Deformable Registration of Chest CT using Elastix Based on TRE minimization

A Report on Final Project For MIRA (Medical Image Registration and Applications) Coursework

Aroj Hada
Medical Imaging and Applications (MAIA)
University of Girona
u197064@campus.udg.edu

Tewele Weletnsea Tareke
Medical Imaging and Applications (MAIA)
University of Girona
u1970634@campus.udg.edu

***Abstract*—Image registration is an essential process to draw correspondence between images.Non-rigid image registration or Deformable Image registration (DIR) differ with rigid image registration (RIR),such that all pixel-to-pixel relationships change. In this report, we present a TRE (Target Registration Error) minimization based algorithm using Elastix to perform deformable image registration of lungs CT (exhale and inhale) on the DIR-Lab's COPD dataset. Different parameter files were used and parameter tuning was implemented in order to minimize the TRE. The average TRE (in mm) for the four datasets using the final parameters were 1.62 , 4.3 , 1.974 , and 2.398 for datasets COPD1, COPD2, COPD3, and COPD4, respectively.**

***Index Terms*—Non-rigid, Deformable, Elastix, Transformix, Registration**

I. Introduction

Image registration is an important tool in the field of medical imaging. In many clinical situations several images of a patient are made in order to analyze the patient's situation. These images are acquired with, for example, X-ray scanners, Magnetic Resonance Imaging (MRI) scanners, Computed Tomography (CT) scanners, and Ultrasound scanners, which provide knowledge about the anatomy of the subject. Combination of patient data, mono- or multi-modal, often yields additional clinical information not apparent in the separate images. For this purpose, the spatial relation between the images has to be found. Image registration is the task of finding a spatial one-to-one mapping from voxels in one image to voxels in the other image, as shown in Figure 1.

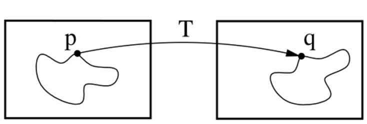

Fig. 1. Image registration is the task of finding a spatial transformation mapping one image to another. Left is the fixed image and right the moving image.

Two images are involved in the registration process. One image, the moving image IM(x), is deformed to fit the other image, the fixed image IF (x). The fixed and moving image are of dimension d and are each defined on their own spatial domain: ■F Rd and ■M Rd, respectively. Registration is the problem of finding a displacement u(x) that makes IM(x + u(x)) spatially aligned to IF (x). An equivalent formulation is to say that registration is the problem of finding a transformation T (x) = x+u(x) that makes IM(T (x)) spatially aligned to IF (x). The transformation is defined as a mapping from the fixed image to the moving image, i.e. T : ■F Rd → ■M Rd.

A. Elastix

Elastix is a software package for image registration.The software consists of a collection of algorithms that are commonly used to solve medical image registration problems. A large part of the code is based on the Insight Toolkit (ITK). The modular design of elastix allows the user to quickly test and compare different registration methods for his/her specific application. The command-line interface simplifies the processing of large amounts of data sets, using scripting.

B. TRE (Target Registration Error)

For most registration tasks, the most important error measure is target registration error (TRE), which is the distance after registration between corresponding points not used in calculating the registration transform.

The error of the target fiducial markers following registration, T(pf)pm where T is the estimated transformation and the points pf,pm were not used to estimate T .

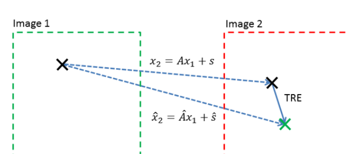

Fig. 2. TRE computation.

C. Registration Parameters

1) Registration: It is recommended to just use the MultiResolutionRegistration method, since multi-resolution is a good idea.

2) Metric: The AdvancedMattesMutualInformation usually works well, both for mono- and multi-modal images. It supports fast computation of the metric value and derivative in case the transform is a B-spline by exploiting its compact support. The number of histogram bins is required to be set, which is needed to compute the joint histogram. A good value for this depends on the dynamic range of your input images, but 32 is usually ok.

3) Sampler: The RandomCoordinate sampler works well in conjunction with the StandardGradientDescent and AdaptiveStochasticGradientDescentoptimisers, which are the recommended optimisation routines. These optimisation methods can be used with a small amount of samples, randomly selected in every iteration. Set the NumberOfSpatialSamples to 3000. Don't go lower than 2000.

Compared to samplers that draw samples on the voxel-grid (such as the Random sampler), the RandomCoordinate sampler avoids what is known as the grid-effect [Th´evenaz and Unser, 2008]. An important option for the random samplers is: (NewSamplesEveryIteration "true") which enforces the selection of new samples in every iteration.

4) Interpolator: During the registration, use the LinearInterpolator. In our current implementation it is much faster than the first order B-spline interpolator, even though they are theoretically the same thing.

5) Transform: This choice depends on the application at hand. For images of the same patient where you expect no nonrigid deformation, you can consider a rigid transformation, i.e. choose the EulerTransform. If you want to compensate for differences in scale, consider the affine transformation: AffineTransform.

6) Optimiser: The StandardGradientDescent method offers the possibility to perform fast registration. The key idea is that you use a random subset of voxels (samples), sequences start with the same step size, but sequence 2 decays much faster. newly selected in each iteration, to compute the cost function derivatives. The number of samples to use is specified using the parameter NumberOfSpatialSamples. Typically, 2000-5000 is enough.

A downside of the StandardGradientDescent method is that you need to tune the parameters of the gain factor ak. The parameters and A define the decay slope of the function. For the parameter the recommended value is 0.6. For A, use something in the order of 50:(SP alpha 0.6) (SP A 50.0)

Another important option related to the optimiser is the maximum number of iterations: (MaximumNumberOfIterations 500) which is, in the case of StandardGradientDescent, not only the maximum, but also the minimum, since there is no other stopping condition implemented for this optimiser. In general, the more iterations, the better the registration result. But, of course, more iterations take more time. A value of 500 is a good start. Use 2000 if computation time is not such an issue. A side benefit of using more iterations is that a wider range of SP a gives good results. Tuning SP a then becomes easier.

The AdaptiveStochasticGradientDescent optimizer is very similar to the StandardGradientDescent, but estimates a proper initial value for SP a automatically. In practice this optimizer works in many applications with its default settings. Only the number of iterations must be specified by the user:

(Optimizer "AdaptiveStochasticGradientDescent")

(ASGDParameterEstimationMethod "DisplacementDistribution")

(MaximumNumberOfIterations 500)

7) Image pyramids: The FixedImagePyramid and the MovingImagePyramid have identical options. Using the FixedSmoothingImagePyramid will not throw away valuable information.Two parameters have to be set to define the multi-resolution strategy: the number of resolutions (NumberOfResolutions) and the specific down-sampling schedule that is used in each resolution (FixedImagePyramidSchedule). In general 3 resolutions is a good starting point. If the fixed and moving image are initially far away, we can increase the number of resolution levels to 5 or 6. This way the images are more blurred and more attention is paid to register large, dominant structures.

The pyramid schedule defines the amount of blurring (and down-sampling in case a FixedRecursiveImagePyramid is used), in each direction x, y, z and for each resolution level. It can be specified as follows:

(NumberOfResolutions 4)

(FixedImagePyramidSchedule 8 8 4 4 2 2 1 1)

II. Dataset

The dataset made available was the Inspiratory and expiratory breath-hold CT image pairs acquired from the National Heart Lung Blood Institute COPDgene study archive. Each available image data set has associated with it a coordinate list of anatomical landmarks that have been manually identified and registered by an expert in thoracic imaging, with repeat registration performed by multiple observers to estimate the spatial variance in feature identification. Included with each case are 2 text files containing coordinate information for the reference landmarks on the inhalation (iBH-CT) and exhalation (eBH-CT) breath-hold CT images. The following table consists of the details on Image Dimension, Voxel spacing in mm, and average Displacement on each CT volumes.

Label	Image Dims	Voxels (mm)	# Features	Displacement (mm)	# Repeats	Observers (mm)
COPD1	512 x 512 x 121	0.625 x 0.625 x 2.5	773	25.90 (11.57)	150/3	0.65 (0.73)
COPD2	512 x 512 x 102	0.645 x 0.645 x 2.5	612	21.77 (6.46)	150/3	1.06 (1.51)
COPD3	512 x 512 x 126	0.652 x 0.652 x 2.5	1172	12.29 (6.39)	150/3	0.58 (0.87)
COPD4	512 x 512 x 126	0.590 x 0.590 x 2.5	786	30.90 (13.49)	150/3	0.71 (0.96)

Fig. 3. Dataset details including Image Dimensions, Voxel spacing , etc.

III. Methodology

This section explains the overall process used for the registration and fin-tuning of the parameter files in detail. The process of parameter selection and fine-tuning of the components was an iterative process and the major step that contributes in the minimization of TRE.

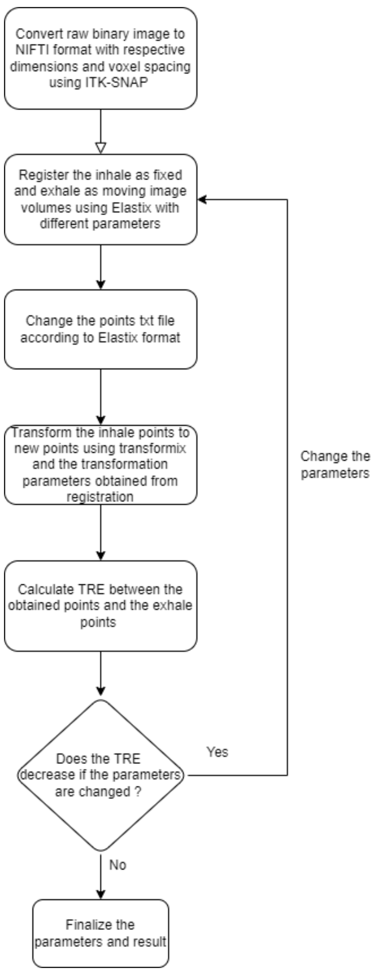

Fig. 4. Flowchart showing the complete algorithm

A. *Conversion of the raw 3D volumes to NIFTI format*

The “*.img” raw binary 3D lung volumes were first properly formatted into NIFTI file format for ease of processing them. This was done using ITK-Snap features that allow the user to input raw binary files while specifying the correct image dimensions and voxel spacings. The images were also reoriented to get them into correct orientation. Finally, the image was saved into NIFTI format. Figure 1 shows a visualization of the raw binary 3D volumes already converted into nifti format with appropriate image dimensions and voxel spacing in ITK-SNAP.

B. *Registration Using Elastix*

The exhale and inhale images in NIFTI format were registered using Elastix. For considerations of the points provided

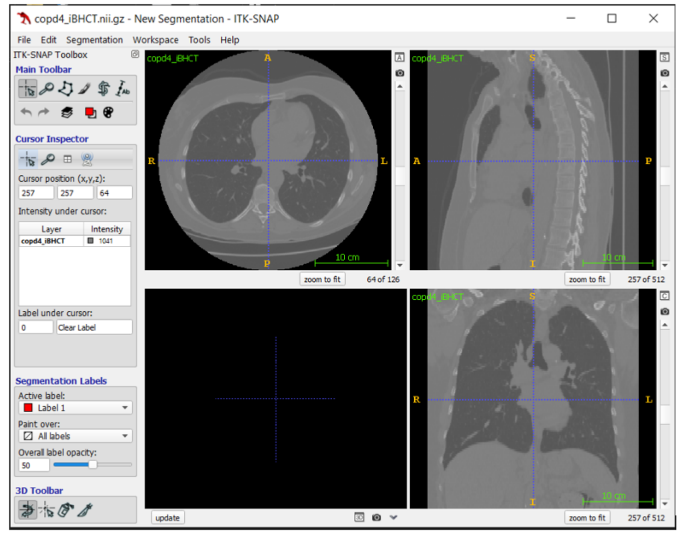

Fig. 5. Visualization of the 3D volume raw binary images (COPD4) in ITK-SNAP with the provided dimensions of (512 X 512 X 126) and voxel spacing of (0.59 X 0.59 X 2.5). Re-orientation of the coronal plane from Superior to Inferior.

to us in the challenge day, the inhale images were taken as fixed and the exhale as moving. Then using the transformation parameters obtained from the previous registration, the inhale points were transformed using the transformix function under Elastix. The input landmarks points .txt file was formatted in order to match the format listed in the Elastix manual.

A code snippet used in elastix for the registration of the inhale volume (fixed) and exhale volume (moving) using non-rigid parameters is given below.

```
elastix -f data/copd1/copd1_iBHCT.nii.gz -m
data/copd1/copd1_eBHCT.nii.gz  -out output/d
efault_nonrigid/copd1 -p parameter_affine.tx
t -p parameter_bspline.txt
```

A code snippet used in elastix to transform the given inhale points using transformation parameters obtained from the previous registration of the respective image volumes is given below.

```
transformix -def data/copd1/copd1_300_iBH_xyz
_r1.txt -out  output/default_nonrigid/copd1/
transform -tp output/default_nonrigid/copd1/
TransformParameters.1.txt
```

Finally, the TRE (Target Registration Error) was calculated between the newly obtained transformed points and the given moving points (exhale points). Based on the idea of minimization of TRE, we fine-tuned the registration parameters.

C. *TRE Calculation*

In each dataset, the TRE was calculated using Matlab between the transformed output index points obtained by transforming the input fixed points (inhale points) and the exhale points that have been made available for the given dataset.

The output of the transform is a text file with multiple columns of input/output points as well as indices. The output index points were extracted from this file which is taken as the new landmark co-ordinates after transformation. A separate matlab function was implemented in order to extract the output index points from the file

D. Parameter Selection and Registration Fine-tuning

For registration, the default affine and B-spline parameters were used as intial base parameter files and changes of options available within these parameter files were made in-order to minimize the TRE. //

The major parameter components for the final affine parameter file are listed below:

- (Registration " MultiResolutionRegistration")
- (Metric " AdvancedNormalizedCorrelation")
- (ImageSampler " RandomCoordinate")
- (Interpolator " LinearInterpolator")
- (ResampleInterpolator " FinalBSplineInterpolator")
- (Resampler " DefaultResampler")
- (Transform " AffineTransform")
- (Optimizer " AdaptiveStochasticGradientDescent")
  ********* Pyramids
- (NumberOfResolutions 6)
- (FixedImagePyramid " FixedSmoothingImagePyramid")
- (MovingImagePyramid " MovingSmoothingImagePyramid")
- (ImagePyramidSchedule 14 14 3 10 10 2 8 8 2 4 4 1 2 2 1 1 1 1)
  ********* Transform
- (AutomaticScalesEstimation " true")
- (HowToCombineTransforms " Compose")
- (AutomaticTransformInitialization " true")
  ********* Optimizer
- (AutomaticParameterEstimation " true")
- (ASGDParameterEstimationMethod " DisplacementDistribution")
- (UseAdaptiveStepSizes " true")
- (SP A 50.0)
  ********* Interpolator
- (FinalBSplineInterpolationOrder 3)
  ********* Image Sampler
- (MaximumNumberOfSamplingAttempts 20)
- (NumberOfSpatialSamples 7500)
- (UseRandomSampleRegion " true")
- (SampleRegionSize 150.0 150.0 35.0)
- (NewSamplesEveryIteration " true")

The major parameter components for the final non-rigid parameter file are listed below:

- (Registration " MultiResolutionRegistration")
- (Metric " AdvancedMattesMutualInformation")
- (ImageSampler " RandomCoordinate")
- (Interpolator " LinearInterpolator")
- (ResampleInterpolator " FinalBSplineInterpolator")
- (Resampler " DefaultResampler")
- (Transform " BSplineTransform")
- (Optimizer " AdaptiveStochasticGradientDescent")
- (NumberOfResolutions 6)
- (FixedImagePyramid " FixedSmoothingImagePyramid")
- (MovingImagePyramid " MovingSmoothingImagePyramid")
- (ImagePyramidSchedule 14 14 3 10 10 2 8 8 2 4 4 1 2 2 1 1 1 1)
  ******** Transform
- (AutomaticScalesEstimation " true")
- (HowToCombineTransforms " Compose")
- (AutomaticTransformInitialization " true")
- (FinalGridSpacingInVoxels 8.0 8.0 4.0)
  ******** Optimizer
- (AutomaticParameterEstimation " true")
- (UseAdaptiveStepSizes " true")
- (ASGDParameterEstimationMethod " DisplacementDistribution")
- (SP A 50.0)
  ********* Interpolator
- (FinalBSplineInterpolationOrder 3)
  ********* Image Sampler
- (MaximumNumberOfSamplingAttempts 20)
- (NumberOfSpatialSamples 25000)
- (NewSamplesEveryIteration " true")
- (UseRandomSampleRegion " true")
- (SampleRegionSize 150.0 150.0 35.0)
  ********* Metric
- (NumberOfHistogramBins 64)

IV. Result and Discussion

The TRE and Standard Deviation values were calculated for different scenarios; no registration , registration using default non-rigid parameters, and registration using final non-rigid parameters. As seen clearly in the figure 6, the TRE and SD were very high initially for the non-registered points and decreased by a fair amount when the images were registered and the points were transformed using even just the default parameters provided by Elastix.
Figure 7 shows the axial view of the COPD1 data volume with landmarks overlayed on top of the slice number 60. The leftmost image has inhale landmarks overlayed on inhale volume. The middle and the rightmost image are exhale volume slice 60 with exhale points and transformed inhale points overlayed on top of them. It can be clearly seen that the landmarks do not completely match up contributing towards the TRE (Target Registration Error). However, the points that do match up are accurate in their position compared with the actual exhale landmarks.
Tuning the parameter components one by one, helped further minimize the TRE and the SD. Among all the parameter components, the major effects were observed from the changes in the Number of Resolutions (Pyramid), Number of Histogram Bins, Number of Spatial Samples, and Sample Region Size.

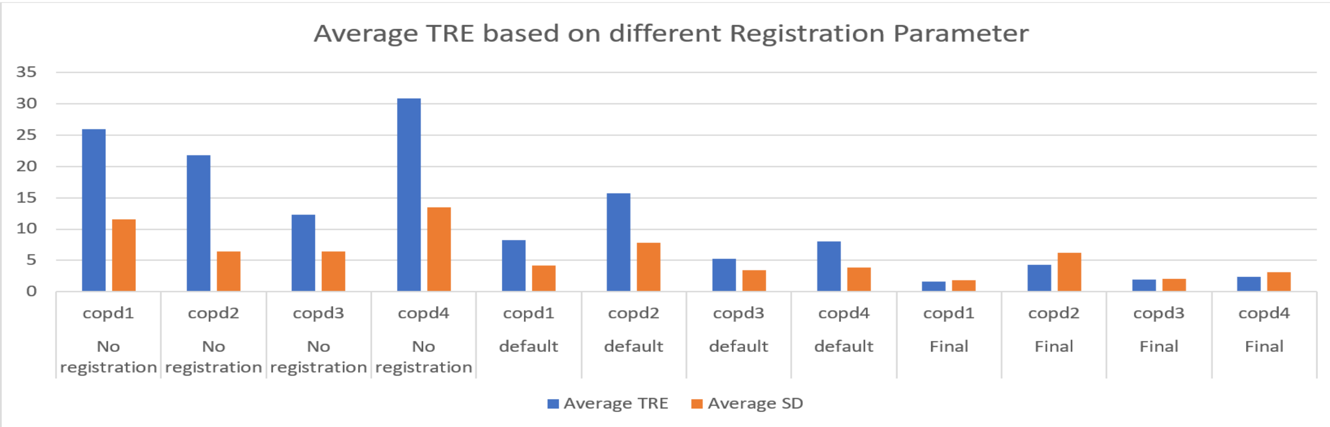

Fig. 6. Average TRE and SD between all image volumes (COPD1 - COPD4) with different registration scenarios; No registration , Registration using default non-rigid parameters, and Registration using final non-rigid parameters.

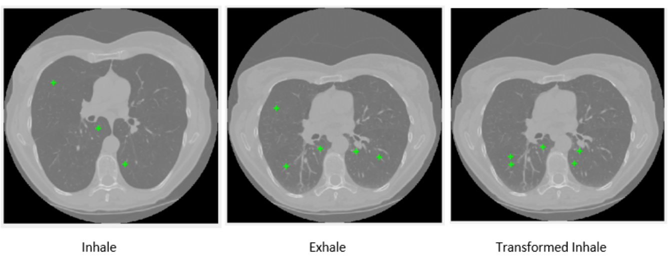

Fig. 7. Axial view of COPD1 volume slice 60 with inhale (left), exhale (mid) , and transformed inhale points (right) shown as green cross.

V. Computation Time

All computations were performed using a personal machine with Intel i7-9750H CPU (2.6 GHz) and 32 GB of RAM. Each image volume had a different overall time requirement for the registration to be complete. The time required are given below:

Dataset	Time for Registration	Time for Transformix
COPD1	2m49s	34s
COPD2	3m28s	38s
COPD3	2m34s	40s
COPD4	2m43	34s

VI. Conclusions

TRE minimization in-order to obtain better image registration is a very robust algorithm that can be paired with registration algorithms such as Elastix. Although the algorithm we have chosen to follow here is quite exhaustive as it requires the user to fine-tune the Elastix registration parameters one by one, it has its own advantages of begin simple to implement as well as interpret the results. Through the proposed algorithm, we were able to achieve low TRE that signifies very low error in estimation of the registration points.

The following table lists all the TRE and SD values obtained.

Parameters	Dataset	Average TRE	Average SD
No registration	copd1	25.9	11.57
No registration	copd2	21.77	6.46
No registration	copd3	12.29	6.39
No registration	copd4	30.9	13.49
default	copd1	8.21	4.23
default	copd2	15.72	7.812
default	copd3	5.271	3.39
default	copd4	8.05	3.88
Final	copd1	1.62	1.861
Final	copd2	4.3	6.217
Final	copd3	1.974	2.03
Final	copd4	2.398	3.1

Fig. 8. Average TRE and SD obtained

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