

DCEFit Plugin for OsiriX

Reference Manual v1.2

Tim Allman Ph.D.

dr.tim.allman@gmail.com

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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 on Github (<https://github.com/TimAllman/DCEFit/releases>) as an archive which contains a bundle called *DCEFit.osirixplugin*. It is suitable for both 32 and 64 bit versions of *OsiriX* and requires OS X version 10.8 (Mavericks) or higher.

The most convenient method to install the plugin to double click it in *Finder*.

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. There are two registration methods available. The first is a two stage (rigid followed by B-spline deformable) multi-resolution scheme in which each of the stages is optional. The second is the Demons² method. 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.³ There are also many footnotes to the programming documentation in this manual because it often contains useful information for the user. For information about registration in general the Slicer wiki is a good place to look.⁴

4.1 Rigid Registration

If the series contains 2D images the ITK Centered Rigid 2D Transform⁵ which rotates the image about its centre and translates it in two dimensions. The Regular Step Gradient Descent⁶ (RSGD) optimizer is used. If

1 <http://www.itk.org>

2 J. P. Thirion. Fast non-rigid matching of 3D medical image. Technical report, Research Report RR-2547, Epidure Project, INRIA Sophia, May 1995. Available here: <http://hal.inria.fr/docs/00/07/72/68/PDF/RR-2547.pdf>. This is recommended reading.

3 <http://www.itk.org/ItkSoftwareGuide.pdf> (This is always a link to the latest version.)

4 http://www.slicer.org/slicerWiki/index.php/Main_Page

5 http://www.itk.org/Doxygen/html/classitk_1_1CenteredRigid2DTransform.html

6 http://www.itk.org/Doxygen/html/classitk_1_1RegularStepGradientDescentOptimizer.html

the series contains 3D images the ITK Versor Rigid 3D transform⁷ and the Versor Transform⁸ (VT) optimizer are used. These are not user selectable.

Either the Mean Squares⁹ (MS) or the Mattes Mutual Information¹⁰ (MMI) metric may be selected although the latter is almost always the better choice.

4.2 B-spline Deformable Registration

Both 2D and 3D series are treated the same way for deformable registrations. The ITK BSpline Transform¹¹ 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^{12,13} (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 defect¹⁴. 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.

4.3 Demons Deformable Registration

This method² seems to be the method of choice for DCE MRI. It is faster than the Rigid + B-spline method, has fewer parameters to set and gives better results. It tends not to produce holes in the outer boundaries of the images as the edges of the image do not get pulled in as much. There is no registration region defined so the whole image is registered at once.

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 both a two stage (rigid followed by B-spline deformable) or a Demons deformable multi-resolution registration scheme. Both stages are optional although at least one must be enabled.

7 http://www.itk.org/Doxygen/html/classitk_1_1VersorRigid3DTransform.html

8 http://www.itk.org/Doxygen/html/classitk_1_1VersorTransformOptimizer.html

9 http://www.itk.org/Doxygen/html/classitk_1_1MeanSquaresImageToImageMetric.html

10 http://www.itk.org/Doxygen/html/classitk_1_1MattesMutualInformationImageToImageMetric.html

11 http://www.itk.org/Doxygen/html/classitk_1_1BSplineTransform.html

12 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSBOptimizer.html

13 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSOptimizer.html

14 <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 type of registration. You can select one of *Rigid*, *B-spline*, *Rigid followed by B-spline* and *Demons*. All registrations are potentially multi-resolution, implemented with 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 ends 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.

At the top of the *DCEFit* Registration tab is a section which contains the attributes common to all registration methods. Below it you can set parameters for the different registration methods.

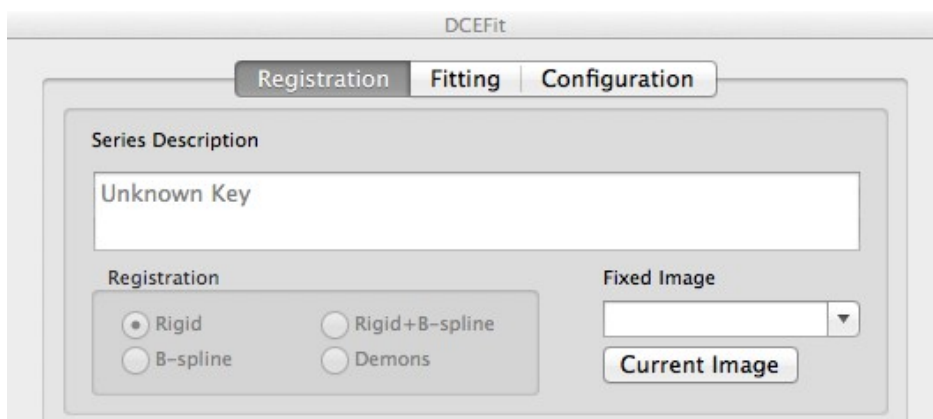


Figure 1: Common registration parameters.

6.1.1 Common Parameters

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).
Registration	Select the registration sequence here.
Fixed Image	The fixed image is the reference image to which all of the others (the moving images) are registered. When <i>DCEFit</i> is launched it looks for the first image containing a region of interest (ROI) named “dcefit” (case insensitive) and chooses it as the default fixed image. The region is kept and used as a registration region if appropriate. (If no ROI is found the region will be set to be the whole image ¹⁵ .) You can choose the fixed image by selecting an image in the list or setting it to the

¹⁵ It is recommended that the smallest possible region be used to reduce time required for registration.

image currently viewed in OsiriX by pressing the Current Image button.

Note that this behaviour was created to support the non-Demons methods which make use of a region to register. Demons fits the whole image and does not make use of the region defined by the ROI.

The Fixed Image 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 Specific Registration Parameters

The middle section of the *DCEFit* window contains the controls used to set the parameters for each kind of registration. Use the tabs to select the registration type. The parameters are described below.

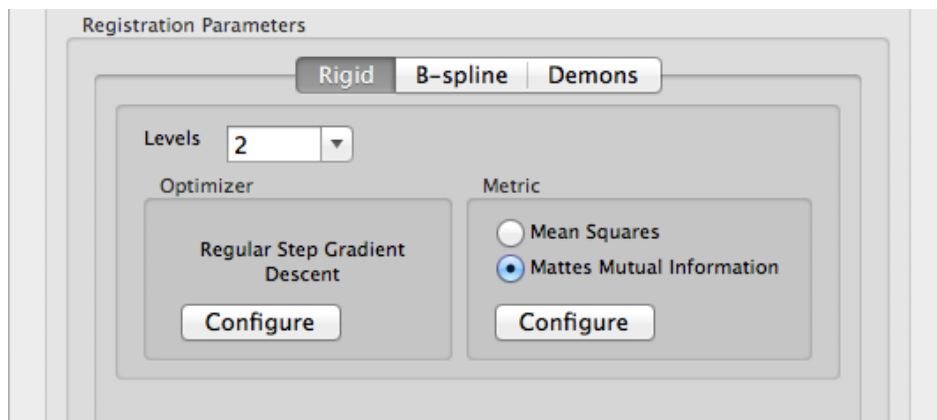


Figure 2: Use these tabs to configure specific registration methods.

6.1.3 Rigid Registration

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	<p>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.</p> <p>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</p>

	<p>more precise fits at the expense of longer registration times.</p> <p>Relaxation Factor When the optimizer reduces the step size it does so by this factor. (<i>i.e.</i> new step size = current step size * relaxation factor)</p> <p>Trans. Scaling (<i>Versor only</i>) 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.</p> <p>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.</p>
Metric	Configure the metric by pressing the Configure button.
Mean Squares	Select to use the mean squares metric. There are no adjustable parameters for this metric.
Mattes Mutual Information ¹⁶	Select to use the MMI metric. The following parameters can be set only if MMI is selected.
	<p>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.</p> <p>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.</p>

6.1.4 B-spline Deformable Registration

Levels	Select the number of levels to use in multi-resolution registration.
Optimizer	Select the desired optimizer and configure it by pressing the <i>Configure</i> button.

¹⁶ <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.

LBFGSB ¹⁷	<p>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.</p> <p>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.</p> <p>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.</p>
LBFGS ¹⁸	<p>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.</p> <p>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.</p> <p>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.</p>
RSGD ⁶	<p>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.</p> <p>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.</p> <p>Relaxation Factor When the optimizer reduces the step size it does so by this factor. (<i>i.e.</i> new step size = current step size * relaxation factor)</p>

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

18 http://www.itk.org/Doxygen/html/classitk_1_1LBFGSOptimizer.html

	<p>Max. Iterations</p> <p>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.</p>
Mattes Mutual Information	Select to use the MMI metric. The following parameters can be set only if MMI is selected.
Metric	
Mean Squares	Select to use the mean squares metric. There are no adjustable parameters for this metric.
Mattes Mutual Information	Select to use the MMI metric. The following parameters can be set only if MMI is selected.
	<p>Bins</p> <p>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.</p> <p>Sample Rate</p> <p>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.</p>
B-spline Grid Size	<p>The deformable registration is based upon ITK's BSplineTransform¹⁹. 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.</p> <p>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 Wiki²⁰.</p>

19 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.

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

6.1.5 Demons Deformable Registration

Levels	Select the number of levels to use in multi-resolution registration.
Optimizer	<p>RMS Difference The optimizer stops when the RMS difference in the metric values obtained in consecutive iterations reaches this parameter. Watch this parameter as the registration progresses. If it is too large you may get convergence on the first iteration. If it is too small you will see the value hovering around a best fit value but never converging.</p> <p>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.</p>

6.2 Fitting Tab

This code is not yet implemented.

6.3 Configuration Tab

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

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

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. However, you can move the windows and scroll through the series to see how the registration is progressing.

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 after quitting *DCEFit*, 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`). You can set the amount of information that is logged by changing the *Logging level* in the Configuration tab. This information is useful to the developer in tracking down problems with the plugin. It is recommended that it be set to Debug

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.

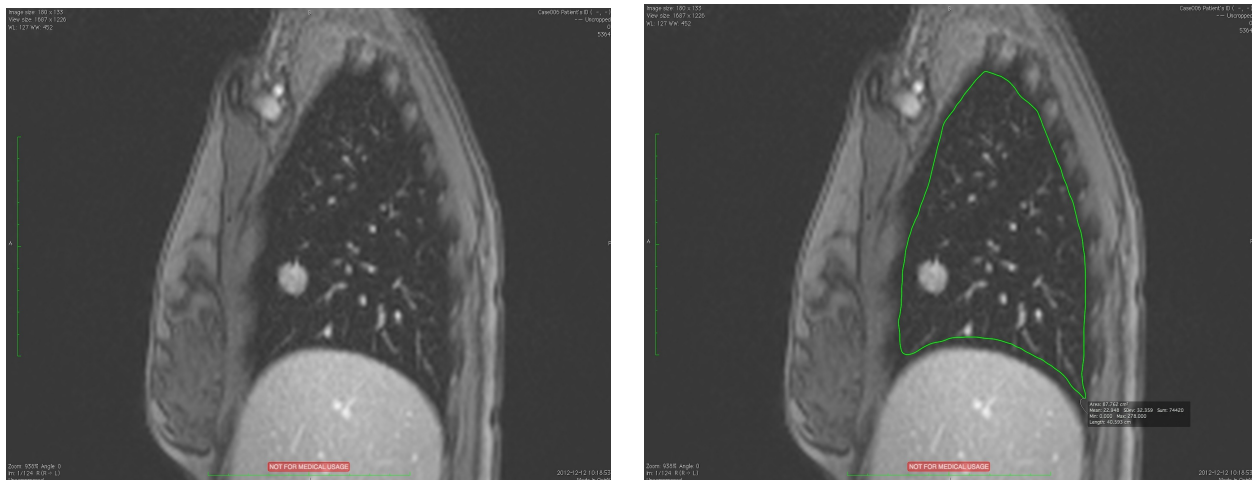


Figure 3: Preparation for B-spline deformable registration. *Left:* Image slice as received. *Right:* Region of interest marked out with the *OsiriX* pencil ROI tool.

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. The B-spline method is method is

8.2 Choice of Registration Sequence

The Demons algorithm is the method of choice to remove motion from a DCE-MRI series of images. Although it is possible to register DCE-MRI images with B-spline, it is difficult to use and is highly dependent upon the choice of fixed image and fitting parameters. Demons is much more forgiving in these

matters. Furthermore, it is faster and it registers the whole image. Also the pixels at the image boundaries tend to stay there, mostly avoiding the holes that B-spline registration can make in the outer slices of a 3D image.

8.3 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.

8.4 Choice of Grid Size in B-spline Registration

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 $30 \times 30 \times 10 \times 3 = 27000$ parameters. Optimizing a series of several hundred images with a fine grid can take a while to complete.

8.5 Choice of Optimizer

8.5.1 Rigid and B-spline

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.¹⁴ If this happens try another optimizer or another fixed image.

8.5.2 Demons

The optimizer is not selectable in Demons registration.

8.6 Choice of Metric

8.6.1 Rigid and B-spline

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.

8.6.2 Demons

The metric is not selectable in Demons registration.