BIOMECHANICALLY CONSTRAINED ULTRASOUND TO COMPUTED TOMOGRAPHY REGISTRATION OF THE LUMBAR SPINE

by

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Abstract

Spinal injections for back-pain management are frequently carried out in hospitals and radiological clinics. Currently, these procedures are performed under fluoroscopy or CT guidance in specialized interventional radiology facilities, and thus incur a major financial burden on the healthcare system. Additionally, the current practice exposes patients and surgeons to X-ray radiation. The use of US for image guided navigation of the spine would greatly reduce the exposure of both the patient and the physician to ionizing radiation and allow the procedure to be performed outside of a specialized facility. However, US as the sole guidance modality has its own challenges. In particular, due to the significant level of occlusion in spinal US images, it can be difficult to accurately identify the appropriate injection site.

Here, a groupwise US to CT registration algorithm for guiding percutaneous spinal interventions is presented. In our registration methodology, each vertebra in CT is treated as a sub-volume and transformed individually. A biomechanical model is used to constrain the displacement of the vertebrae relative to one another. The sub-volumes are then reconstructed into a single volume. In each iteration of registration, an US image is simulated from the reconstructed CT volume and an intensity-based similarity metric with the real US image is calculated. Validation studies are performed on datasets from a lamb cadaver, five patient-based phantoms designed to
preserve realistic curvatures of the spine and a sixth patient-based phantom where the curvature of the spine is changed between preoperative and intraoperative imaging.

For datasets where the spine curve between two imaging modalities was artificially perturbed, the proposed methodology was able to register initial misalignments of up to 20 mm with a success rate of 95%. For the phantom with a physical change in the curvature of the spine introduced between the US and CT datasets, the registration success rate was 98.5%. Finally, the registration success rate for the lamb cadaver with soft tissue information was 87%. The results demonstrate that our algorithm robustly registers US and CT datasets of the spine, regardless of a change in the patients pose between preoperative and intraoperative image acquisitions.
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Finally, thank you to my parents, Diane and Howard Gill, and my sister Krissy. Their love and support has given me the opportunity to be where I am today and is my inspiration to strive to improve and always do the best I can.
Glossary

2D  Two Dimensional.
3D  Three Dimensional.
BCLC$^2$ Biologically Constrained Linear Correlation of Linear Combination.
CC  Cross Correlation.
CMA-ES Covariance Matrix Adaptation - Evolutionary Strategy; an optimization method which uses an evolutionary algorithm to converge to a solution.
CR  Correlation Ratio.
CT  Computed Tomography.
ICP Iterative Closest Point.
Intraoperative During operation.
LC$^2$ Linear Correlation of Linear Combination.
MI  Mutual Information.
MR  Magnetic Resonance Imaging.
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<tr>
<td>NMI</td>
<td>Normalized Mutual Information.</td>
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<tr>
<td>Phantom</td>
<td>An anatomical model of a human or an animal organ.</td>
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<td>Preoperative</td>
<td>Prior to operation.</td>
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<td>TRE</td>
<td>Target Registration Error.</td>
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<td>US</td>
<td>Ultrasound.</td>
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Chapter 1

Introduction

1.1 Motivation

In 2002, almost two thirds of Canadian adults reported at least a mild level of back pain, leading to approximately $16.4 billion lost to the cost of treatment and lost productivity [18]. In the United States, this cost has been reported as $62 billion [1, 42]. A more recent survey suggests these costs may be a lower estimate and real costs are in the range of $84.1 to $624.8 billion [10]. Oral medication is the standard primary method of treatment, however Raj et al. [37] found that 21% of patients reported no improvement and nearly half the patients surveyed reported little improvement in back pain. More recently, improved results for oral medication have been reported [30], however for many patients, it is simply not an effective form of treatment. For such patients, the next step is spinal injections. These percutaneous interventions involve inserting a needle through the skin into the targeted tissue region, which in this case is the facet joint. A local anesthetic and steroid are then injected to reduce pain and inflammation. Spinal injections for back pain management are frequently carried
out in hospitals and radiological clinics. Currently, these procedures are performed under fluoroscopy or computed tomography (CT) guidance. Intraoperative CT and fluoroscopy can provide detailed images of the patient anatomy and needle location throughout the procedure. However, in order to use CT or fluoroscopic guidance, the procedure has to be performed in specialized interventional radiology facilities, thus imposing a major financial burden on the healthcare system. Another drawback with the current practice is patient and surgeon exposure to X-ray radiation. In CT-guided procedures, a minimum of three scans are required for identifying the needle target, rescanning the patient with a fiducial marker placed in the target plane and confirming an acceptable insertion. This number can increase for more difficult cases, such as scoliotic patients. A typical intervention can take between 10-45 minutes, depending on the experience of the physician and complications that arise. A significant portion of this time can be attributed to the medical staff needing to leave the room when an image is acquired. The work presented in this thesis is part of a larger effort to develop an ultrasound (US)-guided percutaneous spinal intervention system and eliminate the need for intraoperative X-ray-based imaging. Additionally, an US-guided intervention system would allow the procedure to be performed in a neurosurgeon’s office, eliminating the use of expensive specialized facilities and reducing the wait time and travel for patients.

Galiano et al. [14] performed a cadaver study using US as the guidance modality for facet joint injections and successfully inserted the needle tip into the targetting tissue region. While, US imaging is portable and inexpensive with no known side effects, the use of US as a sole guidance modality introduces its own challenges. US images are acquired from the propagation of sound waves through tissue. The
transmission and reflection of the signal is dependent on the interaction of the signal at inhomogeneous tissue interfaces. One of the major factors in this interaction is the density of the tissue. The transition from soft to bony tissue, a large change in density, often causes full reflection of the US signal. This occludes any anatomy below the bony and soft-tissue interface, making it impossible to visualize in the US image. Due to the significant reflection occurring at these interfaces, the surface of the bony structure appears bright in the image, but is often blurred and difficult to identify exactly. Additionally, not all bone surfaces are visible in US. If a US signal reflects at a bony and soft-tissue interface that is angled away from the US transducer, the signal will not return to the transducer and the surface will not appear in the US image. Finally, US images contain a significant noise in the soft-tissue portion of the image. For these reasons, US as a sole modality for guidance is not ideal, as a clear depiction of the location of the needle relative to the target anatomy is essential for a clinically viable guidance system.

It is common for patients who require a percutaneous spinal intervention to have a CT image acquired as a diagnostic step. This CT would contain information on the shape and structure of the spine, including anatomy not visible in US. Therefore, this work considers the fusion of intraoperative US with preoperative CT for guiding percutaneous spinal injections. Figure 1.1 shows an example of corresponding anatomy in slices from US and CT and an overlay displaying the CT bone edges in US space.

The use of a preoperative CT image introduces an additional challenge to the fusion of US and CT. In order to minimize motion artifacts, the preoperative CT is acquired with the patient in a supine position. Conversely, the intervention is performed with the patient prone. Thus, the intraoperative US image will be of the
CHAPTER 1. INTRODUCTION

Figure 1.1: Transverse slice from an US volume (left); the corresponding CT slice (center); and an overlay of the CT bone contours with the US slice (right) in a lamb cadaver.

patient in the prone position, introducing a change in the curvature of the spine across the US and CT datasets. The registration of the US and CT data will need to account for any change in the curvature of the spine caused by the change in pose.

In this thesis, a novel biomechanically constrained US to CT registration of the spine is presented [15]. The registration technique is validated on data from patient-based phantoms and a lamb cadaver. The phantoms containing replicas of actual human vertebrae have been designed to preserve a realistic representation of the curvature of the spine.

1.2 Proposed Registration Method

In this thesis, a novel US to CT registration of the lumbar spine is proposed, to be used for percutaneous spinal injections. The algorithm is designed for bone-based registration and is robust to significant occlusion in US image caused by bony and soft-tissue interfaces. In addition, a groupwise registration framework has been developed that incorporates the US to CT registration and allows for the registration
of datasets where the curvature of the spine differs between preoperative and intraoperative images.

This registration technique extends the work presented by Wein et al. [48, 47] on US simulation and registration to CT. While this work focused on US simulation from CT for registration of soft-tissue images and training purposes, this case required emphasizing the registration of bone. An example of the general workflow of the registration, including example intermediate images, is presented in Figure 1.2. The combination of intermediate images into the final US simulation incorporates intensity information from overlapping voxels in the real US image, however, the shape of the occluded region in the image is determined solely by the simulated US reflections in the CT.

The majority of CT image acquisitions are performed with the patient in the supine position. This is done for the comfort of the patient and to minimize motion artifacts in the CT scan. Conversely, percutaneous spine interventions are most often performed with the patient in the prone position. This change in pose introduces a change in the curvature of the spine across the datasets. To account for this, a framework is developed where each vertebra in CT is treated as an individual body in the registration. All vertebrae are registered simultaneously, each allowing for six degrees-of-freedom. After transformation, the vertebral subvolumes are reconstructed to a single volume, to which the US simulation is applied. As \textit{in vivo} vertebrae do not move independently, a biomechanical model is introduced, which is combined with the intensity-based similarity metric, to constrain the motion of the vertebrae relative to one another. This ensures that convergence will only occur with biologically realistic alignments. An example of this registration workflow, for a three vertebrae
Figure 1.2: The workflow of the proposed US to CT registration.

registration, is presented in Figure 1.3. This registration framework is validated for datasets where the alignment of the vertebrae has been perturbed in CT, as well as for a range of weights for the biomechanical model.
1.3 Thesis Objectives

The work presented in this thesis is part of a larger project to develop a guidance system for percutaneous spinal interventions. The objective of this work is to develop a robust and accurate US to CT registration that is able to account for changes in the patient orientation between preoperative and intraoperative imaging. This technique, used as part of an US image based guidance system, would allow percutaneous spine injections to be performed without fluoroscopic guidance. This would reduce
the cost of such interventions by removing the need to perform them in specialized fa-
cilities and would decrease the exposure of both the patient and physician to ionizing
radiation. This objective can be divided into three separate goals:

- The development of a method for accurate and robust registration of US and
  CT images of the spine. This will require a registration technique robust to
  significant occlusion in the US images due to bony and soft-tissue interfaces.

- The development a registration framework that is able to account for a change
  in the curvature of the spine between preoperative and intraoperative imaging.

- Comprehensive validation of the proposed registration technique to ensure it is
  robust to the challenges found in clinical data.

1.4 Contributions

In this thesis, I have:

- Developed a novel volume-to-volume intensity-based US to CT registration that
  required no segmentation of bone surfaces in either US or CT images. In addi-
tion, the algorithm makes no assumptions as to the direction of the US signal
  passing through the patient anatomy.

- Developed a framework for registering datasets where a change in the curvature
  of the spine has occurred between preoperative and intraoperative imaging. The
  algorithm:

1. Treats each vertebrae in CT as an individual body.
2. Registers all vertebrae simultaneously to the US volume to avoid propagating error through sequential registration.

3. Constrains the motion of the vertebrae to biologically realistic orientations through the use of a biomechanical model.

- Validated the proposed US to CT registration and the registration framework for a range of challenges found in a clinical setting. This was done using data collected from a lamb cadaver and from phantoms designed to preserve the shape and structure of real patient anatomy.

1.5 Thesis Outline

The thesis is divided into six chapters that present the registration technique, describe the experimental set up and discuss the registration results. This thesis is organized as follows:

Chapter 2 Background: provides a brief description of image guided surgery and presents the prior work in this area.

Chapter 3 Methods: details the US simulation from CT and the workflow of both the rigid and groupwise registration frameworks. The biomechanical model used to constrain the groupwise registration is presented as well as the method for blending the model with the intensity-based similarity metric.

Chapter 4 Experimental Setup: describes the set of tests used for validation of the proposed registration. Data acquisition is detailed along with an explanation of the construction of the patient-based phantoms.

Chapter 5 Results: presents the registration results for both the rigid and
CHAPTER 1. INTRODUCTION

groupwise registration approaches. In addition, the groupwise registration results are presented when the technique is constrained by a biomechanical model. Quantitative results are given for patient-based phantoms and lamb cadaver data. The implications of the results are discussed throughout the chapter.

Chapter 6 Conclusion and Future Work: presents the key conclusions of the thesis and possible areas of future work that can aid in preparing this work for clinical use.

Our group’s work for rigid and groupwise registration of US to CT images of the lumbar spine has been presented in the SPIE Medical Imaging Conference [16]. The biomechanically constrained groupwise registration has been presented in the Medical Image Computing and Computer Assisted Intervention (MICCAI’09) conference [15]. Additionally, a comprehensive validation of this work has been submitted to Medical Image Analysis (MEDIA) for review.
Chapter 2

Background

In this chapter I will examine the important aspects of the anatomy of the spine for this application and the prior work for multimodal registration of US images. This work will be divided into sections focusing on soft-tissue and bone based applications.

2.1 Anatomy of the Lumbar Vertebrae

Percutaneous spinal injections for pain management have specific target sites in the anatomy defined by the goal of the intervention. This work focuses on the facet joint injection procedure for lower back pain management. The facet joint is the location of overlap of the superior and inferior articular processes on adjacent vertebrae. The most common injection sites are at the L3-L4 and L4-L5 facet joints. An image of a lumbar vertebra are shown in Figure 2.1 with major anatomical landmarks labelled. For a facet joint injection to be successful, the steroid injection must be released close enough to the target so that it can reduce inflammation of the tissue around the facet joint.
CHAPTER 2. BACKGROUND

Figure 2.1: A model of a human lumbar vertebra with major anatomical landmarks labelled.

While the articular processes are the focus of the injection site, the spinous process will prove to be an important anatomical landmark in this work. Due to its proximity to the skin surface, the spinous process and the occlusion caused by US reflecting off the bone surface constitute a significant portion of the US and CT images acquired of the lumbar spine. A surface model of a lamb lumbar spine (L2 to L4) is shown in Figure 2.2.

2.2 Multimodal Registration of Soft-Tissue US Images

Registration techniques are generally divided into two types: Feature-based and Intensity-based. Feature-based registration techniques extract feature information
from both modalities, for example surface features or fiducial markers, and register the images by maximizing the alignment of these feature sets. Iterative closest point (ICP) [3] is the most commonly used method for aligning point-based feature datasets. Intensity based registration does not require the extraction of feature information, but instead uses the pixel intensity values to determine the accuracy of the image alignment. For multimodal registration, mutual information (MI) [45] is one of the most commonly used similarity metrics.

2.2.1 Feature-based

The fusion of US with another modality for image guidance has been a source of interest for many soft-tissue based applications. These applications often have the added challenge of registering tissue that has deformed between image acquisitions. Porter
et al. [36] presented a method for registering US and MR images of vasculature that treats major vessels in the volumes as fiducial markers. The vessels were extracted using a threshold filter and morphological operators. After a manual initialization, the correlation of the two sets of vessels was maximized within a user defined search region. Firle et al. [12] presented registration of preoperative US and CT images of the prostate. This was performed through manual segmentation of the urethral surface and subsequent registration using ICP. Lange et al. [27], presented a similar method where US and magnet resonance (MR) images of the liver were registered through an ICP optimization performed on the center lines of vessels extracted with a region growing algorithm. After a rigid alignment, deformable registration was performed to account for changes between the preoperative and intraoperative images. Narayanan et al. [33] proposed an interesting extension to the feature-based registration of soft-tissue. For improved guidance in prostate interventions, they proposed initializing and registering a statistical shape atlas of the prostate to the intraoperative US data. This approach required the segmentation of the prostate from US. The atlas was then deformed to maximize the overlap with the segmented data.

2.2.2 Intensity-based

Intensity-based registrations for soft-tissue are popular as they do not require the segmentation of surfaces of organs. This segmentation is time consuming and cumbersome, particularly in US images where tissue boundaries are blurred and poorly defined. Roche et al. [39] augmented their similarity metric Correlation Ratio (CR) to incorporate both intensity and gradient information. This new metric was tested
on US and MR images of the brain and proved to be sufficiently accurate and robust for the application. Leroy et al. [28] also used CR for the registration of US and CT images of the kidney, but implemented significant preprocessing to focus the algorithm to their application. In US, occluded regions were masked and speckle in the image was reduced using the sticks filter. In CT, a median blur was applied and the surface edges were emphasized. This intensity-based registration performed similarly to the authors’ ICP based “bronze standard.” Firle et al. [13] found accurate results were achievable when registering US and CT images of a prostate phantom using Mutual Information (MI). The registration was performed only on a user-defined bounding box within the volumes. The authors showed successful registration of their datasets, however the images used did not accurately represent clinical US data. Chan et al. [7] performed registration of models of the carotid artery in US and MR. Normalized Mutual Information (NMI) based rigid and deformable registration was performed, resulting in acceptable accuracy for the application. As multimodal US registration is often performed for intraoperative guidance, keeping registration runtimes low is essential. Huang et al. [21] explored this by examining the effect of subsampling the image volumes throughout the registration. This registration technique was performed for US to MR images of a beating heart. A threshold filter was applied to emphasize the most apparent anatomical features and MI was used as the similarity metric. The authors showed the potential for successful registration, but provided no absolute errors. In their work for registering US and fluoroscopic data of the prostate with implanted brachytherapy seeds, Karimaghaloo et al. [24, 25] tested a variety of preprocessing steps to augment the appearance of the seeds in US. These preprocessed images were then registered using a rigid MI-based optimization. Using
their preprocessing techniques, the authors were able to register their datasets with sub-millimeter accuracy.

A necessity for this application is the ability of the registration algorithm to robustly register images in the presence of significant occlusion in US and minimal soft tissue structure in CT. The above mentioned soft-tissue registration approaches lack this ability.

2.3 Multimodal Registration of Bone US Images

2.3.1 Feature Based

Much of the early work in US to CT registration of bony structures was centered on feature-based registration. Surfaces would be extracted from the US and CT and registered using ICP and its variations. One common issue in these feature-based registrations is the need to extract surface information from US. US images are noisy and only display portions of the bone surface; this makes automatic segmentation of the bone surface difficult to accomplish and manual segmentation cumbersome to reproduce accurately. An additional issue with the use of ICP is the need for a sufficiently accurate initial alignment.

Working with cadaveric and clinical data for the placement of iliosacral screws, Carrat et al. [6] and Tonetti et al. [43] manually extracted bone surfaces from US, which were subsequently registered to CT images of the sacrum using ICP. While no quantitative errors for the registration process was calculated, screw placement was found to improve under the use of the system. Herring et al. [20] collected US images of a plastic spine phantom submerged in water and automatically extracted surface
points using a combination of morphological operations and ray tracing. Using ICP to register this set of points to an extracted CT surface produced promising results; however, in this preliminary work they lacked a system to track the US probe and so the results were not quantitatively verified. Muratore et al. [32] collected tracked US and CT data of a plastic spine phantom submerged in water. Surfaces were extracted automatically, using a modified marching cubes algorithm for CT and a similar extraction approach to Herring et al. [20] for US. Using ICP, registration was performed for each vertebra sequentially, with errors below 2 mm. A plastic model submerged in a water bath produces cleaner US images than would be found clinically, making extraction of the bone surface easier. While the authors show a visual extraction of bone surface in a human US image, no quantitative results were presented. Amin et al. [44] performed an ICP registration on US and CT data collected from a pelvic phantom submerged in water and also from intraoperative patient data. Their approach differed from prior work in that from the US data 2D regions that are likely to be bone surface were extracted. During ICP registration, pixels in these regions were weighted according to their proximity to the initial estimate of the registration, the intensity of the pixels and the shadow region beyond the pixels. In phantom tests, translation error was below 1 mm and 1° along each axis. When comparing this registration technique to registration of physically acquired points on intraoperative patient data, an average difference of less than 2 mm and 1° along each axis was found. No absolute errors for patient data were reported though. This approach puts further emphasis on the initial alignment of the datasets due to the weighting of the ICP registration according to the initial pixel proximity of US to the CT surface. More recent work has focused on eliminating errors within the registration optimization procedure.
Barrat et al. [2] presented a method for concurrent registration and calibration of the US probe \textit{in vivo} based on segmented US and CT surfaces. The optimization scheme minimized the distance between surface points, but in place of ICP a general non-linear optimization scheme is used. Updating the calibration throughout the registration produced less error compared to previous registration techniques. However, the published implementation used manually segmented US surfaces. Additionally, this work was tested on data from the pelvis and femur, which produce significantly different US images from those of the spine. Similarly, Moghari and Abolmaesumi [31] improved upon the registration process with the implementation of an Unscented Kalman Filter replacing the ICP algorithm. This approach was only reported for manually extracted US points. While they improved on feature-based registrations of US to CT images, they are still reliant on extraction of bone surface points from US, which is difficult to reproduce and not robust for automatic implementation.

### 2.3.2 Intensity-based

Intensity-based registration eliminates the need for segmentation of bone surfaces and allows for the inclusion of information in the images that would otherwise be discarded in feature-based registrations. Brendel et al. [4, 5] and Winter et al. [51, 52] based their registration algorithm on the fact that the brightest points in US images are most often caused by the reflection of the signal on the bone surface. After extracting the bone surface from the CT volume, the surface was degraded to only what was expected to be visible in US. This degraded surface was then registered to the US volume, maximizing the overlapping grey scale value. While this approach eliminates the need to extract the bone surface from US, the degradation of the CT
surface requires prior knowledge of the orientation of the US probe when it scans the tissue. Shao et al. [41] presented a similar approach in registering transrectal US to MR images of the pubic arch, where the bone surface was extracted from MR and registered to the US volume. Three similarity measures were compared in this work: Maximizing overlapping intensity in US, maximizing the gradient in US and maximizing the image intensity while minimizing the intensities of the region below the surface. The inclusion of shadow information was found to significantly improve the registration results. This approach still required prior knowledge of the probe orientation. Standard intensity-based approaches assume a mapping between the two modalities. This assumption fails in US images as the intensity is not solely based on the tissue properties, particularly in images with significant occlusion due to bony and soft tissue interfaces. For this reason, preprocessing has been attempted to make intensity-based registration possible. Working with an abdominal phantom, von Berg et al. [46] applied preprocessing to the CT image to bring it closer to the US image. Bone edges were identified and any regions beyond were masked using a ray casting approach. This approach introduces a possible source of error: If the assumed beam direction is incorrect, it will decrease the similarity of the images. The authors tested both NMI and Cross Correlation (CC) as similarity metrics. Results were only reported for 2D to 3D and in-plane registration, and resulting errors were above what would be acceptable for most percutaneous spinal interventions. Huang et al. [21] presented a similar method, designed to register US and CT images of the rib cage as a form of initialization for US to MR registration of the heart. The US images were preprocessed to remove the background noise with a threshold filter. For CT preprocessing, a morphological operator and gradient based threshold filter were
applied to eliminate bone edges that would not be visible in US. As the registration technique was tested on a phantom submerged in water, the US images remained cleaner than clinical images would have been. Like previous work, this approach also requires prior knowledge of the US scan direction. Chen and Abolmaesumi [8] presented a MI-based US to CT registration of the radius bone. In their tests they were able to achieve sub-millimeter accuracy. Penney et al. [34] extended their previous US to MR registration [35] and presented a novel approach for registration of the pelvis and femur where both the US and CT images are converted to intermediate images, that are then registered together. In this work, each voxel in both US and CT was given a probability of being a bony edge. In CT, features for each voxel were extracted for the current intensity and the maximum intensity within a region around the voxel. In US, the features were identified as the current voxel intensity and the number of voxels that were not identified as shadow below the current voxel. The probability of a voxel with a given set of features was determined by the number of voxels identified to be a bone edge with the same set of features. While this approach produced accurate registrations, for clinically relevant probabilities, a large set of prior CT and US images would have to be manually segmented and would be dependent on the region being registered.

2.4 US Simulation Based Multimodal Registration

A recent approach for intensity-based registration focuses on US simulation from CT that is updated throughout the registration. Wein et al. [49] first presented this approach for a rigid US to CT registration of the head and neck. The algorithm extracted slices from the CT volume that corresponded to the scan plane of the US
probe. These CT slices were then processed to extract edge information and used to calculate a weighted MI similarity metric composed of several components, including skin clamping and edge alignment. The algorithm limited the registration region of interest to non-occluded areas within the CT slices. In their subsequent work, Wein et al. [47, 48] presented a method that simulates US reflection from the CT data based on US signal propagation. This was then combined with a CT volume with intensities mapped closer to US values. By updating this combination of images at each iteration of the registration, the algorithm was able to optimize the simulation as the registration proceeded. This work was presented for registration of the liver and was found to be more robust and accurate than directly registering the images with either MI or CC. This algorithm was extended by Shams et al. [40] to create a more realistic simulation for training physicians and technicians in the use of US imaging. This technique required preprocessing to create a scatter volume of the CT data using the Field II US simulator [22, 23], which remains time consuming and makes this approach less appropriate for intraoperative registrations. Reichl et al. [38] and Kutter et al. [26] presented an iterative US simulation and registration implemented in GPU, resulting in significantly decreased algorithm run time. Previously, our group [16] proposed an extension of the work from Wein et al. [47, 48], focusing on bone-based registration, and introduced a groupwise US to CT registration of the lumbar spine in a phantom of L3, L4 and L5. This algorithm allowed free motion of the vertebrae and registers all three simultaneously. This work is further extended by introducing a biomechanical model to constrain the motion of the vertebra, in order to maintain clinically realistic orientations [15].
Chapter 3

Methods

In this section the proposed US to CT registration technique is presented and the biomechanical model used to constrain the groupwise registration is detailed. The registration technique iteratively simulates an US image at each step of the registration. This is performed in three stages: An US signal is simulated passing through the tissue to produce a map of the reflections from the tissue interfaces, the intensities in the CT volume are mapped to corresponding values found in US and finally, these two intermediate images are weighted and combined to best match the current overlapping US voxels. This simulation is updated iteratively throughout the registration. The similarity metric, based on Correlation Ratio (CR), is calculated by comparing the US volume with the simulated US volume.

This registration technique extends the work presented by Wein et al. [48, 47] on US simulation and registration to CT. While this work focused on US simulation from CT for registration of soft-tissue images and training purposes, this case required emphasizing the registration of bone. This required extending areas of the US simulation from CT and in the metric calculation. This registration workflow
differs from most in that the preprocessing of the CT “moving image” is performed within the registration optimization loop. This means that the US simulation from CT is updated iteratively as the registration proceeds. This is essential, as changes in rotation of the spine with respect to the direction of the US signal can produce significantly different occlusion within the US image. Accordingly, by allowing the US simulation to update throughout the registration, there is no need for prior knowledge of the direction of the US signal through the patient anatomy.

The rigid registration optimizes a single set of six parameters (three rotations, three translation) for the entire volume. This is used to initially align the US and CT data. To account for changes in the curvature of the spine between the preoperative and intraoperative imaging, the groupwise registration treats each vertebra in CT as an independent rigid body and registers them simultaneously to the US volume. This results in an optimization of $n \times 6$ parameters, where $n$ is the number of vertebrae registered to the US. Finally, to improve the groupwise registration accuracy and restrict the registration to biologically realistic alignments, a biomechanical model is introduced to constrain the orientation of vertebrae relative to one another.

### 3.1 Rigid Registration and US Simulation

The workflow for the US simulation and registration is shown in Figure 3.1. The six degrees-of-freedom are represented by an Euler transform. Covariant Matrix Adaptation - Evolution Strategy (CMA-ES) [19] is used as the optimization strategy. CMA-ES was chosen since in our group’s previous work [16] we found it to be robust for US to CT simulation and registration when compared with Gradient Descent and Simplex optimization schemes.
There are three distinct steps in the simulation of US from CT: The Simulation of the US reflection from CT, the mapping of the CT values to those found in US, and calculation of the weights for these two images and a bias. The weights are chosen so that the simulation best represents the real US image.

As in the work of Wein et al. [48, 47], the simulated ultrasound reflections model the ultrasound beam passing through the tissue as a ray. The assumption is made that the CT intensities (in Hounsfield units) can be related to the acoustic impedance values used to calculate ultrasound transmission and reflection. The simulated beam passes through each column of the volume. The transmission and reflection of the beam is calculated at each voxel based on the following equations,

\[
\Delta r(x, y, d) = (d^T \nabla \mu(x, y)) \frac{|\nabla \mu(x, y)|}{(2\mu(x, y))},
\]

\[
\Delta t(x, y) = 1 - \left(\frac{|\nabla \mu(x, y)|}{(2\mu(x, y))}\right)^2,
\]

\[
r(x, y) = I(x, y - 1) \Delta r(x, y, d),
\]
\[ I(x, y) = \begin{cases} 
I(x, y - 1) \Delta t(x, y), & |\nabla \mu(x, y)| < \tau \\
0, & |\nabla \mu(x, y)| \geq \tau 
\end{cases} \, , \quad (3.4) \]

where \( d \) is the direction of the US beam, \( \mu \) is the intensity of the CT image, \( \Delta r \) is the reflection coefficient, \( r \) is the simulated reflection intensity, \( \Delta t \) is the transmission coefficient, \( \tau \) is the threshold for full reflection and \( I \) is the intensity of the simulated US beam. Any gradient value greater than a set threshold causes full reflection of the US beam intensity at that point, setting the incoming US beam intensity for all subsequent points on the scan line to zero. The value of the threshold was set to 250 h.u. We compared many values across the phantoms, lamb cadaver and patient datasets and found this value to provide an adequate capture of true bone edges, while minimizing the number of false bone edges produced. The value of \( \tau \) could be increased to approximately 315 h.u. or decreased to approximately 200 h.u. without a significant change in the edges captured. Any threshold values above or below this missed large sections of the bone to soft-tissue interface or included reflections in the soft-tissue, respectively. Voxels where full reflection occurs are flagged as a bone-soft tissue interface. At any point in the simulation, if the intensity of the simulated US beam reaches zero, due to gradual reduction of beam intensity or from full reflection, the remaining voxels along the scan line are flagged as occluded. A log-compression is applied to the simulated reflection image to amplify small reflections,

\[ r(x, y) = \frac{\log(1 + ar(x, y))}{\log(1 + a)}. \quad (3.5) \]

where \( a \) is a user defined value which was selected to give a clear difference between bone edge and soft-tissue reflections. In this case the value of \( a \) was set to 30, however
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this value may change for clinical cases.

Reflections from tissue interfaces only comprise a portion of the US image. To include further tissue information, the CT intensities are mapped to values closer to those corresponding to the tissues in the US data. This is done using an approximation of the curve presented in Wein et al. [48, 47],

\[ p(x, y) = 1.36\mu(x, y) - 1429. \]  \hspace{1cm} (3.6)

The final step of the US simulation is the weighting of the simulated US reflection, the mapped CT and a bias term. A set of weights is calculated based on the set of overlapping US voxels. Similar to the work of Wein et al. [48, 47], a least-squares optimization is used to calculate the weights, such that the values in the simulation best match the corresponding intensities in the real US volume. Any voxels that are occluded in the simulation are not included as part of the weight calculation. Occluded voxels are instead treated as a separate region within the image. The intensity value of occluded voxels in US is dependant on many factors, and can vary between datasets. However, the occluded voxels have approximately the same intensity in any given scan. As such, the value of all occluded voxels is set in the simulation to be the mean of the intensity values in the US that overlap the occluded region. An example of the occluded voxels treated as a separate region is shown in Figure 3.2. The final simulation is calculated as,

\[ f(x, y) = \begin{cases} 
\alpha p(x, y) + \beta r(x, y) + \gamma, & I(x, y) > 0 \\
\psi, & I(x, y) = 0 
\end{cases} \]  \hspace{1cm} (3.7)
where \( f \) is the simulated US image, \( \psi \) represents the mean US intensity from voxels overlapping the occluded voxels in the simulation and \( \alpha, \beta, \gamma \) are the weights of the mapped CT, US reflections and a bias, respectively. The values of \( \alpha, \beta, \gamma \) and \( \psi \) are not static and will vary at each iteration of the optimization. Additionally, any voxels that are flagged as a bone-soft tissue interface are set to the maximum value found in the US dataset. This is done to force the interface to remain bright in the simulation, regardless of what voxels it overlaps in the US. While the US image is used to determine the weights of the intermediate images and the intensity value of the occluded region, the shapes of the soft-tissue and occluded regions in the simulated US are based solely on the CT image. The US voxels used to calculate the weights and the occluded intensity value for these regions varies based on the current alignment.
of the datasets. As the alignment of the CT and US improves, the accuracy of the simulated US will increase. An example of the simulated US is shown in Figure 3.3.

![Image of transverse slices from registered (Top) and misaligned (Bottom) datasets, including CT (Left), simulated US Reflections (Center Left), Simulated US (Center Right) and US (Right).](image)

Figure 3.3: Transverse slices from registered (Top) and misaligned (Bottom) datasets, including CT (Left), simulated US Reflections (Center Left), Simulated US (Center Right) and US (Right).

Similarity between the actual US image and the simulated US image is calculated using the Linear Correlation of Linear Combination ($LC^2$) metric presented by Wein et al. [48, 47],

$$LC^2 = \frac{\sum (U(x, y) - f(x, y))^2}{N \times Var(U)},$$

(3.8)

where $N$ is the number of overlapping voxels between the US and CT images, and $U$ is the actual ultrasound image intensity. All voxels, including occluded voxels, are used in the calculation of the similarity metric.
3.2 Groupwise Registration

In a clinical setting, the preoperative CT of the patient will be acquired in the supine position, while the intervention will be performed with the patient in the prone position. This introduces a change in the curvature in the spine which must be accounted for in the registration process. This issue is alleviated through a groupwise registration that treats each vertebra as a distinct rigid body that moves independently and registers all vertebrae simultaneously. The workflow of the groupwise registration is presented in Figure 3.4.

A rigid registration is performed over the entire US and CT volumes to determine the initial alignment for the groupwise registration. The rigid registration provides a global alignment for the US and CT volumes, while the groupwise allows for the registration of any discrepancies in the orientation of the vertebrae between the volumes. For the groupwise algorithm, the CT volume is initially cut into sub-volumes, each
containing a single vertebra. Voxels in the sub-volumes corresponding to bone from an adjacent vertebra were masked. The registration treats each vertebra independently, allowing for six degrees-of-freedom. All vertebrae are registered simultaneously, resulting in an optimization with $n \times 6$ parameters, where $n$ is the number of vertebrae being registered. After the transformations are applied, the sub-volumes are reconstructed into a single volume. For any overlapping voxels the maximum intensity is selected for the reconstructed volume, thus preserving bone structure. Any gaps in the final volume are filled with a default value approximating the intensity of soft tissue in the CT. This reconstruction process is demonstrated in Figure 3.5. The US simulation is applied to this reconstructed volume and the similarity metric is calculated between the resulting simulated US volume and the actual US data.

Figure 3.5: An example of the subvolume cutting, transformation and reconstruction of the CT volume for groupwise registration. Displayed are sagittal slices from the original CT volume (Left), the CT subvolumes after independant transforms have been applied (Middle) and the reconstructed CT volume (Right) after the subvolumes have been stitched together and gaps have been filled with a simulated soft tissue value.
3.3 Biomechanically Constrained Registration

Allowing free motion of vertebrae during registration is not ideal as it does not distinguish between anatomically realistic orientations of vertebrae and orientations where the vertebrae are colliding, unreasonably oriented or far apart. As in vivo vertebrae do not move independently, a biomechanical model is introduced. This model is combined with the intensity-based similarity metric, to constrain the motion of the vertebrae relative to one another. This ensures that convergence will only occur with biologically realistic alignments. The final workflow of the groupwise registration is modified to include the biomechanical model and is shown in Figure 3.6.

Figure 3.6: Workflow of the biomechanically constrained groupwise US to CT simulation and registration. The transforms in this workflow are initialized by a rigid registration.

The biomechanical model used is based on the work by Desroches et al. [11], which models the relation between the displacement of the intervertebral structures,
the reaction forces and moments:

\[
\begin{bmatrix}
F_x \\
F_y \\
F_z \\
M_x \\
M_y \\
M_z
\end{bmatrix} =
\begin{bmatrix}
100 & 0 & 50 & 0 & -1640 & 0 \\
0 & 110 & 0 & 150 & 0 & 580 \\
50 & 0 & 780 & 0 & -760 & 0 \\
0 & 150 & 0 & 1.48E5 & 0 & -8040 \\
-1640 & 0 & -760 & 0 & 1.52E5 & 0 \\
0 & 580 & 0 & -8040 & 0 & 1.53E5
\end{bmatrix}
\begin{bmatrix}
T_x \\
T_y \\
T_z \\
R_x \\
R_y \\
R_z
\end{bmatrix},
\]

(3.9)

Where \( T \) and \( R \) are the translation and rotation of the vertebrae along a given axis. The \( 6 \times 6 \) stiffness matrix representing the intervertebral structures is defined as \( K \). The vector of translations and rotations is defined as \( x \). For this case, \( x \) is calculated as the relative transform between two consecutive vertebrae, represented as translation in millimeters along each axis and rotation in radians about each axis. Each vertebra is expected to have no change in rotational orientation and no translation along the transverse and sagittal axes. The expected translation along the coronal axis is defined as the distance between the centers of consecutive vertebrae in the patient’s US data. This can be difficult to measure exactly; however it is meant only as an approximation of the vertebral resting position.

The energy of the system is calculated using the general spring equation,

\[
U = \frac{1}{2}(x^TKx).
\]

(3.10)

The energy is calculated across all vertebrae and normalized based on the energy of a maximum misalignment (10 mm translation along each axis and 10° rotation about each axis),

\[
E = \frac{\sum_{i \in V} U_{Li,Li+1}}{|V| \times U_{max}}
\]

(3.11)
where $E$ is the normalized energy of the system, $V$ is the set of vertebrae to be registered, $U_{Li,Li+1}$ represent the energy of the model calculated for adjacent vertebrae, and $U_{\text{max}}$ is the energy of the maximum misalignment.

This normalized energy is then combined with the $LC^2$ metric to give the Biomechanically Constrained Linear Correlation of Linear Combination ($BCLC^2$),

$$BCLC^2 = LC^2 - \sigma E,$$

where $\sigma$ is a user defined weight used to blend the biomechanical model measure with the $LC^2$ intensity-based measure.
Chapter 4

Data Collection and Experimental Design

Validation of the registration technique has been performed on three different types of data. First, patient-based phantoms were constructed and used for validation of the rigid and groupwise registration techniques. These phantoms, containing spine models based on segmented patient CT data, are designed to preserve a realistic curvature of the spine. Second, a patient-based phantom, where a change in the curvature of the spine was introduced between US and CT image acquisitions, was used to further validate the groupwise registration technique with more clinically realistic data. Finally, US and CT datasets were collected from a lamb cadaver in order to validate the registration techniques on realistic tissue. This chapter will discuss the construction of the patient-based phantoms and justify the use of each type of dataset for validation. Additionally, the registration tests performed on each dataset to validate the accuracy of the registration technique will be described.
CHAPTER 4. DATA COLLECTION AND EXPERIMENTAL DESIGN

4.1 Data Collection

A freehand US sweep was acquired for each dataset using an L14-5/38 linear-array transducer and a Sonix RP ultrasound machine (Ultrasonix, Richmond, BC, Canada) operating at 6.6 MHz with a depth of 5.5 cm. The speed of sound was assumed to be 1540 m/s, the speed of sound in soft-tissue. The gel used in the phantoms was designed to approximate this speed. The lamb used for data collection had undergone rigamortis and cooling for storage, therefore this assumption is only an estimate. Differences between the assumed and actual speed of sound may have introduced artifacts or scaling error to the image. An approximate slice spacing of 0.5 mm was maintained through the scans. This, however, varies locally within each dataset, depending on the speed at which the sweep was acquired for a given location of the phantom or cadaver. The probe was tracked using an Optotrack Certus System (Northern Digital Inc., Waterloo, ON, Canada). This involved the affixing an active DRB to US probe, which was tracked, along with a reference DRB, by the Certus camera. External fiducial markers were identified in physical space using a tracked stylus. The US transducer, stylus and an active DRB are shown in Figure 4.1. The US transducer was calibrated to the tracking system using an N-wire US phantom [9]. The set of US image was then reconstructed to a 3D volume[17]. The reconstructed volumes had a voxel spacing of 0.5 mm × 0.5 mm × 0.5 mm.

A high-resolution CT volume was acquired from each test subject using a GE Light-Speed series (GE Healthcare, Waukesha, USA). The CT was collected as a series of axial slices, which were reconstructed into a volume. The CT volumes for the phantoms were captured at 0.46 mm × 0.46 mm × 0.625 mm, while the resolution of the CT scan for the lamb cadaver was slightly lower at 0.70 mm × 0.70 mm ×
0.625 mm. The difference in resolution is due to the larger field of view required to capture the increased width of the lamb cadaver. Locations of the external fiducial markers were identified manually in the volumetric data. In clinical cases, the CT scan will be restricted to the targeted anatomical region resulting in resolutions closer to that of the phantoms scans.

4.2 Patient-Based Phantoms

4.2.1 Construction

The patient-based phantoms are comprised of two main parts: the spine model based on segmented patient CT data, and the surrounding gel designed to mimic the speckle found in soft-tissue. Vertebrae L1 to L5 were manually segmented from five patient CT datasets, using ITK-SNAP. The segmented data was converted to a surface model
and the spine was printed using a Cimetrix 3D shape printer (Cimetrix Solutions, Oshawa, ON, Canada). This approach preserves the natural curvature of the spine between the patient CT and the printed spine model. These are defined as natural phantoms. The model was placed in a box and was filled with soft-tissue mimicking gel. This material is based on an agar-gelatine recipe [29] and made from a recipe of 1.17% agar (A9799, Sigma-Aldrich, St. Louis, MO, USA), 3.60% gelatin (G9382, Sigma-Aldrich), 1% Germall® Plus (International Specialty products, Wayne, New Jersey, USA) as a preservative, 3% cellulose (S5504, Sigma-Aldrich) for speckle, and 3.2% glycerol (G6279, Sigma-Aldrich) to adjust the speed of sound to approximately 1540 m/s. Note that the recipe percentages are by mass, not volume. This gel is designed to simulate the appearance of soft tissue in US, including speckle and refraction.

4.2.2 Rigid Registration

The registration was performed on vertebrae L2-L4 and the US volume was cropped to correspond, as seen in Figure 4.2. The middle vertebrae were chosen for the registration as they contained overlap from other vertebrae at the facet joints. This produces more clinically realistic images in US and CT than including L1 and L5, as in the phantoms they have no overlap on the processes. One hundred registrations of the CT and US data were performed on the data with initial misalignment ranging from 0 mm to 20 mm Target Registration Error (TRE). After aligning the CT and US volumes using the fiducial-based gold standard transform, the CT volume was misaligned by a random transformation chosen from a uniform distribution of ±10 mm translation along each axis and ±10° rotation about each axis. The misaligned CT
volumes were then registered back to the US volume using the registration algorithm. Accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE was calculated from the Root Mean Squared (RMS) error of the corners of the bounding box for each vertebra after registration. A registration was considered failed if any of the three vertebrae have a final TRE greater than 3 mm. The accuracy required for a percutaneous spinal injection will vary based on the specific procedure being performed. In the case of the facet joint injection, 3mm is considered to be an acceptable error and will be used as the measure of success for all our registration tests.

Figure 4.2: Surface model of L1 to L5 (top left); US slice of L2 to L4 (top right). Overlaid US with surface model (bottom left) and corresponding extracted slice (bottom right).
4.2.3 Misaligned Vertebrae Rigid Registration

This set of tests is designed to determine the accuracy of a rigid registration when a change in curvature of the spine has occurred between US and CT image acquisitions. For this data, the change in curvature was introduced artificially by perturbing the orientation of each vertebra individually. Similar to the rigid registration tests, the registration was performed on vertebrae L2-L4. After aligning the CT and US volumes to the fiducial-based gold standard transform, the CT volume was initially misaligned to a range of 0 mm to 20 mm TRE using the same set of transforms as the rigid registration tests. Each vertebra was then further misaligned by individually applying a random transform using a uniform distribution of $\pm 5$ mm translation along each axis and $\pm 5^\circ$ rotation about each axis. While this misalignment is larger than what would be seen in a realistic situation, this distribution was chosen to ensure that the registration capture range will be greater than that of a clinical setting. One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE and success was determined as in Section 4.2.2.

4.2.4 Groupwise Registration

Similar to the previous tests, the registration was performed on vertebrae L2-L4. Registration is performed simultaneously for all three vertebrae, producing an 18 parameter optimization loop ($3 \times 6$ rigid parameters). After aligning the CT and US volumes to the fiducial-based gold standard transform, the CT volume was initially misaligned to a range of 0 mm to 20 mm TRE using the same set of transforms as the rigid registration tests. Each vertebra was then further misaligned by individually
applying a random transform using a uniform distribution of $\pm 5$ mm translation along each axis and $\pm 5^\circ$ rotation about each axis. The registrations were repeated for $\sigma$ values of 0, 0.5, 1 and 2, representing the weight of the biomechanical model relative to the $LC^2$ similarity metric (Equation 3.12). A $\sigma$ value of 0 corresponds to using no biomechanical model at all, while values of 0.5, 1 and 2 correspond to half, equal and double weighting of the biomechanical model relative to the intensity-based similarity metric. Values for $\sigma$ above 2 were considered to put too much emphasis on the biomechanical model, constraining the vertebrae alignments too tightly to the model’s expected alignment. One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE and success was determined as in Section 4.2.2.

4.3 Curved Patient-Based Phantom

4.3.1 Construction

In addition to testing the registration algorithm on artificially misaligned data, the accuracy of the technique on datasets where the physical curvature of the spine differed between US and CT data acquisition was tested. To accomplish this, an additional patient-based phantom was constructed using the same method previously described in Section 4.2.1, to produce a natural phantom. After US and CT datasets were collected from the phantom, the spine model was removed and modified to introduce an increased curvature along the transverse axis. An approximate increase of $4^\circ$ was introduced between each vertebrae. The modified model was then remade into a phantom, defined as a curved phantom. The difference between the two datasets are
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shown in Figure 4.3.

Figure 4.3: Sagittal slices of the natural curved patient-based spine phantom (Right) and of the increased curved patient-based phantom (Left).

4.3.2 Rigid Registration

The rigid registration was tested by registering L2 to L4 from the natural phantom CT to curved phantom US and vice versa. This was done to more accurately mimic the difference that will be observed in clinical data, where the curve in the anatomy will not match across US and CT. One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. After initially aligning the datasets using a rigid registration, the CT volume was initially misaligned to a range of 0 mm to 20 mm. To measure the accuracy of this registration, four fiducial markers that are visible in CT were attached to the vertebral bodies. The fiducial markers were placed so that they would not be directly visible in the US data. The gold standard was calculated by registering each vertebra based on the fiducials visible in CT. For example, the gold standard alignment for L2 in the natural CT and curved US datasets is calculated by
aligning the fiducials on the L2 vertebra in the natural CT and the curved CT. TRE and success was determined as in Section 4.2.2.

4.3.3 Groupwise Registration

The groupwise registration was tested by registering L2 to L4 from the natural phantom CT to curved phantom US and vice versa. Registration is performed simultaneously for all three vertebrae, producing an 18 parameter optimization loop (3×6 rigid parameters). One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. After aligning the CT and US volumes to the fiducial-based gold standard transform, the CT volume was initially misaligned to a range of 0 mm to 20 mm TRE using the same set of transforms as the rigid registration tests. Unlike the previous groupwise tests, no additional displacement of the vertebrae was introduced. The registrations were repeated for σ values of 0, 0.5, 1 and 2, representing the weight of the biomechanical model relative to the $LC^2$ similarity metric (Equation 12). One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. The gold standard was defined similar to the rigid registration tests. TRE and success was determined as in Section 4.2.2.

4.4 Lamb Cadaver

A lamb cadaver was used to test the accuracy of the registration technique for images containing realistic soft-tissue structures. Lamb was chosen as it has been found to
have a sufficiently realistic approximation of the human spine, particularly in the thoracic and lumbar area [50]. External fiducial markers were placed on the outside of the box as well as on the skin surface of the cadaver. The entire lumbar spine, L1 to L6, was imaged in both US and CT.

4.4.1 Rigid Registration

The rigid registration was validated using a similar method to the patient-based phantom tests. The registration was performed on vertebrae L3, L4 and L5. L6 was omitted from the cadaver as there was significant overlap with the sacrum which produced different images than those found in human data. One hundred registrations of the CT and US data were performed on the data with initial TRE ranging from 0 mm to 20 mm. The CT and US volumes were aligned using the fiducial based gold standard transform and the CT volume was then misaligned by a random transformation chosen from a uniform distribution of ±10 mm translation along each axis and ±10° rotation about each axis.

The misaligned CT volumes were then registered back to the US volume using the US simulation-based registration algorithm. One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE and success was determined as in Section 4.2.2.

4.4.2 Misaligned Vertebrae Rigid Registration

Similar to the patient-based phantom tests, an additional 100 rigid registrations were performed, where prior to registration the vertebrae were perturbed in CT to produce a different alignment than that found in US. Each vertebra was misaligned by
individually applying a random transform using a uniform distribution of $\pm 5$ mm translation along each axis and $\pm 5^\circ$ rotation about each axis. The volumes were then reconstructed, filling in any gaps with a simulated soft tissue value. This CT volume was then misaligned by the same set of transformations used in the previous rigid registration tests. One hundred rigid registrations were performed and accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE and success was determined as in Section 4.2.2.

### 4.4.3 Groupwise Registration

Validation of the groupwise registration was performed similarly to the method used for the patient-based phantoms. The registration was performed on vertebrae L3, L4 and L5 and the US volume was cropped accordingly. Registration was performed simultaneously for all three vertebrae, producing an 18-parameter optimization loop ($3 \times 6$ rigid parameters). Similarly to the rigid registration experiment, the CT volume was initially misaligned to a range of 0 mm to 20 mm TRE. Each vertebra was then further misaligned by individually applying a random transformation using a uniform distribution of $\pm 5$ mm translation along each axis and $\pm 5^\circ$ rotation about each axis. One hundred misalignments and registrations were performed. Accuracy was determined by the ability of the registration to recover the gold standard alignment. TRE and success was determined as in Section 4.2.2.
Chapter 5

Registration Results

Through the registration tests of the patient-based phantoms, the curved patient-based phantom and the lamb cadaver, the registration is shown to be robust to a variety of challenges that are presented in a clinical case. The rigid registration of the patient-based phantoms shows that the algorithm can accurately register US and CT datasets containing significant occlusion due to bony and soft-tissue interfaces. The groupwise registration tests for the patient-based phantom demonstrates that changes in the curvature of the spine can be robustly accounted for through the use of a biomechanical model constraining the motion of the vertebrae throughout the registration optimization. Rigid and groupwise registration for actual curved phantoms show that this will hold true not only for artificially misaligned datasets, but for US and CT data where a change in curvature has been introduced between preoperative and intraoperative imaging. Finally, in the registration of the lamb cadaver data, the algorithm will be shown to be robust to the addition of soft-tissue structures in the US and CT images.


5.1 Phantom Data

5.1.1 Rigid Registration

The results of the rigid registration for the patient-based phantoms are shown in Table 5.1. Successful registrations are defined as any registration with a final TRE of less than 3 mm. The registration algorithm was successful for 98.8% of the tests across all phantoms, with a mean TRE of 1.44 mm in the successful cases. An example of an initial misalignment and final registration is presented in Figure 5.1. The results of the rigid registration for the patient-based phantoms are shown in Table 5.1. Successful registrations are defined as any registration with a final TRE of less than 3 mm. The registration algorithm was successful for 98.8% of the tests across all phantoms, with a mean TRE of 1.44 mm in the successful cases. An example of an initial misalignment and final registration is presented in Figure 5.1. While these results show that the algorithm can accurately register US and CT images of the spine, they represent a best case scenario. The curvature of the spine in CT and US data exactly match. This is unlikely to be the case in a clinical setting where the patient has changed pose.

Table 5.1: Final TRE for the rigidly registered CT volumes from the patient-based phantoms are presented for vertebrae L2-L4 for all successful registrations. Success rate (SR) is defined as the percentage of registrations where all vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.95/0.13</td>
<td>0.80/0.09</td>
<td>0.66/0.08</td>
<td>99.0</td>
</tr>
<tr>
<td>2</td>
<td>0.94/0.08</td>
<td>0.83/0.08</td>
<td>0.80/0.08</td>
<td>98.0</td>
</tr>
<tr>
<td>3</td>
<td>1.07/0.05</td>
<td>0.87/0.04</td>
<td>0.76/0.04</td>
<td>100.0</td>
</tr>
<tr>
<td>4</td>
<td>1.36/0.09</td>
<td>1.47/0.06</td>
<td>1.57/0.09</td>
<td>100.0</td>
</tr>
<tr>
<td>5</td>
<td>1.05/0.05</td>
<td>1.36/0.05</td>
<td>1.65/0.08</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Figure 5.1: Sagittal US slice of patient-based phantom 1 (Top) overlaid with bone contours from the initially misaligned CT volume (Middle) and registered CT volume (Bottom).

from supine to prone between the preoperative and intraoperative imaging.

5.1.2 Misaligned Vertebrae Rigid Registration

The results of the rigid registrations for the patient-based phantoms with misaligned vertebrae, perturbed up to 5 mm in CT, are shown in Table 5.2. The registration algorithm was successful for 47.9% of the tests across all phantoms. As is to be expected, when the vertebral misalignments are small, the algorithm is able to find an orientation that brings the CT volume close to the appropriate orientation. However, as the misalignment of the vertebrae increases, it is no longer possible for the registration to find an alignment with acceptable errors for percutaneous spinal interventions.
Table 5.2: Final TRE for the rigidly registered CT volumes from the patient-based phantoms, after individual vertebrae were perturbed, are presented for vertebrae L2-L4 for all successful registrations. Success rate (SR) is defined as the percentage of registrations where all vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.49/0.50</td>
<td>1.57/0.60</td>
<td>1.30/0.50</td>
<td>45.0</td>
</tr>
<tr>
<td>2</td>
<td>1.55/0.51</td>
<td>1.63/0.63</td>
<td>1.58/0.58</td>
<td>48.0</td>
</tr>
<tr>
<td>3</td>
<td>1.66/0.48</td>
<td>1.65/0.63</td>
<td>1.46/0.59</td>
<td>55.0</td>
</tr>
<tr>
<td>4</td>
<td>1.75/0.44</td>
<td>1.86/0.52</td>
<td>1.95/0.41</td>
<td>44.0</td>
</tr>
<tr>
<td>5</td>
<td>1.46/0.44</td>
<td>1.82/0.57</td>
<td>1.91/0.45</td>
<td>47.0</td>
</tr>
</tbody>
</table>

5.1.3 Groupwise Registration

Results for the groupwise registration tests on the patient-based phantoms are found in Table 5.3. The success rate across all the phantoms was 65.0% without biomechanical constraint and 96.4% when the biomechanical model was included. The success rate for the phantom data was highest with a $\sigma$ value of 1, an equal weighting of the biomechanical model and the intensity-based $LC^2$ metric. An example of the initial misalignment and the final registration is displayed in Figure 5.2; CT contours are overlaid on to US slices extracted along the principle axes. A demonstration of the effect of the rigid initialization is shown in Figure 5.3, with sagittal slices from US overlaid with CT contours showing alignment prior to registration, after the rigid registration initialization and after the groupwise registration. As can been seen, the rigid registration brings the CT volume closer to the correct alignment, but the groupwise registration results in alignments that could not be achieved with a strictly rigid registration. Through the groupwise registration of the vertebrae subvolumes in CT to the US volume, the change in bone curvature is accounted for. Without
a biomechanical model, the groupwise registration results were only slightly better than the rigid registration of perturbed datasets. This is likely due to two challenges associated with the groupwise registration. As a set of 18-parameter are being optimized simultaneously, the search space is much more complex than a standard rigid registration. Additionally, as the 18 parameters are made up of three sets of six parameters that pertain to the three distinct subvolumes, it is difficult to determine which transformed subvolume is most responsible for a change in the similarity. For example, a change in the translation on the transverse axis applied to a single vertebrae will have a smaller impact on the similarity metric than if the change in translation corresponded to the entire set of vertebrae, as is the case in the rigid registration. The impact of this challenge is reduced through the use of a biomechanical model, as seen in the results. The best results were for a $\sigma$ value of 1, indicating that
an equal weighting of the biomechanical model with the intensity-based similarity metric. Interestingly, the accuracy of the successful registrations does not change significantly with the different weights for the biomechanical model. This suggests that the model is mostly useful for holding the vertebrae subvolumes to a realistic shape, not for fine tuning the alignment for an improved accuracy. The rigid initialization step has proved to be important to the success rate of the groupwise registration. In our group’s prior work [16] that did not include this initialization step, validation of the groupwise registration on a similar set of experiments was only able to register 82% of misalignments up to 20 mm. From this, it is clear that a good initial alignment of the vertebrae subvolumes is required for a successful groupwise registration and that a rigid registration is sufficient for this purpose.
CHAPTER 5. REGISTRATION RESULTS

Table 5.3: Final TRE for vertebrae L2-L4 of the patient-based phantoms and the mean error of the volume are presented for all successful groupwise registration. Success rate (SR) is defined as the percentage of registrations where all the vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th>Phantom</th>
<th>( \sigma )</th>
<th>( \text{L2} ) (mm/std)</th>
<th>( \text{L3} ) (mm/std)</th>
<th>( \text{L4} ) (mm/std)</th>
<th>Overall (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0</td>
<td>1.83/0.66</td>
<td>1.68/1.34</td>
<td>1.15/0.34</td>
<td>1.56/0.50</td>
<td>64.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>1.95/0.68</td>
<td>1.46/0.52</td>
<td>1.06/0.22</td>
<td>1.49/0.35</td>
<td>86.0</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.56/0.34</td>
<td>0.90/0.24</td>
<td>0.95/0.24</td>
<td>1.14/0.17</td>
<td>95.0</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.66/0.30</td>
<td>1.77/0.22</td>
<td>0.91/0.13</td>
<td>1.44/0.15</td>
<td>93.0</td>
</tr>
<tr>
<td>2</td>
<td>0.0</td>
<td>1.74/0.25</td>
<td>1.19/0.21</td>
<td>2.41/1.62</td>
<td>2.14/0.56</td>
<td>57.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>1.68/0.19</td>
<td>1.20/0.36</td>
<td>2.22/0.81</td>
<td>1.53/0.27</td>
<td>89.0</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.61/0.17</td>
<td>1.32/0.35</td>
<td>1.56/0.41</td>
<td>1.50/0.14</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.66/0.27</td>
<td>1.36/0.33</td>
<td>1.67/0.47</td>
<td>1.55/0.18</td>
<td>94.0</td>
</tr>
<tr>
<td>3</td>
<td>0.0</td>
<td>2.03/0.42</td>
<td>0.88/0.11</td>
<td>2.48/1.19</td>
<td>1.80/0.45</td>
<td>63.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>1.88/0.31</td>
<td>0.83/0.09</td>
<td>2.15/1.08</td>
<td>1.62/0.37</td>
<td>84.0</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.76/0.25</td>
<td>0.79/0.10</td>
<td>1.52/0.37</td>
<td>1.36/0.15</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.65/0.29</td>
<td>0.83/0.08</td>
<td>1.55/0.70</td>
<td>1.32/0.16</td>
<td>94.0</td>
</tr>
<tr>
<td>4</td>
<td>0.0</td>
<td>2.32/0.51</td>
<td>1.73/0.43</td>
<td>2.25/0.48</td>
<td>2.11/0.25</td>
<td>81.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>2.15/0.43</td>
<td>1.81/0.30</td>
<td>2.05/0.16</td>
<td>2.00/0.19</td>
<td>96.0</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.96/0.32</td>
<td>1.92/0.27</td>
<td>2.01/0.12</td>
<td>1.99/0.18</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.83/0.23</td>
<td>2.03/0.27</td>
<td>2.14/0.11</td>
<td>2.00/0.14</td>
<td>96.0</td>
</tr>
<tr>
<td>5</td>
<td>0.0</td>
<td>1.56/0.34</td>
<td>1.98/0.71</td>
<td>2.70/0.91</td>
<td>2.07/0.30</td>
<td>60.0</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>1.50/0.30</td>
<td>2.53/0.32</td>
<td>2.06/0.33</td>
<td>2.03/0.18</td>
<td>90.0</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.49/0.26</td>
<td>2.59/0.30</td>
<td>2.03/0.18</td>
<td>2.04/0.15</td>
<td>93.0</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.45/0.22</td>
<td>2.49/0.18</td>
<td>2.05/0.16</td>
<td>2.00/0.12</td>
<td>91.0</td>
</tr>
</tbody>
</table>

5.2 Curved Patient-Based Phantom Registration

The results of the registration of the curved phantom are reported in Table 5.4. For these cases, rigid registration alone was unable to successfully register the datasets. Across the registrations in both directions (curved/natural, natural/curved), the algorithm had a success rate of 98.5%. The highest success rate for the registration of the curved-phantom CT to the natural-phantom US was with a \( \sigma \) value of 1, while the registration of the clinical case, the natural-phantom CT to the curved-phantom
CHAPTER 5. REGISTRATION RESULTS

US, was most successful with $\sigma$ values of both 0.5 and 1.

Table 5.4: Final TRE for vertebrae L2-L4 of the curved patient-based phantom and the mean error of the volume are presented for all successful registrations. Success rate (SR) is defined as the percentage of registrations where all the vertebrae have a final TRE of less than 3 mm. In this table, Natural CT signifies the CT acquired from the natural phantom, Curved US signifies the US acquired from the curved phantom and vice versa.

<table>
<thead>
<tr>
<th>CT-US</th>
<th>$\sigma$ (mm/std)</th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>Overall (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curved-</td>
<td>0.0</td>
<td>1.96/0.26</td>
<td>2.00/0.17</td>
<td>2.34/0.49</td>
<td>2.10/0.17</td>
<td>52</td>
</tr>
<tr>
<td>Natural</td>
<td>0.5</td>
<td>1.97/0.13</td>
<td>1.95/0.09</td>
<td>2.27/0.31</td>
<td>2.06/0.12</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>2.03/0.13</td>
<td>2.02/0.09</td>
<td>2.33/0.26</td>
<td>2.13/0.10</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>2.07/0.10</td>
<td>2.13/0.06</td>
<td>2.42/0.24</td>
<td>2.21/0.09</td>
<td>95</td>
</tr>
<tr>
<td>Natural</td>
<td>0.0</td>
<td>1.50/0.20</td>
<td>1.24/0.14</td>
<td>1.49/0.20</td>
<td>1.56/0.13</td>
<td>87</td>
</tr>
<tr>
<td>Curved</td>
<td>0.5</td>
<td>1.46/0.16</td>
<td>1.11/0.24</td>
<td>1.46/0.17</td>
<td>1.35/0.11</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.42/0.19</td>
<td>0.97/0.22</td>
<td>1.57/0.22</td>
<td>1.32/0.12</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>1.38/0.19</td>
<td>0.94/0.22</td>
<td>1.90/0.28</td>
<td>1.40/0.13</td>
<td>98</td>
</tr>
</tbody>
</table>

The registration of the natural-phantom CT to the curved-phantom US produced significantly more robust results than in the other patient-based phantom tests. Additionally, both a $\sigma$ value of 0.5 and 1 produced the best results for this dataset, where as for all the other phantom tests the best results were only from a $\sigma$ value of 1. It is possible that in the introduction of the curve, the overlapping articular processes at facet joint separated slightly, making them more defined in the US volume. This would reduce the ambiguity of the vertebral alignment at the facet joint and make it easier for the intensity-based similarity metric to correctly identify the proper alignment of the vertebrae.

With regards to the high success rates for $\sigma$ values of both 0.5 and 1, the curved-phantom US does not match the biomechanical model’s expected orientation to the
same degree as the unmodified patient-based phantoms. Particularly, the biomechan-
ical model makes the assumption that there will be no rotational difference between
subsequent vertebrae. Like in clinical cases, this does not hold true for the curved-
phantom US, thus it is logical that a reduced weight to the model would produce
better results. A trend was observed, in that if too much weight is placed on the
biomechanical model, in this case a $\sigma$ value of 2, the proportion of successful registra-
tions will decrease. To confirm this hypothesis a set of tests was performed with the
inverse set of data, registering the curved-phantom CT to the natural-phantom US.
The results from this test were similar to those of the previous phantom tests and
support this hypothesis explaining the improved accuracy in the natural-phantom CT
and curved-phantom US registrations.

5.3 Lamb Cadaver

5.3.1 Rigid Registration

The results of the rigid registrations of the lamb cadaver are shown in Table 5.5. The
registration algorithm was successful for 99% of tests, with a mean TRE of 1.25 mm
in the successful cases and a standard deviation of 0.14 mm. An example of an initial
misalignment and final registration is presented in Figure 5.4.

The results from the rigid registration of the lamb cadaver shows that the algo-

rithm is able to account for the soft-tissue structure found in the US and CT images.
However, like the rigid registration of the patient-based phantoms, this is a best case
results and does not take into account the change in the curvature of the spine that
will appear in clinical data.
Table 5.5: Final TRE for the rigidly registered CT volumes from the lamb cadaver are presented for vertebrae L3-L5 for all successful registrations. Success rate (SR) is defined as the percentage of registrations where all the vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th></th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.67/0.18</td>
<td>1.66/0.17</td>
<td>1.72/0.17</td>
<td>95</td>
</tr>
</tbody>
</table>

Figure 5.4: Sagittal US slice from the lamb cadaver (Left), overlaid with bone contours from the initially misaligned CT volume (Center) and registered CT volume (Right). Vertebrae in these images from left to right are L3, L4 and L5.

### 5.3.2 Misaligned Vertebrae Rigid Registration

The results of the rigid registrations of the lamb cadaver with misaligned vertebrae, perturbed up to 5 mm in CT, are shown in Table 5.6. As was expected, the registration algorithm is only able to successfully register for 32% of the misalignments.

### 5.3.3 Groupwise Registration

Results for the groupwise registration tests on the lamb cadaver are found in Table 5.7. The maximum success rate for the lamb cadaver data was 87% with a $\sigma$ value of 0.5. An example of the initial misalignment and the final registration is displayed.
Table 5.6: Final TRE for the rigidly registered CT volumes from the lamb cadaver, after individual vertebra were perturbed, are presented for vertebrae L3-L5 for all successful registrations. Success rate (SR) is defined as the percentage of registrations where all the vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th></th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.03/0.41</td>
<td>2.07/0.42</td>
<td>2.00/0.47</td>
<td>32</td>
</tr>
</tbody>
</table>

in Figure 5.5.

Table 5.7: Final TRE for vertebrae L3-L5 of the lamb cadaver and the mean error of the volume are presented for all successful groupwise registrations. Success rate (SR) is defined as the percentage of registrations where all the vertebrae have a final TRE of less than 3 mm.

<table>
<thead>
<tr>
<th>σ</th>
<th>L2 (mm/std)</th>
<th>L3 (mm/std)</th>
<th>L4 (mm/std)</th>
<th>Overall (mm/std)</th>
<th>SR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>1.71/0.76</td>
<td>0.72/0.30</td>
<td>2.26/1.10</td>
<td>1.56/0.42</td>
<td>66</td>
</tr>
<tr>
<td>0.5</td>
<td>1.70/0.79</td>
<td>0.62/0.27</td>
<td>1.81/0.71</td>
<td>1.38/0.38</td>
<td>87</td>
</tr>
<tr>
<td>1.0</td>
<td>1.33/0.44</td>
<td>1.09/0.23</td>
<td>1.94/0.67</td>
<td>1.46/0.29</td>
<td>84</td>
</tr>
<tr>
<td>2.0</td>
<td>1.44/0.38</td>
<td>1.59/0.27</td>
<td>2.00/0.56</td>
<td>1.68/0.23</td>
<td>83</td>
</tr>
</tbody>
</table>

The registration algorithm proved to be robust to noisy and non-ideal data. As can be seen in Figure 5.6, in the lamb cadaver, the US signal passed through the vertebra. Strong reflections are visible on the top and bottom of the bone, as well as the bone surface found below the superior articular process. This occurred several times throughout the US data and the algorithm was still able to successfully register both datasets.

Of note is that for the lamb cadaver data, the registration was the most robust with a σ value of 0.5. This is likely due to the fact that the model is based on human data and is not as accurate of a representation of the lamb anatomy.
5.4 Discussion

In the rigid registration of both the patient-based phantoms and the lamb cadaver, the results showed the algorithm to be robust for registration of US and CT datasets. However, these results should be interpreted as a proof of concept for the registration technique, as this was a best case scenario and did not represent the clinical case. When misalignments were introduced to the relative positions of the vertebrae, the rigid registration was only able to register small misalignments. As the misalignment of the vertebrae increased, it was no longer possible for the rigid registration to find a successful alignment.

The groupwise approach was able to account for these changes in spine curvature. Without a biomechanical model, the groupwise registration results were only slightly
better than the rigid registration of perturbed datasets. This is likely due to the increased complexity of simultaneously optimizing 18 parameters, compromised of three sets of six parameters each pertaining to distinct subvolumes. Interestingly, the accuracy of the successful registrations does not change significantly with the different weights for the biomechanical model. This suggests that the model is mostly useful for holding the vertebrae subvolumes to a realistic shape, not for fine tuning the alignment for an improved accuracy.

The registration of the natural-phantom CT to the curved-phantom US produced significantly more robust results than in the other patient-based phantom tests. It is possible that in the introduction of the curve, the overlapping articular processes at facet joint separated slightly, making them more defined in the US volume. Which in turn would reduce the ambiguity of the vertebral alignment at the facet joint and make it easier for the intensity-based similarity metric to correctly identify the proper alignment of the vertebrae. With regards to the high success rates for $\sigma$ values of
both 0.5 and 1, the curved-phantom US does not match the biomechanical model’s expected orientation to the same degree as the unmodified patient-based phantoms. Particularly, the biomechanical model makes the assumption that there will be no rotational difference between subsequent vertebrae. Like in clinical cases, this does not hold true for the curved-phantom US, thus it is logical that a reduced weight to the model would produce better results. This hypothesis is confirmed from the registration results of the inverse set of data, where they were similar to those of the previous patient-based phantom tests.

The results of the groupwise registration of the lamb cadaver data differed from the patient-based phantom tests in that the registration was the most robust with a $\sigma$ value of 0.5. The lamb vertebrae are approximately half the size of the human vertebrae tested. As the biomechanical model was developed using human data, it is likely it does not present as accurate of a representation of the lamb anatomy.

Various values of $\sigma$ for weighting the biomechanical model in order to determine how much emphasis should be placed on the model when compared to the $LC^2$ metric. If the weight of the model is too low, it will have limited impact, however if it is weighted too high, it will not allow for the accurate registration of anatomy that lies outside the model’s expected orientation. Detailed results are presented for $\sigma$ values between 0 and 2. Across our datasets, the best registration results were with $\sigma$ values of either 0.5 or 1. Values above these showed a trend of decreasing capture range as the biomechanical model weight increased. To ensure this trend continued with larger weights, $\sigma$ values of 5 and 10 were also tested. As was expected, the registration capture range continued to decrease as the emphasis on the biomechanical model increased and the influence of the intensity based similarity measure was decreased.
In the tests on patient-based phantoms, it was found that an equal weighting of the model and intensity metric produced the best results. The benefits of this biomechanical constraint are clearly tied to how closely the model estimates the actual pose of the spine and how flexible the model is in allowing the registration of anatomies that differ from the expected alignment. This particular model was able to successfully register the CT and US from curved patient-based phantom. The anatomy in the curved version of the phantom differs from the expected orientation of the vertebrae, but was still reliably registered. It is possible that if the patient anatomy differs substantially from the biomechanical model’s expected alignment, the model could prove a hindrance rather than a benefit.

In the lamb US volumes, there appears to be US reflections found below the bone to soft-tissue interface. These reflections can be seen as horizontal lines passing through the shadowed region. It is unclear whether this corresponds to reflections from lower in the lamb tissue, scattering of the signal at the bone surface or if there is in fact some US signal that passes through the interface. Regardless, the registration technique was still able to successfully register these datasets.

Through the simultaneous registration of all three vertebrae in the groupwise registration, the chance of propagating error that can occur with consecutive registrations of vertebrae is eliminated. This introduces a challenge to the registration as the 18 simultaneous parameters are more difficult to optimize than three independent sets of six parameters. Particularly, when all three vertebrae are fairly close to the appropriate alignment, changes in one vertebra have a small impact on the similarity metric value. This is an implicit challenge of distilling 18 parameters representing
three independent bodies into a single similarity metric. The inclusion of the biomechanical model aids in this issue and helps the algorithm converge faster, however it is necessary to have very strict convergence criteria.
Chapter 6

Conclusion and Future Work

This chapter summarizes the contributions and results of this thesis. It then discusses the future work to improve the technique and further validate the approach in a clinical setting.

6.1 Summary of Contributions

In this work an US to CT registration technique for the lumbar spine was presented. This is intended for fusion of intraoperative US and preoperative CT data, to be used for guidance in percutaneous spinal injections. In order to have a clinically viable registration technique, the algorithm was designed with the following features:

1. The US simulation from CT allows for the accurate and robust registration of US and CT datasets containing significant occlusion due to bony and soft-tissue interfaces. Additionally, this simulation requires no prior knowledge of the direction of the US signal through the patient anatomy.
2. The registration technique requires no segmentation of the US data. US segmentation is time-consuming and difficult to be reproduced accurately.

3. Through the groupwise registration and biomechanical constraint of motion, the registration of US and CT images of the spine is robust to clinically reasonable changes in the curvature of the spine between preoperative and intraoperative imaging.

The registration tests of the patient-based phantoms, the curved patient-based phantom and the lamb cadaver have shown the registration to be robust to a variety of challenges that are presented in a clinical case. The rigid registration of the patient-based phantoms shows that the algorithm can accurately register US and CT datasets containing significant occlusion due to bony and soft-tissue interfaces. The groupwise registration tests for the patient-based phantom demonstrates that changes in the curvature of the spine can be robustly accounted for through the use of a biomechanical model constraining the motion of the vertebrae throughout the registration optimization. The curved phantom experiments show that this will hold true not only for artificially misaligned datasets, but for US and CT data where a change in curvature has been introduced between preoperative and intraoperative imaging. Finally, in the registration of the lamb cadaver data, the algorithm has proven to be robust to the addition of soft-tissue structures in the US and CT images.

All registrations began with an initial misalignment between 0 mm and 20 mm. The groupwise registration algorithm applied iterative US simulation from CT images while allowing independent motion of each vertebra. A biomechanical model was introduced to represent the intervertebral link and the system energy was calculated based on the relative transforms between the vertebrae. Integration of a
biomechanical model to constrain the registration greatly improved the consistency of the algorithm. For the patient-based phantoms, 98.8% of rigid registrations using matching data were successful. Only 47.9% of tests with perturbed vertebrae were successfully registered with the rigid registration, while the groupwise registration, with a $\sigma$ biomechanical model weight of 1, achieved a clinically acceptable registration for 95% of the tests. For the patient-based phantom with the introduced curvature between imaging acquisitions, rigid registration was unable to successfully register the datasets. The groupwise registration of the curved-phantom CT to the natural-phantom US was successful for 97% of tests with a $\sigma$ value of 1. Tests for registering the natural phantom CT to the curved phantom US had a success rate of 100% for $\sigma$ values of 0.5 and 1. For the lamb cadaver data, 99% of rigid registrations for matching data were successful. When the lamb cadaver vertebrae were perturbed up to 5 mm in CT, 32% of the rigidly registered datasets were successful and 87% of groupwise registrations were successful. For this case, the $\sigma$ value for the biomechanical model was set to 0.5.

These results have shown the simulation of US from CT allows for the registration of datasets without the segmentation of surface information from US and the biomechanically constrained groupwise registration enables the accurate registration of datasets with changes in curvature between US and CT image acquisition. The registration technique has proven to be robust to a wide variety of challenges presented in a clinical setting. When combined with a needle tracking system, this could prove to be a viable option for a percutaneous spinal injections guidance system and eliminate the need for intraoperative CT or flouroscopy.
6.2 Suggestions for Future Work

While the registration procedure has shown promise in the tests, it still requires further improvements to the implementation and must be further validated to be ready for a clinical application. The future work will focus on reducing the registration runtime and on validating the registration technique as a method for guiding needle placement in percutaneous spinal interventions. The following are my suggestions for future work:

- For this registration technique to be viable in a clinical setting, the registration runtime must be reduced. A means of accomplishing this is through GPU hardware acceleration. The nature of the US simulation lends itself well to the parallel processing available on a GPU and will be a source of significant reduction in computation time. A preliminary version of the algorithm has been implemented in GPU and has reduced the registration run time to approximately 7 minutes.

- Another challenge in the registration procedure is the need for identifying individual vertebrae in CT. Currently this is accomplished manually. If this could be done automatically, it would reduce the amount of manual input necessary to initialize the registration process. Currently, our group is working on CT atlas to US registration of the lumbar spine, which would eliminate the need to identify individual vertebrae entirely.

- It is difficult to compare the results of this registration technique with previously published algorithms, due to the groupwise registration framework we have used. To compare the accuracy of this registration technique with prior work, the
algorithms would need to be extended to work with the groupwise framework presented here. This would allow us to directly determine the benefits of this US to CT registration technique compared to prior algorithms.

- While an extensive validation of the registration technique has been provided, to ensure the accuracy of this technique for clinical applications, a thorough validation should be performed on human cadaver data.

- Finally, as the main purpose of this US to CT registration technique is to assist in guiding needle placement in percutaneous spinal interventions, a user interface for needle guidance should be developed and the accuracy of the guidance system will need to be validated.
Bibliography


[41] Wei Shao, Ruoyun Wu, Keck Voon Ling, Choon Hua Thng, Henry Sun Sien Ho, Christopher Wai Sam Cheng, and Wan Sing Ng. Evaluation on similarity


