# SPAMALIZE's Cerebellum Segmentation routine.

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## Introduction:

This program attempts to segment the cerebellum from the whole brain. It was designed to work on T1-weighted MRI images that have the following tissue signal relationship:

background < CSF < GM < WM.

It will probably work on other data (CT, MRI T2-weighted) but you would have to examine the signal from each tissue type and perhaps make some minor adjustments to the code. This program was specifically designed to process single-spectral MRI data; if multi-spectral data also exist (e.g. T1 AND T2- or PD-weighted MRI) there are other approaches which may work better.

The inputs to this program are as follows:
1) T1-weighted MRI (ANALYZE format).
2) Whole-brain mask, including cerebellum (ANALYZE format).
3) Thresholds indicating boundaries between tissue types.
4) Locations of selected points defining cerebellum and brainstem.

This program is approximately 90% accurate. It has problems with the most superior portion of the cerebellum, and with mid-level posterior regions. Some hand editing is usually necessary, particularly if the data are noisy or have a low dynamic range. It takes approximately 10 minutes per cerebellum, with a breakdown of the tasks as follows:
1) (1 min) Load data, set threshold levels.
2) (2 min) Select reference points.
3) (1 min) Run cerebellar segmentation algorithm.
4) (6 min) Edit cerebellar mask. This step can take up to 45 minutes.
I am not particularly pleased with this program, because the results are quite variable; sometimes it works well and other times not. At the very least it saves you about half of the time required to draw the cerebellum completely manually, and also provides criteria for severing the brainstem. At best it takes a few minutes and requires minimal editing, but these instances can be few and far between, particularly if you are in a hurry…

Upon completion, a new mask-file is created, containing the whole-brain and the cerebellar mask. The volumes of the whole-brain, brain less cerebellum, and cerebellum are printed in SPAMALIZE's information window (cubic cm).

**Data Inputs:**

1) T1-weighted MRI (ANALYZE format).
Load this image volume into BrainMaker when you begin. We normally use a MRI volume with dimensions of 256 x 256 x 124 (x, y, z), which always covers the entire brain and usually includes the entire cerebellum. If part of the cerebellum is missing, the accuracy of this program may suffer. The image data should have the following tissue signal relationship:
background < CSF < GM < WM.

2) Whole-brain mask, including cerebellum (16-bit ANALYZE format).
This is usually created using the "Brain Stripper" program in SPAMALIZE. The mask volume should be the identical size as the MRI volume. Brain areas (including GM, WM, CSF, ventricles, cerebellum, brainstem, and perhaps surface blood vessels) should have a value of "1", all other values should be 0.
Load this volume by clicking on the "Anatomy" button in BrainMaker's small main menu, then select "ROI- File -> Find File" and browse for the whole-brain mask. It is usually named something like "MRIfile_wb_mask.img".

SPAMALIZE will read the file and scan it for valid ROIs. An entry for "Whole_brain" should appear in the Anatomy menu. Select "Both", then select "ROI- Current -> Extract from Group" to extract the whole-brain mask to the current working mask. You may edit the whole-brain mask if you wish at this point. Move the "Anatomy" menu toward the bottom of the screen.

3) Thresholds indicating boundaries between tissue types.
Select "Segmentation" in BrainMaker's small main menu. If the MRI has been processed, the tissue boundaries will be read from the corresponding text-file and displayed. You need to re-set the boundaries as follows:
- CSF/GM: Set just on the left lower shoulder of the GM peak.
  We want to include as much CSF as possible in the CSF search.
- GM/WM: Set on the right lower shoulder of the GM peak. We want to
  include as much WM as possible in the WM searches.
  Typically, cerebellar WM does not appear as bright as mid-brain WM.
- WM/Top: Set just above the right shoulder of the WM peak.

Set the boundaries by clicking with the mouse at the desired location (left button:CSF/GM; middle button: GM/WM; right button: WM/Top), by editing the associated text-boxes, or by clicking on the text-box arrows.

4) Locations of selected points defining cerebellum and brainstem.
Within the Segmentation menu, select the button that says "Smooth". From the pop-up menu, select "Find Cerebellum". For each point in the pop-up menu labeled "Reference", place the BrainMaker cursor over the point, and then click on the "Set" button to accept the coordinates. (The location criteria are defined in another section.)

To display (go to) any of the reference points after they have been set, select the "Show" button. To save the coordinates to a text-file, select "Save". If the file already exists and contains reference points, you will be warned, but you can overwrite the existing points if you wish.

**Algorithm Steps:**

Following is a short description of each of the steps performed by this algorithm. For more details refer to the source-code, which is liberally commented.

1) Check data. Make sure MRI and mask data have been loaded, reference points have been selected. Get histogram threshold levels.

2) Extract sub-region of MRI and mask based on reference points.

3) Sever the brainstem. Remove pixels from cerebellar mask if they are above a line drawn between the anterior and posterior brainstem points. Remove mask pixels above and anterior to the anterior brainstem point.

4) Make a "roof" over the cerebellum defined by lines drawn from the superior cerebellum point to the Left and Right cerebellar points. Points above the roof are excluded from the mask.

5) Remove temporal lobes if they intrude behind cerebellum anterior point. The largest single object in the lower planes is called cerebellum.

6) Extract lower part of cerebellum. Assume that all of the tissue in the "whole_brain" mask below the lowest of the user-selected points for the left, right, and posterior cerebellum points are either cerebellum or brainstem. This forms the basis for the cerebellar mask.

7) Extract all of the White Matter (WM) in the sub-region using histogram thresholds. Add WM to cerebellar mask.

8) Remove all WM that intrudes or dangles from the roof. This is usually WM in the brain cortex, not the cerebellum. If a strip of WM is connected to the lower part of the cerebellum it is not removed.

9) Fill in the WM mask with a morphological "fill" (dilate/erode) operator. This connects all of the WM regions and fills in the GM regions between them.

10) Expand the cerebellum up to the CSF boundary with the brain in the coronal view. This is the most important step to define the upper cerebellar boundary. Frequently it will reach into the brain, so all pixels above the roof are removed from the mask.

11) Expand up to CSF in sagittal view for region surrounding the superior cerebellar point.

12) Remove all CSF from mask.

13) Remove vertical "shafts" protruding upwards.

14) Remove (clean) small isolated regions of mask, then fill in the mask.

15) Make sure that below the lowest brain point, the cerebellar mask exactly matches the original brain mask. This ensures that the cerebellum is not too large relative to the whole brain mask. Errors in the whole brain mask will thus be carried through to the cerebellar mask in this area.

16) Store the cerebellum into the original mask. Then save to a new file containing the whole-brain and cerebellum ROIs. Editing should happen to the new data. Make sure edits do not stray outside of the whole brain ROI.

**Display:**

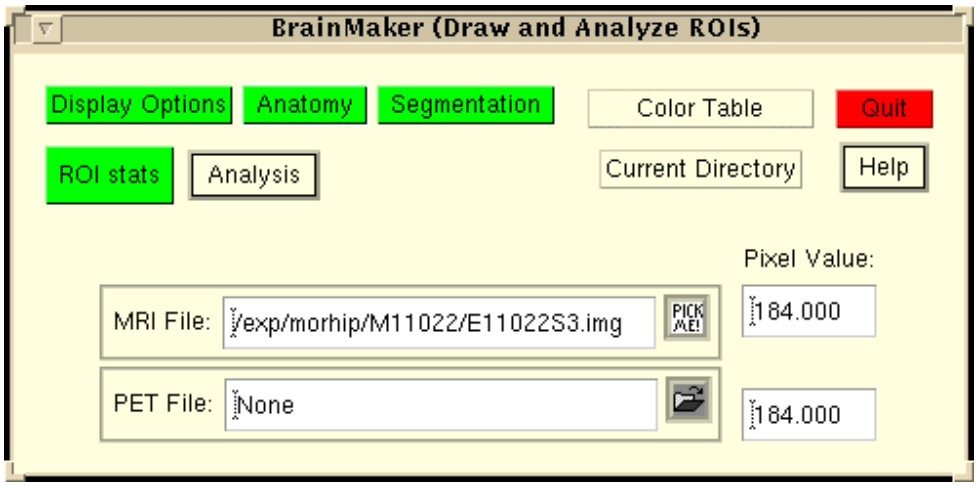
Displaying the images is useful for understanding what the program does, and also as a troubleshooting aid in case it does a less-than-acceptable job. On a SUN/Ultra2, the algorithm takes 50 seconds without display, and 3 minutes with display.

All of the steps are listed below, with an indication of whether or not the step will be displayed if you select the "Display" flag from the menu. It is easy to display more (or fewer) steps by simply changing the appropriate flags in the source-code.

| | |
|---|---|
| 1) Check data. | No display. |
| 2) Extract sub-region. | No display. |
| 3) Sever brainstem | Displayed. |
| 4) Make "roof". | Displayed. |
| 5) Remove temporal lobes. | No display. |
| 6) Extract lower cerebellum. | No display. |
| 7) Extract WM. | Displayed. |
| 8) Remove dangling WM. | Displayed. |
| 9) Fill WM mask. | No display. |
| 10) Expand to CSF (coronal). | Displayed. |
| 11) Expand to CSF (sagittal). | Displayed. |
| 12) Remove CSF. | Displayed. |
| 13) Remove vertical "shafts". | No display. |
| 14) Remove isolated regions. | No display. |
| 15) Match original brain. | No display. |
| 16) Store into original mask. | No display. |

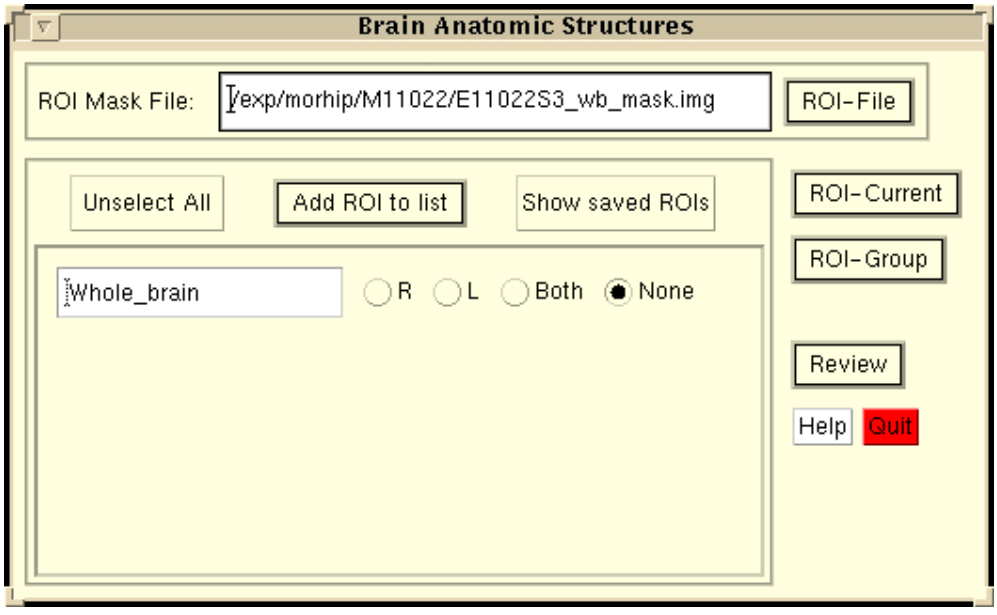
**Example with menu selections**

This section shows all of the menus needed to run the Cerebellum Segmentation program, and also shows various parameters and locations that are needed. The menus appear in the order they are used or needed, and demonstrate how to segment the cerebellum from a sample brain.




The menu above shows BrainMaker's small main menu. When you start BrainMaker, you must first load in a MRI image volume in ANALYZE format. (Refer to the Help button for more details.) Click on the flashing "Pick Me!" button, and browse for the MRI file.

After it has been loaded and displayed, you must load a whole-brain mask file. Select the "Anatomy" button from the above menu. The following menu will appear. Move it to the bottom of your screen.

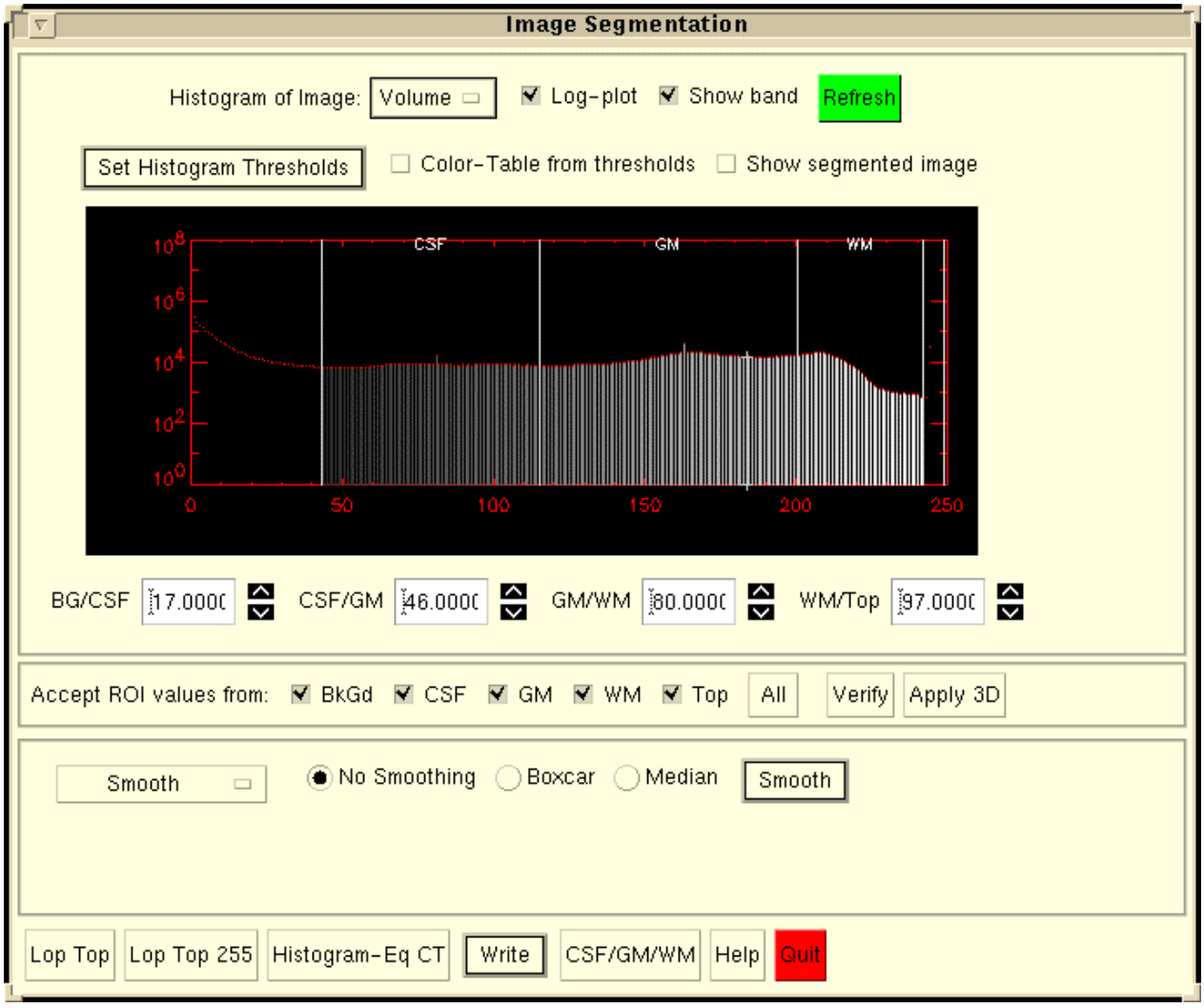



Select the button "ROI- File", then choose "Find File" from the pop-up menu.

Browse for a previously created whole-brain mask. It is usually named something like /pathname/MRIfilename_wb_mask.img .
If you do not have a whole-brain mask, you need to stop and create one using BrainStripper. When you select a whole-brain mask, SPAMALIZE will scan it to see what types of ROIs are stored in it. If it is a simple whole-brain mask, you should see a row with the label “Whole_brain” as in the menu above. If there is not a whole-brain mask in the file, you may see a message like “No ROI currently loaded”. This means you have to stop and go to BrainStripper. (All roads lead to Rome…)

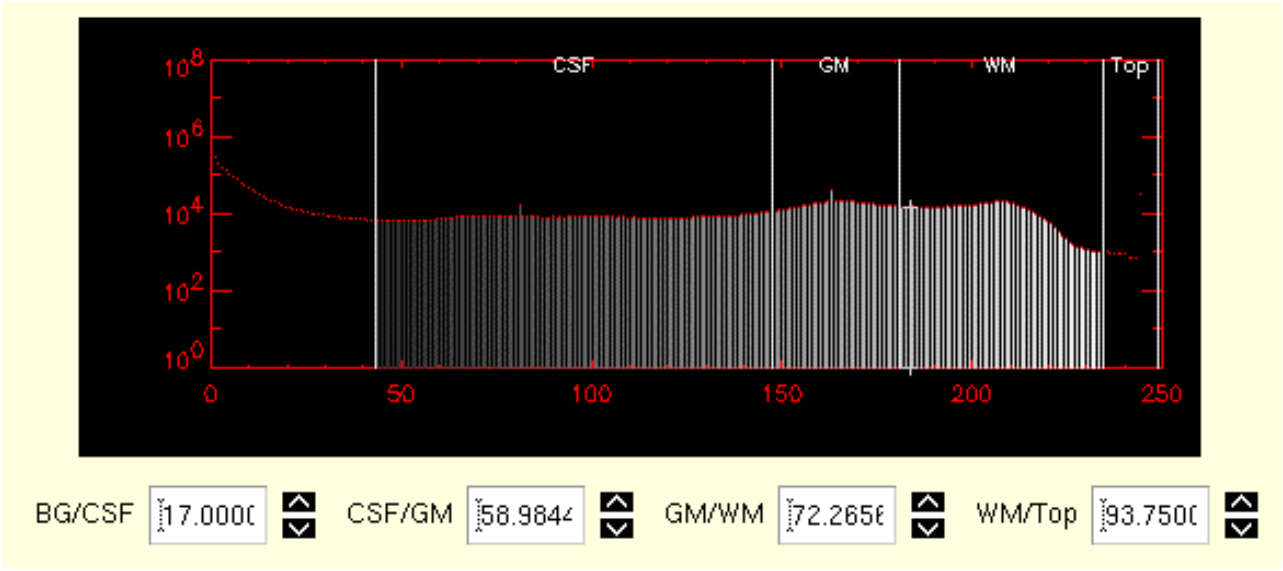
Now you need to extract the whole-brain ROI from the file so SPAMALIZE can work with it. Click on “ROI- Current” and select “Extract from Group" to extract the whole-brain mask to the current working mask. You should see an outline of the brain in red on the images. You may edit the whole-brain mask if you wish at this point. (Remember to save any changes.)

The next step is to set the thresholds that separate each tissue type.
Select "Segmentation" in BrainMaker's small main menu. If the MRI has been processed, the tissue boundaries will be read from the corresponding text-file and displayed. The thresholds typically appear as in the following histogram:

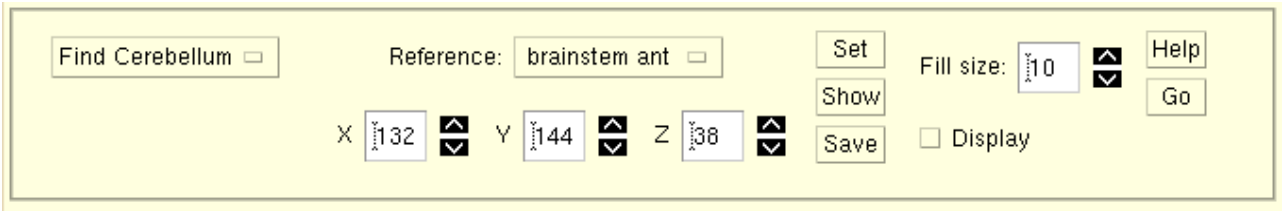


You need to re-set the boundaries as follows:
- CSF/GM: Set just on the left lower shoulder of the GM peak.
  We want to include as much CSF as possible in the CSF search.
- GM/WM: Set on the right lower shoulder of the GM peak. We want to include as much WM as possible in the WM searches.
  Typically, cerebellar WM does not appear as bright as mid-brain WM.
- WM/Top: Set just above the right shoulder of the WM peak.

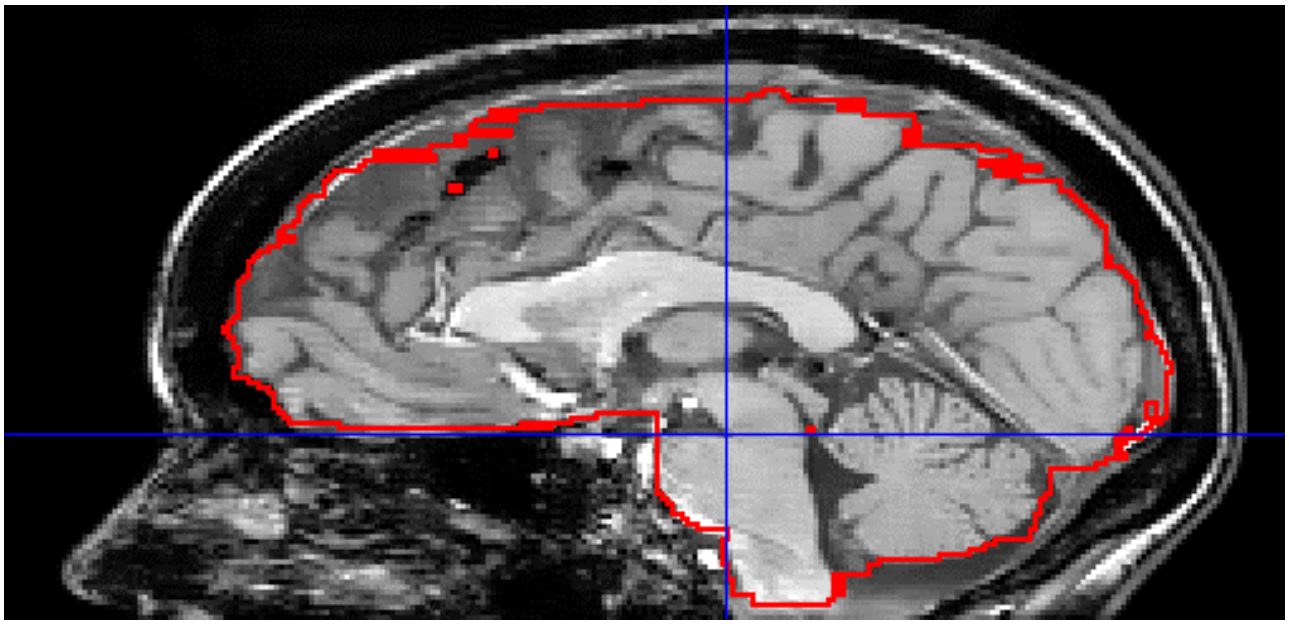
Set the boundaries by clicking with the mouse at the desired location (left button:CSF/GM; middle button: GM/WM; right button: WM/Top), by editing the associated text-boxes, or by clicking on the text-box arrows. The boundaries should now appear something like the following:



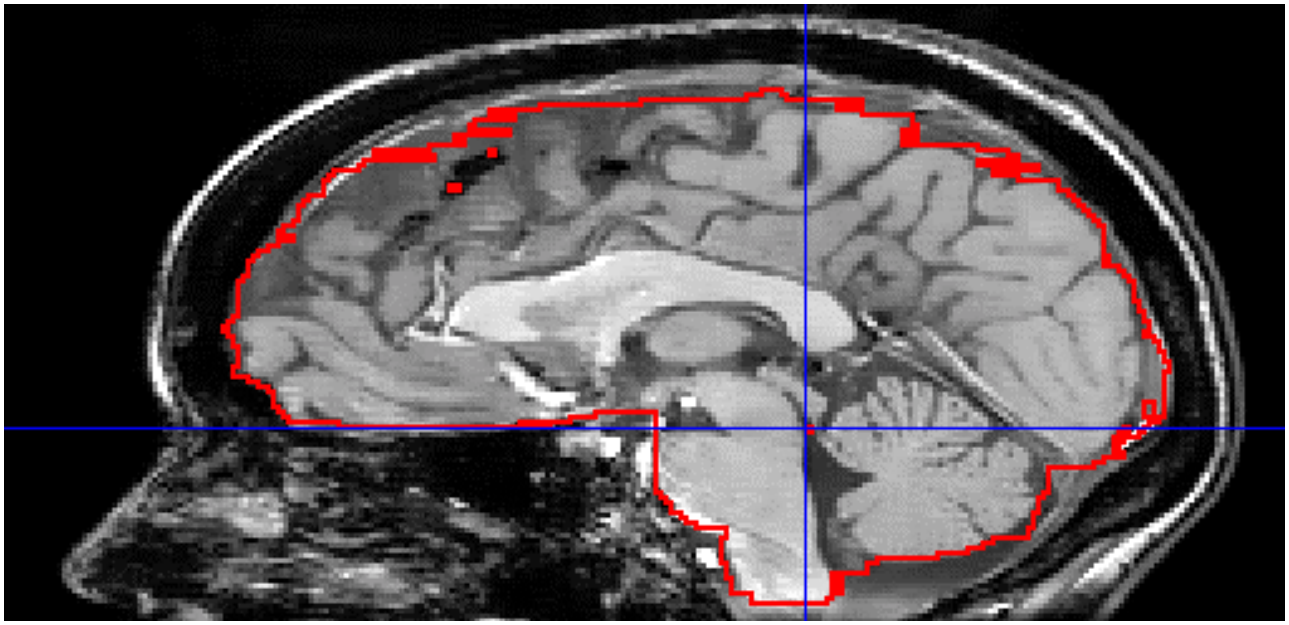

Next, you should go to the “Find Cerebellum” menu. From the Segmentation menu, select the button that says "Smooth". From the pop-up menu, select "Find Cerebellum". You will see a menu that looks like this:



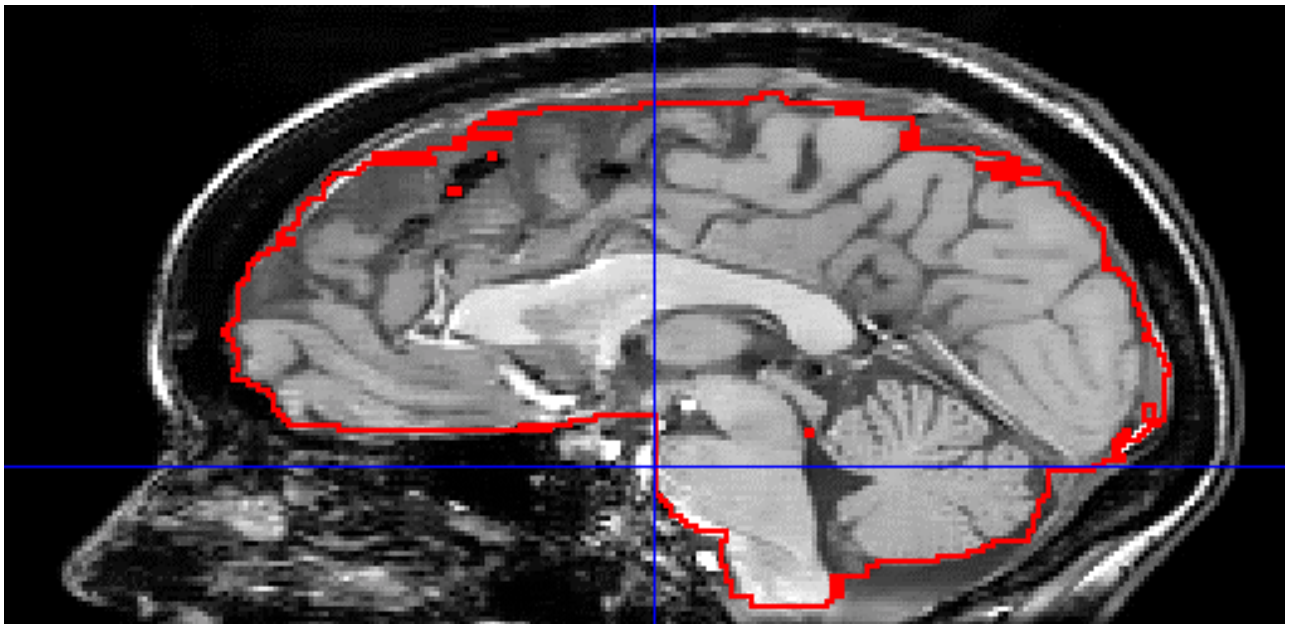

You must find several reference points within the MRI image volume that define the edges of the cerebellum and define where the brainstem will be severed.
For each point in the pop-up menu labeled "Reference", select the point from the pull-down menu. Then, place the BrainMaker cursor over the desired location in any of the three images (axial, coronal or sagittal), and then click on the "Set" button to accept the coordinates. Each of the locations is shown below.



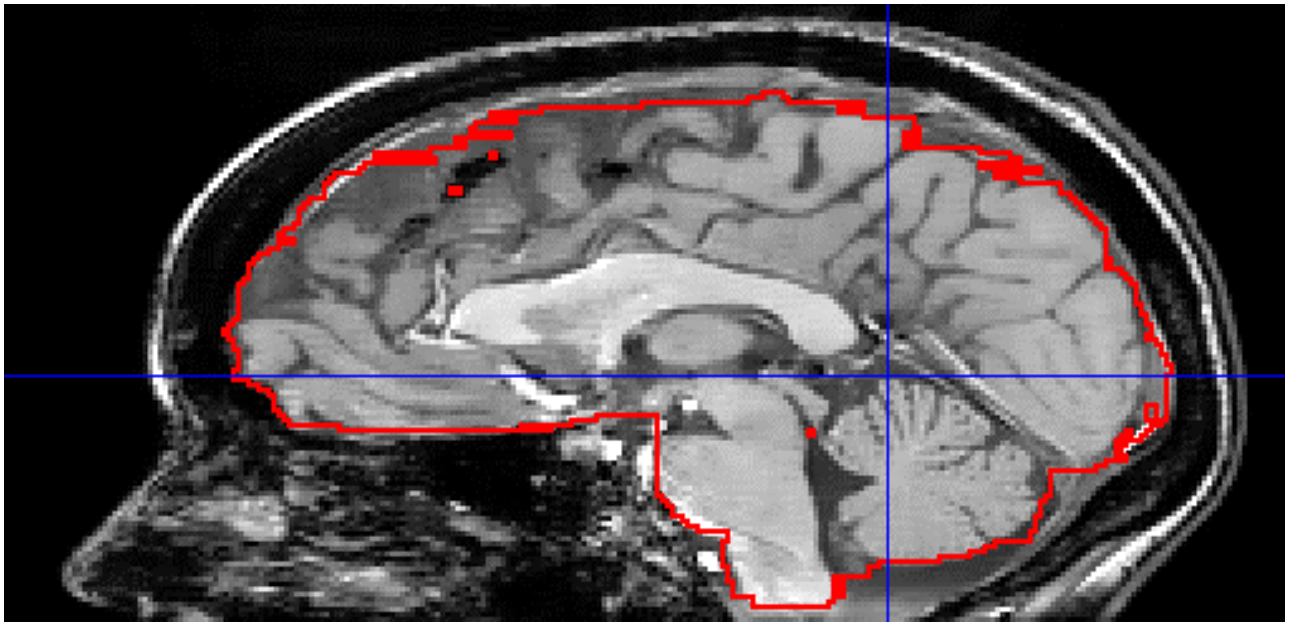
1) brainstem ant : The anterior brainstem location, at the crux of the pons and the brainstem, in the midline plane.



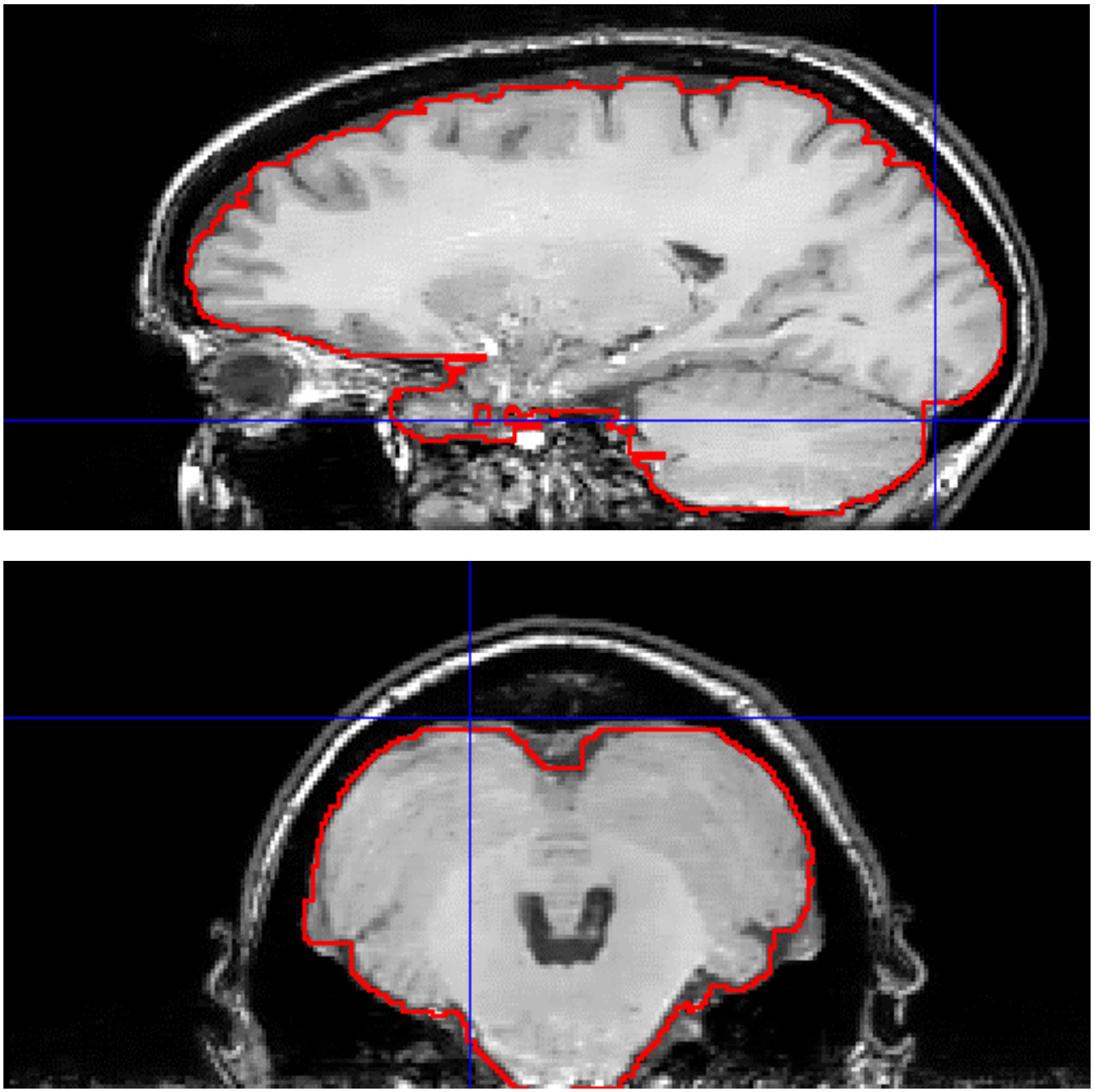
2) brainstem post : The posterior brainstem location, in the midline plane.



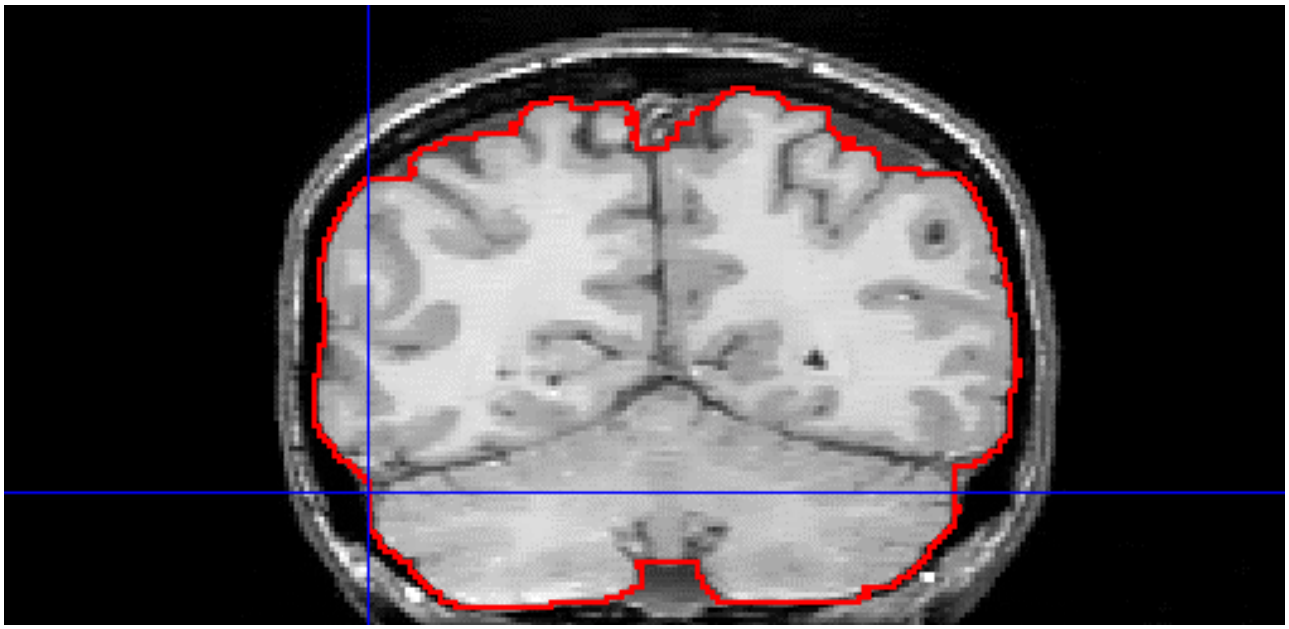
3) cerebel ant : The most anterior portion of the cerebellar volume, which is usually at the tip of the pons. Usually this is in the central plane but not always. If the brain is tilted relative to the cardinal directions of the image volume, this point may not be in the same sagittal plane as the previous two points.



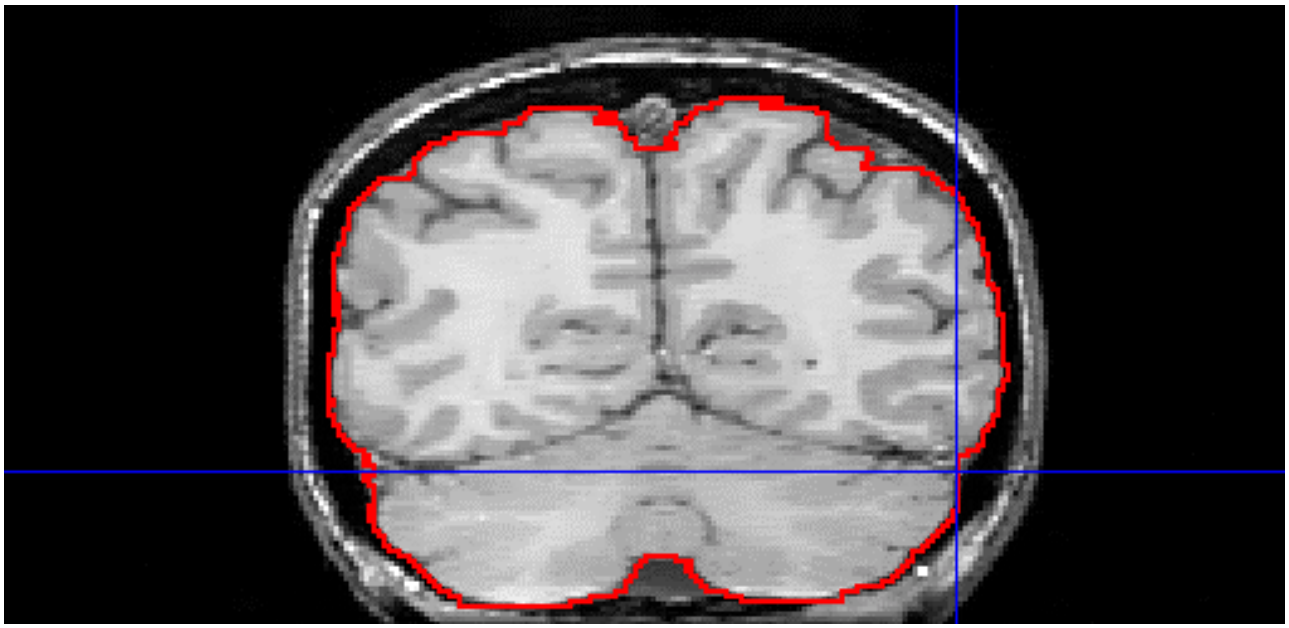
4) cerebel sup : The most superior portion of the cerebellum, which is usually along the midline.



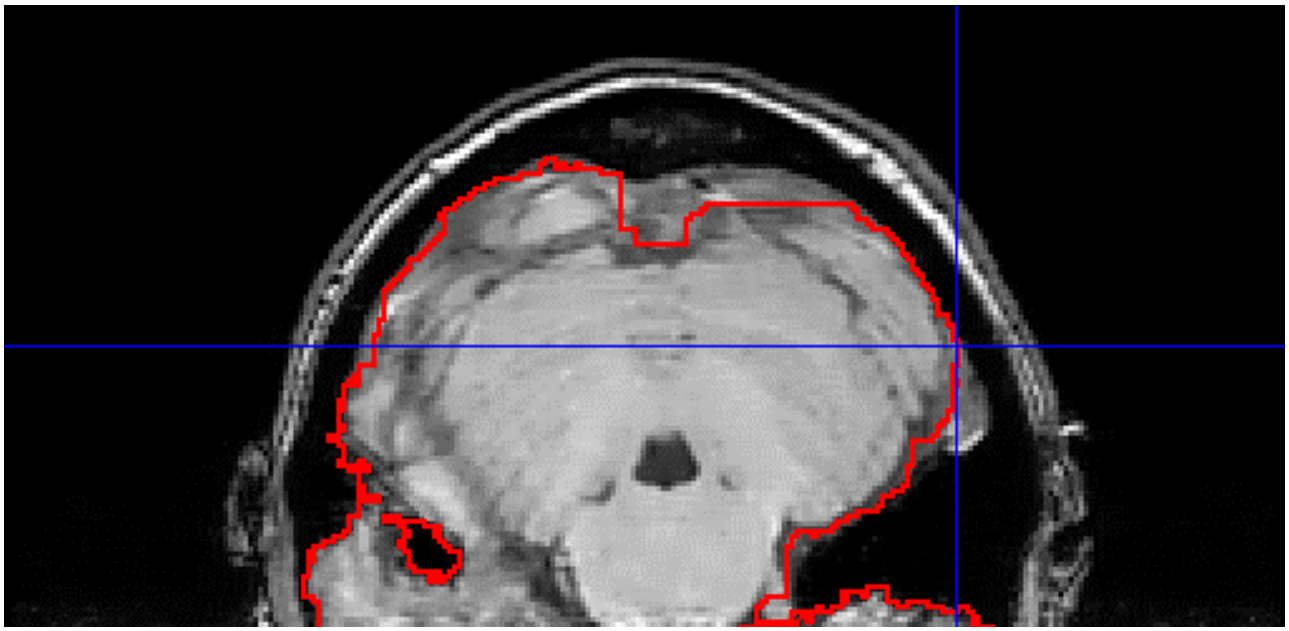
5) cerebel post : The most posterior aspect of the cerebellum. This is usually NOT on the midline, but will be toward one side or the other, as shown in the axial (lower) picture above. Note in the sagittal view how the reference point is positioned as high as possible without encroaching on non-cerebellar brain. A good position for the reference point is in the CSF or blood vessel at the location indicated.



6) cerebel L : The Left-most aspect of the cerebellum. This is according to the neurological convention where Left is on the left-hand side of the screen, even if your data are not. Again, note how the reference point is positioned as high as possible without encroaching on non-cerebellar brain. It is a good idea to scan the axial and sagittal views to make sure you are at the extreme left-hand edge of the cerebellum.



7) cerebel R : The Right-most aspect of the cerebellum. This is according to the neurological convention where Right is on the right-hand side of the screen, even if your data are not. Again, note how the reference point is positioned as high as possible without encroaching on non-cerebellar brain. It is a good idea to scan the axial and sagittal views to make sure you are at the extreme left-hand edge of the cerebellum, as shown in the following picture.



The above picture shows the axial view of the Right-most cerebellar point. Note that it does not have to coincide with the edge of the whole-brain mask or with the edge of other brain tissue; we only want to define the edge of the cerebellum.

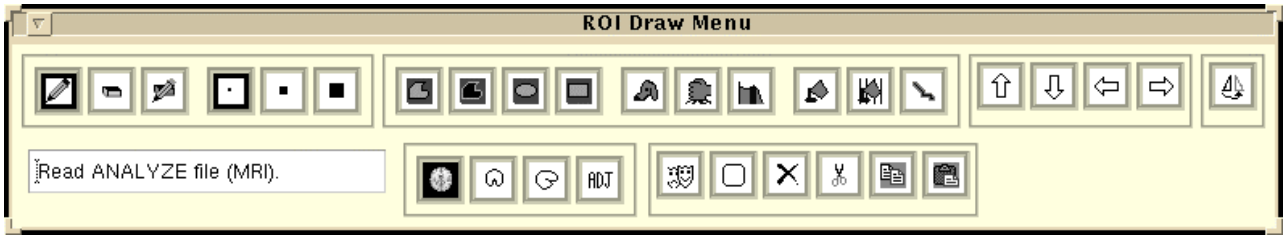
To display (go to) any of the reference points after they have been set, select the "Show" button. To save the coordinates to a text-file, select "Save". It is a good idea to save the points, both to save time if you have to repeat this, and more importantly to document what you did. If the file already exists and contains reference points, you will be warned, but you can overwrite the existing points if you wish. If the file does not exist, or if no cerebellar reference points are contained in it, an informational message will be printed to SPAMALIZE's bulletin board and you can proceed.

If things have gone smoothly, all of the preceding steps will have taken 2-3 minutes.

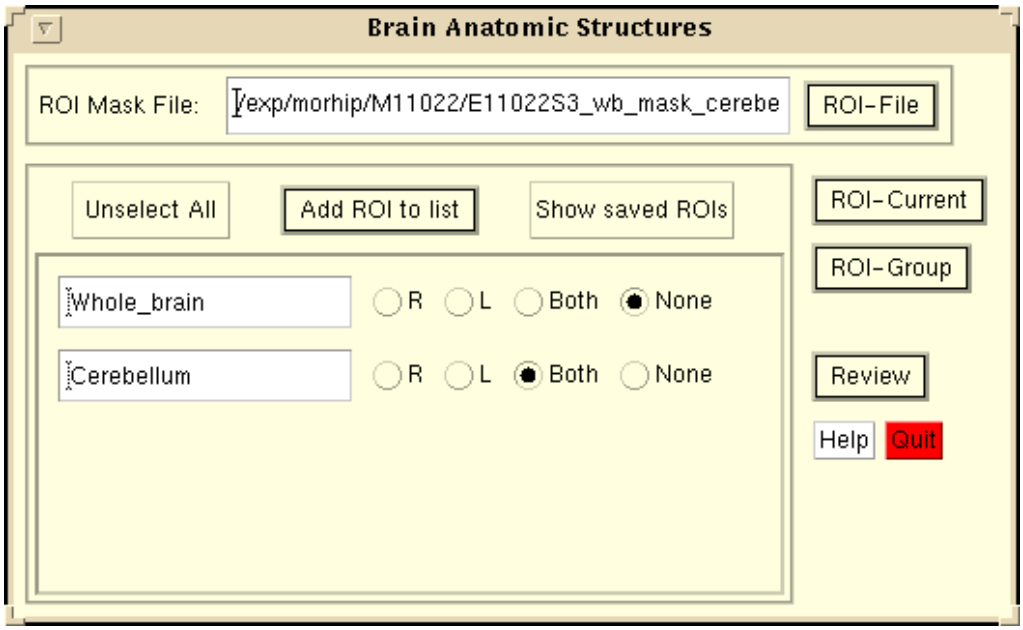
The next step is to actually segment the cerebellum and the lower part of the brainstem and pons. Get your mouse-clicking finger warmed up and select "Go". If you opt not to see the display (the default) the program will be done in a minute or so. If you check the "Display" box in the "Find Cerebellum" menu, most of the intermediate steps will be displayed and it will take approximately 3 minutes to complete.

When the cerebellum has been segmented, the cerebellum Volume-of-Interest (VOI) will be stored in the group ROI volume, and the group ROI will be saved to a new file called something like:
/pathname/MRIfilename_wb_mask_cerebel_000406_112356.img
The final numbers are the date and time (yymmdd_hhmmss) so you cannot inadvertently overwrite other mask files. This file contains BOTH the whole-brain and the cerebellar VOIs. The volumes of the whole brain, cerebellum, and [whole brain – cerebellum] are printed to SPAMALIZE's bulletin board.

To examine your data, you must first delete the whole brain from the current working ROI, then read in the cerebellum from the new group. Select the “X” icon from the icon menu (bottom row, fourth from the right):




Answer “Yes” to the pop-up question that warns you about destroying the current ROI. Really. Now you must extract the Cerebellum from the Group ROI.




Set the “Whole_brain” ROI to “None” and the “Cerebellum” ROI to “Both” (or “Left” will also work). Click on “ROI- Current” and select “Extract from Group" to extract the cerebellum mask into the current working mask. You should see an outline of the cerebellum in red on the images. If you only have the axial view open, you may need to hunt for it. You can open other views by clicking on the axial, coronal, and/or sagittal icons in the icon menu (bottom row, left side).

You may now examine and edit the cerebellum VOI using all of the tools available in BrainMaker. Remember to save!