DCEFit Plugin for OsiriX

Reference Manual v1.1.4

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1 Introduction

This OsiriX plugin performs registration of DCE (dynamic contrast enhanced) MRI time series images, either 2D or 3D, and DCE analysis of the registered images. These are two distinct steps. The registered images are stored as a series in the OsiriX database. The user can then select a series to analyse. **Currently only the registration portion is implemented.**

2 Installation

The plugin is distributed as a Zip archive, *DCEFit.zip* which contains a bundle called *DCEFit.osirixplugin*. It is suitable for both 32 and 64 bit versions of *OsiriX* and requires OS X version 10.7 (Lion) or higher.

Unzip the DCEFit.zip file to obtain DCEFit.osirixplugin. The most convenient method to install the plugin to double click it in *Finder*.

You can also use the following steps.

```
unzip -d “/Library/Application Support/OsiriX/Plugins” DCEFit.zip
```

To install *DCEFit* for yourself only, type

```
unzip -d “~/Library/Application Support/OsiriX/Plugins” DCEFit.zip
```

When OsiriX is restarted, *DCEFit* will appear in the `Plugins/Image Filters` menu.

3 Technical Description

DCEFit has been compiled to run on either a 32 or 64 bit Macintosh with either 32 or 64 bit *Osirix*. It uses the Insight Segmentation and Registration Toolkit (ITK)[1] for registering the images. The registration section uses a two stage (rigid followed by deformable) multi-resolution scheme in which each of the stages is optional. The user can select up to four resolution steps for each of the rigid and deformable registrations.

4 Getting Help

The first place to look is the ITK Software Guide.[2] There are also many footnotes to the programming documentation in this manual. It often contains useful information for the user. For information about registration in general the Slicer wiki is a good place to look.[3]

1 http://www.itk.org
2 http://www.itk.org/ItkSoftwareGuide.pdf (This is always a link to the latest version.)
3 http://www.slicer.org/slicerWiki/index.php/Main_Page

4.1 Rigid Registrations

If the series contains 2D images the ITK Centered Rigid 2D Transform[4] which rotates the image about its centre and translates it in two dimensions. The Regular Step Gradient Descent[5] (RSGD) optimizer is used. If the series contains 3D images the ITK Versor Rigid 3D transform[6] and the Versor Transform[7] (VT) optimizer are used. These are not user selectable.

Either the Mean Squares[8] (MS) or the Mattes Mutual Information[9] (MMI) metric may be selected although the latter is almost always the better choice.

4.2 Deformable Registrations

Both 2D and 3D series are treated the same way for deformable registrations. The ITK BSpline Transform[10] is used with the number of B-spline nodes selectable in each dimension.

There is a choice of optimizers, two versions of the Limited memory Broyden Fletcher Goldfarb Shannon optimizer[11,12] (LBFGS and LBFGSB) and the RSGD optimizer. The reason for this choice is that the LBFGSB optimizer generally gives the best results but occasionally fails, probably because of an internal software defect[13]. The LBFGS, RSGD optimizers are not as well suited to the high dimensionality of deformable registration but will work if needed.

Either the MS or the MMI metric may be selected although, as above, the latter is almost always the better choice.

5 Running DCEFit

As with any *OsiriX* Image Filter plugin, a series must be loaded into the *OsiriX Viewer* in order to load the plugin. Because we are working with time resolved series the images must be loaded with the *Osirix 4D Viewer*. After loading the plugin (menu item `Plugins/Image Filters/DCEFit`) the images will be loaded (this may take a few seconds) and the main window or dialog will appear and associate itself with the key viewer. (If more than one series is loaded, the key viewer is the one with the red border.) Be sure to select the correct one before loading *DCEFit*. If you wish to change series do the following.

1. Close the *DCEFit* dialog.
2. Open the new series or select the viewer containing the new series thus making it the key viewer.
3. Relaunch *DCEFit*.

6 Image Registration

DCEFit implements a two stage (rigid followed by deformable) multi-resolution registration scheme. Both stages are optional although at least one must be enabled.

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4 http://www.itk.org/Doxygen/html/classitk_1_1CenteredRigid2DTransform.html
5 http://www.itk.org/Doxygen/html/classitk_1_1RegularStepGradientDescentOptimizer.html
6 http://www.itk.org/Doxygen/html/classitk_1_1VersorRigid3DTransform.html
7 http://www.itk.org/Doxygen/html/classitk_1_1VersorTransformOptimizer.html
8 http://www.itk.org/Doxygen/html/classitk_1_1MeanSquaresImageToImageMetric.html
9 http://www.itk.org/Doxygen/html/classitk_1_1MattesMutualInformationImageToImageMetric.html
10 http://www.itk.org/Doxygen/html/classitk_1_1BSplineTransform.html
11 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSBOptimizer.html
12 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSOptimizer.html
13 http://www.itk.org/pipermail/insight-users/2013-September/048794.html

6.1 Registration Tab

There are a number of parameters that can be set to control the registration. The general scheme is that an optional rigid registration can be performed before an optional deformable registration. Both registrations are potentially multi-resolution, implemented by image pyramids.

The ITK manual describes image pyramids as having the largest shrink factor, that is the smallest image, at the top. Conceptually, the registration starts with the top image and end with the bottom one. In *DCEFit* the `Optimizer` and `Metric` tables show the parameters as if the pyramids were inverted. The top entries are for a shrink factor (divisor) of 1 and these increase by factors of 2 down the tables. If, for instance, you selected 3 levels the parameters would correspond to shrink factors 1, 2 & 4 going down the tables. Again, *DCEFit* goes from the bottom of the tables to the top as it processes the image pyramids.

6.1.1 Common

Series Description	When the registered series is stored in the OsiriX database this is appended to the existing series description. The series description corresponds to DICOM attribute (0008, 103e).
Fixed Image	The fixed image is the reference image to which all of the others (the moving images) are registered. When *DCEFit* is launched it looks for the first key image in the series and chooses it as the fixed image. This can be reset by the user. If there is an ROI on the new image it will be used as the registration region. Otherwise the region will be set to be the whole image[14]. This control shows both the image number and its acquisition time (DICOM attribute (0008, 0032)) as shown also in the lower right corner of the *OsiriX* viewer.

6.1.2 Rigid Registration

Enabled	Check to enable the rigid registration step.
Levels	Select the number of levels to use in multi-resolution registration.
Optimizer	Configure the optimizer by pressing the *Configure* button. The RSGD optimizer is used for 2D images and its close relative the VT optimizer is used for 3D images.
Versor and RSGD	Initial Step Size This is the step size in mm that the optimizer starts with in searching for optimum parameters. The step size is reduced as the optimizer closes in on the best fit. Setting this too large may cause the optimizer to “get lost” immediately while setting it too small will increase search time. Min. Step Size As this optimizer converges it reduces the step size (in mm) until this value is reached. Larger values will give poorer but faster fits while smaller values will give

14 It is recommended that the smallest possible region be used to reduce time required for registration.

	more precise fits at the expense of longer registration times. Relaxation Factor When the optimizer reduces the step size it does so by this factor. (*i.e.* new step size = current step size * relaxation factor) Trans. Scaling (*Versor only*) Adjusting the translation scaling factor can be used to fine tune the registration. The optimization is more sensitive to translations than rotations so the translation parameters are scaled internally to reduce sensitivity to them. The default value of 0.001 should be acceptable in most cases. Max. Iterations This sets the maximum number of iterations allowed. The optimization will stop when this number of iterations has been reached even if convergence is not achieved.
Metric	
Mean Squares	Select to use the mean squares metric. There are no adjustable parameters for this metric.
Mattes Mutual Information[15]	Select to use the MMI metric. The following parameters can be set only if MMI is selected.
	Bins The MMI algorithm generates joint probability histograms based upon the values of corresponding pixels in the two images. These are used to calculate the mutual information between the two images. The original authors recommend 50 bins for 3 dimensional registrations but fewer might work well here. Sample Rate This is the fraction of the total number of pixels to sample at random to generate the histograms. A value of 1.0 indicates that all pixels should be used. Lower values will lessen the computational burden.

6.1.3 Deformable Registration

Enabled	Check to enable the deformable registration step.
Levels	Select the number of levels to use in multi-resolution registration.
Show deformation	If enabled a grid showing the deformation field will be “burned” onto the image. Normally this should be disabled as the grid cannot be removed.

15 http://www.itk.org/ItkSoftwareGuide.pdf and Mattes et al., PET-CT image registration in the chest using free-form deformations. IEEE Trans Med Imaging 2003;22:120-128.

Optimizer	Select the desired optimizer and configure it by pressing the *Configure* button.
LBFGSB[16]	Convergence Factor The L-BFGS-B optimizer stops when $\Delta m < c * mp$ where Δm is the change in the metric between iterations, c is the entered convergence factor and mp is the machine precision. The authors recommend using 1.0E12 for low accuracy, 1.0E7 for moderate accuracy and 1.0E1 for extremely high accuracy. In registration problems values in the range 1.0E10 to 1.0E12 appear to work well. Gradient Tolerance This optimizer can also be set to stop when the projected gradient becomes smaller than this number. Setting it to zero disables this feature. Max. Iterations This sets the maximum number of iterations allowed. The optimization will stop when this number of iterations has been reached even if convergence is not achieved.
LBFGS[17]	Gradient Convergence The LBFGS optimizer converges by finding the smallest gradient in its parameter space. It stops when the projected gradient is smaller than the number set here. Initial Step Size This is the step size in mm that the optimizer starts with in searching for optimum parameters. The step size may be reduced as the optimizer closes in on the best fit. Setting this too large may cause the optimizer to “get lost” immediately while setting it too small will increase search time. Max. Iterations This sets the maximum number of iterations allowed. The optimization will stop when this number of iterations has been reached even if convergence is not achieved.
RSGD[5]	Min. Step Size As this optimizer converges it reduces the step size (in mm) until this value is reached. Larger values will give poorer but faster fits while smaller values will give more precise fits at the expense of longer registration times. Max. Step Size This is the step size in mm that the optimizer starts with in searching for optimum parameters. The step size is reduced as the optimizer closes in on the best fit. Setting this too large may cause the optimizer to “get lost” immediately while setting it too small will increase search time. Relaxation Factor

16 http://users.eecs.northwestern.edu/~nocedal/lbfgsb.html and http://www.itk.org/Doxygen/html/classitk_1_1LBFGSBOptimizer.html
17 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSOptimizer.html

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B-spline Grid Size	The deformable registration is based upon ITK's BSplineTransform[18]. A grid of cubic B-spline nodes (or control points) is laid out over the registration region. During optimization these are moved in the x, y and (possibly) z directions. These translations are the optimization parameters. In the table, the dimension labels are X: horizontal, Y: vertical and Z: orthogonal to the screen. The Z column is enabled only when the images are 3D. Because the number of parameters scales with the square (2D) or cube (3D) of this value, it is the most important parameter in determining the speed of the registration. The grid size can be set arbitrarily in each dimension with a minimum size of 4. Some guidance on the selection of grid sizes is given in the Slicer Wiki[19].

6.2 Fitting Tab

This code is not yet implemented.

18 The ITK Software Guide does not document this transform although its predecessor (DeformableBSplineTransform) is documented. See also http://www.itk.org/Doxygen/html/classitk_1_1BSplineTransform.html.

19 http://www.slicer.org/slicerWiki/index.php/Documentation/4.3/FAQ#What.27s_the_BSpline_Grid_Size.3F

6.3 Configuration Tab

There are a few parameters which control the operation of *DCEFit* that can be set here.

Logging Level	While *DCEFit* is running it logs information to the file "`ca.brasscats.osirix.DCEFit.log`" in ~/Library/Logs. It can be viewed with the *Console* application (*/Applications/Utilities/Console.app*). This controls the amount of information logged to the file.
Number of ITK threads	Most ITK classes are designed to be multi-threaded and *DCEFit* takes advantage of multiple processors when possible. Each thread requires its own memory and while this is not a problem for the 64 bit *OsiriX* version, it can be a problem when using the 32 bit version because *OsiriX* and *DCEFit* use the same limited memory space. Unfortunately the first symptom of memory shortage is for *OsiriX* to crash. Should this happen, reduce the number of threads after restarting *DCEFit* but before starting a registration.

6.4 Starting the Registration

The *Start* button starts the registration. This causes the current viewer on *OsiriX* to be copied. The new viewer becomes the key viewer, the one with the red border. As slices are registered they are copied into the new viewer and you can follow the quality of registration by viewing the images in the new viewer as they are stored. Do not close either of the viewers while registration is in progress.

6.4.1 Progress Dialog

At the start of registration a dialog is presented to show the progress of the registration and to allow you to abort the registration if necessary. If you press *Stop* and confirm that you wish to abort the registration, it will stop when the current image iteration is finished.

If you wish to save the registered images in *OsiriX*'s database press *Save*. Otherwise press *Quit* to abandon the data. Should you change your mind, you can use *File/Export/Export to DICOM Files* in *OsiriX* while the 2D Viewer is active.

7 Implementation Notes

1. While *DCEFit* is running it logs information to a file "`ca.brasscats.osirix.DCEFit.log`" in ~/Library/Logs. It can be viewed with the *Console* application (*/Applications/Utilities/Console.app*).

8 Comments on Registering DCE-MRI Images

I gained some experience with registration was gained while writing *DCEFit*. What follows are comments based upon this experience.

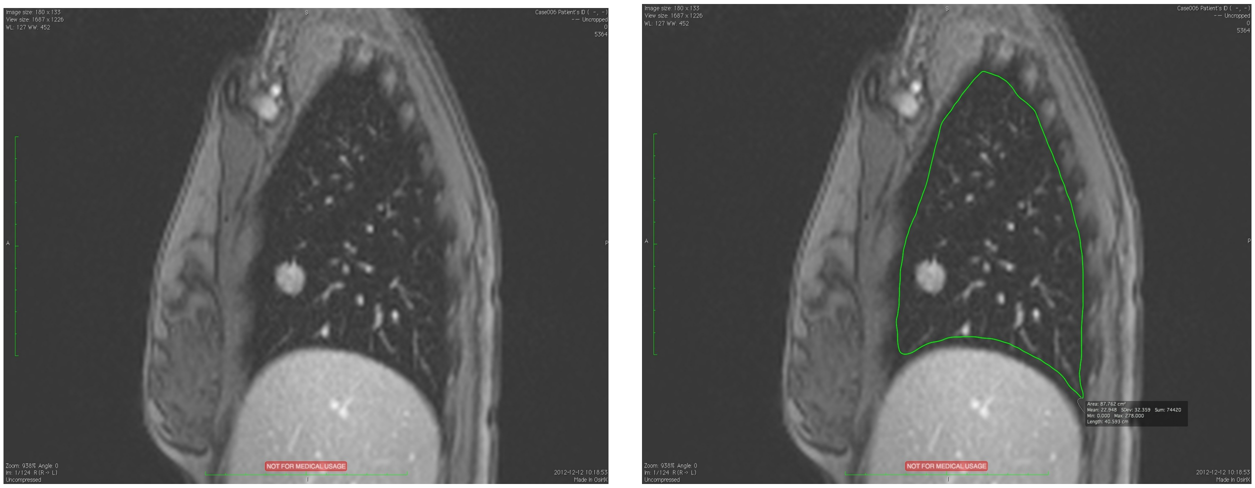

Figure 8.1: Preparation for registration. *Top left:* Image slice as received. *Top right:* Region of interest marked out with the OsiriX pencil ROI tool.

8.1 Choice of Fixed Image

Essentially registration is the process of making one image, the *moving* image, look as much as possible as another, the *fixed* image. In DCE-MRI one image in the series must be chosen as the fixed image and the others one by one become the moving images. Ideally, the fixed image should be somewhere the middle of the field in terms of its deformations and not an extreme.

8.2 Use of Rigid Registration

It is common to apply a rigid deformation to the moving image first. In *DCEFit* this consists of a rotation around the centre of the image and translation in both spatial directions. This is followed by a deformable registration based upon B-splines directions.

My experience with registering DCE-MRI images is that rigid registration is not necessary and may be counterproductive. Rigid registration is usually used to correct offsets in two images produced at different times or with different modalities. In the case of DCE-MRI, there is no offset to correct unless the subject actually shifts position. The differences in the images are due to breathing, not shifts in the patient's position, and are therefore best treated as deformations.

I have also found that rigid registration often fails completely on these images because there is no smooth rigid transformation between the fixed image and the moving image and the optimizer may not be able to deal with this situation.

8.3 Choice of Grid Size

Image registration is an iterative optimization process and can be quite slow. The rigid transform has few parameters (a rotation and a translation for each dimension) so it is quite fast even without restricting the region. The B-spline transform parameters consist of a translation vector for each node in the B-spline grid so for a grid size of 30 x 30 x 10 nodes we have 30 x 30 x 10 x 3 = 27000 parameters. Optimizing a series of several hundred images with a fine grid can take a while to complete.

8.4 Choice of Optimizer

The L-BFGS-B optimizer is described as being the best for large multidimensional problems and this seems to be the case. Unfortunately there seems to be a bug in the L-BFGS-B optimizer which shows up as a severe failure of the registration.[13] If this happens try another optimizer.

8.5 Choice of Metric

Mattes Mutual Information is often used for multi-modality registrations because of its tolerance for variations in the appearance of the images. Mattes et al. in their original paper describe the 3D registration of PET and CT images. This method works well even if only a small fraction of a large image is sampled at random, thereby improving performance. In 2D slices there are not enough pixels to require reduction of the computational load by random sampling so it is probably best to choose a sample rate between 0.50 and 1.00. For 3D registrations a sample rate of 0.01 to 0.1 appears to give good results.

The mean squares metric is ideally used if the intensities of the homologous regions are the same in both images. This is not strictly true with DCE-MRI image series but all of the features that we wish to register appear in all of the images with reasonable intensity. Experience has shown that it is faster than MMI but may not work well for some images.