Coregistration with FireVoxel: Quick Start Guide

FireVoxel is developed by Artem Mikheev and Henry Rusinek
Department of Radiology, NYU School of Medicine
The Guide was prepared on Apr 2014 by Brian Park

FireVoxel (FV) is software for visualizing and analyzing medical images. The main types of data analyzed by FV are:

- 3D volumes from MRI, CT, PET, SPECT, ultrasound acquisitions
- 4D datasets, typically representing a dynamic time series of 3D volumes
- 3D/4D regions of interest (ROIs) linked to above data

wp.nyu.edu/FireVoxel is a web page where you can download the software, tutorials, and sample data.

Introduction

Among its many features, FireVoxel implements several image coregistration tools. Image coregistration refers to the alignment of images across time or different imaging modalities. This document represents a step-by-step guide through the program's coregistration features using three examples: 1) aligning two brain MRIs of the same patient taken four years apart, 2) coregistering MRI and CT of the brain using a more complex algorithm, and 3) aligning MRI and ultrasound of the prostate using anatomical landmarks. This guide refers to FV build 311B.

In FireVoxel, coregistration requires loading two images as separate documents: 1) source (moving image); and 2) target (still image). FireVoxel computes the transform and applies it to the source image. The transformed version of the source image will be resampled in the target space and it will appear as a new layer in the target document

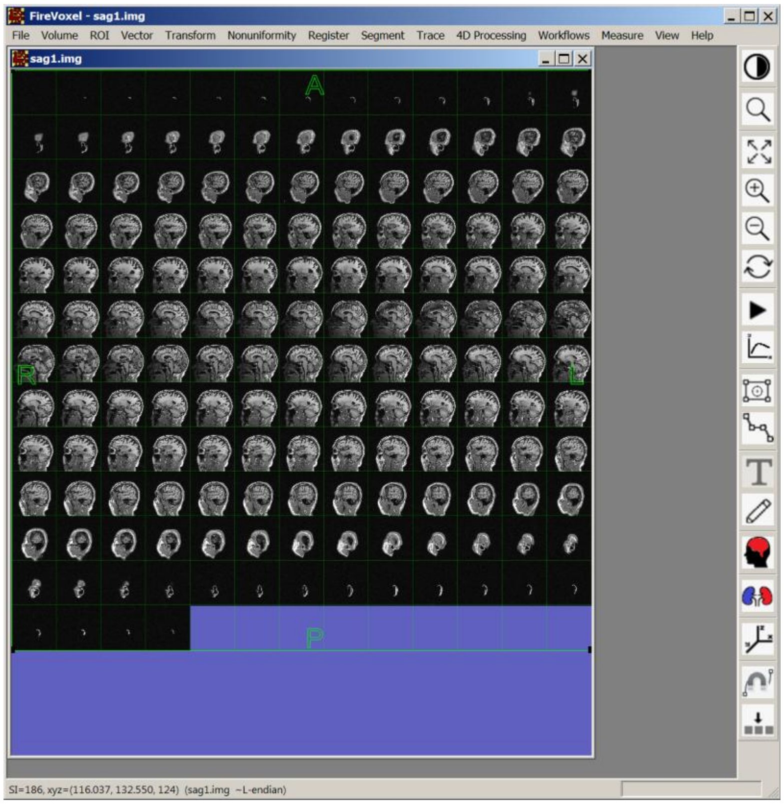
Step 1– LOADING

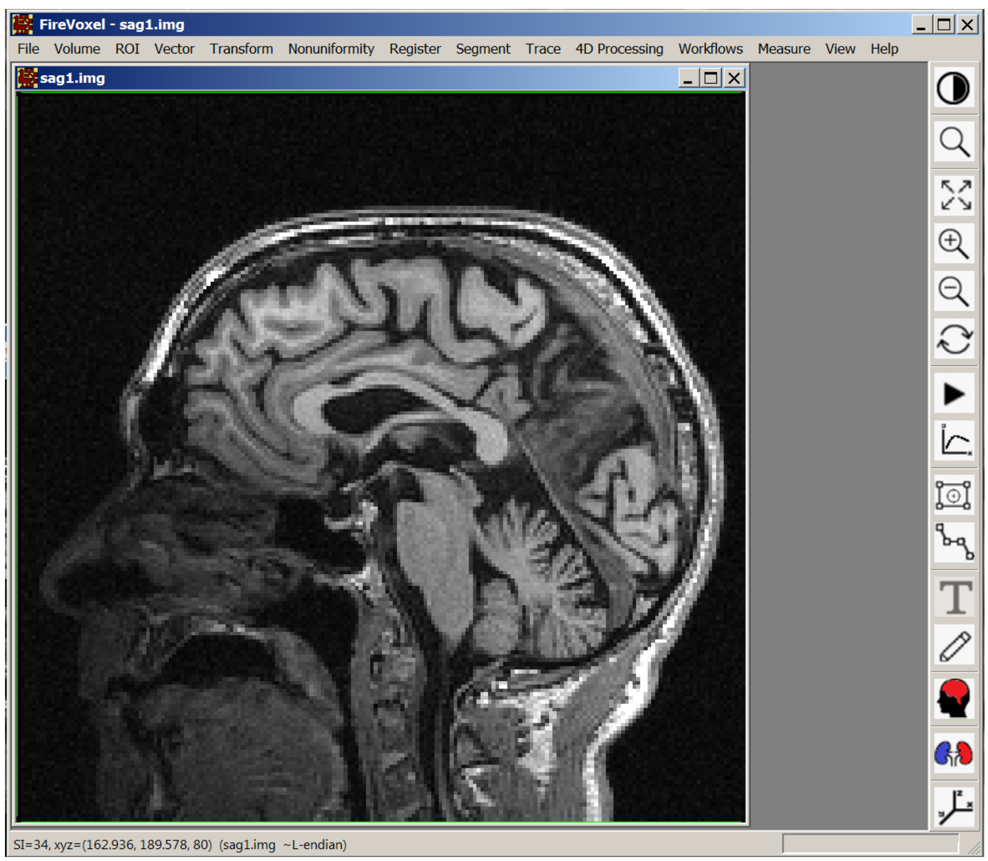
When you start FireVoxel you will see its main window, toolbar along the right margin, and four menu items: File, Applications, Dynamic Analysis, and Help. The gray document area is initially empty. Make sure that the vertical resolution of your screen is fine enough to view the entire toolbar (17 icons).

Next, we will load sagittal T1-weighted brain MRI images stored in a popular format called Analyze. In this format, a volume of data is represented in two files: a header file with the extension .hdr and the data file with the extension.img. Go to File→Open Image, select Analyze in the dropdown menu for file type, find sag1.img from downloading and extracting the sample data folder (from wp.nyu.edu/FireVoxel/quick_start), and click Open.

Step 2 – VIEWING

A new Document window will appear inside the main window. Many new main menu items (Volume, ROI…etc.) will also appear. The Document window will initially show the entire collection of slices. This is the Film view. Position the mouse cursor on any slice and right double-click to switch to a Single Slice view. In Single Slice view, use the mouse scroll wheel or the keyboard up/down arrow keys to view different slices. Repeating right double-click brings you back to the Film view.

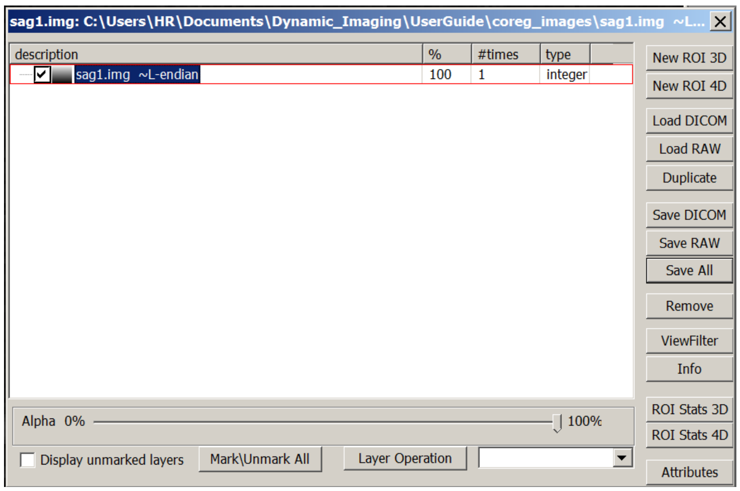

FireVoxel - sag1.img
File Volume ROI Vector Transform Nonuniformity Register Segment Trace 4D Processing Workflows Measure View Help
sag1.img
A
R
L
P
SI=186, xyz=(116.037, 132.550, 124) (sag1.img ~L-endian)


FireVoxel - sag1.img
File Volume ROI Vector Transform Nonuniformity Register Segment Trace 4D Processing Workflows Measure View Help
sag1.img
SI=34, xyz=(162.936, 189.578, 80) (sag1.img ~L-endian)

You can load multiple volumes in separate resizable documents. Independently, you can resize the volume relative to the document window using the four zoom icons located near the top of the toolbar. Before performing an operation, the relevant object needs to be selected with a mouse click. If a volume is selected, a green rectangular frame appears around its border.

Step 3 – LAYERS

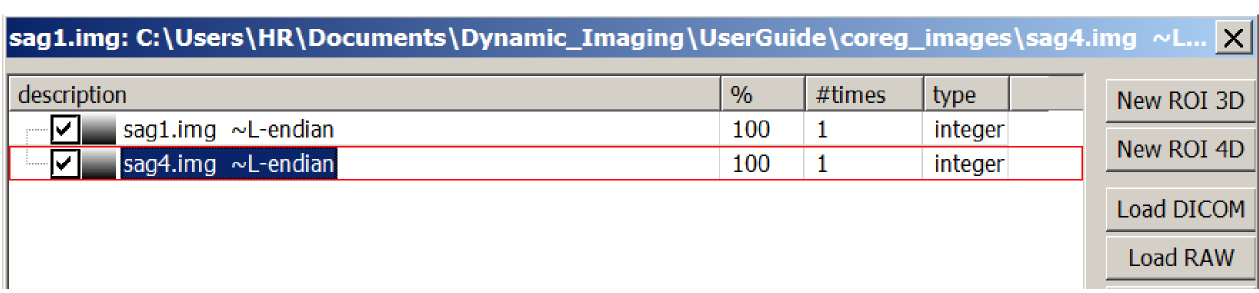
Bring up the Layers dialog box by left double-clicking anywhere over the volume. Layers enable you to work on multiple volumes in unison. All layers must have the same resolution to be loaded in the same document.



Our sample data is loaded as a single layer (sag1.img),which is 100% opaque (non-transparent). The transparency of the layer is controlled with the horizontal slide bar at the bottom of the window. Click on the leftmost box to unselect the layer. Press the Info button to display information about the volume. Press the ViewFilter button to change how voxel intensities are mapped to colors, i.e. gray level window and color maps.

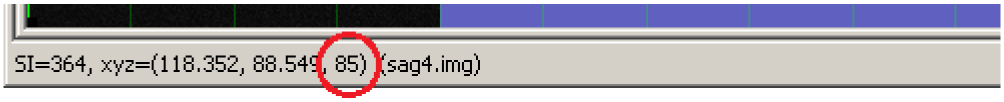
Step 4 – LOADING SECOND IMAGE IN THE SAME WINDOW

A second MRI of the same patient was taken 4 years later. This image is also in Analyze format, stored assag4.hdr and sag4.img. With Layers box open, click on the Load RAW button (fourth button from the top), set file type to All, select the file sag4.img, and click Open.

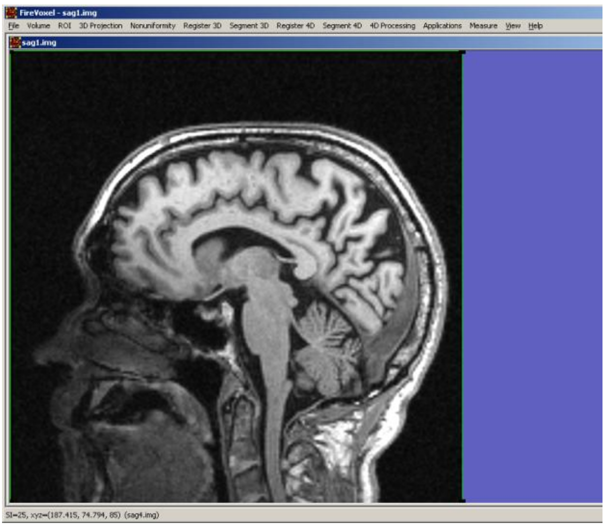


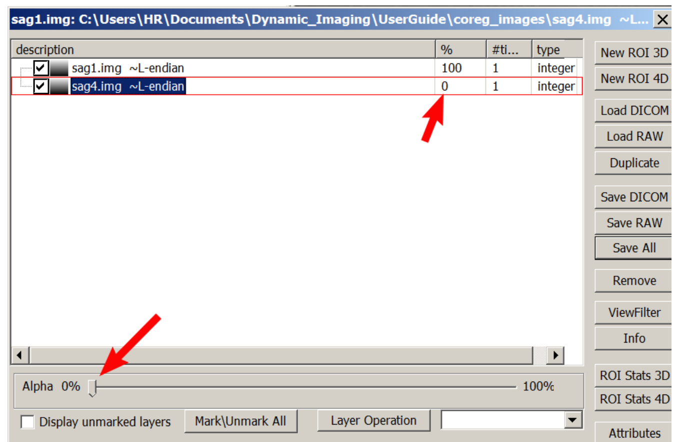
We now have two layers in the same window. Note the name of the second layer is highlighted and the entire row is outlined in red. This signifies that the layer is active or selected. The active layer is the (only) one affected by tools such as Save RAW, ViewFilter, Info, etc. These tools are on the right side of the Layers dialog box. To make another layer active, click on its name.

Let's now display slice number 85 located near the middle of the brain. Click on the MRI. The slice number is shown at the bottom left frame under the image. It is the third number in parentheses.

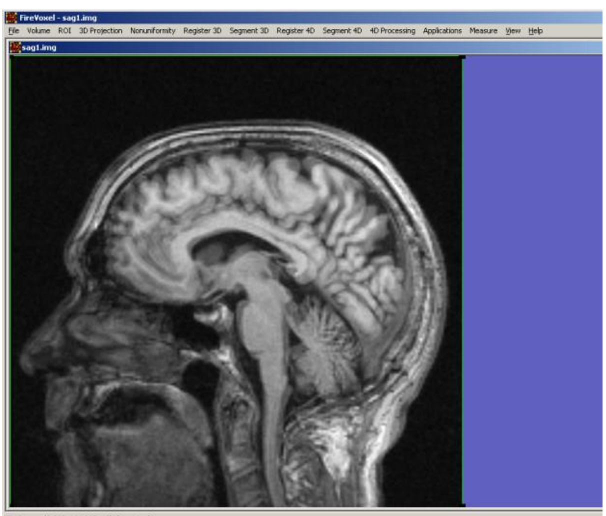


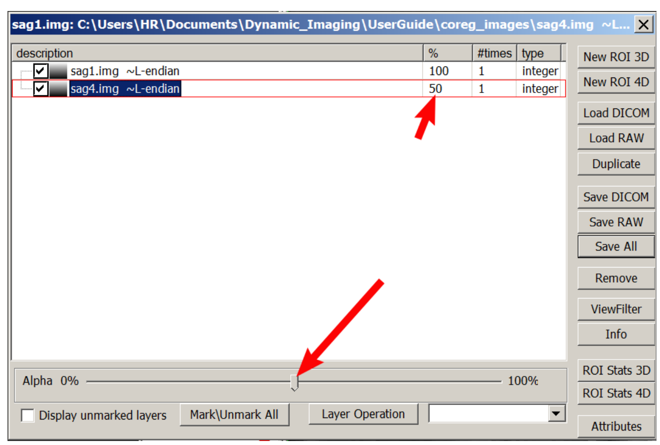
There are several ways to check brain alignment across the two layers. First, we will try viewing these two brains simultaneously by altering transparency. We change the image transparency using the horizontal slide bar at the bottom of the Layer Control dialog box. Make the second layer active and set the transparency slice first to 0%, then to 50%, and finally to 100%.You should see a misalignment of the brain across the two MRIs, highlighting the importance of coregistration.





Transparency of sag4.img at 0%



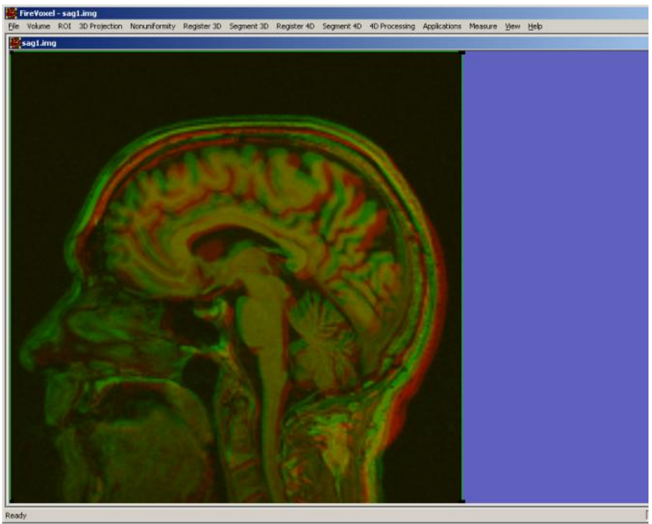


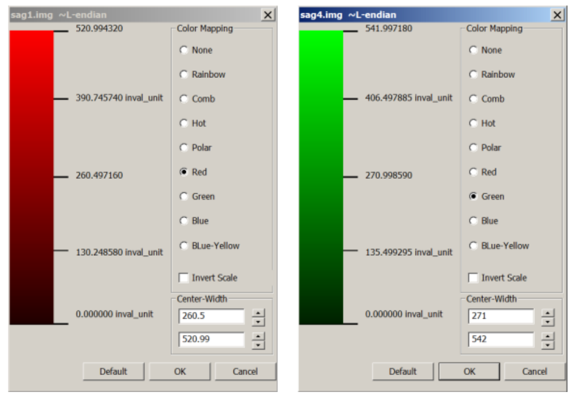
Transparency of sag4.img at 50%

Step 5 – VIEWING IN DIFFERENT COLORS

Another way to check brain alignment is to view the two layers simultaneously in different colors. Image colors are changed by the ViewFilter button in the Layers box. Let's change the color of MRI signal for sag1.img to red and sag4.img to green. In Layers dialog box select sag1.img active by clicking on its name. Press the ViewFilter button, and on the right side of the View Filter dialog box under Color Mapping select Red. Press OK. Next, select sag4.img in the Layer Control dialog box and press ViewFilter. Select Green and press OK.

Make sag4.img active and change its opacity α from 100% to 50% using the horizontal slide bar. This will allow you to view sag4.img (in green) superimposed on sag1.img (in red), showing misalignment.



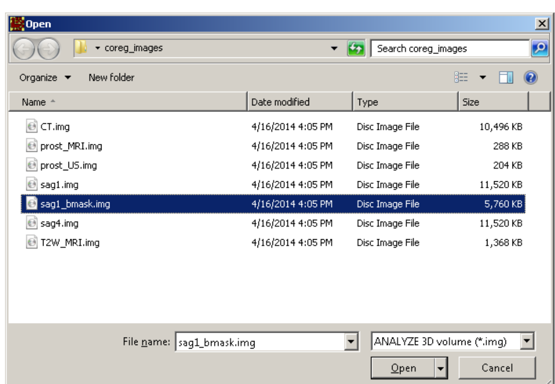


Switching ViewFiler for sag1 to red and sag4 to green.
On the left, the transparency of sag4.img was at 50%

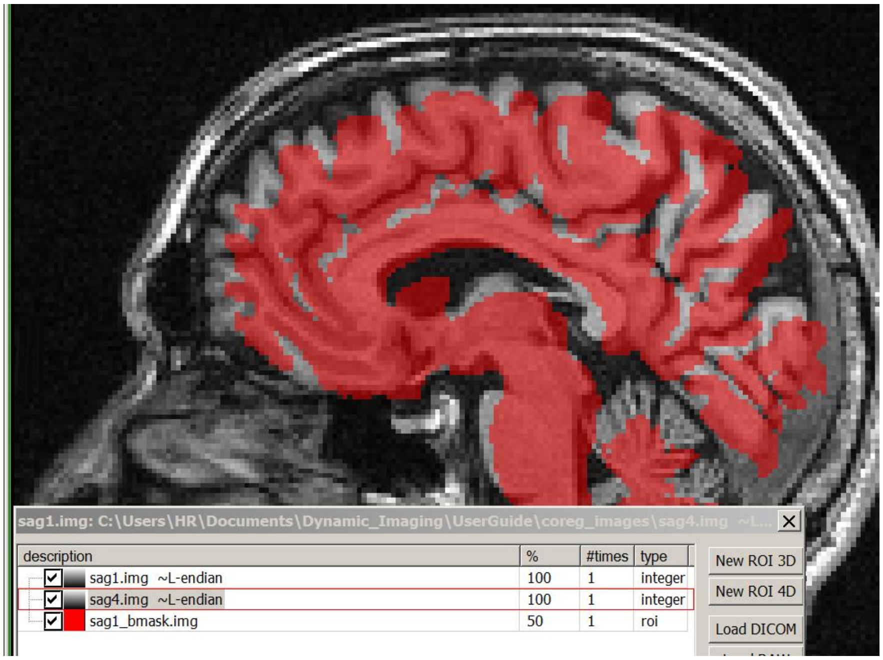
Step 6 – USE MASK LAYER

A third way to check brain alignment is to superimpose a brain mask layer derived from one image onto the second image. The brain mask layer is included in the sample data (sag1_bmask.img). Another tutorial (Introduction to FireVoxel) explains how such masks are generated using segmentation tools. Before loading the brain mask, return the color of the images to back to grayscale by selecting each of the images from the Layer Control dialog box, pressing the ViewFilter button, and selecting None.

In order to load the brain mask, press the Load Raw button in the Layers box, set file type to Analyze, and select the file sag1_bmask.img.



The Layer Control dialog box will now have three layers. You should verify that sag1_bmask provides a reasonable brain tissue segmentation for the baseline MRI sag1.img. Do this by temporarily disabling sag4.img -- uncheck the small square box on the left of its layer. Then view the baseline brain mask on top of the follow-up MRI (sag4.img) to see the misalignment.



Viewing the baseline brain mask in red (layer 3) superimposed on the follow-up MRI sag4.img (layer 2). Since the opacity of sag4.img is 100%, we don't see the baseline MRI sag1.img.

Example I: Coregistering two MRI images of the same brain

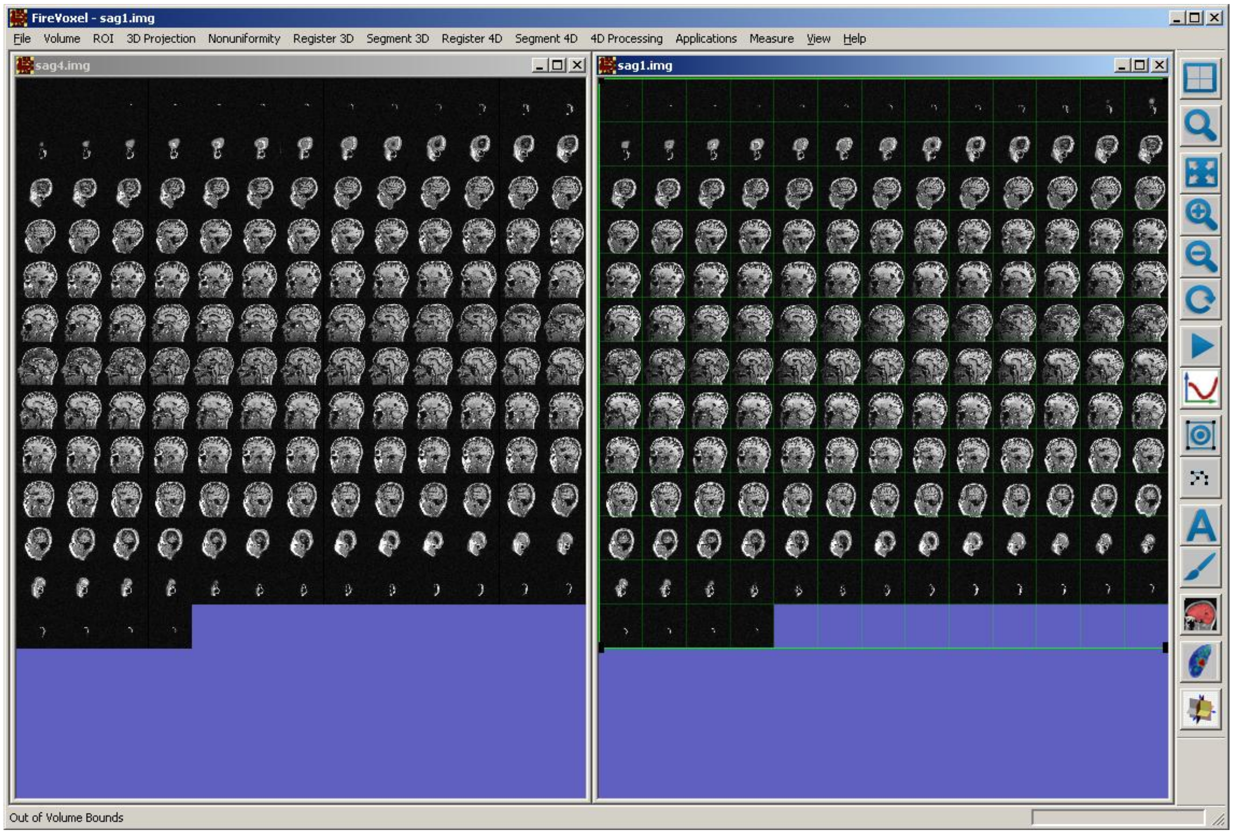
Step 7 – LOADING THE SOURCE AND THE TARGET VOLUMES

Now that we viewed the extent of misalignment, we will proceed to fix the problem. Close the document and let's begin with coregistration.

Load the baseline MRI as before. Go to File→Open Image from the main menu, then select and load the file sag1.img.
Next, do again File→Open Image and then select and load the file sag4.img. The two documents will appear side-by-side with sag1.img on the right, and sag4.img on the left.

Let's go over a few basic terms. We will refer to the still image, the one that we wish to keep in place, as the target of coregistration. The other image will be called the source, or the floating image. FireVoxel will manipulate the source image (translate, rotate, etc.) to align it with the target image. At the end of the process, a copy of the source image will be inserted as a new layer in the target window.

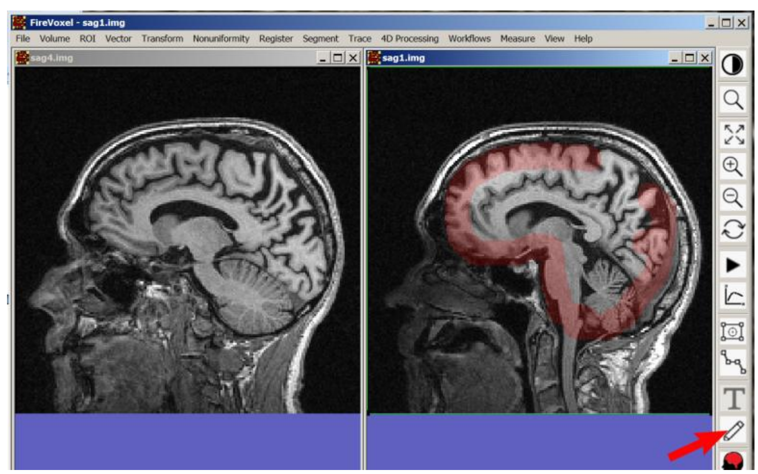
To select the target, click on its document sag1.img. This makes the title bar turn blue and the image becomes outlined by a green line. The source image window title bar (sag4.img) is gray.



The next step involves marking the target region of interest (ROI). There are two reasons for making a target ROI:

1. It restricts coregistration to the organ we care about. For example. in abdominal image we may want to coregister two images of the right kidney and ignore other organs.
2. Targeting a region speeds up the computations. You will soon find out that coregistration is a CPU-intensive task.

Step 8 – MAKING TARGET ROI



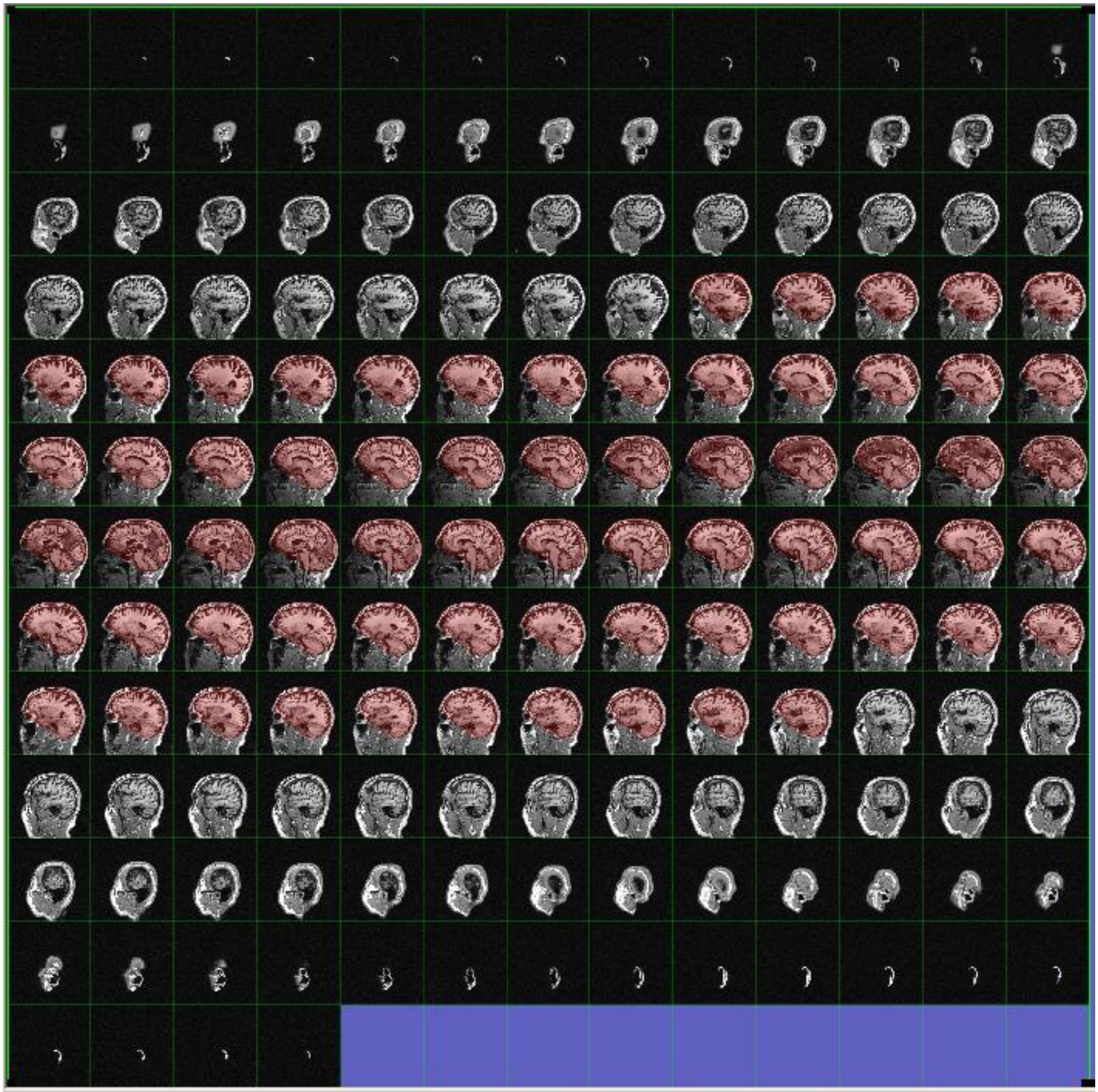
Place the cursor on the target image (sag1.img) and bring up the Layers dialog box using left double-click. Press the New ROI 3D button in the Layer Control dialog box which creates a new layer called New ROI 3D.

Next, we will mark our area of interest (i.e. the brain) on three different slices. Start by selecting the middle slide (slice number 85) from the Film view and right double-click to see the Single Slice view.

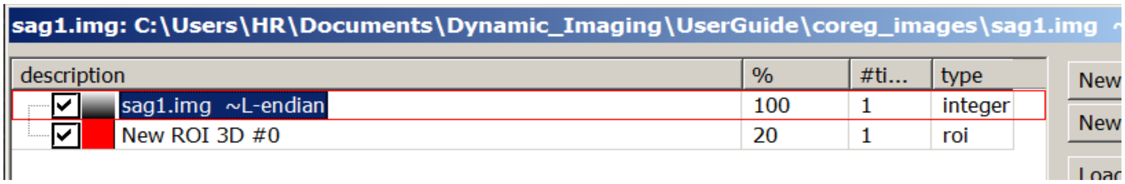
Painting an ROI is done by holding down the Ctrl key and the left mouse button. Holding down the Ctrl key and the right mouse button will erase the ROI. The size of the paintbrush can be adjusted by simultaneously holding down the Ctrl key and turning the mouse scroll wheel. You could also control the Paintbrush using the crayon icon on the right toolbar in the main FireVoxel window (see red arrow in the figure above).

After marking the area of interest in the middle slice (slice 85), use the mouse scroll wheel or the keyboard up/down arrow keys to view different slices. Select temporal lobe slices from the left and the right hemispheres (slices around 48 and 114, respectively) and use the paintbrush tool to outline the brain. Don't include the skull in the mask. The color and transparency of your ROI is not important.

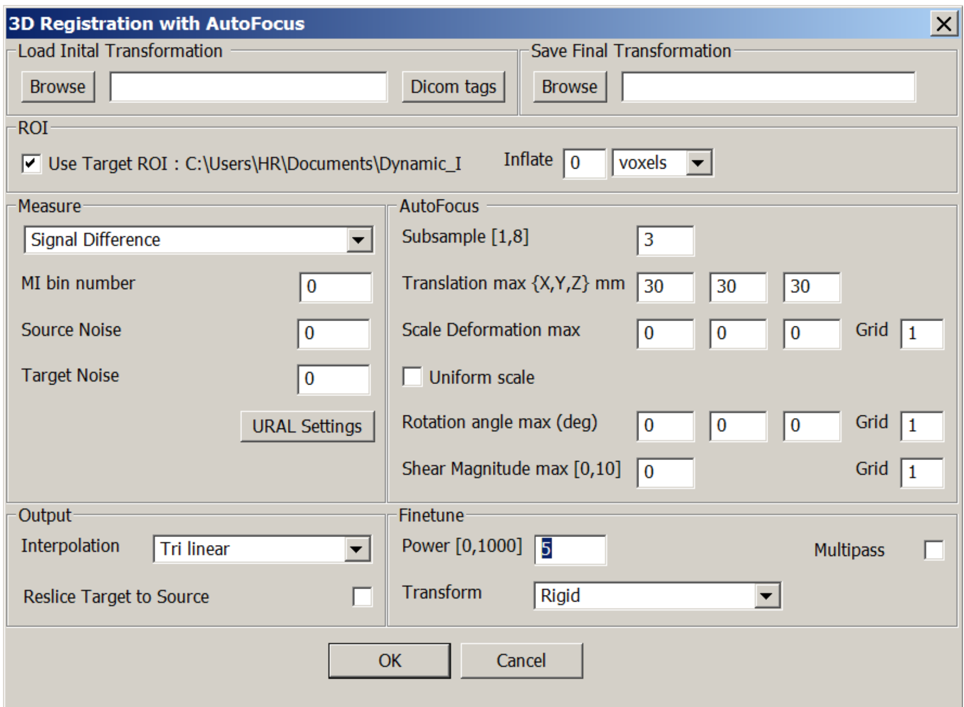
Next, return to the Film view using right double-click. Select ROI→Morph -> Fill 2D Contours and Morph Convex from the main menu. After a brief calculation, your ROI will be automatically filled and appear in all slices in-between the ones that you outlined. The target ROI is done!



Step 9 – COREGISTRATION DIALOG BOX



Select the image layer, not the ROI layer, as the active layer. From the Main Menu, select Register → Signal Difference with AutoFocus. A complicated dialog box will pop up.



The parameters for AutoFocus are grouped on the right side of the 3D Registration dialog box. FireVoxel computes the transformation in two stages: the first is the AutoFocus stage, and the second stage fine-tunes the transform.

In the AutoFocus stage, we examine combinations of parameter values that span a multidimensional grid. Even though by default we only consider translations (excluding rotations, etc., in this stage) and we subsample the volume, independent combinations of left/right translations, up/down translations, and through-slice translations yield thousands of choices. These transformations will be ranked based on how well they manage to match the two volumes. The matching involves a “similarity” measure (left side of the 3D Registration dialog box). FireVoxel offers multiple different similarity measures (from simple and quick to more complex and powerful). The options for measures in the dropdown menu include:

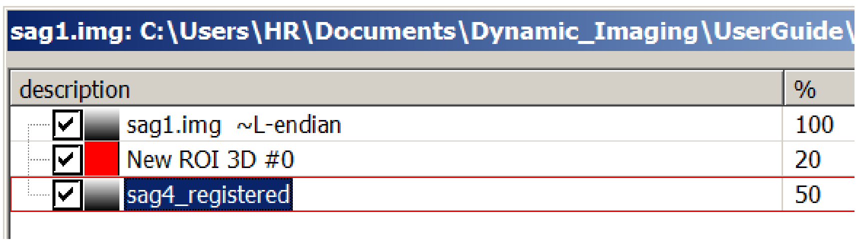
- Signal difference
- Cross Correlation
- Image Ratio Uniformity
- Mutual Info
- Mutual Info Normalized
- URAL (basic, log, and normalized versions)

A number *P* of best transformations from the Autofocus stage are retained for the second, fine-tuning stage. This number appears in the Power text field of the dialog box. Fine-tuning consists of iterative adjustments of transformation parameters until we reach a local optimum of similarity measure. Finally, the transformed source image is interpolated and saved as a new layer in the target image.

With the exception of setting Power to 5, keep the default settings in the 3D Registration dialog box. Before launching coregistration, please double check :

- Make sure target window is active and target ROI is visible
- Make sure Use Target ROI box is checked in 3D Registration dialog box

Press OK and wait a few minutes, depending on the power of your computer. On a modern PC, coregistration of two MRIs by signal difference should about a minute (306 seconds in this case). You should now see another layer called sag4_registered in the sag1.img window. If so, congratulations, you have fused two brain MRIs!



Step 10 – VERIFYING ALIGNMENT AFTER COREGISTRATION

In order to view the results of the coregistration and the alignment of the two images (baseline and follow-up MRIs) return to single slice view, slice 85, using right double-click. Next, use left double-click to open the Layers. The first layer, sag1.img, is the baseline MRI. The second layer, New ROI 3D, is the target ROI. The third layer, sag4_registered.img, is the follow-up MRI coregistered to the same space as the baseline exam. Because of our use of the brain mask (layer 2), FireVoxel was able to focus on aligning the brain by ignoring the mouth, skin, next and other irrelevant tissue. We can now unselect the brain mask New ROI 3D #0 layer by unchecking the small square box.

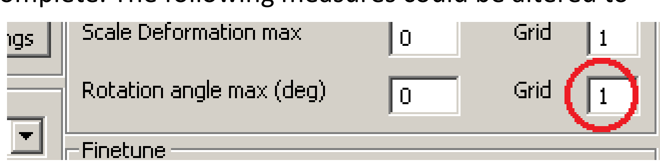
Now use the method from Step 4 above to verify how well did the coregistration work. Briefly, select the third layer sag4_registered.img by clicking on it. Then moving the horizontal slide bar at the bottom of the Layers box between 0% and 100%. You should see that the location of the brain is pretty much the same as you switch from the baseline MRI to the coregistered follow-up MRI. Notice that the skin and bone are not registered. Can you see biological changes due to aging in this brain?

STOPPED HERE… SUBSAMPLE

Step 11 – IMPROVING THE ACCURACY OF COREGISTRATION

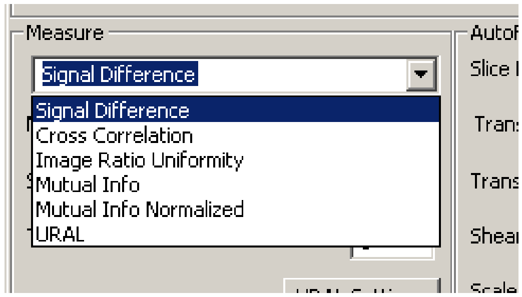
FireVoxel offers several means to increase coregistration accuracy over the simplest approach we did in step 9. However, these will make the program take longer to complete. The following measures could be altered to improve accuracy:

1. Increasing the Rotation angle max Grid



2. Increasing the Power

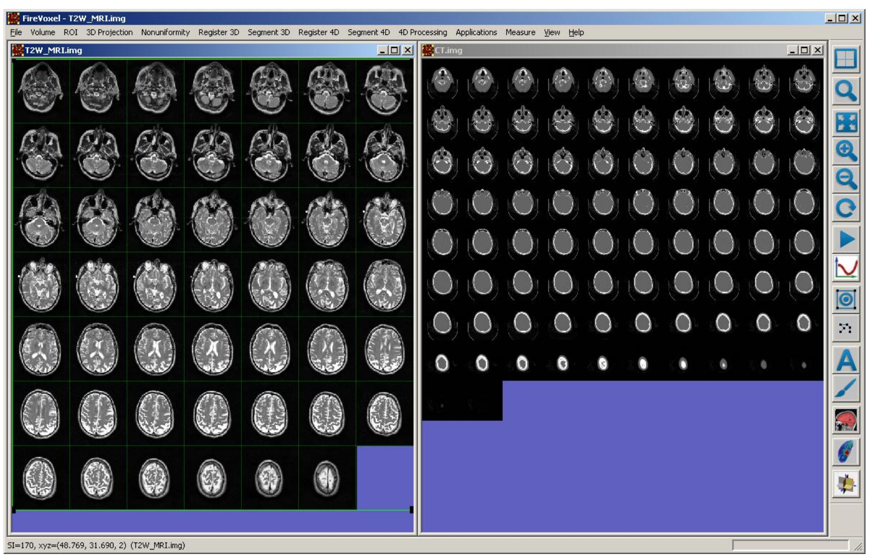
3. Selecting more complex similarity measure (i.e., Cross Correlation or Mutual Info) from the Measure drop-down menu.



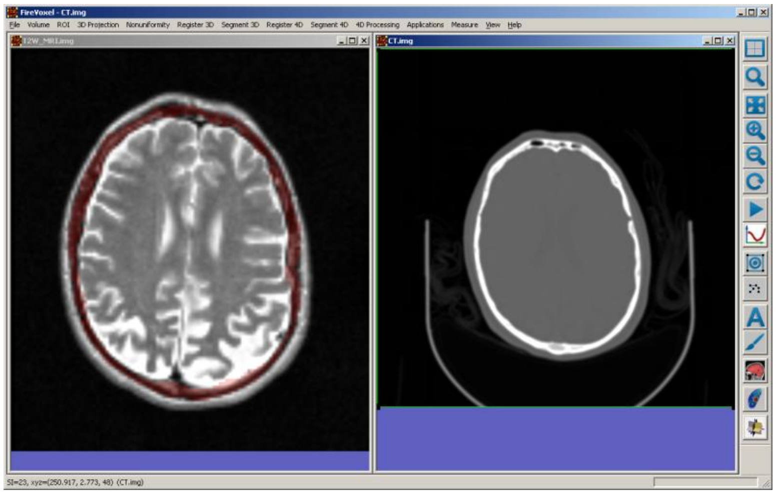
Example II: Coregistering different modalities (CT and MRI)

Step 12 – MAKING TARGET ROI

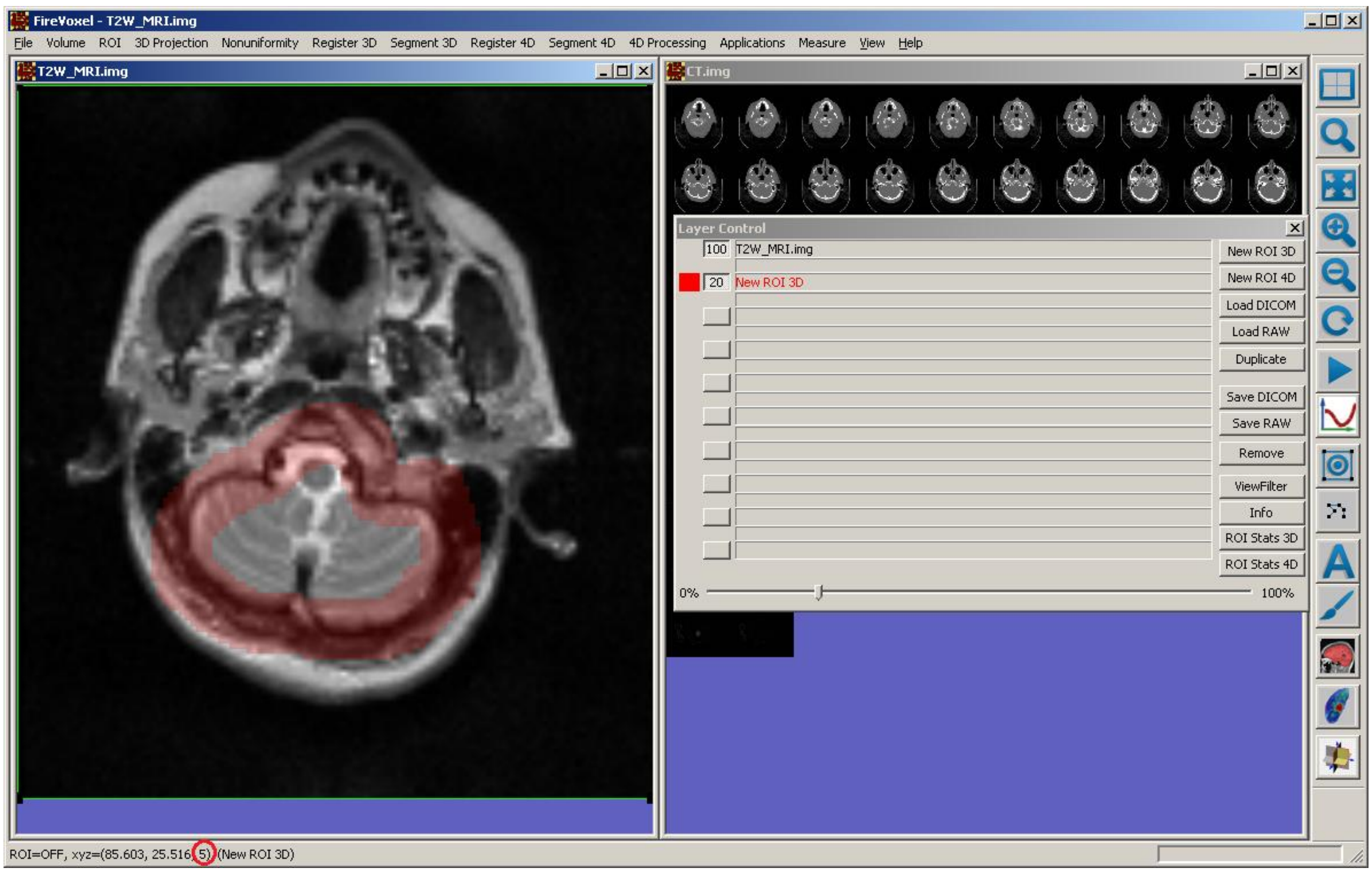
We will proceed to coregister images derived from different modalities: T2-weighted MRI and CT brain scans. Load the CT volume, CT.img. Next, load the MRI volume,T2W_MRI.img.

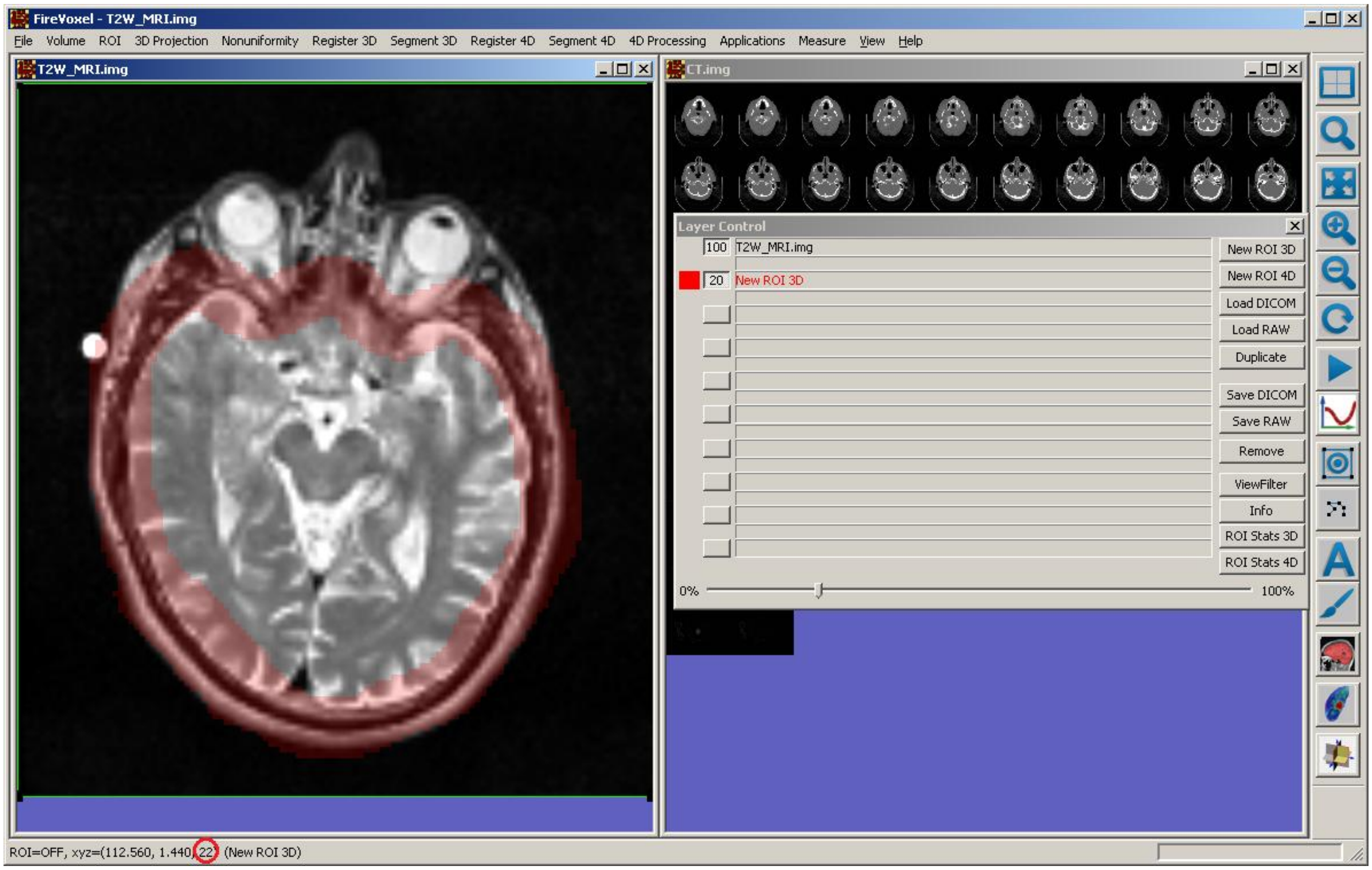


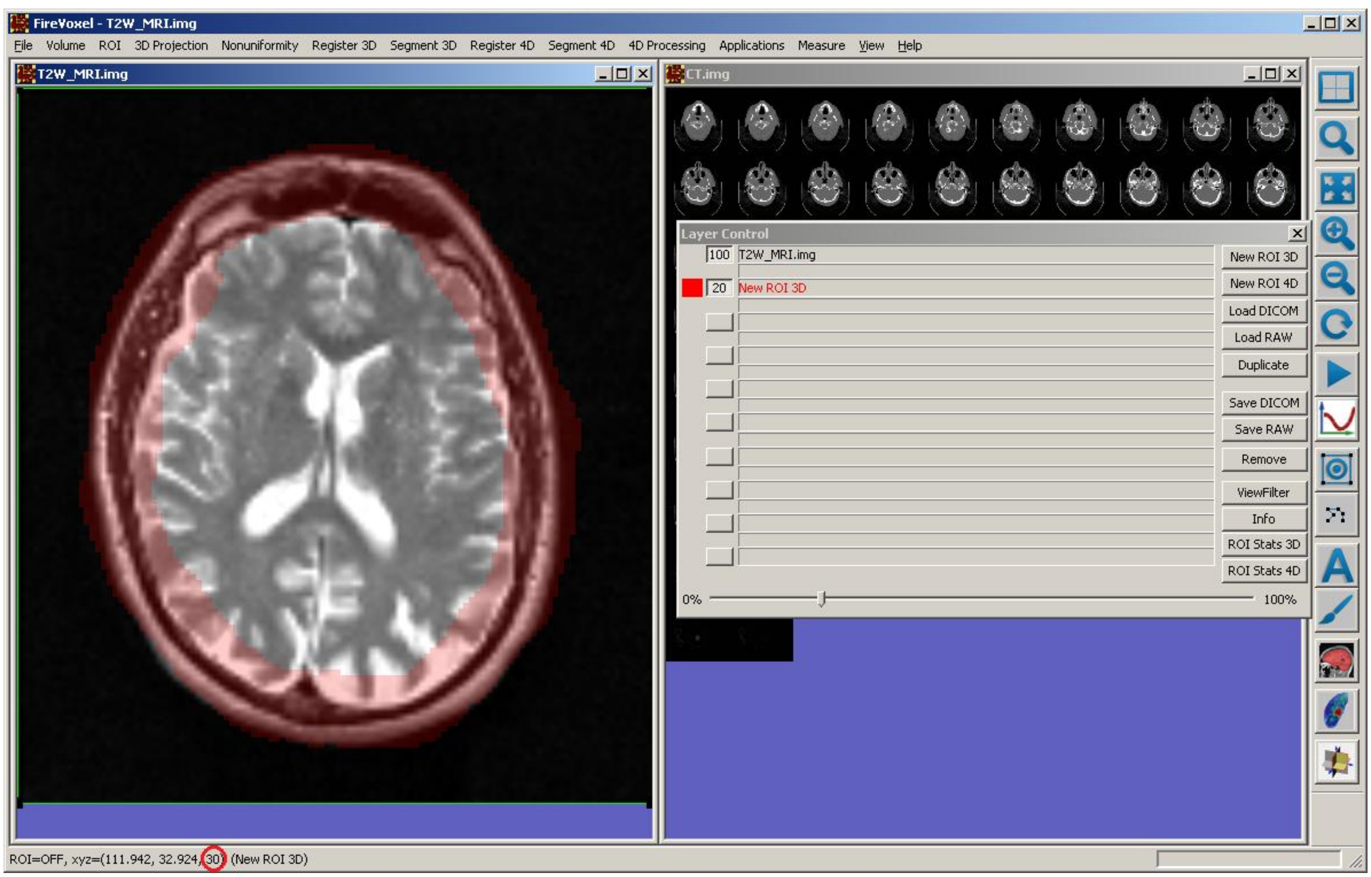
The next step involves marking the target ROI. Because CT is most sensitive for depicting bone (skull), we will try to include the bone on the target MRI images. Bone is dark on T2-weighted MRI (highlighted in red in the image below simply for viewing purposes), while bone is bright on CT.

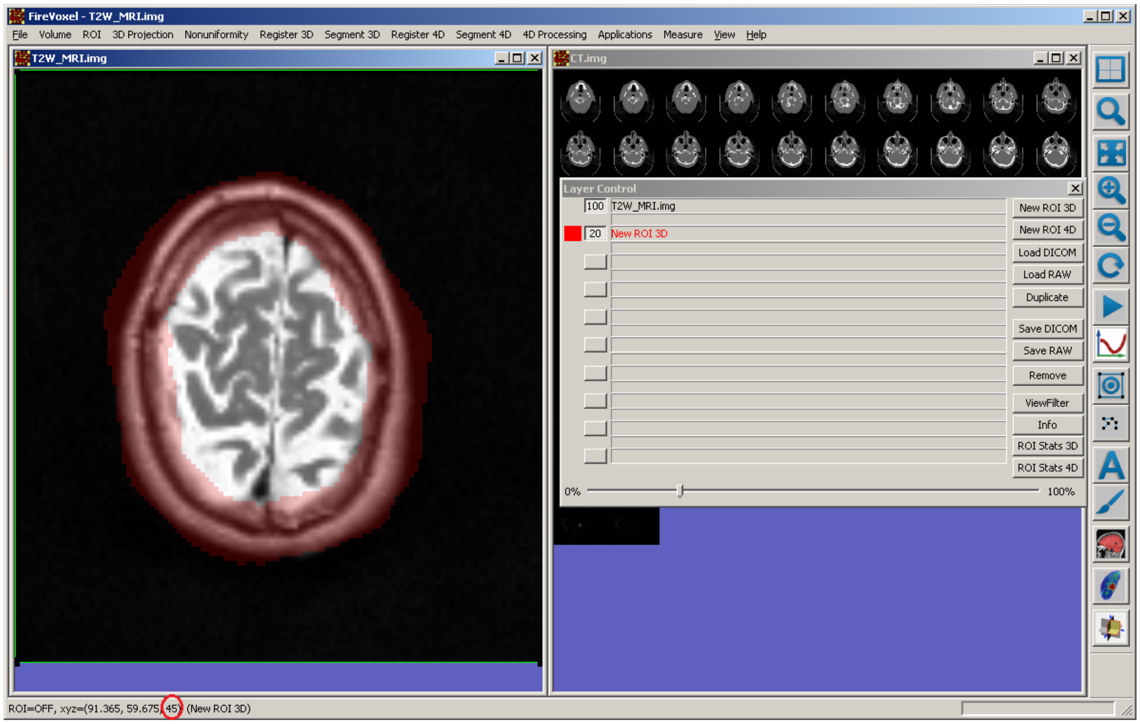


We will then create a new ROI and make a rough outline of the brain and the skull on 4 different MRI slices (5, 22, 30, 45) as shown below.

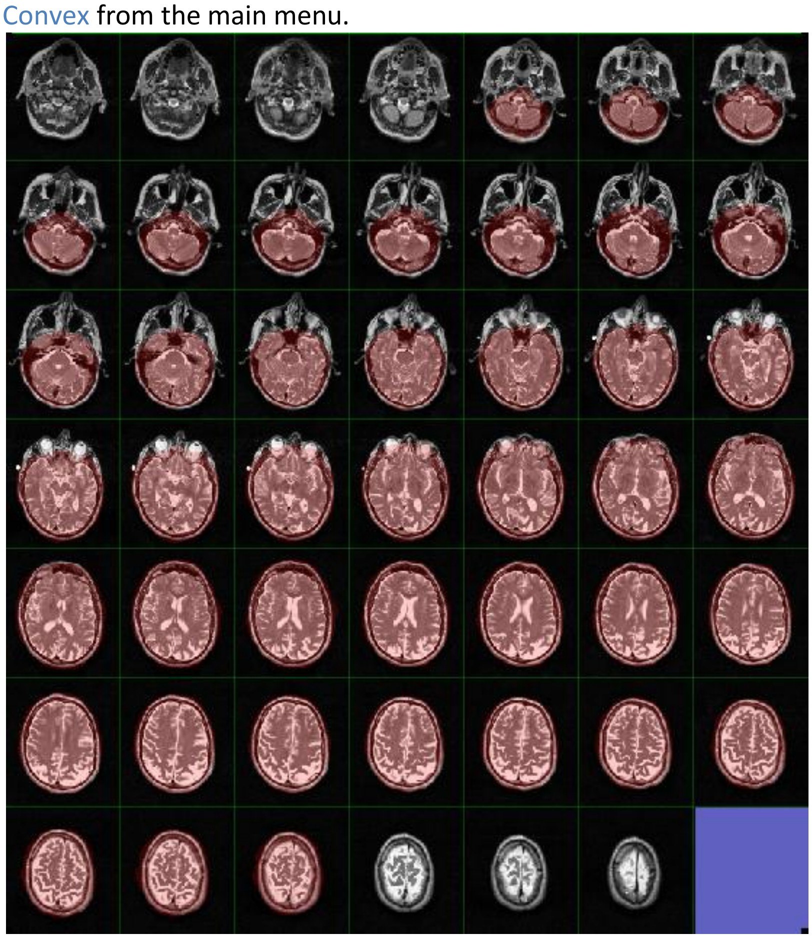



FireVoxel - T2W_MRI.img
File Volume ROI 3D Projection Nonuniformity Register 3D Segment 3D Register 4D Segment 4D 4D Processing Applications Measure View Help
T2W_MRI.img
CT.img
Layer Control
100 T2W_MRI.img
20 New ROI 3D
New ROI 3D
New ROI 4D
Load DICOM
Load RAW
Duplicate
Save DICOM
Save RAW
Remove
ViewFilter
Info
ROI Stats 3D
ROI Stats 4D
0%
100%
ROI=OFF, xyz=(112.560, 1.440, 22) (New ROI 3D)


FireVoxel - T2W_MRI.img
File Volume ROI 3D Projection Nonuniformity Register 3D Segment 3D Register 4D Segment 4D 4D Processing Applications Measure View Help
T2W_MRI.img
CT.img
Layer Control
100 T2W_MRI.img
20 New ROI 3D
New ROI 3D
New ROI 4D
Load DICOM
Load RAW
Duplicate
Save DICOM
Save RAW
Remove
ViewFilter
Info
ROI Stats 3D
ROI Stats 4D
0%
100%
ROI=OFF, xyz=(111.942, 32.924, 30) (New ROI 3D)



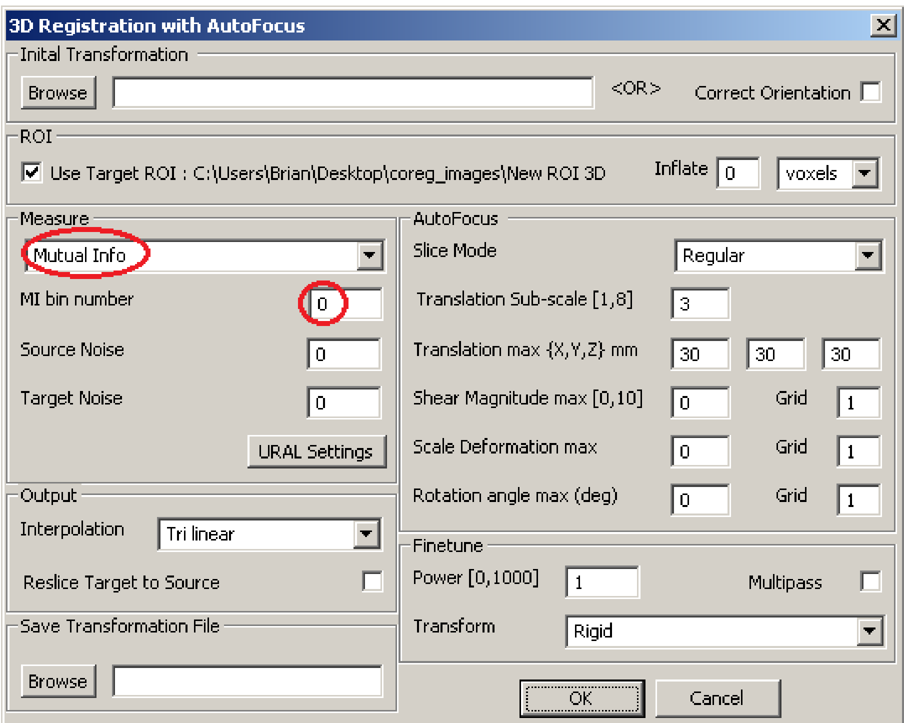
Next, we will create the brain mask by returning to Film view and selecting ROI→Fill 2D Contours and Morph Convex from the main menu.



Step 13 – COREGISTRATION DIALOG BOX

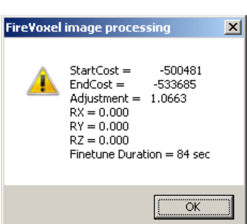
After creating the target ROI, we can coregister the CT and MRI brain images. Make certain that the target image (T2W_MRI.img) is selected as the active layer (red) in the Layer Control dialog box. Aligning images derived from different modalities requires the use of a more complex algorithm. Consequently, using Register 3D→Signal Difference with AutoFocus operation or Register 3D→Cross Correlation with AutoFocus will fail to produce satisfying alignment (you can attempt these by selecting and running the above operations).

Instead, in order to perform the coregistration of MRI and CT images, we will select Register 3D→Mutual Info with AutoFocus from the main menu. The 3D Registration dialog box will appear with Mutual Info selected as the similarity measure.



Note the MI (Mutual Info) bin number is set to 0 by default. Maximum signals are computed separately for the source and target volumes. The signal range [0, S_{max}] for the source volume and [0, T_{max}] for the target volume are each divided into *bn* bins. The transformation during coregistration is iteratively computed to maximize the mutual information of the binned joint histogram. When *bn* = 0 (default value), the number of bins follows Sturges estimate: *bn* = log2 (# target voxels) + 1.

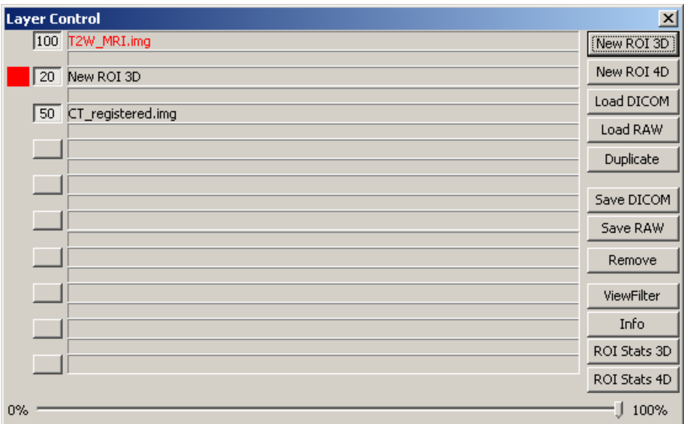
Keep these default settings and press OK. The transformation process might take a few minutes, depending on the power of the computer you are using. After its completion, the Image Processing window will appear.



Because in this example we have fewer slices, lower MRI image resolution, and set Power=1, the coregistration took less time (84 seconds) than the previous example.

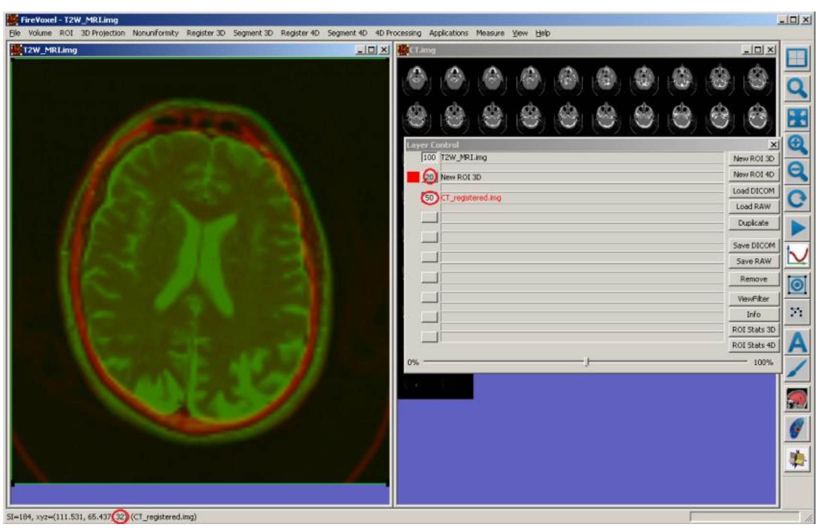
Step 14 – VERIFYING ALIGNMENT AFTER COREGISTRATION

In order to view the results of the coregistration and the alignment of CT and MRI, return to Single Slice view using right double-click while the cursor is placed on the MRI image. Next, use left double-click to open the Layer Control window. The dialog box will show 3 layers.

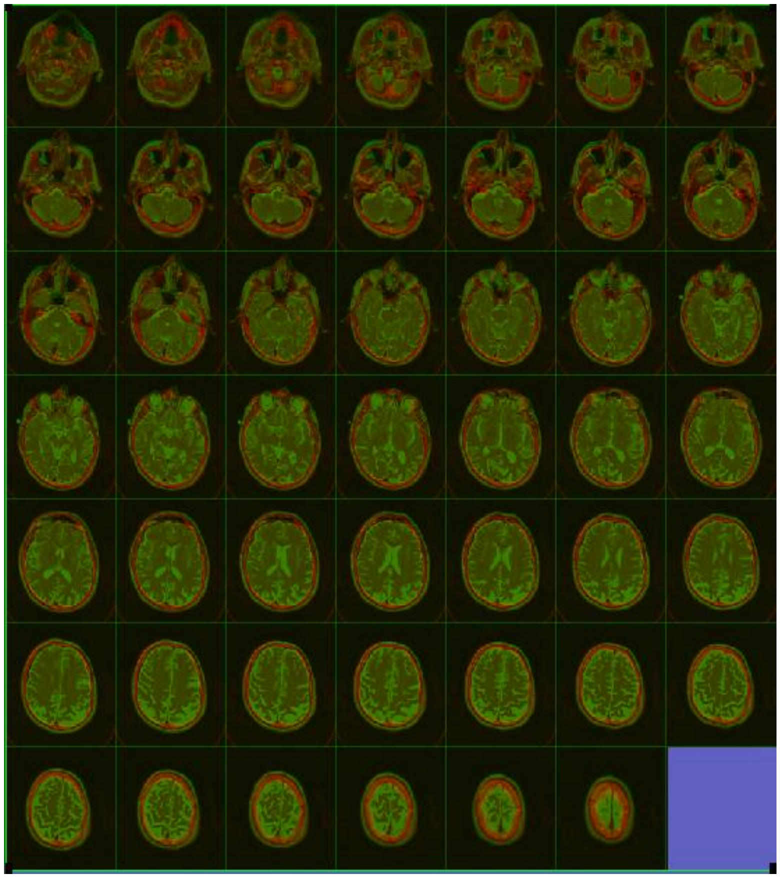


The first layer, T2W_MRI.img, is the MRI image. The second layer, New ROI 3D, is our target ROI which can now be disabled. The third layer, CT_registered.img, is the CT image after coregistration.

In order to verify the alignment across the two layers we will view them simultaneously in different colors (see step 5). Using the ViewFilter tool in the Layers box, change the color of the MRI layer to green and the coregistered CT layer to red. Then, change the transparency of CT_registered.img to 50% using the horizontal slide bar. This will allow you to view the green MRI layer on top of the red CT layer. In the image below, slice 32 was selected, New ROI 3D (currently at 20) disabled, and transparency ofCT_registered.img set to 50.



A Film View shows overall coregistration between the MRI and CT images.



Example III: Manual coregistration using landmarks (last resort)

Step 15 – PLACING AND LABELING GREEN BOXES (VROIs)

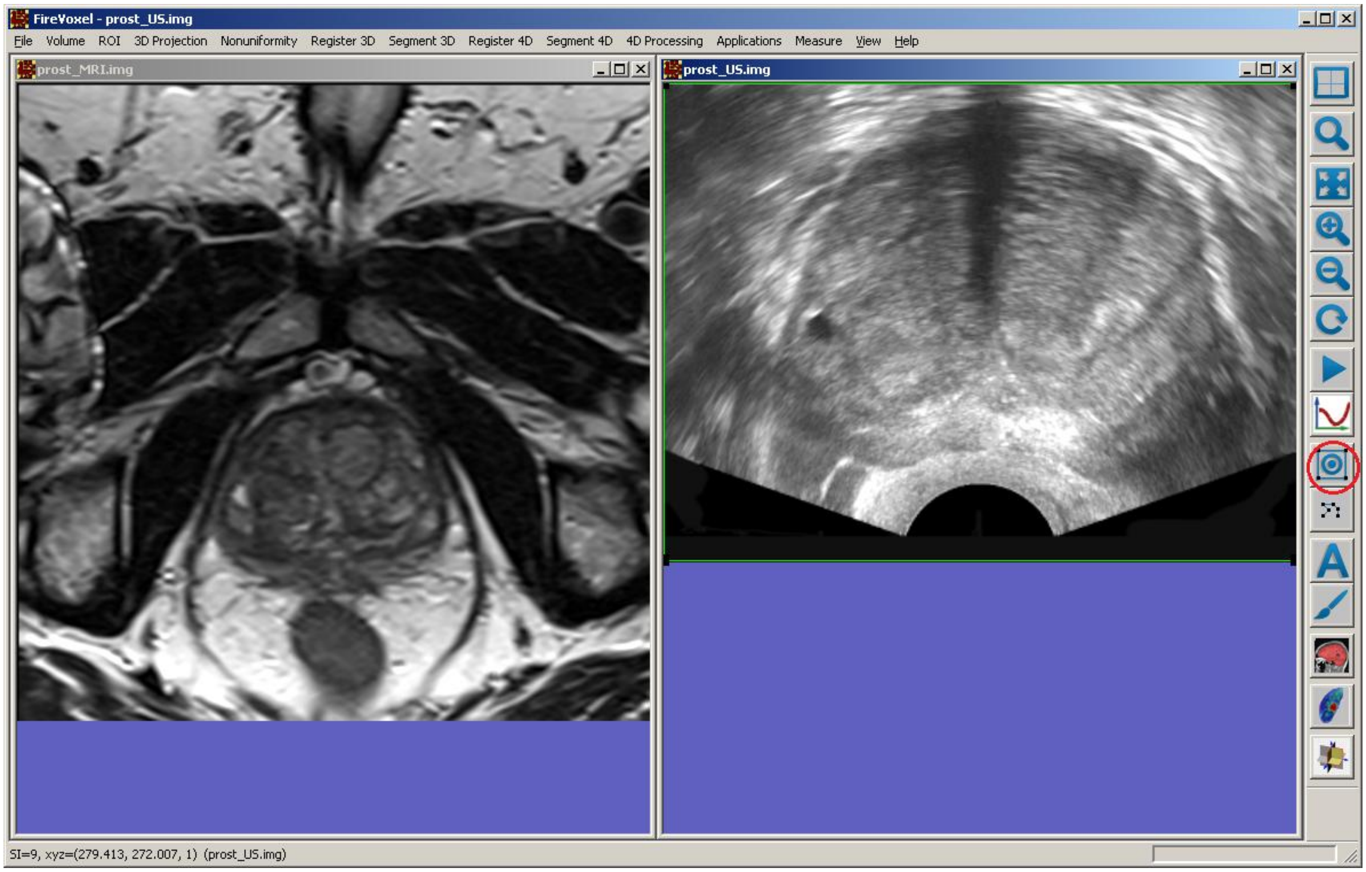
In the third example we will use anatomical landmarks to align MRI and US (ultrasound) images. Because of the marked difference between these two imaging modalities, a fully automatic coregistration process will not provide accurate results (you can attempt this by marking ROIs for both images and running Signal Difference, Cross Correlation, or Mutual Info with AutoFocus operations from the Register 3D menu). In order to coregister images derived from such disperse modalities, points or landmarks based registration may be required. We will demonstrate this process by using MRI and US images of a prostate.

Load the US volume, prost_US.img. Next, load the MRI volume, prost_MRI.img. Both volumes comprise of only 1 slice. Note how different the two modalities are and how little information is visible on US.

The next step involves picking, placing, and labeling at least 3 corresponding points or landmarks in the prostate. The landmarks we choose must represent the same detectable features in both US and MRI.

To facilitate the accuracy of the alignment, we should try to identify landmarks that are spread far apart and across different areas of the prostate.

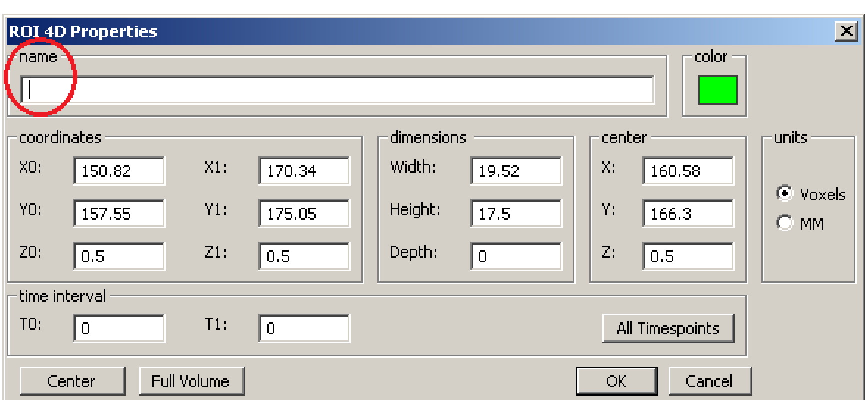
We will begin by selecting the US image. In order to mark the first landmark, click on the square target shaped icon located in the middle of the toolbar (circled in red below).



Place the mouse cross-hair cursor a bit to the left and below the area you wish to mark, click the left mouse once and move the crosshair to the right and over the landmark. Note that a green hatched box will appear, with intersecting red lines marking the center of the box. Move the mouse to make the lines intersect at the center of the landmark, and left-click again. This will create your first landmark.

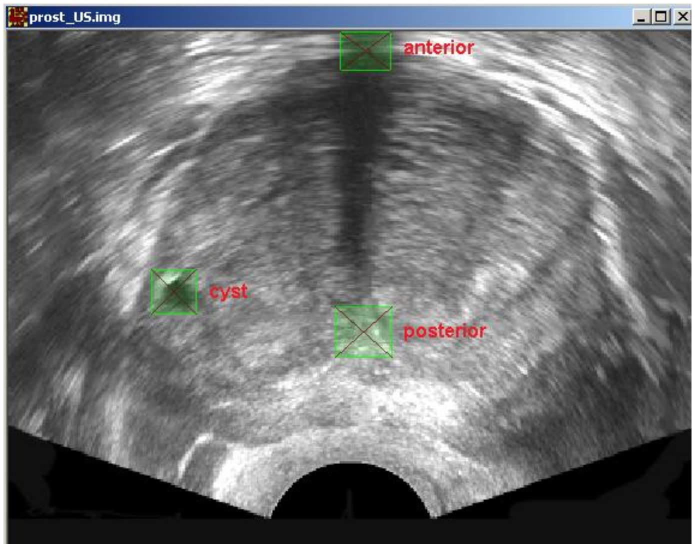
FireVoxel refers to green boxes used for landmarking as vector ROIs (VROIs). There are two ways to adjust a landmark after left clicking on it to make it active (two gray squares will appear on the bottom left and top right corners). In order to move the entire landmark, place the mouse over the VROI, then click and hold the right mouse button to move. In order to increase or decrease the size of the landmark, place the cursor on the VROI's bottom left or top right corner(marked by the gray squares) and click and hold the left mouse button to resize. To delete VROI, select it by a left click and press delete.

Next, name the landmark by left double-clicking while the mouse cursor is inside the landmark and typing a name.

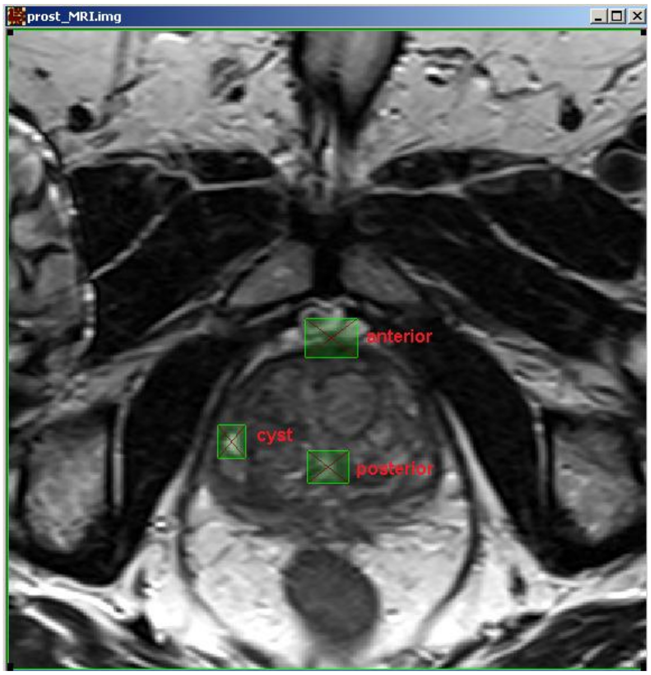


To coregister US and MRI, we will create 3 landmarks: 1) a cyst that happens to be visible on the left side of prostate. The cyst shows up dark on US and bright on T2-weighted MRI. 2)The point of the reflective curve of the anterior fibromuscular stroma, the most anterior point of the prostate (superior most aspect on the images). And 3)the verumontanum, located near the conjunction of the two ejaculatory ducts, at the posterior point of the prostate (inferior aspect on the images).

Generate 3 VROIs in the US as shown in the image below. Use the nomenclature cyst, anterior, and posterior for the respective VROIs.

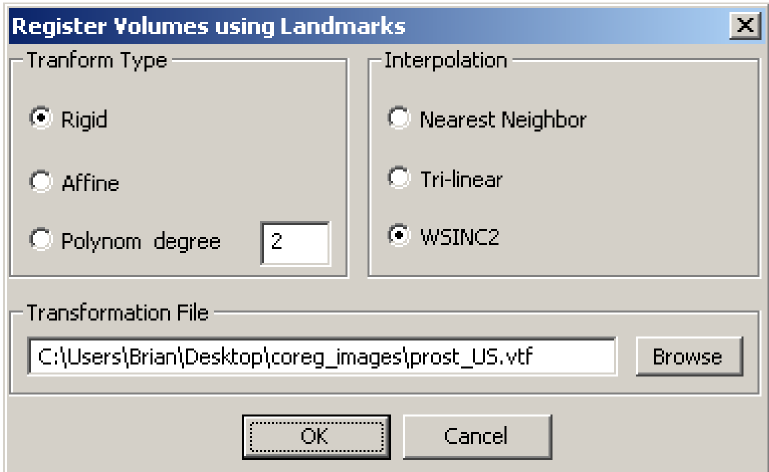


Next, generate 3 VROIs in the MRI at the same locations and use the same nomenclature used for the US landmarks: cyst, anterior, and posterior.

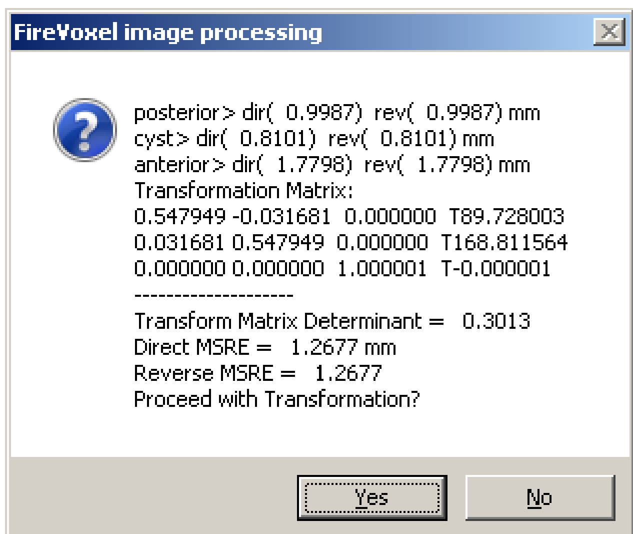


Step 16 – LANDMARK BASED COREGISTRATION

Return to the ultrasound image to make it active and select Register 3D→Landmark Registration from the main menu.



Keep the default settings and click OK. At this point, if no gross mistakes were made in landmarking, the Image Processing window will appear providing important data concerning the accuracy of the landmarks.

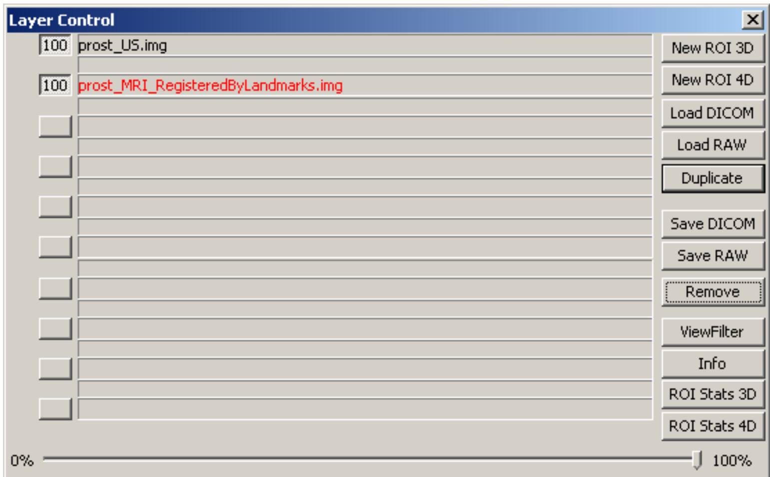


If mistakes or omissions were made during landmarking, an error window will appear. For example, if you forgot to label one of the landmarks or if different nomenclature was used for the same landmarks across the two images.

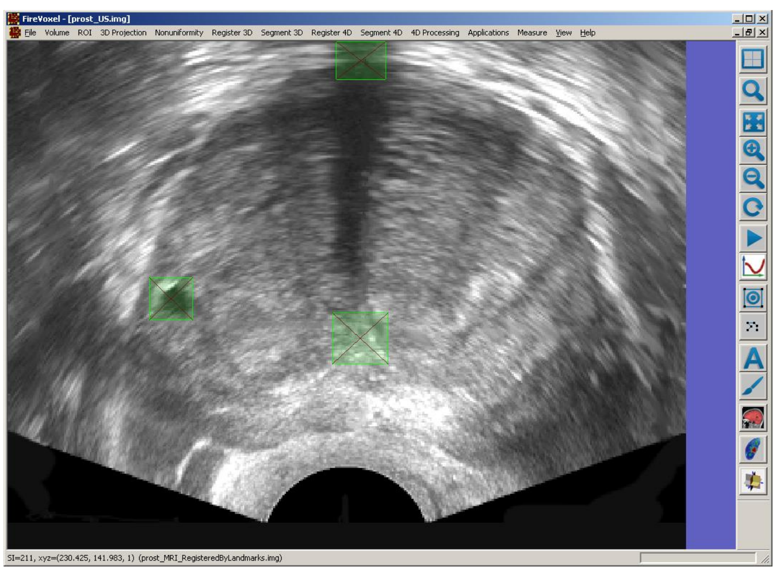
Mixing up the labels, on the other hand, may not result in an error message, but in large coregistration errors, as indicated by the values next to the landmark names in the Image Processing window. Large values indicate large registration errors. Overall errors lower than 2-3 mm for prostate US, as shown here by MSRE (root-mean-squared error) values, are indicative of a high degree of accuracy. If you are satisfied with the values, proceed with pressing Yes.

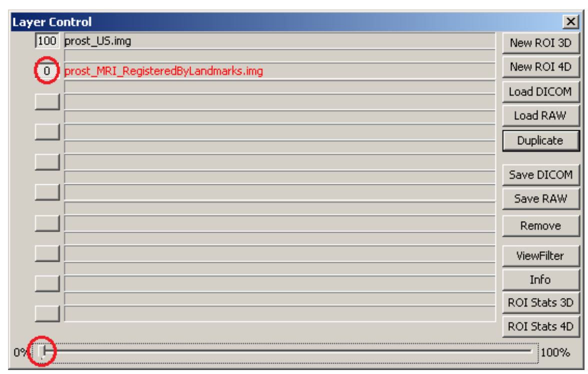
Step 17 – VERIFYING ALIGNMENT AFTER COREGISTRATION

In order to view the results of the coregistration of the two images (prostate MRI and US), left double-click the US image to open the Layer Control dialog box. A second layer, post_MRI_RegisteredByLandmarks.img, is the coregistered MRI image.

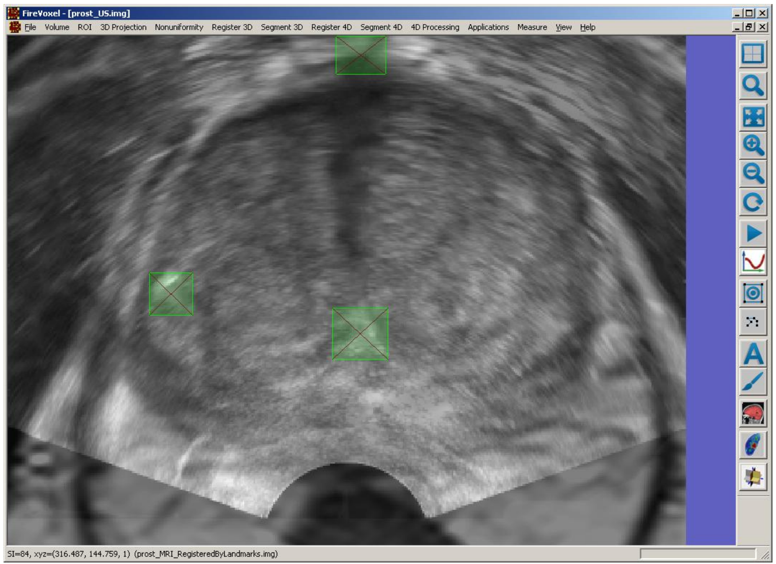


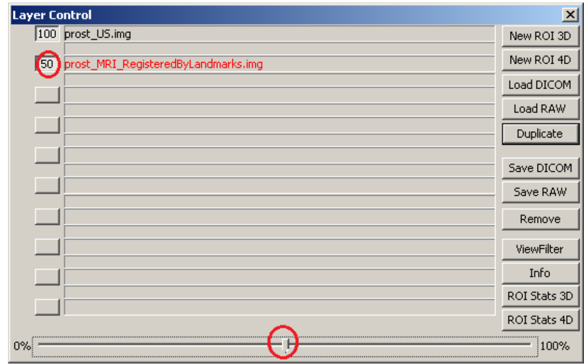
Change the transparency of the coregistered MRI image by making it active (red letters) and moving the horizontal slide bar at the bottom of the Layer Control dialog box. You will see that the location of the prostate is not affected much by switching from the US image to the coregistered MRI.



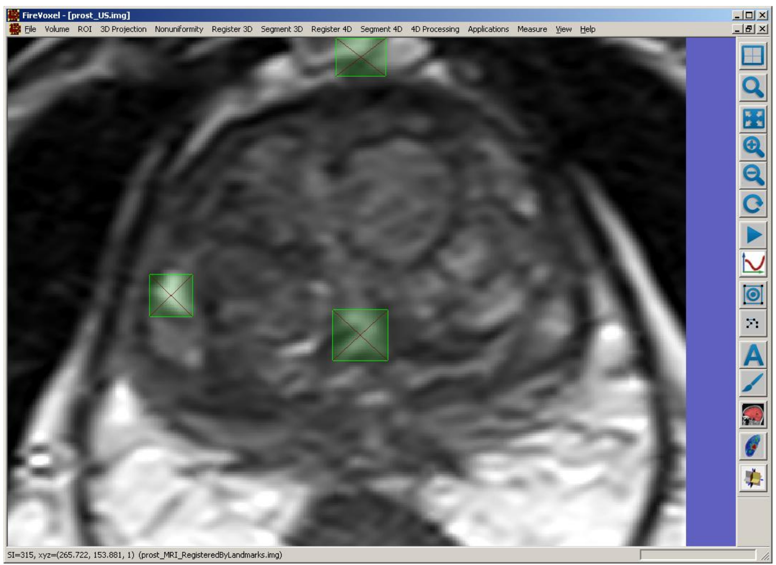


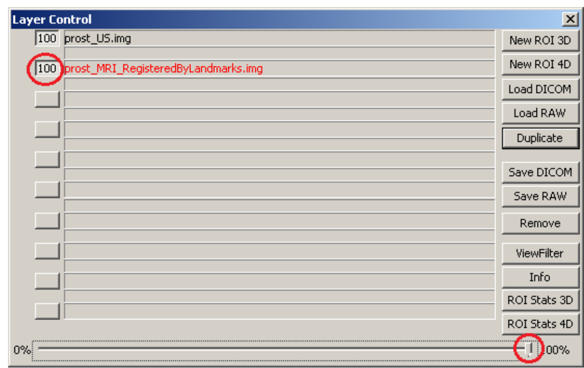
Transparency of prost_MRI_RegisteredByLandmarks.img at 0%





Transparency of
prost_MRI_RegisteredByLandmarks.img at 50%





Transparency of
prost_MRI_RegisteredByLandmarks.img at 100%

Conclusion

We have reviewed the key coregistration features offered by FireVoxel in which images of varying degrees of disparity were aligned using signal difference, mutual information, and landmark based procedures. More advanced coregistration tools not covered here include affine transformation that allow stretching and motion correction (or 4D coregistration) that performs together a large number of 3D coregistrations.