MARS: <u>M</u>ultiple <u>A</u>tlases <u>R</u>obust <u>S</u>egmentation

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1. Purpose

A lot of medical-imaging-based studies demand accurate segmentation of anatomical structures, in order to quantitatively measure structure differences across individuals or between two groups [1, 2]. For example, multiple brain regions need to be automatically delineated for hundreds of brain MR images before constructing brain connectivity network [3, 4]. To this end, automatic ROI (Region of Interest) labeling has been a hot topic in medical image processing areas, as evidenced by many labeling and label fusion methods that have been developed to improve both segmentation accuracy and robustness.

The software is hosted at IDEA lab webpage of University of North Carolina at Chapel Hill (http://bric.unc.edu/ideagroup/free-softwares/) and NITRC (http://www.nitrc.org/projects/mars/). Our software is free to use for the academic research purpose Please cite the paper [5, 6] as references if your studies use this software.

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2. System and Installation

This software is developed using QT (http://qt.nokia.com/) and has been tested on Windows XP (32-bit/64-bit), Window 7 (32-bit/64-bit), MAC (64-bit, OS X 10.9.2), and Linux (64-bit, kernel version 2.6.18-194.el5). Since GLIRT is for the large data analysis, we suggest the computation machine has more than 2G memory and 10G free disk space.

2.1 Overview of MARS

In general, MARS has integrated several state-of-the-art multi-atlas based segmentation methods, such as majority voting, local weighted voting, and non-local patch based segmentation methods. Specifically, we also included our recently-developed patch based segmentation method in this software. Compared with convention methods, our method has the following advantages: (1) add sparsity constraint to suppress the influence of misleading patches; (2) reduce the joint risk of two patches jointly making the same segmentation errors, (3) augment the conventional image patch with multi-scale representation and label-specific patch partition, and (4) use iterative framework to correct the possible mis-segmentations. In order to efficiently segment the the imaging-based researches, we developed user-friend GUI to facilitate the fast and easy processing of hundreds of images.

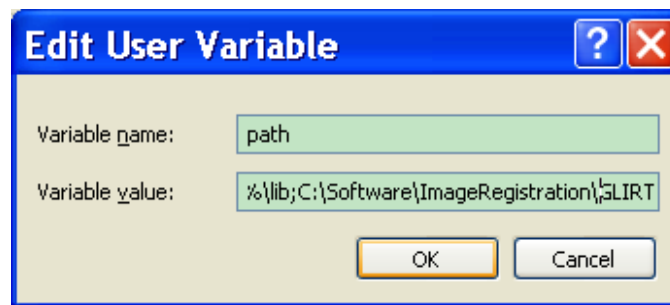### 2.2 Installation for Windows User

Fig. 1. Set up the path in desktop.

Fig. 2. Welcome screen of GLIRT in window XP.

2.3 Installation for Linux User

For linux user, please download the software (Spartacus.tar.gz) and extract (using command tar xzfv Spartacus.tar.gz) to certain folder, for example, /home/usrname/GLIRT. If you ar using C-Shell, you can set up the path by typing "setenv PATH ${PATH}:/home/usrname/GLIRT" your c-shell profile (~usrname/.cshrc). If you are using BASH, type "export PATH=${PATH}:/home/usrname/GLIRT" in your bash profile (~usrname/.bashrc). Then, use the "source" command to make the change take effect immediately ("source ~usrname/.cshrc" for C-Shell user and "source ~usrname/.bashrc" for BASH user). To test if you have successfully use the GLIRT software, you can type "Spartacus_GUI" in terminal window. If you can see the welcome screen shown in Fig. 3, congratulations, you are able explore your medical image data by GLIRT.

Fig. 3. Welcome screen of GLIRT in Linux.

3. The MARS GUI

The welcome screen is shown in Fig. 2 (Windows) and Fig. 3 (Linux). If you have a set of MR brain images, you may select "Groupwise Registration Package" button to simultaneously register all of your images to the common space without specifying the template. If you have longitudinal data on hand, you may select "Longitudinal Registration Package" button to jointly align all these longitudinal data as well as preserve the temporal continuity in each longitudinal sequence. Next, we will illustrate how to use our software in application of groupwise and longitudinal application one by one.

3.1 Groupwise Registration by GLIRT

After you click the "Groupwise Registration Pack" button on the welcome screen, you will ask to select the groupwise registration method, i.e., "Groupwise Registration with Group Mean Image" and "Hierarchical Feature-Based Groupwise Registration", which is shown in Fig. 4.
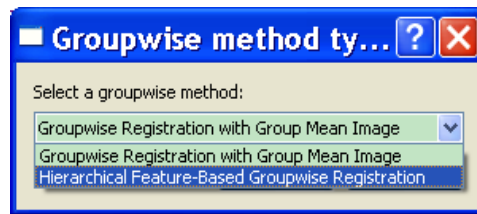

Fig. 4. The interface of the selection of groupwise registration method.

Groupwise Registration with Group Mean Image

If you select "Groupwise Registration with Group Mean Image" method and click "ok", you will see the user interface in Fig. 5. Please follow the steps below to perform the groupwise registration upon your dataset in GLIRT.

1. *Add the images to process*
   Click the "add" button to load all the data to do the groupwise registration. You can also delete any selected files or all selected files by click the "Delete" and "Clear" button. Note, we only accept the image data in Analyze type (with a pair of '.hdr' and '.img'). The image size and the overall number of subjects for groupwise registration are shown on the top of control panel. GLIRT will automatically detect whether the sizes of input images are equal.

2. *Tune the parameters for best performance*
   There are several parameters need to setup. We list the role of each parameter, value range and their default value in Table 1. You are free to change their values in the control panel.

3. *Run and check the groupwise registration result*
   Click the "Run" button to start the groupwise registration if every parameter is correctly set. Before running, you will see the dialog (in Fig. 6) to do the final check of parameters and input images. If you find any not correct, you can click "cancel" button to go back to the main window. Otherwise, click "ok" to perform the groupwise registration. The status will keep updating in the "Output Information" area and the progress bar in the bottom of the main window. Note, groupwise registration usually takes long computation time than pairwise one. Take the standard

PC (2.4GHz duo-core CPU, 3G memory) as example, it takes 12 hours to complete the groupwise registration on 18 brain images with image size 256×256×124.
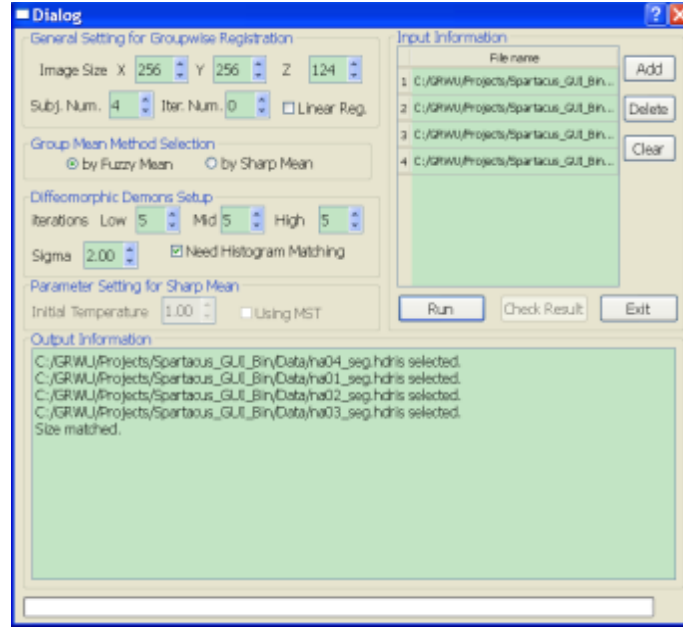

Fig. 5. The interface of "groupwise registration with group mean image" method.

Table 1. The specification of the parameters used in "groupwise registration with group mean image" method.

| Name	Meaning	Value Range	Default Value
Iteration Number	The overall iteration of groupwise registration	1~100	20
Linear Registration	If checked, GLIRT will do the linear registration before groupwise registration	true, false	false
by Fuzzy Mean	If check, GLIRT will perform the conventional unbiased groupwise registration [7]	true, false	true
by Sharp Mean	If check, GLIRT will perform our proposed groupwise registration with sharp mean [8]	true, false	false
Demons iterations Low	The iteration of demons registration in low resolution	1~100	5
Demons iteration Mid	The iteration of demons registration in low resolution	1~100	5
Demons iteration High	The iteration of demons registration in low resolution	1~100	5
Demons Sigma	The sigma value used in Demons for smoothing	0.1~5	2.0
Need Histogram Matching	If checked, GLIRT will match the histograms of all images to the first selected images	true, false	false
Initial Temperature	The initial temperature in annealing system. Lower degree, the sharper of the group mean image.	0.1~5.0	1.0
Using MST	If check, tree-based registration will be used	true, false	false
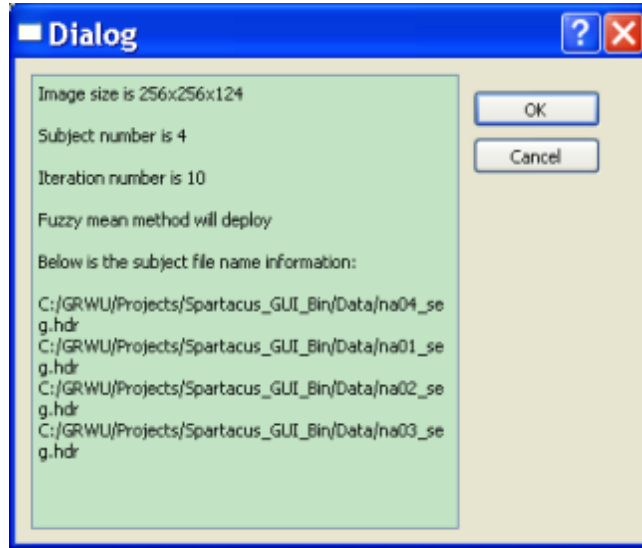
Fig. 6. The interface of check dialog before running.

Groupwise Registration with Group Mean Image

If you select the "Hierarchical Feature-Based Groupwise Registration" in the interface in Fig. 4, you will see the interface like Fig. 7. Please follow the steps below to perform the groupwise registration upon your dataset in GLIRT.

1. *Add the images to process*
   Click the "add" button to load all the data to do the groupwise registration. You can also delete any selected files or all selected files by click the "Delete" and "Clear" button. Note, we only accept the image data in Analyze type (with a pair of '.hdr' and '.img') and the '**unsigned char**' type. The image size and the overall number of subjects for groupwise registration are shown on the top of control panel. GLIRT will automatically detect whether the sizes of input images are equal.

2. *Tune the parameters for best performance*
   There are several parameters need to setup. Here, we divide the parameters into two groups, i.e., basic and advance, as shown in Fig. 8. We list the role of each parameter, value range and their default value in Table 2. You are free to change their values in the control panel.

3. *Run and check the groupwise registration result*
   Click the "Run" button to start the groupwise registration if every parameter is correctly set. Before running, you will see the dialog (in Fig. 6) to do the final check of parameters and input images. If you find any not correct, you can click "cancel" button to go back to the main window. Otherwise, click "ok" to perform the groupwise registration. Here, both the intensity and segmented image are supported. Thus, after you click "ok" button, you will see the dialog in Fig. 9 asking you to specify whether the input data are all intensity image or segmented image. For the segmented data, you must label the white matter as 250, gray matter as 150, and cerebral spinal fluid as 10. For the detail on how to get the segmented image, we encourage you to download our HAMMER_GUI software at http://www.nitrc.org/projects/hammer_suite and use that software to

do the image preprocessing, including skull strip, bias correction and segmentation. The status will keep updating in the "Output Information" area and the progress bar in the bottom of the main window.
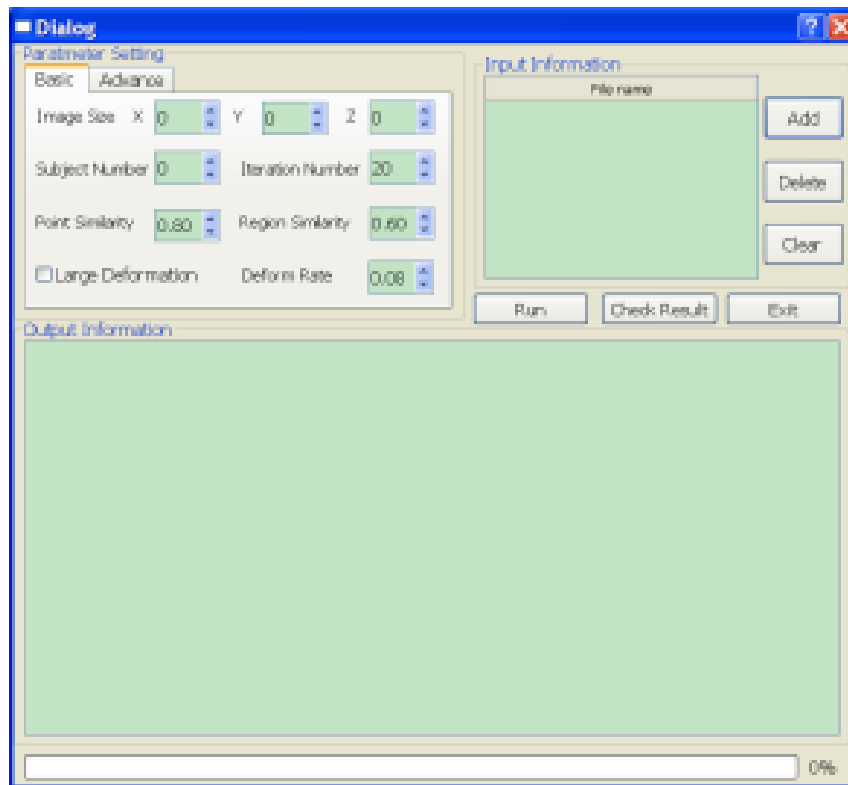

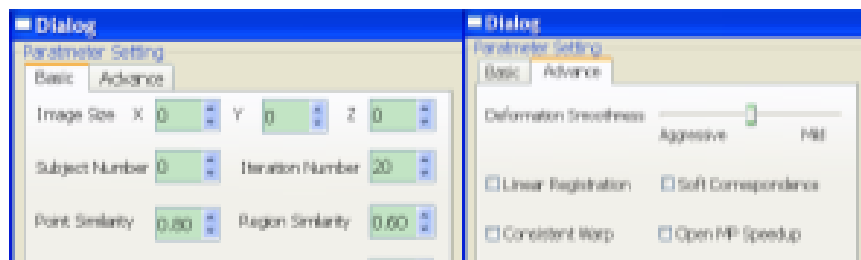**Fig. 7.** The interface of "Hierarchical Feature-Based Groupwise Registration" method.

Fig. 8. The parameters for "Hierarchical Feature-Based Groupwise Registration" method.

Fig. 9. The dialog for choose either segment or intensity based groupwise registration method.

Table 2. The specification of the parameters used in "Hierarchical Feature-based Groupwise Registration" method.

Name	Meaning	Value Range	Best Value
Iteration Number	The overall iteration of groupwise registration	1~100	50
Point Similarity	The threshold in computing the similarity between two points	0~1.0	0.8
Region Similarity	The threshold in comparing the similarity between two sub-volumes	0~1.0	0.6
Large Deformation	If checked, GLIRT will consider the anatomical difference is large among the group	true, false	false
Deform Rate	The step in updating the deformations in each iteration	0~1.0	0.05
Deform Smoothness	The strength of smoothing on deformation field	0~1.0	0.5
Linear Registration	If checked, GLIRT will do the linear registration before groupwise registration	true, false	false
Soft correspondence	If check, the soft correspondence detection strategy will be used in establishing the correspondence	true, false	false
Consistent Warp	If check, both the forward and backward deformation will be considered	true, false	false
OpenMP Speedup	If check, the multi-thread technology will be used	true, false	false

3. 2 Groupwise Longitudinal Registration by GLIRT

After you click the "Longitudinal Registration Pack" button on the welcome screen (Fig. 2 or Fig. 3), you will first to ask how many sequences of longitudinal data do you have, as shown in Fig. 10. After you click the "ok" button, you will see the main window for longitudinal registration by GLIRT (in Fig. 11). For example, we have input the sequence number as '5' in Fig. 10. Then you will see there are 5 sequences (S#1, .., S#5) listed in the "Input Information" panel (in the right part of Fig. 11). Then you can add the longitudinal data in each sequence by first specifying the underlying sequence number in the drop-list shown in the red circle of Fig. 11. Then click "Add" button in the bottom of "Sequence Information" panel to add the longitudinal data. Note, here only the segmented images in ANALYZE format are supported. If you only have the intensity image, please download our another software at http://www.nitrc.org/projects/hammer_suite and use that software to do the image preprocessing (including skull strip, bias correction and image segmentation). Our software will automatically check whether all the image sizes are matched. The image size and the overall number of images loaded will be shown in the top-left of the main window.

Before running the groupwise longitudinal registration, you need to setup the correct parameters in the left panel in main window. The detailed information on all parameters are listed in Table 3. Finally, you can click "Run" button to start the groupwise longitudinal registration. The check list will be shown in Fig. 12, you can use the scroll bar to check the parameters and the input image files.
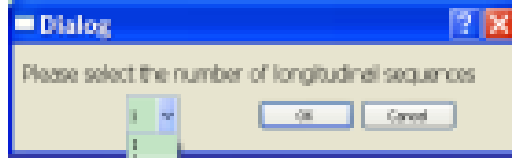
Fig. 10. The dialog for determining the number of longitudinal sequences.
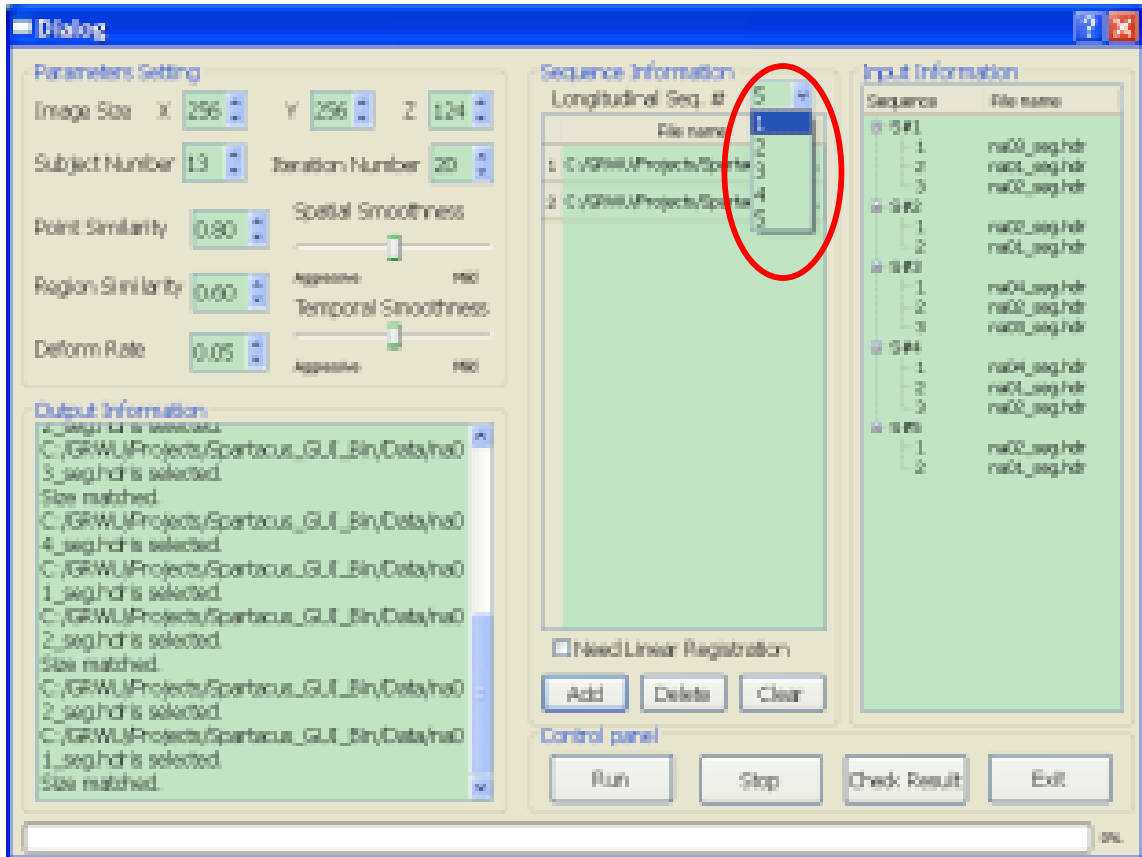

Fig. 11. The main window for longitudinal sequences registration package.

Table 3. The specification of the parameters used in "Groupwise Longitudinal Registration" method.

| Name	Meaning	Value Range	Best Value
Iteration Number	The overall iteration of groupwise registration	1~100	50
Point Similarity	The threshold in computing the similarity between two points	0~1.0	0.8
Region Similarity	The threshold in comparing the similarity between two sub-volumes	0~1.0	0.6
Deform Rate	The step in updating the deformations in each iteration	0~1.0	0.05
Spatial Smoothness	The strength of smoothing on deformation field	0~1.0	0.5
Temporal Smoothness	The strength of temporal smoothing	0~1.0	0.5
Need Linear Registration	If checked, GLIRT will do the linear registration before groupwise registration	true, false	false
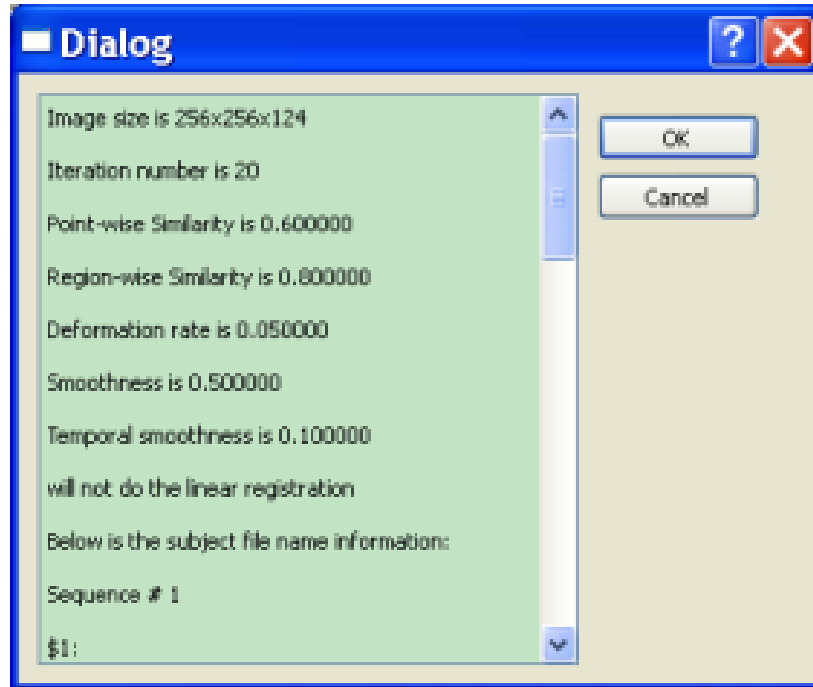
Fig. 12. The check box for longitudinal sequences registration package.

3.3 Check the Registration result in GLIRT

Once the registration is finished, a message will pop-up (in Fig. 13) to notify the registration is done. Then you can click the "Check Result" button to get the direction to check the registration results. In the current version, our registration software will provide the registered subject images and their corresponding deformation fields to warp them to the destination space. To view the image, you can use Mricro (can be downloaded at http://www.cabiatl.com/mricro/) to go through the data. We record the displacement vector for each voxel, by considering the top-left as the origin. To read our deformation field, please see the example C code in section 4.1. Also we will show the information on registration results on the "Output Information" panel, as displayed in Fig. 15.
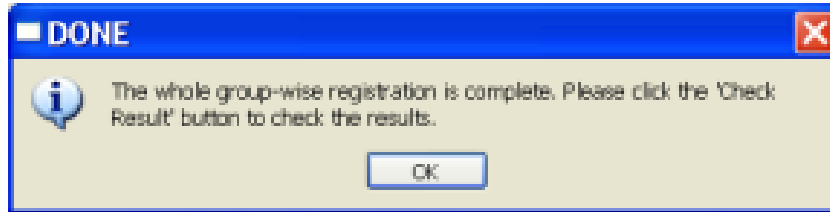
Fig. 13. The message box to notify the registration is done.

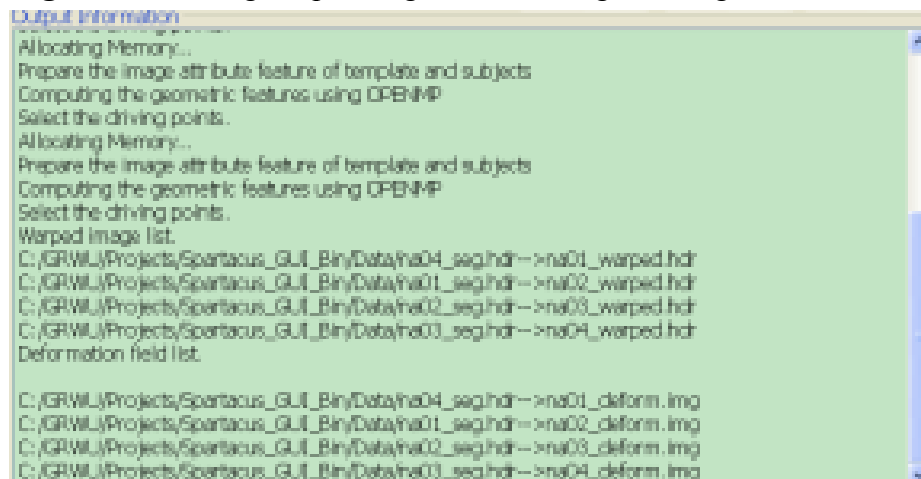**Fig. 14.** The dialog for pointing out where to get the registration results.

Fig. 15. The dialog for pointing out where to get the registration results.

4. **Miscellaneous**

4.1 Read the Output Deformation Field by GLIRT

Below is the sample C code to show how to use the output deformation field in GLIRT.

```
structure DeformationType
{
        float    x;
        float    y;
        float    z;
}Fvector3d;

void ReadDeformationField(char *filename, Fvector3d ***Deform, int x_size,
int y_size, int z_size)
{
        FILE *fp;
        int i, j, k;
        int image_size, image_z_size;
        fp = fopen(filename, "rb");
        if(fp!=NULL)
        {
                for(k=0;k<z_size;k++)
                        for(i=0;i<y_size;i++)
                                fread(Deform[k][i], sizeof(Fvector3d), x_size, fp);
        }
        fclose(fp);
}
```

5. **Contact us**

For any questions or bug reports, please email to grwu@med.unc.edu.

6. **References**

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