Image registration of chest CT volumes: 4DCT DIR-Lab

*Medical Imaging Regristarion and Applications

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***Abstract*—Medical image registration is a pivotal computational technique widely employed in medical imaging applications to align and synchronize information from multiple imaging modalities or time points. In this project, we conducted non-rigid image registration of Chest CT images employing a BSpline transform. The primary goal was to align Inhale to exhale images based on provided landmarks. The Target registration metric served as a benchmark, resulting in a registration accuracy of 1.69 in the training set and 1.33 in the testing set.**

***Index Terms*—Registration, Chest CT, Elastix, Lung Segmentation**

I. Introduction

Registration is the process to transform one or more images onto the coordinate of another image. For decades, optimization-based methods that solve the transformation parameters by maximizing the image similarity have successively received many applications [1]. Lung MRI registration, between exhalation and inhalation phases, is a critical process in medical imaging that involves aligning lung images captured during different breathing phases to observe and measure the movement and changes within the lung tissue. The Target Registration Error (TRE) is employed as a key metric for assessing the accuracy of this registration. TRE quantifies the discrepancy between corresponding points in the registered images, offering a measure of precision and reliability in the registration process.

A. Objectives

The primary goal of this project is to establish a comprehensive Registration Strategy for chest CT scan images. The specific objectives encompass:

1) Develop a registration baseline pipeline for chest CT scan images.
2) Utilize provided landmarks to assess the Target Registration Error (TRE) after registration.
3) Develop an algorithm with the aim of automating the registration process.
4) Leverage the TRE metric for comparative analysis, aiming to minimize registration discrepancies through iterative method refinement.

II. Materials

A. Dataset

The data set consists of 4 CT scans of different subjects with exhalation and inhalation images from DIR-Lab. The data of these images comes in raw format which needs to be converted to usual formats. Additionally, the dataset includes corresponding landmark annotations for each image, crucial for calculating the Target Registration Error (TRE) during the registration process.

For each training case, the dataset contains:

1) Inhale chest CT scan
2) Exhale chest CT scan
3) Landmarks associated with the inhale CT scan
4) Landmarks associated with the exhale CT scan

In the testing subset, only landmarks for the inhale CT scan are provided.

III. Methodology

A. Preprocessing

Since the data consists of a raw file we need to create all the metadata necessary for the *Simple ITK* to be able to read it. In our project, we created a function called *read_raw_sitk* to tackle this challenge. The function defines a dictionary to map *SimpleITK* pixel types to their corresponding *MetaImage* (MHD) types, and it constructs the necessary image header information based on the provided arguments. This header is written to a temporary *MetaImage* header file (.mhd), allowing *SimpleITK* to read the raw image file (.raw) associated with this header. The image is loaded with the specified spatial orientation, spacing, and origin, and the temporary header file is deleted after use.

B. Mask Segmentation

In this project, we develop an algorithm composed of two functions: *get_segmented_lungs* and the *get_segmented_lungs_3d*, designed for the creation of masks for lung MRI. The first function operates on a single 2D image. The first step is to create a binary image by a threshold of 400, typically representing lung tissue. Then we apply some operations to clean and obtain a better mask: clearing the border, labeling connected regions, and removing smaller regions based on area comparison. The next step is erosion and closing operations using disk-shaped structuring elements to refine the lung region's shape. Robert's edge detection method is applied, followed by filling holes to achieve a more accurate lung segmentation. The second function extends this approach to 3D image volumes like MRI scans. It iterative applies the first function constructing a binary mask for the entire volume.

C. Registration

Medical image registration is a pivotal computational technique widely employed in medical imaging applications to align and synchronize information from multiple imaging modalities or time points. This process is crucial for tasks such as image fusion, treatment planning, and monitoring disease progression. This lab report presents a simple yet effective registration pipeline designed to align a "moving" medical image with a reference or "fixed" image. The pipeline, Fig 1, involves the selection and configuration of key components, including a similarity metric, transformation model, and optimization algorithm.

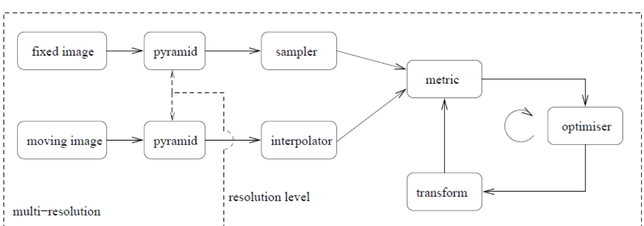


Fig. 1: The basic registration components.

- **Fixed and Moving Images:** The fixed image serves as the reference point, while the moving image undergoes spatial transformations to achieve alignment.
- **Similarity Metric:** A similarity metric quantifies the agreement between corresponding pixel intensities or features in the fixed and moving images. Common metrics such as Mean Squared Difference (MSD) or Normalized Cross-Correlation (NCC) are employed to guide the optimization process.
- **Transform Model:** The transformation model defines the spatial relationship between the fixed and moving images. The choice of a transformation model, such as rigid, affine, or deformable, depends on the nature of the images and the required level of alignment precision.
- **Optimizer:** An optimizer iteratively adjusts the transformation parameters to minimize the dissimilarity metric between the fixed and moving images. Gradient descent, stochastic gradient descent (SGD), and simulated annealing are commonly employed optimization algorithms.
- **Multiresolution:** Multiresolution registration involves a hierarchical approach, performing the registration at multiple levels of image resolution. This strategy aids in overcoming local minima and accelerates convergence.
- **Multimetric:** Multimetric registration employs multiple similarity metrics during optimization, enhancing the robustness and accuracy of the registration process.

Understanding and effectively configuring these components are critical for the successful implementation of a registration pipeline. The iterative refinement of the transformation parameters ensures the alignment accuracy required for subsequent analysis and interpretation of medical images.

In the subsequent sections, we will delve into the specific parameters chosen for our registration experiments, discuss the rationale behind their selection, and present the results obtained from this registration pipeline.

D. Target Registration Error

For most registration tasks, the primary error measure is the target registration error (TRE), which represents the distance after registration between corresponding points not used in calculating the registration transform. In Fig. 2, the TRE, measured at a point relative to some given origin, is the distance after registration between the anatomical location (filled square) represented by *r* in one space and the corresponding anatomical point in the other space (filled circle) [2]

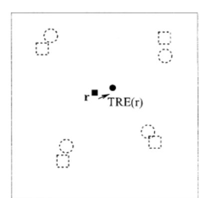


Fig. 2: Taget Registration Error

E. Elastix

Elastix is an open-source software package commonly used for medical image registration in modalities like CT, MRI, and PET [3]. We opted for *Elastix* based on its user-friendly interface and flexibility, experiences from our previous labs.

The heart of the registration process lies in the parameter file—a text document defining the components and their values. As these choices significantly impact the registration outcome, thoughtful parameter selection is crucial. In our case, we experimented with various parameters from the *Elastik* Model Zoo [4], tailored for applications like 3D Lung CT.

F. Parameter file

Given the multitude of options—more than 14, each with its unique settings—we have chosen to investigate two extremes: Par0054 (2018) and Par003 (2010), [4].

Par004: This particular configuration addresses the registration of intra-patient thoracic CT scans in the presence of respiratory motion, leading to compression/expansion of lung parenchyma. It emplys the *SumSquaredTissueVolumeDifference* metric and adopts a *MultiMetricMultiResolutionRegistration* approach.

As outlined in the *elastix* documentation, here are the recommended values for various components:

TABLE I: Component Recommendations

Component	Recommendation
Registration	MultiResolutionRegistration
Metric	AdvancedMattesMutualInformation
Sampler	RandomCoordinate
Interpolator	LinearInterpolator
ResampleInterpolator	FinalBSplineInterpolator
Resampler	DefaultResampler
Transform	Depends on the application
Optimizer	AdaptiveStochasticGradientDescent
FixedImagePyramid	FixedSmoothingImagePyramid
MovingImagePyramid	MovingSmoothingImagePyramid

For our CT lung volumes, we have chosen to adapt the parameter file Par0054. Notable changes were made to several parameters, outlined in the table below:

TABLE II: Parameter Variations Parameter Par0054

Parameter	Values
Metric	SumSquaredTissueVolumeDifference TransformBendingEnergyPenalty AdvancedMattesMutualInformation
NumberOfSpatialSamples	10000 3000
NumberOfResolutions	4 8
MaximumNumberOfIterations	100 200
FinalGridSpacingInPhysicalUnits	8 12
Optimizer	StandardGradientDescent AdaptiveStochasticGradientDescent
ImagePyramidSchedule	1 1 1 1 1 1 1 1 1 1 1 1 4 4 4 3 3 3 2 2 2 1 1 1 -

These adjustments cater to the specifics of our CT lung volumes, aligning the registration parameters with our imaging requirements.

Following a systematic exploration of parameter values, adjusting each one individually to observe improvements, and referencing the *Elastix* manual [5], we arrived at the following insights:

1) Metric Selection: The *AdvancedMattesMutualInformation* metric demonstrated effectiveness for both mono- and multi-modal images.
2) Optimizer Considerations: The critical aspect related to the optimizer is the maximum number of iterations. Generally, a higher number of iterations yields better registration results. A recommended starting point is 500 iterations, and if computational time allows, increasing it to 2000 can further enhance results.
3) Number of Resolutions: Initiating with 3 resolutions is a commonly effective starting point. However, if the fixed and moving images are initially distant, increasing the number of resolution levels (e.g., 5 or 6) is beneficial. This strategy prioritizes the registration of large, dominant structures.
4) Pyramid Schedule: The pyramid schedule defines blurring in each direction (x, y, z) for each resolution level. Adjusting this schedule can influence the registration outcome.
5) Optimizer Choice: The *AdaptiveStochasticGradientDescent* optimizer proved effective, especially due to its adaptive nature, eliminating the need for intricate parameter specification and tuning. This simplifies the optimization process, particularly when parameter tuning is challenging.

These observations serve as valuable guidelines for optimizing the parameter selection process based on the specific characteristics and requirements of our CT lung volumes.

Following the successful reduction of the Target Registration Error (TRE) through parameter adjustments, our attention shifted to experimenting with different transformation types. The choice of transformation depends on the specific application requirements:

1) AffineTransform: This transformation is suitable for compensating differences in scale.
2) BSplineTransform: Ideal for nonrigid registration problems, the B-spline nonrigid transformation is defined by a uniform grid of control points.

To further expand our parameter exploration, we delved into the specifics of Par003. This parameter set investigates the influence of the multiresolution strategy on the registration process. For each patient, baseline and follow-up scans were registered using both a nonrigid B-spline transformation and an Affine transformation.

Within Par003, there are 8 options, each employing 8 resolution levels. Each option presents two variations:

1) Constant Grid Resolution (Isotropic): The resolution of the B-spline control point grid is maintained at a constant value of 12 mm across all resolutions.
2) Refined Grid Resolution: The grid is refined after each resolution, ensuring that at the final resolution, the control points are spaced 12 mm apart again.

This parameter exploration aims to discern the impact of multiresolution strategies on the registration outcomes, providing valuable insights into the nuances of the transformation and resolution choices.

For Par003, we extended our exploration by combining the final parameter variation with additional modifications. The table below outlines the variations introduced:

TABLE III: Parameter Variations using Par003

Parameter	Values
NumberOfResolutions	1 6 8
Transformation	BSplineTransform Affine
NumberOfResolutions	4 8
MaximumNumberOfIterations	1000 2000 3000
NumberofSamples	3000 10000
FinalGridSpacingInPhysicalUnits	8 12
GridSpacingSchedule	Fixed: (1 1 1 1 1 1 1 1) Decreasing: (16 16 16 16 8 4 2 1)
ImagePyramid	Smoothing Recursive
NumberOfHistogramBins 32	32 16

These variations encompass adjustments to the number of resolutions, transformation types, iteration counts, sample numbers, grid spacings, pyramid strategies, and histogram bins. This comprehensive exploration aims to refine the registration process further

Following a meticulous exploration of parameters and their impact on the registration process, we arrived at a final parameter configuration that balances accuracy and efficiency. The table below outlines the chosen registration configuration:

TABLE IV: Final Registration Configuration Parameters

Parameter	Value
AutomaticTransformInitialization	true
AutomaticParameterEstimation	true
UseAdaptiveStepSizes	true
Registration	MultiResolutionRegistration
FixedImagePyramid	FixedRecursiveImagePyramid
MovingImagePyramid	MovingRecursiveImagePyramid
Interpolator	BSplineInterpolator
Metric	AdvancedMattesMutualInformation
Optimizer	AdaptiveStochasticGradientDescent
ResampleInterpolator	FinalBSplineInterpolator
Resampler	DefaultResampler
Transform	BSplineTransform
NumberOfResolutions	8
FinalGridSpacingInPhysicalUnits	12
GridSpacingSchedule	16 16 16 16 8 4 2 1
MaximumNumberOfIterations	2000
NumberOfHistogramBins	16
NumberOfSpatialSamples	3000

G. *Registration Algorithm*

In this project, we implemented the function to automatically register our test from the different parameter fields. This function is designed to process the dataset using specified parameter maps and an experiment name, with an option to include masks. The algorithm iterates through each item, extracting essential data such as the case name, voxel size, displacement mean, and standard deviation.

For each sample, the algorithm sets up necessary paths for data storage and processes parameter maps. Depending on whether masks are used, it invokes the *elastix_wrapper* function to perform image registration, recording the time taken for this operation. Post-registration, the algorithm modifies field parameters in the transformation map and proceeds to transform landmark points using *transformix_wrapper*.

It calculates the target registration error between transformed landmarks and expected landmark points, providing both mean and standard deviation values. These statistics, along with the registration time and mask usage status, are stored in a results dictionary for each case. The function ultimately returns this comprehensive results dictionary, encapsulating all key outcomes of the registration process.

IV. Results

A. *Lung Segmentation*

In Fig. 3, we present a 2D cut of the new image created from the raw data algorithm of the 3D volumes provided in this project. In the inhalation images, the lungs appear well-expanded with air, which makes the lung tissue look darker due to the lower density of inhaled air. The bronchial tubes are open and the diaphragm is lowered to allow for the expansion of the lungs. In contrast, the exhalation images show the lungs in a state of deflation, where the lung tissue is denser and appears lighter on the CT images. The bronchial tubes may seem narrowed due to the decreased lung volume, and the diaphragm rises because the lungs are expelling air.

In Fig. 4, we present the results of the mask creation algorithm of a 2D cut from one of the 3D volumes provided in this project. Initially, the image is binarized to distinguish lung tissue, then refined by clearing the border artifacts. Subsequent steps include labeling connected regions, selecting the two largest areas representing the lungs, applying erosion with a disk radius of 2 to separate connected structures, and finally performing a closing operation with a disk radius 10 to smooth lung boundaries and fill gaps.

B. *Registration with elastix*

n our best experiment without using the mask, we achieved optimal results with Elastix using the Par0003 parameter file and 8 resolutions for COPD patients (COPD1, COPD2, COPD3, COPD4). The final mean of the Mean Target Registration Error (TRE) is recorded at 4.58 mm, as detailed in Table V. Despite the extended computation time, exceeding 40 minutes, Elastix demonstrated superior performance in achieving precise image registration, showcasing its effectiveness in our experiments without any use of segmentation.

We conducted experiments with the final parameter set, both with and without incorporating the mask during the registration process. The results, presented in Table VI (without mask)

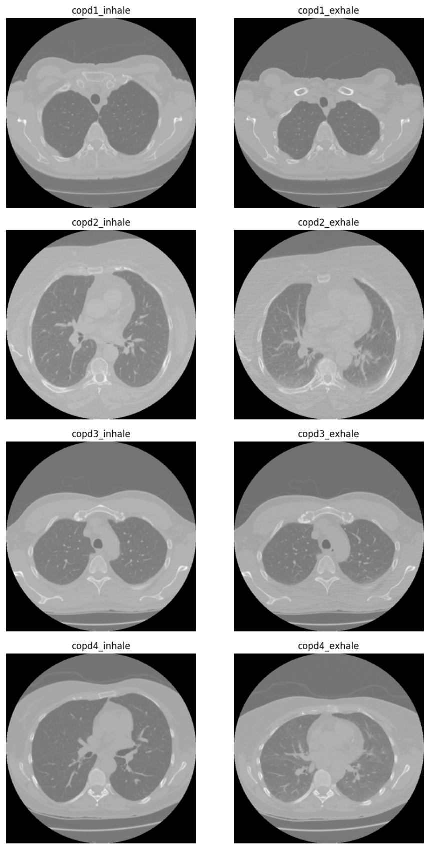
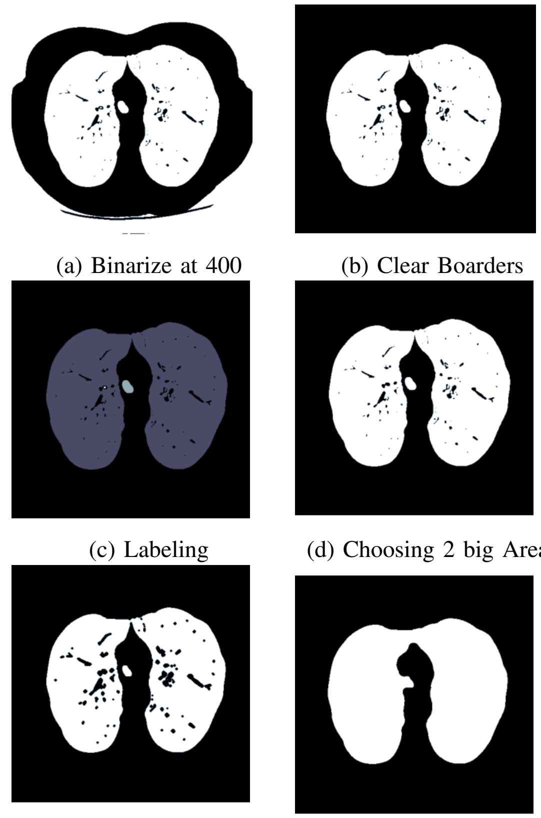


Fig. 3: Reading the new files

TABLE V: Par0003 8 resolutions NormalizedMI Results - COPD Patients

Patient	Mean TRE	Std TRE	Time (s)
COPD1	4.36	4.0	1058.62
COPD2	5.84	6.07	996.82
COPD3	2.93	2.69	946.36
COPD4	5.58	5.28	936.15



(a) Binarize at 400 (b) Clear Boarders

(c) Labeling (d) Choosing 2 big Areas

(e) Erosion Closing

Fig. 4: Masks Algorithm Result

TABLE VI: Results Final Parameter without mask

Patient	Mean TRE	Std TRE	Time (s)
COPD1	7.17	4.6	132.12
COPD2	12.4	7.01	129.18
COPD3	4.19	3.27	146.54
COPD4	8.04	4.17	136.15

and Table VII (with mask), showcase the impact of the mask on improving registration outcomes for COPD patients.

Without the mask, the Mean Target Registration Error (TRE) ranged from 4.19 mm to 12.4 mm, with corresponding standard deviations and computation times. In contrast, the incorporation of the mask led to a significant reduction in the Mean TRE, with values ranging from 1.15 mm to 2.86 mm. The standard deviations also exhibited a decrease, indicating enhanced precision in the registration process. Although there was a slight increase in computation times, the improved accuracy achieved by utilizing the mask demonstrates its effectiveness in refining the registration outcomes. The results underscore the importance of incorporating additional information, such as lung masks, for optimizing the registration performance in medical imaging.

In Fig. 5 is shown the TRE mean and standard deviation of our trials without the masks. The image shows in the x-axis the names of all the parameter files used in the trials. We can observe that the test with the best TRE is *best_untilnow* and the *Par0003.bsR8-fg_NormalizedMI*. Meanwhile, the last one shows good results it comes with a high computational cost. At last, the result without a mask still has room for improvement since we have TRE around the 10 mm mark.

In the 6 shows a good improvement in the reduction of the TRE across all the file parameters. In this batch of test, the *Par0003.bsR8-fg_NormalizedMI* was not considered due to the high computational cost of the registration. The *best_untilnow* is our best result so far given an average TRE of 1.6 across all the training files. Is notable the overall reduction of the TRE with the mask in Fig. 5 the average TRE is near 10 here we can see an average of 1.

Registration with ANS

In our literature review for a solution implementing another tool we encounter ANS, after testing around with some of the parameters. We did 5 different registrations with differents settings in Fig 7 we can observe that the TRE was multiplied

TABLE VII: Results Final Parameter - COPD Patients with mask

Patient	Mean TRE	Std TRE	Time (s)
COPD1	1.32	1.44	133.76
COPD2	2.86	4.04	127.41
COPD3	1.15	0.99	147.38
COPD4	1.46	1.12	138.95

by 5 times the TRE provided us in the dataset. We concluded that our *elastik* implementation was good enough to not do a further incursion on *ANTS*.

Testing-Challenge

During the challenge were provided three new volumnes, after performing the final registration the gave us a mean TRE of 1.3385. The TRE per patient is shown in table VIII. Additionally, in Fig 8, are shown soome examples of the registration result.

TABLE VIII: Results Testing COPD Patients with mask

Patient	Mean TRE	Time (s)
COPD5	1.4674	0
COPD6	1.6330	0
COPD0	0.8850	0

Discussion and Conclusion

In this project, we focused on refining a baseline for image registration for chest CT scans of patients during inhalation and exhalation phases. The adaptation of appropriate parameters to the dataset proved crucial for improved results.

Utilizing Elastix, we achieved a mean Target Registration Error (TRE) of 4.58 mm, demonstrating precise registration even without masks. Incorporating lung masks significantly reduced the Mean TRE to a range of 1.15 mm to 2.86 mm, enhancing accuracy at a slight computational cost. This emphasizes the effectiveness of incorporating lung masks for superior results.

Comparison with ANTs highlighted Elastix's effectiveness, providing results five times better in terms of TRE. In a testing challenge with new volumes, our approach exhibited a mean TRE of 1.3385, showcasing adaptability to diverse datasets.

In conclusion, our strategy proves robust with Elastix, offering accurate registration with the potential for clinical relevance. Future work may focus on further optimizing computational efficiency for practical implementation.

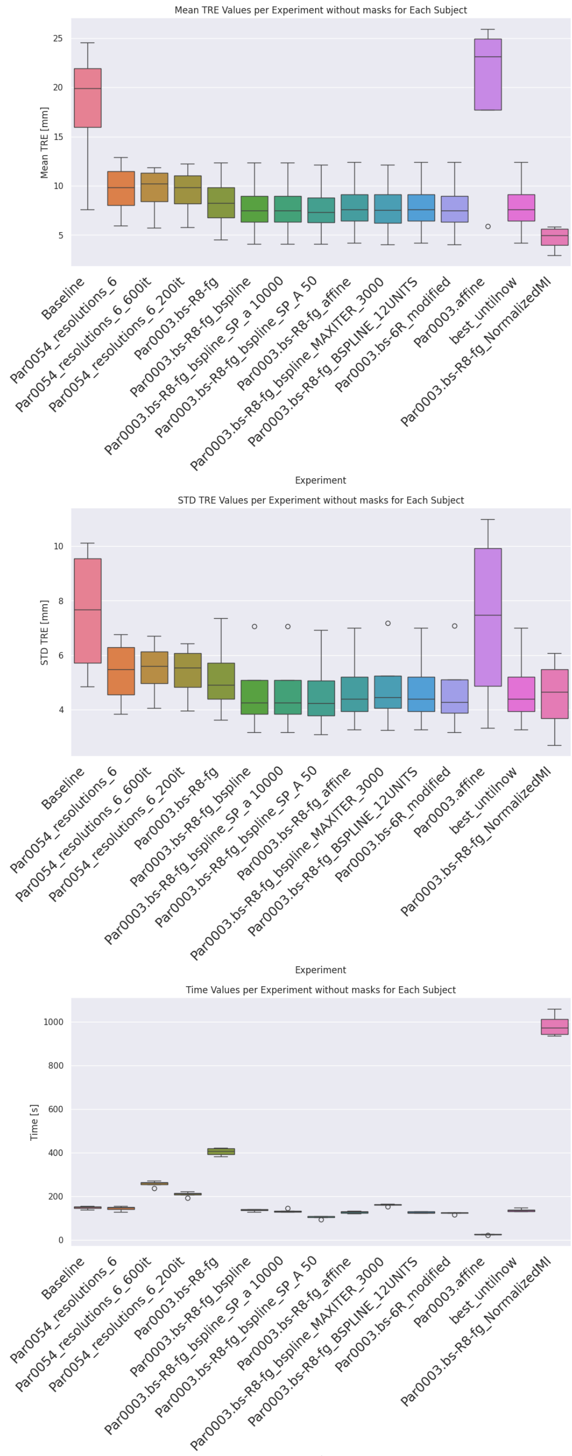


Fig. 5: Elastik without masks

References

[1] L. Chen, X. Cao, L. Chen, Y. Gao, D. Shen, Q. Wang, and Z. Xue, "Semantic hierarchy guided registration networks for intra-subject pulmonary ct image alignment," in *Medical Image Computing and Computer Assisted Intervention – MICCAI 2020* (A. L. Martel, P. Abolmaesumi, D. Stoyanov, D. Mateus, M. A. Zuluaga, S. K. Zhou, D. Racoceanu, and L. Joskowicz, eds.), (Cham), pp. 181–189, Springer International Publishing, 2020.

[2] J. Fitzpatrick and J. West, "The distribution of target registration error in rigid-body point-based registration," *IEEE Transactions on Medical Imaging*, vol. 20, no. 9, pp. 917–927, 2001.

[3] S. Klein*, M. Staring*, K. Murphy, M. A. Viergever, and J. P. Pluim, "elastix: a toolbox for intensity-based medical image registration," *IEEE Transactions on Medical Imaging*, vol. 29, pp. 196 – 205, January 2010.

[4] "Elastix model zoo," n.d.

[5] S. Klein and M. Staring, *Elastix Manual*, October 10, 2019.

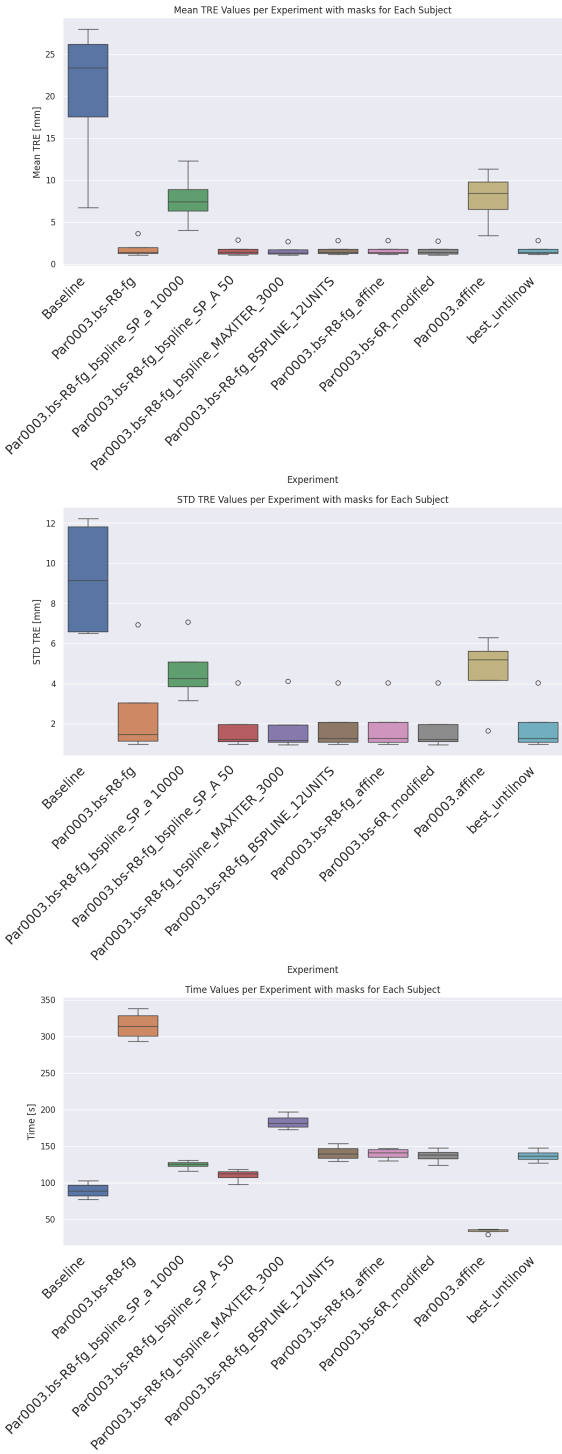


Fig. 6: Elastik with masks

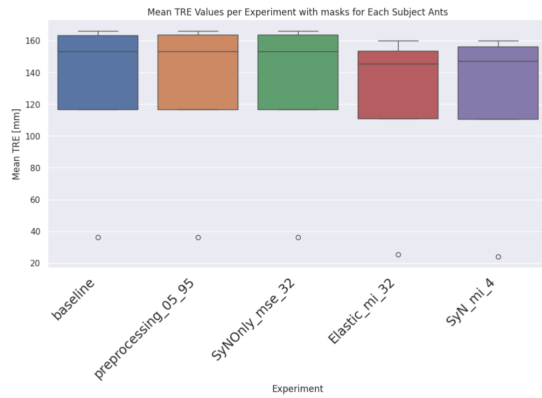
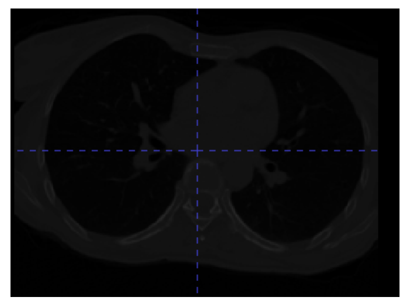
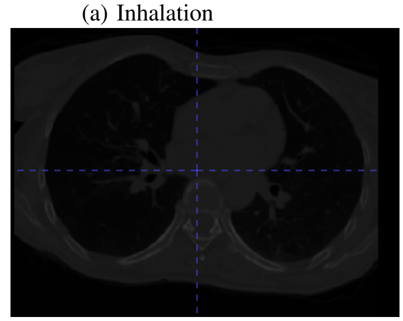


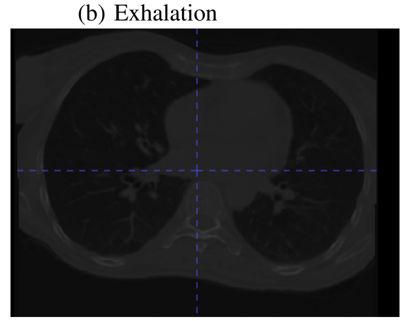
Fig. 7: Ants: TRE mean per tests



(a) Inhalation



(b) Exhalation



(c) Inhalation transform

Fig. 8: Test registration Result