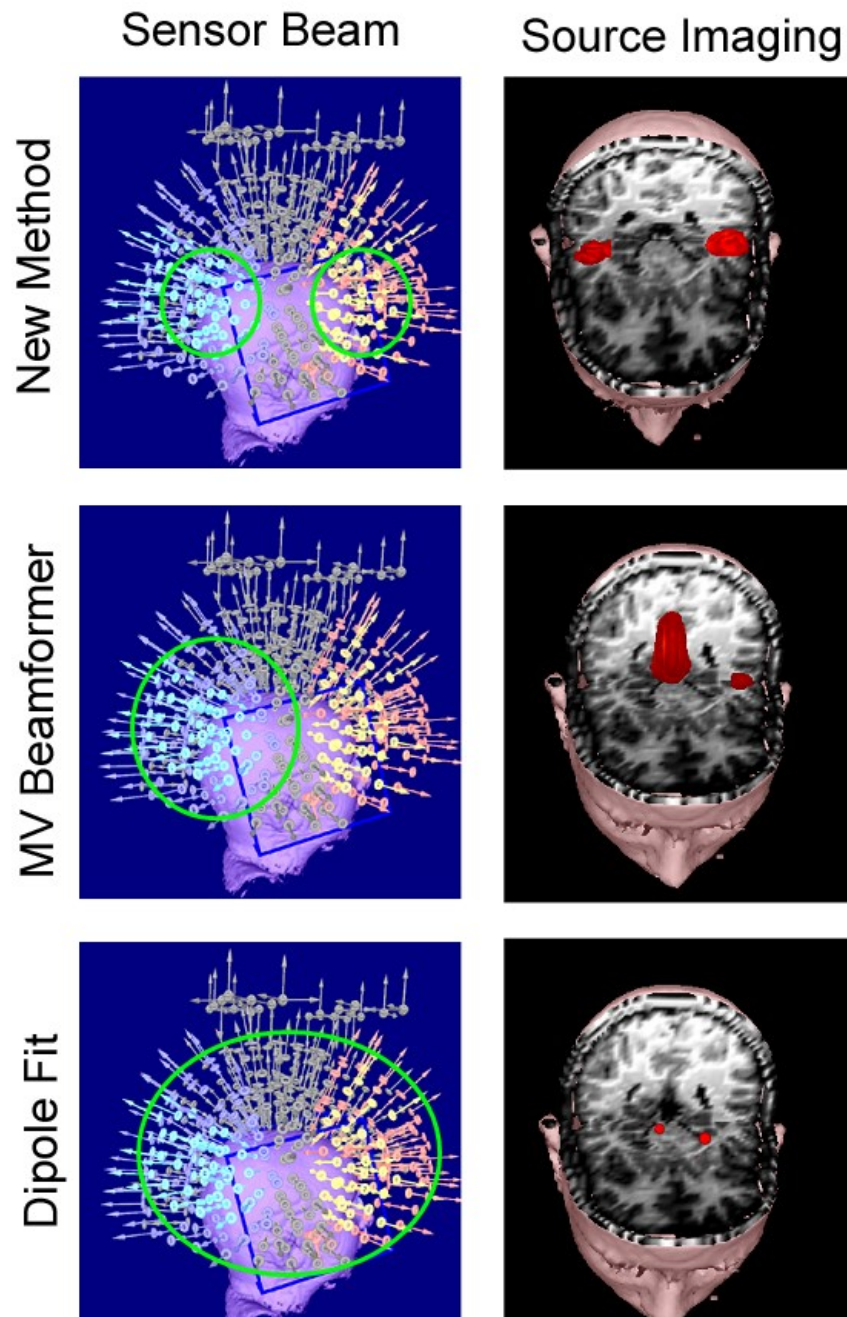


MEG Source Scan

Software Guide



DISCLAIMER

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Features and specifications of this software program are subject to change without notice. This manual contains information and images about MEG (magnetoencephalography) source scan software and its user interface, GUI and its other signal processing algorithms, publications that may be protected by copyright.

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Sending Your Comments and Critiques: We'd like to hear from you. Your comments and suggestions for improving this document are welcome and appreciated. Please e-mail your feedback to MEG_Processor@live.com

Thank you.

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Warnings and Cautions

There are a set of source localization algorithms in the program. Each source localization algorithm has been designed and tested for specific reasons. To ensure the quality and visibility, all source localization algorithms will generate a volumetric source image, which can be considered as an image with millions of “dipoles” or multi-value-voxel. Building on our tests with thousands of MEG dataset, this approach is very reliable and reproducible. It is significantly different from the conventional magnetic source imaging (MSI) or equivalent current dipoles.

The source localization software does not test if the active and control time windows overlap one another. Meaningful designation of integration time windows is the responsibility of the user. It is strongly recommended that the number of samples integrated into the active and control states are close to equal. Failure to do so will lead to bias in images of difference and ratio.

The accuracy of the structural images (MRI/CT) may also affect the MEG results if the conventional magnetic source imaging (MSI) is used. If MRI/CT is distorted, the combination of MEG/MRI/CT will be low-quality. In addition, multiple local sphere, head model or other structural constrained source localization may internally use the MRI/CT images. Any analysis based on those distorted images may yield unexpected or poor results.

The co-registration is only as good as how closely the lipid markers correspond to the placement of the head localization coils during an MEG collection, and how accurate the head coil locations are relative to the sensors. Please See the Head Localization Guide for more details on head coil localization methods and accuracies. In addition, if the MRI contains any distortions which may distort the locations of the lipid markers, the co-registration of the MEG data results and the MR image may also be compromised.

For source localizations on the surface of the brain, there is little or no difference in results between the MSI Studio shape data extraction methods (“cortical hull”, “head” and others). However, for deep sources (e.g., those located in the hippocampus or inferior temporal lobes), the cortical hull extraction method results in source localizations that more closely approximate the true model. This method is the default selection in the MSI Studio software.

The accuracy of the multiple local spheres head model used for the mathematical analysis of MEG data is dependent on the accuracy of the MRI itself. If MR images are poor (i.e., distorted), the shape data created in MSI Studio and the resulting multiple local spheres model created by the local spheres application will likewise be inaccurate. Any analysis based on this multiple local spheres model may yield poor results.

It is a good idea to use input data generated by MEG Processor software when processing and analyzing data. For example, the multiple local spheres model created by the local spheres model in MSI Studio has only been tested and validated using shape data files generated by MEG Processor. Use of other software to generate input files for MSI Studio is at the discretion of the user.

When the source volume is not overlay correctly on an MRI, it is possible due to the source localization methods, MR images and/or co-registration errors. The following warnings and cautions appear in this guide. Please ensure you are aware of all the operations and interpretations.

During source localization, the software may overwrite a pre-existing middle data such as covariance data; it is deleted at the beginning of the process and cannot be recovered. It is recommended to save a copy of the important file as a backup.

Preface

This guide describes the operation of MEG/EEG source localization. The source localization module is one of the core functions in MEG/EEG data analysis. It is used as the primary tool to analyze functional activity/activation or abnormality for research or clinical purposes. Importantly, the source localization module provides graphic user interface (GUI) for access other functions.

Intended Audience

This guide is intended for persons responsible for localizing functional brain activity/activation with MEG and EEG data. This reference is useful to anyone who performs source analysis techniques for MEG/EEG data. Operations of source localization require some expertise to satisfy requirements of accuracy and fitness for use of the results. Technicians may use the application under review by highly trained analytical staff. The guide assumes the reader is familiar with standard MEG/EEG procedures and is familiar with the Windows operating systems.

There are many MEG/EEG source localization algorithms. In this manual, we will discuss the well-tested algorithms with waveform, covariance, spectral and spectral covariance data.

References

This document assumes familiarity with many terms related to computer operations and physiology. This document also assumes you are familiar with the principles of source localization and the data collection and recording process. It also assumes some knowledge of MEG/EEG analysis. The document uses terms related to computer operations and physiology as well as many acronyms.

Document Structure

Documents are generally provided in both Microsoft Word® format and Adobe® Acrobat® PDF (Portable Document Format). All editions are distributed on Flash Driver, CD or websites with the related software, and include bookmarks and hyperlinks to assist navigating the document. Please feel free to send your critiques, corrections, suggestions and comments to: MEG_Processor@live.com.

Conventions

Numeric: Numeric values are generally presented in decimal but in special circumstances may also be expressed in hexadecimal or binary. Hexadecimal values are shown with a prefix of 0x, in the form 0x3D. Binary values are shown with a prefix of 0b, in the form 0b00111101. Otherwise, values are presumed decimal.

Units: Units of measure are given in metric. Where measure is provided in imperial units, they are typically shown in parenthesis after the metric units. Magnetic signal strength is given in Teslas (T), the

SI unit of flux density (or field intensity) for magnetic fields, also known as the magnetic induction. Typical signal strengths in MEG measurements are in the order of pT (picoteslas = 10^{-12}) or fT (femtoteslas = 10^{-15}).

The conventional source localization method is dipole modeling, which provides “point-like” description of brain activity/activation. Since 2004, this software started to replace dipoles with volumetric source images. In our new volumetric source image, each 3D point has many values or each voxel has many values. Therefore, each voxel can have all the information that a conventional dipole has. Therefore, the dipole modeling is becoming obsolete.

Changes from Previous Releases

If you used the software before, please read the ReadMeFirst.doc file for late changes that did not make it into this manual and for a list of new functions or options, changes, additions, bug fixes, and known bugs for the application. The discussion of the source localization or source scan will focus on volumetric source scan, which generates a volumetric source image. This manual will still mention dipoles. However, the description of dipoles is mainly for back compatible purposes. Noteworthy, the values in volumetric source images depend on source localization algorithms.

Introduction

This manual describes the various graphical elements that make up source localization module and defines the volumetric source data throughout the software applications. There are several ways to localize MEG/EEG sources. In this guide, the source localization methods will be discussed according to the data types that will be used for source scans (see Figure 1). The mathematic algorithms will be explained briefly.

Menu for Launching Source Localization Windows

The menu for launching source localization windows is in the Main Frame of the MEG Processor program, which is under the Source Menu (Figure 1). MEG data for source localization can be the conventional waveform data and/or spectral data. Those waveform and spectral data can be used to compute covariance matrix, which is the product of channel-cross-channel operation (CxC). In this manual, we typically use CxC to refer data generated by operations applied to channel-pairs.

To localize sources, we can use waveform (Wave Amp Source Imaging), waveform CxC matrix data (Wave CxC Source Imaging) and both (Wave Amp CxC Source Imaging). In the similar way, we can also use spectral data to localize sources. This manual describes the various graphical elements that make up source localization module and defines the volumetric source data throughout the software applications.

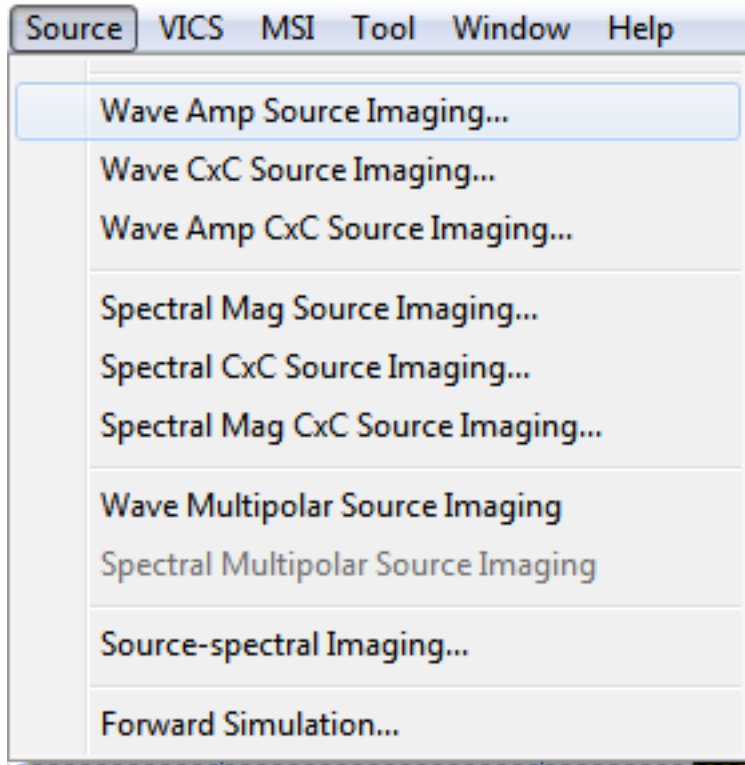


Figure 1. Menu for launching Source Localization Windows.

Wave Amp Source Imaging

The “Wave Amp Source Imaging” launches the main window for localizing sources with wave form data and generates a volumetric source image, which may have multiple time slices. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

Source analysis is performed after a dataset has been acquired and reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- a) If there are structural data available, import the MRI/CT data
- b) Use MSI Studio to check and view MEG sensor and MR/CT data.
- c) Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.
- d) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- e) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).

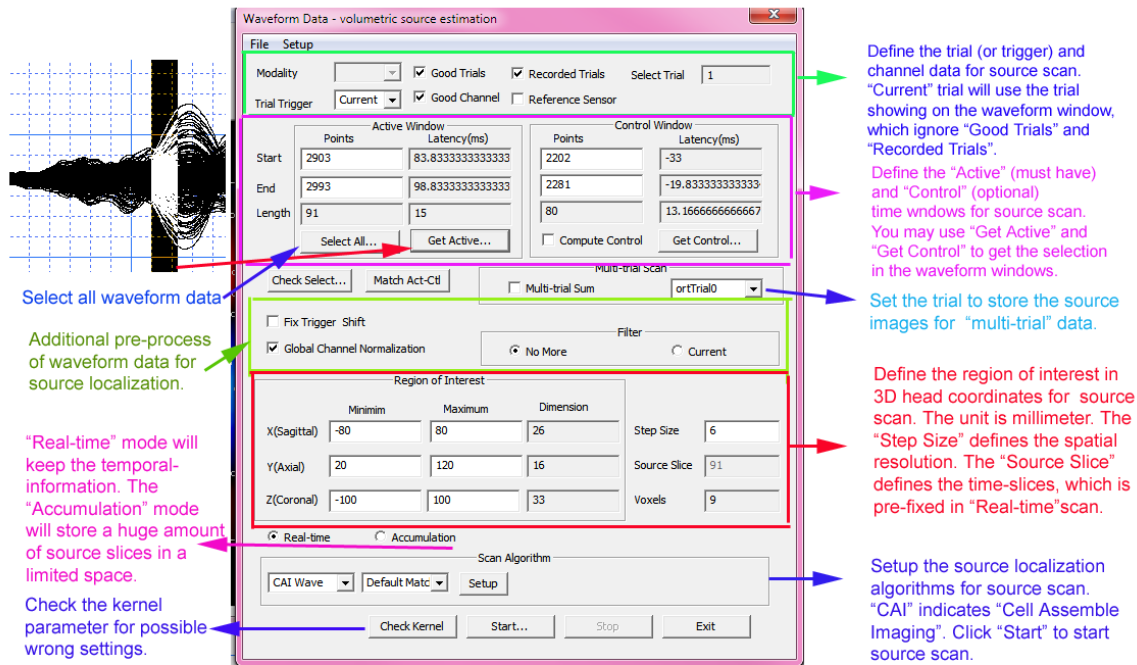


Figure 2. Source scan window for MEG/EEG waveform data.

- f) For each dataset for the patient referred to by the Main Frame waveform viewer and MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing waveforms, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- g) Use the waveform viewer to inspect each dataset. If required or necessary, marking trials, channels, or segments bad. Also use waveform viewer to generate markers identifying the time of occurrence of events to be imaged by source localization program. For details, see MEG Processor Main Frame Guide.
- h) If required or necessary, use "Select-Cut" and "Select-Cut settings" to remove bad segments or use Segmentation marks to select "good" data segments for source scan.
- i) For each dataset, you may select the "good data segments" such as the responses in evoked neuromagnetic data. If all time samples are to be selected, click the "Select All". If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.
- j) For each source scan for a dataset, the program will generate a volumetric source image with at least one time-slice.
- k) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the "Refresh" button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

Main Module in Waveform Amp (amplitude) Source Scans

The full suite of waveform source scan comprises the following components.

- ❖ Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution
- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target data (Time windows)

The data selection specifies the trial, channels to be used for source scan. The time window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing in the time windows manually.

By default, source scan will integrate the selected data in the waveform viewer into the source scan matrix unless one or more time windows are specified, in which case only data within the time ranges are used. Time windows are defined relative to some event in the data — either the beginning of the trial (time zero) or a marker. Triggers (one group of Markers) are added automatically by the Data Acquisition application when the data is acquired. Typical markers are added by the adding Marker programs. They can also be added manually to mark an event of interest using the Selection Mark application.

If you are generating a single-state image, only active-state windows can be defined. If you are generating a dual-state image, both active- and dual-state windows can be defined.

To define a window:

- 1) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the waveform viewer window.
- 2) You may click the “Select All...” to select all data points.
- 3) To use the control data, you must select “Compute Control” checkbox.
- 4) The Check Select will check the selection of the data.
- 5) The Match Act-Ctl will match the size of the active and control selection so that they have the same length.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 1) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 2) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Hint: Sources can be constrained to stay in the vicinity of a given region. Thus, it is possible to include prior knowledge from imaging modalities such as fMRI, PET, or SPECT.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control data for source scan.

Storage of source images

For source images based on one trail, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that

the source difference between active and control states over the entire head should be small compared to the common mode.

$$p = \sum_{i=1}^v (a_i - c_i) / (a_i + c_i)$$

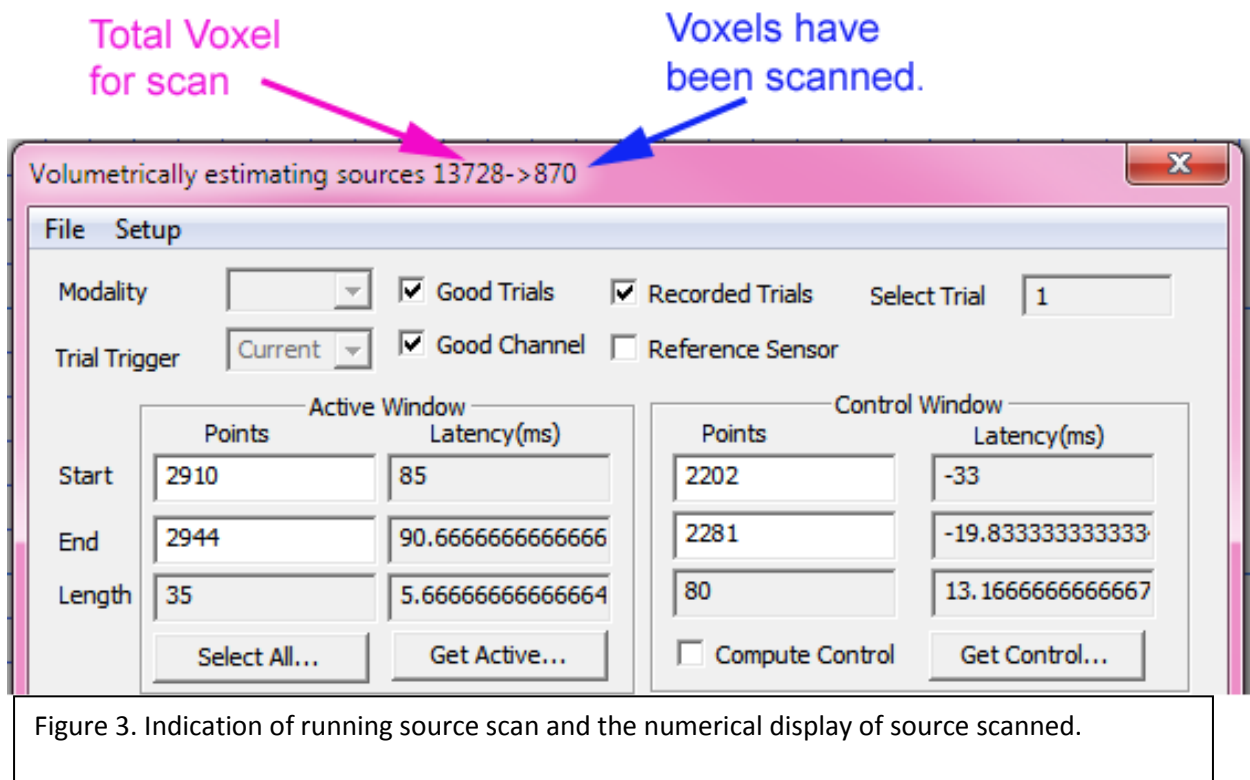
Source scan applies an equation to all non-zero voxels (only within the head boundary), where a and c are the active and control source power of each voxel. In this simple test, if the ratio exceeds a 25% threshold, poor suppression of common mode brain activity is indicated. This, in turn, suggests either poor experimental design or corrupted MEG data.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan (see Figure 3).

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Filters data and computes covariance of data if necessary
- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth
- 7) Computes two sets of source time-series for source peak (maxima) — one using full bandwidth and one using the high-pass filter.
- 8) Finds and marks peak (or spikes) in the source time-series using the covariance with the high-pass filter.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.



Analyzing Source Images

Volumetric source scan is a unified analysis for MEG/EEG data (without the uncertainties of dipole fitting) in which the locations of brain activation or spike activity and the source activation/activity from those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio, coregistered with the subject's MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

- Misidentification or lack of identification of spikes if they have insufficient amplitude relative to background brain activity and noise.
- Erroneous results from a dipole fit where the topography of visible spikes is not strictly dipolar due to activation of a large cortical area.
- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

Wave CxC Source Imaging

The “Wave CxC Source Imaging” launches the main window for localizing sources with waveform CxC data and generates a volumetric source image, which may have multiple time slices. The waveform CxC dataset is the result of an operation applied to two channel-pair, or channel-cross-channel (CxC) operation. The CxC dataset is typically a square matrix: $N \times N$. Here, N is the number of channels.

The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

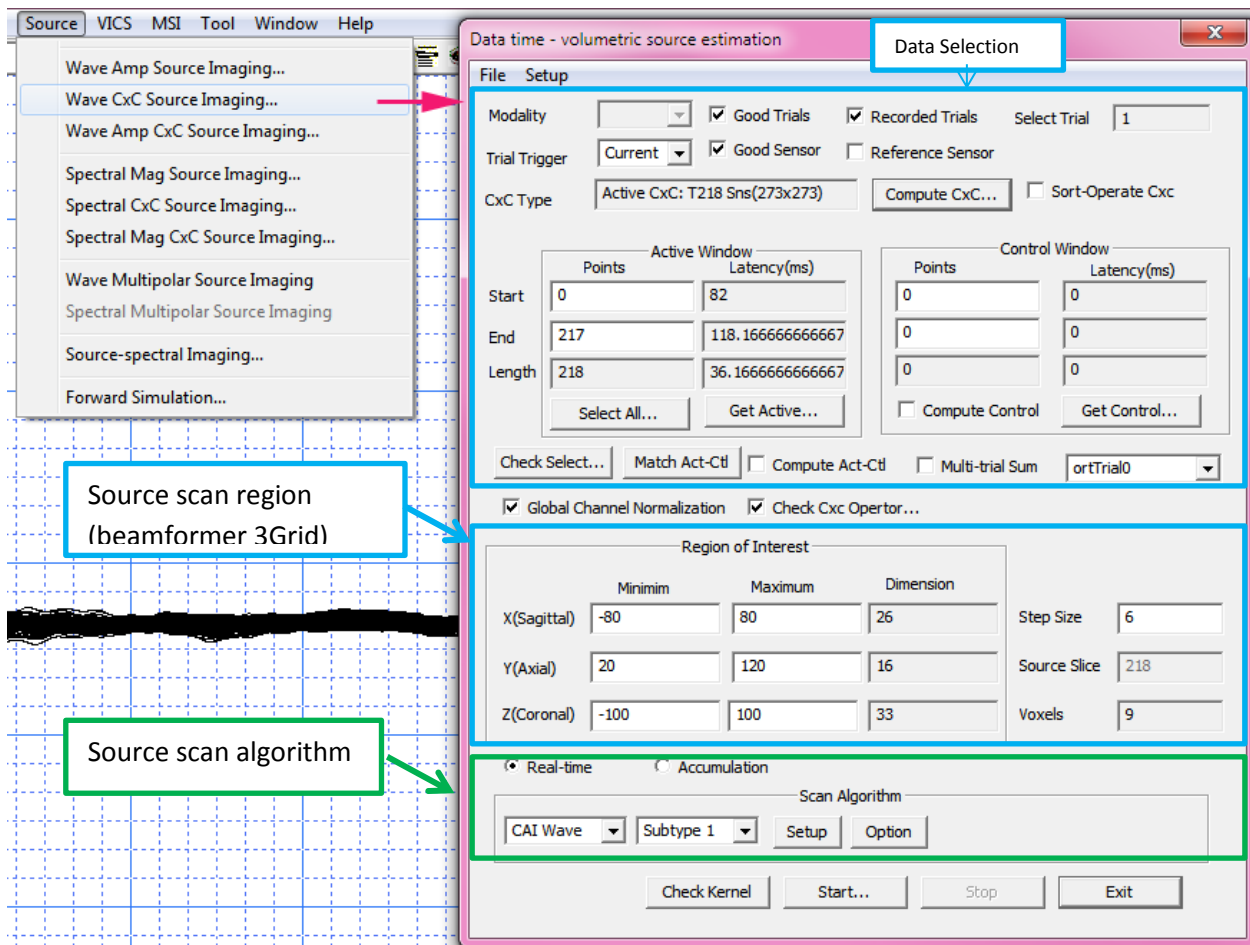


Figure 4. Source Scan for waveform CxC data.

Source analysis is performed after a CxC dataset has been acquired, reviewed and a head shape file created from the MRI/CT or digitalization devices. The recommended procedures for a standard analysis using wave CxC source localization programs are similar to that for “Wave Amp Source Imaging”.

Main Module in Wave CxC Source Scans

The full suite of wave CxC source scan comprises the components are similar to that for “Wave Amp Source Imaging”.

- ❖ CxC Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution
- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target CxC data (Time windows)

The data selection specifies the trial, channels to be used for source scan. The time window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing in the time windows manually.

By default, source scan will integrate the selected CxC data in the CxC waveform viewer into the source scan matrix unless one or more time windows are specified, in which case only data within the time ranges are used. Time windows are defined relative to some event in the data , which is typically predefined by the computing of CxC data

If you are generating a single-state image, only active-state windows can be defined. If you are generating a dual-state image, both active- and dual-state windows can be defined.

To define a window:

- 1) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the waveform viewer window.
- 2) You may click the “Select All...” to select all data points.
- 3) To use the control data, you must select “Compute Control” checkbox.
- 4) The Check Select will check the selection of the data.
- 5) The Match Act-Ctl will match the size of the active and control selection so that they have the same length.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis

by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 1) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 2) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control data for source scan.

Storage of source images

For source images based on one trail, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared to the common mode. The formula is similar to that for “Wave Amp Source Imaging”.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan (see Figure 3).

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Filters data and computes covariance of data if necessary

- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth
- 7) Computes two sets of source time-series for source peak (maxima) — one using full bandwidth and one using the high-pass filter.
- 8) Finds and marks spikes in the source time-series using the covariance with the high-pass filter.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

The analysis and view of volumetric sources generated by Wave CxC Source Scan are similar to that for “Wave Amp Source Imaging”.

Wave Amp CxC Source Imaging

The “Wave Amp CxC Source Imaging” launches the main window for localizing sources with waveform amplitude and CxC data. This program will use waveform data as well as internally generated CxC data to perform source scan. This program generates a volumetric source image, which may have multiple time slices. The waveform CxC dataset is the result of an operation applied to two channel-pair, or channel-cross-channel operation. The CxC dataset is typically a square matrix: $N \times N$. Here, N is the number of channels.

The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

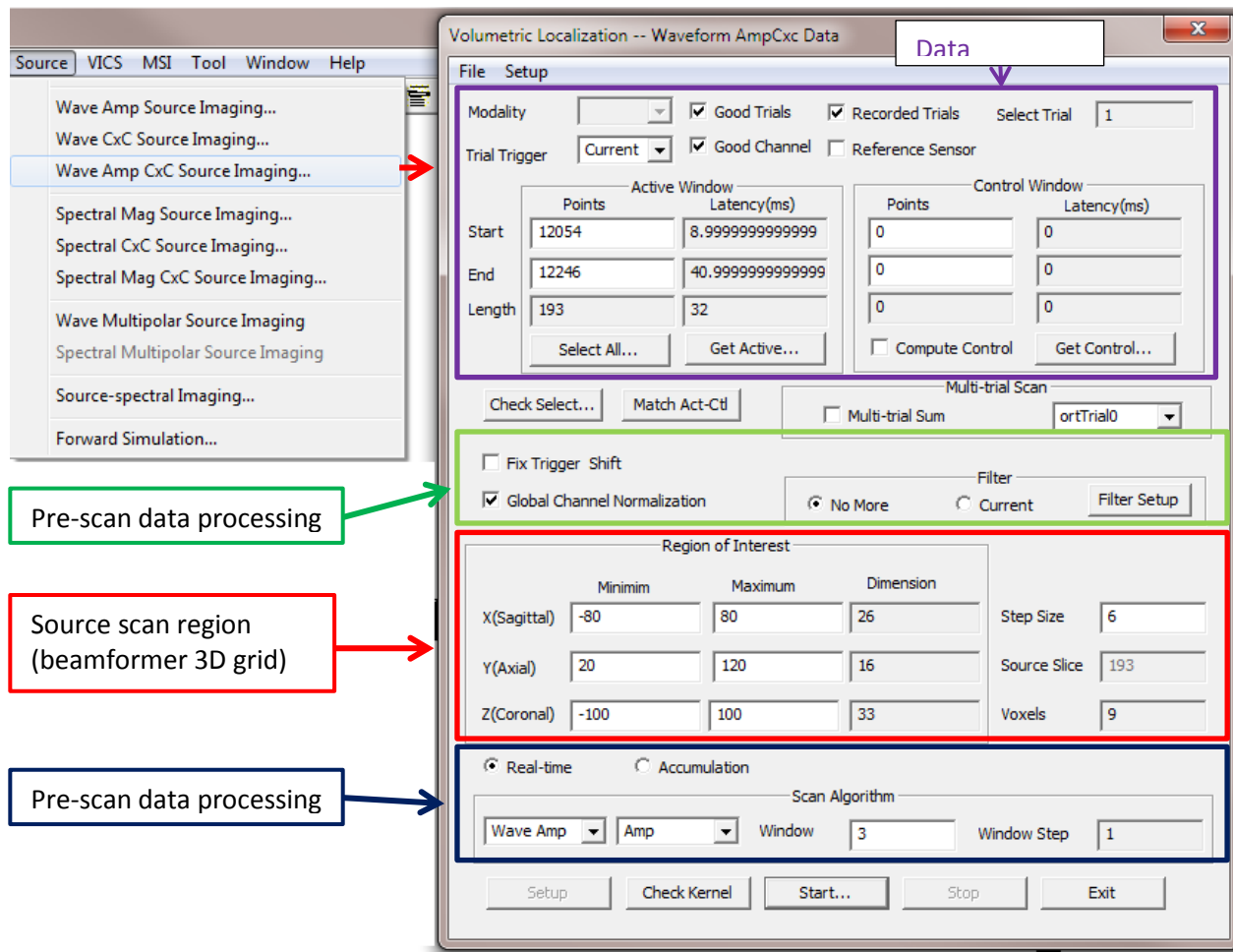


Figure 5. Wave Amp CxC Source Scan.

Source analysis is performed after a waveform dataset has been acquired, reviewed and a head shape file created from the MRI/CT or digitizing devices. The recommended procedures for a standard analysis using “Wave Amp CxC Source Localization” programs are similar to that for “Wave Amp Source Imaging”.

Main Module in Wave Amp CxC Source Scan

The full suite of wave Amp CxC source scan comprises the components are similar to that for “Wave Amp Source Imaging”.

- ❖ CxC Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution

- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target Wave data (Time windows)

The data selection specifies the trial, channels to be used for source scan. The time window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing in the time windows manually.

By default, source scan will integrate **the selected wave data in the waveform viewer with internally generated CxC dataset into the source scan matrix** unless one or more time windows are specified, in which case only data within the time ranges are used. Time windows are defined relative to some event in the data, which is typically predefined during the study design and analyzed in waveform viewers.

If you are generating a single-state image, only active-state windows can be defined. If you are generating a dual-state image, both active- and dual-state windows need to be defined.

To define a window:

1. Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the waveform viewer window.
2. You may click the “Select All...” to select all data points.
3. To use the control data, you must select “Compute Control” checkbox.
4. The Check Select will check the selection of the data.
5. The Match Act-Ctl will match the size of the active and control selection so that they have the same length.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 1) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 2) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control data for source scan.

Storage of source images

For source images based on one trial, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared to the common mode. The formula is similar to that for “Wave Amp Source Imaging”.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan (see Figure 3).

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Filters data and computes covariance of data if necessary
- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth
- 7) Computes two sets of source time-series for source peak (maxima) — one using full bandwidth and one using the high-pass filter.

- 8) Finds and marks spikes in the source time-series using the covariance with the high-pass filter.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

The analysis and view of volumetric sources generated by Wave Amp CxC Source Scan are similar to that for “Wave Amp Source Imaging”.

Spectral Mag Source Imaging

The “Spectral Mag Source Imaging” launches the main window for localizing sources with spectral data and generates a volumetric source image, which may have multiple time slices. This source localization method mainly utilizes the magnitude of spectral data. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

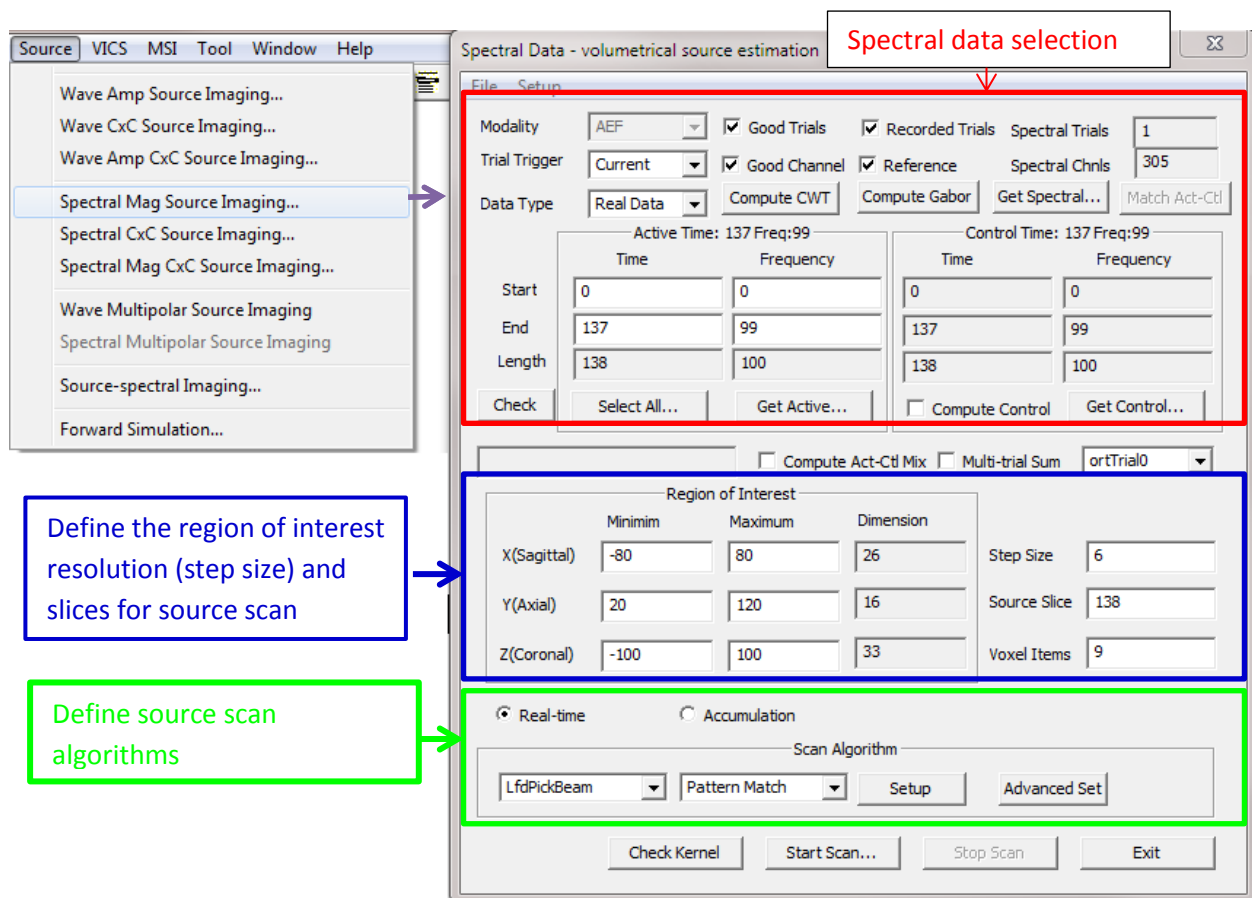


Figure 6. Spectral Mag (magnitude) Source Scan.

Source analysis is performed after spectrograms have been computed, reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- a) If there are structural data available, import the MRI/CT data.
- b) Use MSI Studio to check and view MEG sensor and MR/CT data.
- c) Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.
- d) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- e) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).
- l) For spectrograms showed in spectral viewer and the sensors showed in MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing spectrogram, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- m) Use the spectral viewer to inspect each spectrogram. If required or necessary, marking trials, channels bad. For details, see Spectral Analysis Guide.
- n) For each spectral dataset, you click the “Select All” to select all the spectral data. If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.
- o) For each source scan for a spectral dataset, the program will generate a volumetric source image with at least one time-slice and one frequency band.
- p) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the “Refresh” button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

Main Module in Spectral Mag (magnitude) Source Scans

The full suite of spectral source scan comprises the following components.

- ❖ Spectral Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution
- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target spectral data (Time-frequency windows)

The data selection specifies the time-frequency ranges for source scan. The trial, channels and time-window are supposed to be appropriately determined during spectral computing. Therefore, all the spectral data are assumed to be appropriate for source scan. The time-frequency window parameters specify active- and control-state time windows relative to named triggers or markers or the trial

synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing.

By default, source scan will integrate the selected data in the spectral viewer into the source scan matrix unless one or more time windows are specified, in which case only spectral data within the time-frequency ranges are used. Time-frequency windows are defined relative to some event in the, which has been discussed in waveform source scan. The spectral data are linked to waveform data, therefore, the temporal information is available for users to track the time or latency.

If you are generating a single-state image, only active-state time-frequency windows can be defined. If you are generating a dual-state image, both active- and dual-state time-frequency windows can be defined.

To define a time-frequency window:

- 6) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the spectral viewer (single channel-spectral viewer).
- 7) You may click the “Select All...” to select all data points.
- 8) To use the control data, you must select “Compute Control” checkbox.
- 9) The Check Select will check the selection of the data.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 3) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 4) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control spectral data for source scan.

Storage of source images

For source images based on one trial, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred to as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared to the common mode.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan.

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Computes covariance of data if necessary
- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-frequency-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth
- 7) Computes two sets of source time-series for source peak (maxima)
- 8) Finds and marks peaks in the source data.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

Analyzing Source Images

Volumetric source scan is a unified analysis for MEG/EEG data (without the uncertainties of dipole fitting) in which the locations of brain activation or spike activity and the source activation/activity from those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio,

co-registered with the subject's MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

- Misidentification or lack of identification of spikes if they have insufficient amplitude relative to background brain activity and noise.
- Erroneous results from a dipole fit where the topography of visible spikes is not strictly dipolar due to activation of a large cortical area.
- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

Spectral CxC Source Imaging

The “Spectral Mag Source Imaging” launches the main window for localizing sources with spectral data and generates a volumetric source image, which may have multiple time slices. This source localization method mainly utilizes the magnitude of spectral data. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

Source analysis is performed after spectrograms have been computed, reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- f) If there are structural data available, import the MRI/CT data.
- g) Use MSI Studio to check and view MEG sensor and MR/CT data.
- h) Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.
- i) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- j) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).
- q) For spectrograms showed in spectral viewer and the sensors showed in MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing spectrogram, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- r) Use the spectral viewer to inspect each spectrogram. If required or necessary, marking trials, channels bad. For details, see Spectral Analysis Guide.

- s) For each spectral dataset, you click the “Select All” to select all the spectral data. If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.
- t) For each source scan for a spectral dataset, the program will generate a volumetric source image with at least one time-slice and one frequency band.
- u) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the “Refresh” button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

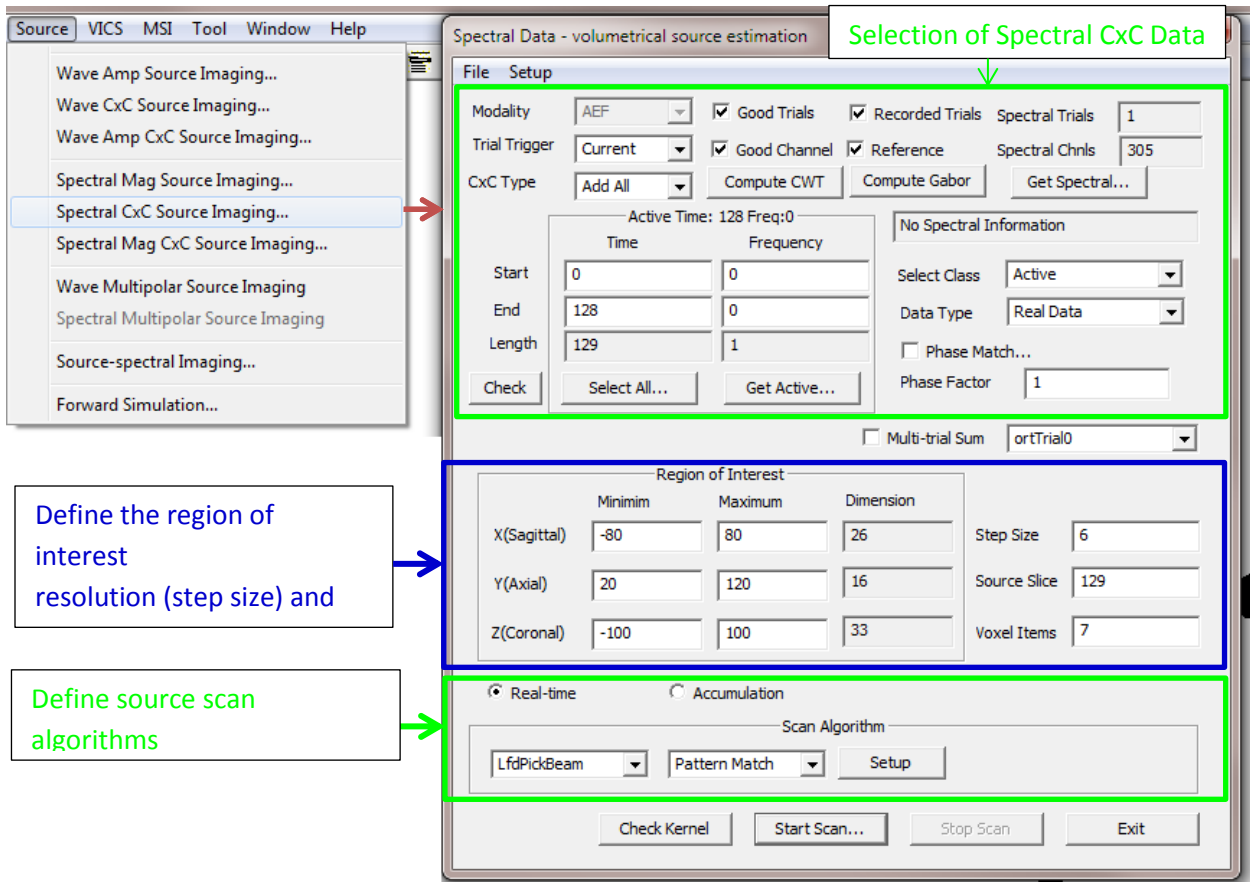


Figure 7. Spectral CxC Source Scan.

Main Module in Spectral Mag (magnitude) Source Scans

The full suite of spectral source scan comprises the following components.

- ❖ Spectral Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution

- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target spectral data (Time-frequency windows)

The data selection specifies the time-frequency ranges for source scan. The trial, channels and time-window are supposed to be appropriately determined during spectral computing. Therefore, all the spectral data are assumed to be appropriate for source scan. The time-frequency window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing.

By default, source scan will integrate the selected data in the spectral viewer into the source scan matrix unless one or more time windows are specified, in which case only spectral data within the time-frequency ranges are used. Time-frequency windows are defined relative to some event in the, which has been discussed in waveform source scan. The spectral data are linked to waveform data, therefore, the temporal information is available for users to track the time or latency.

If you are generating a single-state image, only active-state time-frequency windows can be defined. If you are generating a dual-state image, both active- and dual-state time-frequency windows can be defined.

To define a time-frequency window:

- 1) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the spectral viewer (single channel-spectral viewer).
- 2) You may click the “Select All...” to select all data points.
- 3) To use the control data, you must select “Compute Control” checkbox.
- 4) The Check Select will check the selection of the data.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 1) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 2) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control spectral data for source scan.

Storage of source images

For source images based on one trail, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared to the common mode.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan.

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Computes covariance of data if necessary
- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-frequency-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth

- 7) Computes two sets of source time-series for source peak (maxima)
- 8) Finds and marks peaks in the source data.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

Analyzing Source Images

Volumetric source scan is a unified analysis for MEG/EEG data (without the uncertainties of dipole fitting) in which the locations of brain activation or spike activity and the source activation/activity from those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio, co-registered with the subject's MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

- Misidentification or lack of identification of spikes if they have insufficient amplitude relative to background brain activity and noise.
- Erroneous results from a dipole fit where the topography of visible spikes is not strictly dipolar due to activation of a large cortical area.
- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

Spectral Mag CxC Source Imaging

The "Spectral Mag Source Imaging" launches the main window for localizing sources with spectral data and generates a volumetric source image, which may have multiple time slices. This source localization method mainly utilizes the magnitude of spectral data. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

Source analysis is performed after spectrograms have been computed, reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- k) If there are structural data available, import the MRI/CT data.
- l) Use MSI Studio to check and view MEG sensor and MR/CT data.
- m) Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.

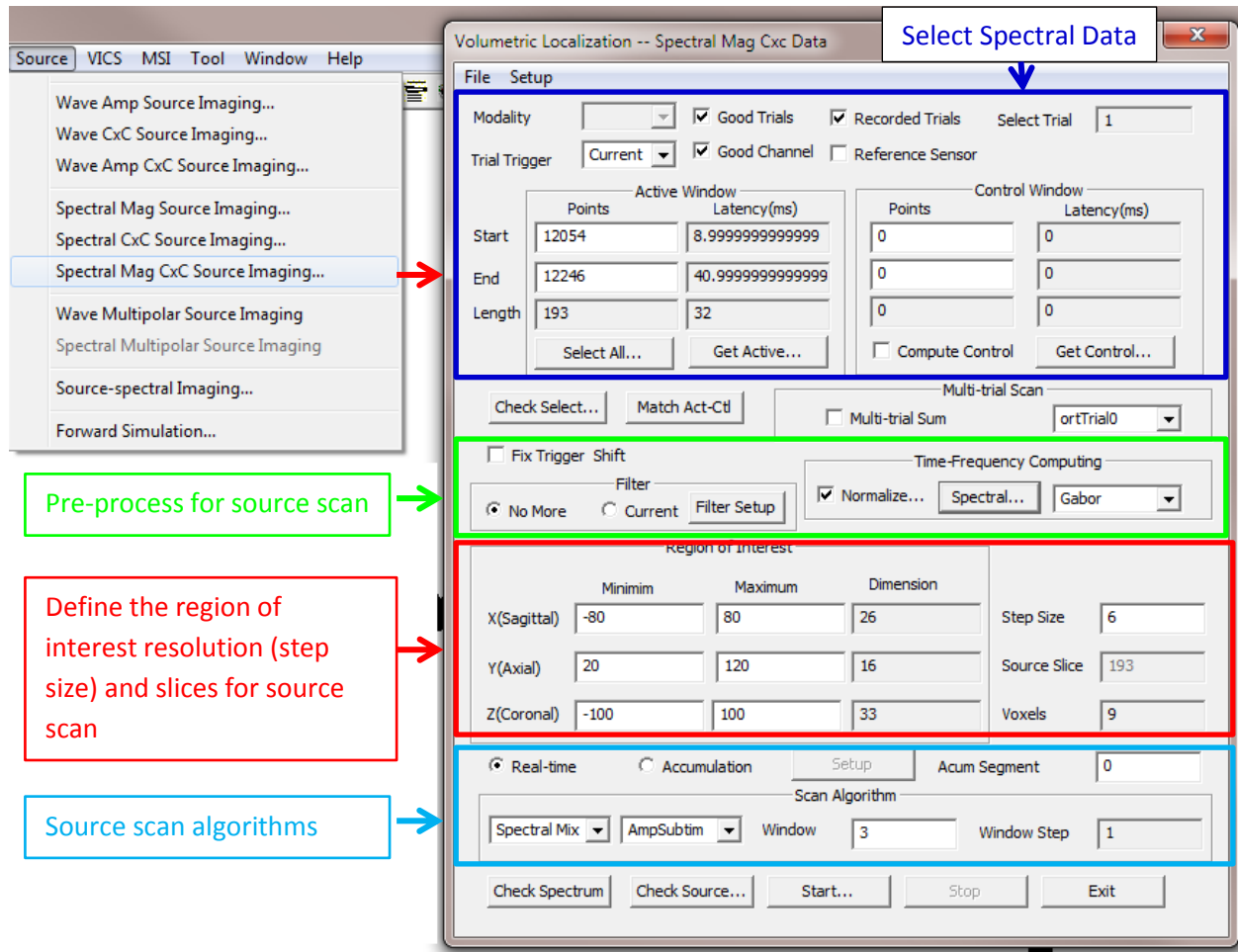


Figure 8. Spectral Mag (magnitude) and Channel-cross-channel (CxC) Source Scan.

- n) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- o) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).
- v) For spectrograms showed in spectral viewer and the sensors showed in MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing spectrogram, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- w) Use the spectral viewer to inspect each spectrogram. If required or necessary, marking trials, channels bad. For details, see Spectral Analysis Guide.

- x) For each spectral dataset, you click the “Select All” to select all the spectral data. If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.
- y) For each source scan for a spectral dataset, the program will generate a volumetric source image with at least one time-slice and one frequency band.
- z) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the “Refresh” button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

Main Module in Spectral Mag (magnitude) and Channel-cross-channel (CxC) Source Scans

The full suite of spectral source scan comprises the following components.

- ❖ Spectral Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution
- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target spectral data (Time-frequency windows)

The data selection specifies the time-frequency ranges for source scan. The trial, channels and time-window are supposed to be appropriately determined during spectral computing. Therefore, all the spectral data are assumed to be appropriate for source scan. The time-frequency window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing.

By default, source scan will integrate the selected data in the spectral viewer into the source scan matrix unless one or more time windows are specified, in which case only spectral data within the time-frequency ranges are used. Time-frequency windows are defined relative to some event in the, which has been discussed in waveform source scan. The spectral data are linked to waveform data, therefore, the temporal information is available for users to track the time or latency.

If you are generating a single-state image, only active-state time-frequency windows can be defined. If you are generating a dual-state image, both active- and dual-state time-frequency windows can be defined.

To define a time-frequency window:

- 5) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the spectral viewer (single channel-spectral viewer).

- 6) You may click the “Select All...” to select all data points.
- 7) To use the control data, you must select “Compute Control” checkbox.
- 8) The Check Select will check the selection of the data.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 3) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 4) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from active state data. To generate a dual-state image, you must select both active and control spectral data for source scan.

Storage of source images

For source images based on one trial, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared

to the common mode.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan.

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 10) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 11) Computes covariance of data if necessary
- 12) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 13) Computes the source power or kurtosis of the source time-frequency-series if necessary
- 14) Finds local maxima in the source image.
- 15) Computes covariance of data in full bandwidth
- 16) Computes two sets of source time-series for source peak (maxima)
- 17) Finds and marks peaks in the source data.
- 18) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

Analyzing Source Images

Volumetric source scan is a unified analysis for MEG/EEG data (without the uncertainties of dipole fitting) in which the locations of brain activation or spike activity and the source activation/activity from those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio, co-registered with the subject’s MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

- Misidentification or lack of identification of spikes if they have insufficient amplitude relative to background brain activity and noise.
- Erroneous results from a dipole fit where the topography of visible spikes is not strictly dipolar due to activation of a large cortical area.
- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

Wave Multipolar Source Imaging

The “Wave Multipolar Source Imaging” launches the main window for localizing sources with waveform data and generates a volumetric source image, which may have multiple time slices. This source localization method mainly utilizes the magnitude of spectral data. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

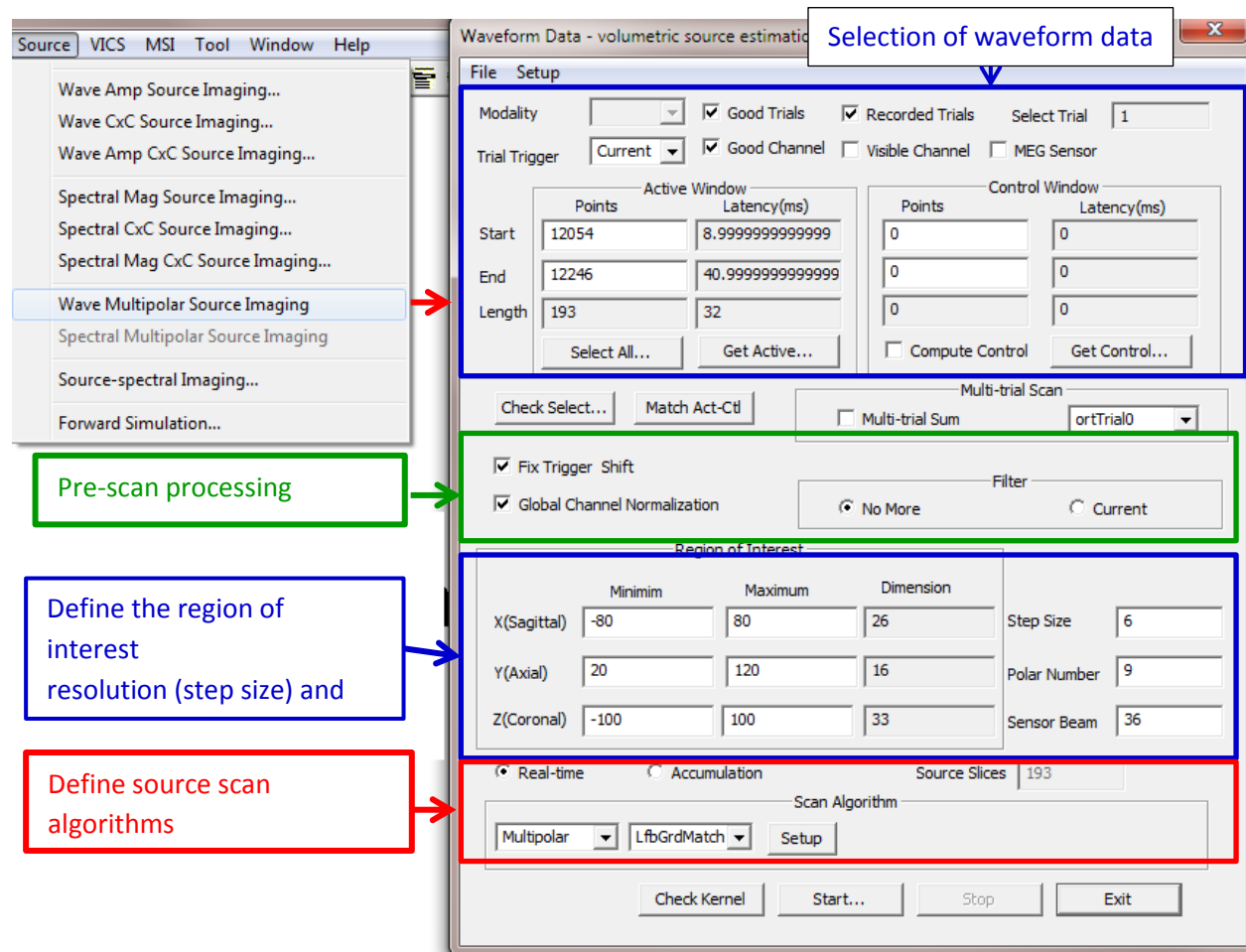


Figure 9. Wave Multipolar Source Scan.

Source analysis is performed after spectrograms have been computed, reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- If there are structural data available, import the MRI/CT data.
- Use MSI Studio to check and view MEG sensor and MR/CT data.
- Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.

- d) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- e) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).
- f) For spectrograms showed in spectral viewer and the sensors showed in MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing spectrogram, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- g) Use the spectral viewer to inspect each spectrogram. If required or necessary, marking trials, channels bad. For details, see Spectral Analysis Guide.
- h) For each spectral dataset, you click the “Select All” to select all the spectral data. If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.
- i) For each source scan for a spectral dataset, the program will generate a volumetric source image with at least one time-slice and one frequency band.
- j) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the “Refresh” button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

Main Module in Wave Multipolar Source Scans

The full suite of spectral source scan comprises the following components.

- ❖ Spectral Data Selection
- ❖ Pre-scan data processing
- ❖ Region of Interest for source scan
- ❖ Source spatial resolution
- ❖ Source scan mode: real-time (e.g. task-based functional activation) or accumulating (e.g. epileptic activity)
- ❖ Source scan algorithms
- ❖ Parameter checking
- ❖ Starting source scan

Target Waveform Data (Time windows)

The data selection specifies the time-frequency ranges for source scan. The trial, channels and time-window are supposed to be appropriately determined during spectral computing. Therefore, all the spectral data are assumed to be appropriate for source scan. The time-frequency window parameters specify active- and control-state time windows relative to named triggers or markers or the trial synchronization time point (typically zero). You may use the “Get...” button to get the selection for either active or control time window. You may also change or add the parameters by typing.

By default, source scan will integrate the selected data in the spectral viewer into the source scan matrix unless one or more time windows are specified, in which case only spectral data within the time-frequency ranges are used. Time-frequency windows are defined relative to some event in the, which has been discussed in waveform source scan. The spectral data are linked to waveform data, therefore, the temporal information is available for users to track the time or latency.

If you are generating a single-state image, only active-state time-frequency windows can be defined. If you are generating a dual-state image, both active- and dual-state time-frequency windows can be defined.

To define a time window:

- 1) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the waveform viewer.
- 2) You may click the “Select All...” to select all data points.
- 3) To use the control data, you must select “Compute Control” checkbox.
- 4) The Check Select will check the selection of the data.

Target region (ROI for Source Scan)

The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

To define a ROI or target volume:

- 1) Enter the start (Minimum) and end (Maximum) values for each axis. (See “Head Coordinate System” in MSI Studio Guide for a description of X, Y, Z coordinates.).
- 2) Set the Step Size (resolution) to the desired value in millimeter. Note: Although it is possible that a strong (spiky) signal that falls between grid points will be missed, a smaller resolution value will significantly increase computation time.

The meaning of the “coefficients” depends on the source localization algorithms.

Single-state or Dual-state Image

The single-state option generates a functional map based on the active state only (i.e., measurements taken when the brain is being stimulated). The dual-state option generates a functional map that results from the subtraction of control-state data (measurements taken when no stimulation is applied) from

active state data. To generate a dual-state image, you must select both active and control spectral data for source scan.

Storage of source images

For source images based on one trial, the results are typically stored with the trial. For source images based on multiple trials, the results, which are typically referred as “sum-images”, are stored in a selected trial. It is necessary to define the targeted trial for storing the results before source scan.

Sanity Checks

If both active and control data are used, the source localization program applies a “sanity check” to differential images to examine whether active and control MEG measurement conditions are well balanced. Differential imaging should cancel out the “common mode” brain activity. This implies that the source difference between active and control states over the entire head should be small compared to the common mode.

Running Source Scan

Click the “Start” button will start to run the source scan. Once it is started, the window title bar will show the progress of the source scan.

The source scan calls several internal dynamically linked libraries to perform a variety of analyses. Here are some steps:

- 1) Generates the multiple-sphere origin information needed for an accurate head model, if necessary.
- 2) Computes covariance of data if necessary
- 3) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 4) Computes the source power or kurtosis of the source time-frequency-series if necessary
- 5) Finds local maxima in the source image.
- 6) Computes covariance of data in full bandwidth
- 7) Computes two sets of source time-series for source peak (maxima)
- 8) Finds and marks peaks in the source data.
- 9) As usual, the resulting volumetric source image is available to be viewed using MSI Studio.

Analyzing Source Images

Volumetric source scan is a unified analysis for MEG/EEG data (without the uncertainties of dipole fitting) in which the locations of brain activation or spike activity and the source activation/activity from those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio, co-registered with the subject’s MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated

and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

- Misidentification or lack of identification of spikes if they have insufficient amplitude relative to background brain activity and noise.
- Erroneous results from a dipole fit where the topography of visible spikes is not strictly dipolar due to activation of a large cortical area.
- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

Source-Spectral Source Imaging

The “Wave Multipolar Source Imaging” launches the main window for localizing sources with waveform data and generates a volumetric source image, which may have multiple time slices. This source localization method mainly utilizes the magnitude of spectral data. The Window GUI application allows you to configure parameters and processing options for source scan as well as other kinds of analysis.

Source analysis is performed after spectrograms have been computed, reviewed and a head shape file created from the MRI/CT or digitalization devices. Here is the recommended procedure for a standard analysis using waveform source localization programs:

- a) If there are structural data available, import the MRI/CT data.
- b) Use MSI Studio to check and view MEG sensor and MR/CT data.
- c) Use MSI Studio to designate the nasion and bilateral pre-auricular fiducial marks to agree with the positions of the MEG/EEG System head coils or fiducial points.
- d) If necessary, use MSI Studio to create a head shape data containing only the head boundary voxel coordinates.
- e) If MRI/CT data are not available, you may use MEG sensor array and its spatial relationship to the MEG/EEG fiducial points to define a region of interest (ROI).
- f) For spectrograms showed in spectral viewer and the sensors showed in MSI Studio, the source localization program will automatically create a realistic head model. Noteworthy, the program modules for viewing spectrogram, sensor array (Dewar) position and the MRI/CT fiducial points are internally linked.
- g) Use the spectral viewer to inspect each spectrogram. If required or necessary, marking trials, channels bad. For details, see Spectral Analysis Guide.
- h) For each spectral dataset, you click the “Select All” to select all the spectral data. If specific time windows or active and control states are designated, then a time window parameter file containing these specifications must be given appropriately.

- i) For each source scan for a spectral dataset, the program will generate a volumetric source image with at least one time-slice and one frequency band.
- j) The source images will be available to analyze by MSI studio. If the source images are not visible, please click the “Refresh” button. Alternatively, you may launch/re-launch the MSI Studio Window; it will automatically check and show the newly computed source images.

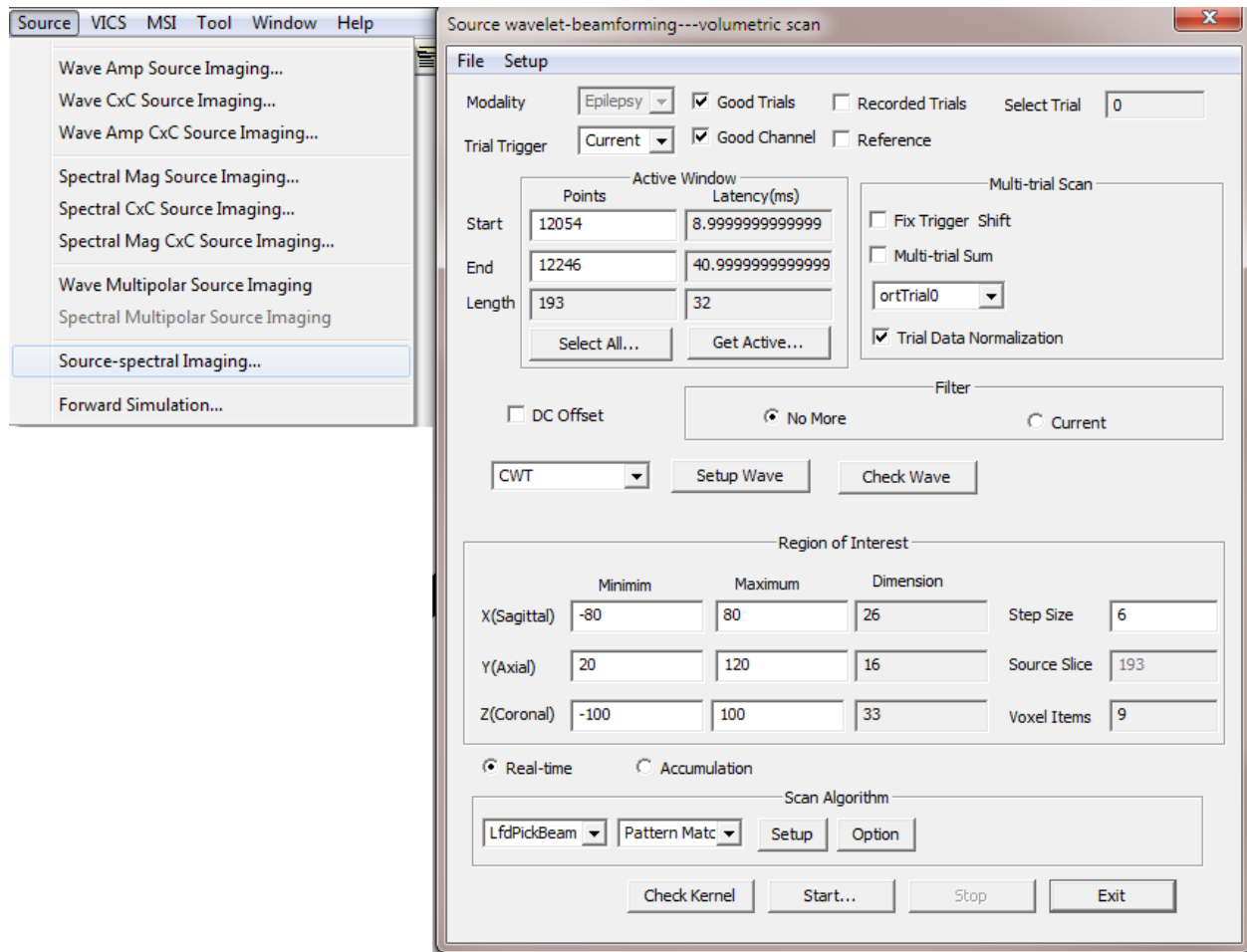


Figure 10. Source-Spectral Imaging.

Main Module in Source-spectral Scans

The full suite of spectral source scan comprises the following components.

- ❖ Spectral Data Selection
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- ❖ Source spatial resolution

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If you are generating a single-state image, only active-state time-frequency windows can be defined. If you are generating a dual-state image, both active- and dual-state time-frequency windows can be defined.

To define a time window:

- 5) Click the “Get Active” or “Get Control” button (Active States or Control States) to get the selection in the waveform viewer.
- 6) You may click the “Select All...” to select all data points.
- 7) To use the control data, you must select “Compute Control” checkbox.
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The Image Dimensions panel provides options for specifying which voxels to use when computing an image. The minimum and maximum volumes in the X, Y and Z directions specifies the bounding coordinates of the target volume cube, or region of interest (ROI) in millimeters. The dimension values define the grid size in voxel unit. This target volume contains a 3-D grid of points, separated on each axis by the specified Resolution, or step size. To generate volumetric source image, each voxel within the specified ROI will be evaluated. In other words, the region of Interest for source scan defines a volumetric grid or 3D grid with a list of coordinates for which a set of source coefficients are to be computed.

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- 11) Computes covariance of data if necessary
- 12) Computes sensor lead fields and/or weights on a grid of points throughout the head.
- 13) Computes the source power or kurtosis of the source time-frequency-series if necessary
- 14) Finds local maxima in the source image.
- 15) Computes covariance of data in full bandwidth
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those locations are estimated from the data. A source analysis generates a volumetric image of the source activity (time-series) throughout the brain. This source image file can be viewed using MSI Studio, co-registered with the subject's MRI/CT. Markers corresponding to local peaks in the image may be loaded into MSI Studio from one of the weights files generated by the program. The source time-series for these locations can be viewed by animating each time-slice. Viewing the source activity enables identification and characterization of spike activity, and gives relative timing of brain activation and/or spikes when more than one spike locus has been found. The volumetric analysis method is automated and unbiased. Besides automating the process of localizing brain activity, volumetric source scan also reduces the risk of error compared to the manual process. For example, dipole fit based on visual identification of spikes is prone to the following errors:

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- Failure to fit one or more dipoles when signal-to-noise ratio (SNR) is poor, and inability to signal-average spikes due to non-stationarity
- Erroneous choice of baseline when performing a dipole fit.

3D Coordinate Systems in Source Reconstruction

The spatial volume of the brain can be represented in a variety of three-dimensional coordinate systems. All forms can be expressed as points in three axes: (x, y, z). The issues are the location of the origin and the orientation of the axes. At various times, the source localization software may need to work with data from any of the following systems:

- 1) MEG/EEG system, based on the fiducial points.
- 2) MRI/CT system, based on the image slice orientation.
- 3) Digitizer: such as Polhemus "raw" system based on the digitizer's transmitter location and orientation.

Each has their own distinct coordinate systems. Co-registration is needed for the system to translate locations to a common reference. The common reference used is the head coordinate system. The head coordinate system sets the origin and axes orientation on a reference determined by the three head localization coils: the left preauricular fiducial point (green), right preauricular fiducial point (red), and nasion (blue). The origin is defined as the midpoint between the left and right preauricular fiducial points. This means the head coordinate system uses both positive (to the patient's left) and negative values (to the patient's right).

Talairach Coordinates and Atlas Support

By specifying AC, PC, and the brain extensions, results can be transformed into Talairach coordinates and extensive anatomical and functional atlas information (Brodmann areas) can be accessed..

Anatomy-based Coordinates

Landmarks (Nasion, Pre-auricular points) and brain extensions serve for anatomy-based coordinate output. Output coordinate systems can be changed and co-registered with other modality at any time.

Co-registration of Coordinate Systems in Source Localization

Co-registration is the process of defining a common reference so that objects can be mapped from one system to the other. The fiducial points are used as the common reference for all 3D data in the source localization software. When the system knows their location in each coordinate system, it can translate points between the two.

Co-registering with MRI/CT Data

The MSI Studio application is used to mark the fiducial points on the image to co-register with the head localization coil positions stored with the MEG/EEG dataset. Having the fiducial points indicated in the MRI/CT requires the placement of MRI/CT (radiological) contrast markers on the fiducial points prior to recording the MRI/CT. These markers appear as distinctive bright ovals or rings on the image.

Co-registering with Digitized Data

The position of electrodes in EEG typically localized with Electrode Digitizer, whose application software typically requires that you digitize the head coordinates (fiducial points) before collecting electrode location or head shape data. This same application performs the necessary coordinate translation to yield data files in the head coordinate system.

Head Model

This software can perform source reconstruction using the well-known spherical shell head models. In addition, one of its unique and powerful features is to generate a high-resolution realistic head model based on anatomical information. Such a realistic head model derived from individual MR Images (or CT) increases the localization accuracy of source analysis. A built-in procedure performs fully automatic generation of the realistic head model geometry (triangle nets) from T1-weighted MR images. This software also comes with pre-computed realistic head models, which have been developed with a normative database in different age groups. The head models are applicable to all EEG data, including an FEM mesh with anisotropic skull layer.

Averaged Structural Data (Templates)

MRI/CT data files may be averaged to create an averaged database. Normalization using Talairach space allows the differently sized brains to be averaged together with minimal distortion.

Volumetric Source Reconstruction and Dipole Fit

The new version of software performs volumetric source reconstruction instead of the conventional dipole fits. To ensure the quality and visibility, all source localization algorithms will generate a volumetric source image, which can be considered as an image with millions of “dipoles” or multi-value-voxel, which is significantly different from the conventional equivalent current dipoles. By selecting waveform source localization, the software can do advanced “dipole fitting”. Dipole fit is based on the measured EEG and/or MEG data, the sensor positions and the head model, a fit of one or more dipoles can be done. The position of the dipoles can be completely free (moving dipole) or can be restricted (rotating or fixed dipole, mirror or regional constraints). Source reconstruction can be constrained to stay in the vicinity of a given region (see the description of spatial region of interest). Thus, it is possible to include prior knowledge from imaging modalities such as fMRI, PET, or SPECT.

Source Reconstruction and Source Localization Algorithms

The description of source reconstruction in the new version of the software is based on the data such as waveforms, spectral data. It is important to clarify that each source localization methods have implemented and optimized a set of source localization algorithms. Those algorithms can be found in the professional version of the software.

Current Density Reconstructions (CDR)

A current density map is an independent analysis. It computes a current pattern on a regular 3D grid or the cortex that would explain the measured EEG or MEG at a certain time point. Now, all points on the surface can be active simultaneously. In order to come up with a solution, additional assumptions are needed. For example, the minimum norm constraint (L1, Lp, or L2 norm), maximum smoothness constraints (LORETA), and statistical measures (sLORETA) can be applied. SWARM can also be applied providing a sLORETA-weighted minimum-norm CDR.

Goodness of Fit, Deviation and Beamformer Scans

During a scan, many locations throughout the brain are considered. For each location, a measure is calculated for the possibility that activity in that location could account for the measured EEG or MEG signal. Deviation scans determine if a dipole in this location would be correct. Beamforming is a technique that increases the spatial selectivity for each location.

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