save the Interictal to MRI matrix file.

Menu (continued)

File > Input/Output ports (continued):

- **MRI:** Right clicking on the MRI port provides the following options:
 - **Unload MRI:** Unloads the current MRI input volume.
 - **Export Matrix:** Allows users to save the following registration transformation matrix files. Note that these are only available for output once the Register SPECT/MRI step is complete.
 - MRI > Ictal:** Save the MRI to Ictal matrix file.
 - MRI > Interictal:** Save the MRI to linterictal matrix file.
- **Hyper:** Right clicking on the Hyper port provide the following options:
 - **Export Hyper Map:** Saves a copy of the hyperperfusion map in the space of the Ictal input to the workspace.
 - **Export Thresholded Hyper Map:** Saves a copy of the hyperperfusion map, thresholded based on hyper Z-Score, in the space of the Ictal input to the workspace.
 - **Export Restricted Hyper Map:** This export option is only available if the Restrict Hyper option is enabled. Saves a copy of the hyperperfusion map, thresholded based on hyper Z-Score and restricted using the Restrict Hyper parameter, in the space of the Ictal input to the workspace.
 - **Export Registered Hyper Map:** Saves a copy of the hyperperfusion map in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.
 - **Export Registered Thresholded Hyper Map:** Saves a copy of the hyperperfusion map, thresholded based on hyper Z-Score, in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.
 - **Export Registered Restricted Hyper Map:** This export option is only available if the Restrict Hyper option is enabled. Saves a copy of the hyperperfusion map, thresholded based on hyper Z-Score and restricted using the Restrict Hyper parameter, in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.



Menu (continued)

File > Input/Output ports (continued):

- **Hypo:** Right clicking on the Hypo port provide the following options:
 - **Export Hypo Map:** Saves a copy of the Hypoperfusion map in the space of the Ictal input to the workspace.
 - **Export Thresholded Hypo Map:** Saves a copy of the Hypoperfusion map, thresholded based on Hypo Z-Score, in the space of the Ictal input to the workspace.
 - **Export Restricted Hypo Map:** This export option is only available if the Restrict Hypo option is enabled. Saves a copy of the Hypoperfusion map, thresholded based on Hypo Z-Score and restricted using the Restrict Hypo parameter, in the space of the Ictal input to the workspace.
 - **Export Registered Hypo Map:** Saves a copy of the Hypoperfusion map in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.
 - **Export Registered Thresholded Hypo Map:** Saves a copy of the Hypoperfusion map, thresholded based on Hypo Z-Score, in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.
 - **Export Registered Restricted Hypo Map:** This export option is only available if the Restrict Hypo option is enabled. Saves a copy of the Hypoperfusion map, thresholded based on Hypo Z-Score and restricted using the Restrict Hypo parameter, in the space of the MRI input to the workspace. Note this option is only available for output once the Register SPECT/MRI step is complete.
- **Extracted Brain:** Right clicking on the Extracted Brain port provide the following option:
 - **Export Extracted Brain:** Saves a copy of the greyscale segmented brain from the MRI input to the workspace. Note that this option is only available once the MRI brain segmentation step has been completed.

Exit: Closes SISCOM.



Menu (continued)

Other

The Other menu provide users with access to the Options menu and Powerbar Editor.

Options: When selected opens the Options menu providing access to Module configuration options, including:

- **Auto Note Update:** Allows the Auto Note Update option to be enabled or disabled.
- **Threads:** Allows users to specify the number of threads used in a multi-threaded rendering process. By default, the number of threads is set to the number of processors on the system.

Powerbar Editor: When selected opens the PowerBar editor allowing users to add additional shortcut buttons to the tools area of the Segment window.

Help

The Help menu provides users with quick access to help resources including:

About: View version, system and environment information.

User's Guide: Opens a link to the Analyze 15.0 SISCOM User's Guide.

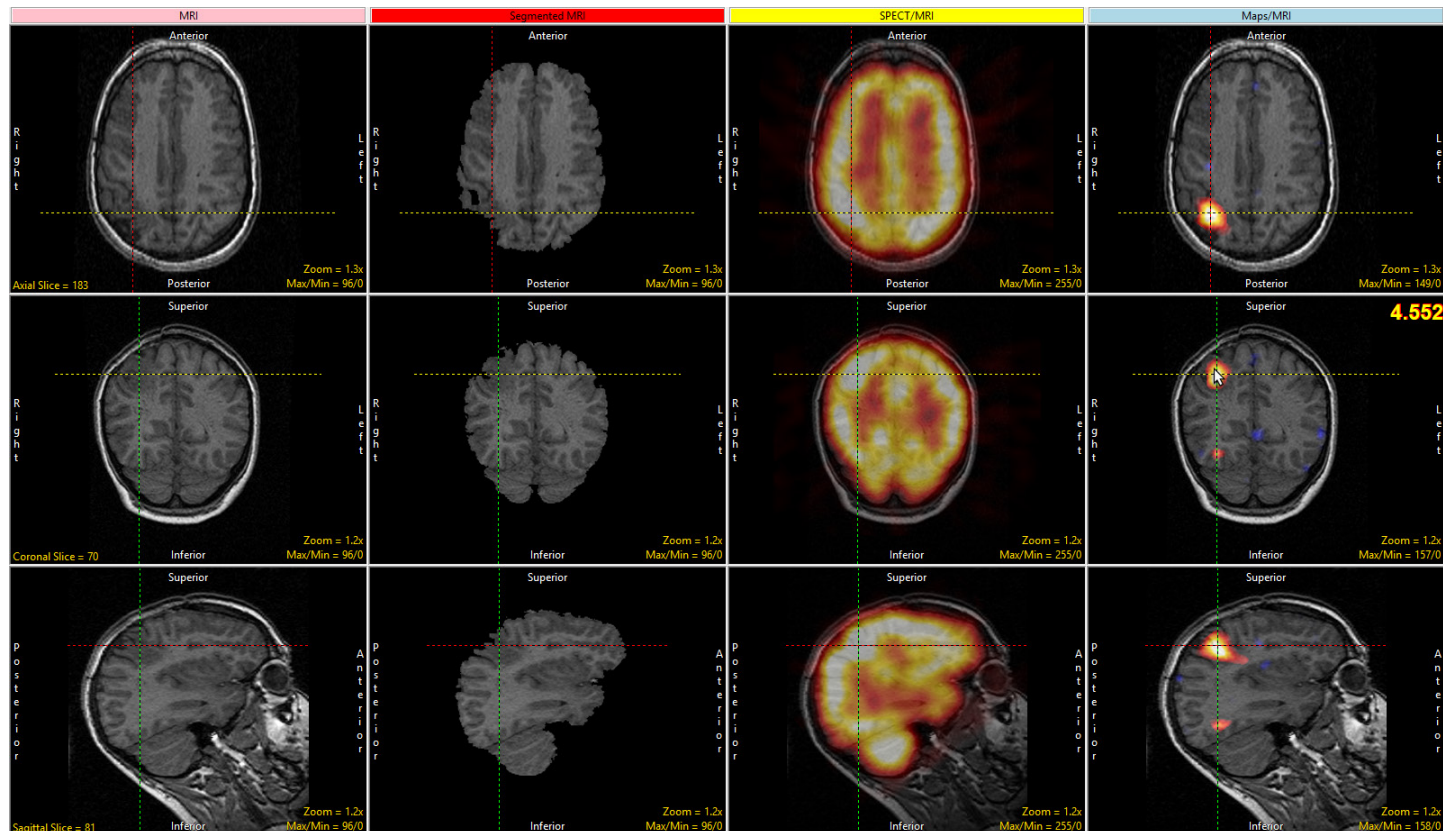
Display Tools

The Display Tools options provide access to the Toggle Cursor Link, Input/Output Ports and the Set Note State tools.

Cursor Link

The cursor link allows users to interactively navigate through the image data. The tool can be controlled from any of the 2D orientations or from the 3D rendering on the review tab. Moving the cursor will interactively update the corresponding slice displays.

The linked cursor can be enabled or disabled using the Toggle Cursor Link button.





Display Tools (continued)

Input/Output Ports

The Input/Output ports tool displays a Volume area at the bottom of the SISCOM module window. This area facilitates the dragging and dropping of image data into the module. The area also displays the volumes created during the SISCOM process. See the description of Input/Output ports under File above for a full description of the options available.

Notes

The set note state button allows users to enable the Notes tool. The Notes tool allows users to annotate the 2D slice data or 3D rendering. Notes are automatically associated with the data set and can be displayed in other modules. Notes can be hidden or deleted at any time.

To annotate a data set using notes click on the Notes button in the toolbar. (Note that the Edit mode will be activated.) Click on any 2D slice or the 3D rendering to create a note.

SISCOM Processing Tabs and Tools

The SISCOM workflow is divided into three processing tabs;

- SPECT Processing
- MRI Processing
- Review

Each of these processing tabs, and the tools contained therein, are now described.

SPECT Processing

The SPECT Processing step in the SISCOM workflow accomplishes several important tasks:

- Determine thresholds for ictal/interictal SPECT images to segment cortical voxels for registration and analysis.
- Register the ictal and interictal SPECT volume images.
- Segment the brain from the ictal and coregistered interictal volumes images and create a combined mask for the brain.
- Normalize and subtract the ictal/interictal SPECT images.
- Determine the statistical regions of hyperperfusion and hypoperfusion from the subtraction SPECT image.

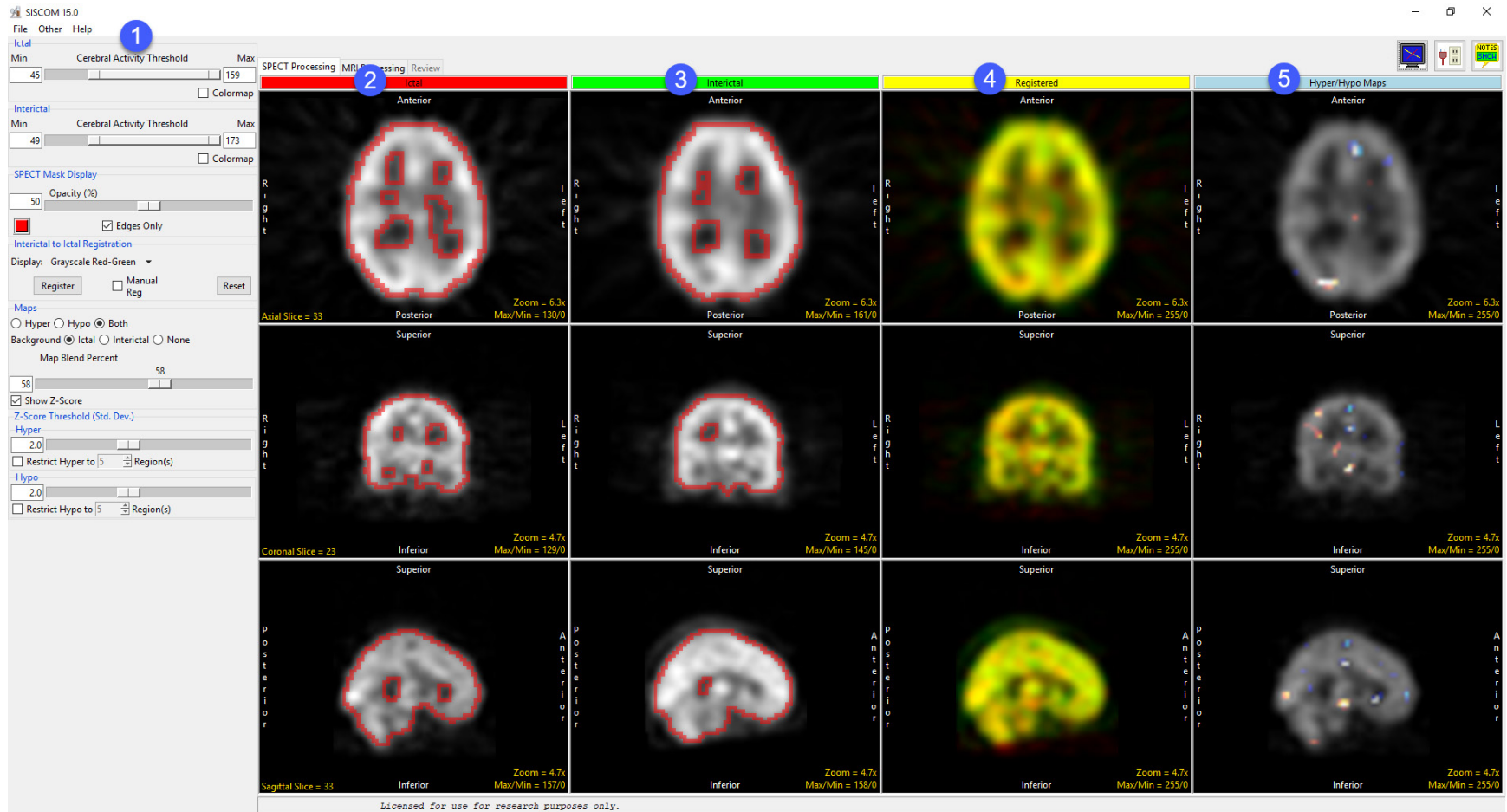
These tasks are done automatically when the SPECT Processing workflow panel is invoked. The registration, segmentation and functional map computation often need no user intervention. The user can establish appropriate statistical cutoffs for the hyperperfusion and hypoperfusion maps based on the signal strength and desired functional representation. The main components of the SPECT Processing workflow panel are shown in the next image and described below. **Note:** The linked cursor, shown in all image panels, can be used to move through the registered volume images. Each image window also has zoom and window/level controls for enhanced viewing of the images.

The SPECT Parameter Controls (left menu): This contains all of the controls for the tasks in this process. Each will be described below. [1]

Ictal (red column): The left column of images (red column) contains the ictal SPECT volume image shown as transverse, coronal and sagittal images. This is the base image set to which the interictal volume is registered. The current cerebral activity threshold is shown as a red boundary. [2]

Interictal (green column): The next column of images (green column) contains the registered interictal SPECT volume image. Note that these images have already been transformed by the registration transform that is automatically determined when the SPECT Processing panel is invoked. [3]

SPECT Processing (continued)



Registered (yellow column): The fused representation of the registered ictal and interictal SPECT volume images is shown with red/green color blending for direct evaluation of the registration results. The type of fusion can be controlled by the Interictal To Ictal Registration Display selection. [4]

Hyper/Hypo Maps (blue column): The right column shows the hyper- and hypoperfusion maps fused with one of the SPECT input volumes (ictal by default). The amount of functional signal depicted in the map is controlled by the statistical cutoffs. [5]

Cerebral Activity Thresholds / SPECT Mask Display

Thresholds are established for each SPECT input to select signal specific to voxels within the cortex. By default, the exterior boundary of the threshold region is shown as a red overlay on the SPECT images. These two masks are combined into a single mask of cortical activity, which is applied to the functional maps to limit the activity to within the bounds of the cortex. The thresholds should be optimized to eliminate any background activity, with the boundary on the outer edge of signal from the cortex.

Ictal Cerebral Activity Threshold: this double-ended slider establishes the range of signal values for cortical signal in the ictal SPECT volume image. All signal between and including the Min and Max values will be part of the ictal mask. The Colormap check box will turn on/off the colored representation of the SPECT signal.

Interictal Cerebral Activity Threshold: this double-ended slider establishes the range of signal values for cortical signal in the interictal SPECT volume image. All signal between and including the Min and Max values will be part of the interictal mask. The Colormap check box will turn on/off the colored representation of the SPECT signal.

SPECT Mask Display: the Opacity slider controls the opacity of the red overlay used to depict the cortical signal threshold mask on the SPECT image: 0% = no overlay, 100%=full intensity overlay. The Edges Only check box changes the display of the mask between just the boundaries (checked) or the entire set of voxels in the threshold range (unchecked).

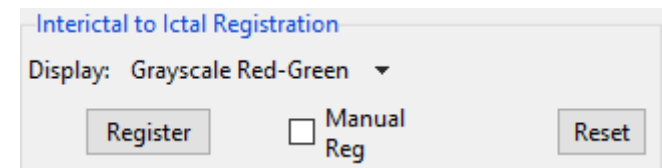
The screenshot displays a control panel with three main sections:

- Ictal:** A double-ended slider for 'Cerebral Activity Threshold' with 'Min' set to 40 and 'Max' set to 159. A 'Colormap' checkbox is present and unchecked.
- Interictal:** A double-ended slider for 'Cerebral Activity Threshold' with 'Min' set to 43 and 'Max' set to 173. A 'Colormap' checkbox is present and unchecked.
- SPECT Mask Display:** An 'Opacity (%)' slider set to 50. A red square icon is visible on the left, and an 'Edges Only' checkbox is checked.

Interictal to Ictal Registration

The registration of the interictal volume image to the ictal volume image is accomplished automatically using a normalized mutual information registration algorithm, making it very robust to localized differences in signal value, orientation and threshold determination. By default, this registration is carried out automatically when the SPECT Processing panel is invoked. Upon visual evaluation of the registration results as depicted in the Registered (yellow) column, if the registration is incorrect, the transformation between the interictal and ictal volumes images can be manually adjusted.

Display: controls the type of visual fusion between the ictal and registered interictal images as shown in the Registered (yellow) column. The fusion options are as follows:



- **Grayscale Red-Green:** (Default) Ictal colored red and registered interictal colored green, with intensity of color modulated by SPECT signal. Overlapping signal with common intensity will be yellow.
- **Grayscale Yellow-Cyan:** Ictal colored yellow and registered interictal colored cyan, with intensity of color modulated by SPECT signal. Overlapping signal with common intensity will be white.
- **Binary Red-Green:** Ictal colored red and registered interictal colored green, with only those voxels within the current SPECT thresholds shown as a single binary intensity. Overlapping voxels will be yellow.
- **Binary Yellow-Cyan:** Ictal colored red and registered interictal colored green, with only those voxels within the current SPECT thresholds shown as a single binary intensity. Overlapping voxels will be white.
- **Difference:** The registered interictal will be subtracted from the ictal and the difference shown as a grayscale image. Zero-valued differences will be a mid-gray intensity.

Register: this button will invoke the registration process starting from the current registration transformation between the interictal and ictal volumes.

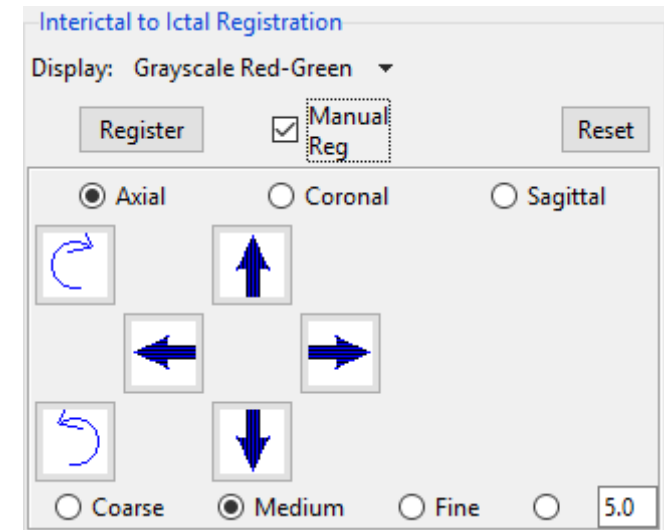
Interictal to Ictal Registration (continued)

Manual Reg: when checked, the manual registration control panel will be displayed below the check box enabling manual manipulation of the interictal volume in register with the ictal volume. When unchecked, a registration will be done automatically when the SPECT Processing panel is first invoked and whenever one of the controls is changed, such as the SPECT thresholds.

The **Manual Registration Controls** allow manual application of rotation and translation in all six degrees of freedom to transform the interictal volume into registration with the ictal volume. options are as follows:

- **Orientation:** The orientation buttons at the top of the panel choose which orientation a limited set of two translation degrees of freedom and one rotational degree of freedom can be applied: axial allowing translation along X and Y, rotation about Z; coronal allowing translation in X and Z, rotation about Y; and sagittal allowing translation in Y and Z, rotation about X.
- **Rotation and Translation:** The translation and rotation buttons apply an incremental change in these transformations, with the size of the increment controlled by the options on the bottom
- **Increment:** Course=10 voxels/10 degrees, Medium=5 voxels/5 degrees, Fine=1 voxel, 1 degree. An optional entry field is provided on the right to set a user-established increment for manual manipulation.

Reset: resets the interictal to ictal registration transform to the identity transform (no registration).



Functional Map Settings

Functional Map Settings – Maps

The Map controls and Map Settings establish the content and statistical significance reflected in the SISCOM hyperperfusion and hypoperfusion maps, as shown in the Hyper/Hypo Maps (blue) column.

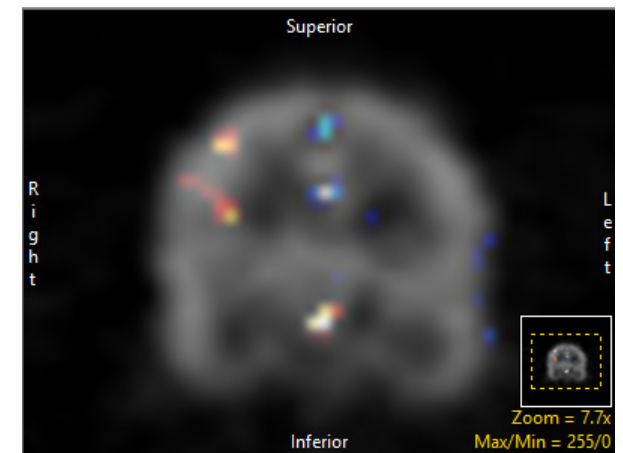
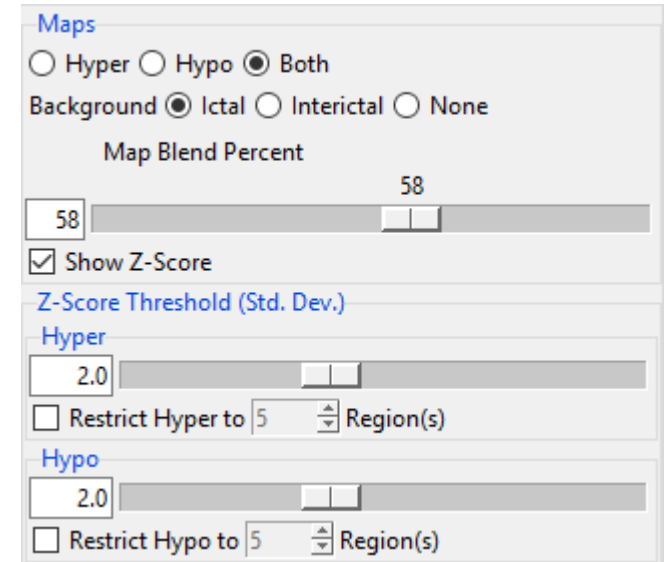
Hyper/Hypo/Both: selects which functional maps are depicted in the fused images shown in the Hyper/Hypo Maps (blue) column. Choose from:

- **Hyper:** only shows regions of hyperperfusion.
- **Hypo:** only shows regions of hypoperfusion.
- **Both:** (Default) displays both the hyperperfusion and hypoperfusion maps.

Background: controls the image upon which the hyper/hypo functional maps are displayed in the fused representation. The following options are available:

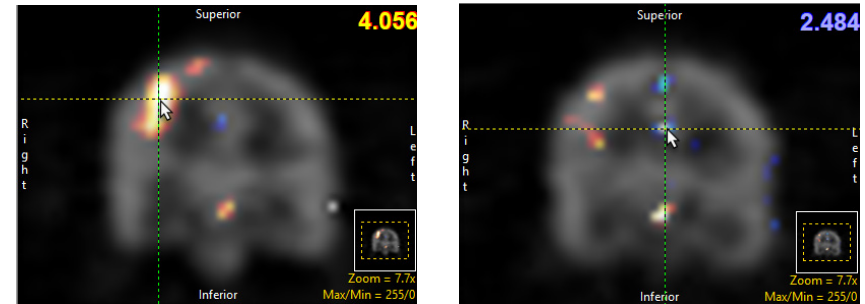
- **Ictal:** (default) Displays the ictal SPECT volume image as a grayscale image.
- **Interictal:** Displays the registered interictal SPECT volume image as a grayscale image.
- **None:** Turns off the display of the SPECT images, showing only the functional SISCOM map.

Map Blend Percent: The Map Blend Percent slider allows users to adjust the blend percent of the background ictal or interictal image with the hyper and/or hypo functional maps.



Functional Map Settings (continued)

Show Z-Scores: The show Z-Score checkbox allows users to enable or disable the display of the hyper and hypo region z-scores. When a hyper or hypo region is selected the z-score is displayed in the upper right-hand corner of the Hyper/Hypo Maps display area. Z-Score are color coded, orange for hyper and blue for hypo, to prevent confusion.



Functional Map Settings – Z-Score Threshold

Z-Score Threshold (Std. Dev): The Z-Score Threshold options provide users with the ability to adjust the parameters used for the generation of the Hyper and Hypo maps. The following options are available:

- **Hyper:** The Hyper slider sets the level of statistical significance shown in the functional SISCOM map for regions of activation (hyperperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 to 5.0 standard deviations.
- **Restrict Hyper to # Regions:** The Restrict Hyper to # Regions check box and numeric value allows further control for the display of the hyperperfusion regions to only the # largest regions of activation, as determined by the number of 3D connected voxels in a specific region.
- **Hypo:** The Hypo slider sets the level of statistical significance shown in the functional SISCOM map for regions of decreased perfusion (hypoperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 to 5.0 standard deviations.
- **Restrict Hype to # Regions:** The Restrict Hypo to # Regions check box and numeric value allows further control for the display of the hypoperfusion regions to only the # largest regions of hypoperfusion, determined by the number of 3D connected voxels in a specific region.

MRI Processing

The MRI Processing step in the SISCOM workflow accomplishes several important tasks:

- Segment the cortical anatomy from the 3D T1-weighted MRI.
- Register the SPECT volume images to the MRI volume.
- Apply the SPECT/MRI registration transform to the hyper- and hypoperfusion maps.
- Fuse the functional maps with the MRI to directly correlate function to structure.

The main components of the MRI Processing workflow panel are as follows (numbers refer to image on the next page):

Tool Control Panel: This column [1] contains all the controls for the tasks in this process. Each will be described later in this section.

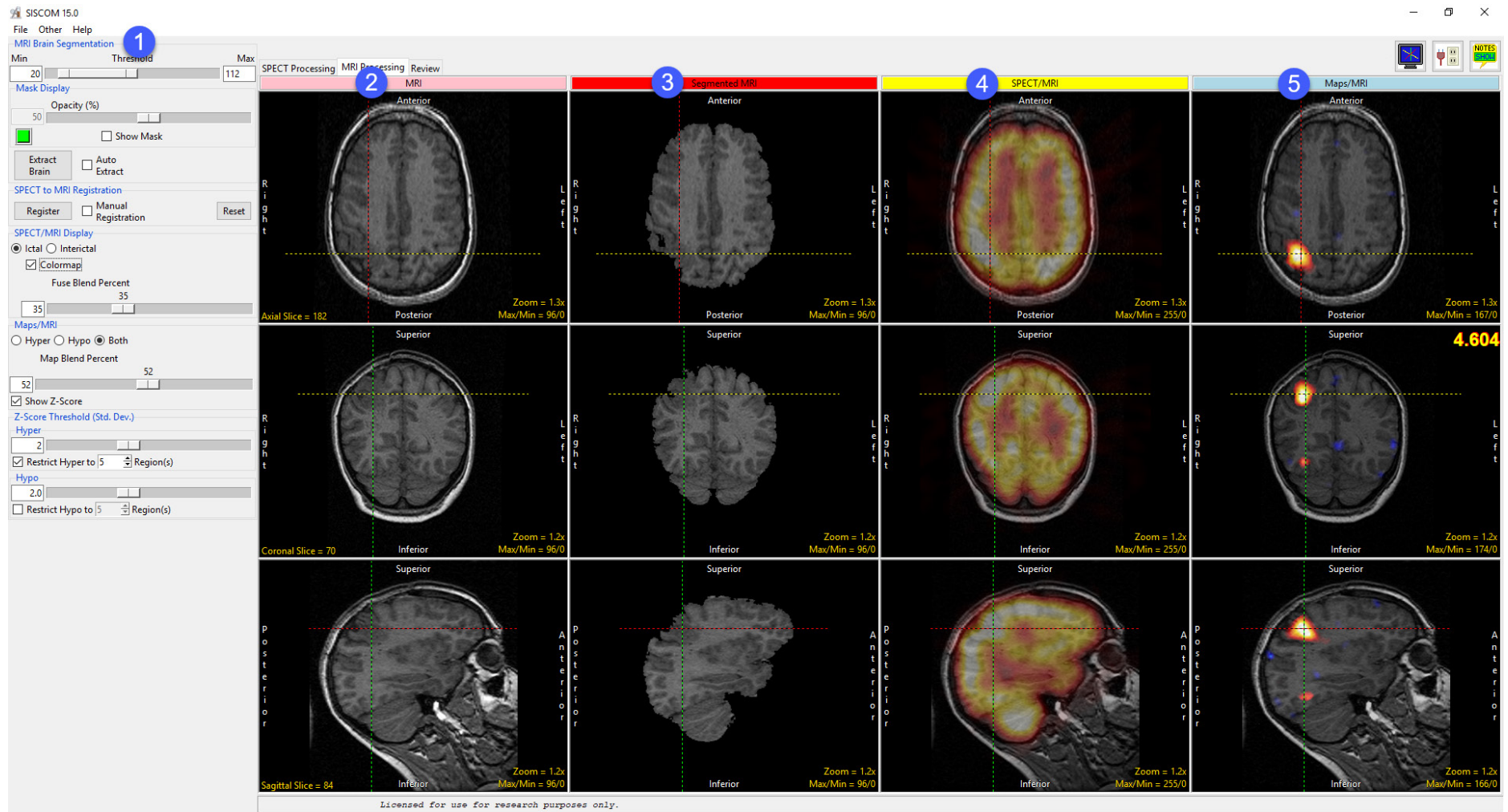
MRI (pink column): The left column of images (pink column) contains the unsegmented MRI volume image shown as transverse, coronal and sagittal images. This is the base volumetric MRI image set to which the SPECT volumes are registered. The green overlay on the images depicts the current threshold setting for the segmentation task, as controlled by the Threshold slider. The red boundary shown on the image corresponds to the current segmentation target [2].

Segmented MRI (red column): The next column of images (red column) contains the segmented MRI volume image. Note that these images will not be present until the Extract Brain button is selected to do the cortical structure segmentation [3].

SPECT/MRI (yellow column): The fused representation of the registered SPECT and MRI volume images is shown with red/green color blending for direct evaluation of the registration results. Note that the registration results will not be shown until the Register action has been completed [4].

Maps/MRI (blue column): The right column shows the hyper- and hypoperfusion maps fused with the MRI volume image. The amount of functional signal depicted in the map is controlled by the statistical significance map settings [5].

MRI Processing (continued)



The linked cursor shown in all of the image panels can be used to move through the registered volume images. Each image window also has zoom and window/level controls for enhanced viewing of the images.

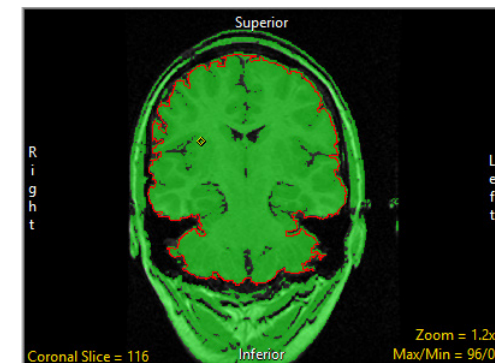
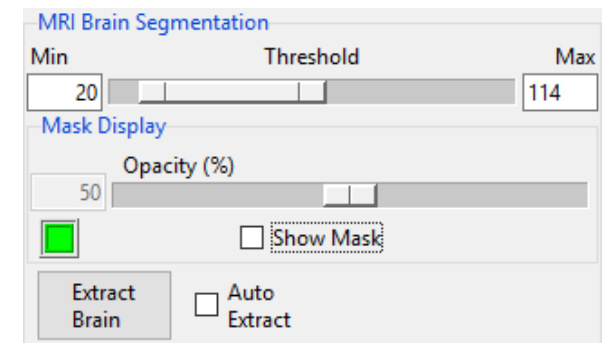
Brain MRI Segmentation

The segmentation of the cortical structure from the 3D T1-weighted MRI volume image is accomplished with an automated morphological segmentation algorithm that requires the definition of the target anatomy to be segmented. To do this, a seed point must be selected in the cortical region and thresholds established to provide a bounded representation of the cortex in one of the orthogonal images displayed in the first column. The seed point from which the bounded cortical region is grown is shown as a diamond-shaped yellow marker, initially displayed on the transverse image. This seed point can be placed using the left mouse button on any of the images in the left column, with image selection done by the user to provide an optimal image in which to define the bounded cortical region (as shown in the MRI Processing Panel image, a coronal section has been chosen). Once the optimal image has been chosen and seed point selected, the controls for defining this target region and doing the cortical segmentation are as follows:

MRI Threshold: this double-ended slider establishes the range of signal values for cortical signal in the MRI volume image. All signal between and including the Min and Max values will be included in the region if spatially connected to the original seed point. The morphologic segmentation process is based on the ability of the process to break connections with anatomy exterior to the bounded red region. To optimize the segmentation process, the Min value should be set to determine a bound on the outer cortex, and to further reduce the connectivity to unwanted structures, reduce the Max value just to the point where voxels interior to the cortical anatomy begin to lose the green overlay color, then raise the value slightly to keep all cortical voxels within the threshold range.

Opacity (%): The Opacity slider controls the blending of the threshold mask overlay on the underlying grayscale MRI image.

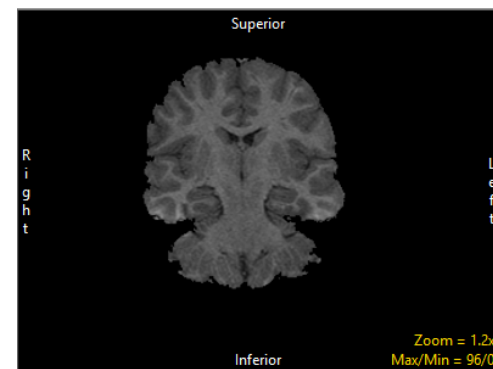
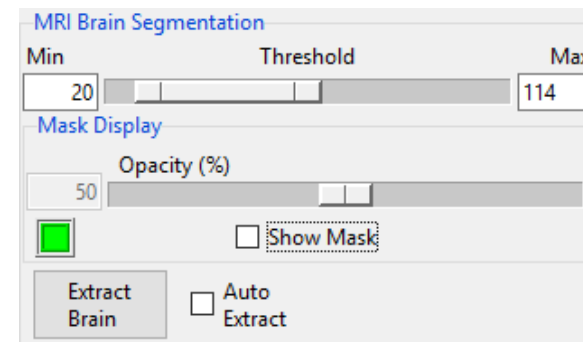
- **Show Mask:** The Show Mask check box will turn on/off the colored representation of the voxels currently within the Threshold range.
- **Color:** The color of the mask can also be controlled by the colored button next to the Show Mask check box.



Brain MRI Segmentation (continued)

Extract Brain: this button will invoke the automated morphologic segmentation process with the current Threshold settings and the current target region. The result of the segmentation will be shown in the Segmented MRI (red) column.

Auto Extract: if this check box is enabled, the morphologic segmentation process will automatically be invoked when the MRI Processing tab is selected in the workflow. If a seed point and threshold had previously been defined for a specific MRI volume image, enabling Auto Extract will allow the segmentation to be done without additional user manipulation of the segmentation parameters. If enabled and the Threshold values are changed, the segmentation process will again be invoked automatically with the new segmentation settings.



SPECT to MRI Registration

The registration of the SPECT volume image to the MRI volume image is accomplished automatically using a surface-based registration algorithm. This registration is carried out following the segmentation of the cortical structure from the MRI volume image. Upon visual evaluation of the registration results as depicted in the SPECT/MRI (yellow) column, if the registration is incorrect, the transformation between the SPECT and MRI volumes images can be manually adjusted.

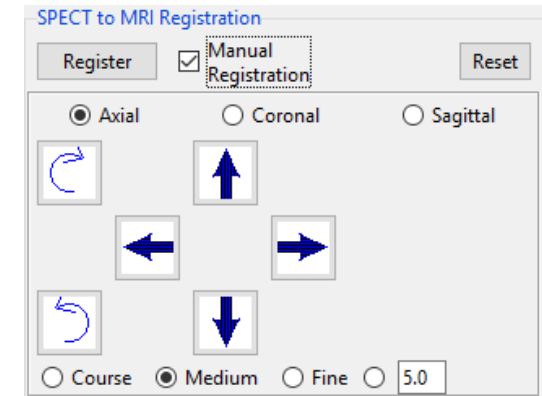
Register: this button will invoke the registration process starting from the current registration transformation between the SPECT and MRI volumes.

Manual Reg: when checked, the manual registration control panel will be displayed below the check box enabling manual manipulation of the SPECT volume in register with the MRI volume. When unchecked, a registration will be completed automatically when the MRI Processing panel is first invoked and whenever one of the controls is changed, such as the MRI segmentation.

The **Manual Registration Controls** allow manual application of rotation and translation in all six degrees of freedom to transform the ictal volume into registration with the MRI volume.

- **Orientation:** The orientation buttons at the top of the panel choose which orientation a limited set of two translation degrees of freedom and one rotational degree of freedom can be applied: axial allowing translation along X and Y, rotation about Z; coronal allowing translation in X and Z, rotation about Y; and sagittal allowing translation in Y and Z, rotation about X.
- **Rotation and Translation:** The translation and rotation buttons apply an incremental change in these transformations, with the size of the increment controlled by the options on the bottom.
- **Increment:** Course=10 voxels/10 degrees, Medium=5 voxels/5 degrees, Fine=1 voxel, 1 degree. An optional entry field is provided on the right to set a user-established increment for manual manipulation.

Reset: resets the interictal to ictal registration transform to the identity transform (no registration).



SPECT/MRI Display

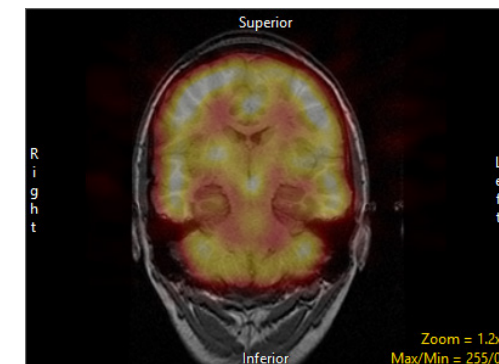
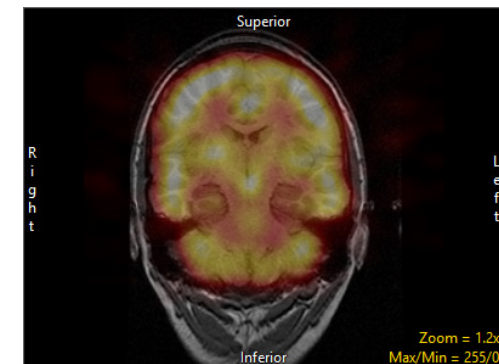
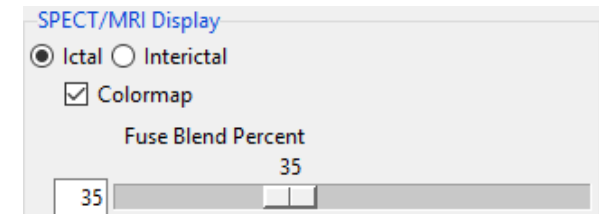
The result of the registration of the SPECT volume image to the MRI volume image is depicted in the SPECT/MRI (yellow) column. This registration should be carefully evaluated to ensure the function to structure correlation is correct prior to further processing with the fused SISCOM volume image. The following controls can be used to optimize the display of the functional SPECT image on the grayscale MRI volume image:

Ictal: selects the registered ictal SPECT volume image to be displayed fused with the MRI volume image.

Interictal: selects the registered interictal SPECT volume image to be displayed fused with the MRI volume image.

Colormap: this check box will enable/disable the display of the SPECT volume images with the standard 'hot-body' colormap.

Fuse Blend Percent: this slider controls the blending of the SPECT volume image and the MRI volume image, with 0% being only the MRI volume, 100% showing only the SPECT volume.



Functional Map Settings - Maps/MRI

The Maps/MRI controls and Map Settings establish the content and statistical significance reflected in the SISCOM hyperperfusion and hypoperfusion maps, as shown in the Maps/MRI (blue) column.

Hyper / Hypo / Both: selects which functional map is depicted in the fused images shown in the Maps/MRI (blue) column. Choose from:

- **Hyper:** only shows regions of hyperperfusion.
- **Hypo:** only shows regions of hypoperfusion.
- **Both:** (Default) displays both the hyperperfusion and hypoperfusion maps.

Show Z-Score: Turns on/off the display of the statistical significance value (z-score) at the location of the linked cursor on the images in the Maps/MRI (blue) column. When checked (default), the z-score of the voxel identified by the 3D position of the linked cursor will be shown in the upper left of the image display window in which the cursor is being manipulated. This allows direct interrogation of the significance of any areas of activation (hyperperfusion) or decrease in function (hypoperfusion). Z-score values are color coded, orange for hyper and blue for hypo, to prevent confusion. When the Show Z-Score option is unchecked, the statistical significance readout is not shown.

Maps/MRI

Hyper Hypo Both

Map Blend Percent

52

Show Z-Score

Z-Score Threshold (Std. Dev.)

Hyper

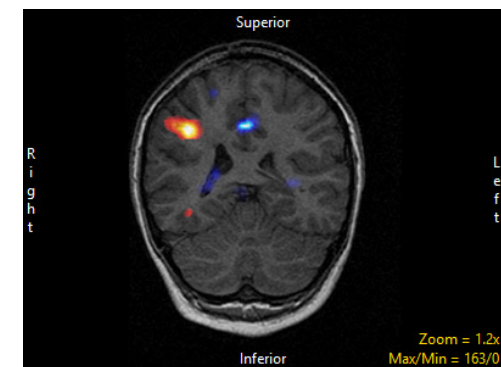
2

Restrict Hyper to 5 Region(s)

Hypo

2.0

Restrict Hypo to 5 Region(s)



Functional Map Settings - Z-Score Threshold

Z-Score Threshold (Std. Dev): The Z-Score Threshold options provide users with the ability to adjust the parameters used for the generation of the Hyper and Hypo maps. The following options are available:

- **Hyper:** The Hyper slider sets the level of statistical significance shown in the functional SISCOM map for regions of activation (hyperperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hyper to # Regions:** The Restrict Hyper to # Regions check box and numeric value allows further control for the display of the hyperperfusion regions to only the # largest regions of activation, as determined by the number of 3D connected voxels in a specific region.
- **Hypo:** The Hypo slider sets the level of statistical significance shown in the functional SISCOM map for regions of decreased perfusion (hypoperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hypo to # Regions:** The Restrict Hypo to # Regions check box and numeric value allows further control for the display of the hypoperfusion regions to only the # largest regions of hypoperfusion, as determined by the number of 3D connected voxels in a specific region.

Review

The Review tab allows users to review the SISCOM images generated in the SPECT processing and MRI processing tabs. SISCOM image data can be reviewed using in 3D mode (Four Panel Display) or in 2D mode (Multi Panel Display).

Display

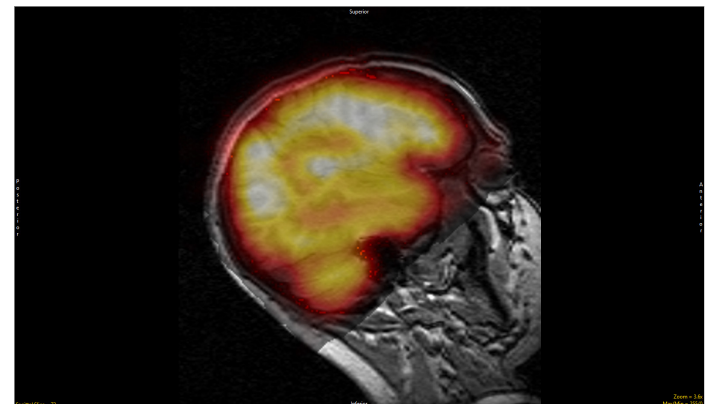
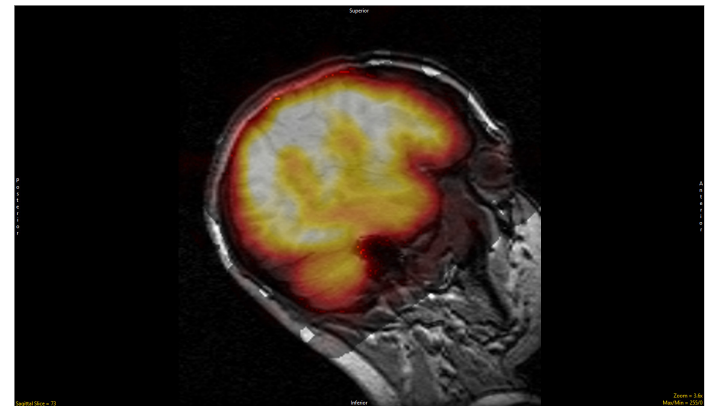
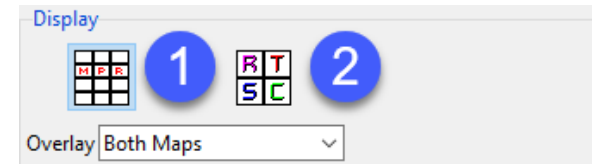
There are two display modes for image review Multi Panel Display [1] mode and Four Panel Display [2] mode. Both modes are described in detail later in this section.

Overlay

The overlay drop-down menu allows users to select which functional map will be displayed with the MRI data set in both Multi Panel Display mode or Four Panel Display mode. Users can choose from:

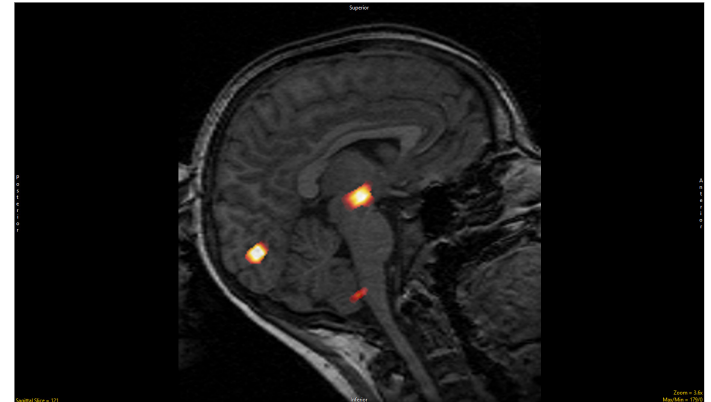
Ictal SPECT: Overlays the registered ictal SPECT image onto the MRI.

Interictal SPECT: Overlays the registered interictal SPECT image onto the MRI.

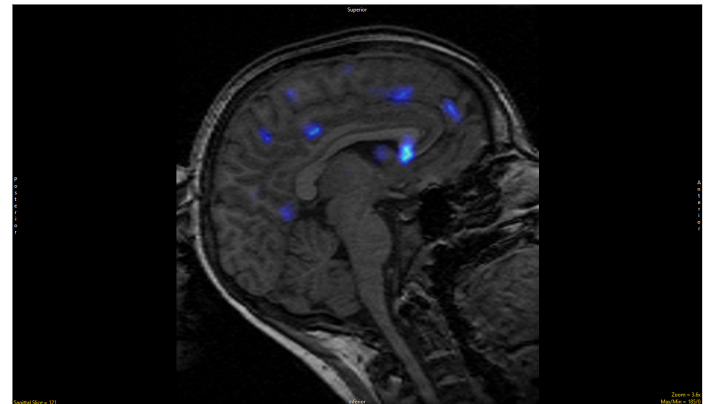


Review (continued)

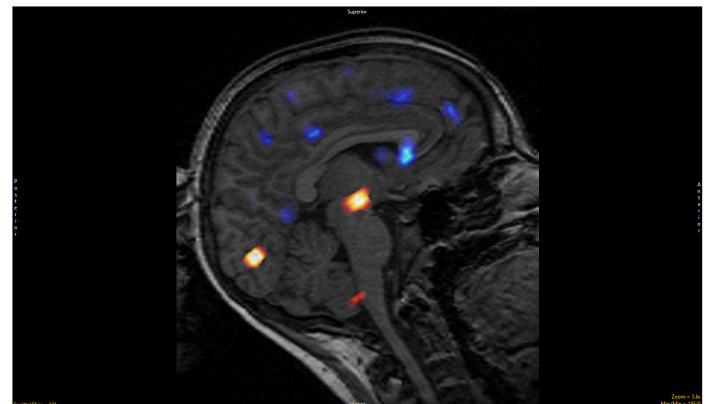
Hyper Map: Overlays the registered hyperperfusion map onto the MRI.



Hypo Map: Overlays the registered hypoperfusion map onto the MRI.

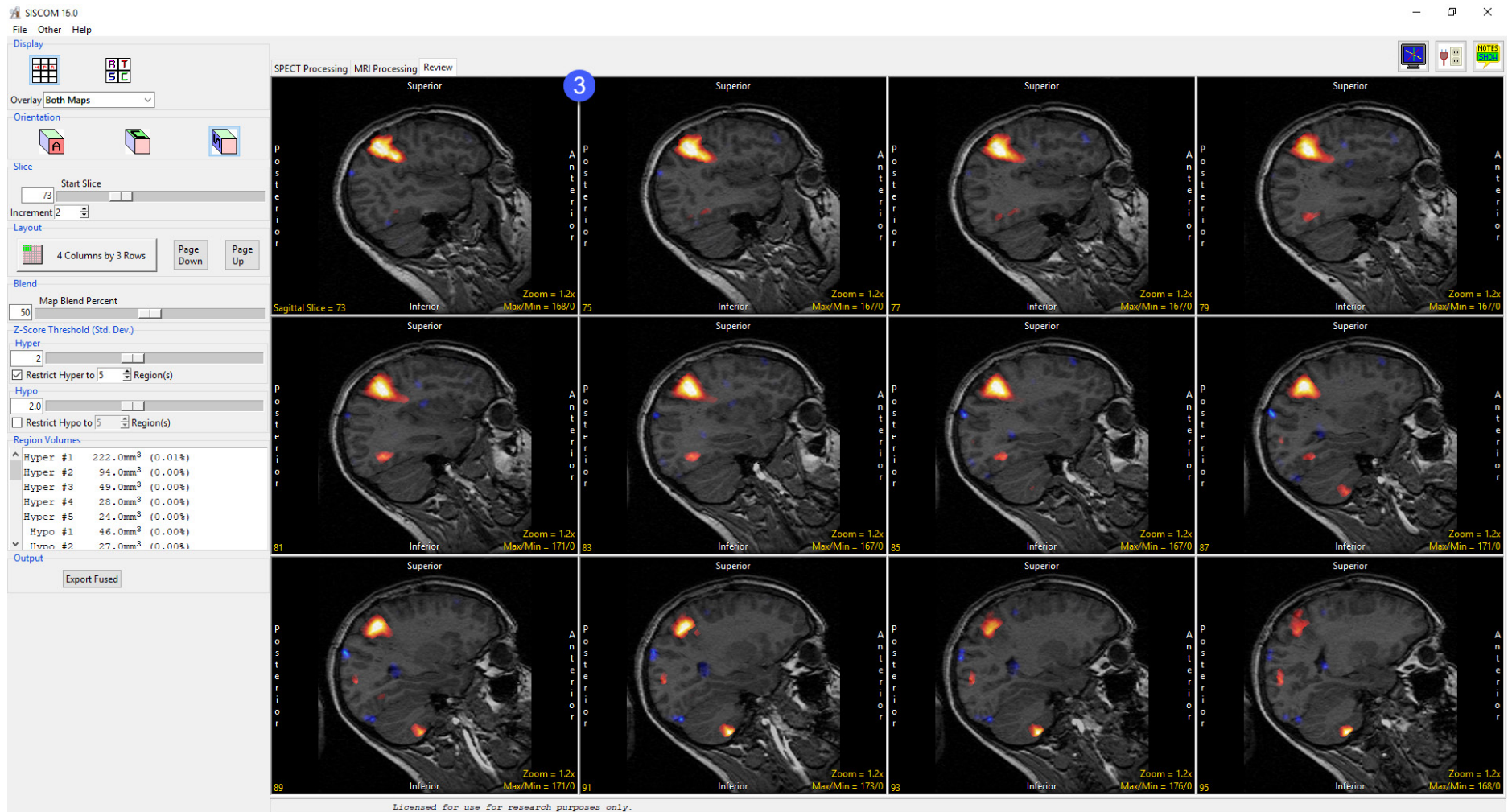


Both Maps: (Default) Overlays both the registered hyperperfusion and hypoperfusion maps onto the MRI.



Multi Panel Display

When Multi Panel Display mode is enabled image data will be displayed as a panel of sections from a single orthogonal orientation [3].

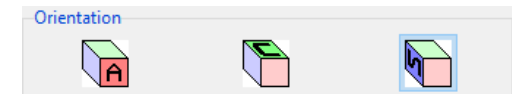


Multi Panel Display (continued)

The following options are available:

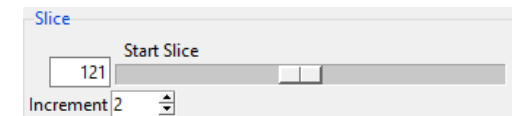
Orientation

Orient: The Orient tool allows users to switch to switch between any of the three orthogonal orientations; Axial, Coronal, or Sagittal. Left click on the Orient tool to cycle through the orthogonal displays or right-click and choose the desired display option from the menu.



Slice

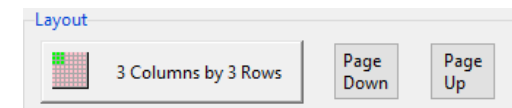
Start Slice: The Start Slice slider allows users to specify the starting slice in the selected orientation for 2D image display. Use the slider to adjust the starting slice or enter the desired value in the slice field.



Increment: The Increment tool allows users to specify the interval used to determine the next image to be displayed. Click the yellow Increment text, the cursor will update to display an up/down INCR cursor. Hold down the left mouse button and slide the cursor upward to increase the increment value and downward to decrease the increment value.

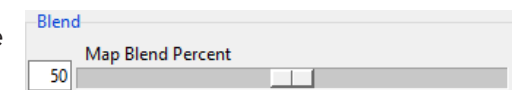
Layout

The number of panels shown can be controlled using the Columns/Rows button. Use the Page Down and Page Up buttons to change the slices shown.



Blend

Map Blend Percent: The Map Blend Percent slider allows users to adjust the percentage blend of the grayscale data and selected overlaid map option.



Multi Panel Display (continued)

Functional Map Settings - Z-Score Thresholds

Z-Score Threshold (Std. Dev): The Z-Score Threshold options provide users with the ability to adjust the parameters used for the generation of the Hyper and Hypo maps. The following options are available:

- **Hyper:** The Hyper slider sets the level of statistical significance shown in the functional SISCOM map for regions of activation (hyperperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hyper to # Regions:** The Restrict Hyper to # Regions check box and numeric value allows further control for the display of the hyperperfusion regions to only the # largest regions of activation, as determined by the number of 3D connected voxels in a specific region.
- **Hypo:** The Hypo slider sets the level of statistical significance shown in the functional SISCOM map for regions of decreased perfusion (hypoperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hypo to # Regions:** The Restrict Hypo to # Regions check box and numeric value allows further control for the display of the hypoperfusion regions to only the # largest regions of hypoperfusion, as determined by the number of 3D connected voxels in a specific region.

Multi Panel Display (continued)

Regions Volumes

The Region Volumes display reports volumes of the hyperperfusion and hypoperfusion regions in accordance to the settings in the Z-Score Threshold section.

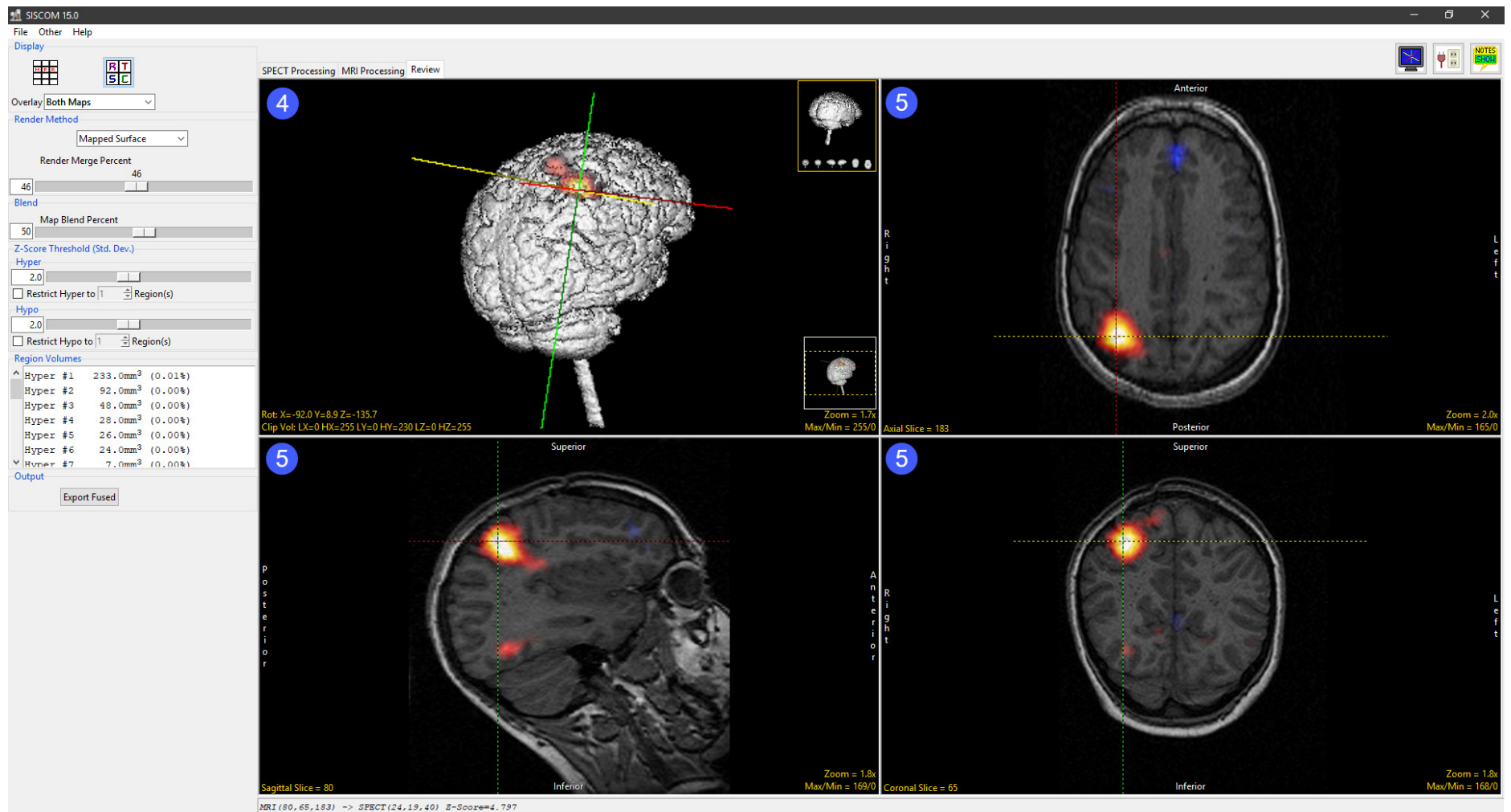
Export Fused

Export Fused allows users to save the SISCOM images to the workspace.

^	Hyper #1	233.0mm ³	(0.01%)
	Hyper #2	92.0mm ³	(0.00%)
	Hyper #3	48.0mm ³	(0.00%)
	Hyper #4	28.0mm ³	(0.00%)
	Hyper #5	26.0mm ³	(0.00%)
	Hyper #6	24.0mm ³	(0.00%)
▼	Hyper #7	7.0mm ³	(0.00%)

Four Panel Display

When Four Panel Display mode is enabled, a rendering of the brain [4] and the three orthogonal images [5] will be displayed. For additional information about the rendering and slice display windows please refer to section 2 – Image Controls and Customizations, of the Analyze 15.0 User’s Guide.



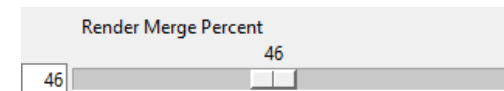
Four Panel Display (continued)

The following options are available:

Render Method

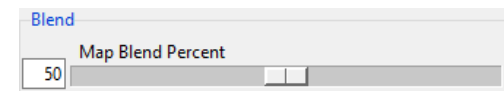
The Render Method drop-down menu allows users to select which rendering method will be used for the 3-D rendering. Users can choose from; Brain Surface, Mapped Surface, Summer Voxel, Weighted MIP, Transparent Colored, Transparent Brain, Composite With, or Composite Without.

Render Merge Percent



The Render Merge Percent slider allows users to adjust the percentage merge between the rendered map and brain.

Blend



The Map Blend Percent slider allows users to adjust the percentage blend of the grayscale data and selected overlaid map option.

Functional Map Settings - Z-Score Thresholds

Z-Score Threshold (Std. Dev): The Z-Score Threshold options provide users with the ability to adjust the parameters used for the generation of the Hyper and Hypo maps. The following options are available:

- **Hyper:** The Hyper slider sets the level of statistical significance shown in the functional SISCOM map for regions of activation (hyperperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hyper to # Regions:** The Restrict Hyper to # Regions check box and numeric value allows further control for the display of the hyperperfusion regions to only the # largest regions of activation, as determined by the number of 3D connected voxels in a specific region.

Four Panel Display (continued)

Functional Map Settings - Z-Score Thresholds (continued):

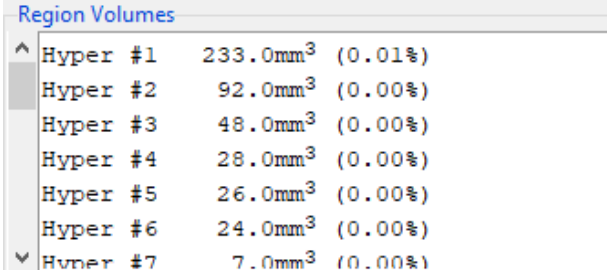
- **Hypo:** The Hypo slider sets the level of statistical significance shown in the functional SISCOM map for regions of decreased perfusion (hypoperfusion). The numeric value unit is in standard deviations of the variance in the SISCOM subtraction image, which is shown in the Standard Deviation = field. By default, this is set to 2.0 standard deviations, with a selectable range from 0.1 standard deviations up to 5.0 standard deviations.
- **Restrict Hypo to # Regions:** The Restrict Hypo to # Regions check box and numeric value allows further control for the display of the hypoperfusion regions to only the # largest regions of hypoperfusion, as determined by the number of 3D connected voxels in a specific region.

Regions Volumes

The Region Volumes display reports volumes of the hyperperfusion and hypoperfusion regions in accordance to the settings in the Z-Score Threshold section.

Output

Export Fused allows users to save the SISCOM images to the workspace.



Region Volumes		
Hyper #1	233.0mm ³	(0.01%)
Hyper #2	92.0mm ³	(0.00%)
Hyper #3	48.0mm ³	(0.00%)
Hyper #4	28.0mm ³	(0.00%)
Hyper #5	26.0mm ³	(0.00%)
Hyper #6	24.0mm ³	(0.00%)
Hyper #7	7.0mm ³	(0.00%)

SISCOM Tutorial

This exercise will demonstrate how to use the SISCOM module within Analyze 15.0. To start, download the following three files:

1. SISCOM_Ictal_SPECT.avw, 2. SISCOM_Interictal_SPECT.avw, and 3. SISCOM_MRI.avw

from <https://analyzedirect.com/data>. Load these three files into the Analyze workspace using the Input/Output module.

Once loaded, select the data sets in the following order (hold down the shift key to select multiple data sets, or click using the middle mouse button):

1. SISCOM_Ictal_SPECT
2. SISCOM_Interictal_SPECT
3. SISCOM_MRI

Note the selection order: Ictal, Interictal, MRI. If the data is not selected in this order the SISCOM procedure will fail to run correctly.

Select SISCOM from the Apps area. The SISCOM module will open to the SPECT processing tab.



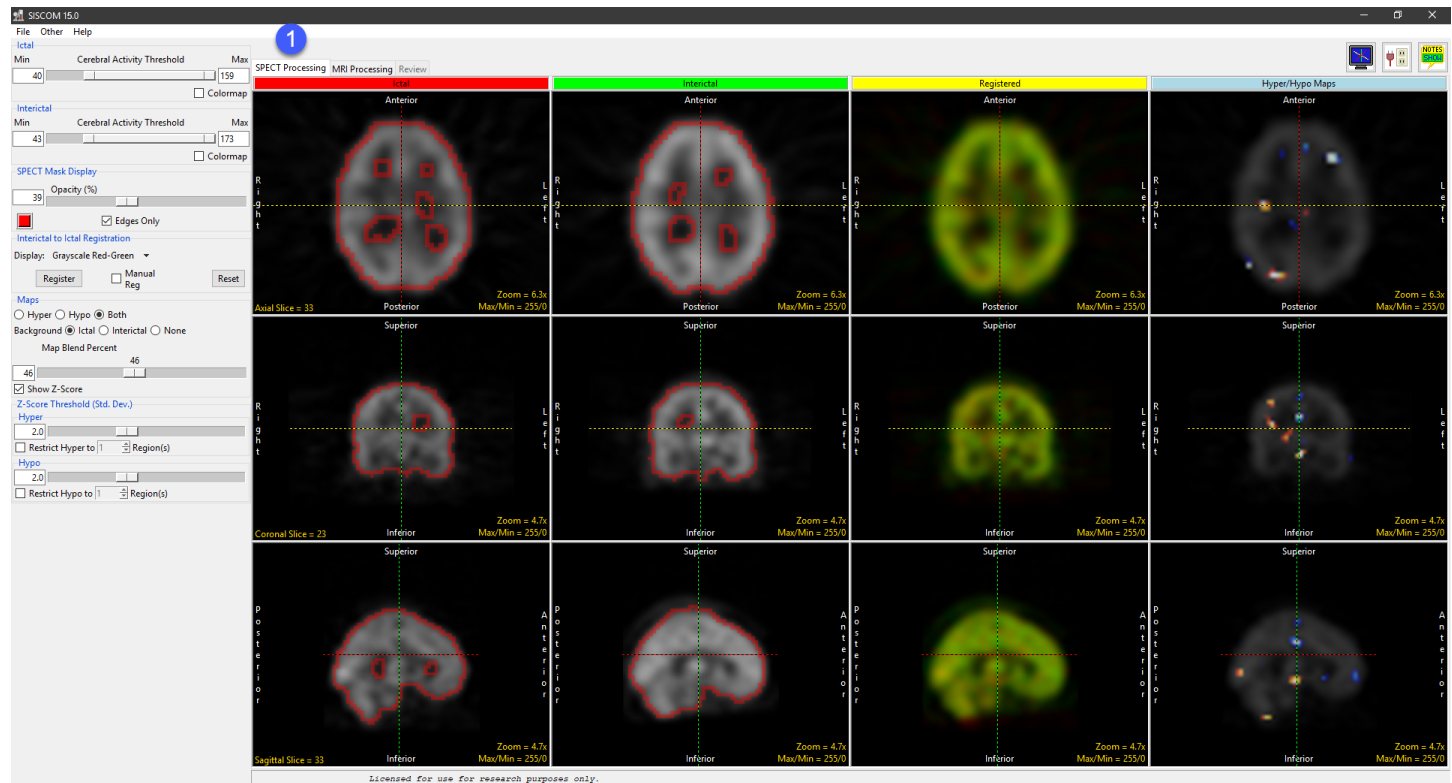
SPECT Processing

The SISCOM module will open to the SPECT processing tab [1]. The SPECT Processing step accomplishes several important tasks:

- Determines thresholds for ictal/interictal SPECT images to segment cortical voxels for registration and analysis.
- Registers the ictal and interictal SPECT volumes.
- Segments the brain from the ictal and co-registered interictal volume images and creates a combined mask for the brain.
- Normalizes and subtracts the ictal/interictal SPECT images.
- Determines the statistical regions of hyperperfusion and hypoperfusion from the subtracted SPECT images.

These tasks are completed automatically when the SPECT Processing panel of the SISCOM workflow is opened. Often the registration, segmentation and functional map computation needs no user intervention, however, sometimes it may be necessary to manually adjust any or all steps.

Next, we will review how to adjust certain parameters manually.



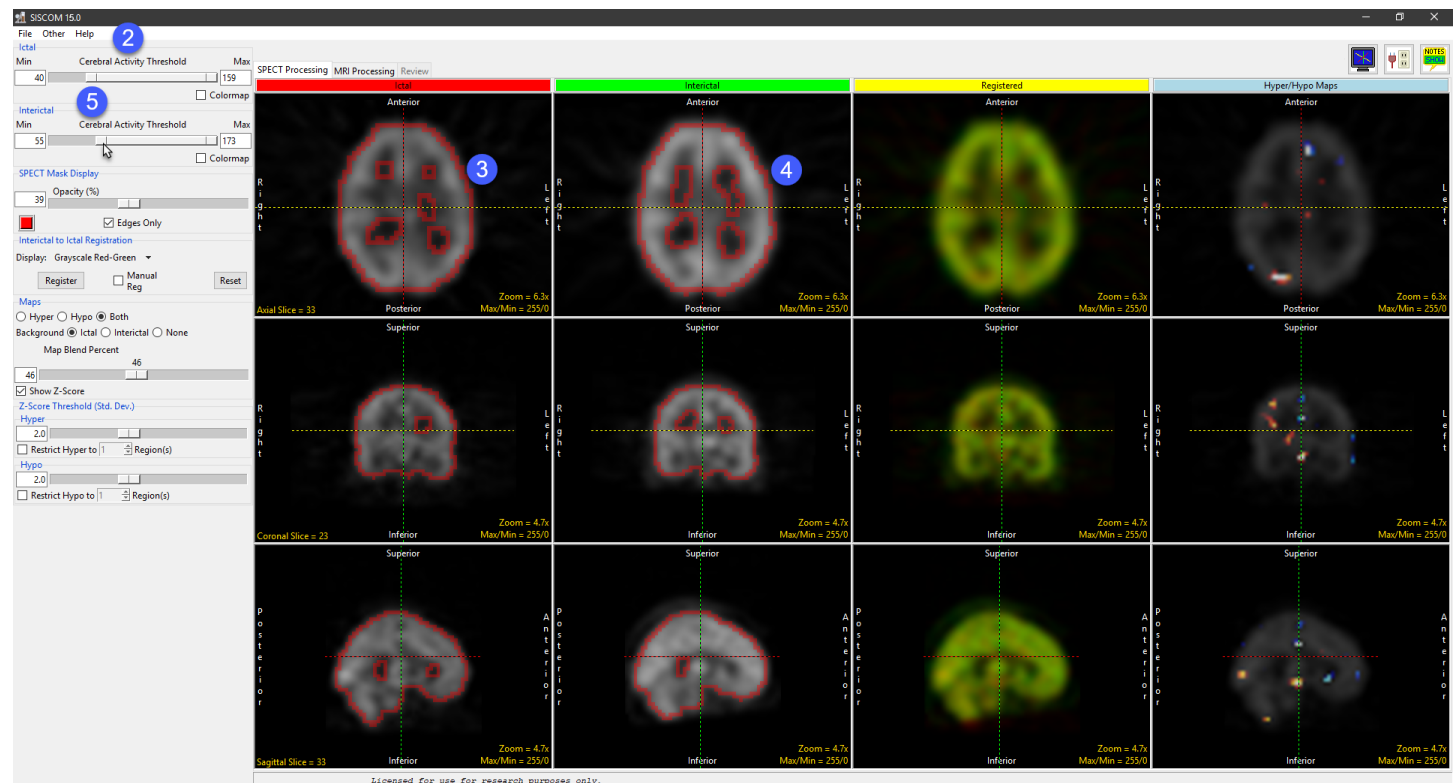
SPECT Processing (continued)

Adjusting the Cerebral Activity Threshold for interictal SPECT images

The thresholds for cerebral activity in the ictal and interictal SPECT volumes are controlled with the sliders at the top of the left menu column [2]. The boundaries determined by this threshold setting are depicted by the red region borders shown on the ictal [3] and interictal [4] images.

Select the box on the Min end of the Interictal threshold slider and raise the threshold from 43 to 55 [5]. Note the change in the red boundary in the Interictal image column. When the mouse button is released, the new threshold minimum will be established and the registration and map determination process will run using the new parameters.

Thresholds should be set to depict a reasonable boundary around cortical activity, with similarity between those boundaries between the ictal and interictal volume images.



SPECT Processing (continued)

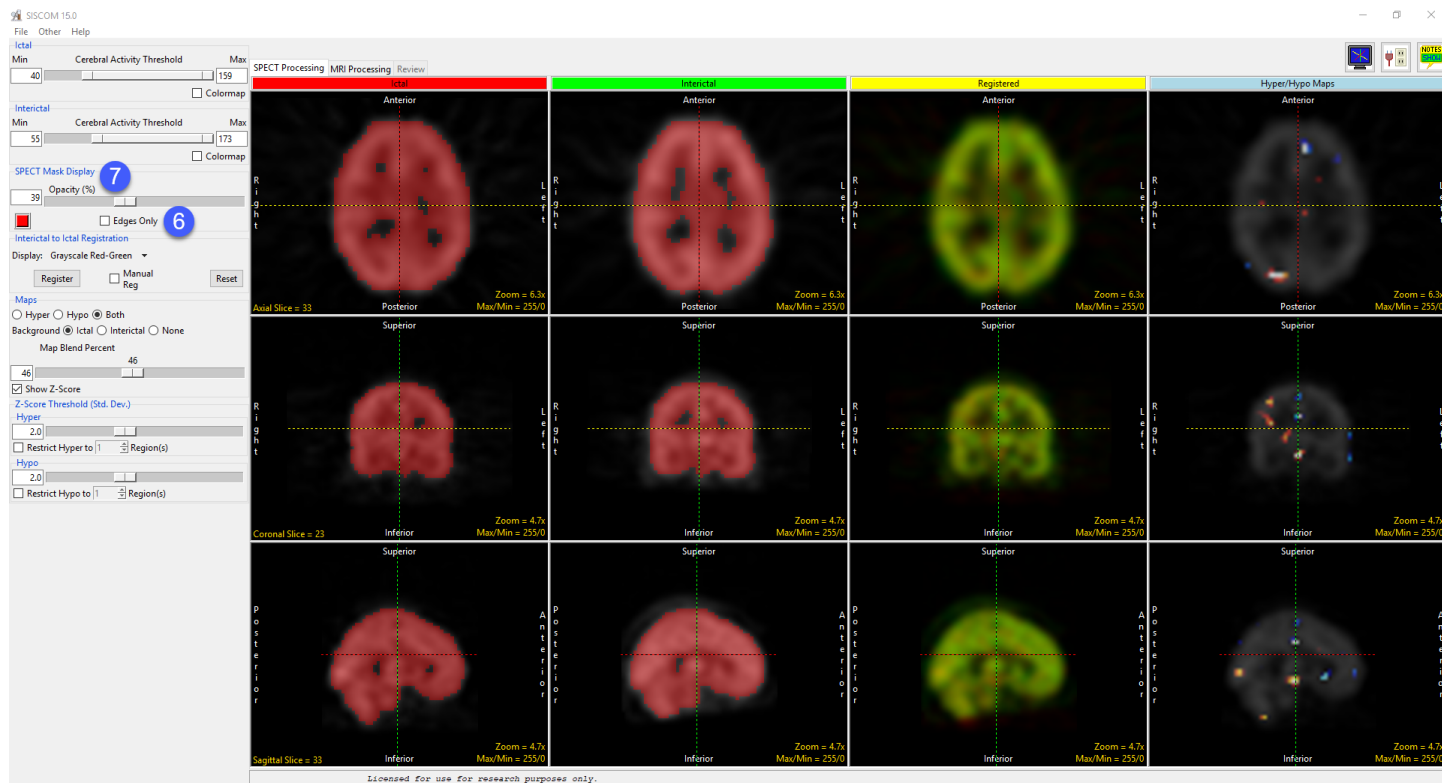
Modifying the SPECT Mask Display

The SPECT Mask Display options change the way in which the thresholds are depicted on top of the ictal/interictal images.

Uncheck the Edges Only check box [6] to see the entire set of voxels within each threshold range shown as a red overlay on the images.

The Opacity (%) control [7] can be used to change the blending of the threshold region with the image itself.

Turn the Edges Only check box back on to show only the edges of the thresholded region.



SPECT Processing (continued)

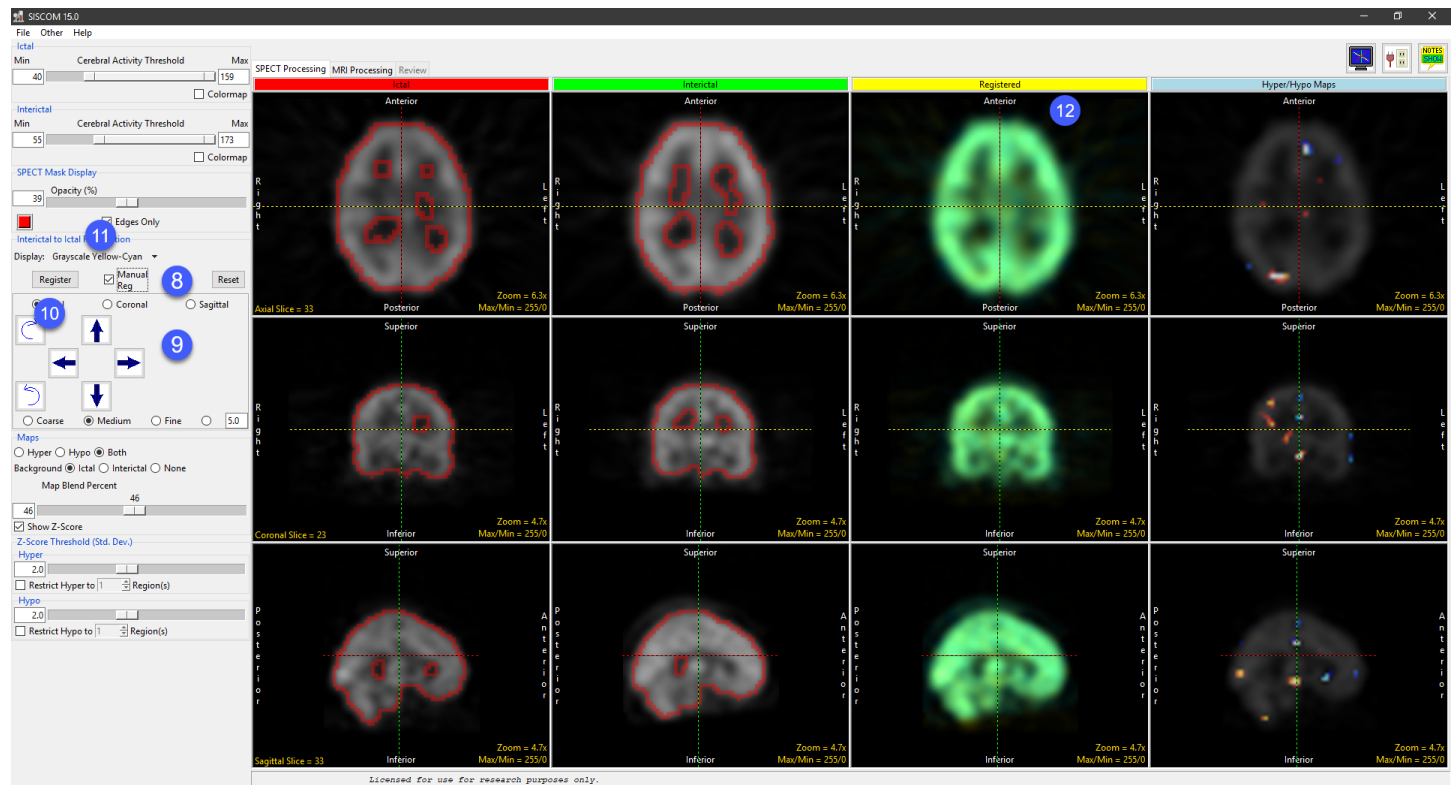
Optimizing registration of the SPECT data

The interictal to ictal SPECT registration is accomplished using a mutual information algorithm, making it robust to localized differences in signal value, orientation and threshold determination. The registration is completed automatically, but manual manipulation of the registration is achieved as follows: Select the Manual Reg check box [8]. Controls for manual rotation and translation are shown in the registration control panel [9], allowing manual manipulation of the registration of the interictal to the ictal volume image. Select the Register button [10] to apply the mutual information algorithm to these unregistered, which will once again register the two SPECT volumes.

Change the Display type [11] to other fusion schemes to review the registration displayed in the yellow Registered column. [12] These blend options are used to visually establish the validity of the interictal/ ictal SPECT registration. It is important to visually verify this part of the SISCOM process to be assured of a valid functional map.

Reset the registration options by changing the Display type to Grayscale

Red-Green and uncheck the Manual Reg check box. Select the Register button to make sure the interictal/ictal SPECT volumes are registered.

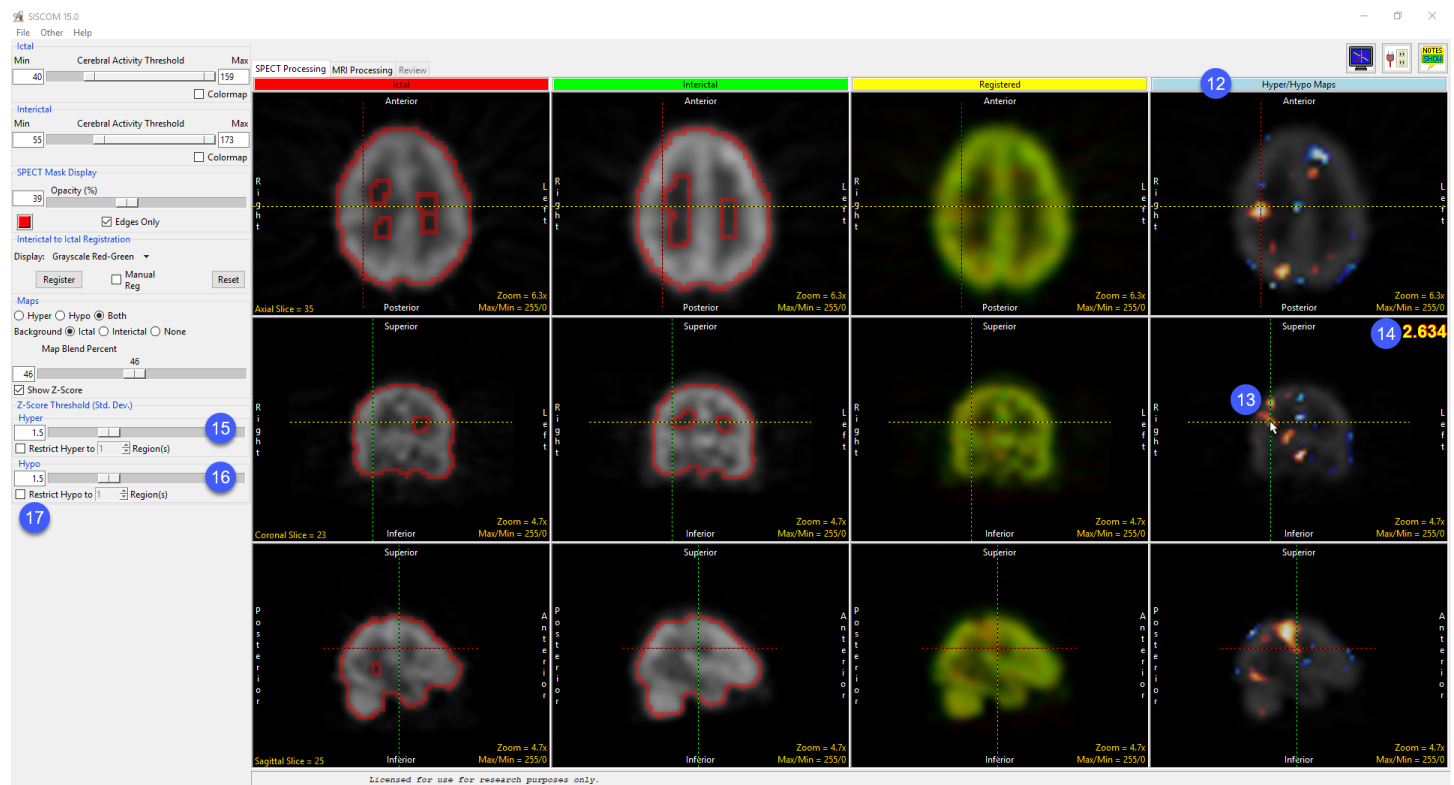


SPECT Processing (continued)

Reviewing the significance levels of both the Hyper- and Hypoperfusion maps

Once the interictal and ictal SPECT images are registered, they can be normalized, subtracted and the level of significance in the functional signal map set to determine which voxels are considered as possible regions of hyperperfusion (increased activation) or hypoperfusion (decreased activation). This level of significance can be controlled by adjusting the amount of signal shown in the functional map. By default, the level of significance is set to 2.0 standard deviations for both the hyperperfusion map and the hypoperfusion map. To adjust the map settings, do the following:

Use the linked cursor on the coronal image in the Hyper/Hypo Maps (blue) [12] column to move the cursor up and to the left, to the area of activation shown in the right, superior aspect of the brain [13]. Note that the level of statistical significance is displayed for the voxel selected by the linked cursor [14], allowing exploration of the signal significance in a focal hyper- or hypoperfused region.



SPECT Processing (continued)

Lower the significance setting for the hyperperfusion regions (Hyper slider in Map Settings) to a value of 1.5 standard deviations [15] and note the increase in the amount of activation signal in the region depicted at the location of the cursor.

Lower the significance setting for the hypoperfusion regions (Hypo slider in Map Settings) to a value of 1.5 standard deviations [16] and note the increase in the amount of focal deficit signal throughout the cortical structure (blue regions).

The map display can be controlled with the check buttons labeled Hyper, Hypo and Both (the default). The maps can be displayed fused with the Ictal SPECT volume (default), Interictal SPECT volume, or without any background SPECT image.

Move the linked cursor throughout the 3D volume image to explore the areas of increased activation (orange regions) and areas of decreased perfusion (blue areas).

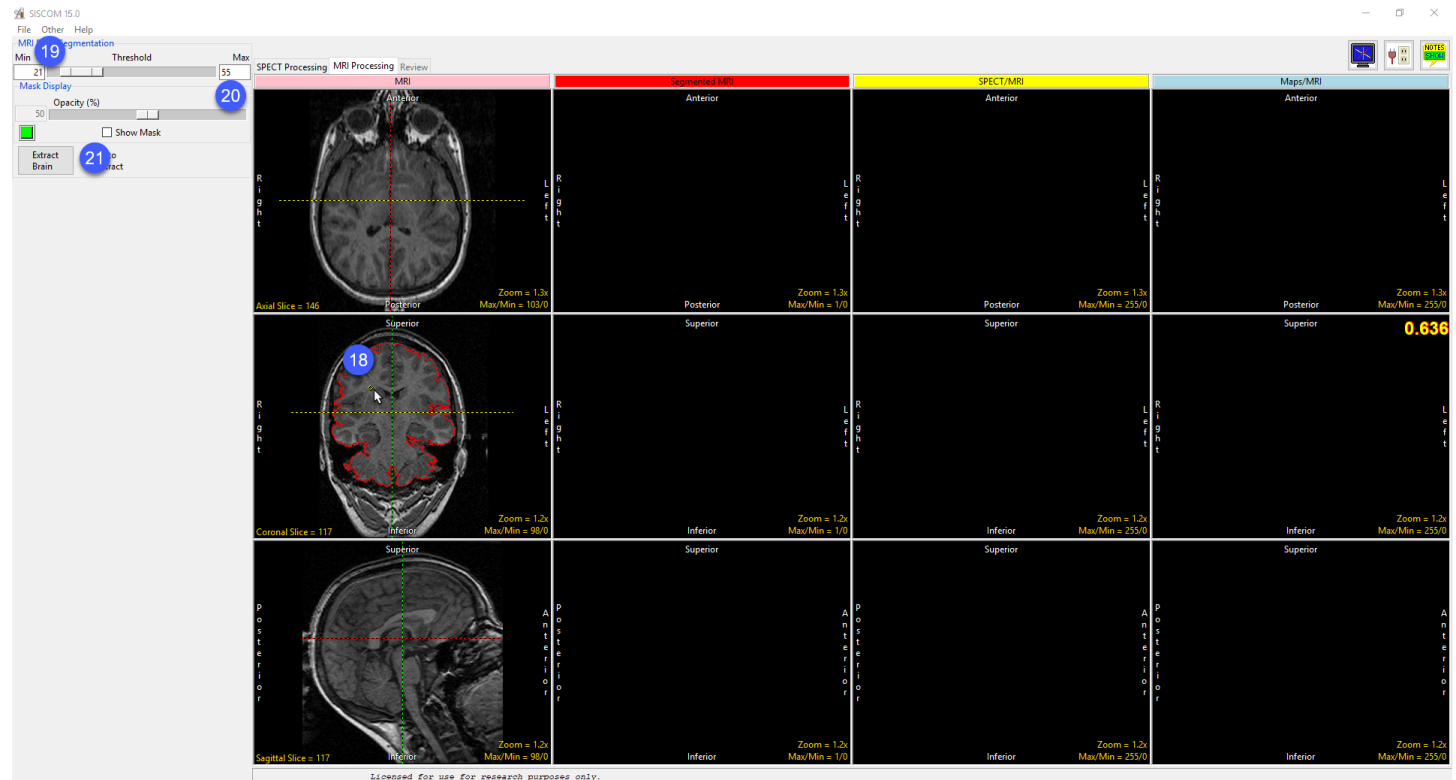
Vary the significance values for both the hyper- and hypoperfusion maps to see the effect of changing statistical cutoff thresholds. Mapped regions can also be restricted based on volume using the Restrict to # Region(s) setting [17]. Note that these regions are all displayed, at the original low spatial resolution of the SPECT volumes, limiting the ability to derive function-to-structure relationships in the cortical anatomy.

When satisfied with the SPECT Processing, reset the threshold values and continue to the MRI Processing step.

MRI Processing

The MRI Processing step in the SISCOM workflow accomplishes several important tasks:

- Segment the cortical anatomy from the 3D T1-weighted MRI
- Register the SPECT volumes to the MRI volume
- Apply the SPECT/MRI registration transform to the hyper- and hypoperfusion maps
- Fuse the functional maps with the MRI to directly correlate function to structure



The first task in the MRI Processing workflow panel is segmentation of the cortical structure from the MRI volume. This is accomplished by establishing a threshold range for cortical voxels and defining a bounded region around the exterior of the brain on a displayed image. To perform this task, do the following:

Using the left mouse button, select a point inside the brain in the coronal image [18] in the MRI (pink) column. A diamond-shaped marker will denote the location of the point selected.

MRI Processing (continued)

The current threshold range causes the red segmentation boundary to surround the entire head. Use the Threshold slider to increase the Minimum threshold value [19] from 16 to 21; the red boundary will now surround the surface of the cortical anatomy.

The morphologic segmentation process is based on the ability of the process to break connections with anatomy exterior to the bounded red region. To further reduce the connectivity to unwanted structures, reduce the Maximum value just to the point where voxels interior to the cortical anatomy begin to lose the green overlay color, then raise the value slightly to keep all cortical voxels within the threshold range - a Maximum value of 55 in this MRI volume image [20].

Select the Extract Brain [21] button to perform the brain segmentation process.

A full 3D segmentation of the cortical anatomy will be completed using the MRI volume image, with the segmentation results appearing in the Segmented MRI (red) column [22].



MRI Processing (continued)

The next task in the MRI Processing workflow is to register the SPECT volumes to the MRI volume. The registration is accomplished automatically after segmentation of the brain is completed, registration uses the initial thresholded SPECT images (SPECT Processing panel) and the Segmented MRI volume. If you wish to manually adjust the registration check the Manual Registration check box to display the manual registration tools, select the Register once manual adjustment of the SPECT image is completed.

Once the SPECT volumes have been registered to the MRI volume, the fused registration result is displayed in the SPECT/MRI (yellow) column.

The final column displays the MRI input with the Hyper and Hypo maps overlaid. The functional maps Z-Score Threshold can be adjusted as described in the SPECT Processing section.

When satisfied with the MRI processing go to Review.

Review

Once the SISCOM volume has been generated by the SPECT Processing and MRI Processing steps of the SISCOM workflow, it can be reviewed using the multiplanar sections and 3D viewer on the Review workflow panel. SISCOM Images can also be exported to the Analyze workspace. To examine the SISCOM volume, do the following:

By default, the first 12 axial SISCOM images are shown in a 4x3 arrangement. To change to a more relevant set of images that demonstrate focal hyper- or hypoperfusion, change the Start Slice slider to image number 170 [23]. If desired adjust the contrast/brightness of the fused image, select any of the Max/Min tool in the lower right-hand corner [24] and move the mouse with the left button held down to change the image display. This new W/L setting will be applied to all displayed images.

Note the statistics for all of the Hyper and Hypo regions are reported in the Region Volume area. [25]

Click the Export Fused [26] button to save the SISCOM images to the workspace.

This concludes the SISCOM tutorial and the SISCOM User's Guide. If you have any questions please email the Analyze support team at support@analyzedirect.com or call +1 (913) 338 2527.

