Chest CT volumes registration: Medical Images Registration and Applications project

1st Gonzalo Esteban Mosquera Rojas
MSc. in Medical Imaging and Applications student
University of Girona
Girona, Spain
gonzalo.mosquerarojas2000@gmail.com

2nd Kazi Saeed Alam
MSc. in Medical Imaging and Applications student
University of Girona
Girona, Spain
saeed.utsha@gmail.com

***Abstract*—The following report presents the results obtained during the final project of the course of Medical Images Registration and Applications.The main objective of the project was to perform intra patient 3D CT chest lung images registration taken in two different respiration moments: inhale and exhale. The training data set consisted on 4 pairs of volumes with their respective annotations (landmark points). The performance of the registration algorithms was initially evaluated through Target Registration Error (TRE), which corresponds to the 3D euclidean distance between transformed landmarks. During the challenge day, 3 pairs of new images were given as well as the inhale landmarks, and the final performance evaluation was done by computing the TRE between the transformed points and the hidden exhale ones. The method proposed in this work achieved TRE of 1.8014, 3.9218, and 1.1823 for the three testing examples.**

***Index Terms*—Chest lung CT volumes, image registration, target registration error, CT imaging, histogram matching.**

I. Introduction

Chest computed tomography (CT) is a medical imaging technique that uses X-rays to create detailed images of the organs and structures in the chest, such as the lungs, heart, and blood vessels. CT scans are commonly used to diagnose and monitor a variety of conditions, including cancer, heart disease, lung infections, and injuries to the chest.

Chest CT registration is the process of aligning or "registering" two or more chest CT images taken at different times or under different conditions. For example, a chest CT may be taken while a patient is inhaling and another while the patient is exhaling. These images could be captured on different days or at different stages of a treatment, such as before and after chemotherapy or radiation therapy. By registering these images, doctors can compare the images and look for changes in the size, shape, or position of the organs and structures in the chest.

Registration of chest CT images can also be used for other purposes in medical practice, such as detecting changes in lung (growth of tumors, presence of infection), monitor the progress of diseases or evaluating the performance of a specific treatment, and guiding the placement of needles and other medical instruments during biopsies or surgical procedures.

There are several techniques that can be used to perform chest CT registration, including manual registration and automated registration using specialized software. Manual registration involves aligning the images by eye, while automated registration uses algorithms to compare the images and determine the best alignment. Automated registration can be faster and more accurate than manual registration. In this project, a method for automatic non-rigid registration of chest CT volumes is explored. The dataset consists of 4 pairs of volumes of patients in two different moments (inhale and exhale) with their respective annotations (landmark points). Therefore, the performance of the registration method is evaluated using Target Registration Error (TRE), which corresponds to the 3D Euclidean between transformed landmarks. The report is divided in the following sections: design an implementation of the proposed solution, in which all the steps for the general pipeline are presented, results section, in which an analysis of the obtained results is presented and finally a conclusions section where the main strengths and limitations of the method are studied.

II. Design and implementation of the proposed solution

The design of the project solution consisted on several steps which are discussed in the following subsections, and depicted in Figure 1.

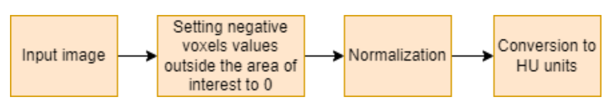

Fig. 1. Block Diagram for Image Preprocessing Steps.

A. Image Preprocessing:

1) Analysis of data:: Figure 1 shows an example of an inhale training images with its corresponding landmarks. As seen in the image, all these landmark points are located within the lung area, and therefore it is of great importance to segment this area accurately in order to have good registration results, and this will be studied in the following sections.

2) Setting negative voxel valus outside the area of interest to zero: First of all an exploration of the image space was carried out and it was found that outside the area of interest (the chest itself) the voxel values were -2000 instead of 0. In

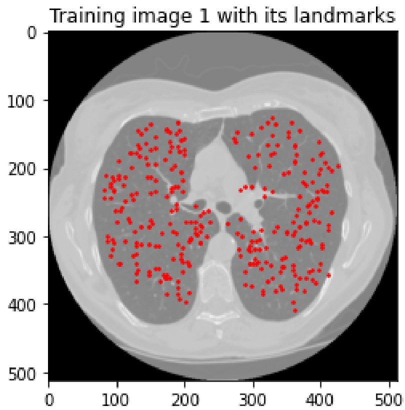

Fig. 2. Training inhale image example with its landmarks

CT imaging, the value of -2000 is often used to represent areas outside the field of view (FOV) or areas that are not imaged due to motion or other artifacts. These areas are sometimes referred to as “air” or ”background” voxels.

One reason to keep these -2000 voxels in the image is that they provide important information about the FOV and the imaging process. For example, in CT imaging, the image intensities are proportional to the X-ray attenuation coefficients of the tissue, and the value of -2000 is assigned to areas where there is no tissue present, such as air or the body’s exterior. By retaining these -2000 voxels, the radiologist can see the spatial relationship between the lung tissue and the surrounding air, which is important for diagnostic purposes. Another reason to keep these voxels is that they can be used to validate the accuracy and reliability of image analysis algorithms. For example, in lung CT imaging, it is important to accurately segment the lung from the surrounding air and other structures, such as the diaphragm. The presence of the -2000 voxels in the image can be used as a check to ensure that the segmentation algorithm is not including voxels outside the FOV or that should not be included.

However, there is a big reason on why not to keep them, and that one is when performing image registration. These “air” voxels could be seen as significant difference between the images, causing the registration to fail. Also, if you are planning to perform lung volume measurement, those “air” voxels would artificially increase the lung volume. Therefore, -2000 voxels were set to zero in all training images.

3) Normalization: For this particular case, min-max normalization was performed on all the training images. This is a preprocessing step that is used to scale the pixel intensities of an image to a specific range, typically between 0 and 1. Min-max normalization is an important preprocessing step for chest CT images because it helps to improve the performance of various image processing tasks, such as image registration, which is this application case.

One of the main reasons why min-max normalization is important in chest CT images is that the raw data can have a wide range of intensity values due to the fact that the pixel intensities are proportional to the X-ray attenuation coefficients of the tissue. This wide range of intensity values can make it difficult for image processing algorithms to work effectively, as some algorithms may be sensitive to small changes in intensity, while others may not be able to distinguish between different types of tissue based on their intensity values. By normalizing the intensities to a specific range, it can be sure that the methods will focus on relevant features rather than the intensity variations. Another important reason for min-max normalization is that it helps to ensure that the images have a consistent appearance, regardless of the specific scanner or imaging protocol that was used to acquire them. Chest CT images are acquired using different scanners with different imaging protocols, and this can result in images that have vastly different intensity distributions. The normalization will put the images in a common scale which will make them more comparable, and more easily processable.

4) Conversion to Hounsfield units: Once the images are normalized, these are converted to Hounsfield units. Hounsfield units (HU) are a measure of radiodensity used in computed tomography (CT) imaging. HU values are assigned to each voxel (3D pixel) in a CT image based on the amount of x-rays absorbed by the tissue at that location. The range of HU values can vary depending on the specific CT machine and imaging protocol used, but in general, air has a HU value of -1000, water has a HU value of 0, and bone has a HU value of around +1000.

When a CT scan is performed, the x-ray beam passes through the body and the amount of x-rays absorbed by the tissue is measured by detectors. These measurements are used to generate a 3D image of the patient’s body, with each voxel in the image assigned a HU value based on the amount of x-rays absorbed at that location. Because different types of tissue have different densities and therefore absorb different amounts of x-rays, they will have different HU values. This means that HU values can be used to distinguish different types of tissue in a CT image, such as bone, fat, muscle, and lung tissue.

Converting chest CT images to HU is important in order to improve registration and segmentation of the lungs. During registration, the CT images from multiple time points are aligned so that corresponding structures in the images are in the same location. However, if the images are not in the same scale, registration may not be accurate. By converting the images to HU, the images will be in the same scale, which improves registration. Additionally, converting to HU can also improve segmentation of the lungs, as it allows for better distinction between the lung tissue and other structures such as blood vessels and bones.

5) Results of image preprocessing: Figure two shows the visual results after applying each one of the preprocessing steps. From these images it can be noted the big importance of setting -2000 pixels to zero, as it allows better visualization of the lungs area, which is very beneficial for working on segmentation approaches that would greatly improve the registration results.

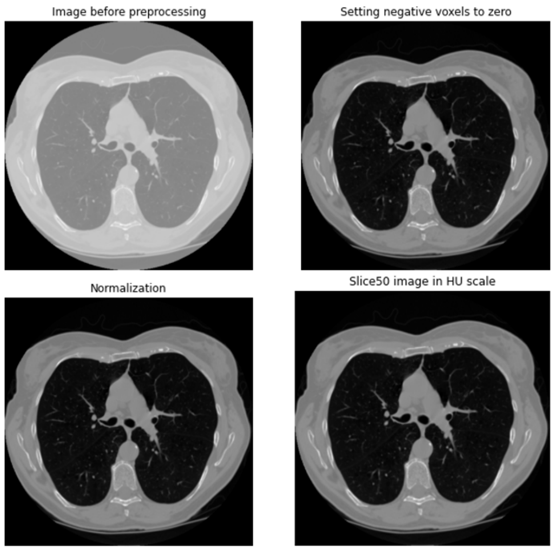

Fig. 3. Visualization of image preprocessing steps

6) Image Registration: Once the images were preprocessed, the registration was performed using Elastix [1]. Taking into account the way the challenge was proposed (the exhale landmarks would be hidden and used for final evaluation), the exhale images were used as fixed image and the inhale ones as moving images. For the registration algorithm a variety of different parameter maps were used, and a total of 15 experiments were done. Also, the experiments were done on the images before and after preprocessing, in order to evaluate the benefit of doing it. The experiments were divided in two important blocks: the first set used default transformation parameters (rigid, affine and spline). These were:

- **Experiment 1:** Rigid registration of images without preprocessing
- **Experiment 2:** Affine registration of images without preprocessing
- **Experiment 3:** Non-rigid registration of images without preprocessing
- **Experiment 4:** Translation-Affine-Bspline registration of images without preprocessing.
- **Experiment 5:** Rigid registration of images without preprocessing
- **Experiment 6:** Affine registration of images without preprocessing
- **Experiment 7:** Non-rigid registration of images without preprocessing
- **Experiment 8:** Translation-Affine-Bspline registration of images without preprocessing.

The second set of experiments was run using customized transformation parameters found in the Elastix Parameter Zoo file. These are parameters that have been tuned to work for specific applications. After a review of all the different possible parameters, the following ones were selected based on how related they were to the application of this project. The parameters selected were:

- **Parameter 15**: This parameter composes an intra-patient registration using B-spline transformation and several similarity metrics, such as normalized crosscorrelation. These parameters were used for the purpose of progression estimation of emphysema. This registration is described in detail in [2]
- **Parameter 35**: This parameter composes intra-subject and intersubject mono-modal and multi-modal registration; rigid, affine and B-spline transformations; mean square difference, normalized correlation, and mutual information as similarity metrics. These parameters have different versions as they were tuned for two applications: brain and chest images registration. This registration is described in detail in [3]
- **Parameter 54**: This parameter composes intra-subject registration of respiratory motion using B-spline transformation. The data in which it was applied were 3D thoracic CT (inhale/exhale phases from 4DCT). This registration is described in detail in [4]

Once having selected the parameters, the second block of experiments was defined:

- **Experiment 9:** Registration using parameter 54 and images with preprocessing
- **Experiment 10:** Registration using parameter 15 and images with preprocessing
- **Experiment 11:** Registration using parameter 15, images with preprocessing and segmentation masks of the lungs.
- **Experiment 12:** Registration using parameter 35 with mutual information metric, images with preprocessing and segmentation masks of the lungs.
- **Experiment 13:** Registraton using parameter 35 with normalized cross-correlation metric, images with preprocessing and segmentation masks of the lungs.
- **Experiment 14:** Registration using two concatenated versions of parameter 15 with normalized cross-correlation and LNC, as well as preprocessed images and segmentation masks of the lungs.
- **Experiment 15:** Registration using combination of parameters 15 and 35, preprocessed images and segmentation masks of the lungs.

As it can be noticed, all these set of experiments run required the tweaking of the parameter files, and for each particular experiment some changes had to be made within the file such as the resampling factor, number of resolutions of the pyramid, optimizer iterations, etc. Experiments 11 to 15 required the segmentation masks of the lungs. Therefore, a segmentation algorithm was used in order to get these masks.

B. Algorithm analysis

1) Segmentation algorithm Watershed: For this project, watershed segmentation algorithm was used. Watershed segmentation is a technique used to separate objects in an image by treating the image as a topographic surface, with peaks and valleys. The idea behind this method is to flood the image from different starting points, also known as “seed points” or markers, and wherever the floods meet, there must be a “catchment basin” or “watershed” that separates the different objects.

Applying the watershed method requires two steps: defining markers for identifying the Region of Interest (ROI) for the segmentation but also to use them as seed for the flooding of the basins (segmentation of the area of interest). In the second step the actual algorithm of the basins flooding happens, and that leads to the resulting image that corresponds to the segmentation. However, this image can still have some unwanted regions, and therefore the result can be refined applying image processing techniques. This was exactly the procedure applied in the project and will be explained in the following subsections.

2) Calculating the markers: Figure 4 presents a pseudo code on how the image markers were calculated. For this case, only the corresponding image is needed as input. Afterwards, the initial thresholding is applied as stated previously. Since the images were converted into hue units, this threshold was defined on the tipical value of lung tissue in HUE units (-400). Afterwards, for each of the slices of the thresholding image a clear bordering step is applied. In the third step, lung labels and region properties and calculated in order to keep the largest area regions (those corresponding to lungs). Finally, the inner and outer markers are built. The first one is just a thresholding of the lung labels and the second one is obtained after applying dilation on the inner marker. Finally, the watershed marker is defined as 2 times the inner marker plus the external marker.

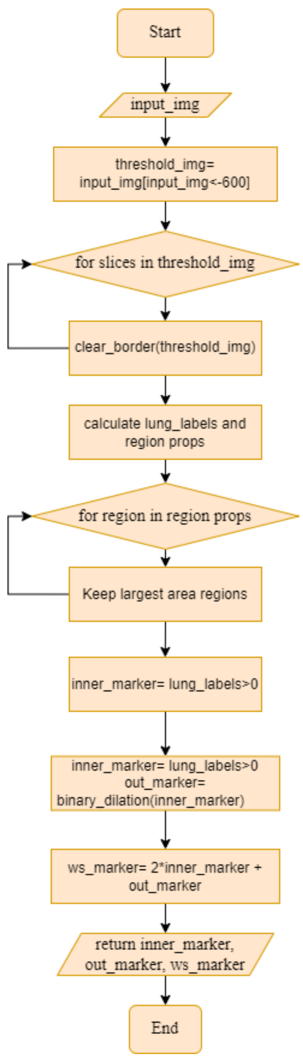

Fig. 4. Images markers calculation flow chart

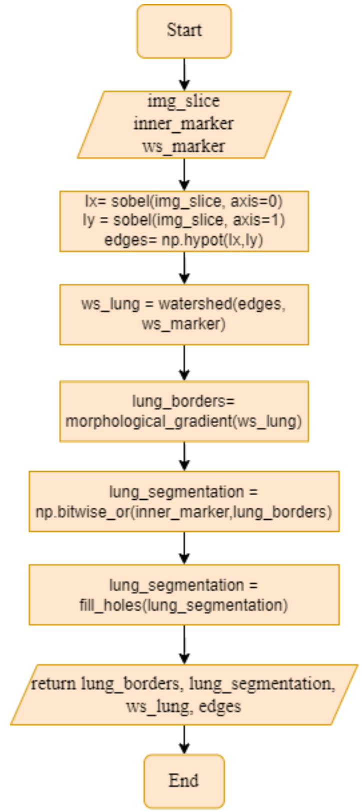

Fig. 5. Watershed lung segmentation flow chart

Once the markes are calculated, the watershed segmentation algorithm takes place. This is depicted in Figure 5. This function receives as input an image slice, as well as the inner and watershed marker. The first step consists on finding the edges in the image in both directions, and it was done using sobel operator. Afterwards, the watershed procedure is applied and the borders of the segmented lungs are obtained by using morphological gradient. In the last stage, the final lung segmentation mask is obtained by applying bitwise or operator and a post processing step of holes filling is applied. Figures 6 and 7 show the results obtained for the calculation of the markers and the final segmentation, respectively. It can be noted visually that the algorithm works very good, since the edges and borders of the lung area are also detected very accurately and small discontinuities in the watershed binary masks are fixed with the holes filling post-processing step.

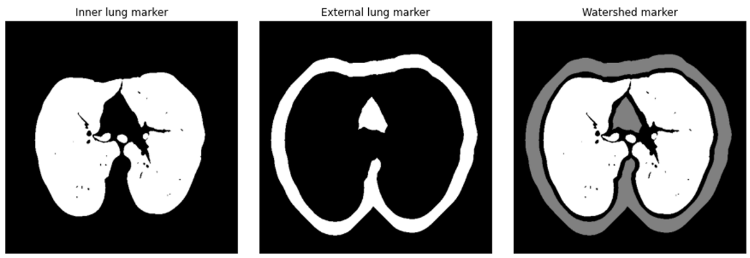

Fig. 6. Watershed markers calculation procedure

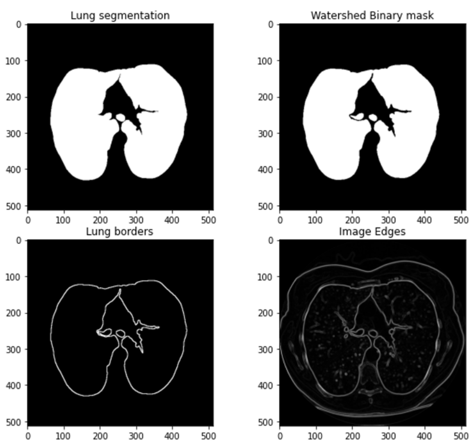

Fig. 7. Watershed segmentation results

TABLE I
MEAN TRE AMONG EXPERIMENTS

Experiment Number	Mean TRE
1	21,885
2	20,431
3	18,201
4	17,555
5	20,935
6	14,276
7	11,096
8	10,102
9	12,869
10	7,280
11	2,223
12	2,993
13	2,690
14	2,049
15	2,043

TABLE II
STANDARD DEVIATION OF TRE AMONG EXPERIMENTS

Experiment Number	Standard Deviation
1	6,568
2	8,620
3	8,665
4	8,534
5	6,136
6	6,694
7	5,880
8	5,451
9	5,680
10	2,407
11	0,909
12	1,791
13	1,472
14	0,911
15	0,776

III. RESULTS

1) Training results: In the training phase, the TRE was evaluated in all 4 volumes for each of the experiments that were done. Tables I and II present the mean and standard deviation of the TRE for all experiments, respectively. Figures 9 and 10 show the same information in a visual way. By analyzing these graphs, it can be noted that the best results (lowest mean and standard deviation of the TRE among all patients) was obtained in experiment 15, which consisted on doing the image registration by concatenating both parameters 15 and 35, and feeding into the registration algorithm both the preprocessing images and the corresponding segmentation from the watershed algorithm. Therefore, this was the method used for generating the final landmark predictions in the test set. Figure 10 shows the distribution of the TRE values among all experiments, and it can be infered from it that the preprocessing and the use of segmentation masks had an important role in improving the results, since all the distributions of experiments that include preprocessing are below 5 TRE. For experiments 11, 14 and 15 the TRE values distribution is very similar. Therefore, this parameters could have been used for generating the exhale landmark points during the challenge day.

2) Challenge results: During the challenge day, 3 new pair of images were revealed to be tested by the algorithm. The main problem faced during this part was generating the predictions of the image COPD0, since it had a very different distribution of voxels intensities when compared to the other 2 testing images and all the other images used for training. Therefore, since the segmentation method used in this work was voxel intensity dependent due to the fact that it started with an initial thresholding of the image in Hounsfield units, the segmentation result obtained was a black image. In order to solve this issue, histogram matching technique was used. Image COPD0 was matched to the second test image

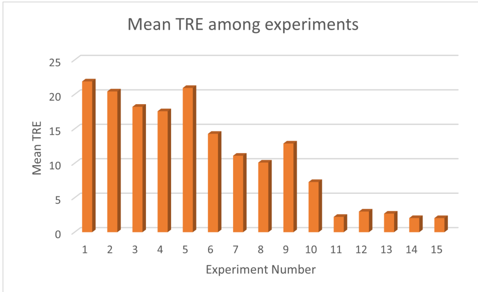

Fig. 8. Mean TRE among experiments

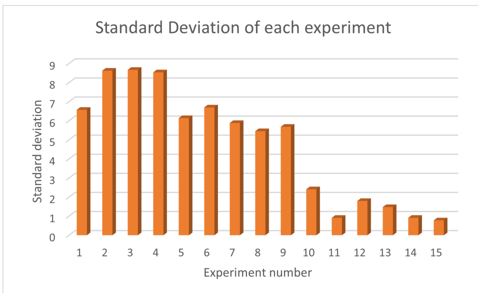

Fig. 9. TRE standard deviation among experiments

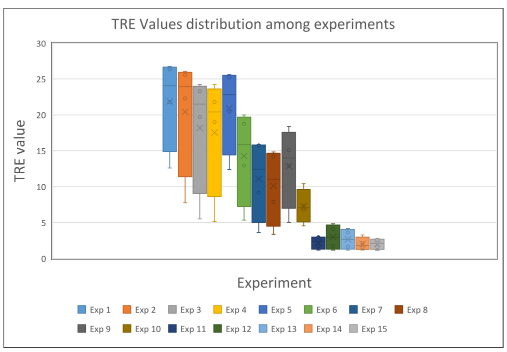

Fig. 10. Distribution of TRE values

and then preprocessed. After that, the segmentation algorithm was applied once again and the final segmentation mask was obtained. The results of the entire process can be seen in figure 12. It can be noticed that in this case the mask generated was not perfectly solid, but it was much better than what was obtained without histogram matching. Once the final masks the submitted, the results obtained for the TRE of the three test volumes copd0, copd5 and copd6 were 1.8014,3.9218 and 1.1823, respectively.

IV. Conclusions

In this study, chest CT volume registration was performed and the results obtained were satisfactory. The key for obtaining good results in this process was the preprocessing and segmentation of the lungs. Preprocessing was essential for removing any noise or artifacts present in the CT scans, which can negatively impact the registration process. Segmentation, on the other hand, was necessary for isolating the lungs

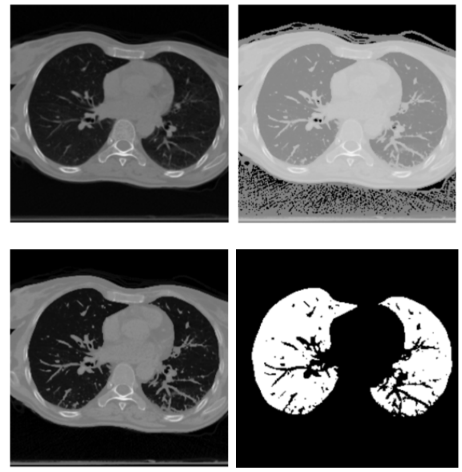

Fig. 11. From top to bottom, from left to right: COPD0 image, COPD0 image after histogram matching, COPD0 image after preprocessing, final segmentation mask of COPD0

which was the area where the landmarks to be transformed were located. Converting the images to Hounsfield Units also played an important role in the general pipeline since it made the segmentation process easier, as the thresholding for the first steps of the watershed method was obtained from the theoretical HU values for the lungs.

Even though the results were good, it can be concluded that the main limitation of the proposed method is the lung segmentation algorithm. It was proved both visually and quantitatively that it was very effective and precise in detecting the lung areas for all the training images. However, since the initial markers that are fed to the method are obtained by thresholding from the image, this makes it to be intensity-dependent and dramatic changes in the range of intensities makes it to fail, since the algorithm would not be able to detect the anatomic structure that is theoretically mapped with that intensity threshold in HU units. This could be solved by choosing a different strategy to select the marker rather than just intensity image thresholding, such as k-means clustering or local maxima detection. Deep learning segmentation methods could also be more robust to intensity range changes, so that could be another way to improve the performance of the overall method.

References

[1] M. K. V. M. P. J. Klein S, Staring M, "elastix: a toolbox for intensity-based medical image registration." 2010.

[2] M. Staring, M. Bakker, J. Stolk, D. Shamonin, J. Reiber, and B. Stoel, "Towards local progression estimation of pulmonary emphysema using ct," *Medical physics*, vol. 41, no. 2, p. 021905, 2014.

[3] Y. Qiao, B. van Lew, B. P. Lelieveldt, and M. Staring, "Fast automatic step size estimation for gradient descent optimization of image registration," *IEEE Transactions on Medical Imaging*, vol. 35, no. 2, pp. 391–403, 2015.

[4] C. L. Guy, E. Weiss, G. E. Christensen, N. Jan, and G. D. Hugo, "Caliper: A deformable image registration algorithm for large geometric changes during radiotherapy for locally advanced non-small cell lung cancer," *Medical physics*, vol. 45, no. 6, pp. 2498–2508, 2018.