Final Project: Lung Image Registration of Chest CT Volumes

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1 INTRODUCTION

The use of image registration within the medical image processing field is a fundamental task with multiple applications. One of these is the alignment of chest Computed Tomography (CT) images of a patient, focusing on the assessment of the lung and its internal structures while performing the inspirational and expiration natural function. Thus, the application of the information obtaining from the images have been rapidly increasing in the fields of diagnosis and surgical or radiotherapy planning.

2 PROBLEM STATEMENT

The aim of the project is to register chest CT volumes corresponding to inspiratory and expiratory breath-hold images using deformable image registration approach. One of the challenge to deal with is to obtain a high accuracy of the registration while taking into account the computational time and visual results of abnormal deformations since they are medical images.

3 DATASET

The dataset provided for this project contains 4 COPD (Chronic Obstructive Pulmonary Disease) cases/patients. Table 3.1 describes the characteristics of each volume in the dataset.

Each one contains 2 raw binary images of chest CT volumes corresponding to the inhalation and exhalation movements of the patient and their coordinate list of 300 anatomical landmark points that identify the area of the lungs. These landmark points are used as a reference for evaluating the registration. Figure 3.1 shows the one slice of the $1st$ expiratory volume with the landmark points marked with green.

Table 3.1: Dataset description

Label	**Volumes**	**Image Dimension**	**Voxel Spacing (mm)**
COPD1	COPD1_eBHCT	512 x 512 x 121	0.625 x 0.625 x 2.5
	COPD1_iBHCT	512 x 512 x 121	0.625 x 0.625 x 2.5
COPD2	COPD2_eBHCT	512 x 512 x 102	0.645 x 0.645 x 2.5
	COPD2_iBHCT	512 x 512 x 102	0.645 x 0.645 x 2.5
COPD3	COPD3_eBHCT	512 x 512 x 126	0.652 x 0.652 x 2.5
	COPD3_eBHCT	512 x 512 x 126	0.652 x 0.652 x 2.5
COPD4	COPD4_eBHCT	512 x 512 x 126	0.590 x 0.590 x 2.5
	COPD4_iBHCT	512 x 512 x 126	0.590 x 0.590 x 2.5

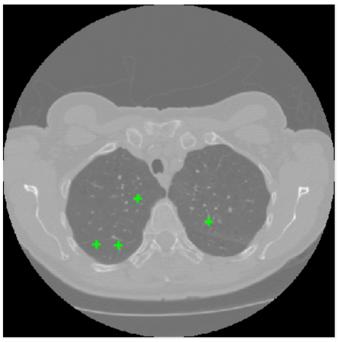


Figure 3.1: Example of one slice of expiratory volume with landmark points shown in green crosses

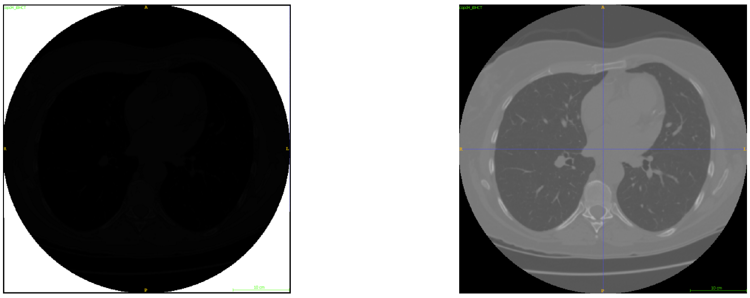
4 METHODS

This section explains the different approaches implemented as part of this project. The main approach is implemented in Matlab with elastix which is explained in Section 4.1 and the other approaches tried using C++ ITK(Insight Took) library and Slicer3D are explained in Section 4.3.

4.1 PROPOSED SOLUTION : RIGID, AFFINE, B-SPLINE REGISTRATION

4.1.1 LOAD DATA

The important point to be taken into account when loading the raw binary volumes provided is the data-type. For instance, these volumes, as indicated on the website XXXXXX, are in 16-bit integer. Figure, 4.1 shows an example of loading the volume as unsigned(left) and signed(right) 16-bit integers.



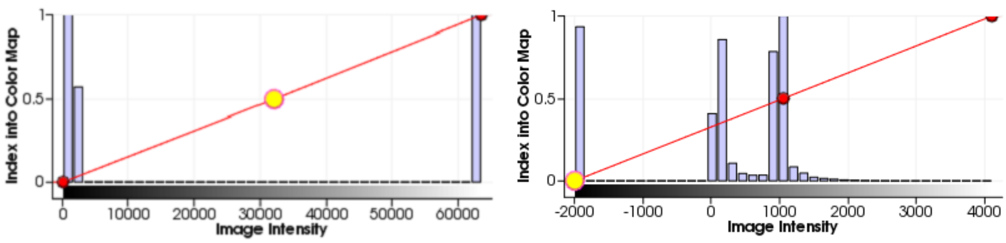
(a) 16-bit unsigned (b) 16-bit integer

Figure 4.1: Example of loading COPD4_iBHCT volume with 2 different data types.

The information associated with the physical spacing between pixels and the position of the image in space with respect to some world coordinate system are also extremely important. Image origin and spacing are fundamental in registration as it is performed in physical coordinates and improperly defined spacing and origins will result in inconsistent results.

4.1.2 PRE-PROCESSING

The pre-processing step mainly involves the removal of the circular disc around the CT volumes as it affects the registration due to its very high or very low intensity value based on the data type selected when loading the volumes. Figure 4.2 shows how the histogram of the intensity distribution varies based on the data type. In this step the circular disc is removed by assigning the intensity value of the disc to 0 and the remaining intensities are normalized to be in a certain range for all the volumes as the intensities play a main role during registration.



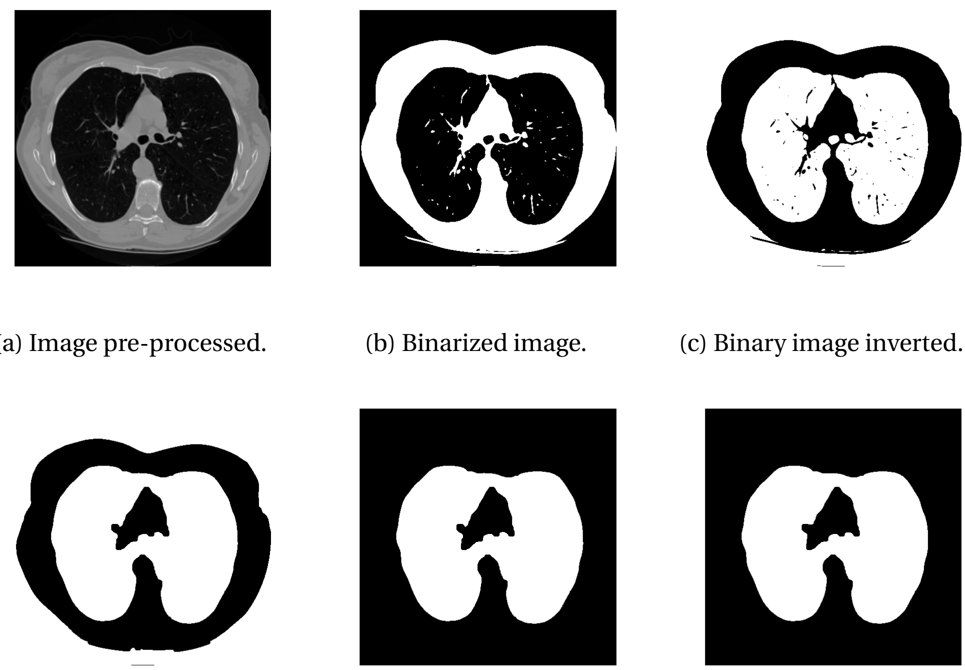
(a) 16-bit unsigned (b) 16-bit integer

Figure 4.2: Histograms of COPD4_iBHCT volume loaded 2 different data types.

4.1.3 Create lung mask

As the final aim of the registration is to register the lungs during different breath movements, a lung mask could allow to register only the area of the lungs or to apply pre-processing to that area in specific in order to enhance the small structures inside the lungs. For this project 2 approaches were followed for creating the mask, mainly morphological filters and active contour, which are described in this section.

- **Morphological filters:** They are simple but very powerful filters that are used to remove imperfections by accounting for the form and structure of the image. Figure 4.3 shows the steps in creating a lung mask with a combination of the below filters:
  - **Dilation :** Expands the size of the object, tends to close holes and gaps.
  - **Erosion :** Shrinks the size of the object and removes small objects depending of the size of the structural element.
  - **Opening :** It is the application of erosion following by a dilation using the same structural element and is used to remove small structures.
  - **Closing :** It is the application of dilation following by an erosion using the same structural element and is used to fill holes.



(a) Image pre-processed. (b) Binarized image. (c) Binary image inverted.

(d) Morphology close. (e) Clear borders. (f) Morphology open.

Figure 4.3: Illustration of steps followed for the creation of lung mask for COPD1_iBHCT volume

- **Active contour:** The active contour algorithm which is commonly called as snake algorithm is a segmentation algorithm which can be used to get the lung mask. It is based on minimization of internal and external energies. Since it is a semi-automatic method it requires initial seed points to start the algorithm and so the other method using filters is preferred over this. It can be automated by fixing the initial points in one volume and performing a basic rigid registration to get the points in the other volume. Fig 4.4 shows the mask obtained from ITK-Snap using its inbuilt snake algorithm with classification as pre-segmentation step.

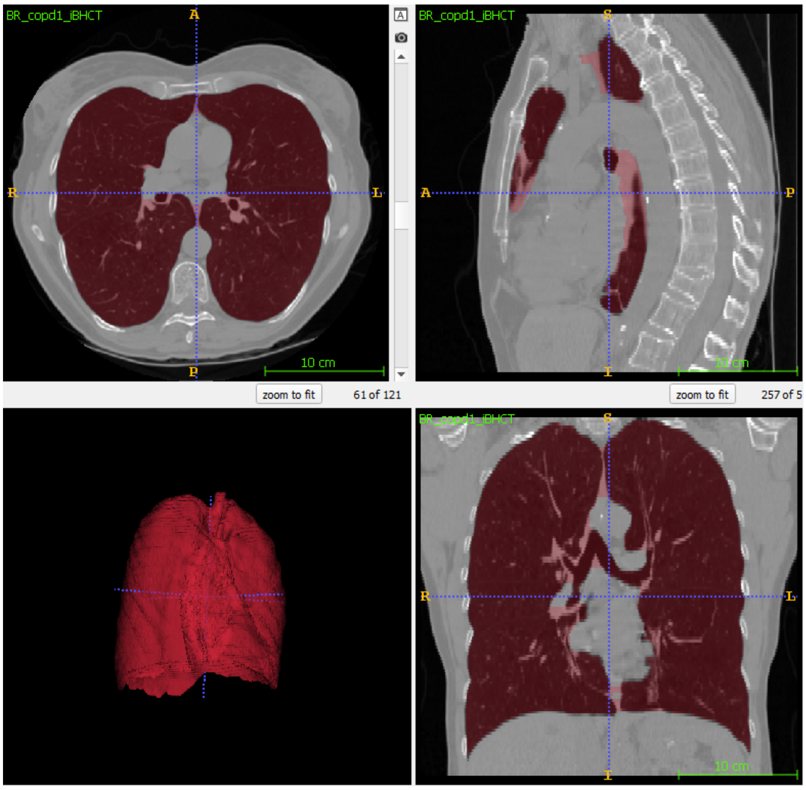


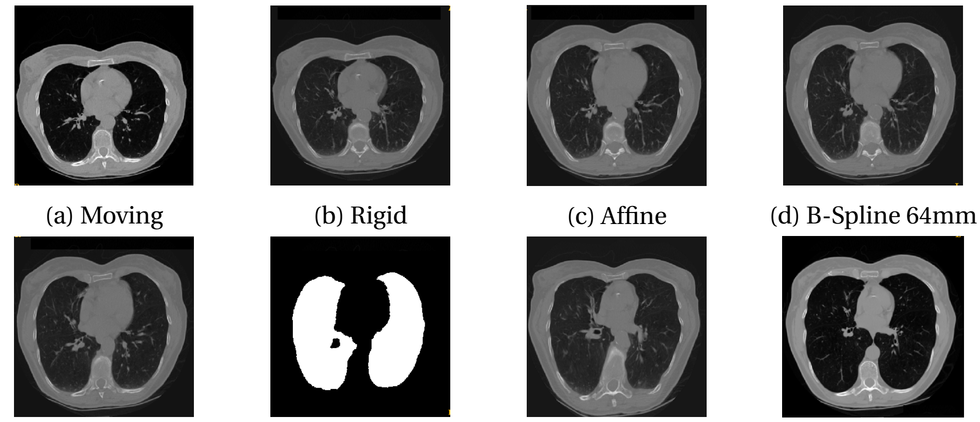
Figure 4.4: Example of segmentation mask created with ITK-Snap for COPD1_iBHCT volume

4.1.4 Registration

The image registration is the task of finding a spatial transformation mapping from one image(moving image) to another image (fixed image). The registration of the inpiratory and expiratory volumes is a challenge because the ribs and the lungs do not move along the exact same direction between these two motions, and in CT volumes the ribs have higher intensities compared to the lung volume. So the approach used here is to first align the whole volume and then apply a mask to register only the lung volumes, therby getting a good overall registration without any irregular deformations.

Figure 4.5 shows the steps in registering the COPD1 expiratory(moving) volume to the inspiratory(fixed) volume. The parameters tuned to get a good combination of transformations are listed in section 5.1. The different transformations used are given below:

- **Rigid :** In this transformation the images are treated as rigid bodies, which can only translate and rotate. It is very important to initially align the two images to their centers before performing other non-rigid transformations.
- **Affine :** In contrast with the rigid transformation, this transformation apart from translation and rotation, also includes scaling and shearing.
- **B-Spline :** It is a type of non rigid transformation which allows deformations with the help of control points provided by the grid. The spacing of the grid is a very important parameter of this transformation in order to allow smaller or larger deformations.



(a) Moving (b) Rigid (c) Affine (d) B-Spline 64mm

(e) B-Spline 32mm (f) Lung mask (g) B-spline 8mm (h) Fixed/Reference

Figure 4.5: Illustration of steps followed when registering from COPD1_eBHCT volume to COPD1_iBHCT volume

4.1.5 Transform landmark points

The transformation applied to get the transformed landmark points is defined as a coordinate mapping from the fixed image domain to the moving domain even though the moving image is said to be deformed to fit the fixed image. The reason for this is that forward mapping from the moving to the fixed image is not always a one to one mapping and it may lead to holes in the transformed image. In order to avoid this the transformation is calculated from the fixed to the moving image which is called as inverse mapping. So the fixed landmark points/indexes are provided to calculate the transformed points which are then compared with the moving landmark points to calculate the registration error.

4.1.6 Registration Evaluation

TRE(Target Registration Error) calculated between the transformed points and the moving points is one important criteria to evaluate the performance of registration. It is the 3 dimensional euclidean distance between the points and given by,

$$TRE(t,f) = \sqrt{(t_1 - f_1)^2 + (t_2 - f_2)^2 + (t_3 - f_3)^2} \tag{4.1}$$

where t and f are the physical coordinates of the transformed and moving landmark point. It is important to note that the points provided are in physical coordinates and measured in mm. In order to calculate the TRE the indexes should be multiplied with their corresponding voxel spacing.

Though TRE is an important criteria to calculate the performance of registration it cannot always say if the entire volume is registered properly and whether it cost effect in real time applications. The other evaluation parameters that can be used are:

- Execution time
- Dice coefficient
- Jaccard coefficient
- Volume overlap

4.2 Implementation

The methodology described in the previous section was mainly implemented in Matlab and given below are the steps followed.

- ***Step 1 :*** The raw binary volumes, both inspiration and expiration, are converted to NifTI(.nii) volumes by opening it in ITK-Snap and providing the correct dimensions, voxel spacing and bit type(16-bit signed).
- ***Step 2 :*** The circular black disk background is removed by setting the lowest voxel values(-2000) in the volume to '0' and normalizing the intensities between 0 and 1023.
- ***Step 3 :*** The lung masks for the volumes are generated by binarizing the volumes using otsu thresholding and performing the morphological operations specified below in the given order.
  - *imbinarize*
  - *imcomplement*
  - *imclose* : Structuring element 'disc' with size 7
  - *imclearborder*
  - *imopen* : Structuring element 'disc' with size 7

- ***Step 4 :*** Register the two volumes and transform the landmark points by calling elastix and transformix command line tool from matlab using *'system'* function passing the volumes and masks as parameters. 'system' matlab command is used. There are 4 elastix batch files created for this purpose since we do registration both with and without mask.
  - *elastixregister.bat* : Call elastix registration without applying mask.
  - *elastixregister.bat* : Call elastix registration with mask.
  - *elastixtransform.bat* : Call transformix to transform only the intensity volume and mask volume.
  - *elastixtransformpoints.bat* : Call transformix and transform only the fixed landmark points.
- ***Step 5 :*** Extract the transformed points from the output file of the *elastixtransformpoints.bat* and find the registration error using TRE.

4.3 Other Approaches : Demon's Registration

Demon's algorithm is another 3D non-rigid registration algorithm which is increasingly being used for medical images. And so as part of this project we have done work on this trying to use the algorithm, and the section below explains the steps followed for each approach.

4.3.1 C++ ITK (Insight Toolkit)

ITK is a C++ library mainly used for registration and segmentation of medical images and it has Demon's algorithm implemented in it. Below are the steps followed for the implementation in C++.

- ***Step 1 :*** Read the raw fixed and moving volumes with *itk::ImageFileReader* using the input/output *itk::RawImageIO* by setting the correct dimension and pixel spacing.
- ***Step 2 :*** The images read are thresholded to remove the circular dark background using *itk::ThresholdImageFilter* by setting the threshold value to 0.
- ***Step 3 :*** The images are type casted to floating points using *itk::CastImageFilter* to proceed with further internal processing.
- ***Step 4 :*** The images are then registered using *itk::DemonsRegistrationFilter* by setting the *SetFixedImage()* and *SetMovingImage()* and the other parameters for registration which is to be tuned to get good results.
- ***Step 5 :*** After the registration is finished the displacement field is stored in an image containing vectors *itk::Image<itk::Vector<float,Dimension>,Dimension>*.
- ***Step 6 :*** The displacement field is used to transform the moving image or mask with the *itk::WarpImageFilter*.

- ***Step 7 :*** The displacement field image can also be used to create a transformation *itk::DisplacementFieldTransform* which allows us to transform the fixed points using the *TransformPoint()* function.

4.3.2 3D Slicer

Slicer is an open source software used mainly in medical image visualization and processing. This software has Demon's registration as one of the modules implemented which can be freely used. It is easier to use because of its interactive graphical user interface unlike elastix. Below are the steps to be followed to use the Demon's algorithm in Slicer.

- ***Step 1 :*** Select the module *'Registration -> Specialized -> Demon's Registration'* from the list of modules in Slicer.

- ***Step 2 :*** Select the input fixed and moving volumes and the output for transformed and displacement field volumes.

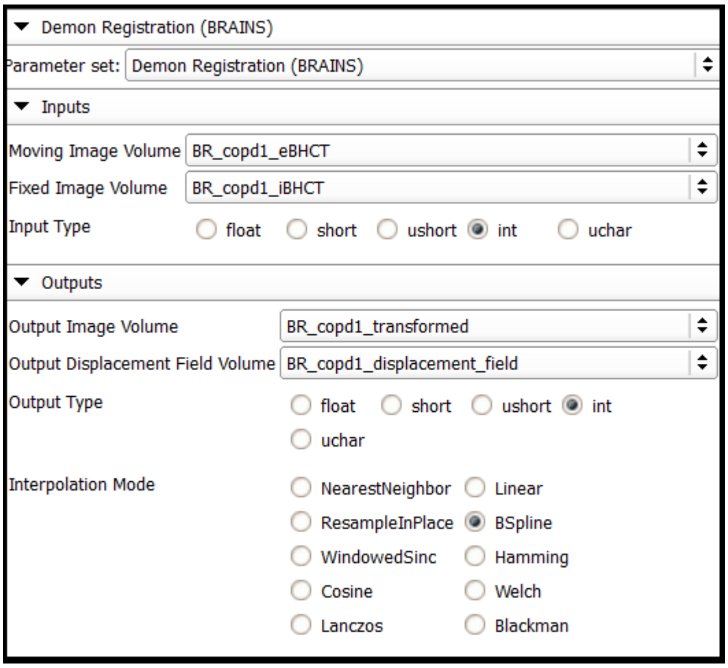


Figure 4.6: Snapshot of Slicer to select inputs and outputs

- ***Step 3 :*** Tune the registration parameters and apply pre-processing and masks for more specific purposes and click the 'Apply' button to start the registration .

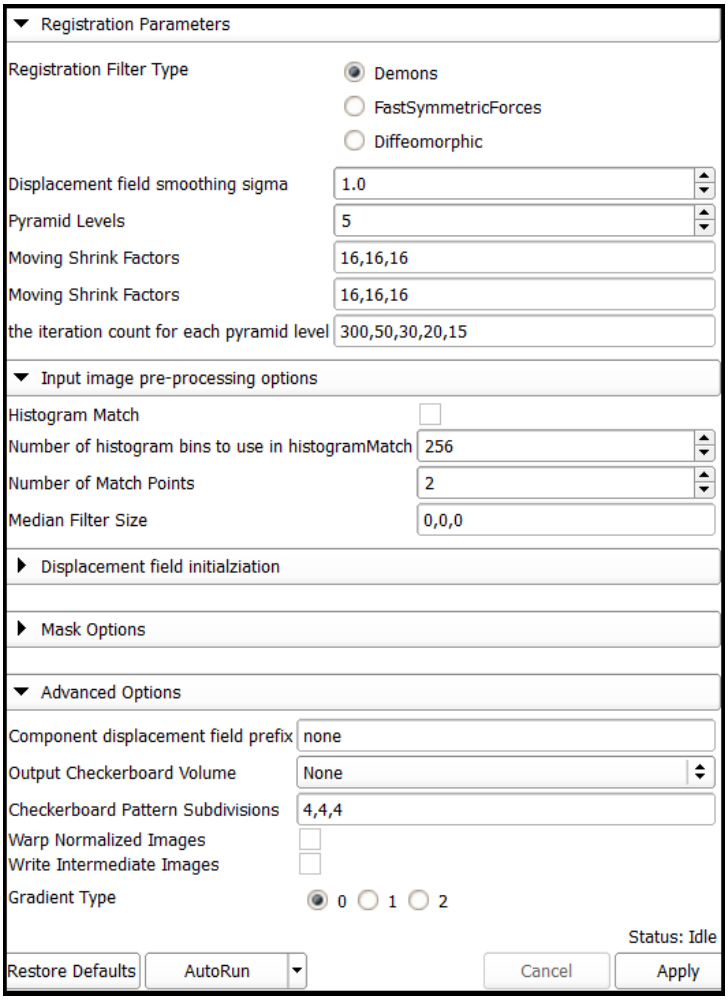


Figure 4.7: Snapshot of Slicer to tune the registration parameters

- ***Step 4 :*** After the registration is finished the output volumes can be viewed in the Slicer viewers and exported outside.

5 Experiments

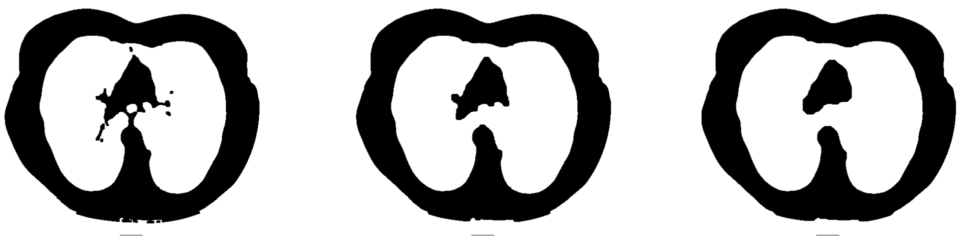
5.1 Tuning elastix registration parameters

Elastix provides us the option to tune the default registration parameters for each transformation we use with the help of parameter files . Most of the work done in this project was to find the best set of transformations with good parameters for registering lung volume. A systematic approach was followed to find the parameters and table 5.1 shows few of the initial tests done with their corresponding registration results.

Table 5.1: Initial tests for tuning elastix parameters			
Test No.	**Modification**	**Observations**	**Error value**
No. 1	Rigid [Increase of iteration from 500 to 2000] + B-Spline [16mm of grid spacing]	More iterations allows to reach the transformation better but longer computation time.	Vol 1: 13.10 Vol 2: 12.47 Vol 3: 5.83 Vol 4: 28.03
No. 2	Rigid [Increase of resolutions from 4 to 6] + B-Spline [16mm of grid spacing]	More resolutions allows better registration for larger structures.	Vol 1: 11.25 Vol 2: 12.099 Vol 3: 4.95 Vol 4: 25.55
No.3	Rigid + Affine + B-Spline [16mm of grid spacing]	The combination of transformation give more free to the deformation for complex transformation needed.	Vol 1: 14.28 Vol 2: 14.47 Vol 3: 6.68 Vol 4: 14.27
No. 4	Rigid [with 700 iterations] + Affine[with 2000 iteration] + BSpline [with 8mm of Grid Spacing], Increase of resolution to 6 for Affine & Rigid.	In case of Rigid Transformation, there are not more translations to do, therefore, it is can be reduced to execute faster.	Vol1: 12.86 Vol2: 12.95 Vol3: 6.37 Vol4: 19.48
No. 5	Rigid + Affine + BSpline, all using 'SmoothingImagePyramid' as option to build the image pyramid.	In combination with a Random or RandomCoordinate Sampler, the downsampling step in the Image pyramid is not necessary.	Vol 1: 14.28 Vol 2: 14.47 Vol 3: 6.68 Vol 4: 14.27
No. 6	Same configuration as Test 5 but the BSpline with 16mm of Grid Spacing	The lower this value, the more flexible the deformation can be. However low values can cause unrealistic deformations.	Vol1: 19.05 Vol 2: 15.01 Vol 3: 6.13 Vol 4: 16.66
No. 7	Same configuration as Test 5 but the BSpline with 10mm of Grid Spacing	Increase of error and presence of abnormal deformations.	Vol 1: 17.96 Vol 2: 14.47 Vol 3: 6.55 Vol 4: 17.79
No. 8	Same configuration as Test 5 but using as Metric the 'NormalizedMutualInformation' only for BSpline.	This metric is the normalization of the 'Mutual information', therefore, for some cases has a better performance.	Vol 1: 15.21 Vol 2: 16.14 Vol 3: 6.43 Vol 4: 13.61

5.2 Selection of structuring element for creating lung mask

The mask for the lung is very important for the final registration step in order to properly register the low intensity structures inside the lungs. So, different structuring elements with different sizes were tried to get a smooth shape for the mask. Figure 5.1 shows in particular the effect on the lung mask created by using different sizes of structuring element.



(a) Disk size = 3. (b) Disk size = 7. (c) Disk size = 15.

Figure 5.1: Example illustrating the effect of using different sizes of Structuring Element (SE) for morphological filters applied to the COPD1_iBHCT binarized volume (slice 50)
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5.3 Contrast enhancement for structures inside lung volume

The lung volume has a very low contrast to guide the registration even after the mask is applied. Few approaches were tried to enhance the contrast of the structures inside the lungs to get better registration results. Figure 5.2 shows the contrast enhanced lung structures done with the help of lung mask, adaptive histogram equalization and morphological filters.

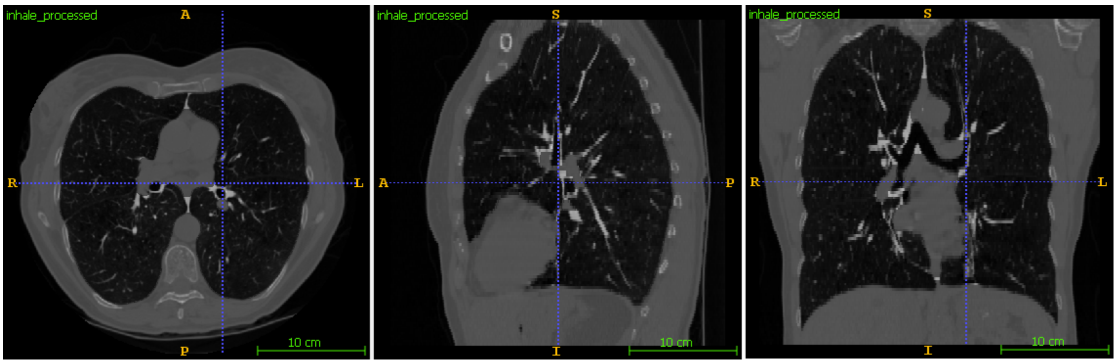


Figure 5.2: Illustration of contrast enhancement for lung volume structures using histogram equalization and morphological filters

6 Evaluation & Results

This section provides the quantitative and qualitative results for the registration of the 4 COPD cases provided.

6.1 Quantitative results

6.1.1 TRE(Target Registration Error)

Table 6.1 provides the TRE metics for each set of inhalation and exhalation volumes.

Table 6.1: Target Registration Error

Volume	**Mean TRE (mm)**	**Standard Deviation TRE (mm)**
COPD 1	8.0518	4.3702
COPD 2	11.3562	7.3449
COPD 3	4.3210	2.2639
COPD 4	9.8877	4.3563

6.1.2 Execution time

Table 6.2 provides time taken for the execution of each transformation in the given order. The execution time includes generating the transformed output volume for each transformation applied. It does not include the time taken to generate the Jacobian or deformation images.

Table 6.2: Execution time

Transformation	**Time taken(s)**
Rigid	60
Affine 2	60
B-Spline 64mm 3	120
B-Spline 32mm	180
B-Spline 8mm(with lung mask)	300
Total	720

6.2 Qualitative results

6.2.1 Comparison of fixed and transformed volumes

This section provides the images of the fixed, moving and the 2 transformed volumes, one before applying the last B-Spline(8mm) with mask and the other is the final transformed volume. The last 2 transformed volumes are provided to appreciate the effect of applying a mask for the transformation.

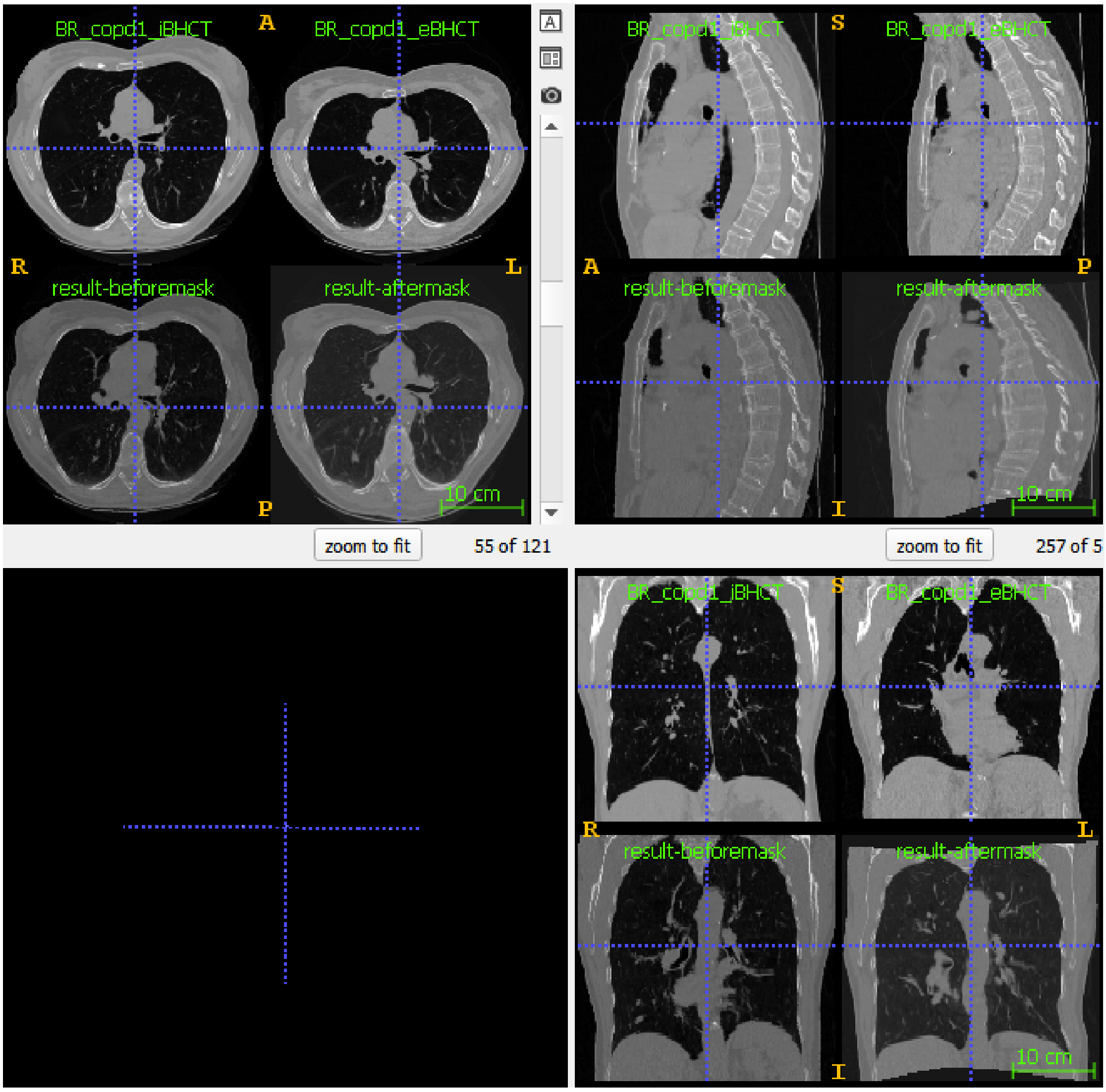


Figure 6.1: Registration result for copd1 data from exhale(moving) to inhale(fixed). Inhale(top left), Exhale(top right), Transformed image before applying mask(bottom left), Transformed image after applying mask(bottom right)

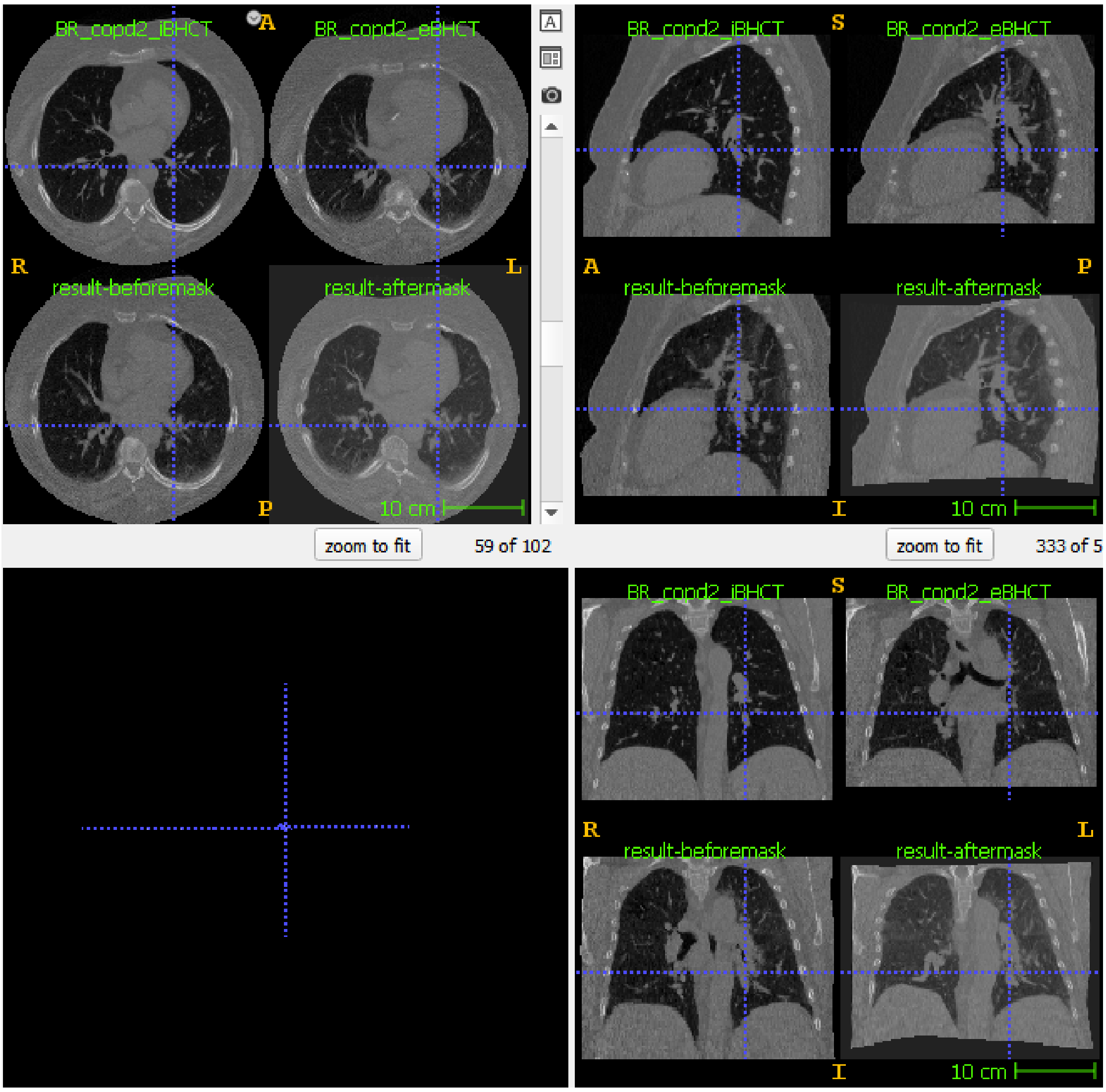


Figure 6.2: Registration result for copd2 data from exhale(moving) to inhale(fixed). Inhale(top left), Exhale(top right), Transformed image before applying mask(bottom left), Transformed image after applying mask(bottom right)

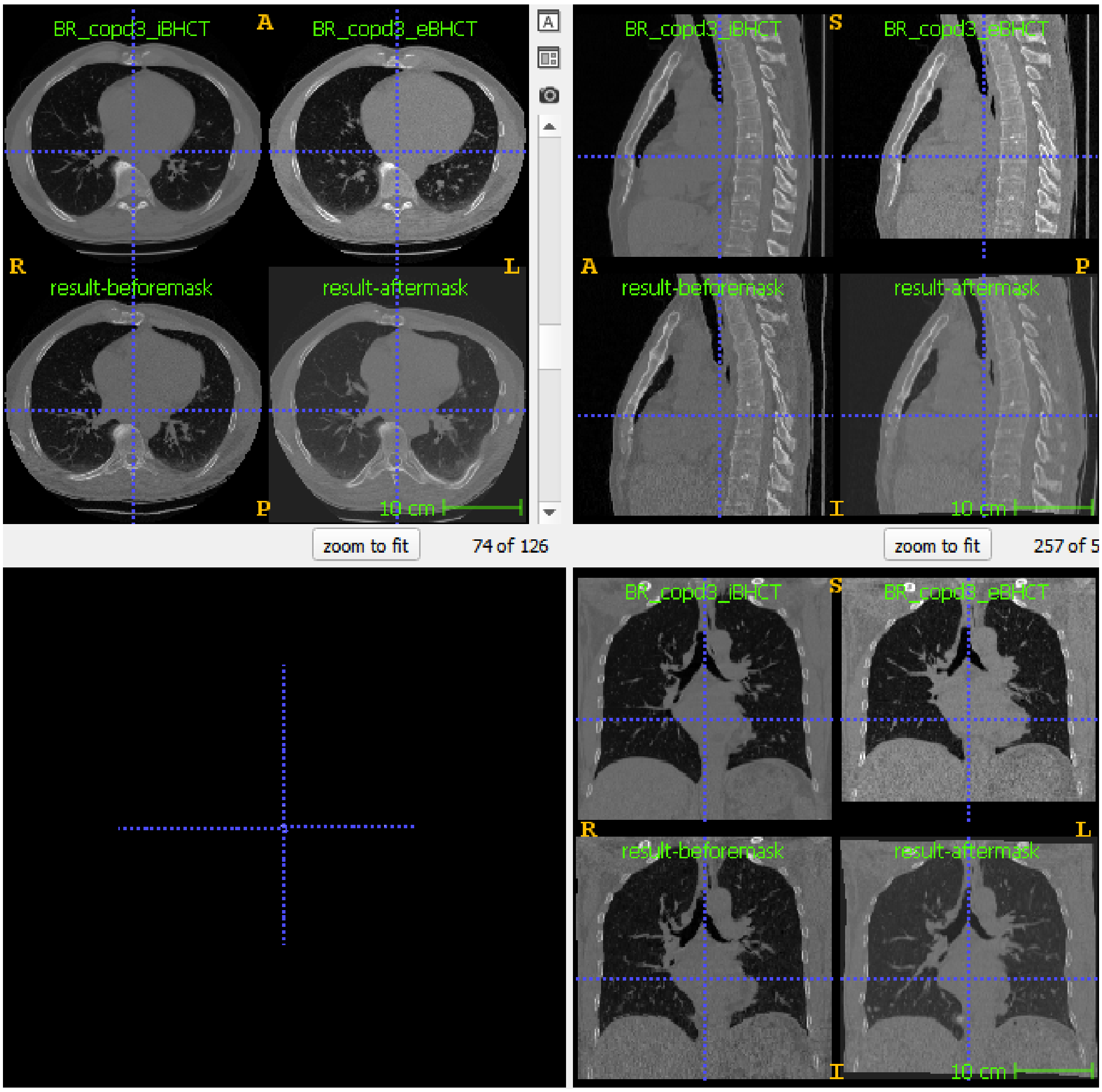


Figure 6.3: Registration result for copd3 data from exhale(moving) to inhale(fixed). Inhale(top left), Exhale(top right), Transformed image before applying mask(bottom left), Transformed image after applying mask(bottom right)

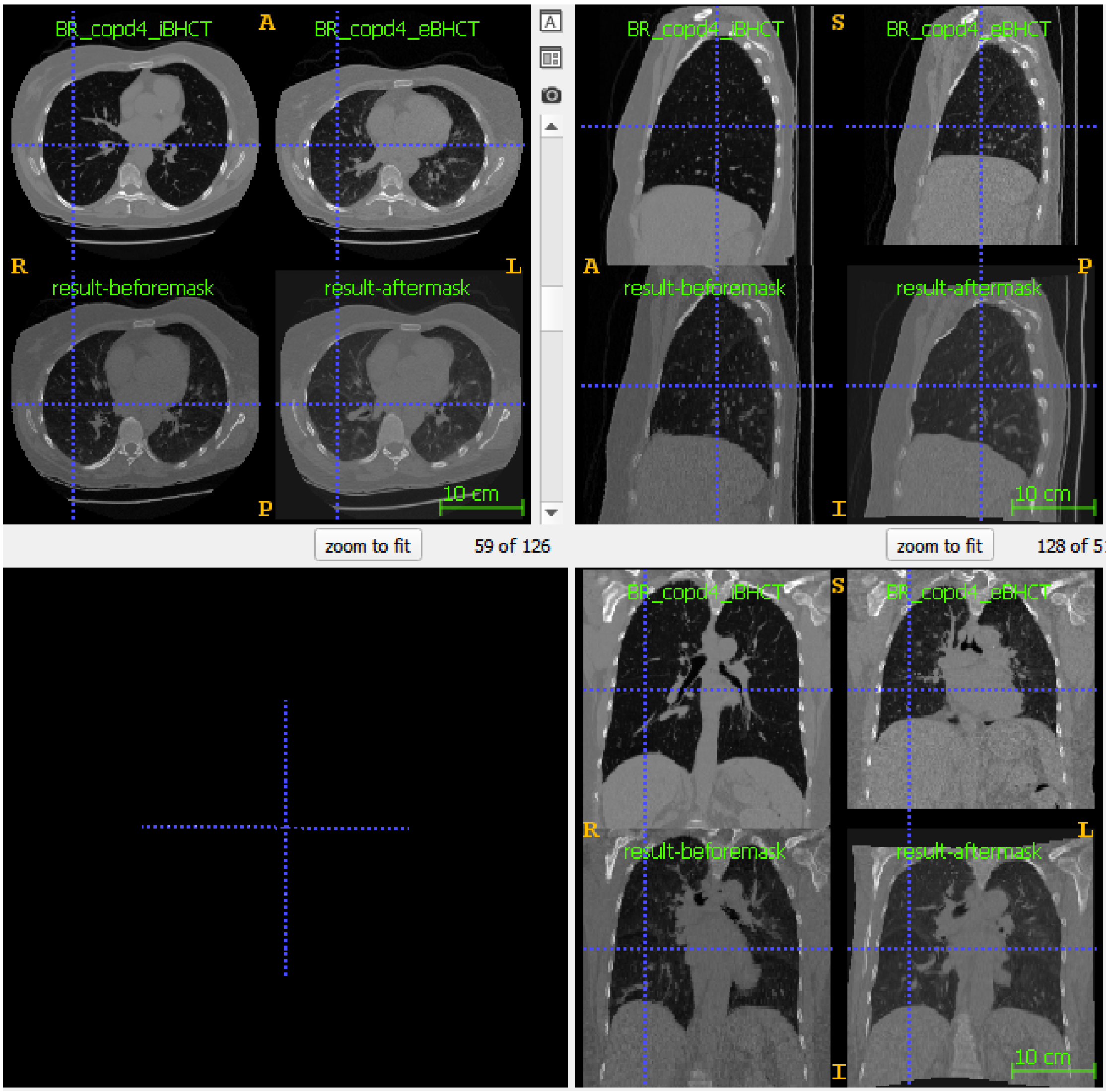
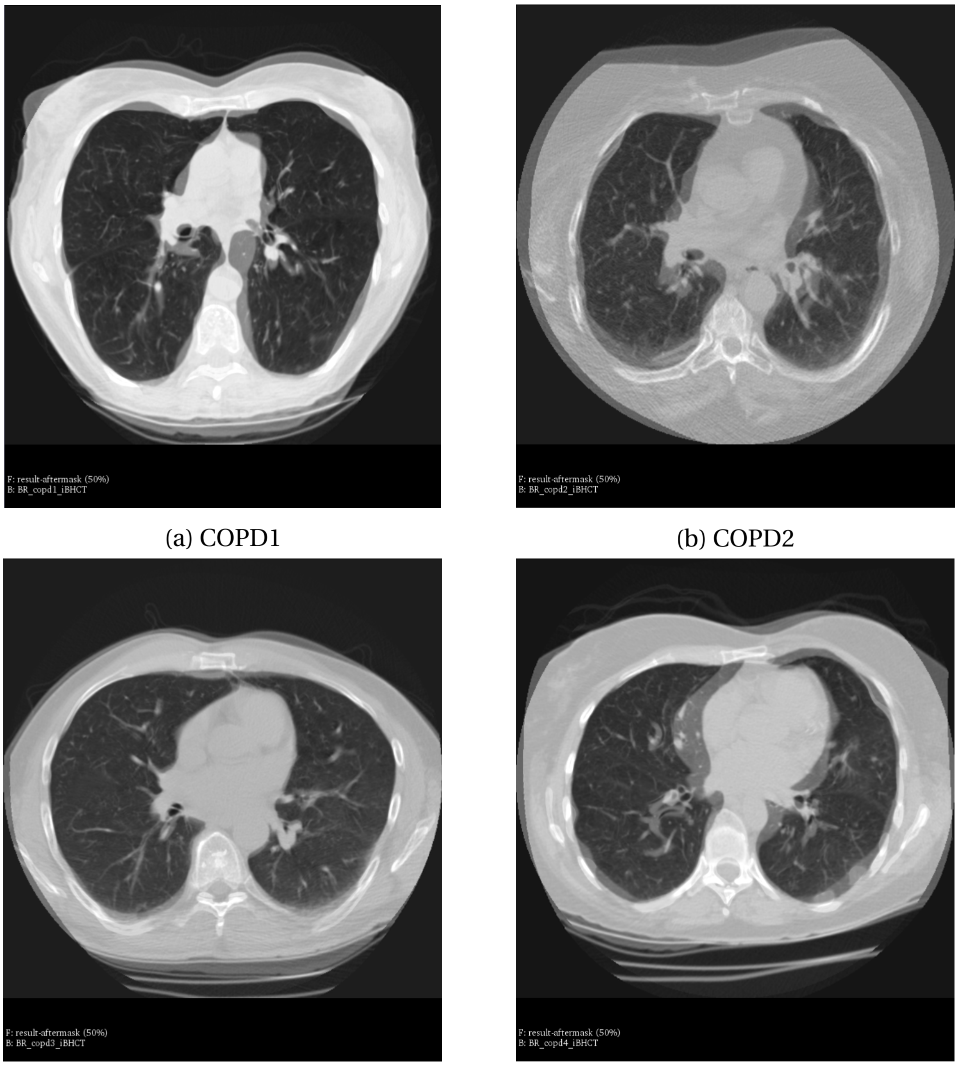


Figure 6.4: Registration result for copd4 data from exhale(moving) to inhale(fixed). Inhale(top left), Exhale(top right), Transformed image before applying mask(bottom left), Transformed image after applying mask(bottom right)

6.2.2 Volume overlay

Figure 6.5 shows the volume overlay between the fixed volume and the transformed volume. It is visually easy to find the regions where the volumes are not properly registered.



(a) COPD1 (b) COPD2

(c) COPD3 (d) COPD4

Figure 6.5: Illustration of volume overlay as a visual tool to check registration accuracy between fixed(foreground) and transformed(background with 50 % opacity) volume slices

6.3 Discussions

Figure 6.6 shows how the use of a mask varies the deformations applied on the volume. It is also observed that even though the deformations happen only within the regions that we wanted but still the deformations are not very smooth and this affects a lot the final accuracy of the registration. So in order to avoid this problem the amount of deformation applied can be penalized if it is more than required.

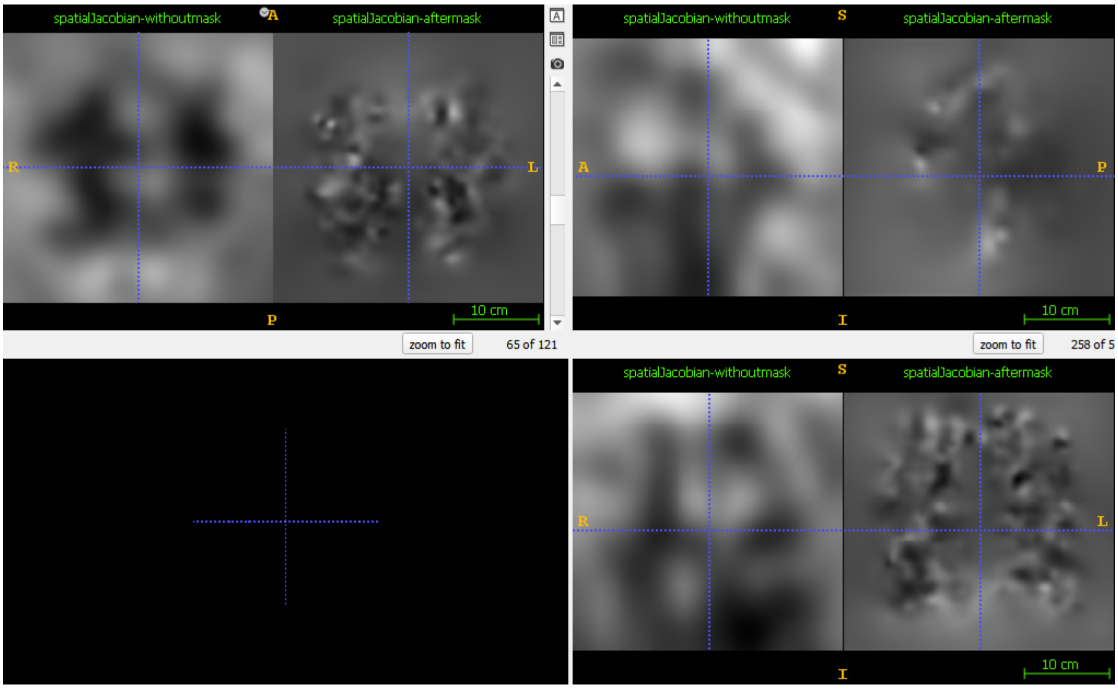


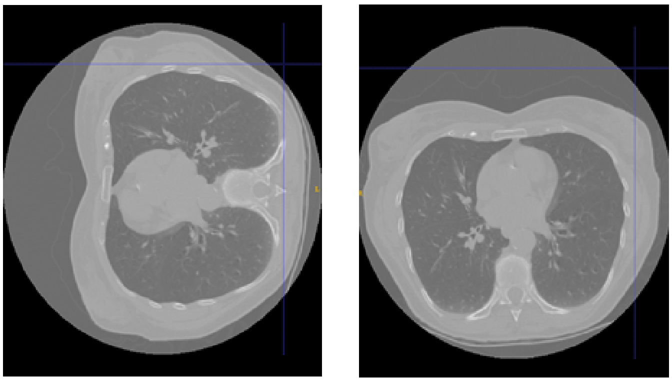
Figure 6.6: Jacobian of COPD 1 transformed volume showing the deformation without the mask(left) and with mask(right)

7 Problems Faced

During the development of the project we were facing some technical problems in different stages of the project. As follow it can be found a description of the most relevant problems faced.

7.1 3D Volume Visualization

At the beginning of the project, when analyzing the dataset, the Raw image (.img) were opened in ITK-Snap with the characteristics of the image (image dimension, pixel spacing), after re-orienting the image and saving it as .nii files to make use of it in the Matlab implementation it was noticed that, when showing the same image, the orientation was different between both the softwares as shown in Figure 7.1.



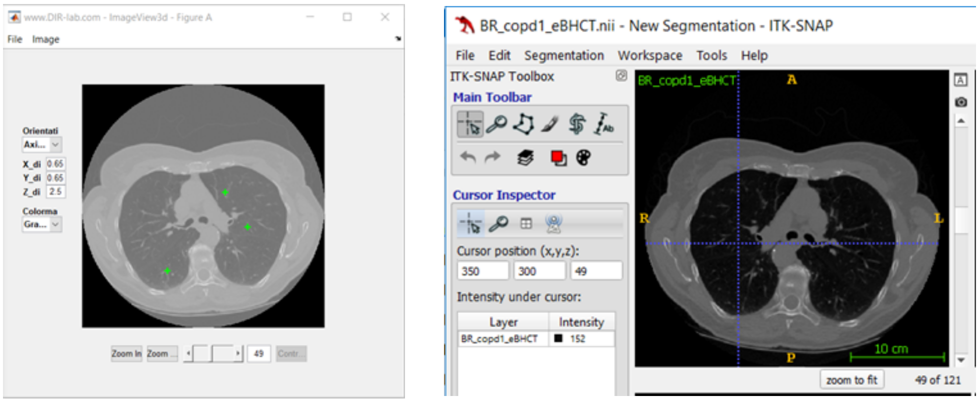
(a) MATLAB (b) ITK - Snap

Figure 7.1: Example of visualization of volume COPD1_iBHCT, slice 50, using 2 different software.

This problem is due to where is the orientation set in the software. However, this was only a visualization problem that did not affect the performance of the registration because, as long as the both images are oriented in the same direction, the registration will be work properly.

7.2 LANDMARK POINTS VISUALIZATION

The other visualization problem was related to the landmark points. In order to evaluate the transformation result it was needed to visualize the landmarks over the volume to check how close and where was mapped the landmarks in the lung region.
Using the ITK-Snap software it was not able the view to the landmark points. In MATLAB it was possible to show them by using the function provided *'imageView3d'* from the **MatlabUtilityPack - v1.0**. See the Figure 7.2



(a) MATLAB (b) ITK - Snap

Figure 7.2: Example of landmarks visualization over the volume COPD1_iBHCT, slice 50, using 2 differents software.

8 PROJECT MANAGEMENT

Table 8.1: Weekly tasks

Week	**Main Tasks**
Week 1	Define methods to approach objective Distribution of the project tasks Familiarize with the dataset
Week 2	Tune elastix parameters Matlab code to automate the process of registering all the volumes
Week 3	Tune elastix parameters Analyze MeVisLab & ITK
Week 4	Analyze methods for creating lung mask Installation of C++ ITK library Project approach presentation with mid-term results.
Week 5	Create lung mask. Implementation of the Mask to all the volumes. Tune elastix parameters Registration evaluation with the mask implementation. Implementation of Demon registration approach with Insight ToolKit (ITK).
Week 6	Registration evaluation with the mask implementation. Tune elastix parameters Analyze Demon registration in Slicer 3D. Report.
Week 7	Analyse contrast enhancement of lung volume. Report.

Table 8.2: Number of working hours

Team Member	**Tasks**	**Week 1-3(hours)**	**Week 4-7(hours)**
Umamaheswaran	Learning	10	15
	Coding	5	15
	Experiments	20	40
	Presentation & Report	3	12
Carmen	Learning	15	8
	Coding	5	10
	Experiments	10	30
	Report	3	15

9 CONCLUSION

The medical image registration are quite important to evaluate patient's evolution of a disease or for diagnosis purpose. Therefore a good performance of the registration is needed, for obtaining this it was notice that pre-processing of the image, creation of mask for the area of interest are quite important and have an impact on the result. Also the understanding of the parameters of the transformation, in this case the one from elastix software, lead to a better manage and manipulation of the deformation of the image.