RegLSM Manual

1 Introduction

1.1 Outline

RegLSM, an image **Reg**istration tool for **l**esion-**s**ymptom **m**apping (**LSM**), is a user interface (UI) in Windows OS that supports registration of CT and MR (DWI, and FLAIR or T2-weighted) brain images to MNI152 space. The lesion masks together with their source images are input of this interface, and the registered source images and lesion masks are the output. The transformed lesion masks can be used for LSM analysis (e.g. the univariate LSM with NPM software in MRIcron package or the recent multivariate LSM such as SVR-LSM). The user can check the registration results of the final step or intermediate steps. The major functions of this UI are based on Elastix and SPM12, so the installation of these two software is essential before you run *RegLSM*.

1.2 Installation

It is required that the user has installed MATLAB (2015a or later version) and SPM before using this UI.

SPM is a package of functions that can be called in MATLAB. To enable SPM in MATLAB, the user should add the address of SPM folder in MATLAB PATH. We recommend the user install SPM12 (the latest version of SPM) in MATLAB. Although previous versions of SPM might also be sufficient, we have not tested for them.

For elastix, its version 4.8 has been embedded in the UI code, so you do not need to install it independently. However, you still have to prepare some basic tools (e.g. Microsoft Visual C++ Redistributable Package) to enable elastix, where you can find help in FAQ of Elastix (http://elastix.isi.uu.nl/FAQ.php).

1.3 Quick start

To open this UI in MATLAB environment, you should change the current folder to that of *RegLSM*, and then type “RegLSM” in the command window. You will see a “Brief Guide” in the major panel that introduces the basic operation of the main functions. In the menu bar, you can realize the functions supported by this UI.

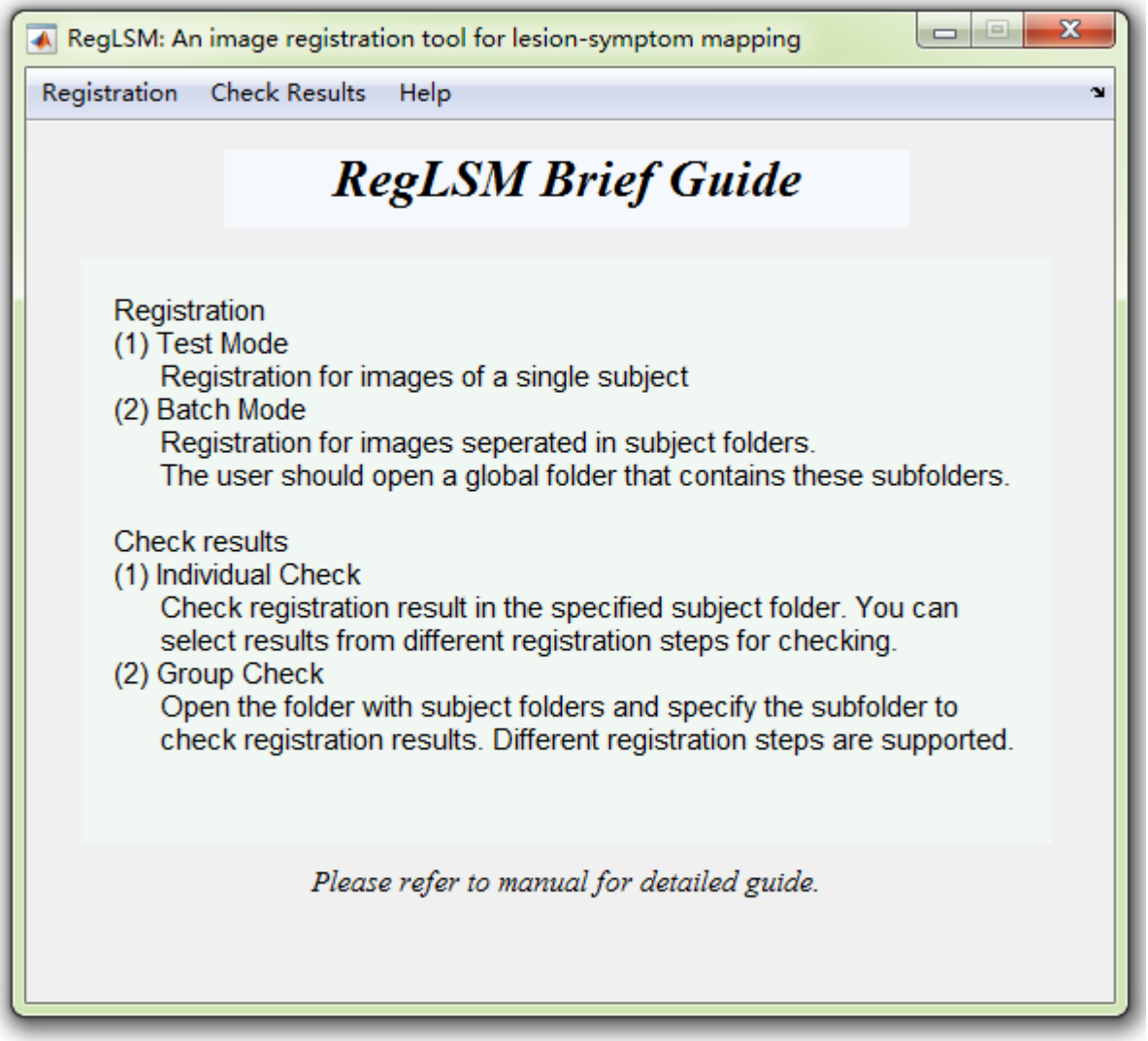

Figure 1. Main panel of *RegLSM*

2 Image registration

2.1 Test mode

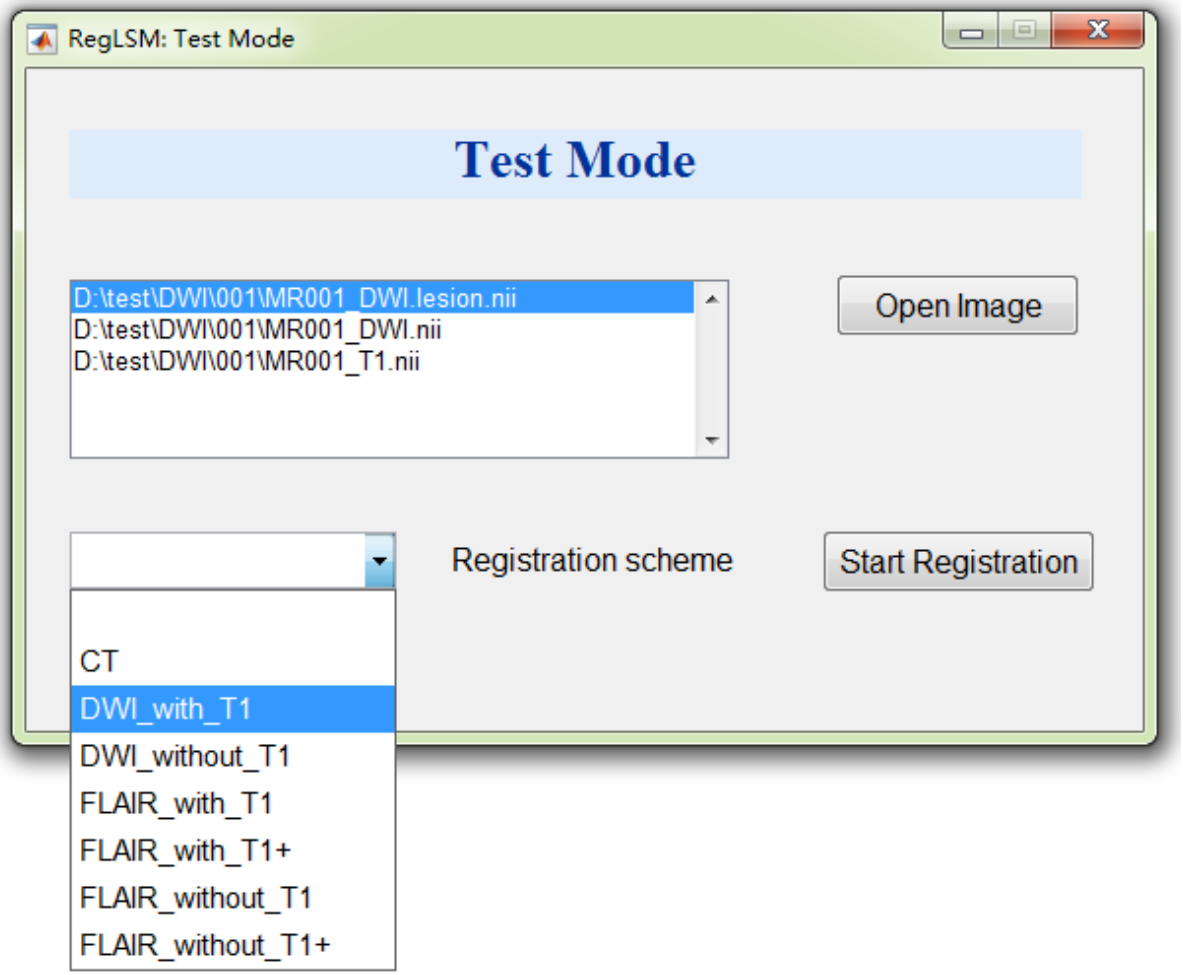

Figure 2.1 Panel of Test Mode

By clicking "Test Mode" in the item of Registration in the menu, you will see a panel like **Figure 2.1**.

- Open image

  The user can select nii files in the same folder and the directories of these files will be displayed in the listbox on the left. We recommend that you specify only the needed images for registration. If you select more than one lesion mask or source image, the registration cannot run.

- Naming of images

  Before selecting images for registration, the user should rename the images like the inputs shown in **Figure 2.1**. For example, if the lesion is delineated on DWI/FLAIR/T2, the source image should bare a string "DWI"/"FLARI"/"T2" respectively (i.e. ID of the subject + sequence name, e.g. MR001_DWI.nii). To name the lesion, you should copy the name of the source image and add ".lesion" to it (e.g. MR001_DWI.lesion.nii). For T1 image, make sure to include "T1" in the name (i.e. ID of the subject + T1, e.g. MR001_T1.nii).

- Presence of 4D images

  If some of the required input images are 4D nii files, they will be converted to 3D nii files automatically, and the first layer of the 4D nii will be taken as the input for registration.

- Registration scheme

  The users need to specify a registration scheme for selected images: CT, DWI_with_T1, DWI_without_T1, FLAIR_with_T1, FLAIR_with_T1+, FLAIR_without_T1, and FLAIR_without_T1+.

  To specify an appropriate registration scheme for your images, there are some tips to follow. If the lesion is delineated on CT, select "CT" as the registration scheme. For MR images, there are different schemes according to the modality of the source image.

  (1) ***DWI_with_T1***: If the lesion is delineated on DWI and you have a T1-weighted image of the same patient, please try this scheme first. However, if the lesion locates near skull, brainstem or cerebellum, and the mapping of the lesion is not good, you may try "*DWI_without_T1*".

  (2) ***DWI_without_T1***: If the lesion is delineated on DWI and you do not have a T1-weighted image of the same patient, please select this scheme.

  (3) ***FLAIR_with_T1***: If the lesion is delineated on FLAIR or T2 and you have a T1-weighted image of the same patient, please try this scheme first. However, if are not satisfied with the registration result, you may to turn to "*FLAIR_without_T1+*".

  (4) ***FLAIR_with_T1+***: If the appearance of T1 and FLAIR is very different (for example the tissue near ventricle), even with affine transformation in (3) will not guarantee a good registration of FLAIR to T1. In this case, this scheme might help due to its nonlinear transformation from FLAIR to T1 (the registration from subject T1 to template T1 is the same as *FLAIR_with_T1*).

  (5) ***FLAIR_without_T1***: If the lesion is delineated on FLAIR or T2 and you do not have a T1-weighted image of the same patient, please try this scheme. If the lesion mapping is not good with this scheme due to large ventricles, please turn to "*FLAIR_without_T1+*".

  (6) ***FLAIR_without_T1+***: This is the last option for FLAIR or T2 images and is better to deal with large ventricles to some degree. There might be bugs for some computers when running "*FLAIR_without_T1*" or "*FLAIR_without_T1+*" in elastix.

  - ❖ It should be noted that the names of the source image and lesion mask should match the name of the registration scheme. For example, if you select "FLAIR_with_T1" for the registration of DWI images, the registration will never run.
  - ❖ Please note that the previous registered source image and lesion mask will be covered with the newly generated results. If you want to compare the results from different registration schemes, please save the previous result (in folder "to_MNI") elsewhere before you rerun the registration.
  - ❖ There might be bugs for some computers when running MR registration schemes without T1. In general, if a bug appears for one registration in batch mode, it will be skipped, and the program will go on with the rest subfolders. When you encounter a disruption error dialog of elastix, close it and contact the developers.

- Start registration

  For now, this interface can only perform image registration if a lesion mask is available among the inputs. If the specified images are not sufficient to match the registration scheme that you specify, an error warning dialog will appear once the user clicks on

"Start Registration". Otherwise, the registration will start immediately with the specified images and registration scheme.

2.2 Batch Mode

By clicking "Batch Mode" in the item of Registration in the menu, you will see a panel as **Figure 2.2**. In batch mode, most functions are similar to those in the test mode. However, there are several differences.

- Open folder

  The user need to select a folder with subfolders that contain images of specific patients. For example, as is shown in **Figure 2.2**, we have 3 subfolders (named 001, 002, and 003) in the global directory "D:\test\DWI". Each subfolder has a source DWI image, a lesion mask delineated on this DWI, and a T1 image of the subject. Here, we do not support image selection for every subject, so the users should rename the images according to the tips mentioned in "Naming of images" of the previous section (Test mode).

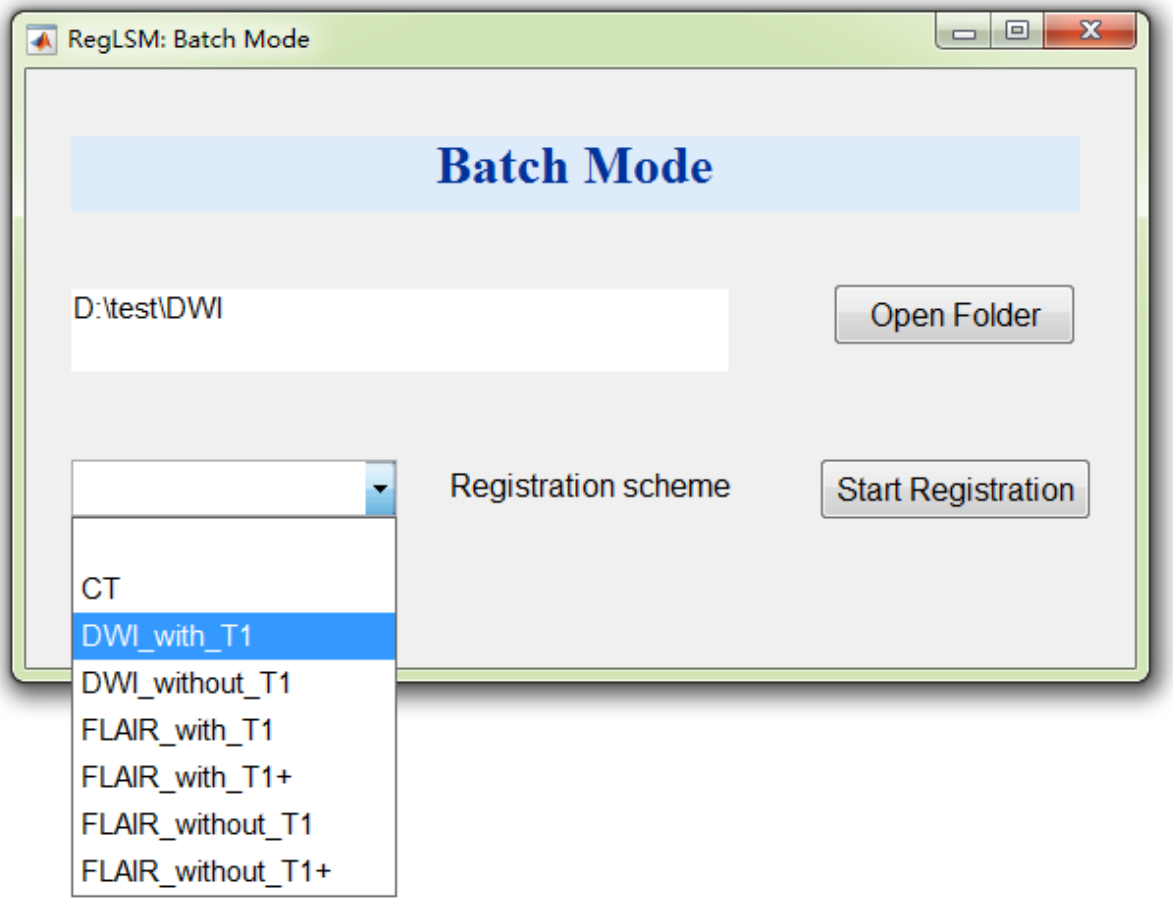

Figure 2.2 Panel of Batch Mode

- Lack of images for registration

  If some subfolders do not have complete images required for specific registration scheme, they will be ignored and the program will run for the following subfolders. Unlike test mode, no error warning dialog will appear here about the lack of images in a folder, but the subfolders with incomplete images will be recorded in an excel file. This record file is named with "batch_record" which locates in the input root folder. **Table 1** is an example of such batch record, with image directories of the inputs for

registration. If any of the required images is empty or more than expected, the number of the image(s) will be displayed instead of its directory. For example, in **Table 1**, subject "003" does not have T1 image in the specified scheme "DWI_with_T1", so "0" is displayed in the directory of T1 image. If more than one required image is missing, the corresponding value of the image may be empty instead of "0" in the record.

- There might be bugs for some computers when running MR registration schemes with nonlinear transformation from DWI/FLAIR/T2 to T1. In general, if a bug appears for one registration in the batch mode, subfolder with bugs will be skipped and the program will go on with the rest subfolders. A text file named "FAILED" would be added to the subject folder with bugs. If you encounter a disruption error warning dialog of elastix and the batch mode fails to go on with the following registration, please contact the developers.

Table 1. Example of batch record

Subject folder name	Lesion mask	Source image	T1 image
001	D:\test\DWI\001\MR001_DWI.lesion.nii	D:\test\DWI\001\MR001_DWI.nii	D:\test\DWI\001\MR001_T1.nii
002	D:\test\DWI\002\MR002_DWI.lesion.nii	D:\test\DWI\002\MR002_DWI.nii	D:\test\DWI\002\MR002_T1.nii
003	D:\test\DWI\003\MR003_DWI.lesion.nii	D:\test\DWI\003\MR003_DWI.nii	0

3 Check Registration

3.1 Individual Check

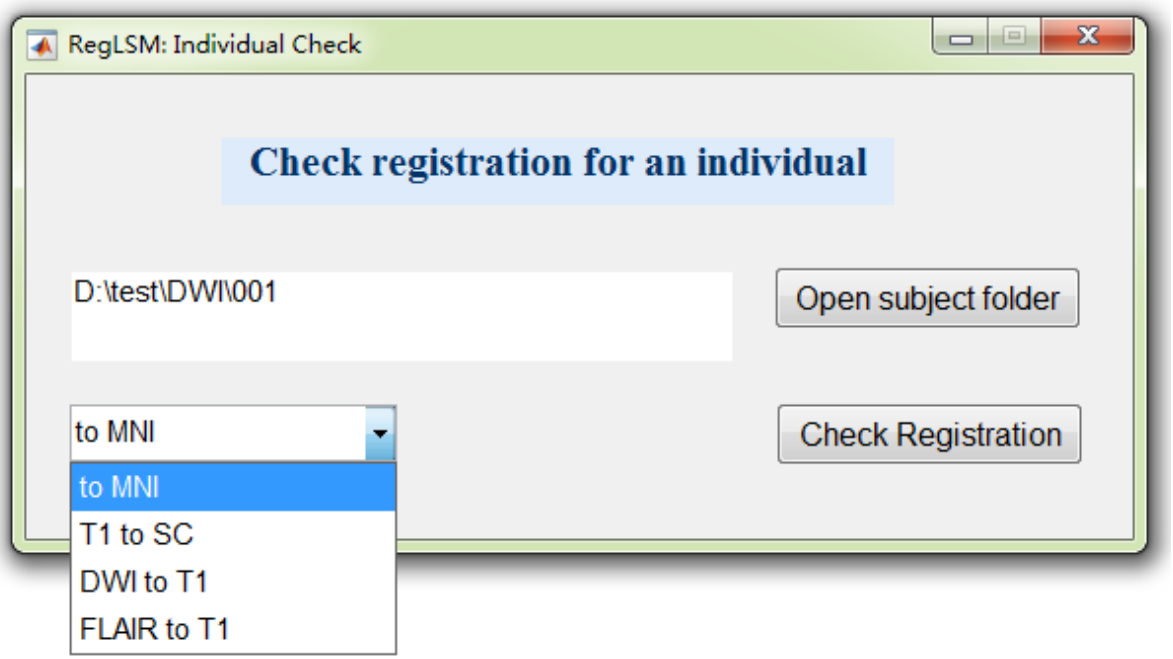

Figure 3.1 Panel of Individual Check

After registration for a single subject, you can check the results of different registration steps (**Figure 3.1**). The default image to check is the final registration result to MNI152 space. In addition, for example, if you have a lesion mask delineated on DWI and the selected registration scheme is "*DWI_with_T1*", you can also check the results from steps of *DWI to T1* and *T1 to SC*, where *SC* is an intermediate T1 template in MNI152 space.

3.2 Group Check

In "Group Check", you can specify a folder with subjects and check the results of different steps. This mode enables selection of subject folder to check (see **Figure 3.2**) compared to "Individual Check".

Taking the example we've mentioned in Section 2.2, where there is a folder named "DWI" with 3 subjects whose lesions are delineated on DWI. If you want to check subject "001", you need to select folder "DWI" instead of "DWI\001". Then input the number "1" in the bottom left frame (indicating ***Subfolder ID***), or just click "***Check Registration***", which will start from the first subject by default. And if you want to check subject 002, you have 2 options. The first option is to type "2" in ***Subfolder ID*** and click "***Check Registration***". The second is to click on "Next" before clicking "***Check Registration***". Also, you can change the registration step ("to MNI" by default) to check for each subject.

- ❖ Although manual correction is sometimes needed for very few of the results (i.e. to correct the registration bias for some lesion masks that are mapped to MNI152 space), it is not yet available in the current version of this UI.

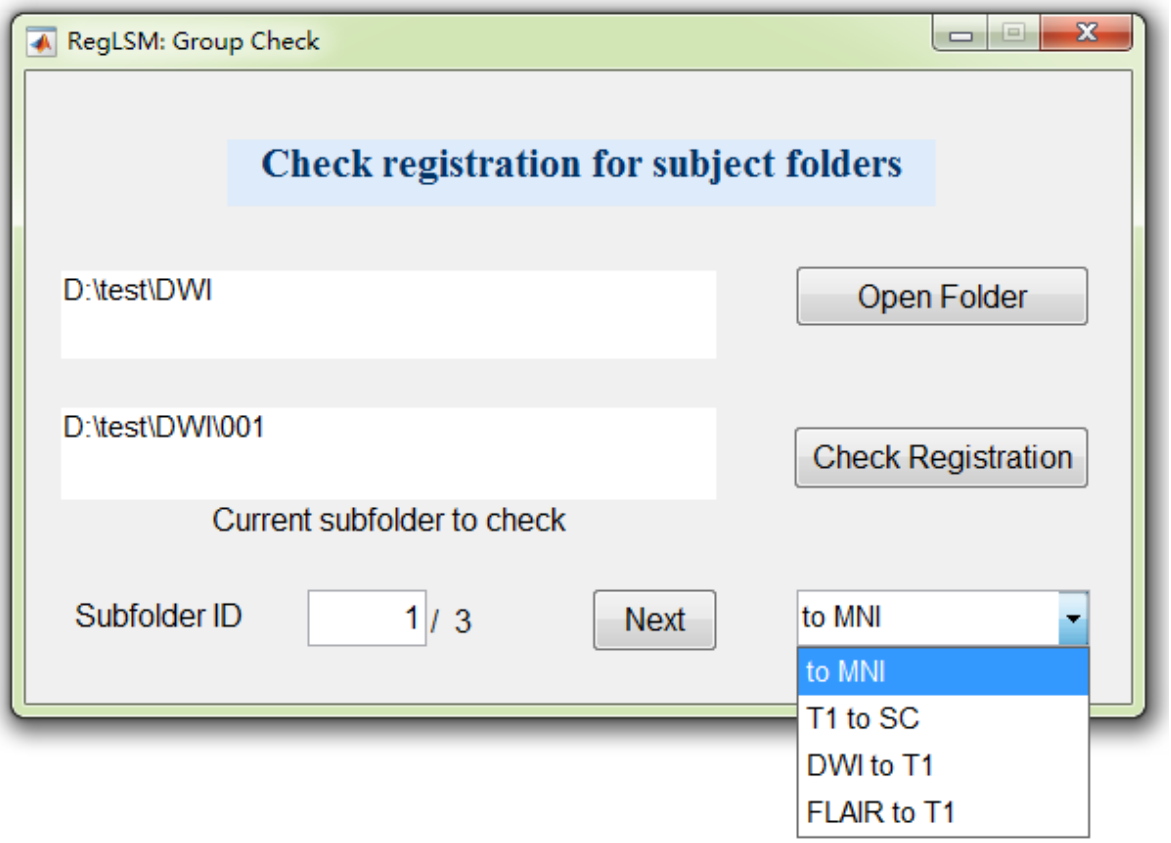

Figure 3.2 Panel of Group Check

4. Paths of the registration results

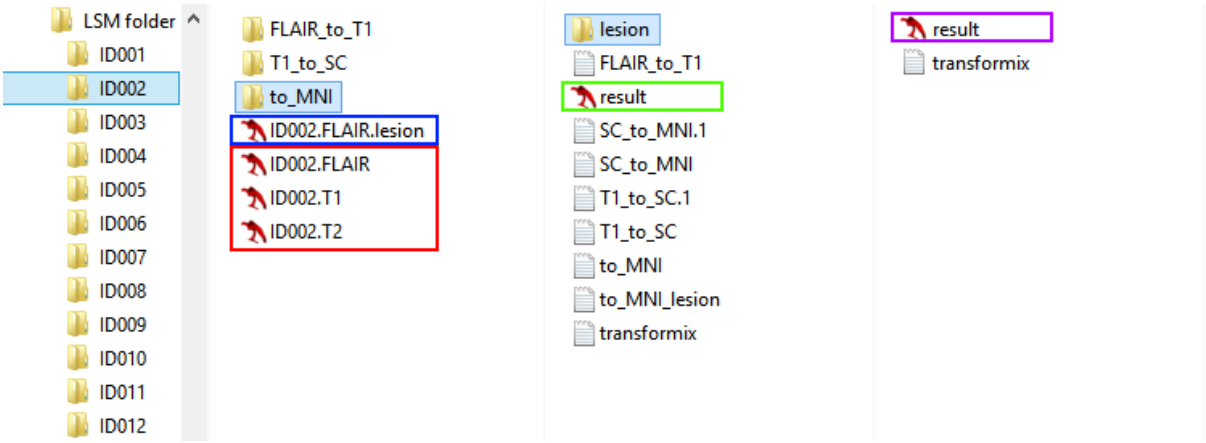

Figure 4. Typical folder structure during image processing for lesion-symptom mapping. The first subfolder for subject ID002 contain three native scans in nifti format (FLAIR, T1 and T2, in red box) and the segmentation of the FLAIR sequence (in blue box). The three subfolders are created during the registration process by RegLSM. The subfolder to_MNI contains the registered segmented scan (in this case the FLAIR, in green box). The subsequent subfolder contains the registered lesion map in standard space (purple box). Of note, RegLSM will be made BIDS-compatible in the upcoming update.