Prostate segmentation and multimodal registration in 3D ultrasound images

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Prostate Segmentation and Multimodal Registration in 3D Ultrasound Images

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Summary

Transrectal ultrasound (TRUS) is the most-commonly used imaging tool in diagnosis (e.g., biopsy) and treatment (e.g., brachytherapy) of the prostate cancer. This thesis addresses two important issues arised in those procedures. One is the prostate segmentation in 3D TRUS image, which helps the urologists to obtain the prostate surface, based on which they can make correct clinical decisions for early diagnosis and effective therapy. The other is the multi-modal registration between pre-operative medical image and the intra-operative 3D TRUS image. Movitation of this study is to provide the anatomic and functional information, which is only obtainable from the pre-operative images, to the real-time ultrasound, so as to aid the biopsy or treatment procedure.

The main contributions of this thesis are as follows:

- Employed the real-value spherical harmonics to describe the 3D prostate shape and built up a much compact statistical model for the prostate based on the parametric representation.
- Proposed a fully automatic prostate segmentation for 3D TRUS image using the statistical shape model. No more than 13 parameters (including shape and pose) are required to be determined for the segmentation.
- Presented a generic framework of a rigid surface-to-image registration technique which can be used in image tracking, mono- and multi-modal image registration associated with ultrasound. This technique can also provide an initial guess of the prostate surface in the 3D ultrasound images when the rigidity assumption is not ideally satisfied.

- Discussed the measurements used in the registration framework and the possible formulations to evaluate the similarity between an organ surface and its ultrasound image. It is necessary to define a similarity measurement most appropriately highlighting the organ's acoustic feature.
- Explored the use of surface parameterization (for point correspondence) and the use of thin-plate spline (for transformation interpolation) to account for the prostate deformation occurred between 3D MRI/MRS and 3D TRUS images. Designed and built up an elastic phantom for the validation of the proposed deformable registration.

In this thesis, all the experiments are conducted on the real patient data. The consistency and accuracy of these methods have been verified quantitatively or qualitatively, with the aid of the human expert or through a phantom study. The segmentation technique has been integrated into the robotic prostate biopsy system developed by our team and successfully used in the patient trials conducted in Singapore General Hospital.

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Chapter 1

Introduction

1.1 Background

Prostate is a gland of the male reproductive system that produces fluid for semen, which helps to transport sperm during the male orgasm. As shown in Figure 1.1, the prostate is located in front of the rectum and just below the bladder. Normally, the prostate is small, about the size of a chestnut and somewhat conical in shape, and consists of a base (which is directed upward near the inferior surface of the bladder), an apex (which is directed downward and in contact with the superior fascia of the urogenital diaphragm), an anterior, a posterior and two lateral (left and right) surfaces. As men age, the prostate become a potential source of problems.

Figure 1.1: Anatomy of the prostate [1].

1.1.1 Prostate Cancer

Prostate cancer is one of the most common cancers affecting elderly men in developed countries. The American Cancer Society estimated that in the year 2009 there would be 192,280 new cases of prostate cancer in the United States and about 27,360 men would die of this disease [5]. Although these numbers have been decreasing over recent years, it is still the second leading cause of cancer death among men. In Singapore, it is ranked as the fifth most common cancer for male [6].

Early detection of prostate cancer can help to gain more chances of successful treatment. However, there are no clear symptoms until the cancer is quite advanced. Digital rectal examination (DRE) and prostate-specific antigen (PSA) blood test are routine screening methods used for diagnosis. When a patient has an abnormal DRE and/or an elevated PSA level ($> 4ng/ml$), he will be suspected to have a cancerous prostate and a needle biopsy will be recommended.

1.1.2 Prostate Biopsy

Prostate biopsy is the procedure to take out small tissue samples from the prostate. These samples will be examined under microscopic observation to verify the cancerous existence. The biopsy procedure should be guided under real-time image monitoring, which is the transrectal ultrasound in most of cases [7]. It is generally accepted that cancer of the prostate appears hypoechoic on sonography [8]. However, the ultrasonic imaging quality is not high enough so that it has very limited ability in identifying tumor foci directly from the image. Therefore, the biopsy cores are generally selected uniformly within the gland following standard biopsy protocols like the sextant or 10-core protocol [9, 10], in which the prostate is divided into a number of zones and one core is randomly sampled from each zone.

The biopsy can be conducted transrectally or transperineally. Figure 1.2(a) shows the ultrasound-guided transrectal biopsy procedure, in which the needle goes into the prostate through the rectum wall. As for transperineal biopsy, the needle goes through the skin of the perineum to reach the prostate. It is commonly recognized that the former has a higher risk of infection and longer recovery time than the latter but more

Figure 1.2: Transrectal ultrasound guided prostate biopsy and brachytherapy. (a) Transrectal biopsy [2]. (b) Transperineal brachytherapy [3].

often used due to its simplicity and less time consumed.

1.1.3 Prostate Brachytherapy

Brachytherapy is a minimally invasive treatment to the localized prostate cancer – the doctor implants permanent radioactive iodine seeds into the prostate where they irradiate the cancer from inside of the gland. After an initial volume assessment, these tiny seeds are placed according to a computer-generated grid by needles inserted through the perineum wall under real-time imaging (e.g., ultrasonography) and template guidance (Figure 1.2(b)). However, when the prostate is of a large volume (> 50 cc) or sometimes even with a volume less than 40 cc, the anterior or the anterolateral parts of the prostate may be blocked by the pubic bone along the needle trajectories [11, 12, 13, 14]. This interfering pubic arch often means the needle may not reach the respective targets and the trajectory shall be altered. Therefore, it is important to assess the pubic arch interference (PAI) before the brachytherapy procedure to prevent the cancer from being inadequately treated. This assessment is applicable to the transperineal biopsy as well.

1.1.4 Related Imaging Modalities

Transrectal Ultrasound (TRUS) is one of the most commonly used imaging tool for diagnosis or treatment guidance, due to its safety, real-time capacity and low cost. Its early application for the prostate concentrates on the ultrasonic appearance of prostate abnormalities. Since the introduction of PSA screening test and early detection of prostate cancer, the role of TRUS has changed to visualizing the prostate and assisting the biopsy and treatment planning. This examination is also used in the prostate volume assessment, which is important in the planning of radiation treatment like brachytherapy. In the prostate imaging, TRUS image is obtained by placing the patient in lithotomy position and scanning the prostate from the rectum using an endorectal ultrasound probe (shown in Figure 1.3), while the probe is held by the urologist's hand or an external probe holder. However, the TRUS-guided transrectal biopsy was reported having a positive cancer detection rate less than 30% [9], as the number of cores is limited and the cancerous region (appearing to be hypoechoic) is hardly recognizable in the image if it is still small. So it may occur that a patient may have an elevated PSA level but have a negative biopsy finding, thus leading to a false negative result.

Computer tomography (CT) scan is a process that uses X-rays and computer technology to make a series of cross-sectional images of the body. CT scan has been widely perceived as an imaging modality of limited value in imaging prostatic cancers. It is used as an additional test to determine whether the cancer has spread beyond the prostate, rather than providing good information for the prostate condition or stage of cancer. This technique is often used in brachytherapy for planning and pre- or postimplant dosimetry [15].

Magnetic Resonance Imaging (MRI) is a well-established technique that produces high-contrast images of tissue components. The anatomical details revealed by the MRI images allow physicians to better evaluate parts of the body that may not be visible with other imaging methods such as ultrasound or CT. When the cancer grows to some extent, it is possible for experienced radiologists to distinguish them from the normal regions, as the cancer is usually identified as an area of low signal intensity within the peripheral zone on T2-weighted images [16].

Figure 1.3: Typical endorectal probes used in TRUS scan and MRS scan of the prostate.

Magnetic Resonance Spectroscopy (MRS) is a combination of MRI imaging and spectroscopic analysis. More than just imaging, it can examine the chemical components in tissue via a series of spatially localized spectrum. The new technology provides not only a tool for early diagnosis and screening but also the opportunity for preferential targeting of biopsy or radiation to regions of high tumor burden in the prostate [17, 18, 19]. To detect cancer, MRSI requires good spatial resolution (1 cm^3 or less), high signal-to-noise ratio, efficient water and fat suppression techniques, and short echo time (TE) for optimum detection of short T2 metabolites. In addition, a supplementary endorectal coil encompassed in a fixation balloon (shown in Figure 1.3) is required to be placed in the patient rectum. The balloon will be inflated with air or water ($40 \sim 200 \text{ ml}$) to hold the coil in place when the patient lies in supine position during the exam. The MRS findings shows that significantly higher choline/creatinine levels and lower citrate levels are usually obtained in regions of cancer compared with benign and normal prostatic tissue, so the ratio of these metabolites (choline/creatinine to citrate) in a local region could indicate a positive suspect [20].

1.1.5 A TRUS-Guided Robotic Prostate Biopsy System

Our team, the former Computer Integrated and Medical Interventional Lab (CIMIL) in Nanyang Technological University, has been working on a TRUS-guided robotic prostate

Figure 1.4: Medical images of the prostate.(a) TRUS image. (b) MRS image.

Figure 1.5: The robotic prostate biopsy system developed by CIMIL.

biopsy system and collaborated with Singapore General Hospital for years (National Medical Research Council of Singapore Grant Ref: 0859/2004) [21, 22, 23, 24]. Figure 1.5 shows the latest design of the whole system. It consists of a ultrasound imaging system (ALOKA Inc., Japan), a transrectal bi-plane probe, a frame grabber system, a robotic control system that pulls the probe and drives the needle guide, and a user control console.

This system is designed for a robotic assisted transperineal biopsy of the prostate and aims at achieving a customized biopsy planning and high accuracy in needle targeting.

Figure 1.6: Implementation of the robotic biopsy system. (a) Acquisition of the 3D TRUS image. (b) Prostate modeling and biopsy planning. (c) Biopsy the prostate at the planned cores.

In order to have a full picture of the prostate and make the biopsy plan in 3D space, the system obtains the 3D image using a traditional 2D probe. This probe is attached to an external probe holder and this holder is controlled by a linear motor so that it is able to pull the probe along the axial direction at regular speed. Then the 3D image is constructed by the series of transverse slices scanned at the intervals and it takes about 1 minute to obtain the whole gland scan. Figure 1.6(a) shows the operational principle of the 3D image collection and how the image data is formed. The image data collected by

the ultrasound machine will be transmitted to the robotic system via the frame grabber, and the 3D image data is stored as an array of the 2D matrices of gray values. When the system has been calibrated, we can get the spatial information of the image data thus obtain the field of view of the image volume with respect to the robotic system. When the 3D image data is rendered in the graphical human interface, the user can manually outline the prostate boundary, construct the prostate shape and make biopsy planning by specifying multiple biopsy sites inside the 3D shape, as shown in Figure 1.6(b). The system will calculate the required needle trajectory for each biopsy site, revolve and advance the biopsy needle guide accordingly (Figure 1.6(c)). Once the needle guide has been properly positioned, the urologist can fire the biopsy gun along the needle guide and take out the tissue sample at the specified target. This procedure will be repeated until the urologist has taken samples from all the planned sites.

1.2 Motivation

Identifying the prostate boundary is an important aspect of TRUS imaging. Boundaries provide the anatomical description of the prostate, useful for biopsy, brachytherapy, cryotherapy, and indirectly the volume required for treatment planning, e.g., brachytherapy and transurethral microwave therapy, and progression monitoring like hormonal treatment. Because of the low signal-to-noise ratio (SNR) and the inhomogeneous intensity distribution in the image, the boundary detection in ultrasound image remains a difficult work, due to the low signal-to-noise ratio (SNR) and inhomogeneous echo attenuation of the image. For this sake, manual contouring on the ultrasound image is considered most close to the truth, but it is time-consuming, arduous and user dependent. This arises a need for an automated system to understand the images.

For decades, many algorithms have been developed for the semi-automatic or automatic segmentation of the prostate in ultrasound image [25, 26, 27, 28, 29, 30, 31], using low-level image analysis or deformable models. The low-level image analysis can be edge-based (including filtering, morphological operation, edge detection and linking) or region-based (denoising and pixel classification). The techniques are relatively simple but have to be tuned properly and often involves human intervention. Their effectiveness in

ultrasound images is limited due to their sensitivity to the image quality. The deformable models are shape models independent of the image but able to deform themselves in the image region to fit with the image features. They can be physical models driven by image force, or statistical models with prior knowledge for prostate segmentation. Comparing with the low-level image analysis, the deformable models can create smooth boundary with inherent topology, and are more resistant to low contrast and edge missing between adjacent region. However, the physical models are gradually deformed; the initial model is required to be close to the boundary of interest, so that it is within the capture range of the deformation. What's more, when the deformation shall be stopped is usually decided empirically. It often occurs in the ultrasound images that the model will grow over the boundary when boundary strength is weak while trapped by noise of strong strength before it goes to the desired position. The statistical models address these problems by capturing plausible samples from a training set and imposing this prior knowledge into the segmentation. The model initialization can be automatically derived from the mean statistical model, while the model deformation is constrained by the principal variation of the statistical model. But so far most of the statistical models developed for prostate segmentation are applicable to a 2D midgland segmentation. Some of them even need a lot of human efforts to label the landmarks in each sample. Extension of 2D model to 3D segmentation is possible by constituting the stack of detected 2D contours to generate the 3D surface [32, 33, 34]. But compared to the direct 3D image segmentation which utilizes the strength continuity of image boundary in 3D, there would be more errors occurred in the surface construction and the number of model parameters to be determined is larger. To eliminate the requirements on landmark labeling and reduce the parameter dimensions, some studies have utilized a parametric representation of the prostate contour and surface [35, 36, 37, 38]. To our knowledge, there are only a few automatic 3D statistical models proposed for prostate segmentation [39, 40, 41, 38, 42] and they are somehow computation expensive, relying on delicate image thresholding and filtering [38, 42], or feature extraction [39, 40, 41]. In this study, we aims to take advantage of the statistical deformable model from parametric denotation and develop an automatic segmentation algorithm for the prostate in 3D ultrasound images. The emphysis of this method is that it should avoid unnecessary processing of the original image data, reduce the number of parameter required to determine the prostate surface

and make it practical for clinical use.

On the basis of intelligent prostate recognition in ultrasound images, the biopsy or brachytherapy procedure can be automated as well. To those TRUS-guided robotic systems developed for the prostate [43, 21, 44, 22, 23, 45, 46, 47], this facility can help the urologists to generate a logic plan of the biopsy or treatment. However, since the TRUS's role in these clinical procedures is limited: it is only used to determine the location of the prostate and the needles within the gland, the biopsy sites are still randomly chosen by urologists based on empirical rules, leading to a significant number of cancer cases undetected in initial biopsy. Similarly occurs to the seed planning in brachytherapy. To target the needle towards highly possible deposits, some researchers proposed to use statistical atlases of cancer distribution of the prostate [48, 49, 50, 51, 52]. Although these atlases are suitable to yield universal cancer occurrence for a population, when they are applied to an individual, its sensitivity of cancer detection is still unpredictable. Compared with the universal models, the patient-specific cancer model established from pre-operative information of an individual would be a better choice. With the recognition of MRS's ability in prostate cancer detection, we wish to merge the information obtained from the pre-operative MRI/MRS data to the intra-operative TRUS, so that the suspected tumor deposits can be used to define the preferential sampling sites for biopsy and design a seed placement pattern for brachytherapy. To fuse multimodal information, a registration procedure is required. This procedure searches for the transformation between the two image spaces. In this study, the registration serves for two purposes - one is the localization of the pubic arch in TRUS image using information from MRI to assess PAI; the other is the integration of MRI/MRS information, i.e., the anatomic details or suspected cancer distribution inside of the prostate, to the TRUS image.

3D Image registration involving the ultrasound modality is still a difficult topic, especially when the transformation to be determined is a deformable one. Manual selection of corresponding anatomic features [53, 54] is a solution to multimodal image fusion. But it is more likely used for rigid or affine transformation, because the number of landmarks identifiable on the ultrasound image is limited. To develop an algorithm to register MRI/MRS and TRUS images of the prostate, we have to understand that ultrasound

images have an higher level of speckle noise and smaller field of view than the MRI images. Therefore the anatomic structural information exhibited in MRI images may not have a correspondence in TRUS image and they may deteriorate the registration quality as outliers. This can cause the intensity-based approaches (or called image-to-image approaches) [55, 56] to fail. Surface-guided approaches (surface-to-surface) [57, 58] are universal and applicable for most of the image modalities. But they need too many efforts on the segmentation, not ideal for intra-operative use. Hence, we wish to have a method to make use of the advantages of both approaches, by enforcing only the necessary processing on the original gray level of TRUS image and filtering out the irrelevant structural information in MRI/MRS images which is hard to find correspondence in the TRUS image.

With regard to the complexity of the transformation, due to the different rectal filling (the endorectal coil in MRS against the transrectal probe in TRUS) and patient posture (supine in MRS against lithotomy in TRUS) [59, 58, 60], the prostate, a soft organ, may have a deformation between the modalities. When this deformation is not significant, a rigid transformation is sufficient. Otherwise, a deformable transformation is essential to account for the change of shape. There are solutions simplifying the deformation to be affine-like in form of linear scaling [61, 62] or polynomial [63]. A more general approach is to solve the global transformation as a rigid one first and then refine the transformation by a non-rigid one. The prostate deformation has been described by biomechanical models [64, 65], the physical model with statistical training on deformation behavior [66, 67], and the transformation expressed by interpolation with respect to feature points [56, 68, 69] or intensity measures [56, 70, 71]. The biomechanical model is superior in describing the complex motion, but it has a high computation requirement and needs prior knowledge on the tissue properties which may vary between individuals and is practically unavailable. Here we hope to develop a registration strategy which is fast in solving the problem and is able to deliver acceptable accuracy. Based on our investigation, the spline-based transformation is good in both accuracy and speed.

1.3 Major Contribution

In this thesis, an automatic segmentation method using a compact statistical model for the prostate in 3D ultrasound images has been proposed. As mentioned, the statistical shape models are superior in automation and intelligent supervision. The major contribution in this part is the proposal of a 3D model that requires less model parameters and is able to detect the 3D prostate shape automatically or with least user intervention. To reduce the model parameters, we propose to represent the closed prostate surface using real-value spherical harmonics parameterization. The coefficients to each harmonic basis, called as shape descriptor, then become the model parameters to be evaluated in training and determined in segmentation. Due to the coarse-to-fine property of the spherical harmonics representation, the number of the harmonics coefficients sufficient for shape representation is much less compared to the traditional point distribution model (PDM). Our results show that the 3D prostate surface can be approximated by a weighted sum of 7 components and its shape can be altered by varying these parameters. In comparison, it is much more efficient than a 2D PDM model [72], in which 10 parameters are needed to denote a 2D prostate contour. The decrease in the parameter dimension determines that less computation is involved in solving the multivariate optimization problem. Another advantage of this parametric representation is that there is no requirement for correspondent landmark labeling as that in PDM. To achieve high speed for real-time use, the proposed method defines an objective function based on the original ultrasound data with only basic denoising applied to it. The automatic segmentation is achieved by maximizing the objective function using the genetic algorithm with respect to the shape and pose parameters whose mean values and variations are obtained from training. To improve its performance in adverse image qualities, a user constraint, i.e., an indication of region of interest in one or more slices, can be incorporated into the method to narrow the search range of the pose parameters for better accuracy.

Under the motivation to bring suspected cancer information retrievable from MRI/MRS to the TRUS-guided procedure, a surface-to-image registration method is presented to solve the rigid transformation between the two image spaces [73, 74, 75, 76, 77]. In comparison with the surface-based approach, this method is superior for real-time applications as it does not require segmentation or complicated processing on the intra-

operative ultrasound image. Compared with the intensity-based approach, it excludes those anatomic structure information presented in MRI/MRS images but not in TRUS images, in the form of surface extraction, since information other than the object surface may deteriorate the registration quality badly as adverse outliers. Via the global search of the genetic algorithm, the best location of the surface in the ultrasound image is found by maximizing a defined similarity function with respect to the transformation. As a generic registration method, the similarity measure formulated in the framework could be customized according to the object's acoustic appearance in ultrasound. This is demonstrated in its applications to the prostate for the information-enriched guidance, as well as the pubic arch, for the evaluation of pubic arch interference. In the experiments with the prostate, it shows that the method is effective when little deformation is involved. Meanwhile the registered result could offer a good guess of the prostate boundary in the ultrasound images, or as a global alignment between the two image spaces. In its application to the pubic arch, we formulate three candidate similarity measures based on different interpretation of the organ boundary and the comparison study shows that it is important to choose an appropriate definition to ensure the success of the registration.

The idea of registering an object surface extracted from MRI image to its corresponding appearance in ultrasound image volume can be extended to any mono- or multimodal medical data fusion concerning ultrasound. However, the restriction of this technique is that the rigidity assumption should be satisfied. In our experiment with the prostate, we found that due to the use of an endorectal coil in MRS imaging, the prostate may have a significant deformation between MRI/MRS and TRUS. In this case, a rigid transformation is insufficient. The deformable registration is then introduced to address this problem in way of a global alignment followed by a non-rigid transformation refinement. The surface-to-image registration method, or the iterative closest point (ICP) method [57], is used for the first step. Based on this alignment, the surface parametrization is used to provide point correspondences based on geometric features. The thin-plate spline [78] is then employed as the radial basis function to describe the nonrigid transformation that accounts for the deformation from the surface to the rest of the volume [79, 80, 81]. On account of the difficulty in finding the ground truth for validation between the two

image modalities, we design an elastic pelvic phantom. This phantom is able to reproduce the deformation caused by different rectal filling. Using the phantom image data with and without the endorectal coil in the rectum, the accuracy of the algorithm is evaluated by the displacement errors of the fiducial markers implanted in the prostate.

In summary, the major contributions of this thesis are:

- Employed the real-value spherical harmonics to describe the 3D prostate shape and built up a much compact statistical model for the prostate based on the parametric representation.
- Proposed a fully automatic prostate segmentation for 3D TRUS image using the statistical shape model. The shape and pose parameters of the prostate are determined using the original ultrasound data through a multivariate optimization constrained by the statistical model.
- Presented a generic framework of a rigid surface-to-image registration technique for image tracking, mono- and multi-modal image registration associated with ultrasound.
- Discussed the measurements used to evaluate the similarity between an organ surface and its appearance in the ultrasound image. It is found that it is necessary to define the similarity measurement most appropriate to highlight its acoustic feature.
- Explored the use of a parametric surface (for point correspondence) and the use of thin-plate spline (for transformation interpolation) to account for the prostate deformation occurred between 3D MRI/MRS and 3D TRUS images. Designed and built up an elastic prostate phantom for the validation of the proposed deformable registration.

1.4 Organization of Thesis

The remaining parts of the thesis are organized as follows.

Chapter 2 gives a brief introduction on the TRUS images. The reported work on the prostate segmentation in 3D TRUS images, and the multimodal registration techniques for the prostate in 3D ultrasound images are reviewed.

Chapter 3 presents a statistical deformable model for automatic prostate segmentation in 3D ultrasound image. The real-value spherical harmonics are employed in the parametric representation of the prostate surface. The statistical model obtained from training finally establish the prior knowledge of prostate in no more than 13 model parameters. Using this statistical model, the automatic or semi-automatic segmentation is then formulated as an constrained optimization problem that searches for the proper set of the model parameters (including the shape and pose) to maximize the image gradient aligned with the surface normal, based on the bright-halo appearance of prostate boundary in TRUS images.

Chapter 4 describes a surface-to-image registration method solving the rigid transformation between the pre-operative image and the intra-operative ultrasound image of the prostate. Based on a rigidity assumption, an object surface segmented from the pre-operative image can be merged into the intra-operative ultrasound image by looking for a best fit of the surface with its acoustic correspondence. The similarity measure in this framework is can be customized based on the acoustic appearance of the object selected for registration. Our experiments with the prostate show that this method is effective and accurate. Although not ideal to account for transformation with deformation involved, it can still offer a gross alignment and provide a good initial guess for the boundary detection. In our tests on the pubic arch, registration results using different similarity measures are compared and the best candidate for the acoustic appearance of tissue-bone interface is derived.

Chapter 5 presents a preliminary work on a deformable solution to the registration between MRI and TRUS images of the prostate. This framework includes a rigid registration as the global alignment, and thereafter a nonrigid transformation to refine the remaining deformation. The prostate surface is used for match, and the deformation field is obtained by propagating the displacement determined by the surface match to the whole volume. The thin-plate spline is employed as the radial basis function for the nonrigid transformation. To evaluate the algorithm accuracy, an custom phantom with

the "prostate", the "rectum", the "pubic arch" and surrounding tissues is designed. The registration error is assessed by the fiducial marks implanted in the prostate.

Chapter 6 summarizes the conclusion and suggestion for future work.

Chapter 2

A Literature Review

This chapter provides a literature review on the techniques developed for the prostate segmentation in 3D ultrasound image and its registration with other image modalities for the fusion of information. To get better understanding of the image data used in this study, a brief introduction of the transrectal ultrasound imaging and the image formation is presented in the first part of this chapter.

2.1 Fundamentals of Transrectal Ultrasound Image

2.1.1 Preliminary Knowledge

Ultrasound (US) is a noninvasive imaging technique that produces pictures of the inside of the body by emitting high-frequency (1MHz~10MHz) sound waves and receiving the echo reflection caused by the impedance difference at the tissue interface. Its image is formed by the time delay and the strength of the reflected echo. In view of its safety, real-time capturing capability and low cost, it has been the most commonly used tool for diagnostic imaging and treatment guidance. There are several modes of the ultrasound imaging, A (amplitude) -mode, B (brightness)-mode, M (motion)-mode and Doppler mode. The B-mode ultrasound is one of the mostly used ultrasound for medical imaging. It produces 2D tomographic or slice image of anatomical structure by sweeping the ultrasound beam repeatedly back and forth through the patient's body and modulate

the brightness of the image pixels by the strength of the reflected echo with regards to its time delay along the beam. The sweeping is achieved either mechanically by using a rocking or rotating transducer, or electronically by using an array of piezoelectric elements.

2.1.2 Image construction, quality and processing

Sonographic images are generated with the assumption that sound waves propagate through tissue at a constant velocity and reflect back in a narrow straight line. Based on the reflected signals with respect to the time, the following steps are involved to construct a ultrasound image: filtering, envelope detection, attenuation correction, log-compression and scan conversion [82]. Due to the nature of the ultrasound imaging, there are several intrinsic features of the acoustic image.

Speckle noise

Speckle is a random pattern of reflection scatter and interference occurred in ultrasound imaging. It is formed with coherent radiation of a medium containing many sub-resolution scatterers. Usually, the texture of the observed speckle pattern does not specifically correspond to any underlying structure. Low-pass filtering, adaptive filtering, wavelet and neural network are the mostly used techniques for the ultrasound image denoising.

Image artifacts

Artifacts refer to the findings visible on the ultrasound image but not existing in reality. Image artifacts can occur from a variety of effects. There are several kinds of artifacts commonly seen in ultrasound images, for example, shadowing, posterior enhancement and reverberation. Acoustic shadowing can be caused by partial or total reflection or absorption of the sound energy - a much weaker signal returns from behind a strong reflector (air) or sound-absorbing structure (gallstone, kidney stone, bone). A thin acoustic shadow may occur behind edges of cystic structures. In posterior enhancement, the area behind an echo-weak or echo-free structure appears brighter, or more echogenic, than its surrounding structures. This is because the neighboring signals pass through tissues of more attenuation and return with weaker echoes. Reverberation is an artifact caused by

the ultrasound signal striking a very echogenic surface near the ultrasound transducer. This signal is reflected back and forth between the transducer and the reflector, taking twice as long to reach the transducer as the prior reflection. In the ultrasound image, this phenomenon is exhibited as a echogenic structure followed by a characteristic series of equidistant bright lines in the deeper tissue layer.

2.1.3 Transrectal Ultrasound of Prostate

Transrectal ultrasound (TRUS) of the prostate is one of the B-mode imaging techniques that provide cross section of the gland. The difference of TRUS with the ordinary B-mode scan is that the transducer will be inserted into the rectum and the sound waves is sent and recorded through the rectum wall. For a TRUS biopsy conducted in clinics, the patient is asked to lie left lateral, lithotomy or knee-elbow. After the transducer is covered by a disposable protective cover and properly lubricated, it is inserted through the anus and placed into the rectum. Nowadays, a bi-plane TRUS probe is often used for biopsy in clinics. This probe is able to generate two intersected imaging planes (i.e., transverse and sagittal) in one embodiment. An instrument path is positioned with respect to the planes such that an instrument may be viewed in two imaging planes. With this facility, the biopsy procedure involves inserting a needle into the prostate gland while the radiologist traces the needle advancing with ultrasound.

In TRUS, shadow artifacts may occur due to the difference of attenuation, or a strong attenuation caused by air bubbles or calcifications. The reverberation is usually caused by the rectal wall and the condom covering the probe and results in multiple hyperechoic arches evenly spaced between the rectal wall and the anterior aspect of the image. Such an effect can be avoided by using copious amounts of coupling medium and ensuring no air is between the probe and the rectum [83].

Three-dimensional ultrasound images can be obtained by adding additional rows of crystal elements to permit sweeping in a direction perpendicular to the plane of the B-mode scan. It can also be realized by using the same transducer as that used for 2D TRUS scan but install a motion mechanism inside the probe to make it moving fast along the probe axis. The third choice is to use the existing 2D probe, but attach it with an external

Figure 2.1: 3D TRUS Image formation. (a) Translate the transducer to obtain a series of transverse slices scanned at regular interval along z axis. (b) Tilt the transducer to obtain a series of sagittal slices scanned at regular interval of azimuth around z axis.

motion driver, so that it can be pulled or rotated in a regular speed to get a stack of cross sections of the prostate. Based on the slicing plane of the 2D cross section, two forms of the image data can be obtained. One is the transverse slices and the other is the sagittal slices in cylindrical arrangement. Figure 2.1 show the operational principles of the two modes. Both of them will constitute an image matrix. In the former mode, the voxels are arranged in cartesian format, and the image data is represented as $I(x, y, z)$, with voxels located at the raster grid and the digital value representing the brightness. This is also the image data structure used in this study. In the latter mode, the voxels is arranged in cylinder coordinate and the image data is represented as $I(r, \theta, z)$, with the in-plane voxels located at the polar grid. However, for the convenience of rendering and processing, this format is often converted into the former format by interpolation (also called as sector reconstruction). The quantization of the brightness can be 8-bit (256 levels), 16-bit (65536 levels), or n -bit (2^n levels). The spatical resolution of the voxel can be iostropic or non-isotropic and is usually computed as "(spatial dimention)/(number of voxels along this dimension)", where the spatial dimension is evaluated as the field of view (FOV) of the image when they are collected.

For more details about the physics and signal processing principles of the ultrasound images, please refer to [84, 82]. For the terms used in this thesis, we refer the set of gray values in matrix form as the image data. The boundary is defined as the image appearance that features the interface of the object with repsect to its surroundings in the image. The term contour or surface is independent of the image, however, it can be

a geometric description of the object shape shown in the image.

2.2 Survey on Prostate Segmentation in Ultrasound Image

Image segmentation is one of the first stages in many medical applications using ultrasound. A correct prostate segmentation in the ultrasound image could aid urologists greatly in providing visual means for inspection of anatomic structures, identification of abnormal and tracking of its progress, preparing for surgical planning and simulation, and real-time guidance for biopsy and treatment. Compared to the general segmentation problem in medical images, there are special challenges of the ultrasound image segmentation of the prostate [41, 85].

- Compared to MRI and CT images, the signal-to-noise ratio (SNR) of the ultrasound image is much lower. The adversities from speckle noise, poor contrast between the prostate region and surrounding tissues, missing boundary segment (due to ultrasound's inability to image interfaces that are parallel to the sound beam or hidden by acoustic shadowing caused by calcifications), bowel gas and protein deposit artifacts (corpora amylacea), makes those algorithms relying purely on the image intensity more likely to fail.
- Although the prostate region appears to be relatively dark compared to its surroundings, the texture appearance may vary significantly inside the gland within one image or across different images. Sometimes, it is hard to get an global characterization between the prostate and non-prostate areas, because different tissues may have similar acoustic appearance while tissues of the same kinds may show different appearance over the areas. These may inhibit robust texture recognition.
- Inhomogeneity of the intensity distribution could be observed in both interior and exterior of the gland, due to depth-dependent signal attenuation and direction-dependent edge contrast. The overlap between each other could lead to the failure of the pixel classification depending on the intensity distribution.

A survey on 2D prostate segmentation in ultrasonographic images was written by Shao et al. [86], in which little work was mentioned for 3D. Although a 3D surface can be constructed from a stack of 2D contours detected on sliced cross sections, it may suffer from the vulnerability to broken boundary in a single slice, the variation of segmentation along slicing axes and the error of interpolation between 2D contours [86]. In this section, we will supplement it with more research progresses observed in recent years, especially those for 3D detection. Based on the techniques used in the image analysis, we classify them into two main categories. The first corresponds to the edge-based or texture-based low level image analysis, which totally rely on a mathematical calculation over the image matrix. The second is the model-based methods that determine the image boundary by physically or statistically constrained deformable models.

2.2.1 Segmentation by Low-Level Image Analysis

The segmentation by low-level analysis refers to those techniques purely depend on the mathematical image analysis, such as image filtering, morphological operation, and other matrix convolution and differential calculations. The processing typically searches for an abrupt change of image features between the prostate and background, by means of edge detection [87, 88, 25, 89, 26, 90, 91] or region classification [92, 93].

Edge-based methods

The edge-based detection methods are often seen in 2D boundary detection. The process usually contains four steps: image smoothing and enhancement, edge detection, edge selection and edge linking. A minimum/maximum filtering and zero-crossing technique was used by Aarnink et al. [87] to generate the edge image from ultrasogography. After the false edges were removed by thresholding and pattern fitting in a radial/linear edge searching process, the candidate edges were linked via interpolation. But even with a multi-scale filtering [88], this method still could not avoid erroneous edges at artifacts and shadowing. Liu et al. [25] suggested a radial bas-relief (RBR) method, which could produce an incomplete edge image of the prostate in 2D ultrasound image. To generate a smooth contour, a harmonics fitting approach was proposed [89]. Pathak et al. [26]

and Awad et al. [94] utilized the Sticks filters to selectively enhance the image edges. To reduce speckle, a weak membrane fitting [26] and Gaussian smoothing [94] may be used before Canny's detection. With the false edges removed by knowledge based filtering, the final results can be overlaid on the transversal image as a visual guidance for user delineation. Abolmaesumi et al. [90] also used the Sticks filters for speckle reduction in US image, but they projected equispaced radii from an arbitrary seed point inside the cavity towards its boundary and the prostate boundary was described as the trajectory of an object whose motion is governed by a model from a finite set of known models at any given radii. In Sahba et al.'s work [91], a coarse-to-fine segmentation procedure was proposed. They incorporated image contrast enhancement, Kalman coarse boundary estimation, selective enhancement and the connection of boundary pieces after edge detection. Summarizing the edge-based methods, the main disadvantage is that they are only effective in those images where the boundaries are clearly defined; otherwise they may lead to spurious boundaries in highly textured areas.

To reduce the false-positive points in smooth edge linking, Badiei et al. [95] segmented the prostate using an ellipse fitting on warped US image. The image was first warped by six points selected along the prostate boundary to make the prostate in the warped image look like an ellipse. Then an initial ellipse fit as used to confine and locally guide an edge detector along the boundary. After a more accurate ellipse was fitted to the edge points thereafter, the inverse warp was applied to get the real prostate boundary.

Region-based methods

Rather than trying to find the edges in an image, the regional-based approaches attempt to characterize regions of different tissues from an image on the basis of the texture features. The object boundary is then determined by generating the border between the classified regions. In another word, the region-based method is more like a pixel classifier.

There are a few studies analyzing the prostate texture in ultrasound image [96, 97]. Richard and Keen [92] presented a texture-based algorithm which segments a set of parallel 2D images of the prostate into regions of prostate and non-prostate to form a

3D prostate description. The algorithm was essentially a pixel classifier based on four texture energy measures associated with each pixel in the image. Assuming a Gaussian distribution for each class, the probability of any image pixel belonging to each class was computed, by means of the Bayes's theorem and using the means and variances collected through an automated clustering technique. Each image pixel was then labeled to the class with highest probability. But as they indicated, the effect of using texture information was marginal. Mohamed et al. [98] extracted texture features from US image using Gabor filtering. Pixels with the similar texture characteristics were clustered and labeled to a region. Misic et al. [93] analyzed the texture feature information of the prostate after a polar conversion centered on the central axis of the outlined prostate. The training procedure extracted texture features from the gray level co-occurrence matrix based on the manually segmentation, establishing corresponding feature vectors for the prostate and surrounding tissues. A nearest neighbor classifier was then trained based on feature vectors and utilized for tissue classification. The resulting prostate boundaries were then post-processed by a 4th degree polynomial fitting to eliminate those points falsely identified as the boundary.

Generally, the low-level image analysis have encountered considerable difficulties when segmenting US image. Success of these techniques relies on the preprocessing of the image with respect to a certain pattern of features. When this pattern was deteriorated in US images, the preprocessing or postprocessing becomes unreliable - the false edge points or regions may be included while the true edge points or regions may be excluded. Due to the difficulty of excluding the false edges and generating topology from scattered edges, the segmentation using pure image information has limited applications.

2.2.2 Segmentation by Deformable Models

To address the mentioned difficulties, the deformable models are proposed. The attraction of deformable models is that they can deliver an analytical representation for closed boundaries, which does not have the problems of edge linking. In addition, they offer increased robustness to both image noise and boundary gaps by constraining the extracted boundaries to be smooth and topological. The boundary segments, which may be scattered in low-level image analysis, are inherently assembled to a coherent and con-

sistent mathematical description. Some deformable models are dynamically driven by forces coming from an unbalanced energy between the model physics and the image before they reach equilibrium at the prostate boundary. Although the physically driven models are efficient for segmentation, issues from ultrasound image quality still exist, e.g. edge missing due to shadowing provides no force to "pull" the model while artifact yields unexpected force to trap the model. In such case, a priori knowledge, such as anatomic shapes, physical characteristics, and radiologic features of imaging, would be helpful to improve the detection. Based on these techniques, the commonly-used deformable models for prostate segmentation can be divided into two types, the physical deformable models and the statistical deformable models. The former are contours or surfaces that automatically deform themselves according to physical laws, e.g. Hooke's law to "push" and "pull" the contours or surfaces toward the prostate boundary. The latter characterizes the prostate shape or texture by a set of parameters estimated from a group of training samples, and this information will serve as the prior knowledge in the segmentation.

Physically based deformable models

One of the most well-known physically based deformed models for image segmentation is the Active Contour Model (ACM, or called 'Snakes') proposed by Kass et al. [99]. Using a prime contour for initialization, ACMs deform the contour by minimizing the contour energy including an internal energy from the contour geometry, and an external energy derived from the image. Using a variational method, the imbalance between the internal energy, which maintains the contour's elasticity and smoothness, and the external energy, which draws the contour to the desired image boundaries, is converted into the force that "push" or "pull" the contour. The process finally stops when the contour energy reaches a minimum (force balance). To avoid the curve's being trapped by spurious isolated edge points, an inflation force was added [100], so that the curve is able to stop if the edge is strong or pass through it if the edge is too weak. This balloon model was later extended to a generalized 3D model which used the finite element method (FEM) to search for the solution [101, 102]. To reduce local minima when using ACM, the US image is often smoothed [103, 104, 105] or selectively enhanced [106, 26]. For example, the ACM

was applied on Sticks-enhanced US image in Pathak et al.'s work [106] to locate the 2D prostate boundary, with its initialization generated by user-specified points, or human-aided zero-cross edge detection [87]. To cope with the low SNR in US images, Jendoubi et al. [103, 104] adjusted the rigidity parameter of ACM dynamically on median-filtered image. Zhao et al. [107] utilized a wavelet transformation to decompose the US image into multiscale edge maps, with coarsest edge map determining the initial contour for ACM and finer edge map deforming the contour gradually. Zhang et al. [105, 108] improved the adaptivity of ACM by applying a tree-structured nonlinear filter, directional wavelet transforms and tree-structured wavelet transformation to the US image, so as to suppress noise and enhance boundary. Knoll et al. [109] proposed a coarse-to-fine segmentation more than pure image filtering. They restricted the deformation of ACM by parameterizing the contour in a localized multiscale form using 1D dyadic wavelet transform. The initialization and deformation of the contour were conducted on a multiscale image edge representation using the modulus maxima of 2D dyadic wavelet transform, with the initial contour derived from a binary multiscale pattern matching at coarse scale, and finer scale for refinement. Yet when the prostate boundaries are blurry or not sharply discerned from the background, standard ACMs tend to have difficulty to seek edges. Saroul et al. [110] presented a semi-automatic segmentation using an edgeless active contour model [111]. Its region energy was defined on the assumption of a Rayleigh distribution for the prostate in TRUS image. Unlike the discrete models used before, the analytical formulation of a deformable super-ellipse was inserted directly into the energy function for minimization. But because of the attenuation and inhomogeneity of US image, they had to build up multiple Rayleigh distributions for different parts of the prostate. An initial region inside the prostate was needed as well. Summarizing the shortcomings of ACM methods, they require an initialization for the deformable contour or surface, and this initialization must close to the desired boundary. The ACM using regional force may not have this restriction, but a known partial region of the object is fundamental in establishing good knowledge of its texture features.

Another physical model used for the prostate segmentation is the Discrete Dynamic Contour (DDC) model [112], which is represented by a sequence of vertices connected by straight-line segments that automatically and iteratively deform to fit features in an

image. At iteration analogous to time, the new position of each vertex is derived from a numerical integration of a weighted combination of internal external and damping forces applied. This process continues until all vertices come to a rest. This model was first used by Ladak et al. [27] for semi-automatic segmentation of the prostate from 2D ultrasound images. The authors initialized the DDC using a cubic interpolation through four points selected by user around the prostate. The estimated contour was then deformed automatically to better fit the boundary. In Chiu et al.'s work [113], the DDC model was cooperated with the dyadic wavelet transform, with DDC refining the initial contour based on the approximate coefficients and the wavelet coefficients generated by the dyadic wavelet transform. Wang et al. [33] extended its use in pseudo-3D segmentation, where the image volume was resliced parallel or rotationally to generate a series of cross sections. The surface was then constructed by interpolation through the contours detected using DDC at each 2D image. They needed an initialization in at least one slice. The remaining slices would be initialized iteratively by propagating the refined result from this slice. To ensure a smooth surface, Ding et al. [114] affixed continuity constraints along the rotational 2D segmentations. A direct 3D segmentation using DDC was implemented by Hu et al. [29]. They used a triangular mesh connected at their vertices for the DDC model, with its initial mesh denoted as a warped ellipsoid and generated from six user-specified prostate ends. As indicated in [115], the DDC model was adopted for its proven performance on noisy medical images and simplicity of implementation. However its current use still requires a few user-selected points in the image to establish a coarse approximation (polynomial interpolation) of the prostate contour or surface. A similar 3D deformable model was proposed by Ghanei et al. [30], in which the model was represented by a discrete structure from a set of vertices in 3D triangle facets, with each vertex moving iteratively in time under a weighted sum of an internal force from surface curvature, an external force from image gradient and a damping force from velocity. Their model was initialized by manual outlines at several 2D cross-sections of the volume image.

The level set based methods [116, 117] can be somehow regarded as a geodesic form of the ACMs. They are numerical techniques that track the interface or shape over time with its evolution controlled by a distance map, front characteristics (e.g., curvature,

normal direction and etc) and image characteristics (e.g., gray level, gradient and etc). Different from ACM, it is adaptable to both 2D and 3D image segmentation, and allows a flexible change of object topology as its evolution is in an implicit form. Whereas, most of the level set based algorithms perform unsatisfactory on prostate ultrasound images because of speckle noise, poor contrast, and the presence of acoustic shadowing. Compared with the classic framework with an ellipse initialization [118], region-based level set methods may be more robust. Shao et al. [31, 119, 120] integrated a regional force in the front evolution, using a Gaussian mixture model (GMM) to parameterize the probability distribution of the intensity and discriminate texture statistics between the interior and exterior 3D prostate region. Similar approach for 2D segmentation was proposed by Kachouie [121], where the textures were classified by local binary pattern operator. However, these approaches require proper initial region inside the prostate to start the evolution and meanwhile gain the prior knowledge of texture statistics.

Statistically based deformable models

The statistical model based algorithms use a priori information, such as the general shape or appearance of the prostate in the acoustic image, in the deformable model to locate the object in a given image. After learning the mean and variation from a suitably annotated training set of typical images, the statistical models should be able to capture any plausible example from the population and be generalized to new images. For this reason, the segmentation using statistical model can be considered as a matching procedure to locate the structure in the images using a deformable model with constrained range of variations. Regarding to the prior knowledge used in the segmentation, the statistical models can be classified as shape-based and appearance-based.

Shape-based statistical model

The point distribution model (PDM), proposed by Cootes et al. [122, 123] for Active Shape Model (ASM) segmentation, was one of the most-frequently used statistical shape models for prostate segmentation [72, 124, 125, 126, 34, 42]. In building PDMs, the contour or surface is typically represented by a shape vector consisting of the Cartesian co-

ordinates of a group of labelled landmarks. After a principal component analysis (PCA) on its covariance matrix, the shape vector can be approximated by a linear combination of a reduced number of orthogonal components. In order to determine the landmarks which are not well-defined naturally in the prostate, three different methods have been suggested [123, 72, 127, 125, 128, 42]: manual, equal spaced sampling (equal space in distance or equal angular increment) and the minimum description length (MDL) method. Based on the determined landmarks, intermediary points are inserted at equal intervals along the contour between landmarks. The shape parameters obtained from training set is used as initial guesses and variation constraints in the generation of new shapes similar to those in the training set. The range of model parameters can be either limited within a hyper-box of an upper and lower bound for each corresponding mode of variation, or as a penalty in the shape estimation through Mahalanobis distances towards their normal distributions [123]. This pioneer use of PDMs for prostate segmentation in ultrasound images was Cosio et al. [72, 32]. The prostate of new image was delineated by optimizing a gray level energy function along the normal profile against the constrained shape parameters using a simple genetic algorithm (SGA). Their method was able to find accurate boundaries on some images but the energy function showed minima outside of the prostate boundary for other images [32]. To improve the robustness, a two-stage strategy was proposed [32, 129, 130]. A initial mean model of the prostate is firstly fitted to a binary image constructed from Bayes pixel classification of original US images. With this initialization, the second stage follows the original way of adjusting the PDM to the Gaussian filtered gray level image. The use of 2D PDMs for 3D prostate segmentation was implemented by Wang et al. [33] and Hodge et al. [34]. The 3D surface was constructed by contours detected on parallel or rotational sliced 2D images using independent PDMs built from their respective ranges. Use of 3D PDM for prostate segmentation was found in Heimann et al.'s work [42]. The literature shown that the number of model parameters (including pose and shape) for 2D PDM of prostate is about one third of the number of landmarks. For examples, in [72], when 45 landmarks are used, the prostate contour can be described by 4 pose and 10 shape parameters with 95% coverage of variations. In another modeling using 25 points, 9 principal modes was derived [124, 125]. A much compressed number number was found in Heimann et al.'s report, in which the authors claimed to be able to use 8 principal modes to constitute

approximately 90% of the overall variation of the 3D shape model, which was trained using 642 landmarks for each sample.

Since the more the number of parameters means a more complex multivariate optimization problem, a compact representation of the prostate shape is preferred. The simplest solution is to describe the shape in polar system [127, 131]; by default the landmarks can be determined by equal angular spacing so that only the radial is required in the shape formula. In the feature model reported by Wu et al. [127], the contour originally denoted by 64 points was approximated by 10 parameters for 99.85% shape variation. A coverage of 95% reduced the number to 3. A similar approach was implemented by Liu et al. [131], except that they use the polar PDM model to connect key points detected on smoothed and attenuation-compensated ultrasound image.

An alternative to the radial annotation of PDM is a shape attribute model attached to each landmark [132, 28]. Shen et al. [28] converted the ordered spatial positions of points to attribute vectors, in way of multi-level triangular areas constructed at each vertex. They used the Gabor filter bank, in a multiscale and multiorientation manner, to characterize the prostate boundaries from the noisy US image.

To reduce the number of parameters to be determined in the segmentation procedure, parametric representations have been proposed for shape annotation. The parametric description used for the prostate shape include the Fourier descriptor [35], the hyperquadrics [133], the superquadrics [134, 135, 136, 36], the medial model (m-rep) [137, 138, 139], the superellipses [37, 140] and the spherical harmonics [141, 38]. The segmentation is realized by varying the model parameters to optimize a fitness measure between the model and the image. The Fourier deformable model was used by Staib et al. [35] to segment 3D image by optimizing the integral of boundary strength in image gradient over a given surface. The work by Gong et al. [37, 140] defined a hybrid energy function to maximize the sum of edge strength [26] at the deformable contour under a priori bias of likelihood on shape parameters. Gong et al. reduced the number of parameters to 8 by using a superellipse representation for 2D prostate contour. A hybrid model using superquadrics for global 3D shape and Fourier descriptor for local variations was proposed by Tutar et al. [140], but 52 parameters were required to generate the prostate shape, making it unfavorable for efficient computation. A substitute parameterization

in spherical harmonics successfully consolidated the parameters to a 20-element vector accounting for 99% shape variations [38]. However, the search for the model parameters was determined by minimizing distances between the fitted surface and a point cloud in edge map [26, 37], in which extra attention had to be paid to eliminating false-positive edge points.

Appearance-based statistical model

The first statistical appearance models are described by Cootes and Taylor [142, 143] for the Active Appearance Model (AAM). Because a given point shall correspond to a particular part of the object, the appearance models examine the similar gray-level patterns about that point in images of different individuals and attempt to synthesize the complete appearance of the target image, choosing parameters which minimize the difference between the target image and an image generated from the model, rather than matching a shape model to boundaries in image.

A statistical appearance model can characterize the variability of both shape and texture in a training set. Zhan and Shen [39, 40, 41] proposed a deformable model for automatic segmentation of prostates from 3D US images, by statistical matching of the shape and texture. More than a shape model defined by geometric attribute vectors, they built up another hierarchical texture model using a set of Gabor-supported vector machine (G-SVM) to differentiate Gabor features between tissues along the prostate boundary and adaptively label the prostate and nonprostate region around subsurfaces. Segmentation was realized by minimizing an energy term over the difference on attributes and the Gabor texture labeling.

An alternative to the appearance template is the texture classification using an artificial neural network (ANN). Prater and Richard [144] developed a method for segmentation of the prostate in transrectal ultrasound images using region classification by feed-forward neural networks. Their method segmented the US image to prostate and non-prostate regions using three neural networks trained by a small portion of a training image manually segmented and then applied to the entire training image. Similar approaches were implemented by Zaim et al. [145] and Dokur et al. [146]. They used a self organization map (SOM) neural network to learn image features from thresholded ultrasound image

or wavelet transformed images. The segmentation was implemented by an automatic thresholding over the distribution of feature vectors in multi-dimensional feature space, and a node coloring for difference visualization.

Statistically guided physical model

The role how statistical models play in segmentation is not only via constrained optimization over fitness measures; they can be integrated with the physical model by deriving the initialization from mean shape of training and supervising the deformation from the statistical variations. [132, 147, 148, 149, 150].

M. Leventon et al. [147] reported a deformable model incorporating the geodesic active contours with the prior shape information. The surface was evolved globally towards the maximum a posteriori (MAP) position, and locally based on image gradients and curvature. Y. Chen et al. [148] also integrated the shape priors into the geometric active contour. Instead of using the probabilistic approach, a model based on a variational method was utilized to minimize an energy functional depending on the image gradient and the shape of interest. In this way, the boundary will be captured either by high gradient magnitude or prior knowledge of the shape. Tsai et al. [149] combined shape and region information within the level set framework for segmentation of MRI images. They derived gradient descent equations to optimize the shape and pose parameters that describe the evolving curve. However, energy minimization may be trapped by local minima and the minimization result generally depends on the initial pose and shape of the model. Gong et al. [150] incorporated prior shape model in parametric representation of deformable superellipse, into the level set based prostate segmentation. This model served as constraint to the curve evolution in terms of a shape regularization energy.

2.2.3 Discussion

As indicated by Shao et al. [31], it is unlikely that automatic prostate boundary detection methods will ever replace physicians, but they will likely become crucial elements in prostate disease diagnosis and treatment, particularly in computer-assisted surgery.

The model-based image segmentation has shown superiority over the methods using low-level image processing, in aspects of better resistance to poor image quality, inherent model smoothness and topology. With the assistant of physical models, the image segmentation problem becomes a model deformation procedure which is driven under the influence of the image energy. However, to guarantee a successful boundary localization, the model has to be initialized close to the object boundary in image to ensure it is within the capture range of its deformation. Meanwhile, when the image energy is determined locally, it is vulnerable to weak boundary strength, speckle noise and other interferences in the US image. The introduction of statistical models addresses these problems by integrating general patterns of the prostate in US images so as to provide an automatic initialization (from the mean model) and constrain the model fitting procedure to produce shapes in a plausible range (from the model variation). Compared with the physical model, the integration of prior information in the segmentation shows much better reliability. We believe the future development will follow the direction in model-based approaches, especially those with incorporated prior knowledge and least user intervention.

2.3 Survey on Methods for Prostate Registration

The prostate segmentation in TRUS-guided procedure provides a basis to make a clinical decision. However, due to the limited imaging ability of TRUS, the prostate biopsy and brachytherapy is still conducted aimlessly. Integration of multiple image modalities, such as, MRI, MRS, CT, SPECT and etc, can increase the amount of diagnostic information available to the procedures, and likely to improve the definition for suspected sites and target volume [151]. The prostate registration have been found in the planning for radioactive seed insertion during brachytherapy [66], the dose tracking for targeted prostate radiotherapy [152], the enhancement of image quality during live-time application [56], the comparison of images before and after the treatment, the serial examinations to follow regression/progression of tumor, and etc.

The prostate registration between MRI/MRS and TRUS image is relatively difficult due to some reasons. Firstly, the ultrasound image is of poor quality, often deteriorated by

artifacts and shadows, and may lack of distinguished anatomic information possessed in MR image. Secondly, compared with the pelvic MRI image, the field of view in TRUS image is smaller, only including the prostate, part of the bladder and the pubic arch and the rectum. Thirdly, the two modalities have different tissue response in gray level; the appearance may not have a one to one correspondence during matching. Lastly, there may be significant prostate deformation between the two modalities due to the use of an inflated endorectal imaging probe in MRS. When this deformation can not be neglected, a deformable transformation is required. Another issue is the validation of the nonrigid registration accuracy. It is hard to establish a ground truth, at the absence of anatomic landmarks in US images.

Image registration is a field of intensive studies. The recent reviews have elaborated the registration techniques developed for images [153, 154, 155, 156, 157, 158, 159, 160, 161]. In general, the image registration can be formulated as a procedure that searches for a transformation between two image spaces so that the correspondent features are matched. It usually consists of two basic components: the representation of the transformation and the determination of the related transformation parameters. The transformation representation is generally chosen based on the nature of the object for registration. This determines the degrees of freedom (DOFs) essentially needed to describe the transformation between the two spaces. For an 3D object of high rigidity, such as bone, a rigid transformation, including three parameters for translation and three for rotation, is enough. An affine transformation allows for another 6 DOFs in scaling and shearing. Both of them can be denoted in a linear representation. When more DOFs is required, a nonlinear formula is essential. The deformable transformation is usually represented by polynomial, a linear sum of basis functions, or deformable models with regularized smoothness. The parameters in the chosen representation, is then determined by a least-square solution, an interpolation through explicit correspondences, or an optimization of a similarity measure.

Table 2.1 lists the general choices used for rigid or nonrigid transformation. Determination of their parameters is somehow related to the availability of explicit correspondences between the source and target, and the selected form of the transformation. If, for example, corresponding landmarks can be identified straightforward (e.g. by human) in

Table 2.1: Representation of 3D transformation.

Transform (DOFs)	Representation	Examples
rigid (6) affine (≤ 12)	linear	
deformable (> 12)	polynomial basis function deformable model	thin-plate spline, B-spline, etc elastic solid, viscous fluid, diffusion model, etc

two image modalities, when the transformation is assumed to be rigid, the parameters can be solved as a least-square problem. When a nonrigid transformation is required, the deformation can be described by an volumetric interpolation through the displacement vectors at sparse landmarks. However, when there is no intuitive correspondences established, the transformation is then solved by optimizing a measure in intensity or distance. The transformation parameters will be iteratively refined from an initial guess according to the change of the measure, and stop until it reaches maximum similarity or minimum difference.

Limited by space, we only concentrate on those techniques proposed for the prostate with ultrasound modality involved. Nevertheless, compared with the overall work on medical image registration, much less work have been reported in this particular area. Therefore, we also include some techniques which were not originally proposed for US image purpose, but can be extended to this application. For simplicity, we classified these algorithms into rigid and deformable methods, based on the rigidity condition of the prostate between the two scans.

2.3.1 Rigid Registration

Rigid registration of the prostate is used in the cases when the scanning conditions are similar, tracking the prostate in a series of images, or determining a rough alignment before the application of a nonrigid technique. Manual registration has been used where an operator cues on segmented structures or anatomical landmarks in the pelvis [162, 53]. This tedious procedure has been automated by some computer-assisted algorithms. According to the data used in calculation, we subdivided them into surface-based, intensity-based or a combination of both. For simplicity, the affine transformation (with extra

freedom for scaling and shear) is also included in this category.

Surface-to-surface methods

Verbally, this techniques utilize the geometric information of the prostate in registration. The geometric data can be point sets with known correspondence, the dense point clouds denoting surface, and etc. Registration using correspondent point sets require intra-prostatic fiducial markers implanted purposely for registration [163, 164], or landmarks, such as prominent geometric features such as corners and intersections of edges identified from both images [162, 63, 54]. Based on a one-to-one correspondence in the point-based registration, a least-square solution can determine the decoupled translation and rotation [165]. The surface-based techniques, although denoted in points as well, do not require an explicit correspondence between the points. They are either formulated as an alignment by principal axes, such as the principal axes registration [166], or an optimization problem which minimizes distance measures, such as the iterative closest point (ICP) algorithm [57] and the chamfer matching algorithm [167, 58, 151]. Fontenla et al. [63] accounted for the affine transformation of the prostate between 2D planning and treatment scans by registering the bony anatomy [168] and thereafter the prostate surface. Kaplan et al. [54] selected six apexes on the prostate shape to fuse MRI information into the transperineal ultrasound guided prostate biopsy. Zaider et al. [61] and Mizowaki et al. [62] aligned the 2D prostate contours in MRS with those in TRUS, assuming a linear scaling in orthogonal directions. In comparison with the marker-based approaches, registration using data directly obtained from the patient image would be a better choice.

In general, the surface-to-surface algorithms often require significant user interaction for identification of markers/landmarks and delineation of object surfaces. But also due to the extraction of data, the computation required in registration becomes less.

Image-to-image methods

The image-to-image registration techniques, also referred as intensity-based approaches, are based on correlation of the entire gray-value volumes. This correlation is often

evaluated as similarity in form of absolute intensity difference, or histogram, such as mutual information (MI), normalized MI, correlation coefficient (CC), correlation ratio (CR) and etc [169, 170, 171, 172, 55, 173]. There is a vast literature on the definition and use of these image intensity information [174, 56, 175, 176, 177, 178, 179].

Voxel-based similarity measures have shown to be robust aligning images obtained from different modalities, and could be user intervention free [158]. A key advantage of these methods based on intensity correlation quality metrics is that tissue segmentation is not required, but long computation time is required for the optimization of cost function. However, use of the intensity information for the registration of ultrasound images against other modalities is challenging [180]. There are quite few literature for the registration between MRI and US scans of the prostate. A related work was implemented by Castro-Pareja et al. [181]. They used the mutual information as the similarity measure in the rigid registration between 3D CT images and US images of prostate. But to ensure its effectiveness, both images have to go through a series of preprocessing and image cropping for region of interest.

Surface-to-image method

In comparison with the two approaches, the surface-to-image techniques take advantages from both the surface and the image, as the segmentation from pre-operative image has no time constrain while least image processing is required in the live time guidance. A real-time tracking of the prostate surface in 3D TRUS image was proposed by our team [73]. This surface can be segmented from any modality (including 3D TRUS) and registered to the intra-operative 3D TRUS image by maximizing the image gradient on the referred surface. A similar work was presented by Brendel et al. [182, 183]. They registered the CT and US datasets using bone structure and defined the similarity measure as the averaged gray value at the bone-tissue interface.

2.3.2 Deformable Registration

Researches have noticed that there could be deformation between different imaging modalities for the prostate, due to different rectal filling and change of patient pos-

ture [59, 60]. When the magnitude of prostate deformation is significant, it shall not be neglected during the biopsy and treatment planning. A number of reported work have taken this into account.

One form of the nonrigid representation is to constitute it by piece-wise rigid transformations. Srikanthana et al. [184] described a neural computation based nonrigid registration of the prostate surfaces in this form. The hybrid approach combined registration without exact point correspondence via multi-object principal axes, and registration with point correspondence via polynomial transformation. Based on a mixture of probabilistic principal axes transformation, a neural network interpretation of the Expectation Maximization (EM) algorithm was used to integrate the individual principal axes solutions for each object in a committee machine formulation and to obtain the polynomial transformation based on extracted control points using a multi-layer perceptrons. Another polynomial form of the deformable transformation was used by Wu et al. [71], for the study of the prostate motion with and without MRS coil. The polynomial coefficients were obtained by optimizing a cost function, which consisted of a similarity energy in mutual information and a regularization energy for the smoothness of the deformation field.

The deformation field can also be denoted as spatial interpolation using radial basis functions, such as thin-plate spline (TPS) [185] or B-spline [186, 187, 188]. Lian et al. [189, 68] studied the feasibility of TPS for the registration of distorted MRI/MRSI data with CT images in phantom deformation. When applying on patient data, they selected four to eight landmarks as the control points used in TPS. Same method was used by Venugopal et al. [69] to implement a nonlinear registration method to account for the prostate deformation between the coil-inflated and coil-deflated MRI/MRS. Fei et al. [56] also utilized the TPS based transformation in the deformable registration between high-resolution MR volumes and live-time iMRI images. To determine the control points, they proposed a semiautomatic detection of feature points [185] in the MRI images, based on 5 manually defined points. They used a multi-resolution solution to refine the correspondence of the detected points and two similarity measures, correlation coefficient and mutual information were adopted for lower resolutions and full resolution, respectively. An octree-spline elastic registration [190] was used in Reynier et al's work

[191] for the integration of 3D MR with 3D TRUS of the prostate. This method used an adaptive, hierarchical and regularized free-form deformation (FFD) based on B-spline and a Levenberg-Marquardt optimization to minimize a distance measure. The hierarchical multi-resolution of the FFD based on B-Splines was also found in Abolhassani et al's work [192] for improving the dosimetry planning in prostate deformation. Their algorithm consists of a global transformation and a local transformation, in which the normalized mutual information was used as the similarity measure. Same measure was used by Castro-Pareja et al. [181] for the prostate registration between treatment planning CT and daily 3D US images. Although the elastic registration was still performed on a 3D grid of B-Splines, the compressibility and rigidity of the deformation field were controlled by a ChainMail algorithm [193]. To avoid the computation over whole image region, Schreibmann et al. [70] applied a narrow band on the deformable model of B-spline FFD. The signed narrow band acted as a shape representation model and was defined on the CT image for prostate and rectum based on the physician-delineated contour. The calculation of the normalized correlation between intensities was restricted to those points contained in the narrow band. Greene et al. [194] also proposed a constrained nonrigid registration algorithm using B-spline FFD. But they forced the control points that lie within the segmented objects to the positions estimated by individual registration of the organs and bones.

Biomechanical models are one of the most frequently used techniques for the registration of prostate between MRI and US images. To compute deformation in the prostate image, the equations are solved in finite element model (FEM), with known boundary conditions or external forces. The boundary conditions are usually specified on some of the nodes in terms of node displacements. Although these displacements are not directly available, they can be derived from a matching of surface regarding to the shifting or change of the object shape visible in the images. Xuan et al. [195] implemented a surface-spine model for the surface match between prostates, in which the surface deformation is governed by Lagrangian motion equations. Yan et al. [196] performed pioneering work on deformable image registration using FEM to calculate fractionated dose in a deforming organ. They segmented a single tissue type, and used fiducials to set boundary conditions. Bharatha et al. [64] evaluated a deformable procedure using FEM of isotropic linearly elastic

material to improve the intra-operative data by pre-operative information. Different material properties was assigned to the central gland and peripheral zone created from pre-operative images. The boundary surface extracted from mesh was then treated as an elastic membrane and deformed iteratively to match the corresponding surface segmented from intra-operative images. The surface deformation obtained from the active surface matching were finally used as inputs in FEM to infer a volumetric field. Instead of the evolving surface matching, Crouch et al. [65, 197] used the m-rep model [137] to represent the prostate surface in both images. When the m-rep models are fit to the deformed and undeformed prostate, they can build up an automatic boundary correspondence for FEM, based on their medial geometry. Before the use of FEM to solve the volumetric warping, Haker et al. [198] modelled the prostate surface as a thin elastic sheet and registered it to the intra-operative surface by an augmented conformal mapping (angle-preserving) with thin-plate spline allowing for pre-specified landmark correspondences defined between surfaces. Hensel et al. [199] developed a multiorgan finite element deformable method for MRS scans acquired with and without an ERC. Similarly they mapped the surface of the bladder and rectum between two images first, then calculated the deformation of the prostate through biomechanical properties. The FEM deformation by external forces was seen in Alterovitz et al's work [200, 201]. The presented prostate model used a 2D FEM and optimized both the applied force vectors and the tissue stiffness parameters to estimate the deformation of the prostate and surrounding tissues. The objective function was defined to maximize the Dice Similarity Coefficient (DSC) and minimize the dependence on external forces. As compared to other biomechanical models, the optimization of stiffness parameter gave an additional in-plane flexibility, but the force vectors came from the image intensity measures which had little value for ultrasound images. In addition, its limitation to two dimensions prevented it from representing any out-of-plane deformation.

Another special technique is a combination of statistical model and biomechanical model. In order to estimate the prostate deformation caused by TRUS probe insertion, Mohamed et al. [66] built up a patient specific biomechanical model to run simulations under different TRUS probe insertion. They extracted the main modes of the prostate deformation and used this information to establish a statistical motion model. This

model was then used in registration to estimate the deformation under known TRUS probe position. Hu et al. [67] also proposed a patient-specific statistical motion model (SMM) of the prostate gland in 3D TRUS image. Similarly, they simulated the motion of the gland using an US-based 3D FE model over a range of plausible boundary conditions and soft-tissue properties. The SMM was then used to both predict the displacement field over the whole gland and constrain a deformable surface registration algorithm. The registration of the deformable gland model to the target surface points was realized by optimizing the weights of the principal modes of variation of the SMM such that the distance between the target point set and the deformed model surface was minimized. This SMM was extended to non-rigid registration between pre-operative MR images to intra-operative TRUS images of the prostate [202], where the prostate surface in MR images was segmented and used for motion training. In the registration, vector representations of this surface, i.e., the surface normal vector field, were computed independently from the MR-derived model and the 3D TRUS image. Expressing the coordinate and normal of a image voxel as a probability mixture model, the registration searched for the optimal transformation parameters by maximizing the likelihood function using EM algorithm.

2.3.3 Discussion

There are several considerations in developing the algorithm to register MRI/MRS and 3D US images of the prostate. First, preprocessing of the US images should be kept at a minimum level to ensure a real-time performance of the algorithm, while there is no such restriction exists for the MRI/MRS images because they are scanned pre-operatively. This makes the surface-based registration unsuitable in the intra-operative situation where delineation of surface is time-consuming. Likewise, complicated US image processing is unfavorable as well. Second, ultrasound images have an inherently high level of speckle noise and a smaller field of view than the MRI images. Besides the prostate, the pubic arch is the most reliable anatomical structure sufficiently visible in 3D TRUS images of the prostate. And because it is a rigid object, the use of this information could be helpful in registration. Third, the lack of correspondent structural appearance in US images is detrimental to the success of intensity-based registration

algorithms.

A deformable registration is required to account for the significant prostate deformation due to rectal filling. FEM can provide a method modeling the physical deformation caused when the MRS endorectal imaging probe compresses the prostate. But it requires substantial work on constructing a patient-specific finite element model and there is difficulty to determine an appropriate set of boundary conditions for this model. In addition, the elasticity and density constants for various tissues are not readily available and have to be found by a trial and error procedure. Moreover, the computation needed to solve the resulting large system of equations is huge [197].

In comparison, the spline interpolation based on correspondent landmarks is computationally efficient. But the problem of determining the correspondences from the two images still exists. Although the intensity based measure is infeasible in this case, it is yet possible for us to follow the idea of selecting surface landmarks, not manually, but automate this process by searching the geometric features from the surface.

Chapter 3

Automatic Prostate Segmentation in 3D Ultrasound Image

To assist the urologist to segment the prostate in TRUS-guided procedures, an automatic 3D prostate segmentation method is proposed in this chapter¹. This method utilizes a statistical deformable model, which is built upon a parametric representation of the prostate shape in real-value spherical harmonics, and the original ultrasound image data, which is collected intra-operatively, for the segmentation. With the prior knowledge obtained from a large number of training samples, the segmentation becomes an constrained optimization problem that searches for the proper shape and pose parameters that can maximize a similarity (i.e., formulated in the objective function) between the parametric surface and its acoustic appearance in the image. By default, the proposed method works fully automatically. To cope with adverse image qualities, such as insufficient scan of the gland, image artifacts or deteriorated boundary, it can incorporate with some image-specific prior knowledge specified by user, such as an indication of the region of interest, so as to narrow the search range of the pose parameters for higher accuracy. Compared with other statistical methods proposed for the 3D prostate segmentation, the proposed method requires less number of model parameters and has less image operation involved. The resulted speed is promising for a real-time application.

¹Materials reported in this chapter have been submitted.

3.1 Introduction

According to the conclusion declared in the literature review, the methods depending on the low level image analysis and physical models are susceptible to image noise and sensitive to the initialization, while combining prior knowledge in the prostate segmentation can dismiss the dispensable human initialization and constrain the shape in a plausible range, leading to a more robust performance. Compared to the traditional statistical shape models, such as the point distribution model (PDM) [123], the parameterized shape models are able to produce a coarse-to-fine representation of the shape using much less parameters. The global nature of the surface parameterization could also eliminate the landmark labeling required during the training. These improvements are shown not only in a more compact representation of the surface data, but also in a reduced dimension involved in the multivariate optimization during the model fitting for segmentation. As for the use for real-time TRUS, it is ideal to utilize the original image data rather than applying complicated processing which not only takes time, but also may introduce false results.

Similar to other statistical approaches for segmentation, the proposed method will solve the problem in two steps – model training and model fitting. Figure 3.1 shows the block diagram of the proposed method. The model training procedure captures the prior knowledge of the prostate from a large number of training samples and builds up the statistical model for its shape and pose in the ultrasound image. The model fitting procedure varies these model parameters in the optimization procedure and determine the proper values that can denote the prostate surface in the new image. Although the existing parametric statistical shape models have had improvement to the point distribution model, the number of parameters is still challenging for an optimization problem. In this study, it is found that the real-value spherical harmonics is able to describe the 3D prostate surface in a coarse-to-fine manner and halves the number of parameters required for the complex-value spherical harmonics. The principal component analysis (PCA) will construct a further reduced data dimension for the shape descriptor, thus a few parameters are sufficient to denote the surface in the image. When applying the prior knowledge in the model fitting procedure, the segmentation is formulated as a constrained optimization problem that searches for the proper values of the model

Figure 3.1: The block diagram of the proposed segmentation method.

parameters in the new image. To reduce the possible errors caused by image processing and also save the computation time for live time application, the object function is defined directly on the gray level of the TRUS images. There are two working modes for this method. One is the automatic boundary detection and the other is to incorporate with a user-specified region of interest (ROI). The latter is helpful to deal with images of poor qualities.

Figure 3.2: The definition of the spherical system.

In the following part, we will explain the principal of the spherical harmonics and its real-valued expression (section 3.2), the procedure of building the statistical model from the harmonics coefficients (section 3.3), and the segmentation procedure that utilizes the statistical deformable model on new images (section 3.4). Validation with respect to expert annotation is conducted to verify the feasibility and accuracy of this method (sections 3.5 and 3.6).

3.2 Global Shape Description Using Real-Value Spherical Harmonics

3.2.1 Spherical Harmonics

Normally, a 3D shape can be represented by a set of points sampled on the surface. The Cartesian form of the surface points, (x, y, z) , can be converted into the spherical coordinate system (r, θ, ϕ) , as shown in Figure 3.2, with r denoting the radial, $r \in [0, \infty)$, θ denoting the polar (colatitudinal) coordinate, $\theta \in [0, \pi]$, and ϕ denoting the azimuthal (longitudinal) coordinate, $\phi \in [0, 2\pi)$. When the shape is single-valued at the radial component r , the bijective mapping between (x, y, z) and (r, θ, ϕ) can be established (Table 3.1).

Spherical Harmonics (SH) are originated from the angular part of the Laplace's equation

Table 3.1: Conversion between Cartesian coordinate system and Spherical coordinate system.

Cartesian system	Spherical system
$x = r \sin \theta \cos \phi$	$r = \sqrt{x^2 + y^2 + z^2}$
$y = r \sin \theta \sin \phi$	$\theta = \cos^{-1} \left(\frac{z}{r} \right)$
$z = r \cos \theta$	$\phi = \begin{cases} \cos^{-1} \left(\frac{x}{\sqrt{x^2 + y^2}} \right) & \text{if } y \geq 0 \\ 2\pi - \cos^{-1} \left(\frac{x}{\sqrt{x^2 + y^2}} \right) & \text{if } y < 0 \end{cases}$

defined in 3D spherical coordinates [203],

$$\left[\frac{1}{\sin \theta} \frac{\partial}{\partial \theta} \left(\sin \theta \frac{\partial}{\partial \theta} \right) + \frac{1}{\sin^2 \theta} \frac{\partial^2}{\partial \phi^2} + l(l+1) \right] Y_l^m = 0 \quad (3.1)$$

The spherical harmonics, $Y_l^m(\theta, \phi)$, are obtained as the decompositions of a spherical function defined on the unit sphere,

$$Y_l^m(\theta, \phi) = (-1)^m \sqrt{\frac{2l+1}{4\pi} \frac{(l-m)!}{(l+m)!}} P_l^m(\cos \theta) e^{im\phi} \quad (3.2)$$

where $P_l^m(x)$ is the associated *Legendre* function defined as

$$P_l^m(x) = \frac{(-1)^m (1-x^2)^{m/2}}{2^l l!} \frac{d^{l+m}}{dx^{l+m}} (x^2 - 1)^l \quad (3.3)$$

where l is a non-negative integer denoting the degree and m is an integer in the range of $[-l, l]$ denoting the order. The *Legendre* polynomials $P_l^m(x)$ can be computed using a closed-form formula. But it may lead to numerical instabilities and inefficiency. Hence it is recommended to use the explicit calculation in single precision (32-bit) for l no more than 6 or 8, or in double precision (64-bit) for l no more than 15 or 18 [173]. For higher degrees, a recursive computation is preferred and defined as follows,

$$\begin{aligned} P_0^0(\cos \theta) &= 1 \\ P_m^m(\cos \theta) &= (2m-1) \sin \theta P_{m-1}^{m-1}(\cos \theta) \\ P_{m+1}^m(\cos \theta) &= (2m+1) \cos \theta P_m^m(\cos \theta) \\ P_l^m(\cos \theta) &= \frac{(2l-1) \cos \theta P_{l-1}^m(\cos \theta) - (l+m-1) P_{l-2}^m(\cos \theta)}{l-m} \end{aligned} \quad (3.4)$$

Figure 3.3: The real (red color) and imaginary (blue color) components of the complexed spherical harmonics basis function (degree $l = 0, 1, 2$).

The spherical harmonics satisfy two important properties. One is the symmetry

$$Y_l^{-m}(\theta, \phi) = (-1)^m \overline{Y_l^m}(\theta, \phi) \quad (3.5)$$

The other is the orthogonality,

$$\int_0^{2\pi} d\phi \int_{-1}^1 d(\cos \theta) Y_l^{m'*} Y_l^m(\theta, \phi) = \delta(l', l) \delta(m', m) \quad (3.6)$$

Therefore, the spherical harmonics form an orthonormal basis for the spherical functions. But due to the presence of item $e^{im\phi}$, the spherical harmonics are in complex form. For example, Figure 3.3 demonstrates the real and imaginary components of the harmonics $Y_l^m(\theta, \phi)$ with $l \leq 2$. The complex form of the basis functions, however, do not fit with most of the applications which involve only real-value functions. Therefore, it will be more reasonable if a real-value form can be used.

3.2.2 Real-Value Spherical Harmonics

The real-value spherical harmonics are defined in terms of their complex analogues. We can choose their real forms by combining complex conjugate functions, corresponding to opposite values of m , based on the spherical symmetry of the complex dependence in ϕ , $e^{im\phi}$. In this way, the real-value spherical harmonics are defined as

$$S_l^m(\theta, \phi) = \begin{cases} \frac{(-1)^m}{\sqrt{2}}(Y_l^m + \bar{Y}_l^m) = \Theta_l^m(\theta)\sqrt{2}\cos m\phi & m > 0 \\ Y_l^0 = \Theta_l^0(\theta) & m = 0 \\ \frac{(-1)^m}{i\sqrt{2}}(Y_l^{|m|} - \bar{Y}_l^{|m|}) = \Theta_l^{|m|}(\theta)\sqrt{2}\sin |m|\phi & m < 0 \end{cases} \quad (3.7)$$

This derivation produces the signless real-value spherical harmonics, which seems to be the most common basis in use. It can be succinctly written as:

$$S_l^m(\theta, \phi) = \Theta_l^{|m|}(\theta)\Phi_m(\phi) \quad (3.8)$$

where

$$\Theta_l^m(\theta) = \sqrt{\frac{2l+1}{4\pi} \frac{(l-m)!}{(l+m)!}} P_l^m(\cos \theta) \quad (3.9)$$

$$\Phi_m(\phi) = \begin{cases} \sqrt{2}\cos m\phi & m > 0 \\ 1 & m = 0 \\ \sqrt{2}\sin |m|\phi & m < 0 \end{cases} \quad (3.10)$$

Given the definitions in Equation (3.9) and (3.10), the real-value spherical functions have the same symmetry and orthonormality as the complexed form (see Figure 3.4). For simplicity, we may use the same annotation Y_l^m to denote the following real-value spherical harmonics.

3.2.3 Shape Descriptor

The classic spherical harmonic is considered as a type of Fourier representations, but limited to "star-like" or convex surfaces, i.e., surfaces obtained by deforming a sphere by moving points only in the radial direction [35]. Given a "star-like" object shape (i.e.,

Figure 3.4: The real-value spherical harmonics basis function (degree $l = 0, 1, 2$).

single-valued on r) with its center at the coordinate origin, its spherical function $f(\theta, \phi)$ can be decomposed into a series of spherical harmonics,

$$f(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^l C_l^m Y_l^m(\theta, \phi) \quad (3.11)$$

where the harmonic coefficients C_l^m , also regarded as the shape descriptor in the literature, provide a measure of the spatial frequency constitutes that compose the shape [141]. Low order coefficients capture gross shape characteristics while higher order coefficients represent surface variations of higher spatial frequency [204]. Thus, the shape function can be approximated as a finite sum of spherical harmonics

$$f(\theta, \phi) \approx \sum_{l=0}^L \sum_{m=-l}^l C_l^m Y_l^m(\theta, \phi) \quad (3.12)$$

where L denotes the highest degree which controls the level of approximation of the 3D shape.

To compute the shape descriptors C_l^m , two methods are available [205]. The first is the *direct method* which projects the sampled points onto the basis of real-value spherical harmonics Y_l^m ,

$$\begin{aligned} C_l^m &= \langle f(\theta, \phi), Y_l^m(\theta, \phi) \rangle \\ &= \sum_{i=1}^{N_1} \sum_{j=1}^{N_2} \hat{f}(\theta_i, \phi_i) \cdot Y_l^m(\theta, \phi) \cdot \Delta\phi \cdot \sin\theta_i \cdot \Delta\theta \end{aligned} \quad (3.13)$$

where $\hat{f}(\theta_i, \phi_i)$ is the sampled function value at (θ_i, ϕ_i) , i.e., the radial coordinate of the i -th point. N_1 and N_2 are the number of samples in θ and ϕ , respectively. $\Delta\theta$ and $\Delta\phi$ are the sampling steps. This method requires that the surface points must be sampled at a regular mesh of θ and ϕ . The other choice, the *least-squared method*, is used more often and does not have such limitation. The harmonic coefficients, C_l^m , can be estimated by minimizing the sum of the square errors between the 3D surface and its functional approximation [206]:

$$e = \sum_{i=1}^n \left[f(\theta_i, \phi_i) - \hat{f}(\theta_i, \phi_i) \right]^2 \quad (3.14)$$

over the n points regularly sampled on the surface.

According to Equation (3.12), in order to represent a spherical function using the set of spherical harmonics of highest degree L , $N = (L+1)^2$ harmonic coefficients are required to be determined. When the spherical function is described by a set of spherical samples (θ_i, ϕ_i) and their function values $r_i = f(\theta_i, \phi_i)$, for $1 \leq i \leq n$, a linear system can be formulated as follows

$$\mathbf{f} = \mathbf{Y} \cdot \mathbf{c} \quad (3.15)$$

where $\mathbf{f}$ is a column vector of n elements denoting the array of the radial coordinates, r_i , of the points sampled on surface at (θ_i, ϕ_i) , where $i = 1, 2, \dots, n$.

$$\mathbf{f} = [r_1 \ r_2 \ r_3 \ r_4 \ \dots \ r_n]^T \quad (3.16)$$

$\mathbf{Y}$ is the $n \times N$ matrix ($n > N$) with its row elements denoting the values of the set of the harmonics, i.e., $\{Y_0^0, Y_1^{-1}, Y_1^0, Y_1^1, \dots, Y_L^L\}$, at the respective spherical sampling (θ_i, ϕ_i) ,

$$\mathbf{Y} = \begin{bmatrix} Y_0^0(\theta_1, \phi_1) & Y_1^{-1}(\theta_1, \phi_1) & Y_1^0(\theta_1, \phi_1) & Y_1^1(\theta_1, \phi_1) & \dots & Y_L^L(\theta_1, \phi_1) \\ Y_0^0(\theta_2, \phi_2) & Y_1^{-1}(\theta_2, \phi_2) & Y_1^0(\theta_2, \phi_2) & Y_1^1(\theta_2, \phi_2) & \dots & Y_L^L(\theta_2, \phi_2) \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ Y_0^0(\theta_n, \phi_n) & Y_1^{-1}(\theta_n, \phi_n) & Y_1^0(\theta_n, \phi_n) & Y_1^1(\theta_n, \phi_n) & \dots & Y_L^L(\theta_n, \phi_n) \end{bmatrix} \quad (3.17)$$

$\mathbf{c}$ is the column vector of N elements representing the array of harmonic coefficients corresponding to the set of harmonics.

$$\mathbf{c} = [C_0^0 \ C_1^{-1} \ C_1^0 \ C_1^1 \ \dots \ C_L^L]^T \quad (3.18)$$

Based on the over-estimated linear system, minimizing Equation (3.14) is same as solving the normal equation $\mathbf{Y}^T \mathbf{Y} \mathbf{c} = \mathbf{Y}^T \mathbf{f}$ using the least squared method [207, 206]

$$\mathbf{c} = (\mathbf{Y}^T \cdot \mathbf{Y})^{-1} \cdot \mathbf{Y}^T \cdot \mathbf{f} \quad (3.19)$$

3.3 Statistical Modeling

In medical images, the general shape, location and orientation of an organ is usually known. The statistical shape model aims at capturing this *a priori* knowledge and integrating it into the deformable model in form of initial conditions, data constraints, constraints on the model parameters in the model fitting procedure.

Unlike the point distribution model, the surface model built from the spherical harmonics based representation is a coarse-to-fine global shape representation thus does not require an explicit landmark labeling. As the surface can be decomposed to a weighted sum of harmonics, when each training individual shares the same angular sampling, the correspondence are inherently guaranteed and the harmonic coefficients become the only parameters needed to be studied by the statistical model.

3.3.1 Preparation of Training Data

We have developed a friendly graphic user interface (GUI) for the interactive boundary delineation so that our experts can manually outline the prostate boundaries from 3D ultrasound images. These boundaries data are used to build a statistical model.

The software is implemented using object-oriented C++ language, as well as libraries from Qt (Trolltech, acquired by Nokia in 2008) for the GUI design and Visualization toolkit (VTK, Kitware) for image and graphics visualization. The stack of 2D image slices or a single 3D image volume is displayed in three orthogonal views including transversal, sagittal and coronal (Figure 3.5(a)). The user can outline a closed contour by specifying several points along the prostate boundary in transversal view. The 2D contour is generated by connecting the points using Non-Uniform Rational B-Spline (NURBS) [208]. Likewise, the prostate surface is generated by interpolating through a stack of parallel 2D contours using NURBS (Figure 3.5(b) and 3.5(c)).

In the utilization of NURBS for prostate shape construction, the image boundary is formulated as a 3rd-degree closed NURBS curve, $C(u)$, $0 \leq u \leq 1$, while the prostate surface in NURBS, denoted as $S(u, v) = [x(u, v), y(u, v), z(u, v)]^T$, is constructed by skinning through the contours $C_i(u)$ drawn on selected slices with two ends closed at the base and the apex. Parameter u is defined clock-wisely in the transversal plane and v defined along direction from inferior to superior. For the brief introduction on NURBS curve and surface, please refer to Appendix A and B. For more details, please refer to [208].

As suggested by Chalana and Kim [209], a delineation produced by a single observer is not a suitable gold standard. They recommended to form a suitable gold standard by averaging the manual outlines built from multiple observers. So, we recruited two observers trained by experienced urologists from Singapore General Hospital, and radiologist from National Cancer Center Singapore. Among the training samples, the first dozen were outlined by the medical experts or by our observers but under the supervision of the experts. The rest were processed by the trained observers independently. The final expert annotation is generated by averaging the two surfaces in radial direction.

(a)

(b)

(c)

Figure 3.5: Boundary delineation and surface construction. (a) Boundary delineation on one slice. (b) Stack of contours. (c) Surface construction.

Figure 3.6: The averaged expert interpretation. The yellow and green boundary denotes the delineation from two observers. The boundary in red color demonstrated their average.

3.3.2 Normalization of Training Set

The normalization accounts for inter-individual morphological variability and allows the direct superposition and comparison of images from a large group of patients, thereby enabling image statistics calculation [52]. Although the scanning condition for each data set is almost the same, the prostate shape, size and location can vary considerably between individuals. It is documented that the prostate volume may vary from 30cc to 80cc. So it is necessary to consider the scaling factors before analyzing the shape descriptors in our statistical model; otherwise the radial values of each individual are not comparable. The procedure of transforming the samples to a common reference system is known as normalization. As a result, the statistical model for prostate shape detection in TRUS image shall include two parts – the first is the pose parameters (also referred as transformation parameters) that normalize the training sets; the other is the shape parameters that characterize the normalized shape descriptors.

Normalizing the training samples may include the following transformations:

- Translation – A translation vector $(t_x, t_y, t_z)^T$ is required to move the samples to a common spherical system (overlapping their centroids).
- Rotation – Sometimes, the prostate does not perfectly lie symmetric in the transverse view. It may be rotated by an angle due to an improper operation of the transrectal probe. But this rotation can be avoided by adjusting the probe angle properly.
- Scaling – The scaling transformation is to ensure all samples are at the same level of volume, so that they can hold comparable shape descriptors. The scaling is anisotropic, represented as the scaling vector $(s_x, s_y, s_z)^T$.

3.3.3 Uniform Sampling in Parameter Space

In order to process every sample equally, we need to choose a homogeneous point distribution on the surface, so that they can approximate the shape with maximum similarity. There are various sampling strategies for this purpose. However a pre-requisite of building our statistical model is that the sample data should share the same spherical harmonics, which means they should have the same (θ, ϕ) sampling.

The NURBS surface formulation shows that the (u, v) parameters are parameterized according to the chord length in the orthogonal directions. Given the number of samples M in $0 \leq u < 1$ and N in $0 \leq v \leq 1$, a uniform sampling in (u, v) space may generate points along the orthogonal (u, v) directions with approximately equal chord length respectively, resulting in a $M \times N$ mesh of (θ_i, ϕ_i) samples, as shown in Figure 3.7(a). However, between different individuals, the resulted (θ, ϕ) sampling may not be the same. Hence, this sampling policy is unsuitable.

An alternative is to sample the (θ, ϕ) parameter space homogeneously (Figure 3.7(b)). Nevertheless, the NURBS tool does not provide a direct facility to generate uniform points on surface in (θ, ϕ) parameter space. A ray-intersection strategy was therefore developed to generate these points: a 3D mesh at uniform (u, v) values is generated first using NURBS surface function. This mesh is then triangulated. For each set of (θ_i, ϕ_i) in their homogeneous distributions, a ray originating from the centroid and along the designated direction will intersect with one of the triangles and the resulted intersection

Figure 3.7: Oblique views of the surface points (a) sampled uniformly in (u, v) parameter space, (b) sampled uniformly in (θ, ϕ) spherical coordinate, (c) sampled uniformly using icosahedron subdivision.

point becomes the surface point sampled at (θ_i, ϕ_i) . Given N_1 is the number of samples for ϕ in the range of $[0, 2\pi)$ and N_2 is the number of samples for θ in the range of $[0, \pi]$, a mesh grid of $N_1 \times (N_2 - 2) + 2$ vertices (only one vertex needed at the south or north polar) and $2N_1 \times (N_2 - 3)$ triangular facets are generated on the surface.

In [141, 38], a homogeneous sphere sampling were used. It is started by sampling the sphere with an icosahedron or octahedron and repeatedly bisecting the triangular facets while moving the vertices to the sphere surface (Figure 3.7(c)). Given k is the number of subdivisions, this process will result in $10k^2 + 2$ facets for an icosahedron initialization [141] or 2^{2k+1} facets for an octahedron initialization [38]. Figure 3.7(c) shown the icosahedron subdivision of $k = 6$ for a prostate surface. The point generation follows the a ray-intersection method mentioned before, except that the group of (θ_i, ϕ_i) values are obtained from the homogeneous sphere subdivision.

Practically, the last two methods are both applicable. But we choose the homogeneous sampling on (θ, ϕ) to build our spherical harmonics due to some considerations. The first is that the prostate shape is far from an ideal sphere. The uniform distribution on a sphere does not mean it may have homogeneous density of points on the prostate surface. The second is that the distribution of the spherical harmonics can be well-defined so that its matrix will not be ill-ranked. The third consideration is that because the image boundary at the apex and base of the prostate is much more blurred than

the midgland, the homogeneous sampling on (θ, ϕ) space can have relative denser points at the two ends of prostate, helping to gather more information from regions of weak strength. In our study, the number of samples on (θ, ϕ) is selected as $N_1 = 30$ and $N_2 = 15$, respectively. Excluding redundant vertices at the two ends, the total number of samples on each surface is 392.

3.3.4 Model Training

After the normalization and uniform sampling on the spherical surface, the shape descriptors for each individual are comparable as they have been converted to the same reference system. Given L the degree of approximation, the number of descriptors required to rebuild the shape is $N = (L + 1)^2$, while the pose involves three parameters for translation and three for scaling. It is observed that a harmonic degree no less than 9 can achieve acceptable shape approximation error, which is calculated between the averaged user-interpreted surface and the approximated surface. This means a total number of 100 shape descriptors is required. The Principal Component Analysis (PCA) is a classical statistical method to reduce the data dimension by highlighting their similarity and differences. After formulating the covariance matrix of a large set of data and performing the eigenvalue decomposition of the matrix, the data dimension can be dramatically reduced without much loss of information. Hence this technique is applied on the set of spherical harmonic coefficients, so that less number of parameters is needed for shape reconstruction.

Capturing Statistical Shape Information

The statistical shape model is built upon the PCA over the shape descriptors, i.e., the harmonic coefficients. Given M samples in the training set, the mean model of the shape descriptor, $\bar{\mathbf{c}}$, is obtained by averaging the respective descriptors of each training samples:

$$\bar{\mathbf{c}} = \frac{1}{M} \sum_{j=1}^M \mathbf{c}_j \quad (3.20)$$

where $\mathbf{c}_j$ is the $N \times 1$ column vector denoting the shape descriptor, i.e., the set of harmonic coefficients, of the j -th training sample ($j = 1, \dots, M$).

The eigen-analysis on the covariance matrix of $\mathbf{c}$ results in the eigenvalue matrix $\mathbf{\Lambda}$ and the eigenvector matrix $\mathbf{W}$, where $\mathbf{\Lambda}$ is an $N \times N$ diagonal matrix holding the descending eigenvalues λ_i ($i = 1, \dots, N$) and $\mathbf{W}$ is an $N \times N$ matrix whose column $\vec{e}_i$ ($i = 1, \dots, N$) defines the eigenvector associated with the corresponding eigenvalue. Hence, the shape descriptor of any prostate surface, $\mathbf{c}$, can be described by a linear sum of the orthogonal eigenvectors, i.e.,

$$\mathbf{c} = \bar{\mathbf{c}} + \mathbf{W} \cdot \mathbf{b} \quad (3.21)$$

where the column vector $\mathbf{b} = (b_1, b_2, \dots, b_N)^T$ denoting the weights to the N orthogonal eigenvectors, with $\bar{b}_i = 0$ and $\text{std}(b_i) = \sqrt{\lambda_i}$, $i = 1, 2, \dots, N$.

Since the first few eignmodes can account for most of the total variations in the covariance analysis, we may use a few principal components to reduce the data dimension. In our study, the least number of principal components chosen for approximation, denoted as q , is determined by the criterion that the sum of their variances should cover no less than 90% of the total variances, i.e., $\sum_{i=1}^q \lambda_i \geq 0.9 \cdot \sum_{i=1}^N \lambda_i$. Equation (3.21) can be re-written as follows:

$$\begin{aligned} \mathbf{c} &= \bar{\mathbf{c}} + \begin{bmatrix} \mathbf{W}_q & \mathbf{W}_{(N-q)} \end{bmatrix} \cdot \begin{bmatrix} \mathbf{b}_q \\ \mathbf{b}_{(N-q)} \end{bmatrix} \\ &= \bar{\mathbf{c}} + \mathbf{W}_q \cdot \mathbf{b}_q + \mathbf{W}_{(N-q)} \cdot \mathbf{b}_{(N-q)} \\ &\approx \bar{\mathbf{c}} + \mathbf{W}_q \cdot \mathbf{b}_q \end{aligned} \quad (3.22)$$

where matrices $\mathbf{W}_q$ and $\mathbf{W}_{(N-q)}$ contain the first q columns and the remaining $(N - q)$ columns of the eigenvector matrix $\mathbf{W}$, respectively. Similarly, $\mathbf{b}_q \in \mathcal{R}^{q \times 1}$ is the vector containing the first q elements in $\mathbf{b}$, and $\mathbf{b}_{(N-q)} \in \mathcal{R}^{(N-q) \times 1}$ for the remaining $(N - q)$ elements.

Rewriting Equation 3.15, the shape function, $\mathbf{f}$, is then represented by a mean shape, $\bar{\mathbf{f}} = \mathbf{Y} \cdot \bar{\mathbf{c}}$, and a variation shape which is controlled by the set of weights $\mathbf{b}_q$ corresponding

to the q principal components,

$$\mathbf{f} = \bar{\mathbf{f}} + \mathbf{Y} \cdot \mathbf{W}_q \cdot \mathbf{b}_q \quad (3.23)$$

When use this shape model to reconstruct a new shape, $\bar{\mathbf{f}}$, $\mathbf{Y}$ and $\mathbf{W}_q$ are known parameters in the statistical model. Therefore the shape function is purely governed by the variables $\mathbf{b}_q$.

Statistical pose parameters

The statistics of the translation vector and scaling vector are collected from the normalization of training samples. We know that the prostate always lies just beyond the rectum where the ultrasound probe is held. The statistical distributions of the translation $(t_x, t_y, t_z)^T$ in x , y and z direction can be characterized by their mean and standard deviation, since the region of interest in the ultrasound image is constrained when the training images are obtained under the same coordinate system. For the evaluation of the scaling vector $\mathbf{s} = (s_x, s_y, s_z)^T$, it is understandable that the prostate dimension in the three orthogonal directions is not totally independent. For example, a prostate which has a larger cross-section size may have a longer apex-base length. Therefore, PCA technique is again employed to de-correlate the scaling vector $\mathbf{s}$ using

$$\mathbf{a} = \mathbf{P} \cdot \mathbf{s} \quad (3.24)$$

where $\mathbf{a} = (a_1, a_2, a_3)^T$ are the scaling parameters calculated as the projection to the eigen space $\mathbf{P}$.

Result

To avoid poor prediction ability resulted from the over-constrained model of insufficient training data [141, 210], a total of 104 sets of patient data were used in model training. The medical images were collected using the Aloka SSD-1700 ultrasound machine (ALOKA Inc., Japan) and a TRUS probe (Aloka UST-672-5/7.5 MHz) from year 2006 to 2008 in Singapore General Hospital. According to our study criterion approved by

IRB (Institutional Research Board), the patients recruited for our test must have had at least one round of traditional biopsy two weeks prior but the findings were negative and subsequently the PSA level keeps increasing before the second biopsy. In order to get the volumetric image of the prostate, the TRUS probe was fixed on an external probe holder and the series of transversal images were obtained by pulling the probe via a servo motor controlled by our robotic system [21, 22] along the axial direction at specified increments. The voxel dimension in image is around $0.18 \times 0.18 \times 0.5 \text{ mm}^3$. The size of the TRUS image is 548×456 pixels and the number of slices varied between patients, from 66 to 143, according to the size of the gland. The expert annotation for each data set is obtained by averaging the drawings from two observers. Figure 3.8 illustrates the 104 prostate shapes before normalization.

To evaluate the inter-observer disagreement quantitatively, the mean absolute radial distance (MeanARD) and maximum absolute radial distance (MaxARD) were calculated between the observers' interpretation of the prostate boundary. They are calculated as radial disagreement at mesh vertices used for spherical harmonics calculation:

$$MeanARD = \frac{1}{n} \sum_{j=1}^n |r1_j(\theta_j, \phi_j) - r2_j(\theta_j, \phi_j)| \quad (3.25)$$

$$MaxARD = \max_j |r1_j(\theta_j, \phi_j) - r2_j(\theta_j, \phi_j)| \quad (3.26)$$

where $r1(\theta, \phi)$ and $r2(\theta, \phi)$ represent the surface data outlined by observer 1 and observer 2, respectively. Table 3.2 summarizes the averaged disagreements over all the training images by mean and standard deviation. It is found that the discrepancy between different observers is larger than those reported in [38]. This is probably because the quality of the collected images is generally not good. Since we do not exclude those ultrasound images of poor quality, while the observers' annotation on those images may have rather different results at boundaries which were blurred or totally missing.

Table 3.2: The inter-observer disagreement on the prostate boundary.

MeanARD (mm)	MaxARD (mm)
1.94 ± 0.64	6.89 ± 1.95

Our test has verified that the spherical harmonic surface approximation using degree

Figure 3.8: Illustration of all the training samples for the prostate.

$L = 9$ is sufficient for the 3D prostate shape. Table 3.3 shows the residuals between the manual interpretation and the approximated surface, also in terms of MeanARD and MaxARD.

Table 3.3: Surface distance between the averaged user interpreted shape and the spherical harmonic approximated shape.

MeanARD (mm)	MaxARD (mm)
0.15 ± 0.06	1.06 ± 0.48

The statistics of the translation parameter and scaling parameters are collected from the normalization of training samples. The translation parameter t_z is not recorded because the number of transversal slice scanned varied between patients. Only t_x and t_y are listed in Table 3.4.

Table 3.4: Mean and standard deviation of the translation parameters (t_x, t_y).

COMPONENT	MEAN (mm)	SD (mm)
t_x	-1.6190	3.0979
t_y	-16.7983	8.0745

The eigen analysis on the scaling vector (s_x, s_y, s_z) shown in Table 3.5 demonstrated that the first two principal components can account for more than 90% of the total variances. So we choose to use (a_1, a_2) to denote the scaling parameter.

Table 3.5: Percentage of total variances for scaling vector.

Eigenmode	λ_i (Variance)	Percentage of total variance (%)
1	0.0478	71.2
2	0.0137	91.6
3	0.0056	100.0

Analyzing the percentage of total variances listed in Table 3.6, we choose to use the first 7 eigenmodes, which covers at least 90% of total variances of the training population.

By varying the parameters b_j ($j = 1, \dots, 7$) within their respective ranges, we can construct any plausible prostate shape using Equation (3.23). Figure 3.9 demonstrates the results of varying the parameter for each mode in turn with $b_j = \{-2\sqrt{\lambda_j}, -\sqrt{\lambda_j}, 0, \sqrt{\lambda_j}, 2\sqrt{\lambda_j}\}$, leaving all other parameters to be zero. The first row representing the first eigenmode accounts for the most significant change while the last shows least influence on the shape.

Table 3.6: Percentage of total variances for shape descriptors.

Eigenmode	λ_i (Variance)	Percentage of total variance (%)
1	2.6637	36.87
2	1.2776	54.55
3	1.0727	69.39
4	0.5222	76.62
5	0.3715	81.76
6	0.3612	86.76
7	0.3067	91.01
8	0.2008	93.79
9	0.1051	95.24
10	0.0899	96.48
11	0.0683	97.43
12	0.0444	98.04
13	0.0360	98.54
14	0.0198	98.82
15	0.0183	99.07
16	0.0154	99.28
$\vdots$	$\vdots$	$\vdots$
100	$1.8420e - 020$	100.0

3.4 Prostate Segmentation

Based on the established statistical models, the prostate segmentation in a new US image becomes an constrained optimization problem that searches for the optimal model parameters, including the shape parameters $\mathbf{b}_q = (b_1, b_2, b_3, b_4, b_5, b_6, b_7)$ and the pose parameters $\mathbf{T} = (t_x, t_z, t_z, a_1, a_2)$, suitable for the given image. The optimum model parameters shall be able to reconstruct a prostate shape with maximum similarity to its appearance in the image.

3.4.1 Objective Function

The similarity between the prostate shape and its acoustic appearance is evaluated by means of the objective function of the optimization problem. Thus special consideration must be paid on choosing a proper definition for the objective function. Firstly, it should be able to evaluate the similarity between the shape and its image. Secondly, its calculation should be as simple as possible as it is computed in every iteration of the optimization. Thirdly, although image denoising and filtering is important, it is not

Figure 3.9: The shape variations for the major modes in row ($j = 1, \dots, 7$) with $b_j = \{-2\sqrt{\lambda_j}, -\sqrt{\lambda_j}, 0, \sqrt{\lambda_j}, 2\sqrt{\lambda_j}\}$ in column. The middle column represents the mean shape obtained from model training.

favorable to introduce too much intermediate processing to extract some image features that may be used in calculating the fitness of the objective function. This is because the processing to the image data may cause possible errors for the future calculation or lead to certain level of information loss. For example, the Processing for edge detection may results in false-positive and true-negative edge points. The errors occurred in every image operation will be accumulated and finally affects the accuracy of the final decision.

It is noticed that in the ultrasound images, the prostate appears to be a dark region surrounded by hyperechoic halo. Hence, high image gradients should lie along its boundary in centrifugal direction. If excluding noise and other tissues, we can take an ideal prostate image as a binary image with the prostate region in black and the surroundings in white. Thus when a surface is perfectly aligned at the prostate boundary (where the high image

gradient exists), for any given spatial point on the surface, the normal vector at that point and the image gradient vector at the same coordinate would be parallel and in a same direction. This directional strength can be regarded as a kind of image energy, or a good fitness measure, for the similarity between a spatial shape and its boundary in image. In this manner, the prostate segmentation problem can be regarded as a procedure that searches for a set of optimal shape and pose parameters, which maximizes the directional image strength fallen on the constructed surface, i.e., the gradient magnitude along the normal of the surface points.

However, the prostate image of a patient is full of noise and contains not only the prostate gland. To reduce the speckle noise, a Gaussian smoothing is applied before the calculation of image gradient. Given the new image I , the objective function for the optimization, $E(\mathbf{b}_q, \mathbf{T})$, is defined as follows,

$$E(\mathbf{b}_q, \mathbf{T}) = \frac{1}{n} \sum_{k=1}^n \langle \vec{G}([h(\mathbf{T}, \xi(\mathbf{b}_q, k))]) \cdot \vec{n}(h(\mathbf{T}, \xi(\mathbf{b}_q, k))) \rangle \quad (3.27)$$

where $\xi(\mathbf{b}_q, k)$ is the function calculating the Cartesian coordinates (x_k, y_k, z_k) of the vertex defined at (θ_k, ϕ_k) on the surface using the shape parameters $\mathbf{b}_q$:

$$\xi(\mathbf{b}_q, k) = \begin{pmatrix} x_k \\ y_k \\ z_k \end{pmatrix} = \begin{pmatrix} r_k \sin \theta_k \cos \phi_k \\ r_k \sin \theta_k \sin \phi_k \\ r_k \cos \theta_k \end{pmatrix} \quad (3.28)$$

with

$$r_k = \bar{r}_k + \sum_{j=1}^7 A_{kj} b_j \quad (3.29)$$

where A_{kj} is the (k, j) element in matrix $\mathbf{A} = \mathbf{Y} \cdot \mathbf{W}_q$.

$h(\mathbf{T}, \xi(\mathbf{b}_q, k))$ is the function that applies the transformation $\mathbf{T}$ to the point:

$$\begin{aligned} h(\mathbf{T}, \xi) &= \begin{pmatrix} s_x \cdot x_k + t_x \\ s_y \cdot y_k + t_y \\ s_z \cdot z_k + t_z \end{pmatrix} \\ &= \begin{pmatrix} (\bar{s}_x + a_1 p_{11} + a_2 p_{12}) \cdot x_k + t_x \\ (\bar{s}_y + a_1 p_{21} + a_2 p_{22}) \cdot y_k + t_y \\ (\bar{s}_z + a_1 p_{31} + a_2 p_{32}) \cdot z_k + t_z \end{pmatrix} \end{aligned} \quad (3.30)$$

where p_{ij} is the (i, j) element for the eigenvector matrix $\mathbf{P}$ for scaling (see Equation (3.24)).

$\vec{G}$ is the Gaussian-smoothed image gradient obtained by

$$\vec{G}(x, y, z) = \nabla(I(x, y, z) * g_\sigma(x, y, z)) \quad (3.31)$$

where $*$ denotes the convolution operator and $g_\sigma(x, y, z)$ is the Gaussian kernel function of $\sigma = 1$ that is used to reduce the noise in the ultrasound images. ∇ is the gradient operator for an image,

$$\nabla I(x, y, z) = \frac{\partial I}{\partial x} \mathbf{i} + \frac{\partial I}{\partial y} \mathbf{j} + \frac{\partial I}{\partial z} \mathbf{k} \quad (3.32)$$

$\vec{n}$ denotes the operator for normal calculation, with surface normal $\vec{n}_k$ defined at point (x_k, y_k, z_k) and is computed by averaging the normal vectors of the adjacent facets.

$$\vec{n}_k = \frac{1}{6} \sum_{i=1}^6 \vec{n}_{ki} \quad (3.33)$$

where $\vec{n}_{ki}$ is the surface normal of the i -th facet, $1 \leq i \leq 6$, adjacent to the point (x_k, y_k, z_k) , as shown in Figure 3.10.

The operator $\langle \cdot \rangle$ calculates the inner product between the normal and the image gradient at the surface point. When the two vectors are parallel, the inner product between them, i.e., the value of the objective function, will be maximum. Because of the discrete

Figure 3.10: Calculation of the surface normal $\vec{n}_k$ at the surface point (x_k, y_k, z_k) .

coordinate of the image voxel in the space, we use the nearest-neighbor operator "[]" to derive the image gray value at any spatial point.

The objective function in Equation (3.27) is calculated as a form of image energy (in terms of the gradient magnitude along the surface normal). This definition satisfies our requirement that the segmentation should feature the strongest directional strength between the image gradient and the normal at all surface points. Meanwhile its computation is direct and simple for the use of the original image data. To illustrate the feasibility of this image energy, a simplified simulation test was conducted to reveal the relationship between the pose parameters and the fitness of the objective function. Figure 3.11 demonstrates a 2D example of the defined objective function that only considers how the pose parameters affect the similarity. Figure 3.11(a) and 3.11(b) show the alignment and misalignment between a 2D prostate contour and the corresponding image generated from the contour. The normal vectors of the contour (shown by long arrows) and the image gradients (shown by short arrows) are demonstrated respectively in the figures. In Figure 3.11(b), when the contour is aligned with the region boundary, its normal vectors will match with the image gradients at the boundary so that the value of the objective function is maximum. Figure 3.11(c) and 3.11(d) illustrate how the value of the objective function changes with respect to the translation and rotation parameters. As can be seen from Figure 3.11(c) and 3.11(d), only when the prostate shape is aligned at its image boundary (in-plane translation $t_x = t_y = 0$ and rotation angle $\alpha_z = 0$), i.e., its contour normal is in the same direction of the gradient at the boundary, the objective function will get maximum value.

Figure 3.11: A 2D example of the directional strength and the alignment between the shape contour and the binary image in way of point normal and image gradient. (a) A misalignment of the contour with in-plane rotation of 30° and translations of (1mm, 2mm). (b) The true match between the contour and the image boundary. (c) The normalized value of the objective function as a function of in-plane translations in millimeters. (d) The normalized value of the objective function as a function of in-plane rotation in degree.

It is difficult to optimize the objective function (Equation (3.27)) analytically and establish the convergence of the optimization procedure theoretically. Hence in our work, we choose the Genetic Algorithm (GA) as the optimization method. In addition, should there be multiple local optima in the solution space, GA will not be easily trapped in the local optima. The experimental results shown in Section 3.6 give further evidence of the appropriateness of the choice of the objective function and the GA method. The details of the GA method used in this work will be explained in the following subsection.

3.4.2 Optimization Using Genetic Algorithm

The genetic algorithm (GA) is a robust search mechanism based on underlying genetic biological principles. In this study, GA is chosen as the search heuristic to maximize the objective function defined in the multivariate optimization problem. It is superior to the gradient search methods because it does not require differential equations or a smooth search space. Hence it has been widely used as an adaptive search method in many applications including the segmentation [72, 211, 126]. The procedure of GA resembles a biological evolution (Figure 3.12). It consists of the chromosomes to encode the variables, selection by fitness, crossover to produce new offspring, and random mutation between new offspring [212]. Each chromosome is taken as a point in the search space of candidate solutions. The populations of chromosomes are processed by GA and successively replaced one by another. The search process evaluates each chromosome, a single solution to the problem, on how well it solves the problem and deserves for survival by assigning a score of fitness, which, is typically obtained by a linear scaling of the user-specified objective function.

We implement the GA optimization using the *Matthew's Genetic Algorithms Library* (GALib 2.4) [213], a C++ library of the genetic algorithm. Table 3.7 lists the respective range of the model parameters encoded in the chromosomes. The associated settings of GA for our application is illustrated in Table 3.8.

Table 3.7: Parameter settings in genetic algorithm.

Parameter	Range
t_x	$-7.81 \sim 4.58$
t_y	$-32.95 \sim -0.65$
t_z	$(z_{max} - 3z_{min})/4 \sim (3z_{max} - z_{min})/4$ ^a
a_1	$-0.44 \sim 0.44$
a_2	$-0.23 \sim 0.23$
$b_j, (j = 1, \dots, 7)$	$-2\sqrt{\lambda_j} \sim 2\sqrt{\lambda_j}$ ^b

^a z_{min} and z_{max} are the range of the image volume on z axis.

^b λ_j can be obtained from Table 3.6.

As GA is a stochastic search algorithm, it is impossible to guarantee that the global optimal solution can be seen within a small number of iterations. According to [214], it seems that by running GA for long enough, its convergence to the global optimum can

Figure 3.12: Typical evolution process in GA [4].

be guaranteed. Nevertheless, due to the time restriction in a real-time application, it is more practical to let it run with a reasonable number of populations and generations. At least based on its operational principles, it is able to find the optimum appeared in its evolution. Meanwhile, GA will not be easily trapped into the local optima as those local optimization approaches (such as the Powell's method used in [38]). Therefore, it does not need to start with an initialization close to the true solution. Instead, it proceeds from several points in the design space to another set of design points, and may have a

Table 3.8: Parameter settings in GA.

Population size	150
Number of generations	150
Crossover rate	95%
Mutation rate	5%
Chromosome representation	Real-value array encoding
Evolution strategy	Incremental GA evolution strategy with crowding replacement
Selection scheme	Tournament

better chance of locating the global optimum in the solution space.

3.4.3 Optional User Constraints

Ultrasound image quality plays an important role in the success of an automatic detection. An ideal TRUS image of the prostate should exhibit a relatively dark-textured prostate surrounded by bright halo but in fact it may not always appear in such a ideal way in every patient data. Even using the same machine, different patients may have vast difference in the image sharpness. Error of the automatic detection will increase if the image is deteriorated by speckle noise or shadow. Even when manual segmentation is performed, it is always difficult to identify the base and the apex of the prostate gland from the 3D TRUS image, specially when part of the prostate is missing due to an insufficient coverage at the axial length. In this case, the automatic detection may not be able to yield a satisfying result. Therefore, we integrate *a priori* knowledge of the new image from the user, in form of a user-specified region of interest. This dimensional constraint is optional in our algorithm, but it may narrow the search ranges of the scaling and translation parameters, and aims at improving the segmentation accuracy for poor image qualities.

Before the automatic detection, the user may draw on any of the three orthogonal slices to demarcate the minimum rectangular region that can enclose the maximum size of prostate in that dimension. Our experience shows that the best location chosen to draw the constraint is at the midgland of the coronal view. This decision is made based on the saddle shape of the gland and the difficulty in determining the prostate length in the inferior-superior dimension.

To combine this constraint in the proposed algorithm, a minor change is made to the pose parameter set. When the user input is imposed, the scaling vector is directly confined from the user-specified constraints, hence the scaling vector $\vec{s} = (s_x, s_y, s_z)^T$ is used rather than the decoupled scaling parameter (a_1, a_2) . Meanwhile, the ranges of the translation in the associated dimensions are also re-defined accordingly. Statistics collected from model training shows that the standard deviation of the scaling factors (s_x, s_y, s_z) are $(0.1231, 0.1342, 0.1845)$ while their mean values are $(1, 1, 1)$.

Other than the user constraint, some mathematical constraints on the shape, such as the smoothness of the surface or contour, may be another physical constraint to the optimization problem. Mostly this kind of constraint is used to confine the evolution of a physical model which is driven by the image force and may have self-intersection or corners due to the unbalanced image force along the front. This constraint is often formulated as a penalty energy in the objective function. Nevertheless, in our approach, the use of the spherical harmonics for prostate shape parameterization has determined that it is almost unlikely to have a self-intersect contour as the prerequisite of using this parameterization is that the closed surface must be a "star-like" shape, which means a single-valued shape function in the spherical coordinate system. Meanwhile, the harmonic representation comes from a coarse-to-fine decomposition of the spherical shape function. The smoothness has been implicitly confined by the selected degrees of harmonics and the number of angular sampling in the spherical space. Therefore, this constraint is not incorporated in the optimization procedure.

3.5 Issues on Validation

Key issues concerning the segmentation of medical images are validity and reliability. Validity refers to the degree to which a study accurately reflects the specific concept that the researcher is attempting to measure. In short, it means accuracy. In many clinical activities, a large disagreement between the detected result and the "truth", i.e., the real target, might result in severe damage to the patient. For this reason, it is an important task to evaluate the algorithm performance before we can use the detected results to make clinical decisions for the diagnosis and treatment of prostate

diseases. Reliability refers to the consistency of performance, which means the ability of maintaining an effective results. In our case, it is shown as the deviation which occurs in repeated experiments within the same conditions (for a single test case) and different conditions (for multiple test cases).

To evaluate the validity, usually a comparison of new measures against an existing gold standard is conducted. However, it is difficult to obtain the "ground truth" when clinical data are concerned. Quite often, the "ground truth" comes from the experienced people. When evaluating an image segmentation algorithm, its result is usually compared with the manually segmented result done by those experienced people. In our study, these people can be the medical experts, such as the urologists and the radiologists, or the observers trained by the medical experts. As a result of their different understanding of the medical images, the human assessment may show inter-observer variability, i.e., the disagreement between different observers, or intra-observer variability, i.e., the disagreement within one observer but doing the same job at different times [215, 216]. Both of them are observer-related variances, but we are only interested in the inter-observer variability here. When a group of experts are available, the average of their opinions can be taken as the golden standard. The discrepancy of the detected result with respect to the averaged manual result is taken as the error. The related validation matrices can be measures on distance and measures on volume.

3.5.1 Distance Measures

The distance measures are error metrics in form of point distance between the manually-outlined surface (the *reference* surface) and the algorithm-detected surface (the *detected* surface). Based on the distance-based error metrics defined in Ladak et al. [27], the surface distance used in our validation experiments include the Hausdorff distance (HD), the mean absolute distance (MAD) and the root of mean square distance (RMSD) [217]. Given the two surfaces represented as point set $\mathbf{P} = (p_1, p_2, \dots, p_m)$ and point set $\mathbf{Q} = (q_1, q_2, \dots, q_n)$, the distance of any point in surface $\mathbf{P}$ to the surface $\mathbf{Q}$ can be expressed as the closest point distance

$$d(p_i, \mathbf{Q}) = \min_{1 \leq j \leq n} \|q_j - p_i\| \quad (3.34)$$

where $\|q_j - p_i\|$ denotes the 3D Euclidean distance between point q_j and p_i . As a description of the largest difference between surfaces, the Hausdorff distance is calculated as the maximum of the closest point distances,

$$d_{HD}(\mathbf{P}, \mathbf{Q}) = \max_{1 \leq i \leq m} d(p_i, \mathbf{Q}) \quad (3.35)$$

However, due to the asymmetry of the Hausdorff distance, $d_{HD}(\mathbf{P}, \mathbf{Q})$ is not equal to $d_{HD}(\mathbf{Q}, \mathbf{P})$. The symmetric definition of HD is as follows

$$HD(\mathbf{P}, \mathbf{Q}) = \max(d_{HD}(\mathbf{P}, \mathbf{Q}), d_{HD}(\mathbf{Q}, \mathbf{P})) \quad (3.36)$$

The mean absolute surface distance tell us how much on average the two surfaces differ. Using the point to surface distance defined in Equation (3.34). we can calculate the mean error $d_m(\mathbf{P}, \mathbf{Q})$ by

$$d_m(\mathbf{P}, \mathbf{Q}) = \frac{1}{area(\mathbf{P})} \int \int_{p \in \mathbf{P}} d(p, \mathbf{Q}) d\mathbf{P} \quad (3.37)$$

and the root of mean square distance in form of

$$d_{rms}(\mathbf{P}, \mathbf{Q}) = \sqrt{\frac{1}{area(\mathbf{P})} \int \int_{p \in \mathbf{P}} d(p, \mathbf{Q})^2 d\mathbf{P}} \quad (3.38)$$

Similarly, the symmetric forms of MAD and RMSD are defined as

$$MAD(\mathbf{P}, \mathbf{Q}) = \max(d_m(\mathbf{P}, \mathbf{Q}), d_m(\mathbf{Q}, \mathbf{P})) \quad (3.39)$$

$$RMSD(\mathbf{P}, \mathbf{Q}) = \max(d_{rms}(\mathbf{P}, \mathbf{Q}), d_{rms}(\mathbf{Q}, \mathbf{P})) \quad (3.40)$$

3.5.2 Volumetric Measures

Due to the bi-directional (inwards and outwards) ambiguity in the surface distance measure, we can not differentiate between the over-estimated and under-estimated situations. A better approach is to take into account the volumetric overlap. The overlap between the referred volume (*detected*) and the reference volume (*reference*) is evaluated in a com-

combination of logics and binary, where logic 1 defined as the truth, and binary 1 defined as the existence. So the four kinds of volume are derived as follows

- True positive (TP) volume: the common voxels contained by both the *reference* surface and the *detected* surface.
- False positive (FP) volume: the volume enclosed by the *detected* surface but outside of the *reference* surface.
- False negative (FN) volume: the volume enclosed by the *reference* surface but is missed by the *detected* surface.
- True negative (TN) volume: the voxels outside of both the *reference* surface and the *detected* surface.

The volumetric disagreement is quantitatively evaluated as the volume difference (VD) and the absolute volume difference (AVD) [109]. The definitions in [109] were slightly changed according to [38] and [218], in which they used the common volume occupied by both RV and DV for comparison, rather than only RV in [109].

$$VD = \frac{RV \cup DV - RV \cap DV}{RV \cup DV} = \frac{FP + FN}{TP + FP + FN} \quad (3.41)$$

$$AVD = \frac{|RV - DV|}{TP + FP + FN} \quad (3.42)$$

In the above equations, RV denotes the *reference* volume and DV denotes the *detected* volume. Calculation of RV and DV follows a similar definition to planimetric volumetry [219] used for prostate volume estimation in ultrasound. This also applies to TP , FP and TN . For example, the TP volume is evaluated as a numerical integration of cross-sectional sub-volumes, each of which is calculated by the **AND** area at that ultrasound cross-section multiplied by the distance between the cross-sections. For higher accuracy, we set the interval as double the size of the spacing and the calculation of the volume is converted to counting the number of the voxels falling inside the volume.

Based on the definitions of the volume difference, another measure, the volume overlap ratio, also referred as the Jaccard index, is defined in [141, 38] as

$$V_o = \frac{RV \cap DV}{RV \cup DV} = \frac{TP}{TP + FP + FN} \quad (3.43)$$

We can see that they are actually the same measurement except that the former evaluates the difference while the latter evaluates the similarity, $V_o = 1 - VD$. Other than the ratio of volume overlap, the sensitivity that measures the actual proportion of positive prediction (which are correctly identified) with respect to the *reference*, is also used in the analysis of the disagreement [27]. Its definition is similar to that of the overlap ratio, except the difference for comparison,

$$sensitivity = \frac{TP}{TP + FN} \quad (3.44)$$

In all of the calculations, the expert surface is taken as the *reference*.

3.6 Experiment and Results

35 sets of patient data are used for the experiments of segmentation, among which 11 sets are new scans (using the same ultrasound system) not included in the training set and the other 24 sets were randomly chosen from the training set. We are able to include the images used for model building because the data for training are not the prostate images themselves, but the surfaces outlined by human experts. In the validation of accuracy, the averaged expert drawing serves as the golden standard. The consistency of the algorithm is evaluated by repeating the same detection procedure for 10 times for each image set.

Besides the fully automatic segmentation, we also performed the semi-automatic segmentation tests on the same set of test data. The user will draw one boundary (or more) at the midland slice (in transversal, sagittal or coronal view) of the prostate. This initialization is not required to be accurately aligned at the prostate boundary but has to enclose the prostate region in minimum size. When more than one user constraint

is specified, the region constraints are then derived from their maximum coverage. By comparing the results obtained from automatic and semi-automatic segmentation, we can verify whether the user input have any obvious improvement on the performance.

For the validation metric, besides the surface distances and volume differences introduced previously, we also evaluated the ratio of area (RoA) and the ratio of volume (RoV) of the *detected* surface with respect to the *expert* surface. Calculation of these two indices aims at determining whether our algorithm tends to get an over-estimated or under-estimated result.

Figure 3.13 shows the box and whisker plots of HD, MAD and RMSD of 10 repeated experiments for each of the 35 test images using automatic technique. Figure 3.14 shows the results of same measures using semi-automatic segmentation. Figure 3.15 and Figure 3.16 demonstrate the distribution of RoAs and RoVs in the repeated tests using the auto and semi-auto approaches. Similar comparison is shown in Figure 3.17 and Figure 3.18 for VD and AVD. Table 3.9 and Table 3.10 summarize the averages of all the validation matrices for each case. The distance measures, including HD, MAD and RMSD, over all the cases using the automated segmentation are 6.25 ± 1.67 mm, 1.66 ± 0.37 mm and 2.17 ± 0.54 mm, respectively, while these errors are decreased to 4.63 ± 1.02 mm, 1.22 ± 0.26 mm and 1.56 ± 0.33 mm respectively when a user indication on the region of interest is available. RoA and RoV in both tests do not show obvious over-estimation or under-estimation of detection. The volume overlap ratio in automatic detection was $76.90 \pm 5.04\%$, compared with $80.05 \pm 4.50\%$ in semi-automatic detection. Based on the analysis over the sensitivity illustrated in Figure 3.19 for the 35 cases, it was found that the user input improved the average sensitivity from $92.13 \pm 4.93\%$ to $96.30 \pm 2.85\%$.

Figure 3.20 to 3.24 demonstrate some of the typical results in our experiments. The detected surface is shown in contrast with the averaged expert drawing. Figure 3.20(a) and Figure 3.20(b) show the results of case 1. The automatic and semi-automatic detection have comparable good performance. But the anterior boundary is pulled to the pubic arch, because the boundary strength at that part is relatively weak. In addition, many of our patient data do not have a full scanning of the prostate along the superior-inferior direction, as shown in image of case 33 (Figure 3.21). Although the algorithm

Figure 3.13: The statistics of the surface distances between the automatically *detected* surface and the *expert* surface. Top: HD (mm). Middle: MAD (mm). Bottom: RMSD (mm).

Figure 3.14: The statistics of the surface distances between the semi-automatically *detected* surface and the *expert* surface. Top: HD (mm). Middle: MAD (mm). Bottom: RMSD (mm).

Figure 3.15: The statistics of the ratio of area and the ratio of volume between the automatically *detected* surface and the *expert* surface. Top: Ratio of area. Bottom: Ratio of volume.

can make a good guess based on the global approximation of the shape, it still may lead to an unnegligible estimation error around the base and the apex (Figure 3.21(a)). In such cases, an indication of the range in depth by the user could help to reduce the uncertainty (Figure 3.21(b)). The user input is also helpful at the presence of interfering bright spots close to the boundary, like the seminal vesicles (Figure 3.22), or an irregular shape of the gland (Figure 3.23). While for the hyperechoic calcifications located inside the gland, the detection is less likely to be affected (Figure 3.24).

The comparison of the surface and volumetric measures between automatic and semi-automatic detection shows that the ratio of overlap is higher when there is some prior

Figure 3.16: The statistics of the ratio of area and the ratio of volume between the semi-automatically *detected* surface and the *expert* surface. Top: Ratio of area. Bottom: Ratio of volume.

knowledge of the prostate region in image. The improvement of semi-automatic detection is verified by a paired Wilcoxon Signed Rank Test [220] (which does not require an assumption of normal distribution for the population). The result verifies that the detection with user indication of region of interest has a significant improvement over the fully automatic detection ($p < 0.05$). Same conclusion is arrived from a one-tailed Student t test ($p < 0.05$) (when the normal distribution assumption can be satisfied). An abnormal increment, although small, was found for AVD when the semi-automatic detection is used. This may due to the fact that when the overlap increases, the union of the volume of the *detected* surface and the *expert* surface actually decreases, leading

Figure 3.17: The statistics of the volume difference between the automatically *detected* surface and the *expert* surface. Top: VD. Bottom: AVD.

to an increase of AVD.

The experiments were run on a personal computer with Intel Core® 2 Quad CPU @ 2.4GHz and 2GB Memory. The typical running time for the detection is around 24 seconds. If including the calculation time spent on the Gaussian smoothing and gradient calculation (for about 3.2 ~ 4.5 seconds and varies due to the different number of slices scanned for each patient), the total time for an automatic segmentation was no more than 30 seconds. Compared to manual delineation which takes about 3 to 5 minutes, this speed is quite acceptable for clinical use. The speed can be further improved by using a multi-population GA (MPGA) instead of the incremental GA. By allowing for evolution of 5 populations in parallel using a steady-state algorithm and 30 individuals for each population, we can segment the prostate from 3D US images in 17 ~ 19 seconds

Figure 3.18: The statistics of the volume difference between the semi-automatically *detected* surface and the *expert* surface. Top: VD. Bottom: AVD.

Figure 3.19: The comparison of the sensitivity between the automatic and semi-automatic methods.

(a)

(b)

Figure 3.20: The repeated detection results with respect to the expert drawing (case 1). (a). Automatic results. (b) Semi-automatic results.

(a)

(b)

Figure 3.21: The repeated detection results with respect to the expert drawing (case 33). (a). Automatic results. (b) Semi-automatic results.

(a)

(b)

Figure 3.22: The repeated detection results with respect to the expert drawing (case 14). (a). Automatic results. (b) Semi-automatic results.

(a)

(b)

Figure 3.23: The repeated detection results with respect to the expert drawing (case 11). (a). Automatic results. (b) Semi-automatic results.

(a)

(b)

Figure 3.24: The repeated detection results with respect to the expert drawing (case 2). (a). Automatic results. (b) Semi-automatic results.

without sacrificing the accuracy. There is no much difference on the execution speed between the fully automatic detection or the semi-automatic.

3.7 Discussion

In our work, we implemented a parametric representation of the prostate shape in the real-value spherical harmonics. This parametrization is able to produce a more compact representation of the prostate shape model, which means less unknown parameters to be determined in the segmentation problem.

When analyzing a real patient image which is full of the speckle noise and other tissue signals, the ideal solution space of the defined objective function may be deteriorated, causing multiple local optima. To guarantee the effectiveness of this formulation, it is desired that the image quality is not too poor, at least most of the prostate boundary information would be strong and well maintained. In the collected image dataset used for modeling training and segmentation test, the major adversities to the image quality include the speckle noise, the inhomogeneous attenuation of the tissues, the insufficient scan of the gland, the blurred boundary at the gland ends, the calcifications inside of the gland, the shadowing, and the interference signals from surrounding tissues. The reverberation is rarely seen in our dataset because this kind of artifact has a great impact to the image quality thus the patient image is always collected by avoiding an inadequate contact between the rectum and the transducer. As the proposed method does not have special treatment to eliminate the quality deficiencies, for example, when the prostate boundary is partially missing, or deteriorated badly by the speckle noise, the image artifacts, or sometimes the structures such as the seminal vesicles and the pubic arch of strong hyperechoic appearance, or the bladder neck connection of hypoechoic appearance, it is possible that the objective function may not be an effective evaluation to the similarity between the prostate surface and its image boundary. For example, the pubic arch may be a significant interference because it is close to the anterior part of the prostate and also has strong echoic reflection at its interface. When its strength is much stronger than that of the prostate, the algorithm may not be able to locate the anterior boundary accurately. Another important impact comes from the insufficient scan of the

gland. Although the harmonic representation can make a guess on the missing parts based on a global smoothness and connectivity of the prostate shape, when the image information about the base, the apex, or sometimes even the lateral lobes, are missing, it is hard to ensure the detection accuracy for those parts of the boundary. To cope with such cases, an optional constraint from the user may be applied. The user can provide a simple region of interest of the prostate based on his interpretation of the image thus exclude the interference and confine the search in a narrow range.

On the selection of image features for image segmentation, both texture and gradient information have been considered. However, it is found that it is hard to establish consistent texture patterns for the prostate and non-prostate regions in the training set because those information exhibited in our dataset are not so regular, specially when some of them were deteriorated by the hyperechoic calcifications, or the inhomogeneous attenuation of the tissues. The difficulties of using the texture information for prostate segmentation have also been discussed in [41, 85]. There may be concerns when gradient information is used for segmenting ultrasound prostate images because ultrasound images are noisy. This may be true for a 2D segmentation problem in which the gradient information is more likely to be deteriorated by the noise presented in the slices. But in a volumetric image, the distribution of the gradient vectors in 3D can form a spatial constraint which is much more reliable than those in a plane, especially when the shape's centroid and dimension are known within certain ranges. Therefore, the uncertainty in one slice is reduced by the shape smoothness (ensured by the spherical harmonic surface representation of our approach) and connectivity along the neighboring slices. On the calculation of the objective function, due to the interference of noise, it may occur that even the surface is aligned with the prostate boundary, the surface normal is not in a good alignment with the image gradient at some points of the boundary, sometimes even reversed. In such case, the negative contributions made by those points shall be excluded, so that they would not mixed with the other positive prediction to bias the value of the objective function.

Since different medical data is used, it is hard to compare our results directly with the similar work reported in [38, 41]. To compare the statistical model, Tutar et al [38] reported that they can use 20 parameters to account for no less than 99% of the total

shape variances, when a highest degree of $L = 7$ is used for a complex harmonic surface approximation. Our findings is that we need 15 parameters (see Table 3.6) for the same level of shape variances but a higher degree ($L = 9$) of real harmonic surface approximation. When comparing the accuracy, we have a larger inter-observer disagreement. Different observers may be a cause. But we think a more likely reason is owing to the quality of the 3D ultrasound image, as both the inter-observer disagreement and the detection errors are found increased. The volumetric images used in our experiments were not obtained by a 3D probe scanner as used in [41]. Instead, they were constructed by a series of transversal images whose quality is not ideal, especially at the base and the apex at which the boundary is broken or blurred for the sake of the parallelism to the transducer, or totally missing due to insufficient scanning of the gland along the superior-inferior direction. More often, this boundary information is deteriorated by the bladder neck connection at the base and the connection with the superior fascia of the urogenital diaphragm at the apex. So quite a lot of cases is like this: when assessing the transversal slice of the mid-gland, the experts' opinions are similar; when assessing to the slices at the two ends, the variations become large. In our experiments with the proposed method, it also has the same findings that generally the detection accuracy at the midgland is much better than that at the base and the apex, as shown in Figures from 3.20 to 3.24. This finding was quantitatively verified in our comparison between the area overlap ratios at a transversal midgland slice and a coronal midgland slice. Figure 3.25 shows an example of the midgland overlap in transversal and sagittal views, respectively.

Let the area overlap ratio S_o calculated as

$$S_o = \frac{S_r \cap S_d}{S_r \cup S_d} \quad (3.45)$$

where S_r and S_d are the areas of *reference* boundary and *detected* boundary. Table 3.11 illustrates the area overlap ratios measured at the transversal and sagittal view of the midgland, denoted as S_{oT} , S_{oS} respectively. The data show that the accuracy at the transversal midgland is higher than sagittal midgland which takes the base and the apex into account.

Figure 3.25: Area overlap analysis at midgland. Left column: the transversal slice of the midgland. Right column: the sagittal slice of the midgland. From top to bottom: the expert annotation, the detected results and the area overlap.

Another finding is that the overlap ratio measure is quite sensitive to small difference at boundaries [141, 108]. For example, when we compare a mean shape (obtained from our statistical model) with the same mean shape but with an $(1, 1, 1)$ mm translation applied, the overlap ratio will decrease to only 87.67. Comparing the surface measures obtained by our method to those from inter-observability, the proposed segmentation method is considered effective and reliable, able to achieve accuracy comparable to human expert.

The experiments show that the time required to determine the prostate surface in the

ultrasound image is no more than 25 seconds. Compared to the time spent on collecting the 3D TRUS image (about 1 minute) using the robotic system designed by our team, this speed is acceptable and also quite promising for a real-time operation and treatment. However, there is a very significant aspect in the practical usage of any algorithm for the medical images. No matter how accurate the algorithm may be in lab experiments, the user should review it thoroughly before it is used for making clinical decisions. So, a procedure of expert examination of the computer-assisted detection is indispensable in the real time procedures. To modify any miss-aligned parts of the shape model in a convenient manner, the surface will be converted into a stack of NURBS contour that can be modified by the user, so that the shape can be corrected by moving the control points generated at intersecting image slices.

Currently, this technique has been integrated into the robotic biopsy system (National Medical Research Council of Singapore Grant Ref: 0859/2004) developed by our team and used in clinical trials at Singapore General Hospital as a tool to obtain the prostate surface for the biopsy planning.

3.8 Conclusion

This chapter presents a statistical deformable model of the prostate and its application to the prostate segmentation in 3D ultrasound image. The experiments show that it can deliver accuracy comparable to a human expert.

The key concept in the proposed method is to use a compact statistical deformable model, which is built from a parametric representation of the surface in real-value spherical harmonics, and the original ultrasound image data, which is collected intra-operatively, for the segmentation. Compared to the existing statistical shape models, this parameterization reduces the number of shape parameters and produces a much compact 3D model description. Using the real-value spherical harmonics to decompose a 3D closed shape, a coarse-to-fine description of the prostate shape is obtained through a set of harmonic coefficients (e.g., $N = 100$ when choosing the highest degree as 9). In contrast to the original point-denoted surface, the number of parameters required for describing the shape is dramatically reduced (from 3×392 to 100). The statistical method is able

to further condense the shape parameters into an orthogonal space. When trained by a large number of samples ($M = 104$), the number of shape parameters needed to represent a plausible prostate shape is reduced to 7.

Once the statistical model of a 3D prostate surface is obtained, the procedure of segmenting the prostate from a given new image is formulated as a constrained optimization problem that searches for the proper values of the model parameters (including both shape and pose) in known ranges that can maximize an object function. Unlike those work relying on preprocessing of the image to extract edge points or texture features [72, 26, 28, 38, 108], the proposed method utilizes the original image data, which is collected intra-operatively, and employs the genetic algorithm to maximize an image energy defined as the gradient strength along the normal profile of the fitted surface.

This approach is able to work fully automatically, with 7 shape parameters plus another 5 parameters implicitly for pose. To obtain better prediction in images of adverse quality, such as insufficient scan of the gland, deteriorated boundary caused by shadows or interference from neighboring tissues, it is able to cooperate with a user-specified region of interest, leading to an explicit representation of the pose by 6 parameters.

In summary, this method is superior in the prior knowledge about the prostate, less errors possibly caused by image processing, free of initialization and less computation involved in the optimization. The experiment results show that the accuracy is comparable to human expert and the running time (within 25 seconds) is quite promising for a real-time image-guided medical interventions. Currently, this segmentation algorithm has been integrated into the latest prototype of the robotic prostate biopsy system (see introduction in Subsection 1.1.5) in trial tests and helps the urologists to obtain the prostate surface for the following planning of biopsy cores.

Table 3.9: Experimental results using fully-automatic segmentation.

case	HD (mm)	MAD (mm)	RMSD (mm)	RoA	RoV	VD (%)	AVD (%)	Sens. (%)
1	4.0764	1.0898	1.3975	1.0178	1.0200	18.53	11.58	95.73
2	4.5721	1.2702	1.6399	1.0315	1.0450	20.65	11.94	94.86
3	5.3802	1.3887	1.7197	0.9126	0.8922	14.42	3.45	91.57
4	7.2345	1.9767	2.6788	0.8906	0.8413	20.67	10.18	83.72
5	6.3276	1.5687	2.0953	1.0130	1.0099	19.16	8.22	93.51
6	5.5965	1.5395	1.9330	0.9671	0.9480	20.92	8.78	91.80
7	6.8657	1.8290	2.3953	0.9417	0.9275	22.33	3.98	88.82
8	11.7064	2.0809	3.3937	0.9153	0.8609	22.75	5.59	84.83
9	6.6841	1.9256	2.4920	0.9642	0.9329	22.57	8.61	89.31
10	7.1721	1.9205	2.4906	1.1125	1.1403	22.41	16.41	96.25
11	6.6408	1.8100	2.3586	0.8100	0.7526	22.38	17.49	79.58
12	6.8580	2.0263	2.5959	0.8577	0.8056	19.41	12.57	83.67
13	9.6617	2.2715	3.0707	0.8673	0.8374	21.23	7.04	85.46
14	7.5339	2.1474	2.7952	1.0402	1.0328	28.76	5.73	85.50
15	6.2188	1.3887	1.8458	1.0308	1.0263	27.99	16.26	92.43
16	8.0622	2.4013	3.1512	1.1696	1.2540	32.16	29.89	98.46
17	5.8225	1.7179	2.1479	1.0699	1.0700	24.85	15.32	94.05
18	7.4938	1.8982	2.6029	0.9928	0.9600	22.87	6.44	89.44
19	5.6450	1.4082	1.8482	1.0459	1.0321	20.98	14.46	96.11
20	4.5596	1.3205	1.6575	1.0940	1.1114	26.09	22.31	97.55
21	5.5555	1.5549	2.0125	1.0140	1.0162	28.24	24.02	97.29
22	5.0538	1.5745	1.9450	1.1362	1.1767	32.30	29.76	98.21
23	5.8607	1.7499	2.1956	1.1082	1.1476	24.53	20.14	97.37
24	5.6287	1.3360	1.8222	0.9118	0.9072	18.96	5.71	91.47
25	7.8491	1.7443	2.4943	1.1407	1.1842	31.09	29.11	98.58
26	4.9451	1.3189	1.6864	0.9350	0.9203	17.15	4.73	91.77
27	4.3907	1.0718	1.4137	0.9557	0.9467	20.67	11.58	94.68
28	5.5614	1.6127	2.0352	0.9701	0.9679	24.58	7.70	90.01
29	3.7794	1.0403	1.3354	1.0075	0.9966	14.36	10.43	97.77
30	4.6661	1.2999	1.6390	1.0039	1.0037	19.44	7.15	92.91
31	3.6722	1.0650	1.3214	0.9274	0.9079	14.62	4.58	92.80
32	6.9569	2.1894	2.7921	0.9916	1.0444	29.31	14.70	90.76
33	6.9856	2.2626	2.8207	1.1699	1.2320	34.02	27.88	95.46
34	5.5237	1.5937	2.0451	1.0294	1.0381	22.89	15.58	95.76
35	8.2344	1.6909	2.1488	0.9000	0.8954	25.22	6.25	87.09
mean	6.2507	1.6596	2.1719	0.9985	0.9967	23.10	13.02	92.13
std	1.6658	0.3745	0.5382	0.0904	0.1194	5.04	7.87	4.92
worst	11.7064	2.4013	3.3937	0.8100	1.2540	34.02	29.89	79.58

Table 3.10: Experimental results using semi-automatic segmentation with user-specified constraint.

case	HD (mm)	MAD (mm)	RMSD (mm)	RoA	RoV	VD (%)	AVD (%)	Sens. (%)
1	3.7675	0.9282	1.1792	1.0326	1.0393	17.72	13.07	97.29
2	4.9723	1.2816	1.6977	1.0500	1.0876	21.48	15.56	96.41
3	3.9793	1.0157	1.2835	1.0116	1.0244	16.48	11.12	96.96
4	4.4339	1.0909	1.4467	0.9679	0.9526	12.24	2.73	94.01
5	3.9166	1.0222	1.3190	0.9789	0.9787	12.56	5.40	96.08
6	5.3882	1.5410	1.9864	0.9397	0.9008	14.79	4.11	93.19
7	5.0036	1.2943	1.6437	1.0249	1.0581	20.51	14.64	96.45
8	4.1358	1.0890	1.3768	1.0082	1.0041	14.15	9.08	97.15
9	5.1741	1.5038	1.8795	1.0282	1.0411	19.55	13.55	96.41
10	4.7904	1.1423	1.4805	0.9797	0.9810	13.19	3.57	94.77
11	3.2917	0.8703	1.0950	0.9358	0.9093	14.80	2.26	91.61
12	5.6533	1.5330	1.9947	0.9383	0.9099	17.69	1.75	89.68
13	7.0165	1.8937	2.3829	0.9293	0.9109	21.76	1.38	87.88
14	4.6835	1.0646	1.3676	1.0832	1.1112	19.13	11.69	95.62
15	6.6370	1.5011	2.0419	1.1128	1.1548	27.75	26.10	98.90
16	4.6656	1.3517	1.6610	1.0481	1.0547	20.10	17.32	98.30
17	4.1074	1.0727	1.3582	1.0568	1.0610	18.68	15.19	97.90
18	4.0723	1.2761	1.6028	1.1122	1.1500	21.34	20.73	99.62
19	4.5992	1.2752	1.5937	1.0934	1.1086	23.39	20.63	98.25
20	3.9828	1.0394	1.3028	1.0654	1.0960	24.20	21.34	98.18
21	4.5700	1.5145	1.8979	1.0219	1.0344	28.49	25.85	98.19
22	3.8663	1.2113	1.4764	1.0761	1.1018	27.49	25.18	98.45
23	5.5907	1.9925	2.4324	1.1920	1.2736	29.48	28.94	99.62
24	4.1772	1.1034	1.4007	1.0329	1.0587	21.49	17.33	97.43
25	4.9961	1.1928	1.6082	1.0845	1.1125	25.82	24.60	99.19
26	3.2105	0.8707	1.0775	1.0013	1.0182	14.89	11.54	98.08
27	4.6017	0.9801	1.2579	0.9926	0.9842	18.60	15.28	98.02
28	4.9661	1.4172	1.8030	1.0150	1.0075	24.17	10.49	91.91
29	3.1293	0.8986	1.1135	1.0722	1.0891	19.65	18.07	99.02
30	4.5103	1.1577	1.4718	1.0938	1.1384	20.30	18.21	98.71
31	4.1971	1.1596	1.5095	1.0423	1.0617	19.66	14.31	96.86
32	4.1413	1.1753	1.4641	0.9477	0.9632	16.07	8.76	95.85
33	3.6880	1.1898	1.4676	0.9875	0.9426	19.22	6.73	92.92
34	4.1264	1.0882	1.4032	1.0302	1.0390	20.72	17.20	97.86
35	7.9487	1.0854	1.4864	0.9628	0.9737	20.85	10.52	93.89
mean	4.6283	1.2235	1.5590	1.0271	1.0381	19.95	13.84	96.30
std	1.0219	0.2612	0.3283	0.0597	0.0820	4.50	7.61	2.85
worst	7.9487	1.9925	2.4324	1.1920	1.2736	29.48	28.94	87.88

Table 3.11: The transversal and sagittal area overlap ratios at the midgland.

case	Automatic		Semi-automatic	
	$S_{oT}(\%)$	$S_{oC}(\%)$	$S_{oT}(\%)$	$S_{oC}(\%)$
1	88.47	83.07	90.58	82.89
2	86.16	84.17	89.78	86.37
3	88.03	89.05	90.50	87.35
4	91.34	79.74	94.47	88.23
5	88.47	84.94	93.37	89.29
6	87.58	80.55	91.97	88.16
7	91.23	79.75	91.08	83.76
8	91.60	76.42	93.32	89.96
9	89.99	82.89	89.93	85.06
10	88.37	82.45	94.19	89.33
11	80.50	89.36	89.09	91.45
12	85.69	84.80	88.91	84.15
13	85.71	85.13	86.40	87.68
14	78.21	81.23	93.23	89.15
15	86.52	73.45	92.67	74.54
16	89.25	70.42	93.76	81.97
17	81.42	86.55	92.40	83.03
18	89.28	81.72	91.43	84.45
19	88.73	85.48	90.43	81.17
20	89.59	75.77	90.86	76.28
21	88.88	72.45	89.18	72.17
22	91.48	69.04	92.25	72.51
23	89.88	82.78	89.17	77.81
24	89.06	83.77	88.66	76.96
25	89.64	70.62	92.94	75.61
26	91.11	84.33	91.64	83.15
27	92.72	80.18	91.71	81.60
28	86.15	79.31	84.93	77.18
29	88.53	88.31	91.71	79.39
30	89.23	85.35	92.95	83.36
31	87.43	89.02	89.73	82.87
32	81.85	76.02	90.13	87.75
33	85.33	72.15	86.87	81.09
34	89.08	80.87	93.27	83.01
35	85.68	76.85	87.85	79.74
mean	87.78	80.80	90.90	82.81
std	3.27	5.63	2.29	5.15
min	78.21	69.04	84.93	72.17

Chapter 4

A Surface-to-Image Registration Technique for 3D Ultrasound Images

This chapter¹ presents the general framework of a surface-to-image registration technique applicable to 3D ultrasound images. Under this framework, an object surface segmented from the pre-operative images can be merged into the intra-operative ultrasound images by searching for a best fit between the surface and its acoustic appearance in image. The formulation of a proper similarity measurement is then investigated in its application to the multimodal registration between the MRI pelvic images and the 3D TRUS images of the same patient. We apply it on the prostate to justify the accuracy and robustness of this registration method with respect to rigidity. The importance of formulating the similarity measurement according to the object's acoustic characteristics is discussed in the registration using the pubic arch.

4.1 Introduction

Ultrasound is a real-time and cheap tool in the guidance of the prostate biopsy or cancer treatment. But due to its low SNR, it is hard to have most of the anatomic and

¹Materials reported in this chapter have been published in [73, 74, 75, 76, 77]

and metabolic details in acoustic imaging. Integrating such information from other image modalities to the ultrasonography, will be beneficial to the clinical diagnosis and treatment planning guided by ultrasound.

Compared with the patient MRI scan, the most reliable information identifiable in ultrasound image is the interface between organs. Therefore, when we try to correlate MRI data with TRUS, information other than the boundary can be omitted, as the structures visible in MRI but not in TRUS may deteriorate the match of correspondences as disturbance. For the real-time requirement in intra-operative usage, it is better to have least image processing and human intervention on the original ultrasound data. The proposed surface-to-image registration technique takes advantage from the popular surface-to-surface and image-to-image methods. It extracts the surface from pre-operative images without time limitation, and correlate it with the voxel intensities obtained intra-operatively. The correlation between the surface and the image is then formulated as the similarity measurement used in the registration, as the object function of an optimization operator, to determine the transformation parameters.

In the following sections, we first describe the general framework of this method (section 4.2). We then apply it to register the prostate from pre-operative T1- or T2-weighted MRI images to intra-operative 3D TRUS scans of the same patient, using the averaged image gradient aligned with the surface as the similarity measurement, so as to study its performance under different rigidity (such as situations with and without prostate deformation) (4.3). Based on this study, we then apply the method to the pubic arch in the following part of this chapter. The pubic arch is considered as a better choice for the multimodal registration due to its rigidity in all scans. This technique is quite helpful for the assessment of the pubic arch interference in transperineal biopsy and treatment (section 4.4). Three possible similarity measurements are formulated to interpretate the echoic characteristics of the tissue-bone interface and a comparative study is conducted to examine their respective effectiveness.

4.2 Methods

Prerequisites to the surface-to-image registration technique, are that the boundaries of the object used for registration shall be visible in both image modalities and their shapes shown in the two modalities are similar. The transformation in between is defined from the source image space to the target image space, that is, from the pre-operative images to the intra-operative images.

4.2.1 Registration Framework

The registration method requires the surface extraction from the pre-operative medical images (usually MRI or CT). This is not considered as a difficult task, because the image quality of MRI or CT is usually much better than that of the ultrasound. Most importantly, the user can outline it in substantial time as they are processed off-line. We follow the same procedure introduced in Chapter 3 (for the expert segmentation from TRUS images) to delineate the object surface from the pre-operative images.

Given the surface $S(u, v) = [x(u, v), y(u, v), z(u, v)]^T$ ($0 \leq u \leq 1, 0 \leq v \leq 1$) extracted from the source image, a set of uniformly-sampled surface points, (x, y, z) , can be generated based on the respective arc length along u and v . The 3D ultrasound image is defined in the target coordinate system with gray value $I(x', y', z')$ at the voxel coordinate (x', y', z') . The pair of data to be correlated by the registration becomes the spatial coordinates (x, y, z) and the image $I(x', y', z')$. Coordinate (x, y, z) is different from (x', y', z') in not only their origin system, but also the continuity, i.e., the former is defined continuously while the latter is discrete at voxel grid only. The rigid transformation T is described by the three translation parameters, (t_x, t_y, t_z) , and the three Euler angles, $(\alpha_x, \alpha_y, \alpha_z)$, which define the rotation against the x , y and z axis, respectively. To determine the six parameters, the registration procedure is formulated as an optimization problem that maximizes a customized similarity measurement f with respect to the transformation parameters $T = [t_x, t_y, t_z, \alpha_x, \alpha_y, \alpha_z]^T$:

$$T_{opt} = \arg \max_T f(T, x, y, z, x', y', z', I(x', y', z')) \quad (4.1)$$

Generally, the similarity between the geometric surface and the volumetric image is defined as a measure of the image intensity values associated with the voxels where the surface falls on. Nevertheless, the glandular tissues and the bony structures have entirely different characteristics in the echoic imaging. The formulation of the similarity measurement shall be customized accordingly based on the acoustic properties of object selected for registration. We continue to use the genetic algorithm (GA) as this optimization algorithm to maximize the similarity measurement. It is better than those local optimization methods because it does not require an initial guess for the transformation and the global search will not be easily trapped by local optimums. Under this mechanism, the similarity measurement used in registration is treated as the fitness function for GA search.

When applying this method to the multimodal registration between MRI and TRUS images of the prostate, the prostate boundary, as well as the pubic arch interface, are the two structures most reliably identifiable in the ultrasonography. Hence, it is reasonable for us to apply this method on either of them to verify the feasibility of our method. Since the similarity measurement plays a key role in the success of registration, it is important to choose a suitable formulation for either of them, based on an appropriate interpretation of their respective acoustic characteristics.

4.2.2 Issues on Validation

Although GA is well-known for its ability of searching for the solution in a global space, repeated experiments may not arrive at the same answer due to its random nature. Therefore, the accuracy and consistency of the registration method shall be evaluated before it is ready to be applied to the cross-modal application.

An important issue in the registration validation problem is the establishment of the "ground truth", because it is not truly available for the clinical data sets, especially for the multimodal image data. The marker-based assessment approach is widely accepted as a golden standard in registering medical images from different modalities [221], but it concerns ethical issues when implanting fiducial marks into live body. Meanwhile, the markers may not have better visibility than the anatomic structures like bony surface in

the ultrasound image. Thus, we seek for a "bronze standard" [222], which is a fuzzy gold standard with some errors included. This is realized by a so-called "self-registration" test in our study. The idea is to register the object surface segmented from the 3D TRUS image to the image itself using the proposed approach. According to the theory that a perfect registration algorithm should be able to register the surface back to its original location in the image where it was extracted, a "bronze standard" can be established as an identity transformation. Consequently, the deviation of the registration-solved transformation parameters with respect to the identity transformation will serve as the quantitative evaluation of the algorithm performance. Under this framework, the rigid-body assumption is strictly satisfied. The result can be regarded as an inherent error of this registration method under the defined conditions.

In cross-modal registration, even a "bronze truth" is hard to obtain. Therefore we only evaluate the consistency in cross-modal registration and leave the accuracy assessment to either experts or the discrepancy of the centroids between the registered MRI surface (referred as the floating surface) and the manually-segmented TRUS surface (referred as the reference surface).

4.3 Registration of Prostate

Choosing the prostate as the object to be registered is straightforward in matching the two image spaces, as we aim at integrating the anatomical and metabolic information of the prostate in ultrasound-guided application. Although there may be a hidden requirement in the surface-to-image registration that there should be no deformation in between, it may not be strictly met due to different modal conditions imposed on the gland. Hence, in this section, we would like to apply this method to the MRI and TRUS image of the prostate and validate its feasibility with rigid, small-deformed and large-deformed bodies.

4.3.1 Formulation of Similarity Measurement

Under a rigid-body assumption, the prostate surface in ultrasound images should be identical or similar to that in MRI images for the same patient. As the prostate appears to be relatively dark compared to its surroundings, high image gradients may exist along its boundary in centrifugal direction. Therefore, the similarity measurement is designed to characterize the alignment of the surface with respect to the image gradients at the surface. Quantitatively, it is evaluated as the averaged image gradients along the normals of the surface points [73]. This measure is referred as "Projective Gradient" (PG) in our study and defined as:

$$f_{PG}(T) = \frac{1}{N} \sum_{i=1}^N \langle \vec{G}([T(x_i, y_i, z_i)]) \cdot T(\vec{n}(x_i, y_i, z_i)) \rangle \quad (4.2)$$

where $\vec{G}$ is the intensity gradient calculated from the Gaussian-smoothed ultrasound image I (see Equation 3.31). $\vec{n}(x_i, y_i, z_i)$ is the normal vector at the i -th surface point (x_i, y_i, z_i) . Operator $\langle \cdot \rangle$ denotes the inner product. The nearest-neighbor operator $[]$ is used to calculate the image intensity value at any surface point. This definition is the same as that defined for the prostate segmentation problem. When the surface aligns with the boundary of high gradients, the value of the similarity function will be maximal.

4.3.2 Experiments and Results

To examine the algorithm's performance with objects of different deformation, the experiments are conducted between the TRUS images and pre-operative MRI images of the same patient. Usually, the patient will have two kinds of MRI scans. One is the T1 weighted images of a resting prostate, i.e., the prostate lies in its natural condition; the other is the T2 weighted images using an extra endorectal MRS coil, in which the prostate is pushed against the pubic arch and deformed by the rectum filling caused due to a water-inflated balloon that encapsulates the imaging coil.

Image data

All MRI examinations were performed on 1.5 Tesla whole body GE MR systems. The ordinary fast spin-echo T1 weighted images were taken at $TR/TE = 600 - 700 / \sim 12$ msec, with image size 512×512 pixels in field of view of $16.0 \times 16.0\text{cm}^2$, 3.0mm slice thickness and 1.0mm interslice gap. The endorectal FSE T2 weighted images were acquired at $TR/TE = 4100 - 5200 / 92\text{ms}$, with image size 512×512 pixels in field of view of $16.0 \times 12.0\text{cm}^2$, 3.0mm slice thickness and 0.5mm inter-slice gap. The intra-operative TRUS system was still the Aloka SSD-1700 system (ALOKA Inc., Japan), set to yield image resolution to $0.18 \times 0.18\text{mm}^2$. An external motor driving system was used to pull the ultrasound probe to scan the prostate at an even interval of 1.0mm. Image size was cropped to the region of interest (ROI) only, about 400×290 pixels. Due to the experiment complexity and data availability, 5 sets of patient data (including TRUS, MR T1, and MR T2) were collected for this study.

Experiment settings

A test of GA on different combination of chromosome encode schemes and evolution strategies was conducted by Wu et al [127]. Based on this founding, we choose the GA parameters used for our experiments as shown in Table 4.1.

Table 4.1: Parameter settings in genetic algorithm.

Population	600
Number of generations	300
Crossover rate	95%
Mutation rate	5%
Chromosome encoding	Real-value array encoding
Evolution strategy	Incremental GA evolution strategy with crowding replacement
Selection scheme	Tournament selection

The source surface is constructed by a set of parallel contours drawn by expert at the transversal slices. Once it is imported into the target image volume, a group of points are generated on the parameterized surface. Ideally these points should be uniformly distributed on the surface. For that, we extract 20 equally spaced iso-curves from the surface and sampled 30 equally-spaced points along long curves and less along shorter

ones so that the interval between points can be as equivalent as possible. Usually less than 300 points are generated. The coordinates (x_i, y_i, z_i) and normal vectors $\vec{n}(x_i, y_i, z_i)$ defined at these points are then passed to the GA engine.

To simplify the problem, the transformation solved by GA is defined in the local coordinate system of the prostate, whose origin is at the object centroid. If this transformation is denoted as T_{GA} and all transformations are in the form of homogeneous matrix, the final transformation T between the two image systems (what we actually looking for) can be determined by applying translation before the local transformation T_{GA} .

$$T = T_{GA} \cdot T_c \quad (4.3)$$

where T_c is the transformation of moving the MR surface centroid to the origin of the TRUS coordinate system. Once the shape has been segmented from the source images, T_c would be known. Transformation matrix T_{GA} is defined in the Rodrigues' Formula, in which the rotation is computed by an angle θ about a fixed axis $\vec{e}$ (a unit vector) according to the right-hand rule (referred as axis-angle).

The rotation axis $\vec{e}$ can be determined by its latitude ψ and longitude ϕ to a spherical system as

$$\vec{e} = (e_x, e_y, e_z) = (\cos \psi \cos \phi, \cos \psi \sin \phi, \sin \psi) \quad (4.4)$$

where $-\pi \leq \phi \leq \pi$ and $-\pi \leq \psi \leq \pi$. Let $\vec{t} = (t_x, t_y, t_z)$ be the translation vector, the homogeneous matrix T_{GA} can be described as

$$T_{GA} = \begin{bmatrix} e_x^2(1-\cos\theta)+\cos\theta & e_x e_y(1-\cos\theta)-e_z \sin\theta & e_x e_z(1-\cos\theta)+e_y \sin\theta & t_x \\ e_x e_y(1-\cos\theta)+e_z \sin\theta & e_y^2(1-\cos\theta)+\cos\theta & e_y e_z(1-\cos\theta)-e_x \sin\theta & t_y \\ e_x e_z(1-\cos\theta)-e_y \sin\theta & e_y e_z(1-\cos\theta)+e_x \sin\theta & e_z^2(1-\cos\theta)+\cos\theta & t_z \\ 0 & 0 & 0 & 1 \end{bmatrix} \quad (4.5)$$

Table 4.2 lists the six parameters, (t_x, t_y, t_z) and (ψ, ϕ, θ) , encoded in the chromosomes and their respective range of search.

The self-registration is applied to the 3D TRUS image and the manually-extracted sur-

Table 4.2: The transformation parameters encoded in the GA chromosomes, where D_x , D_y , D_z are the dimension of the 3D TRUS image. The ranges of these parameters are under the assumption that the coordinate origin of (x', y', z') is at the center of the image volume.

Parameter	Description	Range
t_x	Translation of the surface centroid in x direction. (unit: mm)	$-D_x/2 \sim D_x/2$
t_y	Translation of the surface centroid in y direction. (unit: mm)	$-D_y/2 \sim D_y/2$
t_z	Translation of the surface centroid in z direction. (unit: mm)	$-D_z/2 \sim D_z/2$
ψ	Latitude of rotation axis, which passes through the surface centroid. (unit: radian)	$-\pi/2 \sim \pi/2$
ϕ	Longitude of rotation axis, which passes through the surface centroid. (unit: radian)	$-\pi \sim \pi$
θ	Rotation angle around the rotation axis. (unit: radian)	$-\pi/2 \sim \pi/2$

face from the image. The accuracy and consistency of this method itself is assessed by evaluating the absolute translation error and residue angle against a rotation axis. Once the inherent errors are obtained, we apply the method on the cross-modal image pairs, where the prostate surface in MRI images is segmented and imported to TRUS image volume. We can therefore study how the prostate deformation (from different modalities) affects the registration accuracy and under what circumstance the method is workable. Two sets of cross-modal tests are performed, one is the surface from MRI T1-weighted image to the 3D TRUS image for resting prostate and the other is the surface from MRI T2-weighted image to the same TRUS volume for deformed prostate. For consistency, 10 times of registration are applied for each of the surface-image pair. And the error is measured by the centroid distance and angular difference between the floating surface and the reference surface.

To study whether there is any directional rotation error involved in the cross-modal registration, we choose to use the Euler angles, rather than the absolute rotation angle about a rotation axis. The conversion from the axis-angle representation $(\vec{e}(e_x, e_y, e_z), \theta)$ to the Euler angles (α, β, γ) are as follows:

if north pole singularity is detected, i.e., $(e_x e_y (1 - \cos(\omega)) + e_z \sin(\omega)) > 0.998$,

$$\begin{aligned}\alpha &= 2 \arctan 2(e_x \sin(\theta/2), \cos(\theta/2)) \\ \beta &= \pi/2 \\ \gamma &= 0\end{aligned}\tag{4.6}$$

else if south pole singularity is detected, i.e., $e_x e_y (1 - \cos(\phi)) + e_z \sin(\phi) < -0.998$,

$$\begin{aligned}\alpha &= -2 \arctan 2(e_x \sin(\theta/2), \cos(\theta/2)) \\ \beta &= -\pi/2 \\ \gamma &= 0\end{aligned}\tag{4.7}$$

else,

$$\begin{aligned}\alpha &= \arctan 2(e_y \sin(\theta) - e_x e_z \cdot (1 - \cos(\theta)), 1 - (e_y^2 + e_x^2)(1 - \cos(\theta))) \\ \beta &= \arcsin(e_x e_y (1 - \cos(\theta)) + e_z \sin(\theta)) \\ \gamma &= \arctan 2(e_x \sin(\theta) - e_y e_z (1 - \cos(\theta)), 1 - (e_x^2 + e_z^2)(1 - \cos(\theta)))\end{aligned}\tag{4.8}$$

Results

Figure 4.1 shows a self-registration example of patient 1 in which we can see the registered prostate surface is very closed to its original location. Table 4.3 demonstrates the experiment results over the 5 cases and the findings is that the translation error is $0.59 \pm 0.28\text{mm}$, the rotation error is $1.45 \pm 0.53^\circ$. Considering the possible error in segmenting the shape, we think that the registration algorithm is quite robust and reliable for ultrasound image.

The above results show the possible registration error under a rigid-body assumption. If the assumption is not satisfied, it may result in an increased error. Figure 4.2 shows an example using the registration between MRI T1 and TRUS data of patient 1. Table 4.4

Figure 4.1: Registering the prostate surface to the TRUS image where it is segmented from. The three images are orthogonal planes of the 3D image volume. The green contours and solid surface indicate their original location, while the yellow ones are the registered result.

Table 4.3: Experimental results of accuracy and consistency in self-registration of us surface-image pairs.

Patient No	Translation $ t $ (mm)		Rotation $ \theta $ ($^{\circ}$)	
	MEAN	SD	MEAN	SD
1	0.55	0.41	1.54	3.41
2	0.71	0.35	1.15	1.08
3	0.86	0.46	1.09	2.63
4	0.46	0.44	2.33	0.61
5	0.35	0.82	1.14	5.57
avg	0.59	0.20	1.45	0.53

summarizes the standard deviation of the solved translation and rotation. The results show that the consistency in translation is comparable with the self-registration result but the consistency in rotation is directional, that is, the variations in rotation around the y and z axes are relatively larger. This may be caused by the symmetry-analog shape of the prostate and the influence from the noise prevalent in ultrasound images. The error evaluated by centroid displacement shown in Table 4.5 is about 2.67mm on average between the MRI T1 and TRUS registration, considerably larger than the error found in the self-registration test. We contribute the increase of error to the shape change between the two modalities, potentially caused by the use of endorectal probe in TRUS compared to a totally relaxed rectum in MRI T1 scan, or the change of patient posture

from lithotomy in TRUS to supine in MRI.

Table 4.4: Surface-to-Image registration consistency and error evaluation (between MR T1 Images and TRUS Images).

Patient No	Translation (mm)	Rotation ($^{\circ}$)		
	SD ($ t $)	SD (α)	SD (β)	SD (γ)
1	0.44	2.9	22.22	13.97
2	0.25	2.67	15.96	9.63
3	0.80	3.20	7.00	15.32
4	0.24	3.96	6.42	20.13
5	1.14	1.74	3.67	3.48
avg	0.60	3.09	11.05	12.51

With an increased deformation in between the scans (e.g., over 10mm between surfaces), such as the use of the endorectal coil in the MRI T2 images for prostate cancer diagnosis, the registration results in an increased error to more than 5mm in the centroid displacement, as illustrated in Table 4.5. Figure 4.3 shows a partially matched result between MRI T2 images and TRUS images of patient 1 using the surface-to-image method. Therefore, we can conclude that the algorithm works effectively and robustly with noisy images and small-deformed object, but may result in a misalignment at part of the boundaries when the deformation is large.

Table 4.5: Registration error with object of different amounts of deformation.

US Images with		Centroid Distance (mm)	
		MEAN	SD
MR T1 Images (no or small deformation)	case 1	1.57	0.45
	case 2	4.12	0.44
	case 3	2.28	1.80
	case 4	2.38	0.30
	case 5	2.95	0.42
	avg	2.67	0.68
MR T2 Images (large deformation)	case 1	4.31	1.20
	case 2	6.07	6.38
	case 3	7.02	3.08
	case 4	2.44	0.33
	case 5	7.00	2.22
	avg	5.36	2.64

The registration takes around 10 seconds on a Pentium® 4 2.4GHz PC with 512MB RAM [73] and the time is reduced to around 1 second on a Intel Centrino® 2 Notebook (2.0GHz CPU and 4GB Memory). This speed is considered sufficiently fast for an intra-

(a)

(b)

(c)

Figure 4.2: Experimental result of TRUS to MR T1 registration using case 1 data. (a) The MR T1 image stack and the segmented prostate surface. (b) The initial location of the prostate surface in (a) with respect to the ultrasound volume before registration. (c) The registered result.

(a)

(b)

(c)

Figure 4.3: Experimental result of TRUS to MR T2 registration using case 1 data. (a) The endorectal MR image stack and the segmented prostate surface. (b) The initial location of the prostate surface in (a) with respect to the ultrasound volume before registration. (c) Registration result (with large-deformed body).

operative use.

4.3.3 Discussion

We have demonstrated the GA-based surface-to-volume registration method and its application in ultrasound and multimodal image matching. In the experiments of the registration between the MRI T1 image (of resting prostate) and the ultrasound images, the results show that the global registration can approximately locate the prostate boundary in the noisy US images in acceptable accuracy, and applicable to intra-operative cases which required a real-time localization of the prostate gland in ultrasound-guidance procedures.

In another aspect, although the registered surface in the ultrasound images may not align perfectly with the real image boundaries, it is still not far from the truth and can serve as a proper initialization of a deformable segmentation model, such as the active contour model (ACM, or called "snakes") [99], and the level set method [117]. To demonstrate the feasibility, a test of using the registered result for further segmentation is conducted. For demonstration only, the 3D image segmentation is simplified into a series of 2D boundary detection problems like the way in [102], except that the initial contour of each slice comes from the cross-section of the registered surface at that slice, not the curve propagated from the neighboring slices.

Given the total energy of an active contour as E_{total} . E_{total} is composed of the internal energy E_{int} and external energy E_{ext} , where the internal energy reflects the elasticity and bending of the contour, and the external energy comprises the image energy E_{image} derived from image contents, and constraints E_{con} imposed by human intervention. Segmentation is realized by iteratively minimizing the total energy of the active contour. When no human constraint is involved, the energy in discrete form can be written as

$$E_{total} = \sum_{i=1}^M [E_{int}(v_i) + E_{ext}(v_i)] \quad (4.9)$$

$$E_{int}(v_i) = (\alpha(v_i)|v_i - v_{i-1}|^2 + \beta(v_i)|v_{i+1} - 2v_i + v_{i-1}|^2) \quad (4.10)$$

$$E_{ext}(v_i) = -\langle \nabla g_\sigma * I(v_i), \vec{n}(v_i) \rangle \quad (4.11)$$

where v_i is the i th point on the contour ($0 \leq i \leq M$); $\alpha(v_i)$ and $\beta(v_i)$ are coefficients that control the relative importance of the membrane term (the first-order term) and the thin-plate term (the second-order term), respectively; g_σ is the Gaussian smoothing kernel for the US image I ; $\vec{n}$ represents the normal vectors on the contour. The dynamic programming [223] is used to look for the optimal solution.

Figure 4.4 demonstrates the segmentation result based on the initialization from registration using the classic active contour model. Since the initial contour is already quite close to the boundary, the number of iterations towards convergence is quite few. The experimental results shown in Figure 4.4(a) indicated that most of the contours correctly converged to the actual boundaries, while some of them may need manual intervention due to ambiguous image information. In fact, there is an issue in the sequential 2D segmentation. Only those 2D slices with the initialized contours covered are processed. Slices which contribute to the prostate region but do not intersect with the registered surface will be falsely excluded, while those initialized slices which are not actually part of the prostate are falsely included. An active surface model which works for 3D shape directly is able to overcome these problems. Early work has been done for the segmentation using a 3D model [101, 30, 29]. However, the purpose of illustrating the ACM segmentation here is only to verify the feasibility of using the registered result as the initial model for further segmentation. Currently it is not our emphasis thus will be left to future work.

4.4 Registration of Pubic Arch

Previous studies show that the prostate deformation in MRI T2 images is prominent thus registration using the prostate is not ideal in recovering the rigid transformation between the MRI T2 and TRUS image spaces. Hence, it is more reasonable to choose the pubic arch, a rigid bone structure visible in both scans, for the registration.

In addition, the pubic arch is also an important anatomical structure requiring special attention in prostate transperineal biopsy and brachytherapy. In such clinical practice, the assessment of the pubic arch interference (PAI) is important, especially when the prostate is enlarged by disease. To our knowledge, only a few work has been done

Figure 4.4: Segmentation based on registered result. (a) Initial active contours for segmentation, which comes from the result of the surface-to-volume registration. There are still some discrepancies along the boundary. (b) The segmentation result using active model which based on the initialization of (a).

on the automatic registration or segmentation of the pubic arch. Mostly, the tissue-bone interface is identified manually [13, 224, 225, 14]. A more advanced technique was proposed by Pathak et al. [226], in which they fitted a parabola over a group of edge points thresholded from the enhanced ultrasound image [227] to conform to the interface.

4.4.1 Candidate Similarity Measurements

As a bony structure, the posterior interface of the pubic arch manifests hyperechoicity in ultrasound images, like the boundary of the prostate. The difference is the rear of the tissue-bone interface is dark as it is hard for echo to penetrate through the dense structures. Hence, based on the possible interpretations of the acoustic appearance of the pubic arch in ultrasound, three forms of the similarity measurements are formulated as candidates and applied in GA as the fitness functions.

The first one is the similarity between surface point and image voxels of high intensity. Based on the fact that the object surface (like bone surface) should be of high gray level in the ultrasound image (Figure 4.5), the similarity measurement can be defined as the averaged intensity value aligned on the surface, similar to that defined in [182, 183]. We refer it as "Aligned Intensity" (AI) and formulate it by

$$f_{AI}(T) = \frac{1}{N} \sum_{i=1}^N I([T(x_i, y_i, z_i)]) \quad (4.12)$$

where N is the number of points uniformly sampled on the pubic arch surface in MRI space. (x_i, y_i, z_i) is the i th point sampled on this surface and $[T(x_i, y_i, z_i)]$ is the corresponding voxel coordinate of the referred point in the US image at which the intensity value is $I([T(x_i, y_i, z_i)])$. The nearest-neighbor operator $[]$ is used to transform the point coordinate to the image voxel grid. For any point falling outside the 3D image region, its contribution to the fitness function would be zero. Inherently, this measure characterizes the high reflection of echo at the tissue-bone interface and is evaluated in terms of gray level in the ultrasound image.

The second is the similarity between the surface normal and the image gradient, which is derived from the fact that there is high image gradient at the tissue-bone interface

Figure 4.5: The interpretation of the similarity between the surface and the image.

as the echo reflection at the bone surface is much strong than that on tissues. So the metric is formulated as the averaged image gradients along the normals of the surface, which has been defined and used in registration of the prostate. This measure, referred as "projective gradient" (PG), is formulated in Equation (4.2).

The third is the similarity between the surface and voxels of high intensity with dark rear shadow. This comes from the acoustic characteristics of the bone structures in ultrasound, which shows that the echo wave has very strong reflection at the tissue-bone interface and can hardly penetrate it. Therefore the inner surface of the pubic arch appears hyper-echoic while the area at its anterior rear shows as a homogeneously dark shadow. Accordingly, this measure is evaluated as the averaged radial "gradient" between the voxels falling on the surface against those at its rear, referred as "Intensity Shadow" (IS) measure [76].

$$f_{IS}(T) = \frac{1}{N} \sum_{i=1}^N (I([T(x_i, y_i, z_i)]) - \frac{1}{D} \sum_{k=1}^D I([T(x_i, y_i, z_i) + k \cdot \vec{v}(T(x_i, y_i, z_i))])) \quad (4.13)$$

where D is the user-defined depth of the posterior region (counted in terms of voxels). $\vec{v}(x, y, z)$ is the unit vector defined in image of depth z , that denotes the direction of the echo emission from the transducer to any point (x, y) in its planar field of view. Since our 3D TRUS image is constructed by a series of transrectal images (in $x - y$ plane) scanned at equal intervals (in z direction), the gray value at any voxel is only determined by the echo reflection in plane (i.e., energy emitted and received at the same z depth of the voxel). According to this rule, the intensity "gradient" is calculated radially, along

Figure 4.6: Another interpretation of the similarity between the surface and the image.

the echo propagation direction, from the transducer center to the surface point, in the planar slice at this depth. The radial vector $\vec{v}(x, y, z)$ at any point (x, y, z) is represented as

$$\vec{v}(x, y, z) = \frac{(x, y, z) - (x_p, y_p, z)}{\|(x, y, z) - (x_p, y_p, z)\|_2} \quad (4.14)$$

where $\vec{x}_p(x_p, y_p)$ is the probe center shown at the transversal plane. Accordingly, The z component of unit vector $\vec{x}_i(x_i, y_i, z_i)$ is 0 due to the assumption of the echo coplanarity. It is noted that the IS measure does not follow the conventional concept of the image "gradient" since it is computed between the voxel at the surface and its posterior along the ultrasound propagation direction.

4.4.2 Experiments and Results

Based on the candidate similarity measures formulated for the registration of the pubic arch, a comparative study is conducted to determine the one which is most appropriate for the search of the tissue-bone interface in ultrasound images.

Image Data

We collected fourteen sets of patient data for the comparative study, among which 1st to 11th patients have complete set of MR T2 and TRUS images and 12th to 14th patients have the TRUS images only. The MRI images were acquired from the same GE MR

systems used before and we only collected the T2-weighted images as the pubic arch shown in T1-weighted images shall be identical. The 3D TRUS images of these patients were collected using the same machine and settings as we mentioned before.

Experiment settings

The number of surface points evenly generated for registration is 450 ($N = 450$). The parameter D in the IS-measure fitness function is chosen as 40, which represents a depth of $7.2 \sim 10.2$ mm beneath the pubic arch surface. The configuration of GA in this study is similar to those used previously (shown in Table 4.1), except that we use 300 populations and 100 generations. The final transformation T is also determined using Equation (4.3). After an initial translation to offset the centroid of the source data to the origin of the target TRUS image, the subsequent transformation is solved by GA but the axis-angle rotation is replaced by the three Euler angles (α, β, γ) . Table 4.6 lists the six parameters encoded in GA chromosome for transformation matrix T_{GA} .

Table 4.6: The transformation parameters encoded in the GA chromosomes, where D_x , D_y , D_z are the dimension of the 3D TRUS image. The ranges of these parameters are under the assumption that the coordinate origin is at the center of the image volume.

Parameter	Description	Range
t_x	Translation of the surface centroid in x direction. (unit: mm)	$-D_x/2 \sim D_x/2$
t_y	Translation of the surface centroid in y direction. (unit: mm)	$-D_y/2 \sim D_y/2$
t_z	Translation of the surface centroid in z direction. (unit: mm)	$-D_z/2 \sim D_z/2$
α	The Euler angle around x axis. (unit: radian)	$-\pi/18 \sim \pi/18$
β	The Euler angle around y axis. (unit: radian)	$-\pi/18 \sim \pi/18$
γ	The Euler angle around z axis (unit: radian)	$-\pi/18 \sim \pi/18$

The TRUS image data of the 1st to 14th patients are used in the self-registration test. The pubic arch surface in each TRUS image is extracted by an expert. To simplify the comparison, the absolute translation $\|t\|$ and the axis-angle θ for rotation are used. The relationship between θ and the three Cartesian rotation angles (α, β, γ) is illustrated in Equation (4.15).

$$\|\theta\| = \cos^{-1} \left(\frac{1}{2} (\cos \alpha \cos \beta + \cos \beta \cos \gamma + \cos \gamma \cos \alpha + \sin \alpha \sin \beta \sin \gamma - 1) \right) \quad (4.15)$$

Statistics in forms of mean and standard deviation is calculated over the 15 repeated experiments of the three sets of patient data. Accuracy of the registration is indicated by the mean value of the translation and rotation vectors, while the algorithm consistency is revealed by the averaged standard deviation of those parameters. An "objective" criterion is introduced in the self-registration test that a match would be considered acceptable if the resulting error is within an absolute displacement of 5mm and a rotation of 5° , otherwise we consider it failed.

The MRI and TRUS image pairs available in patients 1st ~ 11th are used in the subsequent cross-modal registration test. We only evaluate the standard deviations of the registration results to its performance, while relying on expert opinions in the process of justifying its accuracy and feasibility. The robustness of the algorithm is estimated by a rating system obtained from a "subjective" visual assessment by an expert.

Results

Figure 4.7 shows the box and whisker plots of the resulting translation and rotation obtained by self-registration experiments. The IS measure is found to deliver generally the highest accuracy and consistency among the three measures, while the AI measure results in two complete misalignment, with a translational error beyond 10 mm, and the PG measure yields the worst consistency in repeated runs. Table 4.7 illustrates the quantitative evaluation of the self-registration test. The best registration quality is obtained by the IS measure, with 2.22 ± 0.74 mm in translation and $3.43 \pm 1.50^\circ$ in rotation. The Wilcoxon Signed Rank Test (when the population cannot be assumed to be normally distributed), and the paired Student t test (when population are assumed to be normally distributed) are used here to compare the differences between the measurements. The Wilcoxon test shows a significant improvement when IS measure is used ($p < 0.05$), except that no significant difference is found comparing its rotation error with those obtained by the AI measure. Comparing the AI measure against the PG measure, there is a significant improvement ($p < 0.05$) in rotation error but not in translation. The one-tailed paired t tests obtain the same findings.

We also compare the failure rating of the three measures using the "objective" criterion

Figure 4.7: Comparison of the self-registration quality over 14 patients using the similarity measurement AI, PG and IS, respectively. From top to bottom: AI, PG and IS measures. From left to right: translation error and rotation error. The data were collected from 15 repeated experiments on each set of patient data.

we define before. The IS-based self-registration is found to have the best accuracy (22.9% failure) among the total 210 experiments, while the AI-based method is moderate (46.7%) and the PG method is the worst (65.7%).

Another finding about the IS-registration is that the rotation error does not show a distinguished skewness with respect to the x , y and z directions, however, the translation

Table 4.7: Self-registration results using 14 sets of TRUS patient data over the similarity measurement AI, PG and IS.

Patient No.	Accuracy						Variability					
	Mean of Transl.(mm)			Mean of Rotation(°)			SD of Transl.(mm)			SD of Rotation (°)		
	AI	PG	IS	AI	PG	IS	AI	PG	IS	AI	PG	IS
1	2.12	3.48	2.10	4.21	6.78	3.24	0.89	1.45	0.80	2.10	1.80	0.92
2	2.75	4.22	2.53	2.51	3.12	1.87	0.57	1.15	0.53	1.11	1.27	1.41
3	1.24	2.21	0.89	2.94	4.64	2.53	0.59	0.84	0.38	1.69	2.70	1.06
4	0.67	1.69	0.85	2.09	4.54	2.35	0.48	0.49	0.54	0.96	3.35	0.99
5	27.38	5.57	1.12	5.85	9.48	5.51	0.62	8.80	0.53	2.00	2.22	2.94
6	2.07	3.37	1.50	5.08	7.39	3.62	1.12	1.46	0.63	1.79	3.75	1.33
7	7.23	5.94	7.25	1.90	3.64	2.23	0.22	1.24	0.36	0.76	3.50	1.20
8	2.10	3.71	1.63	4.26	9.34	2.59	0.97	2.37	0.63	2.74	1.36	1.07
9	1.06	2.96	1.41	3.12	4.07	3.23	0.39	1.04	0.55	1.65	3.07	1.19
10	35.03	7.16	3.68	13.79	9.09	5.29	1.28	2.78	2.06	1.65	2.68	2.23
11	6.53	4.11	3.46	10.00	8.47	6.35	1.15	1.09	1.32	1.79	2.19	1.97
12	6.89	4.17	2.40	4.54	7.75	4.26	0.45	1.14	0.75	1.98	3.70	2.67
13	1.94	5.70	1.31	3.96	7.58	2.73	0.87	3.89	0.72	1.30	3.28	1.08
14	0.94	1.88	0.97	2.01	2.46	2.18	0.64	0.40	0.52	0.77	1.11	0.91
Avg.	7.00	4.01	2.22	4.73	6.31	3.43	0.73	2.01	0.74	1.59	2.57	1.50

error in z direction is more significant than the errors in x and y directions. On average, it accounts for 42.6% of the total displacement. Figure 4.8 to Figure 4.11 demonstrate a few of the registered results of the self-validation. Figure 4.8 and Figure 4.9 show comparable accuracy among the three methods. However in Figure 4.10, the AI measure delivers a totally wrong prediction of the pubic arch surface because of some highly reflective tissues existing inside of the gland. Figure 4.11 shows a uttermost situation of the axial displacement - the three methods produce similar results and all of them may not be able to obtain good accuracy for its axial position in image. In our repeated experiments of case 7 (Figure 4.11), the IS-method shows an averaged axial mismatching larger than 7 mm, approximately 85.9 of the total displacement error. Two causes are suspected causing this error. One is the surface delineated from the TRUS image. We usually delineate the pubic arch surface by outlining a few curves at selected slices in the transversal view. Due to the limited view of the pubic arch reflection in the echoic image, we usually select those slices with strong boundary strength at the arch interface and avoid those weak ones. This may lead to an incomplete description of the true surface, especially at the two ends. Sometimes, the incompleteness can also be caused by human,

such as the surface delineated for case 7 in which the superior part of the surface was not fully outlined by the expert although the pubic interface is quite clear at those slices. Since the partial surface is somehow wedge-like due to the junction at the pubic symphysis, the registration of the surface back to its image may be "slipped" along the superior-inferior direction of the pubic interface, without causing much difference in the fitness value of the optimization. The image spacing between adjacent slices is another cause of the error in axial direction. Because we use the nearest neighborhood interpolation to locate the corresponding voxel with regards to the surface point, the spatial resolution of the image would affect the accuracy of registration. Comparing with the image resolution in the $x - y$ plane ($0.18 \sim 0.27$ mm), the slice spacing along the z -direction is much coarser (1.0 mm). Therefore we can imagine a larger error may occur in locating the z direction translation.

Therefore, in order to ensure high accuracy when using the surface-to-image registration method, it is desired to delineate the surface information as much as possible. Comparatively, a partial surface is less resistant to the speckle noise and less accurate to locate the objects without much shape features or corners.

Figure 4.12 demonstrates the cross-modal registration results of the three measures using the MRI-TRUS image pair of patient 1st $\sim$ 11th. We can not justify the accuracy from the figure due to the absence of the "ground truth". Therefore only the variation of solutions in the repeated experiments is assessed. A conclusion can be drawn from Figure 4.12 that the PG measure exhibits the worst consistency in the experiments, as it yields a wider range of possible solutions compared to the other two. However, there is no outright winner between the AI and IS measures, because the difference between their performance is not obvious. Summarizing the standard deviations listed in Table 4.8, we can see that IS-based method possesses a relatively better consistency than that of the AI method in average, but it does not outperform AI dominantly in the variability of rotational solutions.

Although a quantitative evaluation of the multimodal registration accuracy is unavailable due to the limitation of our experimental design, we conduct a visual assessment of the registered results with the help of an expert. By superimposing the registered pubic arch surface onto the patient TRUS image volume (as shown in Figure 4.14–4.16), the expert

Figure 4.8: The self-registration results for case 1. (a) The transverse view before the registration. (b) The sagittal view before the registration. (c) The result using IA-based registration. (d) The result using PG-based registration. (e) The result using IS-based registration.

is able to assess whether the surface position is far from the bright echogenic tissue-bone interface. The statistics of the 165 experiments in Table 4.9 shows that the IS measure obtains the highest percentage of excellence. For example, in case 1 (Figure 4.13), the AI measure fails to obtain accurate registration because of the presence of some highly-reflective tissues between the pubic arch interface and the anterior boundary of the

Figure 4.9: The self-registration results for case 4. (a) The transverse view before the registration. (b) The sagittal view before the registration. (c) The result using IA-based registration. (d) The result using PG-based registration. (e) The result using IS-based registration.

prostate. In case 4 (Figure 4.14), all three measures can produce acceptable results. In case 5 (Figure 4.15), however, only the IS measure can overcome the interference from the highly-reflective structures inside of the gland. The case 7 (Figure 4.16) obtain comparable results with the AI measure and the IS measure, but the PG measure may fail to locate it accurately. Case 8 (shown in Figure 4.17) is the only exception in our

Figure 4.10: The self-registration results for case 5. (a) The transverse view before the registration. (b) The sagittal view before the registration. (c) The result using IA-based registration. (d) The result using PG-based registration. (e) The result using IS-based registration.

test dataset, that is, even the IS measure may not deliver satisfying results. It is found that one third of the IS-based experiments are less accurate in axial positioning. The reason is similar to those found in the self-registration test. That is, the pubic surface outlined for the registration is not large enough and it is in a wedge-like shape.

Figure 4.11: The self-registration results for case 7. It is the only case that IS measure does not outperform the other two. (a) The transverse view before the registration. (b) The sagittal view before the registration. (c) The result using IA-based registration. (d) The result using PG-based registration. (e) The result using IS-based registration.

Based on our observations of the overall experimental results, the IA-based registration may lead to a complete misalignment when other tissue interfaces, such as the prostate boundary, the prostatic concretion or highly-reflective fiber, show a similar level of brightness as that of the pubic arch interface. Both the PG-measure and the IS-measure are found to be more likely to fail when using an incomplete surface or small-sized surface.

Figure 4.12: Comparison of the cross-registration quality over 11 sets of patient data using the similarity measurement AI, PG and IS, respectively. From top to bottom: AI, PG and IS measures. From left to right: translation and rotation error. The data were collected from 15 repeated experiments on each pair of patient data.

The former is more likely influenced by the speckle noise or tissue interfaces of high image gradient, due to its poor resistance to the noise. The latter is more vulnerable to the axial positioning due to the wedge shape of the pubic arch interface and the similar fitness values of the objective function along the bony slope.

Table 4.8: Experimental results using 11 sets of MRI-TRUS patient images over the similarity measurement AI, PG and IS.

Patient No.	Variability					
	SD of Translation(<i>mm</i>)			SD of Rotation (°)		
	AI	PG	IS	AI	PG	IS
1	0.62	2.47	0.54	1.02	2.84	1.20
2	0.70	3.22	0.48	1.11	2.82	0.56
3	0.15	4.68	0.09	0.61	2.61	1.02
4	0.46	2.07	0.37	2.01	2.85	0.71
5	0.97	1.62	0.82	2.22	1.92	1.94
6	0.57	2.03	0.30	1.29	2.63	0.93
7	0.18	1.48	0.32	1.55	2.00	1.63
8	0.80	3.80	1.24	1.55	3.42	2.48
9	1.85	0.33	0.34	1.29	1.28	1.24
10	1.04	0.82	0.66	1.35	1.58	1.21
11	0.46	1.42	0.61	1.28	2.72	1.85
Avg.	0.71	2.58	0.53	1.39	2.42	1.34

Table 4.9: The expert rating over the results obtained using the similarity measurement AI, PG and IS. (P: poor. M: moderate. E: excellent)

Patient No.	AI			PG			IS		
	P	M	E	P	M	E	P	M	E
1	15	0	0	8	4	3	0	0	15
2	1	10	4	12	3	0	0	0	15
3	0	0	15	11	0	4	0	0	15
4	0	0	15	2	0	13	0	0	15
5	15	0	0	15	0	0	0	0	15
6	2	13	0	15	0	0	0	0	15
7	0	0	15	6	3	6	0	0	15
8	15	0	0	15	0	0	0	5	10
9	1	0	14	15	0	0	0	0	15
10	15	0	0	15	0	0	0	0	15
11	0	0	15	15	0	0	0	0	15
Percentage of excellence	47.27%			15.76%			96.97%

Figure 4.13: Comparative results for case 1, in which the AI measure may fail. (a) Pre-registration (original pubic arch surface from MRI directly merged to the TRUS image volume). (b) The result using IA-based registration. (c) The result using PG-based registration. (d) The result using IS-based registration.

Figure 4.14: Comparative results for case 4. All methods deliver acceptable results. (a) Pre-registration (original pubic arch surface from MRI directly merged to the TRUS image volume). (b) The result using IA-based registration. (c) The result using PG-based registration. (d) The result using IS-based registration.

Figure 4.15: Comparative results for case 5, in which both AI and PG measures may fail. (a) Pre-registration (original pubic arch surface from MRI directly merged to the TRUS image volume). (b) The result using IA-based registration. (c) The result using PG-based registration. (d) The result using IS-based registration.

Figure 4.16: Comparative results for case 7. (a) Pre-registration (original pubic arch surface from MRI directly merged to the TRUS image volume). (b) The result using IA-based registration. (c) The result using PG-based registration. (d) The result using IS-based registration.

Figure 4.17: Comparative results for case 8, in which only the IS measure is possible to deliver satisfying result. (a) Pre-registration (original pubic arch surface from MRI directly merged to the TRUS image volume). (b) The result using IA-based registration. (c) The result using PG-based registration. (d) A moderately acceptable result using IS-based registration.

The robustness of the IS measure in the cross-modal test is found to be much higher than that in the self-registration test. We believe this is caused by the difference between the "objective" and "subjective" criteria: the inspect of human eyes is usually more tolerant than a specific threshold. In general, the comparative results verify our previous conclusion obtained from the self-test that the IS criterion outperforms the others in the pubic arch registration problem.

The time needed for the pubic arch registration varies depending on the computation complexity of the used similarity measurements. Running on a notebook of Intel Centrino® 2 CPU and 4GB Memory, the time used for the three methods are 1.2, 2.0 and 8.6 seconds respectively.

4.4.3 Discussion

In this study, the surface-to-image registration method shows its adaptivity to the pubic arch with another acoustic characteristics. According to the different interpretation of the echoic appearance of the tissue-bone interface, three forms of the similarity measurements are presented. The first is the AI ("aligned intensity") measure which aims to align the surface at position of highest intensity values. The second is the PG ("projective gradient") measure which tends to register the surface at a high-gradient image boundary and the IS ("intensity shadow") measure that matches the surface at a bright echogenic boundary with a dark rear region. The comparative studies have shown that the similarity based on IS is most accurate and consistent in the interest of the pubic arch.

Due to the similar reasons discussed in Chapter 3, the genetic algorithm is chosen as the optimization in the registration for its advantages of not being trapped by local optimums in the solution space and free of initial guess of the transformation parameters. Another reason for choosing GA is its simplicity of implementation and usage. The shortcoming of the genetic optimization is that due to the limited number of population and generations, it still cannot guarantee that the final result will be the true global optimum in the solution space. Based on our experience, GA appears to work well for the registration applications. To study the behavior of the solution space of the three

similarity measurements, we choose one of the patient data (case 1) used in the self-registration test and monitor the change of the similarity value, i.e., the fitness value in GA, under respective displacement or rotation. Given the reference solution an identity transformation, the fitness score would be intuitively maximum when the translation and rotation parameters $(t_x, t_y, t_z, \alpha, \beta, \gamma)$ are zero. By successively introducing relative translation and rotation in x , y , and z directions on the reference solution, the change of the fitness function could be recorded. Figure 4.18 shows the fitness map of the three similarity measurements, by decoupling the transformation into translation only and rotation only, and reducing the variables from six to two (fixing the other four dimensions to zero). We find that the fitness maps of f_{IS} have the most concentrated distribution of high values around the ideal solution (unimodality), which means that even if the genetic optimization may converge to a local optimum other than the global maximum, the final result will not be far from the truth. f_{AI} is fairly smooth but the unimodality is not sharply converged to guarantee the accuracy. f_{PG} is far from unimodal function with many local maxima present over the space. Obviously the function with a sharp unimodality is the best choice for the global optimum searching. Hence we can conclude that the GA-optimized registration using the IS measure as the fitness function, will be more reliable to find the transformation solution closer to the truth.

Figure 4.18: Comparison of fitness function f over the six transformation parameters $(t_x, t_y, t_z, \alpha, \beta, \gamma)$. (a) Fitness map over translation (t_x, t_y, t_z) without rotation, where $-25mm \leq t_x \leq 25mm$, $-25mm \leq t_y \leq 25mm$, $-25mm \leq t_z \leq 25mm$ and $\alpha = \beta = \gamma = 0$. From top to bottom: $f = f_{AI}$, $f = f_{PG}$, and $f = f_{IS}$. From left to right: $f(t_x, t_y, 0, 0, 0, 0)$, $f(t_x, 0, t_z, 0, 0, 0)$, and $f(0, t_y, t_z, 0, 0, 0)$. (b) Fitness map over rotation angle $(\alpha_x, \alpha_y, \alpha_z)$ without translation, where $-25^\circ \leq \alpha_x \leq 25^\circ$, $-25^\circ \leq \alpha_y \leq 25^\circ$, $-25^\circ \leq \alpha_z \leq 25^\circ$, and $t_x = t_y = t_z = 0$. From left to right: $f(0, 0, 0, \alpha_x, \alpha_y, 0)$, $f(0, 0, 0, \alpha_x, 0, \alpha_z)$, and $f(0, 0, 0, 0, \alpha_y, \alpha_z)$.

Compared to methods in [228] and [229], our approach is free of pre-processing of the image and is more robust as we utilize the original intra-operative image content rather than the selective edges unreliably filtered from the content. The idea presented in [183] is much like our first definition of the similarity measurement (i.e., the averaged gray value). The difference is that they excluded the part of surface that was not orthogonal to the transducer transmission and a deepest-descent optimization method is used. Our experimental results have shown that this measure does not fit well with our application because of the interference from other highly-reflective tissue interface. We also find that the PG measure is unsuitable to the open surface of the pubic arch, although it performs well for the prostate in the same TRUS image, as the description of open surface may be incomplete, making it less resistant to the noise and interferences.

4.5 Discussion

In the first part of the chapter, the prostate is the organ selected as the registration object and the transformation is from pre-operative T1- or T2-weighted MRI images to intra-operative 3D TRUS image. This is useful for integrating the structural and functional information (such as the suspected cancer information) obtained from MRI/MRS to the ultrasound. As a soft organ, the prostate may have no/little deformation (in T1-weighted MRI) or some deformation (in T2-weighted MRI and MRS) compared with its status in TRUS. The similarity measurement used in this registration is defined as the strength of image gradient alongs the surface normals. Using the MRI images with and without prostate deformation, the behavior of the rigid registration method is investigated. The results show that the method is superior in solving a rigid transformation, e.g., from MRI T1 images to the ultrasound scans. Although it may not be an ideal choice to account for the deformation occurred in MRI T2 images, it still can serve as a rough guess of prostate location in 3D TRUS image. This information can either serve as an initialization of a refined segmentation of the prostate or provide a global alignment between the pre- and intra-operative images.

In the second part of the chapter, the registration is applied to the pubic arch surface and the transformation is from the pre-operative T2-weighted MRI image to the intra-

operative 3D TRUS image. This is useful for the assessment of the pubic arch interference possibly occurred in the transperineal needling. As the rigid-body assumption is satisfied, three possible interpretation of the echoic characteristics for the pubic arch surface are formulated and studied in the following comparative experiments. It is shown that the best criterion for the tissue-bone interface in ultrasound image is the strong hyperechoic edge with rear shadow.

Feasibility of the surface-to-image registration approach has been verified in its respective experiments with the prostate and the pubic arch, organs of different rigidity properties and acoustic appearance. When little deformation is observed for the prostate between the pre-operative MRI image and the ultrasound, the registration using the prostate data is able to establish the transformation between the two image spaces. The anatomic and functional information, such as some sensitive structures, e.g., the urethra, in MRI, or the suspected cancer distribution from MRS, can be superimposed onto the ultrasound image to provide visual guidance for a targeted biopsy and brachytherapy. When a large deformation occurs, this method may not be an ideal solution. However, it still can provide a global alignment between the two images. This may be helpful to solve the following deformable registration problem. Meanwhile, the registered result provides an initial guess of the prostate boundary in the ultrasound image thus is able to serve as an initialization for a further segmentation. The registration with the pubic arch is quite useful in assessing the pubic arch interference in transperineal biopsy and brachytherapy. Extracting the pubic arch surface from pre-operative medical data is much more convenient and easier than extracting it from the ultrasound. When the pre-operative data is available, it is reasonable to take this advantage and reduce the human intervention on intra-operative data.

When a real-time 3D ultrasound monitoring is available, it is possible to use the surface-to-image registration method to track the organ surface in a live video. The experiments show that the time needed for the registration (1 ~ 9 seconds) is quite promising to track the organ movement (if there is any due to the patient motion) in a real-time 3D TRUS image. However, due to the limitation of the equipments (see Subsection 1.1.5) used in this study, currently we are unable to scan the prostate in 4D (i.e., a time-varying 3D image). Even a still 3D image is obtained with a time delay about 1 minute.

4.6 Conclusion

This chapter has presented a generic framework of a surface-to-image registration technique for 3D ultrasound image. This framework has been applied to organs of different rigidity and acoustic appearances in the ultrasound image (e.g., the prostate and the pubic arch), to verify its feasibility in solving the rigid transformation between mono- and multimodal images. We also discuss the significance of choosing a similarity measurement based on the appropriate acoustic appearance of the organ.

Motivation of this study is to enhance the guidance ability of the ultrasound, by integrating the structural and functional information from other sources of medical data, such as the pre-operative MRI/MRS images, to the intra-operative TRUS image. However, registration with regards to the ultrasound is challenging. Due to the lack of anatomical details in the acoustic images, it is hard to establish a one to one correspondence for those structures presented in the pre-operative MRI images but not in the ultrasound image. Because of this reason, the image-based techniques, which rely on the voxel intensity, is less likely to be feasible. The surface-based techniques can tackle the problem whereas they require to extract the organ surface from both sides of the images, which is not desired in a real-time procedure.

The principle of the proposed registration framework is that it matches the organ surface, which can be extracted off-line from the pre-operative image, with the image data directly obtained from the intra-operative ultrasound, based on the similarity between the geometric surface and its acoustic appearance in the ultrasound image. Under this framework, the registration becomes an optimization procedure that determines the set of rigid transformation parameters by maximizing the defined similarity measurement (using genetic algorithm). This concept is able to take advantages from both the surface-based and the image-based methods - it uses the reliable surface information in both images, except that the surface is shown as the image data (i.e., the gradient profile) in ultrasound image.

In this chapter, the proposed technique has been applied to two organs identifiable in the TRUS image, the prostate and the pubic arch. The test on the prostate is to examine the behavior of this algorithm with regards to the rigidity of the organ. The test on

the pubic arch is to discuss several possible formulations of the similarity measurements and the importance of choosing an appropriate measurement based on the appropriate interpretation of the organ's acoustic feature. Two conclusions can be made from the above tests. The first is that the surface-to-image registration is a feasible approach to solve the rigid mono- and multi-modal registration with the ultrasound image. The second is that the similarity measurement used in the optimization should be customized according to the appropriate interpretation of the organ's acoustic appearance.

The consistency and accuracy of these methods have been verified mathematically, or with the aid of the human expert. From the practical point of view, it is able to register the organ surface in $1 \sim 9$ seconds, which is considered acceptable for a real time application. Meanwhile, as a generic framework for the multimodal registration associated with the ultrasound, this method can be able to extended to applications of other organs, such as the kidney, the spine and etc.

Chapter 5

A Preliminary Study on Nonrigid Registration of Prostate between 3D Ultrasound and MRI/MRS Images

The surface-to-image registration technique presented in the Chapter 4 aims at solving the rigid transformation between MRI image and TRUS image. However, the use of the endorectal coil in MRS, for the retrieval of the suspected cancer information from MRI, may cause a significant deformation to the prostate compared with its status in the TRUS scan. In order to deal with the deformation caused by the different rectal filling, as well as the change of patient postures, it is necessary to implement a strategy to refine the transformation so that it can take the deformation into account. This chapter¹ presents a preliminary work in the nonrigid registration of the prostate between its 3D MRI/MRS and 3D TRUS images. A framework including a global rigid alignment and a non-rigid transformation is established to match the two prostate surfaces and thereafter their volumes. In the absence of the ground truth, a phantom validation platform is built up to verify the accuracy of the registration algorithm.

¹Materials reported in this chapter have been published in [79, 80, 81]

5.1 Introduction

Due to the limitation of ultrasonography's ability to interpret tumor foci, the traditional ultrasound-guided biopsy protocols may lead to inaccurate or false negative results for patient cancer detection. A possible way of ameliorating this problem is to target the biopsy needle toward areas where the cancer is mostly suspected. Such *prior* knowledge could be obtained from a patient-specific model on the prostate cancer distribution. Compared with those statistical atlases of prostate cancer distribution [48, 49, 50, 51, 52], the patient-specific model established from the pre-operative MRI/MRS images, is premium in providing suspected tumor deposits of the patient during the TRUS-guided procedures. Nevertheless, their use is complicated by the fact that the rectal filling caused by the MRS imaging probe pushes the prostate upward and flattens it against the pubic bones. To account for the deformation in between, the matching process is divided into a rigid registration that grossly aligns the two image spaces, and a nonrigid registration that allows local displacements based on it. The following sections describe the techniques on solving the deformable transformation between the MRI/MRS images and the intra-operative TRUS images. Experimental results on phantom and patient data are demonstrated as well.

5.2 Methods

To spatially deform an image volume with respect to the other, usually two stages are taken: firstly a rigid transformation that compensates for the global change in position and orientation, secondly a non-rigid registration that refines the transformation with more degrees of freedom (DOFs) based on local similarities. A hidden assumption of the non-rigid registration is that the transformation should vary smoothly over the entire field to avoid splitting or folding. This kind of transformation can be described in 3D as local translation, i.e., the deformation field that stores a displacement vector at each node position in a dense cubic lattice. In the multimodal integration for the biopsy roadmap, information from MRI/MRSI (such as the structural features or the cancer distribution) is regarded as the floating data, and supposed to be transformed to match with the TRUS images, i.e., the reference data.

Due to the difficulty of identifying intensity features in the TRUS images, we cannot use the intensity-based approaches to search for correspondences based on the similarity in features. Based on our discussion over the methods applicable to this application, we choose to solve this problem by matching the surfaces first, then based on the boundary correspondence obtained, we use the spline interpolation to apply its deformation to the overall volume. To be more specific, the prostate surfaces from the two image modalities are extracted first. After a global alignment of the two surfaces, a non-rigid transformation is obtained by interpolating the displacements on corresponding feature points identified on the surfaces using thin-plate spline [78].

5.2.1 Global Registration

The global registration aims at aligning the two image spaces grossly. It searches for a rigid transformation that can compensate the overall translation and rotation between the pre-deformed prostate (in TRUS images) and deformed prostate (in MRI/MRS images).

Chapter 4 has described an automatic surface-to-image registration method applicable for the rigid transformation between MRI and US images [74, 79]. Hence, it could serve as the global alignment of the prostate between the two modalities, given that the deformation is comparatively small. In our experiments we find that the prostate registration using the fitness function of "Projective Gradient", aligns the surface (extracted from MRI/MRS scans) with respect to the image boundary in the 3D TRUS images, rather than its centroid. Therefore, when the requirement of the global registration is emphasized on the centroid (in most of the cases), this method is only applicable when deformation is small. For a prostate with a large deformation, it is hard for this method to obtain a good alignment because the similarity between the surface and the image boundary is almost diminished. At the absence of anatomic details inside the gland, a better solution is to use the surface information, and register the two surfaces by minimizing the distance between them. Since the prostate segmentation in ultrasound is a common procedure and has been tackled in Chapter 3 and section 4.3.3, the surface-based registration should be able to produce satisfying result without much trouble [85]. The iterative closest point (ICP) algorithm [57], a well-known surface-based registra-

tion method, can be used to register the two prostate surfaces to determine the global transformation, denoted as T_g , between the MRI/MRS and TRUS scans.

5.2.2 Deformable Registration

To simplify the complexity of the deformation, an assumption is made for the change of the prostate in between MRI/MRS and TRUS images. That is, once the prostate has been grossly matched by the a rigid registration, the transformation involved in superior-inferior (SI) direction is only scaling, that is, the deformation only occurs in axial plane. Consequently, the non-rigid registration was solved in a pseudo-3D manner, that is to determine the planar deformation slice-by-slice then reconstruct the 3D deformation by a stack of the 2D deformations.

To describe the local deformation, the displacement field is not used directly. Instead we employ the thin-plate spline [78] as the radial basis function to interpolate the displacement vectors defined at boundaries. Therefore, it is necessary to determine the surface correspondence before we can propagate the sparse displacements from the boundary to the whole image volume, especially to the region of interest for the cancer.

Establishment of surface correspondence

Manual selection of landmarks based on intensity information is difficult and arduous for the prostate in ultrasound image. Hence, the geometric information, such as the curvature information, as well as the arc-length-based parameterization of the pre-deformed and deformed surface, is utilized to establish the correspondence between the two surfaces.

Based on the NURBS representation of the surface, the prostate surface extracted from TRUS images, $S_{US}(u, v) = [x(u, v), y(u, v), z(u, v)]^T$, is supposed to follow the same way of parameterization as how the prostate surface in MRI image, S_{MR} , is parameterized. The rigidly-transformed surface $T_g(S_{MR})$ will be re-parameterized to accommodate the US image coordinate system. Once the two surfaces are correlated in the same reference system, a rough one-to-one mapping T can be established based on the (u, v) coordinate.

Let $\mathbf{P}$ and $\mathbf{Q}$ denote the corresponding points between the two surfaces:

$$\mathbf{P} \in \{\Omega_{MR} : T_g(S_{MR}(u, v))\} \xrightarrow{(u, v)} \mathbf{Q} \in \{\Omega_{US} : S_{US}(u, v)\} \quad \forall (u, v) \in \mathbb{R} \quad (5.1)$$

where Ω_{MR} and Ω_{US} represent the respective image space domains, and $\mathbb{R}$ is the parametric space with $0 \leq u \leq 1$ and $0 \leq v \leq 1$. The matching on (u, v) is actually relevant to the arc length along the orthogonal parameterization directions. Let Θ denote the conversion from parametric coordinate (u, v) to the Cartesian coordinates (x, y, z) in the NURBS surface formulation, $(x, y, z) = \Theta(u, v)$, and Θ^{-1} the reverse conversion, $(u, v) = \Theta^{-1}(x, y, z)$, the nonrigid transformation T in the Cartesian coordinate system can be represented using the radial basis functions to interpolate the displacements determined by the two point sets $\mathbf{P}$ and $\mathbf{Q}$ of same projections in parametric coordinate system.

However, this matching might fail for irregular shapes [128]. The solution to this problem is to take additional geometric information, such as the curvature information, into account [80]. When the deformation is decoupled into u - and v -space according to our assumption, some feature points are to be identified within each image plane. These prominent features selected to characterize the 2D prostate contour in MRI/MRSI scanning are the anterior corner (AC), the posterior corner (PC), the left corner (LC) and right corner (RC) (see Figure 5.1). The reason we choose these features as the control points of the deformation is that they are relatively easy to be identified, and able to ensure a maximum coverage of the prostate region.

After a global alignment with respect to the centroid, the slice correspondence is firstly set up by proportional scaling with respect to the centroid along the z axis (v -space). Secondly, the prominent corner points ($\mathbf{P}_{AC}$, $\mathbf{P}_{PC}$, $\mathbf{P}_{LC}$ and $\mathbf{P}_{RC}$) are identified automatically in MRI data based on the Gaussian curvature calculated along the contour in each slice. By connecting cross sections of the same feature points, four ridges are constructed and represent the global frame of the prostate shape. The point coordinates (x, y) on each ridge will be a function with respect to the section depth z : $(x, y) = [f_1(z), f_2(z)]$. Due to the slice-by-slice processing, the points on the ridge may not be continuously smooth. A low-pass filtering (Gaussian smoothing) is therefore applied to reduce the

Figure 5.1: The four feature points on a prostate boundary.

inter-slice fluctuation in planar point identification, $(x', y') = [G_{\delta 1}(f_1(z), f_2(z))]$. The smoothed ridge is then projected back to each section contour and the projection will be the updated feature points. This procedure is repeated until the projection distance is within a threshold. Thirdly, the corresponding $\mathbf{Q}_{AC}$ and $\mathbf{Q}_{PC}$ points in TRUS data are still identified based on curvature and arc length information. But the correspondence of the other two features, $\mathbf{Q}_{LC}$ and $\mathbf{Q}_{RC}$, will be determined based on arc length information, that is, proportional arc length in the left (or right) half segment. This relationship is formulated as follows:

$$u'_{LC} = u'_{PC} - \frac{u'_{PC} - \tilde{u}'_{AC}}{u_{PC} - \tilde{u}_{AC}}(u_{PC} - u_{LC}) = \Theta^{-1}(\mathbf{Q}_{LC}) \quad (5.2)$$

$$u'_{RC} = u'_{PC} - \frac{\hat{u}'_{AC} - u'_{PC}}{\hat{u}_{AC} - u_{PC}}(u_{RC} - u_{PC}) = \Theta^{-1}(\mathbf{Q}_{RC}) \quad (5.3)$$

where

$$\tilde{u}_{AC} = \begin{cases} u_{AC} & 0 \leq u_{AC} \leq 0.5 \\ u_{AC} - 1 & 0.5 < u_{AC} \leq 1 \end{cases} \quad (5.4)$$

$$\hat{u}_{AC} = \begin{cases} 1 + u_{AC} & 0 \leq u_{AC} \leq 0.5 \\ u_{AC} & 0.5 < u_{AC} \leq 1 \end{cases} \quad (5.5)$$

Here u_{PC} , u'_{PC} stands for the parametric coordinate of $\mathbf{P}_{PC}$ and $\mathbf{Q}_{PC}$, and so on. To ensure deformation accuracy over the prostate region, denser points are sampled along the contour, according to a criterion of uniform interval within each of the four segments partitioned by feature points. The two sets of points, $\mathbf{P}$ and $\mathbf{Q}$, build up a boundary correspondence, which is proportional along the z axis or in v space, and are equal in a piecewise manner in the u spaces, or (x, y) domain. The number of the sampling points within each segment is selected empirically, considering the balance between accuracy and computation expense.

Volumetric interpolation using thin-plate spline

The thin-plate spline has been successfully used to account for prostate deformation [56, 230, 185, 68, 69]. Therefore it is also feasible for us to explore its application in the cross-modal registration.

Thin-plate spline

Thin-plate spline (TPS) was originally proposed for aircraft wing designs. It was later employed to describe deformations as an interpolant or radial basis function that minimizes the bending energy through control points [78, 231]. The control points, $\mathbf{P}$, are usually chosen at feature points or landmarks.

Generally, the TPS-based transformation is decoupled into sub-transformation in each dimension of the space domain $\mathbb{R}^d$. Given N pairs of corresponding landmark points between the source and target spaces, the general TPS transformation from the source $\mathbf{x}$ to the target $\mathbf{y}$ can be expressed by

$$T_k(\mathbf{x}) = \sum_{i=0}^d c_{ik} \mathbf{x}(k) + \sum_{j=1}^N w_{jk} \phi(|\mathbf{x} - \mathbf{P}_j|) \quad k = (1, \dots, d) \quad (5.6)$$

where $\mathbf{x}$ represents the homogeneous coordinate of a point in the source space, $\mathbf{x} = (1, s_1, \dots, s_d)^T$. In 3D space, it can be denoted as $[1, x, y, z]^T$. $\mathbf{x}(k)$ stands for the k -th coordinate in $\mathbf{x}$. That is, $\mathbf{x}(0) = 1$ and $\mathbf{x}(k) = s_k$ when $1 \leq k \leq d$. T_k is the sub-transformation defined in the k -th dimension of the space and $T_k(\mathbf{x}) = \mathbf{y}(k)$, where $\mathbf{y}$ is the point in the target space after the transformation, $\mathbf{y} = (s'_1, \dots, s'_d)^T$, and $\mathbf{y}(k)$ is its

Figure 5.2: Fundamental solution of biharmonic equation $\Delta^2 U = 0$.

k -th coordinate s'_k . $\mathbf{P}_j$ stands for the j -th landmark (also the control point) defined in the source data and $\mathbf{Q}_j$ would be the corresponding landmark in the target space, where $j = 1, \dots, N$. Function $\phi(r)$ is a radial basis function and defined as

$$\phi(r) = \begin{cases} r^2 \log(r) & \text{if } r \text{ is for 2D space, i.e., } d = 2 \\ r & \text{if } r \text{ is for 3D space, i.e., } d = 3 \end{cases} \quad (5.7)$$

Figure 5.2 shows its form in 2D. c_{ik} and w_{jk} are the coefficients and weights that characterize the affine and non-affine part of the TPS transformation, respectively. In order to determine the $d \cdot (N + d + 1)$ unknown parameters in Equation (5.6), we can form a $d \cdot N$ linear system based on the correspondence between $\mathbf{P}_j$ and $\mathbf{Q}_j$. The constraints on the weights will result in another $d \cdot (d + 1)$ equations.

$$\sum_{j=1}^N w_{jk} = 0, \quad (k = 1, \dots, d) \quad (5.8)$$

$$\sum_{j=1}^N \mathbf{x}_j(k) \cdot w_{jk} = 0, \quad (k = 1, \dots, d) \quad (5.9)$$

where $\mathbf{x}_j(k)$ is the k -th coordinate of the j -th point in the source point set. For example

in 3D space, Equation (5.9) can be reformulated as

$$\sum_{j=1}^N x_j \cdot w_{jx} = 0, \quad \sum_{j=1}^N y_j \cdot w_{jy} = 0, \quad \sum_{j=1}^N z_j \cdot w_{jz} = 0 \quad (5.10)$$

where (x_j, y_j, z_j) is the point coordinate and (w_{jx}, w_{jy}, w_{jz}) is the associated weights.

Accordingly, a linear system (based on Equation 5.6 and Equation (5.9)) is formulated in matrix form as

$$\begin{cases} \Phi W_k + \mathbf{X}^T C_k &= \mathbf{Y}^T(k) \\ \mathbf{X} W_k &= 0 \end{cases} \quad (k = 1, \dots, d) \quad (5.11)$$

where Φ is the matrix composed of the radial function with $\phi_{ij} = \phi(|\mathbf{x}_i - \mathbf{P}_j|)$ at element (i, j) . W_k is the weight vector $(w_{1k}, \dots, w_{Nk})^T$ and C_k is the coefficient vector $(c_{0k}, \dots, c_{dk})^T$. $\mathbf{X}$ is the matrix with each column representing the homogeous coorindates of a point in source space, $\mathbf{X} = (\mathbf{x}_1, \dots, \mathbf{x}_N)$. $\mathbf{Y}$ is the matrix with each column representing the coordinates of the corresponding point in the target space, $\mathbf{Y} = (\mathbf{y}_1, \dots, \mathbf{y}_N)$, and $\mathbf{Y}^T(k)$ is the column vector that contains the k -th coordinate of the point array in target space.

The above equations can be combined into the form as follows:

$$\left[\begin{array}{c|c} \Phi & \mathbf{X}^T \\ \hline \mathbf{X} & 0_{(d+1) \times (d+1)} \end{array} \right] \cdot \left[\begin{array}{c} \mathbf{W} \\ \hline \mathbf{C} \end{array} \right] = \left[\begin{array}{c} \mathbf{Y}^T \\ \hline 0_{(d+1) \times d} \end{array} \right] \quad (5.12)$$

where matrix $\mathbf{W} = (W_1, \dots, W_d)$ and $\mathbf{C} = C_1, \dots, C_k$. If we define a $(N + d + 1) \times (N + d + 1)$ matrix $L = \left[\begin{array}{c|c} \Phi & \mathbf{X}^T \\ \hline \mathbf{X} & 0_{(d+1) \times (d+1)} \end{array} \right]$ and a $(N + d + 1) \times d$ matrix $Y = \left[\begin{array}{c} \mathbf{Y}^T \\ \hline 0_{(d+1) \times d} \end{array} \right]$, we can get the TPS transformation

$$L \cdot \left[\begin{array}{c} \mathbf{W} \\ \hline \mathbf{C} \end{array} \right] = Y \quad (5.13)$$

In 3D, this equation can be expressed as

$$\left[\begin{array}{cccc|cccc} 0 & \phi(r_{12}) & \cdots & \phi(r_{1N}) & 1 & x_1 & y_1 & z_1 \\ \phi(r_{21}) & 0 & \cdots & \phi(r_{2N}) & 1 & x_2 & y_2 & z_2 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \phi(r_{N1}) & \phi(r_{N2}) & \cdots & 0 & 1 & x_N & y_N & z_N \\ \hline 1 & 1 & \cdots & 1 & 0 & 0 & 0 & 0 \\ x_1 & x_2 & \cdots & x_N & 0 & 0 & 0 & 0 \\ y_1 & y_2 & \cdots & y_N & 0 & 0 & 0 & 0 \\ z_1 & z_2 & \cdots & z_N & 0 & 0 & 0 & 0 \end{array} \right] \cdot \left[\begin{array}{ccc} w_{1x} & w_{1y} & w_{1z} \\ w_{2x} & w_{2y} & w_{2z} \\ \vdots & \vdots & \vdots \\ w_{Nx} & w_{Ny} & w_{Nz} \\ \hline c_{1x} & c_{1y} & c_{1z} \\ c_{xx} & c_{xy} & c_{xz} \\ c_{yx} & c_{yy} & c_{yz} \\ c_{zx} & c_{zy} & c_{zz} \end{array} \right] = \left[\begin{array}{ccc} x'_1 & y'_1 & z'_1 \\ x'_2 & y'_2 & z'_2 \\ \vdots & \vdots & \vdots \\ x'_N & y'_N & z'_N \\ \hline 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{array} \right] \quad (5.14)$$

where $r_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2}$. Taking $\mathbf{P}$ as the source point set $\mathbf{X}$ and $\mathbf{Q}$ as the target point set $\mathbf{Y}$, the transformation parameters are solved by

$$\left[\begin{array}{c} \mathbf{W} \\ \mathbf{C} \end{array} \right] = L^{-1}Y \quad (5.15)$$

The general form of the bending energy through control points, is denoted as the functional J over the domain $\mathcal{R}^d$ and the derivative of order m [232]:

$$J_m^d(T) = \sum_{\alpha_1 + \cdots + \alpha_d = m} \frac{m!}{\alpha_1! \cdots \alpha_d!} \int \cdots \int_{\mathcal{R}^d} \left(\frac{\partial^m T}{\partial x_1^{\alpha_1} \cdots \partial x_d^{\alpha_d}} \right) dx_1 \cdots dx_d \quad (5.16)$$

For example, in 2D space the biharmonic bending energy is given by

$$\iint_{\mathcal{R}^2} \left(\left(\frac{\partial^2 T}{\partial x^2} \right)^2 + 2 \left(\frac{\partial^2 T}{\partial x \partial y} \right)^2 + \left(\frac{\partial^2 T}{\partial y^2} \right)^2 \right) dx dy \quad (5.17)$$

Transformation using TPS

The thin-plate spline based method solves the deformable transformation in an interpolant manner using the displacement between $\mathbf{P}$ and $\mathbf{Q}$, where the displacement vectors are propagated from the sparse control points to their neighborhood. According to Equa-

tion (5.6), its definition in $\mathcal{R}^d$ is as follows,

$$\begin{aligned} (x', y', z') &= T_i(x, y, z) \\ &= \sum_{j=0}^d c_{i,j}(1, x, y, z)_i + \sum_{k=1}^N w_{i,k} \phi(|(x, y, z) - \mathbf{P}|) \quad i = (1, \dots, d) \end{aligned} \quad (5.18)$$

where (x, y, z) and (x', y', z') are coordinate in source and target space, respectively. $c_{i,j}$ and $w_{j,k}$ are the unknown coefficients and weights determined by $\mathbf{Q} = T_i(\mathbf{P})$. Because of the planar assumption on the transformation, the volumetric deformation would be decoupled into the 2D TPS transformation $T_{x,y}$ in $x-y$ plane and a scaling transformation T_z along z -axis,

$$\begin{cases} T_{x,y} &= c_0 + c_x x + c_y y + \sum_{k=1}^N w_i \phi(|\mathbf{P}_k - (x, y)|) \\ T_z &= c_z(z - z_0) \end{cases} \quad (5.19)$$

with the basis function $\phi(r)$ is defined as $\phi(r) = r^2 \log(r)$ according to Equation (5.7). Coefficient c_z was determined by the proportional scaling in z axis with respect to the centroid coordinate z_0 . Figure 5.3 shows an example of the 2D TPS transformation based on the corresponding control points defined on the blue and red contours, respectively.

5.3 Experiments and Results

5.3.1 Experimental settings

Because of the difficulty in establishing the "ground truth" for the deformable registration, we use the phantom data, instead of the patient data, to evaluate the accuracy of the algorithm. A custom-designed elastic phantom, including a "prostate", a "rectum", a set of "pubic arch" and surrounding tissues, is designed for the validation purposes. To make the phantom elastic like human tissue, we choose gelatine as the soft tissue material. Mixed with different proportions of water, the gelatine can mimic tissues of different stiffness and elasticity. To quantitatively evaluate the deformation of the prostate, 45 fiducial markers are seamlessly implanted into the prostate and distributed

Figure 5.3: Use TPS transformation to warp an MRI image slice. (a) Manually-specified control points on prostate boundaries of MRI image (blue color) and TRUS image (red color) (b) Warped MRI image.

in a cylinder manner. These dummy markers are designed as cylindrical seeds of 1mm in diameter and 2mm in length. Our experiments show that choosing the Nylon as the material of the seeds can make them visible in both TRUS and MRI images. The positions of these markers identified from the deformed and undeformed images will act as the golden standard for error estimation. Another superiority of this phantom over the commercially-available tissue-equivalent ultrasound prostate phantom (model 053, Computerized Imaging Reference Systems, Norfolk, VA) is that its "rectum" is designed to be elastic. The diameter of the resting rectum is small ($\sim 10mm$), mimicking the natural status of the human rectum. When the MRS probe is inserted, it is able to expand to accommodate the size of MRS balloon, and when the coil is taken out it can return back to its resting status. The "pubic bone" is placed beyond the "prostate", to simulate the real human condition in which it restrains the prostate from moving anteriorly. Figure 5.4 demonstrates the design of the phantom. Figure 5.5 shows the design of the custom-built phantom box. The real phantom is shown in Figure 5.5 and demonstrates its ability to cater for different rectal fillings.

In the collected TRUS images shown in Figure 5.6(a), the tiny markers are recognized as

Figure 5.4: The design of phantom. (a) The concept design. (b) The CAD design. (c) The phantom box. (d) Master mold for prostate.

bright spots. But these signals are mixed with the speckle noise so that it is still difficult for us to distinguish most of them due to its small size. In MRI images the markers exhibit low intensity against the fair surroundings. Since it is much easier to identify the markers in MRI image, we decide to use MRI scans with a resting rectum to replace the original TRUS image in the validation, as only surface information is needed. In this case, we can not use the surface-to-image registration method for the global alignment. Instead, we use the ICP algorithm.

Upon the collection of MRI image of the phantom, we need at least two sets of images

Figure 5.5: Phantom used in our experiments. (a) The schematic view of the phantom. (b) The "prostate", the "pubic arch" and the "rectum". (c) The rectum with transrectal ultrasound probe inserted. (d) The rectum with MRS endorectal coil inserted

to be collected. One is the image with the resting rectum (pre-deformation) to simulate the prostate condition under TRUS imaging, the other is the one with endorectal coil inserted and balloon inflated with water (post-deformation). In our experiment, we segment the prostate surfaces in both images and choose the ICP algorithm to solve the global alignment. Thereafter, the TPS-based transformation is established using automatically-identified feature points. In our test, the prostate is partitioned into 30 slices along z depth and 20 control points per slice, where every other 4 points are uniformly sampled within each segment.

Registration accuracy is evaluated as the displacement of the marker position between the reference images (undeformed, relaxed) and the recovered images by transformation

(a)

(b)

Figure 5.6: The comparison of the TRUS image and the MRI image of the same phantom. (a) TRUS image of the phantom. (b) MRI image of the phantom.

(deformed). In both images, the markers' location will be identified by an expert. These positions will be recorded, not for the use of registration algorithm itself, but for the evaluation of the registration error thereafter. The registration error is computed as the displacement error of the markers (DE_i) as follows:

$$\begin{aligned} DE_i &= \|\mathbf{x}_B(x, y, z) - T(\mathbf{x}_A(x, y, z))\| \\ &= \|\mathbf{x}_B(x, y, z) - T_d(T_g(\mathbf{x}_A(x, y, z)))\| \end{aligned} \quad (5.20)$$

For comparison, the affine transformation by Zaider et al [61, 62] will be performed on the same data. On the basis of the phantom validation, we apply our method on the real patient data to show the final application of integrating MRI/MRS information onto the TRUS image.

5.3.2 Image Data Collection

The same MRI and ultrasound machines as those used in Chapter 4 are used here for the collection the phantom data and patient data. T2-weighted fast spine-echo scanning is performed under TR/TE of $\sim 6400.0/85.6$ ms. The slice thickness varies between $3 \sim 4$ mm, and slice spacing $0 \sim 1.0$ mm. Imaging resolution is 256×256 pixels in field of view (FOV) of 12.0×12.0 mm². The typical resolution of the transrectal image is 0.18×0.18 mm² while the slice interval is 1.0 mm.

Figure 5.7 shows the three sets of the phantom scan under different rectal fillings. The first is the scan with a resting rectum. The second is the one with endorectal coil inserted but no inflation to the balloon. The third is the one with 40 ml water injected into the balloon.

Due to the expenses and availability of the volunteers, we have collected five sets of patient data including both MRI and TRUS images.

Figure 5.7: MRI scans of the phantom under different rectum filling. Left: phantom with resting rectum. Middle: phantom with endorectal coil inserted but no water filled in yet. Right: phantom with endorectal coil inserted and 40 ml water injected into the balloon.

5.3.3 Results

Phantom test

Figure 5.8 shows the three-orthogonal views of the MRI-scanned phantom image with resting rectum (Figure 5.8(a)), and with the inflated endorectal balloon in rectum (Figure 5.8(b)). The former is used to simulate the TRUS imaging. The prostate surfaces, as well as the implanted markers, are extracted from both of the images. Due to the tiny size of the marker, not all of them can be undoubtedly identified; Only 36 pairs of markers are identifiable between the two set of images. The amount of prostate distortion is quantitatively evaluated as the averaged displacement errors of the corresponding markers before the overall registration, which was 5.46 ± 2.57 mm. Figure 5.9 illustrates the experimental results after deformable transformations. For comparison, registration

Figure 5.8: Transversal, sagittal and coronal views of the phantom in MRI images scanned with resting and deformed rectum. (a) With the resting "rectum". (b) With MRS endorectal balloon inflated in the "rectum".

Figure 5.9: Comparison of the marker displacement errors between the affine registration method and the proposed deformable registration method.

errors using affine transformation [61, 62] are also demonstrated. It shows that our method could achieve an accuracy of about 1.71 ± 0.55 mm in the Cartesian system; the result using affine transformation is 2.05 ± 0.56 mm. Figure 5.10 shows the coincidence of the markers before and after the registration. As comparison, the result using affine method is also demonstrated.

The same experiment is performed on another phantom with different stiffness of tissue

Figure 5.10: Visualization of the marker coincidence before and after registration (in sagittal view). Markers in white color are the reference (identified in the scanned image with empty "rectum"). Markers in orange color are the corresponding markers (identified from the scanned image with endorectal-coil-filled "rectum") registered by transformation. (a) Results of the global alignment. (b) Results of the affine transformation. (c) Results of the deformable alignment.

and amount of inflation. The accuracy is found to be 1.10 ± 0.39 mm using our method versus 2.08 ± 0.86 mm using the affine transformation, under an averaged distortion of 9.08 ± 0.83 mm. In both experimental results, more than 40% error is contributed by the error along the axial direction (z axis), which indicates that the assumption of the deformation in the axial direction, i.e., proportional scaling, may not explain the prostate deformation well enough, so for higher accuracy requirement, it needs to allow more DOFs in the axial direction.

Patient test

Figure 5.11 shows the procedure of the ICP algorithm applied on one patient data. Figure 5.12 is the application of the surface-to-image registration applied to the prostate. Both of them can serve as the global transformation before the non-rigid transformation. In consideration of the consistency, we use the ICP algorithm in our experiments.

Figure 5.13 to 5.17 show the registration results on five sets of patient data.

Figure 5.11: Registration of the prostate using ICP algorithm. (a) Segmenting the prostate from MRI image stack. (b) Segmenting the prostate from TRUS image stack. (c) Registering the MRI surface to TRUS surface.

Figure 5.12: Registration of the prostate by Surface-to-image algorithm using projective gradient similarity measurement. (a) Segmenting the prostate from MRI image stack. (b) Import the prostate surface into TRUS image space. (c) Registering the MRI surface.

5.4 Discussion

The objective of the deformable registration is to provide an anatomical picture and a suspected cancer map to the intra-operative ultrasound guided prostate biopsy and brachytherapy. In this way, the needle can be guided with more known anatomical information so that it will not hit any fragile structures such as the urethra. The cancer information provided by the pre-operative MRI and MRS will further establish a new protocol for the biopsy and brachytherapy planning, reducing the blindness and focusing more on those sites with high possibility of tumor deposits.

Figure 5.13: Experimental results on case 1. The image slices are ordered in inferior-to-superior direction, from left to right and up to down. (a) TRUS image slices. (b) Segmentation from (a). (c) MRI image slices of prostate segmented. (d) The registered results of MRI images with respect to the US images.

Figure 5.18 shows how the deformable registration applied to the prostate between MRI and TRUS, with simulated tumors inside. With the tumors non-rigidly transformed onto the real-time TRUS image volume (Figure 5.19), we can make an optimum plan for the needle trajectory and cancer targets, so as to obtain a visual guidance in the TRUS-guided procedures.

Figure 5.14: Experimental results on case 2. The image slices are ordered in inferior-to-superior direction, from left to right and up to down. (a) TRUS image slices. (b) Segmentation from (a). (c) MRI image slices of prostate segmented. (d) The registered results of MRI images with respect to the US images.

Nevertheless, this work is still at a preliminary stage. According to the distribution of the errors shown in the phantom test, the TPS-based registration method imposes certain assumptions that may not explain the real prostate deformation well. In addition, the detection of the feature points may not be so accurate and the correspondence based on arc length is still considered empiric. The correspondence between points is under an arbitrary relationship of "yes" or "no", or in binary value "1" or "0". The relaxation la-

Figure 5.15: Experimental results on case 3. The image slices are ordered in inferior-to-superior direction, from left to right and up to down. (a) TRUS image slices. (b) Segmentation from (a). (c) MRI image slices of prostate segmented. (d) The registered results of MRI images with respect to the US images.

belonging techniques, which relaxes this constraint and introduces a probabilistic estimation into the relationship, is potential to solve the nonrigid point matching for the distorted prostate surface. The thin-plate spline robust point matching algorithm [233] is an example of introducing the "fuzzy" concept to jointly solve the feature correspondence as well as the geometric transformation.

Figure 5.16: Experimental results on case 4. The image slices are ordered in inferior-to-superior direction, from left to right and up to down. (a) TRUS image slices. (b) Segmentation from (a). (c) MRI image slices of ROI. (d) The registered results of MRI images with respect to the US images.

Meanwhile, it is noticed that in the deformation field of the prostate image, the rectum is the major source of the deformation (caused by different rectal filling) and the pubic arch is a boundary constrain to the deformation (as a rigid body). Therefore, it would be more reasonable to take these two structures into the consideration and use them as the boundary conditions to the volumetric deformation. Thus the registration problem

Figure 5.17: Experimental results on case 5. The image slices are ordered in inferior-to-superior direction, from left to right and up to down. (a) TRUS image slices. (b) Segmentation from (a). (c) MRI image slices of prostate segmented. (d) The registered results of MRI images with respect to the US images.

can be solved by searching for the best match between the resting and deformed rectum, and derive the prostate deformation from the deformation field between the rectum and the pubic arch, so that the prostate boundaries can be perfectly matched.

Figure 5.18: Deformable registration applied to the prostate between MRI and TRUS, with simulated tumor inside. (a) The prostate surface from MRI image (in semi-transparent pink color), the tumor (in opaque pink color), and the prostate in TRUS image (in semi-transparent green color). (b) Sagittal view of (a). (c) The deformed MRI prostate surface (semi-transparent pink), and the transformed tumor (opaque pink). (d) Sagittal view of (c). (e) The surface meshes of the MRI prostate and tumor before registration. (f) The target TRUS prostate surface mesh. (g) The deformed mesh of (e) after registration.

Figure 5.19: Guiding the biopsy needle to the virtual cancer foci superimposed on TRUS image volume (The needle is in purple color).

5.5 Conclusion

We have described some preliminary work on a deformable registration method for the purpose of integrating the MRI/MRSI information into the TRUS-guided prostate biopsy. The suspected cancer distribution diagnosed from MRS images, as well as the anatomic structural information provided by MRI, could assist a targeted planning for the prostate cancer diagnosis and treatment. The framework of our method contains an initial global transformation and thereafter a non-rigid matching using surface information. Based on the geometric features on the surfaces, the thin-plate spline warping is employed to propagate the surface deformation to the overall volume. To validate the proposed idea, an elastic phantom of the pelvic, which can simulate the prostate deformation, was set up. Accuracy of this registration method is evaluated based on the fiducial markers embedded in the phantom and compared with that obtained from an affine transformation. Application of this technique on real patient data is also demonstrated, in a way of virtual cancer foci superimposed on the TRUS image volume.

Chapter 6

Conclusion and Future Work

6.1 Conclusion

Prostate cancer is one of the leading causes of cancer death that threatens men of all ages. This thesis addresses two important problems associated with the TRUS guided cancer diagnosis (e.g., biopsy) and treatment (e.g., brachytherapy) for the prostate. The first is the segmentation of the prostate from the 3D ultrasound image. An automatic ultrasound image segmentation technique based on a statistical model of parametric shape descriptor has been proposed in this study to help the urologists to obtain the prostate surface and make clinical decisions based on it. The second is the image registration between the intra-operative ultrasound and the pre-operative medical data of the same patient, so as to enhance the former's guidance ability by integrating the anatomic and metabolic information available from the latter. A surface-to-image registration framework is presented to tackle the rigid matching of an organ surface, which is visible in both image modalities, with its appearance in acoustic image. When different rectal filling is involved, a nonrigid registration technique based on surface matching and thin-plate spline transformation is explored to account for the deformation occurred to the prostate. The main focus of the studies presented in this thesis is to solve the mentioned problems in view of practical use.

In summary, the major contributions in this thesis are as follows:

- The first is the use of the real-value spherical harmonics for the parametric representation of the prostate surface. The harmonic denotation can produce a much more compact statistical model for the 3D prostate shape compared to other existing methods. A plausible prostate shape can be denoted by only 7 parameters.
- The second is the proposal of a fully automatic prostate segmentation for 3D TRUS image using the statistical shape model. The shape and pose parameters of the prostate are determined through a constrained multivariate optimization of an objective function, which is defined as the similarity between the surface and its appearance in the acoustic image. The reduced number of model parameters (no more than 13 for shape and pose) and the use of the original ultrasound data (with least processing involved) helps to achieve a segmentation speed quite promising for the real-time clinical use (≤ 25 seconds). In addition, a user-specified constraint (in form of a region of interest in one or more slices) can be integrated in this method to cope with adverse image qualities frequently occurred in ultrasound images, such as insufficient scan of the gland, and improve the accuracy of the boundary detection.
- The third is a generic framework of a rigid surface-to-image registration approach for mono- and multi-modal registration with ultrasound images. The main concept in this method is to match the original intra-operative ultrasound data with the organ surface data extracted from the pre-operative medical image. This approach takes advantages from both the surface-based and the image-based methods - it can eliminate the outliers information presented in pre-operative images but not in ultrasound (by extracting the organ surface only) and utilize the raw image data collected real-timely. This method is fast ($1 \sim 9$ seconds depending on the formulation of the similarity measurement) and suitable for organ tracking, mono- and multi-modal registration, or initialization of segmentation in the ultrasound images.
- The last is the proposed solution to the deformable registration between MRI/MRS and TRUS image. The problem is addressed by dividing the whole procedure into a global alignment and a following deformable transformation based on the thin-plate spline. By determining proper feature points on the parameterized prostate shapes,

it is possible to deform the gland surface extracted from MRI to its counterpart in ultrasound and propagate the deformation from surface to the rest of the volume. When applying the deformation to the suspected cancer sites obtained from MRS, a cancer map can be superimposed onto the ultrasound image thus provide suspected targets for the intra-operative biopsy and treatment.

In this thesis, all the experiments are conducted on the real patient data. The consistency and accuracy of these methods are verified with the aid of the human expert, or through a phantom study. The proposed segmentation technique has been integrated into the robotic prostate biopsy system developed by our team and successfully used in its patient trials conducted in Singapore General Hospital.

6.2 Recommendations for Future Work

Future work of this thesis is focused on how to improve the accuracy and robustness of the proposed methods.

For the prostate boundary detection, emphasis will be put on making it more robust to image imperfection and obtaining higher accuracy. It may be a promising direction to combine the proposed statistical shape model with a physical model, such as the active surface model [101, 234] or the level set [120] developed for image segmentation. As the detection result from the statistical deformable model can be regarded as the starting point of these physical modes, we can either use the result to initialize a physical model or constrain the deformation of the physical model in the range captured in the statistical shape model. Actually, this idea is similar to what has been discussed in Subsection 4.3.3- that is to use the registered result as the initialization for further segmentation. As indicated, a 3D model is superior than a series of 2D models. Nevertheless, the computation may become much more complex and heavier. Thus, the future plan supposes to concentrate on how to integrate the statistical shape model into the deformable physical model, thus making it evolving directly and efficiently in 3D.

For the surface-to-image registration technique, it is possible to consider other choices for the speckle noise reduction. As the Gaussian filtering may blur the edge information

(although not so dominant in ultrasound images) as well, it is worthy of consideration to replace it with an edge-preserving filter.

For the deformable registration between MRI/MRS and TRUS, the transformation is obtained based on the establishment of the correspondence on some feature points detected on both surfaces. The correspondence established from surface parametrization is able to eliminate the human efforts for landmark labeling. However, they are determined empirically based on geometric features, which may not be so accurate, and the correspondence is under an arbitrary relationship of "yes" or "no", or denoted by binary value "1" or "0". Any error involved in this relationship may cause a decreased accuracy in the registration. The relaxation labeling techniques, which introduces a probabilistic estimation into the relationship, may potentially be employed to solve the nonrigid point matching on the distorted prostate surface. The thin-plate spline robust point matching algorithm [233] and the topology preserving relaxation labeling (TPRL) algorithm [235] are examples that introduce the "fuzzy" concept to jointly solve the feature correspondence and the geometric transformation. The former updates the correspondence, as well as the transformation, iteratively in the minimization of the TPS energy function. The latter evaluates the point correspondence by a compatibility function and contextual information first. The correspondence is applied in the minimization of the TPS energy function as a regularization energy and again being updated interactively with the transformation. In our future work, it is promising to integrate such a technique to relax the correspondence previously arbitrarily determined on the surface. Under this framework, the deformable registration problem can be formulated as an optimization procedure that simultaneously determines the correspondence and the transformation.

Other than TPS, the biomechanical model is supposed to be a better choice to describe the transformation occurred to the prostate. However, it is difficult to obtain the true tissue parameters and computationally expensive. Thus it is used more for simulation rather than for real practice. Our future work will continue on the direction that seeks for a solution which is able to compromise between the biomechanical model (i.e., accuracy) and the geometric model (i.e., speed). A possible solution is to study a larger deformation field that takes the rectum and the pubic arch into account. As the rectum filling is the main cause of the deformation and the pubic arch is a rigid constraint in the

transformation, we can calculate the deformation field within the region that enclosed by the two structures, thus derive the deformation of the prostate. To be computational efficient, the radial basis function, rather than the finite element method, may be used to describe the transformation.

Author's Publications

Publications related to this thesis:

- (1) **W. Shao** and K. V. Ling, "Automatic prostate segmentation in 3D ultrasound images using real-value spherical harmonics based statistical shape model", *Computerized Medical Imaging and Graphics*, submitted and under review
- (2) **W. Shao** and R. Wu and K. V. Ling and C. H. Thng and H. S. S. Ho and C. W. S. Cheng and W. S. Ng, "Evaluation on Similarity Measures of a Surface-to-Image Registration Technique for Ultrasound Images", in *Medical Image Computing and Computer-Assisted Intervention (MICCAI 2006), 9th International Conference*, Copenhagen, Denmark, LNCS 4191, pp. 742-749, October 2006
- (3) **W. Shao** and R. Wu and C. H. Thng and K. V. Ling and W. S. Ng, "Integrating MRI and MRSI Information Into TRUS-guided Robotic Prostate Biopsy", *International Journal of Humanoid Robotics*, 3(4), pp. 499-522, 2006
- (4) **W. Shao** and R. Wu and C. H. Thng and K. V. Ling and H. Ho and C. Cheng and W. S. Ng, "Automatic Pubic Arch Localization in 3D Ultrasound Images Using Pre-Operative Image Information for Prostate Biopsy and Brachytherapy", *International Journal of Computer Assisted Radiology and Surgery*, 1(Suppl.1), pp. 82-84, 2006
- (5) **W. Shao** and R. Wu and C. H. Thng and K. V. Ling and H. S. S. Ho and C. W. S. Cheng and W. S. Ng, "Deformable Registration for Integration of MRI/MRSI Information in TRUS-Guided Prostate Biopsy", in *Proc. of SPIE, Medical Imaging 2005: Image Processing*, San Diego, California, vol.5747, pp. 1263-1273, February

2005

- (6) **W. Shao** and K. V. Ling and R. Wu and C. H. Thng and W. S. Ng, "Deformable Registration Between MRI/MRSI and Ultrasound Images for Targeted Robotic Prostate Biopsy", in *IEEE Conference on Cybernetics and Intelligent Systems*, Singapore, pp. 345-350, December 2004
- (7) **W. Shao** and R. Wu and K. V. Ling and C. H. Thng and H. Ho and C. Cheng and W. S. Ng, "Evaluation of a Surface-to-Volume Registration Method for Prostate Gland and Its Application to Ultrasound Image Segmentation", in *IEEE International Workshop on Biomedical Circuits and System*, Singapore, pp. S3.7.INV-19–22, December 2004
- (8) **W. Shao** and R. Wu and K. V. Ling and W. S. Ng, "Multimodal Image Registration of the Prostate Gland Using Surface-to-Volume Fitting", in *Sixth IASTED International Conference on Signal and Image Processing*, Honolulu, Hawaii, USA, pp. 395-400, August 2004
- (9) R. Wu and K. V. Ling and **W. Shao** and W. S. Ng, "Registration of Organ Surface with Intra-operative 3D Ultrasound Image Using Genetic Algorithm", in *Medical Image Computing and Computer-Assisted Intervention (MICCAI 2003)*, 6th International Conference, Montréal, Canada, LNCS 2878, pp. 383-390, November 2003

Others:

- (1) H. Chen and **W. Shao** and W. S. Ng and D. Shi and S. B. Wee, "Tumour Margin Segmentation and Tracking in Ultrasound Images Using Registration Approach", in *Proc. 12th International Conference on BioMedical Engineering (ICBME)*, Singapore, December 2005
- (2) D. M. Shi and W. S. Ng and K. V. Ling and **W. Shao** and H. Chen and C. K. Kwoh, "Augmented Reality Assisted Sinus Surgery", in *1st International Bioengineering Conference (IBEC)*, Singapore, pp. 93-96, December 2004

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Appendix

A Construction of NURBS Curve through Point Data Interpolation

The NURBS curve is a piecewise polynomial representation of smooth contour. It is a combination of B-spline basis functions with control points. Each of its segment is determined by control points and continuity between segments is maintained by the basis functions. Let $U = u_0, \dots, u_m$ be nondecreasing sequence of real numbers, i.e., $u_i \leq u_{i+1}$, $i = 0, \dots, m-1$. The u_i are called knots, and U is the knot vector. The i th B-spline basis function of p -degree (order $p+1$), denoted by $N_{i,p}(u)$, is defined recursively as

$$\begin{aligned} N_{i,0}(u) &= \begin{cases} 1 & \text{if } u_i \leq u \leq u_{i+1} \\ 0 & \text{otherwise} \end{cases} \\ N_{i,p}(u) &= \frac{u - u_i}{u_{i+p} - u_i} N_{i,p-1}(u) + \frac{u_{i+p+1} - u}{u_{i+p+1} - u_{i+1}} N_{i+1,p-1}(u) \end{aligned} \quad (\text{A1})$$

Given a range of u in $[a, b]$, the p -degree NURBS curve is defined as

$$C(u) = \frac{\sum_{i=0}^n N_{i,p}(u) w_i \mathbf{P}_i}{\sum_{i=0}^n N_{i,p}(u) w_i} \quad (\text{A2})$$

where $\{\mathbf{P}_i\}$ are the set of control points forming a control polygon of the curve. $\{w_i\}$ are the weights. $\{N_{i,p}(u)\}$ are the p th-degree B-spline basis functions defined on the knot vector

$$U = \left\{ \underbrace{a, \dots, a}_{p+1}, u_{p+1}, \dots, u_{m-p-1}, \underbrace{b, \dots, b}_{p+1} \right\} \quad (\text{A3})$$

where $m = n + p + 1$. Unless otherwise stated, it is assumed that $a = 0$, $b = 1$, and $w_i > 0$. Given the rational basis function $R_{i,p}(u)$ defined as

$$R_{i,p}(u) = \frac{N_{i,p}(u) w_i}{\sum_{j=0}^n N_{j,p}(u) w_j} \quad (\text{A4})$$

Equation (A2) can be rewrite to

$$C(u) = \sum_{i=0}^n R_{i,p}(u) \mathbf{P}_i \quad (\text{A5})$$

In the global curve interpolation to point data, given a set of points $\mathbf{Q}_k$, $k = 0, \dots, n$, we want to interpolate through these points with a p th-degree nonrational B-spline curve. If we assign a parameter value, $\bar{u}_k$, to each point $\mathbf{Q}_k$, and select an appropriate knot vector $U = u_0, \dots, u_m$, we can set up the $(n+1) \times (n+1)$ system of linear equation

$$\mathbf{Q}_k = C(\bar{u}_k) = \sum_{i=0}^m N_{i,p}(\bar{u}_k) \mathbf{P}_i \quad (\text{A6})$$

There are three common methods to choose $\bar{u}_k$: equally spaced, chord length and centripetal method. But the recommended method is the second one which can give a uniform parameterization. So assuming a range of $[0, 1]$, parameter $\bar{u}_k$ is solved by the chord length method as

$$\begin{aligned} \bar{u}_0 &= 0, & \bar{u}_n &= 1 \\ \bar{u}_k &= \bar{u}_{k-1} + \frac{|\mathbf{Q}_k - \mathbf{Q}_{k-1}|}{\sum_{k=1}^n |\mathbf{Q}_k - \mathbf{Q}_{k-1}|} & k &= 1, \dots, n-1 \end{aligned} \quad (\text{A7})$$

Figure A1 demonstrated the relationship between the control points $\{\mathbf{P}_i\}$ and the interpolation point data $\{\mathbf{Q}_k\}$.

B Construction of NURBS Surface by Section Curve Skinning

A NURBS surface of degree p in the u direction and degree q in the v direction is a bivariate vector-valued piecewise rational function of the form

$$S(u, v) = \frac{\sum_{i=0}^n \sum_{j=0}^m N_{j,p}(u) N_{j,q}(v) w_{i,j} \mathbf{P}_{i,j}}{\sum_{i=0}^n \sum_{j=0}^m N_{j,p}(u) N_{j,q}(v) w_{i,j}} \quad 0 \leq u, v \leq 1 \quad (\text{B1})$$

Figure A1: The NURBS curve constructed by interpolation.

where $\{\mathbf{P}_{i,j}\}$ form a bidirectional control net, $w_{i,j}$ are the weights, and the $\{N_{i,p}(u)\}$ and $\{N_{j,q}(v)\}$ are the nonrational B-spline basis functions defined on the knot vectors

$$\begin{aligned} U &= \underbrace{0, \dots, 0}_{p+1}, u_{p+1}, \dots, u_{r-p-1}, \underbrace{1, \dots, 1}_{p+1} \\ V &= \underbrace{0, \dots, 0}_{q+1}, u_{q+1}, \dots, u_{s-q-1}, \underbrace{(1, \dots, 1)}_{q+1} \end{aligned} \quad (\text{B2})$$

where $r = n + p + 1$ and $s = m + q + 1$. Introducing the rational basis function

$$R_{i,j}(u, v) = \frac{N_{i,p}(u)N_{j,q}(v)w_{i,j}}{\sum_{k=1}^n \sum_{l=0}^m N_{k,p}(u)N_{l,q}(v)w_{k,l}} \quad (\text{B3})$$

the surface can be written as

$$S(u, v) = \sum_{i=0}^n \sum_{j=0}^m R_{i,j}(u, v) \mathbf{P}_{i,j} \quad (\text{B4})$$

A NURBS surface can be constructed by skinning through a set of section curves which are defined in planar cross sections. Skinning is a process of blending that interpolates through the section curves together to form a surface. Let v direction is chosen as the

blend direction, the set of 3D section curves $\{C_k^w(u)\}$ are defined in u direction as

$$C_k^w(u) = \sum_{i=0}^n N_{i,p}(u) \mathbf{P}_{i,k}^w, \quad k = 0, \dots, K \quad (\text{B5})$$

Assuming all the rational or nonrational section curves $C_k^w(u)$ are defined on the same knot vector, U , and share common degree p , for a given degree q in v direction, the parameters $\bar{v}_k$, $k = 0, \dots, K$, and a knot vector, V , are computed. Then the $n + 1$ curve interpolations are applied across their control points, yielding the set of control points $\mathbf{Q}_{i,j}^w$ of the skinned surface. Accordingly, $\mathbf{Q}_{i,j}^w$ is the j th control point of the interpolating curve through $\mathbf{P}_{i,0}^w, \dots, \mathbf{P}_{i,K}^w$. If the section curves are not defined on the same knot vector or degree, it is necessary to bring them a to common p and U by degree raising and knot refinement. Similarly, the parameters $\bar{v}_k$ are determined using the chord length method as well.