CHAPTER 1

INTRODUCTION:
IMAGE REGISTRATION &
DEFORMABLE IMAGE REGISTRATION

Highlights of the Chapter

- *Brief overview of the deformable registration for abdominal images*
- *Problems with deformable registration of abdominal images*
- *Objectives, contribution and organization of the thesis*

1.1 Brief Overview Of Image Registration

The process of establishing a coordinate transformation for spatially aligning two or more images is termed as Image Registration. The prime research areas in which it is being utilized frequently are computer vision, remote sensing, astrophotography, and medical imaging. While data can be collected from different sources in multimodal fashion, in order to integrate the data obtained from different sources or to compare them, image registration is a necessary step. The images may have been captured by different imaging equipment or sensors at different times and angles or with the same equipment, from the same scenario with geometrical misalignments [1]. The pixels/voxels in the registered images are supposed to have the same meaning after image registration, so that the comparison of the pixel/voxel value in one image with the value of the corresponding pixel/voxel (with the same coordinates) in the other image makes sense [2].

Moreover, image registration is not only restricted to images only, equivalently it can be applied to surfaces, contours, or point sets extracted from the images.

To compute the best geometric transformation for bringing the images into alignment is the prime issue for the image registration. The basic idea is to determine a mapping from each pixel/voxel position in one image (called source or floating or moving image) to a corresponding position in the other image (called target or reference of fixed image). For computing the transformation and bringing the images into alignment, there are several important aspects to consider, such as the choice of the interpolation method. As per description presented in [3], an image registration method can be subdivided into three major components.

First, to determine a useful transformation between the two images, it is necessary to regulate the set of possible geometric transformations that improves irrelevant differences while preserving the important ones. Rigid and affine transformations are the simplest class of the transformations with the fewest number of parameters (from 6 to 12). Precisely, a rigid transformation is composed of translation and rotation motion. The sizes or shapes of the objects present in the image are not altered and are therefore utilized for intra-subject registrations, intermodality registration (registering two images acquired at different times in a longitudinal study). In addition to translation and rotation, affine transformation, allows for scaling and shear motion too. Thus, it can be used for the inter-subject registration, that is, registering the images of two or more subjects into the same reference space, and serve as initializations for more flexible nonlinear registration techniques, which allow for greater freedom in geometric variation between the images.

The second major component is to find the best transformation for an image registration method. The solution is based on the criterion on which the two images are being registered. This criterion can be found by utilizing geometric (anatomical) properties of the images or image intensities. Traditionally, there are distinctive differences between intra- and intermodality registration. The prime reason for the differences is that, for the case of intra-modality registration, the two images which are going to be registered, are acquired using the same modality, so the two images will look much more alike than in the intermodality case, where the images have been acquired using different modalities. Hence it is often recommended to use different criteria for intra and intermodality registrations.

The numerical algorithm which is utilized to finally perform the registration is considered as the third major component of an image registration method. This is the major segment and has been provided an important consideration because the registration criterion is expressed as a cost function that has to be optimized using a numerical algorithm. So, the image aligning process can be facilitated using carefully chosen optimization techniques and estimators for used auxiliary measures. The final computational time is influenced by the quality of used interpolators too. However, the time complexity increases when the accuracy and higher robustness are required because it usually leads to solutions utilizing the iterations.

1.2. Outline of Medical Image Registration

Medical images especially radiological images are extensively being used by the practitioners within healthcare for diagnosis, planning treatment, guiding treatment and monitoring disease progression. Within clinical research, diagnosis and treatment, these images are utilized to investigate disease processes and consecutively understand normal and abnormal development, as well as ageing. For most of these scientific investigation cases and studies, multiple images are acquired from subjects at different times, and often with different imaging modalities. Common imaging modalities used are X-ray radiography, magnetic resonance imaging (MRI), ultrasound (US), endoscopy, and nuclear medicine functional imaging techniques such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT). Besides being desirable, it is often essential to compare images obtained from patient cohorts rather than just single subjects imaged multiple times for research studies. Moreover, the amount of data produced by each successive generation of imaging system is greater than the previous generation [4]. This notion clearly clarifies that, there are, potential benefits in using image registration in the field of medical images. Thus, medical image registration has been proven to be an important, useful and beneficial tool for the healthcare community by gaining the ability to align the information in the different images (monomodal, multimodal, intra-patient, inter-patient), and providing a common space for visualizing, inspecting and investigating the combined images.

The human abdomen is an essential, yet complex body space. The abdomen contains organs involved with blood reservation, endocrine function, detoxification, urination and digestion while supported by spinal vertebrae, protected by the muscular abdominal wall and bounded by the diaphragm superiorly and pelvis inferiorly; including many important arteries and veins. Computed tomography (CT) and Ultrasound (US) scans are routinely obtained for the diagnosis and prognosis of abdomen-related disease [6]. These radiological images of the abdomen are extremely important for clinical analysis and medical engagement.

Compared to the relatively consistent brain anatomy, human abdomens present a huge number of variations that complicates the registrations [5]. On abdominal images, inter-subject variability (e.g., age, gender, stature, normal anatomical variants, and disease status) can be observed (also intra subject variability in many cases) in terms of the size, shape, and appearance of each organ. The registration gets complicated further by soft anatomy deformation while varying the inter-organ relationships, independent movement of multiple organs, even within individuals (e.g., pose, respiratory cycle, edema, digestive status). Local-affine registration methods are not able to handle multiple independent deformations [7]. This prompts the need for the deformable registration of abdominal images, with a special focus on the development of non-rigid correspondence precisely.

1.3. Notes on Deformable Image Registration

Deformable image registration (DIR) is a process which satisfies this requirement by locally registering image data sets into a reference image set. It identifies the spatial correspondence in order to minimize the differences between two or among multiple sets of images [8]. Deformable registration of images is an important and often crucial step in many areas of medical image processing and analysis, specifically in the field of image-guided therapy and image-guided surgery. The basic idea of the deformable registration is as follows.

Supposing a subject is asked to breathe out and hold breath to capture a slice of the abdominal CT scan at maximum expiration, labeled as image I_f , and similarly to breathe in and hold breath to capture another slice of the abdominal CT scan at maximum inspiration, labeled as image I_m . To acquire still images, in both of the cases during the CT scan, the subject is asked to breathe in/out to the maximum possible and then hold the breath. Although the slice of I_m has been selected such that it best corresponds to the anatomy displayed in image I_f, it is obvious that most of the image structures in the displayed slice of I_m do not match the structures in the displayed slice of image I_f. Now, one needs to find a coordinate transformation T in order to automatically match all image structures, that spatially align both images. As here the alignment requires a nonlinear transformation T, so it is termed as deformable image registration. Using a common generalized terminilogy, one of the images I_m , is denoted as the moving image, which is deformed to fit the other image, I_f, the fixed image. The computed transformation T is applied to the moving image, which is denoted by the function composition $(I_m \; o \; T)(x)$, where x denotes a position in the two/three-dimensional image. The deformed moving image is called the registered image, I_r, which can be defined as, $I_r := I_m\ (T(x))$. Extensive surveys on methods for image registration can be found in [9, 10, 11, 12, 13, 14].

Deformable image registration is a key step in the preprocessing of the images for integrating the information, detection of changes, and for the enhancement of the quality of combined information. As the number of imaging data sets has significantly increased after introducing a diverse range of advanced techniques into radiation oncology, there have been many studies proposing applications of imaging data set use. A lot of work is done; however, automatic image registration remains an open problem. Many authors focus themselves on the creation of fully automated algorithms, but the accuracy and the speed of the algorithms varies for different hyperparameters and for the input data also. These applications commonly require a method to align the data sets at a reference. Automated registration methods are not considered to be sufficiently robust to handle complex deformations and locally deviating intensities.

1.4. Problems with Deformable Registration of Abdominal Images

It is important to remember that the inappropriate registration can introduce changes, which can negatively affect the outcome of the image analysis. It can increase or decrease the size of an evaluated object of the scene (i.e., tumors, skin lesions) and thus influence the final diagnosis. The choice of a method and collection of all a priori information is a significant step in the whole process [15].

The deformable registration is an expanding research area, getting more complex due to the fast increase in the computational power of current computers. Performing the registration (monomodal and multimodal both) precisely while considering the intra-subject and inter-subject abdominal image variabilities including the inter-organ relationships is the biggest challenge for this area of exploration. But, the complexity of registration tasks due to the high variability of analyzed data as well as of modalities and types of acquisition devices somehow limits the expansion of computer-based registration to everyday use in medical diagnosis. This limitation can be defeated by the new development in the area of deep learning approaches, applicable to deformable registration for both matching and direct estimation of transformation parameters. This research is still in its early phase, but it has drawn attention to the lack of ground truth data, which is the key issue for learning. So, the overall problems can be summed up as,

- The uncertainty in the presence/observance of the structures in the abdominal images for multimodal registration (intra patient/ inter patient).
- The unpredictability in the appearance (size, shape) of the structures pertaining to the level of deformation for inter subject registration (monomodal/ multimodal).
- Slower implementation of the conventional registration approach due to complex computation while the learning based registration method is faster but lacks ground truth.

1.5. Thesis Objectives

The principal objective of the thesis is to perform deformable registration of abdominal images by generating an optimal deformation field precisely while utilizing the information present in the images that best aligns the structures of interest. In this view, this thesis aims to fulfill the following objectives.

- For conventional approach, utilizing the distinguishable intensity and gradient measures and structural features of the liver to generate prominent relationship between abdominal images.
- For learning based approach, utilizing the abdominal image features to train a model for generating an integrated deformation field.

1.6. Thesis Contribution

This thesis contributes to the necessary theory and implementations for conventional as well as learning based deformable registration of abdominal images as listed below.

- Employed a similarity criterion based on the intensity and the gradient measures of the liver and its surface, as it is present as the biggest prominent structure in the abdominal images.
- Employed an algorithm utilizing the cost function developed using the similarity criterion for deformable registration along with the registration refinement process.
- Employed an unsupervised learning based deformable registration process which is fast, as the transformation for individual image pair is replaced by a combined registration function.

1.7. Thesis Organization

The thesis is divided in 5 parts and comprises a total of 8 chapters. The remaining thesis has been organized in the following manner in order to provide detailed information regarding the ideas that have been mentioned beforehand.

- **Part-I** is titled as “Background”; contains Chapter 1 (current), Chapter 2 and Chapter 3.
  - **Chapter 2** presents the theoretical background and literature review regarding deformable registration with traditional approach. This chapter also discusses a brief overview of the methods used previously, and their utilization in medical image analysis.
  - **Chapter 3** presents the conceptual understandings and literature survey of deformable registrations with deep neural networks. Besides, outline of the techniques developed and extensively used for supervised and unsupervised learning models are also discussed.

- **Part-II** is titled as “Using Conventional Approach For Deformable Registration”; contains Chapter 4 and Chapter 5.
  - **Chapter 4** presents the implementation of a non rigid registration of multimodal images (Ultrasound and CT) of liver using gradient orientation information. This chapter includes the development of a similarity measure followed by a prominent cost function which is utilized to establish correspondence between US and CT images.
  - **Chapter 5** presents the implementation and performance comparison of two algorithms for non rigid registration (Computed Tomography-Ultrasound) of liver using b splines and free form deformation. This chapter showcases the algorithms with registration refinement; one using gradient information and another using multilevel B-splines. This chapter also includes the performance evaluation of three different optimization techniques used.

- **Part-III** is titled as “Using Learning-Based Approach For Deformable Registration”; contains Chapter 6.

- **Chapter 6** presents the implementation and performance evaluation of a learning based deformable registration method on abdominal CT images. This chapter includes the combination of Convolutional Neural Network based U_Net architecture along with Spatial transformer network which is utilized to narrow down the registration problem to a common registration function. This chapter also showcases the comparison with a conventional registration method.

- **Part-IV** is titled as "Closure"; contains Chapter 7 and Chapter 8.
  - **Chapter 7** summarizes the findings and contributions of the thesis and highlights major achievements.
  - **Chapter 8** discusses the scope of work in future directions based on the studies performed till now.

- **Part-V** is titled as "Accomplishments"; contains the publications related to the thesis work and the achievements during the doctoral studies.

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