Real-time movement compensation for synchronous robotic HIFU surgery

Abhilash Rakkunedeth Hareendranathan

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REAL-TIME MOVEMENT COMPENSATION FOR SYNCHRONOUS ROBOTIC HIFU SURGERY

Abhilash Rakkunedeth Hareendranathan

A thesis submitted to the Nanyang Technological University in partial
fulfillment of the requirement for the award of degree of Doctor of
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ABSTRACT

Open surgical techniques are being replaced by minimally invasive or noninvasive techniques in areas such as oncology, mainly due to reduction in tissue trauma and recovery time. Radiation therapy (RT), which is the most commonly used technique for noninvasive treatment, is known to cause tissue ionization which manifests into side effects such as edema, damage to epithelium and fatigue. It can also be a potential cause for cancer in rare cases. High intensity focused ultrasound (HIFU) is devoid of ionizing effects making it more suitable for organs such as the kidney which have low radiation tolerance. Although the therapeutic potential of HIFU has been proved, its clinical usage is still limited due to inaccuracies in the target tracking and control. HIFU surgery shares a few issues common to noninvasive surgery. Most significant among these is the movement of the target organ due to physiological processes such as respiration. Prevalent HIFU systems either ignore this movement or rely upon breath suppression. In this research, a movement model that can be incorporated into therapeutic system is proposed, so as to achieve real-time movement compensation. Aspects such as the image registration algorithm, movement control strategy and HIFU applicator design which are part of the therapeutic system were also addressed. The target application for this study was the treatment of kidney tumors such as the Renal Cell Carcinoma (RCC).

Initial work deals with measurement and statistical analysis of the kidney from a set of healthy volunteers. The movement patterns observed were complex and subject-specific. Hence generic movement models cannot be used. Therefore, a prediction-correlation based model was proposed and a new empirical model was developed for kidney movement; this was used as the basis for non-linear predictors such as Unscented Kalman Filter (UKF), Extended Kalman Filter (EKF) and Adaptive Neuro Fuzzy Inference System (ANIFS). The movement model also comprised of a correlation network which maps the position of skin markers to current position of the kidney. The correlation module comprised of a new mapping function tuned using ANFIS. The prediction-correlation based approach has two advantages – firstly, it intuitively accounts for the subject specific nature of the movement and secondly, it reduces the length of prediction thereby improving the accuracy. This approach gives an accuracy of more than 92% for movement prediction. The maximum absolute error observed was 2.4 mm.

The model was integrated into a movement adaptive protocol comprising of a pre-operative phase, synchronization phase and treatment phase. The additional synchronization phase ensures that the movement of robot is synchronous with the organ. Model Predictive Control (MPC) was chosen for the synchronization phase due to the repetitive nature of the movement and the availability of the model. Since the treatment plan is a first order point to point movement, a Proportional Integral Derivative (PID) controller would be sufficient. The proposed movement compensation strategy was validated on a laboratory testbed comprising of a movement replicating jig to recreate movement and a robotic arm to implement the movement control strategy. Finally, the HIFU applicator for kidney tumor ablation was simulated with accuracy more than 95%. Results of single probe and multi-probe applicators showed that the multiple probe configurations reduce off-focal hot spots while providing a succinct acoustic window.

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LIST OF SYMBOLS

λ	Wavelength of the acoustic signal
f	Frequency of the acoustic signal
a	Aperture of the ultrasound transducer
z_0	Focal length of the ultrasound transducer
A	Focal length of the focal bowl
S	Curved surface of the focal bowl
A	Half angle of the focused transducer
Ψ	Velocity potential
μ_s	Bulk coefficient of scattering in the medium
μ_a	Bulk coefficient of absorption in the medium
μ	Total attenuation constant
β	Compressibility of the medium
ρ	Density of the acoustic medium
τ	Time delay of the signal
Φ	Phase delay of the signal
J_0	Bessel function of the zeroth order
G	System update matrix used in Kalman filtering
F	Measurement matrix used in Kalman filtering
w	Process noise in Kalman filtering
v	Measurement noise in Kalman filtering
K	Kalman gain
χ	Sigma points
$\pm$	Variance

LIST OF ABBREVIATIONS

ANIFS	Adaptive Neuro Fuzzy Inference System
BMI	Body Mass Index
EKF	Extended Kalman Filter
FUS	Focused Ultrasound Surgery
HIFU	High Intensity Focused Ultrasound
KF	Kalman Filter
MIS	Minimally Invasive Surgery
MPC	Model Predictive Control
MRgFUS	MRI guided Focused Ultrasound Surgery
MRI	Magnetic Resonance Imaging
NIS	Noninvasive Surgery
PID	Proportional Integral Derivative
RCC	Renal Cell Carcinoma
ROI	Region Of Interest
RT	Radiation Therapy
TBI	Total Body Irradiation
UKF	Unscented Kalman Filter
US	Ultrasound
USgFUS	Ultrasound guided Focused Ultrasound Surgery

CHAPTER 1 : INTRODUCTION

The recent decades have witnessed many significant changes in medicine and surgery. Surgical procedures once considered to be dreadfully painful and slow are now performed in less than an hour. This is mainly due to the advent of approaches such as Minimally Invasive Surgery (MIS) and Noninvasive Surgery (NIS) in place of conventional open surgery. Another noticeable change is the increasing presence of robots in the surgical room. Currently surgical robots are being used for a large number of noninvasive and minimally invasive procedures. The role of the robots could be that of a surgical assistant as in the Da-Vinci System or a totally autonomous surgical system such as Cyberknife. The use of robotic techniques effectively addresses the issues of accuracy and repeatability necessary for NIS. Robotic NIS or NIS in general has been used for various procedures such as defibrillation, lithotripsy and tumor resection. In this project issues such as movement compensation and minimization of healthy tissue damage during extracorporeal tumor resection are addressed.

The treatment modality used in this project is High intensity focused ultrasound (HIFU). It can be used for noninvasive treatment of tumors and cancers in various organs such as the brain, prostate, kidney and pancreas. It is safer compared to treatment techniques such as radiation therapy (RT) and chemotherapy. RT uses a beam of atomic particles to achieve the desired effect on the tissue [1]. It has been reported that radiation based treatment causes tissue ionization which manifests into side effects such as edema and fatigue [2, 3]. HIFU on the other hand is devoid of such harmful side effects. This makes it ideally suited for organs such as the kidney which have low radiation tolerance. The error tolerance of HIFU system is tighter when compared to conventional noninvasive surgery. This makes it imperative to integrate HIFU into a robotic system.

Robotic HIFU shares challenges common to NIS robots, such as real-time target tracking and surgical navigation [4]. In thoracic and abdominal organs a major source of error is the respiration induced movement of the organ [5]. The dynamics of respiration induced organ movement is poorly understood and is not considered in most robotic systems.

Most prevalent systems rely upon breath holding and suppression techniques to circumvent this issue. However these techniques do not effectively compensate complicated movement pattern and also tend to increase the treatment time. Hence techniques based on organ movement modeling are being considered. Due to the subject specific nature and large variation in organ movement, generic movement models are not common. However simplified one dimensional movement models have been used for the liver during radiation therapy [6].

This research focuses on the issue of modeling complex movement of abdominal organs such as the kidney for a wide range of subjects. It is hypothesized that such a movement model can be used to derive a movement adaptive control strategy for image-guided robotic surgery. Finally, methods to integrate the movement compensation strategy on a surgical testbed are explored.

1.1 Background

Open surgery is the oldest and most widely used approach for surgical procedures such as tissue excision, ligation grafting, transplantation and tumor resection. It is considered to be the “gold standard” for treatment of tumors in different parts of the body including brain, kidney, prostate [7] and liver [8]. Open surgery offers an unconstrained workspace where the surgeon performs the operation relying mainly upon visual and tactile feedback. However noninvasive and minimally invasive techniques are often preferred over open surgery due to shorter recovery time, reduced tissue damage, reduced blood loss and reduced risk of infection. MIS comprises of laparoscopic and endoscopic techniques which have been used for various procedures such as biopsy, bone repair and tumor ablation [9-12]. In MIS the surgical intervention is through small incisions which are usually chosen at sites closest to the target organ. It has been successfully used for tumor ablation of thoracic and abdominal organs including the liver, prostate and kidney. The extent of surgical intervention is further reduced in NIS which is a scarless procedure performed without physical contact with the target tissue. This results in a substantial decrease in tissue damage and surgical recovery time. However, in NIS the surgeon's

visual perception is limited to a set of intraoperative images which are registered to the pre-operative image. This was considered to be a major drawback. Recent advancements in imaging, localization and navigation techniques have tremendously expanded the realms of noninvasive surgery. Currently NIS is employed in areas such as oncology [13-17], total body irradiation (TBI) and bone healing [18].

Robotic systems are often necessary for achieving high degrees of accuracy and repeatability during NIS. Medical robotic systems are meant to assist the surgeon in carrying out surgical procedure consisting of stages such as pre-operative planning, intraoperative registration to pre-surgical plans and trajectory planning. Discrepancies in the pre-operative plan leads to system latencies and unaccounted organ movement reduces the accuracy of NIS which can result in healthy tissue damage. The major challenges involved in robotic NIS are target localization and tool navigation in a surgical environment, which is highly unpredictable and noisy. These issues are exacerbated due to significant respiration induced movement of the tumor in the vicinity of thoracic and abdominal structures [1, 16, 19, 20].

Conventional approaches for NIS such as radio-surgery or radiation therapy have the important drawback of tissue ionization [7, 21]. Therefore, organs like kidney which have low radiation tolerance are not good candidates for radiation therapy [22]. In such cases, high intensity focused ultrasound (HIFU) is seen as a better option as it does not ionize the medium of transmission [23]. The feasibility of usage of HIFU as a noninvasive treatment modality is well established through a wealth of animal trials [15, 24]. HIFU can be used for noninvasive treatment of tumors in different parts of the body such as liver, kidney, prostate and brain [4]. HIFU uses highly focused acoustic waves to attain a temperature of 70–90 degree Celsius within 1-3 seconds thereby ablating the target tissue [4]. This creates a very sharp, well defined and trackless lesion in the tissue leaving the surrounding healthy tissue unaffected [23, 25].

Applied research in clinical applications of HIFU was comparatively slow due to the lack of accurate imaging and localization techniques [23]. The challenges of high repeatability

and accuracy in targeting can now be addressed by robotic HIFU. Two major factors that reduce the accuracy of HIFU have been considered in this research. One is the intraoperative organ movement and the other is the unintended damage to normal tissue due to off-focal heating. Movement can be due to changes in patient position, tissue deformation due to surgical interventions, HIFU induced tissue deformation [3, 26] and respiration induced tumor movement which is significant in thoracic and urologic organs. This research focuses on the respiration induced movement of urological organs. The movement may follow complicated patterns depending upon the target [19, 20]. The extent of movement was reported to be highly subject specific with maximum movement in the superior-inferior direction for organs such as the liver and kidney [19, 20]. This makes it difficult to use a generic model for the robotic system.

The system latency and real-time performance of imaging modalities also induces an additional predictive component in target tracking and localization. HIFU can be used with imaging modalities such as magnetic resonance (MR) and ultrasound (US). In both these modalities real-time imaging of the tissue deformation and target movement are difficult during a HIFU ablation which lasts for 3-4 seconds. Hence, real-time tracking of the tumor requires precise prediction of tissue movement. Further, the HIFU induced tissue deformation and uncertainties due to cavitation can also cause variations in the treatment volume [5]. A movement compensation technique using a patient specific model of the tissue movement is relatively unexplored for robotic HIFU.

The conventional approach for movement compensation used in radio therapy is to use a planning target volume (PTV) larger than actual clinical target volume (CTV). The PTV is based on prior information regarding the extent of organ movement [3, 19]. In this approach the extent of dose delivery is limited by the tissue tolerance. Several approaches such as breath holding, respiratory gating [27] and dosage compensation based on convolution approaches [28] have been used in RT with varying degrees of success. However, synchronous movement based approaches such as multi-leaf collimator, real-time tumor tracking and the controlled patient support system (PSS) [29] are reported to

yield more accurate results. In this research a new unified prediction-correlation based model is proposed for movement prediction during HIFU surgery.

The kidney is chosen as the target organ in this study due to the relatively large amount of respiration induced movement. As mentioned earlier the low radiation tolerance also makes the kidney an obvious target application for HIFU surgery. The extent of respiration induced movement of the kidney was reported to be approximately 2 -3 cm in the superior-inferior direction and 1-2 cm in the transverse directions [26]. The nature of movement of the kidney is three dimensional and follows complicated patterns. The movement varies widely from subject to subject. Significant variations in magnitude and nature of movement are also observed within samples from the same subject. Statistical models such as the one used by Lujan *et al* [28] have been used for modeling the movement of the liver. This model assumes a one dimensional movement that is completely predictable from the movement of diaphragm. Such approaches cannot be adapted for the kidney as the movement in this case is three dimensional and is affected by many factors such as the movement of the ribs, the cardiac pattern, diaphragmatic movement and functions of the supra-renal glands.

In this study, a prediction-correlation based model for the tissue movement is developed based on data gathered from temporal samples of ultrasound (US) images of the kidney. The model consists of an independent prediction module and a correlation module. The prediction module estimates the organ position at a future point of time while the correlation module estimates the organ position based on the position of external skin markers placed on the patient during surgery. The advantage of this approach is twofold, firstly the correlation based approach intuitively accounts for the subject specific nature of the movement and secondly the prediction horizon for predictor module is reduced. The latter is of great significance in ultrasound guided FUS as the therapeutic system loses the ultrasound feedback during HIFU ablation. This is because the HIFU beam interferes with the diagnostic ultrasound thereby making the image totally white.

A schematic representation of the proposed HIFU surgery system is shown in Figure 1-1. Prior to surgery, the prospective sites for HIFU ablation in the tumor and treatment protocol are identified based on pre-operative images. This treatment plan is used by the controller for tool registration. The first step in surgery is to register intraoperative images to the pre-operative image using image registration techniques. During surgery, the controller servos the HIFU applicator based on data from the prediction-correlation model. As mentioned earlier, the predictor compensates for system latencies while the correlation module estimates the position of the internal organ from the position of the external skin markers. The model is periodically updated using intraoperative image slices.

Figure 1-1: Schematic representation of proposed test set-up for HIFU surgery

The HIFU applicator is coupled to the skin using a water chamber which also acts as a cooling mechanism and prevents skin burns during surgery. Issues inherent to the modality such as scattering and off-focal heating have to be addressed by choosing a suitable HIFU applicator configuration for the selected target. Factors such as depth of the tumor from the surface, size of the tumor and the necessary temperature for ablation are considered while choosing the HIFU applicator. The kidney tumor is found on the surface of the organ in almost all cases [30, 31]. Renal tumors are usually larger than 5

cm, and require a temperature rise of approximately 100°C for coagulative necrosis. The focal power required for tumor ablation in the kidney is in the range $3000 - 6000 \text{ W/cm}^2$ [23]. While dealing with such high focal powers, the HIFU applicator must be capable of optimizing the energy deposition at the target.

The major challenges to be addressed while determining the ideal acoustic parameters for kidney ablation are the presence of ribs in the acoustic window which causes scattering leading to heating of the surrounding tissue [15] and the presence of off-focal hot spots in the acoustic profile causing damage to surrounding healthy tissue [15]. Increasing the aperture of the transducer increases the acoustic power as well as off-focal heating. Therefore, a tradeoff exists between the size of the transducer and extent of off-focal heating. This is due to the presence of secondary harmonics seen as side lobes in the acoustic profile [15, 32]. The harmonics are absorbed faster than the primary frequency of the acoustic beam [33, 34]. A similar tradeoff exists between frequency and depth of penetration. The tissue attenuation coefficient increases at a rate of 1dB/MHz/cm . Due to this, the higher frequencies are used only for smaller depths [25, 34, 35]. Approaches using phased array, multi-probe and segmented transducers are used to circumvent these inherent deficiencies of the single probe applicator.

Finally, the computer integrated system (CIS) for robotic HIFU requires a control strategy to move the applicator based on the empirical models of tissue movement. The operating environment of a surgical robot can be described as complex and unpredictable due to the presence of uncertainties in target position and lack of prior knowledge about the complete system dynamics. The order of the system dynamics and subject specificity of the tissue movement pattern must also be considered while selecting a controller design for a surgical robot. Such considerations often lead to systems with very high order of complexity where more than one controller shall be used for specific tasks. Model Predictive Control (MPC) is proposed for this application due its ability to accommodate system latencies and provide a constrained response to enforce safety limits on the system.

Initially the movement pattern of the kidney was studied for a group of 20 healthy volunteers. The study was then repeated in a clinical environment for a group of 84 subjects. The movement models were trained and tested using clinically observed movement patterns. The patterns could be modeled with an overall accuracy of more than 92% using these models. The study also reaffirmed the necessity of incorporating a movement compensation scheme in the treatment protocol. In this work a movement adaptive surgical protocol is proposed. The proposed protocol was implemented on a laboratory testbed developed in-house. The testbed comprises of a kidney movement replicating jig, an ultrasound imaging system and a robotic arm to implement the movement control strategy. The robotic arm used was a detached limb of the kidney ablation robot FUSBOT-US. Finally the HIFU applicator suitable for this application was modeled. It was found from simulations that a multi-probe applicator using three 60 mm diameter probes was most suitable.

1.2 Objectives

The objectives of this research are:

- Formulate a 3-D empirical model for respiration induced tissue movement based on real-time data obtained from ultrasound images of the kidney and corresponding data from external markers.
- Propose and implement a control technique suitable for an image guided robot capable of movement compensation. The proposed control technique shall be validated using FUSBOT-US, which is a customized robot for kidney ablation developed by the Bio-Mechatronic group Robotic Research Center (RRC).
- Develop an acoustic profile simulation for comparison of existing HIFU applicator configurations in order to determine the most suitable approach for tumor ablation in the kidney and validate the simulations using an existing test jig.

1.3 Scope

The motivation of this PhD project is to implement a real-time compensation technique for respiration induced movement of the kidney which can be used for a HIFU surgical robot. This project includes experimental study of the movement pattern of the kidney using a sequence of ultrasound images. Development of a movement compensation model for respiration induced renal mobility is an important area of focus in this project. As part of the movement modeling non-linear methods such as fuzzy inference systems and Kalman filtering are also studied. In order to implement the model on an image guided surgical system, image registration of the intraoperative images of the moving kidney is studied. Development and implementation of a rigid image registration technique to register the gross position of the kidney comes under the scope of this project. As part of the system integration, implementation of a movement adaptive control technique has been included. The treatment modality proposed in this study is HIFU. Hence the project also deals with acoustic profile simulation for a HIFU applicator suitable for kidney tumor ablation.

1.4 Overview

Chapter 1 contains a brief overview of the project. It defines the research problem objectives and scope of this project.

Chapter 2 presents a literature review which briefly describes currently available systems and techniques. It presents the technical background necessary to analyse the problem and discusses possible solutions.

Chapter 3 presents the methodology adopted during the pre-operative planning phase. This consists of techniques that were used to measure and model the three dimensional movement of the kidney. In the prediction module, a new shape function based empirical model is described along with non-linear prediction techniques such

as EKF, UKF and ANFIS. In the correlation module a new correlation function is discussed. ANFIS is revisited as a technique to fine tune the correlation model

Chapter 4 presents the experimental set-up and the results obtained from movement measurement and modeling. The chapter explains the results of statistical analysis of the raw data along with the normalization scheme used to generalize the results. The accuracy of the prediction and correlation modules is explained in this chapter

Chapter 5 presents the methodology adopted for real-time movement compensation. A motion adaptive treatment protocol is proposed in this chapter. It also describes three modules of the movement compensation strategy namely the image registration technique, hybrid control strategy and choice of HIFU applicator from modeling.

Chapter 6 presents the laboratory testbed designed for testing the surgical protocol. The results obtained for image registration, movement replication and control are presented in this chapter. Finally, the experimental set-up to validate the HIFU applicator profile simulation is presented along with the simulation results obtained for a multiple probe applicator.

Chapter 7 presents the conclusions from this study and the future direction of research and the major contributions made in this area.

CHAPTER 2 : LITERATURE REVIEW

In this chapter, available literature on various areas related to the research topic is reviewed. As mentioned in the previous chapter this study attempts to develop a movement compensation strategy suitable for noninvasive surgery. As part of the study various tumors of the kidney are reviewed. The treatment options for kidney tumors include radical or partial nephrectomy, radio surgery [3], chemotherapy and Focused Ultrasound Surgery (FUS) [2, 9, 14, 36, 37] . The modality chosen in this project is FUS. Hence, prevalent robotic FUS systems are reviewed.

A major challenge encountered during noninvasive tumor resection in kidney is respiration induced organ movement. Organ movement can be accommodated in the surgical protocol, if the movement pattern is quantified and modeled in advance. Hence, a brief review of nature of kidney movement is presented, followed by various techniques that can be used to model the organ movement. Conventional treatment window approaches and respiratory gating suffer from drawbacks such as normal tissue damage and increased treatment time [27]. Hence, there is a need for synchronous movement compensation techniques. In this project movement compensation is viewed from the robotic trajectory planning perspective. Therefore, various approaches for surgical guidance and control in motion adaptive surgery are reviewed. The other topics reviewed in this chapter include various image registration techniques to update the treatment plan as well as various acoustic profile modeling techniques to model HIFU applicators suitable for this application.

The overview of this chapter is as follows. The anatomy of the kidney along with various tumors and treatment options are reviewed in section 2.1. An overview of medical robotic systems is presented in section 2.2. Studies on the quantification of movement and the existing movement modeling approaches are reviewed in section 2.3. Issues in movement adaptive surgery such as image registration and control are reviewed in section 2.4. HIFU applicator configurations and techniques used to simulate them are reviewed in section 2.5.

2.1 Anatomy Of The Kidney, Kidney Tumors And Treatment Options

Urological organs include liver, kidneys, urinary bladder, urethra (for both male and female) and the male reproductive organs. The kidneys are situated in the posterior part of the abdomen, on either side of the vertebral column, behind the peritoneum [38, 39]. They are surrounded by a mass of fat and loose areolar tissue. Figure 2-1 shows the posterior surface of the kidney with the adjoining blood vessels.

Figure 2-1: Kidney and surrounding viscera [39]

The right kidney rests upon the twelfth rib while the left usually rests on the eleventh and twelfth, these are indicated as dotted lines in Figure 2-1. The right kidney is placed slightly lower than the left. The longitudinal axis of each kidney is in the downward-lateral direction while the transverse axis is directed backward-lateral. Each kidney is about 11.25 cm in length, 5 to 7.5 cm in breadth, and slightly more than 2.5 cm in thickness [38, 39]. The left kidney is longer and narrower than the right. The weight of the kidney in the adult male varies from 125 to 170 grams, in the adult female from 115 to 155 grams [38, 39]. A more detailed account of the anatomical and functional aspects of the kidney is presented in [39]. Anatomically the porcine kidney is most similar to the human kidney making it suitable for *in vitro* experiments. Understanding the anatomy of the kidney is also necessary to determine the size of the optimal acoustic window.

The presence of ribs at the superior extremity of the kidney is a major hindrance to ultrasound. Ribs cause scattering and shadowing of soft tissue during imaging. It also causes significant heating of the surrounding tissue during therapeutic dose delivery.

The major tissue properties that are of interest during ultrasound surgery include acoustic speed, impedance, absorption, tissue perfusion rate, scattering and attenuation. These properties cause significant changes to the spatial distribution of acoustic energy during HIFU treatment resulting in different effects. The tissue properties may vary due to factors such as age and pathology. During treatment, tissue properties may also vary due to changes in temperature. In a tissue, attenuation of acoustic waves can be due to scattering (which includes reflection and refraction) and absorption. These are represented by their respective bulk coefficients μ_s and μ_a which sum up to give the total attenuation constant μ . The attenuation constant indicates the relative loss of acoustic power per centimeter. Typical values for tissue properties listed in Table 2-1 are provided for soft and hard tissue in many references [25, 35].

Table 2-1: Acoustic properties of human tissue [25]

Medium	Attenuation (dB/cm/ MHz)
Water	0.0022
Skin	2.35
Abdominal Wall	0.59
Kidney	0.41
Urine	0.05

2.1.1 Kidney tumors

Treatment of tumors in the kidney and liver are subject to considerable research due to the high number of cases reported [30, 31]. RCC - Renal Cell Carcinoma (Renal cell adenocarcinoma) is the most common tumor in the kidney. It is also reported to be the third most common urological tumor [31]. These account for approximately 90% of the tumors in the kidney. According to the Heidelberg classification RCC can be divided into five major categories – clear cell RCC,

papillary RCC, chromophobe RCC and unclassified RCC [30, 40]. Clear cell RCC and papillary RCC accounts for 75% of RCC [40]. The cells that cause clear cell RCC appear pale and hence the name. Papillary RCC is characterized by finger –like projections (papillae) in the tumor. These are also known as chromophilic cancers. Chromophobe RCC and collecting duct RCC are rare types of renal tumors. Renal cell carcinomas which do not fall in any of the above categories are included in unclassified RCC [30].

The next most common kind of kidney tumor is urothelial carcinoma, also known as transitional cell carcinoma. It accounts for 10 to 15% of the renal tumors. Transitional cell carcinomas begin in the renal pelvis, the cancer cells look like bladder cancer cells. Studies have shown that these cancers are often linked to cigarette smoking and workplace exposures to certain carcinogenic chemicals. This type of carcinoma has a greater chance of reappearance when compared to other cancers [30]. Wilms Tumor is a relatively rare type of renal tumor accounting for 5% of kidney cancers; almost entirely seen in children. Renal sarcoma is another rare type of kidney cancer (less than 1% of all kidney tumors) that begins in the kidney's connective tissue [30].

Some of the tumors found in the kidney are non-cancerous. However, they can grow and cause significant damage to the kidney. Renal Adenoma is the most common form of benign kidney tumor. These are usually detected accidentally when imaged using high resolution imaging techniques such as CT or MRI. These tumors hold a close resemblance with RCC and hence are usually treated likewise [30, 40]. Oncocytoma is a type of benign renal tumor that can grow to large volumes. These are also hard to distinguish from cancerous cells hence they are also treated as RCC [30, 40]. Angiomyolipoma is a rare variety of benign kidney tumor. They are seen to develop in people with tuberous sclerosis. These tumors are made up of different types of connective tissues such as blood vessels, smooth muscles, and fat. As they are usually harmless these tumors are closely monitored and are treated only in case of further complications [30, 40].

Growth of renal tumors can be divided into 4 stages. In stage 1, the tumor is well within the boundary of the kidney. The size of the tumor is less than 7 cm. In stage 2, the tumor covers the boundary of the kidney. In stage 3, the tumor grows outside the boundary of the organ which can be considered to be the beginning of metastasis. Stage 4 can be considered to be an advanced stage of metastasis in which the tumor spreads to other organs through the lymphatic system. It is

also noticed that most of the renal tumors are found on the surface of the kidney. A pictorial representation of the various stages of growth of the tumor is shown in Figure 2-2.

Figure 2-2: Stages of growth of tumors in the kidney [41]

2.1.2 Treatment options

Open surgery or invasive surgery for partial and radical nephrectomy is acknowledged to be the classic approach for tumor resection in the kidney. This approach provides the surgeon physical access to the target tissue, so it is considered the 'gold standard' for almost any form of surgery. Open surgery is reported to be effective in stage 1 and stage 2 tumor excision with a low recurrence rate [42]. Figure 2-3a shows an intraoperative picture of open surgery for partial nephrectomy. The efficiency of open surgery depends to a large extent on the expertise of the surgeon. Although the dexterity of a skilled surgeon is trusted for most surgical procedures inaccuracies due to factors such as hand tremor cannot be neglected in the context of highly delicate procedures. Advancements in surgical medicine aim to reduce the extent of intervention through minimally invasive and noninvasive techniques, thereby reducing treatment time and tissue trauma.

Minimally invasive surgery (MIS) is considered as an alternative to open surgery for applications such as oncologic treatment and bone healing. MIS involves the creation of a key hole through which surgical equipment can be inserted towards the target organ. The recovery time and surgical blood loss are reduced considerably in this approach [4, 18]. The laparoscopic surgical management of localized renal cell carcinoma is reported to be feasible. Short-term results indicate that laparoscopic radical nephrectomy is not associated with any increased risk of port

site or retroperitoneal recurrence. Various modalities such as radio waves, lasers, cryoablation [11], microwave energy and High Intensity Focused Ultrasound (HIFU) [9, 14, 15] have been used for laparoscopic tumor resection [9, 12] in the kidney. Out of these techniques HIFU has the advantage that it is devoid of ionization effects on the tissue [14, 23]. A freehand phased array type HIFU probe [9] used for laparoscopic tumor ablation is shown in Figure 2-3b.

Figure 2-3: Treatment of RCC a) Open surgery [42] b) Laparoscopic surgery [9]

Noninvasive Surgery (NIS) goes one step further by completely eliminating contact with the target tissue. This reduces the tissue trauma, operative time and recovery time when compared to MIS and open surgery [2, 17, 43]. In the past couple of decades noninvasive oncological treatment finds immense application in treatment and removal of tumors in the kidney, prostate and lungs [4, 18, 22]. The most common option for NIS is radiation therapy which uses electromagnetic radiation. However, radiation therapy causes ionization in the tissue which manifests into side effects such as edema, damage to epithelium and fatigue [7, 21]. It can also be a potential cause for cancer in rare cases [3]. As mentioned earlier High Intensity Focused Ultrasound (HIFU) offers a non-ionizing alternative to radiation therapy. This makes it ideal for organs like the kidney which have low radiation tolerance.

HIFU exploits two properties of a tightly focused ultrasound beam. Firstly, the high acoustic power at the focus causes heat and secondly the pressure wave exerts an axial force in the direction of propagation [34]. The combination of these two effects is lethal to the tumor. The tumor is subjected to temperatures as high as 65-80 degree Celsius for a burst of 2–3 seconds.

Subsequent bursts are administered at 10 sec intervals so as to allow tissue cooling. This causes cell death due to coagulative necrosis. The ultrasound intensities used in HIFU are mostly in the range of $1500 - 6500 \text{ W/cm}^2$ [23]. It is usually classified alongside high power therapeutic ultrasound applications such as hyperthermia ($\sim 1000 \text{ W/cm}^2$) which uses the heating effect of ultrasound to maintain a temperature of 43-50 degree Celsius in the tissue leading to cell death. Another closely related and popular application of ultrasound is Lithotripsy which uses a very high intensity shock wave ($>10\text{kW/cm}^2$) to break kidney stones.

The mechanism of lesion formation in HIFU is based on thermal and cavitation effects [44, 45]. The initiation of lesion formation can be attributed to the thermal effect of HIFU. The boiling of the tissue causes shape transformations in the lesion. The expected shape of the HIFU induced lesion in the tissue is like a “cigar”. It has been observed that the presence of micro-bubbles in the medium causes a change in the lesion shape [44]. The bubbles impede the propagation of ultrasound in the tissue which results in unequal heating. This causes a larger lesion width towards the transducer which is commonly referred to as a ‘tadpole’ shaped lesion. The formation of the cigar shaped lesion sampled at different time intervals is shown in Figure 2-4a. Similarly, the formation of a tadpole shaped lesion is shown in Figure 2-4b. Micro-bubbles are most commonly caused as a result of non-inertial cavitation. Alternatively micro-bubbles can also be induced by UCAs (Ultrasound Contrast Agents).

Figure 2-4: Lesion formation over a series of images [44]

HIFU can be used for treatment of tumors in organs such as the prostate [7, 13, 46-48], liver [2, 49] and kidney [2, 9, 14, 36, 37]. The surgical treatment of kidney tumors may require a temperature as high as 100 degree Celsius and tumor size can be as much as 8 cm. This is much higher compared to tumors in other parts of the body [15]. Therefore it requires precise dosage planning. The use of HIFU as a surgical modality requires precise localization which can be realized using image guided robotic systems. The major advantages of HIFU as a treatment modality include the following [25, 34]:

- HIFU does not ionize the medium of propagation, so it causes far less damaging side-effects than conventional treatments such as radio therapy.
- When used for non invasive techniques usually HIFU reduces the recovery time and leaves no scars in the patient's body.

In general NIS requires high levels of accuracy in targeting and repeatability. This can now be addressed by medical robots. The next section introduces prevalent robotic systems.

2.2 Medical Robotic Systems

The field of medical robotics is relatively new, with the first recorded medical application of a robot occurring in 1985 [4,18,22,50]. The first surgical robot was a simple CT guided positioning device to orient a needle for biopsy of the brain. The system used an industrial robot PUMA 560 tuned to surgical requirements. PUMA 560 was followed by the prostatic surgery robot 'PROBOT' in 1988. These robots were followed by neurosurgical robots such as IGOR (1992) and Neuromate (1995) in the early Nineties [4, 22, 50, 51]. These systems were basically industrial robots casted into the surgical environment. The concept of building customized robots to cater for surgical requirements gained widespread acceptance in the late Nineties although the idea of using industrial robots was not entirely discarded.

Recent medical robotic systems include a large number of neurosurgical robots such as LANS (2005), Neuroarm (2008), MARS (2006), Pathfinder (2008) and Cyberknife (2008) [18, 50].

The targeting accuracy and tele-surgical potential of robotic neurosurgery is widely accepted in the medical community [18, 50, 51]. The first neurosurgical FDA approved neurosurgical robot was Neuromate. The Cyberknife radio surgery robot is different from its predecessors as it uses a completely frameless approach for neurosurgical target tracking. The Heartlander robot [54, 55] developed at Carnegie Mellon University (CMU) is an epicardial crawling robot for cardiac surgery. This miniature step wise locomotion robot adheres to the epicardium and travels to the treatment site to perform intramyocardial injection under the direct control of a surgeon. The DaVinci (2008) robotic system used for minimally invasive treatment has gained immense popularity in endoscopic and laparoscopic applications. The URObot [13, 52] and FUSBOT-US (2005) [53, 54] are examples of robots for urologic applications. FUSBOT-US is a HIFU based robot for urological organs such as kidney and prostate.

The role of these robots during surgery differs in the levels of autonomy, starting from auxiliary supports and surgeon extenders to fully independent surgical robots which entirely remove the surgeon from the treatment loop. During open surgery and MIS, robotic ‘surgeon extenders’ provide the surgeon with highly desirable capabilities such as elimination of hand tremor and the ability to perform dexterous operations inside the patient’s body [4]. DaVinci system shown in Figure 2-5 is a computer integrated system (CIS) that is used for minimally invasive surgery [10]. Apart from eliminating hand tremor, the system also provides much better synchronization compared to the manual procedure.

Figure 2-5: DaVinci MIS Robot [55]

The quest for totally noninvasive automated surgical treatment leads to robotic NIS. Robotic assistance is used for surgical procedures in areas such as orthopedics, percutaneous surgery and

oncology. The recent popularity of the oncologic applications of NIS can be attributed to availability of high quality imaging and localization techniques [4, 50, 56]. The Cyberknife (Figure 2-6a) and Gammaknife (Figure 2-6b) are the most popular radiation based surgical systems.

Figure 2-6: a) Cyberknife system [57] b) Gammaknife system [58]

2.2.1 Commercial HIFU systems

HIFU based systems can be classified into MRI guided (MRgFUS) and US guided (USgFUS) based on the mode of surgical guidance. Commercially available MRgFUS systems include ExAblate [59], Haifu Shanghai Ashen China Medical [60] and Miangong. Some of these are shown in Figure 2-7. MRI images are used for surgical guidance due its high resolution. The major disadvantages of MRgFUS are the constrained workspace and high cost of an online MRI equipment. The MRI bore restricts surgical access of the robot.

Ultrasound is a cheaper means of imaging. It also offers a much more flexible workspace compared to MRI. The major challenge in using ultrasound for surgical guidance is its low resolution compared to MRI. This issue has been ameliorated to a great extent due to the rapid advances in signal processing and image reconstruction techniques available in ultrasound imaging. The relatively slow response time and presence of image artifacts such as pseudo targets are the other major disadvantages of ultrasound imaging. To circumvent these issues,

USgFUS systems use pre-operative MRI in situations where the quality of ultrasound image is inadequate.

Figure 2-7: HIFU surgical systems a) Exablate [59] b) Sonablate [61] c) HAIFU [60] d) RX 90 [62]

The earliest systems to use USgFUS [56] were Sonablate [61] and Exablate [59] shown in Figure 2-7a-b. These systems use inter-cavitary navigation for dose delivery. A recent approach by Z Qiu *et al* in 2008 attempts to achieve HIFU surgery using a customized industrial six DOF robot RX- 90 (shown in Figure 2-7d) using US guidance [62]. HIFU surgery shares certain issues such as respiration induced organ movement which are common to all noninvasive treatment techniques including radiosurgery [1, 3, 19, 20, 26, 63]. None of the above mentioned HIFU robots have a real-time organ movement compensation scheme. A quantitative understanding of the extent and nature of movement is necessary for movement modeling and compensation.

2.3 Numerical Modeling Of Tissue Movement

The movement in the patient position during operation can cause macro scale changes to the pre-operative plan and are corrected through image registration. Physiological processes such as respiration and heart beat also cause significant tissue movement in thoracic and abdominal

organs such as the liver, kidney and spleen [26, 27, 63]. The movement of liver is up to approximately 30 mm while the kidney moves up to 20 mm in the sagittal plane (in the cranio-caudal direction). This movement can cause significant under dosage and unintended tissue damage during treatment.

A quantitative study of the tissue movement of upper abdominal organs was done by Brussels *et al* [26] using dynamic magnetic resonance imaging; the results are shown in Table 2-2. The values shown in the table indicate the average movement and the extent of variation over subjects (indicated by $\pm$). It can be seen that that predominant movement of the liver and kidney is in the cranio-caudal direction which is from the head end to the opposite end of the body. Cranio-caudal direction is otherwise referred to as the cephalo-caudal or superior-inferior direction. In Table 2-2 sagittal Y and coronal Y components indicate movement in the cranio-caudal direction. The movement is maximum for the liver followed by the kidney. The large respiration induced liver movement is explained by its close proximity with the diaphragm [38, 39]. The three dimensional movement pattern of the kidney could be influenced by various factors such as the respiratory movement of the diaphragm, respiratory movement of the ribs, cardiac movements and the effect of the movement of surrounding viscera.

Table 2-2 : Respiration Induced Movement of Upper abdominal Organs [26]

Organ	Respiration induced movement (mm)			
	Coronal X	Coronal Y	Sagittal X	Sagittal Y
Liver	13.2 $\pm$ 6.9	24.4 $\pm$ 16.4	9.0 $\pm$ 3.5	17.5 $\pm$ 6.7
Pancreas	12.1 $\pm$ 9.0	23.7 $\pm$ 15.9	6.0 $\pm$ 3.4	19.5 $\pm$ 7.3
Right Kidney	4.8 $\pm$ 1.6	16.1 $\pm$ 7.9	-	-
Left Kidney	6.2 $\pm$ 2.8	16.9 $\pm$ 6.7	5.3 $\pm$ 1.8	12.5 $\pm$ 5.3

The kidney does not necessarily retrace its motion path during a respiratory cycle. This phenomenon is called hysteresis [16, 19]. It has also been reported that the movement of the kidney is asymmetric with more time being spent in the exhale position [16, 28]. Hence, the position of the center of gravity (CG) of the kidney at any point of the respiratory cycle can be represented as a probability distribution function. The extremities of the movement in each axis

are 6.2 ± 2.8 mm in the horizontal direction (treated as x axis) with respect to the coronal plane, 5.3 ± 1.8 mm in the horizontal direction (y axis) with respect to the sagittal plane and 16.9 ± 6.7 mm in the superior inferior direction (z axis) with respect to the coronal plane [20, 26]. In this project ultrasound imaging is used to study the respiration induced kidney movement.

Ultrasound images of the kidney taken with respect to the longitudinal planes of the body are usually of sufficient resolution 0.3 - 0.6 mm [64] for image guidance. These images can be used for modeling the respiration induced movement of the kidney. The right kidney is imaged with the patient in the supine position (Figure 2-8a). Images of the left kidney, can be best captured from the right lateral decubitus position (Figure 2-8b) [64, 65].

Figure 2-8: Ultrasound imaging a) Right kidney b) Left kidney [58]

The frequency range for ultrasound imaging of the kidney is 3 -5 MHz [64]. The right lateral decubitus position alters the normal kidney movement pattern. Hence the supine position was chosen for ultrasound imaging of both right and left kidneys during the experimental study. Various approaches have been explored to incorporate the changes due to tissue movement in treatment planning. Arresting the tissue movement using anesthesia is not considered as a viable option as it can create changes in the acoustic properties of the tissue leading to undesirable effects during HIFU treatment. Immobilization of the tissue is another option which however is limited to bone tissue [66]. It cannot be extended to soft tissue as the magnitude of movement of the latter is much larger.

2.3.1 Treatment window based movement compensation

A commonly used approach in radiation therapy is to define a planning target volume (PTV) during pre-operative planning hoping that the CTV (clinical target volume) falls within the PTV. However this does not ensure the desired dosage delivery in the target. Compensation of tissue movement has also been done by gated approaches [27, 67]. Here the beam is switched off when the movement of the organ is detected to be outside the PTV. Kubo and Hill compare various external sensors (breath temperature sensor, strain gauge and spirometer) with respect to their suitability for respiratory gating. By measuring breath temperature, it is possible to determine whether the patient is inhaling or exhaling. However gating based approaches [27] are not preferred in this work as they increase the treatment time and do not effectively solve the issue of insufficient dosage delivery.

An alternate approach is to incorporate an empirical tissue model in the dose delivery unit. This means that the robotic applicator would be moved according to an empirical tissue movement model. A minimally invasive approach to compensate the intraoperative tissue movement is to mount the dosage delivery unit on the tissue. This method has been implemented for cardiac movement compensation [68]. It was observed that this approach eliminates the relative movement almost completely. However such an approach would require placement of the ultrasound source on the surface of the kidney/tumor using laparoscopic techniques. In this project, movement compensation shall be done by synchronizing the robotic end effectors with the tissue movement. The major techniques that are used for tissue movement modeling include modeling based on statistical data, anthropomorphic modeling and modeling based on correlation. These techniques are reviewed in subsequent subsections.

2.3.2 Statistical modeling

A method for incorporating the movement of the liver as part of dose calculation for radiation therapy was investigated by Lujan *et al* [28]. In this approach, the movement in the superior–inferior direction is modeled using the empirical formula 2.1, where z_0 is the exhale position, b is

the maximum extent of movement, Φ is initial phase and τ is the period of the breathing cycle. The term n indicates the degree of asymmetry between exhale and inhale time intervals. The terms are indicated in Figure 2-9a. The probability distribution function $p_{mo}(z)$ is defined as 2.2. This function integrates to 1 over the range of spatial variation $((z_0 - b) < z < z_0)$, the function z depends on the total treatment time T and the starting phase Φ . The pdf moves asymptotically towards infinity at $(z_0 - b)$ and z_0 as shown in Figure 2-9b. The curve increases more steeply for higher values of n .

$$z = z_0 - b \cos^{2n} \left(\frac{\pi t}{\tau} - \Phi \right) \quad 2.1$$

$$p_{mo}(z) = \left\{ nb\pi(z - z_0)^{\frac{2n-1}{2n}} \times \left[1 - \left(z_0 - \frac{z}{b} \right)^{\frac{1}{n}} \right] \right\}^{-1} \text{ for } (z_0 - b) < z < z_0 \quad 2.2$$

Figure 2-9: Liver movement a) Statistical model b) Probability distribution function [28]

Simulation based on this model can be done by two different approaches. First is a direct approach where the breathing movement is simulated for every value of Φ and T . An alternate method is to use a convolution approach where the starting phase Φ and treatment time T are not considered. The latter presents a tradeoff between computation time and accuracy, as the direct approach would consume an enormous amount of time. A comparison in accuracy of these two approaches has been done by Lujan *et al*, which shows that the convolution approach does not reduce the accuracy significantly and hence it is preferred for intraoperative applications. However, this model is based on assumptions that movement of the liver is only in superior-inferior direction and that it directly follows the movements of the diaphragm. These

assumptions are not valid for the movement of the kidney as it follows more complicated three dimensional patterns [16, 28]. Hence, other approaches that account for the patient specific variation in the movement pattern are required. Due to the large variance and poor repeatability of movement, statistical convolution models which are used for the liver [69] cannot be extended for the kidney. Effective tracking needs a predictive component, which computes the system latencies for necessary compensation. This includes latencies induced by actuation of the robotic joints, the imaging modality and the control software. Approaches such as Kalman Filters (KF) [70], Extended Kalman Filters (EKF) [71], Neural Network (NN) [70, 72], LMS based prediction [73], wavelet based multi-scale auto-regression [74] and support vector regression [75] have been used for prediction with varying degrees of success.

2.3.3 Modeling based on anthropomorphic simulation

Anthropomorphic simulation of the liver and diaphragm has been done ex-vivo [6] to simulate the respiration induced movement. This approach uses a ventilator to provide the respiratory movement. The simulator is anthropomorphically modeled analogous to the hepatic section of the human torso. The respiratory movement of the diaphragm induces a related movement in the liver which also undergoes deformation in the process. Fiducial markers placed on the liver were imaged using the POLARIS IR tracking system. The experiments using this simulator were conducted using liver phantoms as well as porcine liver. The movement simulation system is depicted in Figure 2-10. Though the method was tested only for MRI and CT imaging modalities, these can be extended to ultrasound imaging.

However, this approach cannot be directly extended for the kidney as it would require accurate anthropomorphic reconstruction of the human torso including all the surrounding viscera that relates the diaphragmatic movement to the kidney. Moreover the movement of kidney is also affected by many factors other than the diaphragmatic movement as discussed earlier. Hence, this approach was not adapted to model the three dimensional movement of the kidney.

Figure 2-10: Liver Movement Simulator [6]

2.3.4 Modeling based on correlation with external markers

Schweikard *et al* [16, 29] used IR sensors placed on the skin to track the external movement during respiration. The internal movement was tracked using fiducial markers that could be detected by X-ray. This approach works on the assumption that the movement of internal organs/tissue and movement of external markers are correlated. The movement of the internal soft tissue can be predicted based on the correlation with the movement of the external markers. This model is continuously updated based on the actual data obtained from the fiducial markers. The schematic representation of this approach is given in Figure 2-11. The radiation beam source is mounted on a six DOF surgical robot. The internal organ movement is tracked using X-ray while the respiratory pattern is simultaneously tracked using an IR tracking system.

This concept was further extended by researchers at Cyberknife [16]. The POLARIS tracking system was used for tracking infrared markers and AURORA electromagnetic tracking system was used for recording the movement of two needles implanted in a moving swine liver. These were used as inputs for SYNCHRONY, a respiratory tracking system, which establishes a correlation model between these movements [16, 76].

Figure 2-11: Tissue movement tracking using external and internal markers [19]

Image segmentation can be used to determine the movement of the organ from a fixed reference. This approach relies upon accurate segmentation of external markers from camera images to derive a respiratory model which can be updated using online US images. More recent works using MRI [19] also confirm that the target positioning accuracy of more than 85% can be achieved using external marker based prediction. In this project a similar approach is used to capture the movement of the kidney.

2.4 Movement Adaptive Surgery

In this section, two aspects of a movement adaptive surgical system are discussed. Firstly the various medical image registration techniques and secondly the controller options for movement compensation are discussed.

2.4.1 Image registration for medical images

Image registration is a crucial step in robotic surgery. It is the process of overlaying the current image over a previously acquired image template [77, 78]. Online images (data images) are registered to a template image of higher resolution. The template generally covers a larger physical area compared to the data image. Image registration is of immense importance in image guided surgery where the information from both pre-operative images (usually MRI or US) and real-time images (usually ultrasound) are used to determine the robotic trajectory. Registration of images of the same subject by different imaging modalities is referred to as multimodal registration. Registering images taken at different times is called multi-temporal registration. The common types of image transformation used in image registration are shown in Figure 2-12. Image registration can broadly be classified into rigid and nonrigid based on the type of deformation.

Figure 2-12: Different types of image transformations [72]

Rigid registration

Transformations which do not involve a volumetric change in the region of interest are considered rigid. This includes translation, rotation or affine transformation. Point based registration is by far the simplest registration technique [77] for rigid registration. Initially a set of corresponding control points are chosen on both images. The algorithm tries to minimize a cost function involving the distance between these points hence arriving at the optimal transformation. However this approach does not extend well for medical images primarily due to the lack of reliable control points. The problem is worsened in case of multimodal registration of US and MRI images because most control points visible in MR do not have corresponding

visible points in US. Even in the case of intra-modal image registration it is not possible to determine corresponding points automatically in a series of real-time ultrasound images. Hence this approach shall not be investigated further in this work.

Feature based registration has been tried out for medical images. This technique uses a point set which corresponds to the boundary of an identifiable feature in the image. Corresponding point sets identified in the data and the template are matched using techniques such as Iterative Closest Point (ICP), Weighted Geometric Features (WGF) [79, 80]. Feature based techniques are much more accurate than the point based techniques in medical image registration as the former is less susceptible to fiducial localization error due to absence of control points. This approach can be adapted to register US image sequences. Automatic or semi-automatic detection of features in ultrasound images is necessary in this work as there cannot be manual intervention in the process of image registration. Once the corresponding features are identified on the pre-operative and real-time images, feature based image registration techniques can be used. The most commonly used feature based image registration technique is ICP.

ICP attempts to find the rigid transformation T that maps a point set S obtained from the data image to the point set M obtained from the model. Generally the image that has a higher resolution or covers a larger area of the object is considered to be the model and the other image is considered as the data image. In case of a movement sequence the first image is considered to be the model. This is because the first image is likely to contain minimal motion artifacts. ICP attempts to minimize the mean euclidian distance between the data points S and model points M . The ICP algorithm is explained below:

Let S be a point set comprising of N_s points $\{s_1 \dots\dots s_{N_s}\}$, correspondingly point set M contains the N_M model points $\{m_1 \dots\dots m_{N_M}\}$

- i. Make an initial estimate of the transformation T_0
- ii. a) Find the correspondences defined by

$$C = \bigcup_{i=1}^{N_s} \{(T_{k-1}(s_i), CP(T_{k-1}(s_i), M))\}$$

where $CP(s_i, M)$ is the closest point operator that gives the closest point in M for a particular point $s_i \in S$

b) Update the transformation T_k that minimizes the means square error between the point pairs defined in C

Repeat the iteration $k = 1 \dots k_{\max}$. Alternatively the iteration can be stopped upon reaching a termination criterion.

It can be proved that the ICP algorithm monotonically converges to a minimum [81]. Other popular registration techniques include voxel based approaches that use similarity measures such as intensity [80], mutual information, ratio image uniformity and partitioned image uniformity. The underlying concept behind these approaches is the assumption that the similarity measure in the image increases when they are registered. Intensity based approaches have been used in medical applications for multimodal as well as intra-modal registration. However, there are relatively few cases of registration of MRI images to US images based on intensity. This is mainly due to the lack of a direct correspondence in pixel intensity.

Nonrigid registration

Nonrigid registration techniques are necessary when there is a deformation in the target image with an accompanying volume change. These comprise of spline based techniques, elasticity based registration, viscosity based registration and registration based on Finite Element Methods (FEM). The spline based techniques [82] or free form deformations (FFD) offer the most flexible registration technique due to the inherent property of splines. A spline is a piecewise polynomial whose shape can be manipulated by changing the control points or knots of the function. B-spline and thin plate spline based techniques have been used for medical image registration.

B-spline based image registration is done using a mesh as defined in equation 2.3. The terms x_k and y_k are the x and y components of points on the surface P in the source image. These surfaces are mapped to a target image surface Q comprising of point sets q_k . The mapping is done using cubic B-splines defined by $N^3(x)$, the unknowns in the equation are the control points b_{ij} . A constraint as shown in equation 2.4 is used to obtain a “wriggle free” transformation.

$$\sum_{i=0}^r \sum_{j=0}^s b_{ij} N_i^3(x_k) N_j^3(y_k) = q_k \quad q = 1, 2, 3, \dots, n \quad 2.3$$

$$\Delta^{1,1} b_{i,j} = (b_{i+1,j+1} - b_{i+1,j}) - (b_{i,j+1} - b_{i,j}) = 0 \quad 2.4$$

The B-spline based image registration algorithm, used to track the non-linear deformation of the brain tissue during surgery is summarized below [83].

- i. The corresponding surfaces Q_i and P_i are marked in the source and target images.
- ii. Let the initial deformation function be ‘f’ with a 4 x 4 x 4 spline control grid. Embed the source image in the volume.
- iii. Determine the control points with maximum deviation. These are called the FTM (free to modify) control points.
- iv. Compute the least square displacement of the FTM points so as to match the source points to the target.
- v. Check whether the deviation between source and target images is less than the threshold, if so terminate or else repeat from step ii

An example of images registered using the above mentioned algorithm is shown in Figure 2-13. The surfaces P_i and Q_i are marked on the source (Figure 2-13a) and target image (Figure 2-13b). The deformed source image is shown in Figure 2-13c.

Figure 2-13: Image registration brain a) Source b) Target c) Source after deformation d) Hierarchical control grid [77]

However, these techniques suffer from the inherent deficiency of a well established validation scheme as opposed to rigid methods. FEM based techniques are used for registration of tissues such as liver and the brain. In this technique the registration is dependent on patient specific data which is necessary for determining the stiffness matrices. Fluid or viscosity based registration has also been used for medical image registration. These techniques can be visualized as solutions of the modified Navier Stokes equation in the specific domain [82, 84]. This work focuses on registration of intraoperative renal images to compensate for respiration induced tissue movement. Since tissue deformation is minimal in case of kidneys, the nonrigid techniques explained above may not be strictly necessary.

A review of various image registration techniques has been done by Mainz *et al*, Zivoata *et al* [77, 85]. A two stage approach is proposed for image registration of the kidney. Similar approaches have been used to register US images of the brain to pre-operative MR images [79]. The technique uses anatomical landmarks to register the first US slice to the corresponding MR image. Subsequent slices are registered using a camphor matching technique [79]. Automatic image segmentation is a major challenge in ultrasound images. Most image segmentation techniques [84] fail to demarcate the boundary of the kidney in ultrasound images. Canny edge detection [86] outperforms the other edge detection techniques such as sobel, zero cross and log edge detectors. Fisher Tippet edge detection is a relatively recent technique used for edge detection in noisy ultrasound images. This technique is based on the fact that the speckle formation can be effectively represented using a Fisher distribution [87]. In this work, the objective is to track the moving kidney over a sequence of images. The presence of movement induced artifacts makes it difficult to use the above mentioned boundary detection techniques. The alternative chosen was to derive a template of kidney from the first ultrasound frame and use it to track the kidney in subsequent frames. Therefore a correlation based template matching technique is adapted.

2.4.2 Methods for control

The control strategy used for medical robotic systems is usually complex compared to other industrial domains. In most cases hybrid approaches which merge two or more regimes are used

for control. A brief review of the common control strategies that can be used for movement compensation such as Proportional Integral Derivative (PID), robust, adaptive, optimal and predictive are presented in this section. The classical PID controller reduces the error by tuning three gains in the feedback loop namely proportional gain (K_p), integral gain (K_I) and derivative gain (K_D). The proportional gain models the stiffness of the system. The derivative gain increases the speed and stability of the system and the integral gain fine-tunes the system performance thereby reducing the steady state error. Due to its simplicity, PID is the most popular controller used in industrial applications. The proportional, derivative and integral gains of the controller can be independently tuned. It is also possible to entirely remove a component by setting the corresponding gain to zero. This is most commonly done to remove the derivative component which tends to amplify the noise signal. A PID controller was implemented in FUSBOT-BS [56] which showed acceptable performance under normal conditions.

However, rapid disturbances can cause unpredictable response from the controller. Such rapid changes can happen as a result of human interaction. The major deficiencies of the PID controller are that the gains are nonadaptive and require offline tuning. Hence, model based controllers such as robust controllers are required in medical applications. Non model based adaptive controls are most commonly used in conjunction with PID in certain applications. Movement compensation for complex movement patterns such as the movement of the kidney is a challenging task for the PID controller as it involves heuristic calculations. However, the PID controller would be sufficient to execute the pre-operative plan excluding the respiration induced movement.

Robust controllers can be used for medical systems, if the system parameters are completely known as in FUSBOT-BS [69]. This system uses a robust position controller for a HIFU breast surgery robot. The robot positions the HIFU applicator based on feedback information from the system. The robust controller design focuses on the reliability or robustness of the control algorithm. The parameters of the robust controllers are designed such that the performance is assured if the variations in the signals are within the specified range. The target organ is considered stationary inside the surgical window. Hence the controller is based on the kinematic model of the robot. However this approach does not model the non-linear surgical tissue

deformation. Such an approach requires a sound knowledge regarding the operating limits of the systems. The safety factor of the system is directly related to the confidence level of this interval. Robust controllers are generally redesigned in case of upgrades or major modifications. Robust control methods are suitable for applications where stability and reliability are the top priorities and limits of variation of the system variables are known in advance. For movement compensation this is hardly the case, due to the complexity of the system. Uncertainties and disturbances may arise from a combination of internal and external factors.

Adaptive control is another commonly used technique. It can be defined as a feedback control system intelligent enough to adjust its characteristics in a changing environment so as to operate in an optimal manner according to some specified criteria. Adaptive systems are typically suited for applications that do not involve significant time delays. The system dynamics need to be well understood in the case of adaptive controls. Most commonly, adaptive controls are used for gain control along with PID controllers. Adaptive controllers are found to have major impairments in dealing with non-linear, structure variant, or large time delayed processes [88, 89]. They have been used in conjunction with model based as well as non-model based controllers.

Model predictive control (MPC) is an advanced control technique that has been successfully implemented in industrial as well as medical systems. The predictive model, optimization range of the temporal window and the feedback correction are the three major elements of predictive control. These elements are continuously updated by the system. The predictive model provides an estimate of the future value based on prior information as well as future input. The model can be structured as a state equation, transfer function, step response or an impulse response. Predictive control calculates the action based on a penalty function, in this sense the predictive controller provides an algorithm of optimal control. This control strategy also provides feedback control in case of a mismatch between the model and process. The model parameters are adjusted to compensate for system uncertainties. Hence, it can be used as the control strategy for movement compensation as it can incorporate the uncertainties involved in the system. However, MPC controllers are computationally expensive compared to other controllers. Therefore to optimize the performance a hybrid controller consisting of PID and MPC controllers is proposed.

2.5 HIFU Applicators For Tumor Ablation – Acoustic Profile Simulation

FUS also requires astute selection of a HIFU applicator that minimizes off-focal heating thereby ensuring minimal damage to surrounding tissue [33]. In case of urological organs the HIFU applicator must also be able to provide a rib sparing acoustic window so as to prevent skin burns due to scattering and unequal heating at the bony interface. Various applicators configurations have been proposed to optimize the acoustic intensity and minimize healthy tissue damage during HIFU surgery. Configurations such as phased array, segmented probe and multiple probe shown in Figure 2-14 attempt to reduce normal tissue damage by reducing the side lobe power. These approaches are explained in subsequent subsections.

Figure 2-14: Applicator configurations a) Phased array [43] b) Segmented probe [15] c) Multiple probe [33]

The phased array transducer is made up of a large array of piezoelectric elements which can be steered individually as shown in Figure 2-14 a. It is possible to create multiple foci using the phased array transducer. Since the steering is accomplished electronically, the phased array can easily produce the rib sparing window. However, the most significant drawback of the phased array approach is the presence of grating lobes and large secondary intensity maxima in the pressure field. The presence of grating lobes in the pressure field can be reduced by a variety of approaches such as randomly distributed phased array, sparse 2-D phased array, pseudorandom code phase modulation and subset array techniques [2, 43]. Using phased array structures in place of a single transducer makes it difficult to produce even moderate power at the target. Moreover, this approach does not effectively reduce the off-focal hot spots. The presence of

grating lobes in the profile causes a considerable amount of energy to be diverted from the main lobe. Hence the number of elements required for adequate dosage delivery to the kidney is large. The phased array based approach has limited spatial flexibility and hence is not ideal for implementing real-time movement compensation.

The principle of the segmented transducer is similar to the phased array. It uses a large single transducer which is divided into multiple equal area strips that can be independently controlled to give a rib sparing structure [15, 90]. It also has a central hole to accommodate an imaging probe as shown in Figure 2-14b. This approach uses a focused transducer of diameter 110 mm and focal length 150 mm operating at a frequency of 1.7 MHz. This structure can provide a rib sparing acoustic window. The presence of lamb waves from the edges between these segments can significantly alter the acoustic profile generated from the probe. Lamb waves are acoustic waves that propagate in solid plate like media. They comprise of shear or longitudinal waves that have movement in both orthogonal dimensions [25, 34]. Simulations using the Rayleigh integral cannot account for lamb waves. Hence Finite Element Method (FEM) or Boundary Element Method (BEM) based simulations would be more appropriate for this transducer.

Multiple probe applicators are an alternate approach where focused transducers of significantly lower power are oriented such that the constructive interference of the beams occurs only at the focal region. Such an approach was implemented by Fry *et al*, using four transducers placed at four corners of a square but the results were not satisfactory [33]. A multi-probe approach for neurosurgery had been implemented by Chauhan *et al* [33] using three focused transducers. The probes were oriented in the optimal fashion so as to create constructive interference at the target. This approach reduces the side lobe intensity and hence the off-focal heating is reduced considerably. It also forms a rib sparing window due to the spatial separation between the probes. In this work, a similar multiple probe approach is used. Probes of significantly smaller diameter are used to produce constructive interference at the tumor target. This provides high intensity at the target while the off-focal heating is reduced since the individual probes are much smaller compared to a single probe approach. The multiple probe arrangement was simulated at various orientations in order to obtain the optimal orientation of the probes. A schematic representation of the multiple probe transducers is shown in Figure 2-14c.

2.5.1 Simulation and measurement of ultrasound field

A brief review of the propagation of ultrasound waves in a medium is presented to lay a foundation for formulation of simulation models. Wave propagation in finite exiting sources is governed by the Hooke's law which states that the stress in the body is proportional to the strain. This is not strictly true in all finite domains. When the diameter of the transducer is finite, the stress fields will have nodes and antinodes across the diameter. The stress fields can be assumed to be uniform if the diameter is large compared to the wavelength and if the Q factor is sufficiently small. An equivalent acoustic impedance is also attributed by the medium of propagation. This concept is analogous to transmission lines, the stress and strain being the analogues to voltage and current respectively. This is a critical parameter when the application involves the coupling of sound from one media to another [91]. The propagation of the ultrasound wave is governed by the pressure wave equation.

The pressure wave equation in itself is a result of a few basic assumptions and approximations which are meant to make the study of the acoustic profile feasible. The presence of shear waves is neglected while deriving the pressure wave equation. This assumption is valid while considering the wave propagation in soft tissue but for the wave propagation in bone this has to be modified as magnitude of scattering is relatively significant. The compressibility of the medium as well as density has to be considered variable for hard tissue [15]. The starting point for the derivation of the pressure wave equation is the assumption of a stationary medium with a spatially varying density $\rho_0(r)$ where r is the location vector. The ultrasound wave displaces the elements in the medium and imparts a particle velocity $u(x,t)$. This is a Eulerian formalism as the field variables are expressed with respect to a coordinate system fixed in space [15]. The wave creates a pressure change as well as density change in the medium that it passes through which can be written as:

$$p_T(x, t) = p_0 + p(x, t) \quad 2.5$$

$$\rho_T(x, t) = \rho_0 + \rho(x, t) \quad 2.6$$

The particle velocity in a medium is written as the derivative of the particle displacement $\zeta(x,t)$, which is defined in a Lagrangian frame of reference

$$u(x, t) = \partial \zeta / \partial t \quad 2.7$$

The force acting on a particle is equal to the gradient of the pressure p . So Newton's law of motion for this system can be written as:

$$-\frac{\partial p}{\partial x} = \rho_r \frac{D}{Dt} u \quad 2.8$$

The time derivative $\frac{D}{Dt} u$ in 2.8 can be expanded using the Taylor expansion as:

$$\frac{D}{Dt} u(x, t) = \frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} \quad 2.9$$

On substituting 2.9 into 2.8 gives equation 2.10 which is called the Euler equation.

$$-\frac{\partial p}{\partial x} = \rho_r \frac{\partial u}{\partial t} + \rho_r u \frac{\partial u}{\partial x} \quad 2.10$$

Assuming that only small perturbations are generated and that the particle displacement and its derivative are small, such that:

$$|\rho/\rho_0| \ll 1 \text{ and } |p/p_0| \ll 1$$

The Euler equation 2.10 can be reduced to:

$$-\frac{\partial p}{\partial x} = \rho_0 \frac{\partial u}{\partial t} \quad 2.11$$

Another principle used is the law of conservation of mass expressed as in equation 2.12 otherwise called equation of continuity. Upon linearization gives this reduces to equation 2.13.

$$-\frac{\partial \rho_T}{\partial x} = \frac{\partial}{\partial x} [\rho_T u] \quad 2.12$$

$$-\frac{\partial \rho}{\partial x} = \rho_0 \frac{\partial u}{\partial x} \quad 2.13$$

In order to formulate an equation for pressure p there must be a constitutive relation between the variables p and ρ . This relation is expressed in equation 2.14, where β_0 is the (adiabatic) compressibility of the medium defined by equation 2.15 [15].

$$\rho = \left[\frac{d\rho}{dp} \right]_{\rho=0} \rho \equiv \rho_0 \beta_0 p \quad 2.14$$

$$\beta_0 \equiv -\frac{1}{V} \left[\frac{\partial V}{\partial p} \right]_{ad} = \frac{1}{\rho_0} \left[\frac{\partial \rho}{\partial p} \right]_{ad} \quad 2.15$$

Combining equations 2.10, 2.14 and 2.15 gives rise to the non-homogeneous wave equation 2.16. Assuming no fluctuations in the compressibility and density of the medium with respect to time, this can be reduced to the homogeneous pressure wave equation shown in equation 2.17. A more rigorous derivation of the acoustic wave equation can be obtained using reference [34].

$$\nabla^2 p - \frac{1}{C^2} \frac{\partial^2 p}{\partial t^2} = \frac{1}{C^2} \tilde{\beta} \frac{\partial^2 p}{\partial t^2} + \nabla \cdot [\tilde{\rho} \nabla p] \quad 2.16$$

$$\nabla^2 p - \frac{1}{C^2} \frac{\partial^2 p}{\partial t^2} = 0, C \equiv 1/\sqrt{\rho_0 \beta_0} \quad 2.17$$

The pressure wave equation can be solved in a finite domain with appropriate boundary conditions. This provides the pressure at various points in the acoustic field. At equilibrium, the above motioned equations lead to an elliptical PDE that can be solved analytically or numerically. These solutions represent the acoustic pressure at a point in space at a particular time.

2.5.2 Acoustic field simulation techniques

Analytic solution based simulation techniques can be traced back to well established methods such as the Rayleigh, King and Schoch [92]. The impulse response method [93, 94] is a convolution based indirect technique that was developed to circumvent the inaccuracies in the direct approach when applied to pulsed ultrasound. The impulse response based techniques being more general can be used for the continuous wave (CW) as well. All the above mentioned techniques work on the implicit assumption of uniform surface normal velocity. Numerical solutions such as FEM [95] and BEM have to be used for profile simulation of highly complex geometries where this assumption is not valid. The mode of excitation causes significant changes in the properties of the beam in the near field. While using pulsed ultrasound the spatial variation in the near field becomes small and the side lobes merge but such effects are not present in the case of CW. Hence the simulation is significantly different for imaging and therapeutic applications as the former uses pulsed ultrasound.

An early approach to measure the near field for pulsed excitation was by summation of all the components of the frequency spectrum by Papadakis and Flower [94]. This approach could also consider the attenuation loss involved. However, it was difficult to generate sufficient samples of the frequency dependent fields. A widely used alternative was the impulse response approach used by Stepanishen [93, 94] for a circular piston. This was subsequently used for a focused transducer by Penttinen and Luukkala [93] and for rectangular sources by Lockwood and Willette in 1973. In the impulse response approach, the pressure $p(r, t)$ is calculated as the convolution between a source function and the pressure impulse response function $h(r, t)$.

$$p(r, t) = p_0 u_0(t) * h(r, t) \quad 2.18$$

This approach considerably reduces the complexity of computation involved since $h(r, t)$ is a function of the source shape and $u_0(t)$ is a function of the source vibration. In ultrasound field simulation the impulse response is a discretized function of time, so the surface integral in the solution of the pressure equation 2.16 is reduced to a single integral which is evaluated numerically. Shear waves and secondary diffraction are not considered in this approach. FEM,

BEM and finite difference methods can be used for both pulsed and continuous excitation. These numerical solutions can be used for complicated domains where there is significant non-uniformity in the surface of the transducer which can occur even as a result of particular types of apodizations [95]. Apodizations in general are techniques used to reduce the side lobe intensity. This is done by decreasing the input power of elements according to their distance from the center.

Continuous wave is used for therapeutic applications where it is necessary to reduce the beam width or to increase the local pressure amplitude or both. This requires the beams to be focused, which can be achieved using a spherical concave transducer, henceforth referred to as a focal bowl. The continuous wave emitted from the focal bowl can be modeled using the Rayleigh integral. A brief review of the Rayleigh integral approach is presented below.

Hygen's principle as explained by the works of Fresnel [34] forms the basis of the Rayleigh integral. It is the special case of the more general Helmholtz Kirchhoff solution in which the radiating source and boundary lie on the same plane. The Rayleigh-Sommerfeld integral shown in 2.19 gives the complex acoustic pressure generated at a point by a time harmonic radiation source. The terms α and k represent the attenuation constant and wave number respectively, r denotes the distance from the source while c is the velocity of sound in the medium.

$$p(r) = i \frac{pck}{2\pi} \int_S u \frac{e^{-(\alpha + jk)r}}{r} dS \quad 2.19$$

King's integral calculates the velocity potential Φ by solving the homogenous Helmholtz equation 2.20 using the method of separation of variables

$$\nabla^2 \Phi(r, \theta, z) + k^2 \Phi(r, \theta, z) = 0 \quad 2.20$$

This gives rise to a solution involving the Bessel function as shown in equation 2.21. The term A_{mn} represents the velocity at the surface, $J(\alpha y)$ represents a Bessel function, c represents the

speed of sound in the medium and l_{mn} represents the distance. In this case the Bessel function of the first kind would suffice because only finite solutions are considered.

$$\Phi(r, \theta, z) = \sum_{m,n} A_{mn} J_m(a_{mn} r) \cos(m\theta) e^{-il_{mn} z} \quad 2.21$$

The expressions thus derived can also be obtained directly from the Rayleigh integral by employing the free-field Green's function in cylindrical coordinates (Lamb or Sommerfeld integral). The Schoch solution is derived from the Rayleigh integral by transforming the surface integral into a line integral by means of a shift in the origin. Convolution integral approach is another widely used approach which typically models a field generated from an impulse velocity at the transducer face. This is referred to as the spatial impulse response which is analogous to the temporal impulse response used in the linear circuit theory. This forms the basis of the previously mentioned impulse response approach used for pulsed fields. This review illustrates the basic similarities among the analytical approaches.

The acoustic field of a continuous wave can also be modeled using numerical techniques such as FEM [32, 95] or BEM. Commercially available software such as ANSYS and PZFlex [32] can be used for acoustic field simulation using FEM. These techniques are numerical solutions of the acoustic pressure equation. In a domain where the assumption of axial symmetry is not valid the propagation domain is divided into different zones such as transduction, propagation and non-linear focal zone.

2.6 Summary

In this chapter the anatomy of the kidney and types of tumors were reviewed. The major challenges in renal FUS include off-focal heating, obstruction caused due to the ribs and respiration induced organ movement. Movement compensation techniques as applicable to soft tissue were reviewed. Due to the subject specific nature of the kidney movement a correlation based approach using surrogate skin markers is proposed. Possible control schemes for movement compensation such as PID, robust and adaptive control were reviewed and the MPC

controller was chosen due its ability to accommodate system latencies and provide a suitable constrained response. Issues of off-focal heating and rib induced scattering are addressed by using an appropriate applicator configuration. Applicator configurations such as phased array, multiple probe and segmented probe were reviewed. A Rayleigh integral based approach has been adopted for simulation due to its computational simplicity and relatively high accuracy near the focal region.

CHAPTER 3 : PRE-OPERATIVE MOVEMENT MODELING OF THE KIDNEY-METHODOLOGY

In the previous chapter, the key issues in noninvasive surgery were discussed. Intra-operational movement of the kidney was identified as a major challenge during extracorporeal treatment. In this chapter, techniques for estimating and modeling the respiration induced kidney movement shall be discussed. Movement estimation in the scanning plane is done using template matching techniques. Since the out-of-plane movement is not directly measureable from ultrasound images a speckle de-correlation based technique is adopted. Organ movement modeling was decoupled into skin marker correlation modules and kidney movement prediction modules. The idea was to use information from markers placed on various points on the skin to estimate the position of the kidney. The latency of the therapeutic system is then compensated by the prediction modules. This approach has two advantages. Firstly it makes the system independent of any online image feedback during surgery and secondly it reduces the prediction horizon which makes the predictor module more accurate. The prediction and correlation modules are trained separately during the pre-operative planning phase.

The overview of this chapter is as follows. Section 3.1 describes the tracking techniques used in this study. Section 3.2 describes a predictive empirical modeling technique for the kidney. The model can be integrated into predictor formulations such as KF, EKF, UKF and ANFIS. Section 3.3 describes a new correlation function to map skin marker positions to the kidney.

3.1 Estimating The Internal Organ Movement From Ultrasound Images

As mentioned earlier the movement of the kidney is three dimensional. Although three-dimensional ultrasound is available, the temporal resolution of such machines is usually poor and inadequate for real-time tracking. An alternative was chosen to use a two dimensional ultrasound image sequence. Here the movement is divided into two components one in the imaging plane and the other in a plane orthogonal to the probe, henceforth called the out-of-plane movement. The movement estimation approach is schematically represented in Figure 3-1.

Figure 3-1: Estimating the organ movement from ultrasound image slices

Movement of the kidney in the ultrasound plane was estimated using a template matching technique based on image correlation. Initially the coarse boundary of the kidney is indicated on the image, this portion of the image is stored as a template T . The correlation coefficient ρ_i is calculated using equation 3.1 over the entire Region of Interest (ROI) defined by R , which contains the kidney contour. In images where the entire kidney contour is not visible, the renal apex was considered as the template. The apex was chosen due to two reasons: firstly the renal apex is clearly visible across the entire movement sequence and secondly most of the kidney tumors are found around the renal apex. The region with maximum correlation is identified as the possible position of the kidney. Most data sets were preprocessed using median filters to enhance the image quality. This step however is not strictly necessary for all image sets as most of the images contained crisp kidney contours. A smoothness constraint is enforced over the search to suppress random spikes.

$$\rho_i(i, j) = \frac{\sum_{i=1}^m \sum_{j=1}^n T(i, j) * ROI(i, j)}{\sqrt{\sum_{i=1}^m \sum_{j=1}^n T(i, j)^2 \sum_{i=1}^m \sum_{j=1}^n (ROI(i, j))^2}} \quad 3.1$$

The out-of-plane movement was estimated using speckle correlation [96]. In order to do this, the tracked regions are extracted from the image sequences. Speckle de-correlation is based on an approximation of the speckle correlation as a function of the orthogonal displacement as given by equation 3.2, where σ is the cell width resolution. This approximation assumes the intensities to be in the linear scale. Since the RF signal on most ultrasound systems is compressed to the logarithmic scale, it needs to be transformed to the linear scale as given by equation 3.3 before calculating the speckle correlation.

$$\rho_s(I_1, I_2) = \exp\left(\frac{-d^2}{2\sigma^2}\right) \quad 3.2$$

$$I(i, j) = 10^{\rho_s(i, j)/51} \quad 3.3$$

In order to use the speckle de-correlation technique, the de-correlation curves at different orthogonal displacements have to be obtained. This is done prior to actual tracking. For this the tracked region is divided into P patches. B-mode scans are obtained at various values of d and the normalized correlation coefficient $\rho_s(d)$ of the corresponding patches is calculated for the image sequence as given by equation 3.4. I_0 and I_d correspond to the pixel intensity arrays in the corresponding patches, while $\bar{I}_0$ and $\bar{I}_d$ are the mean values of the pixel intensity. The normalized correlation can be directly used to estimate the orthogonal displacement $\hat{d}$ given by equation 3.5.

$$\rho_s(d) = \frac{\sum_{i=1}^m \sum_{j=1}^n (I_0(i, j) - \bar{I}_0)(I_d(i, j) - \bar{I}_d)}{\sqrt{\sum_{i=1}^m \sum_{j=1}^n (I_0(i, j) - \bar{I}_0)^2 \sum_{i=1}^m \sum_{j=1}^n (I_d(i, j) - \bar{I}_d)^2}} \quad 3.4$$

$$\hat{d} = \sqrt{-2\sigma^2 \ln(\rho_s)} \quad 3.5$$

Extracting information from the skin markers

Data extraction from the external skin markers comprises of three essential steps. Firstly the movement is tracked using the template matching technique mentioned earlier. The next step is to obtain the X, Y and Z coordinates of the tracked areas. The Z direction is assumed to be orthogonal to the plane of motion. The three dimensional coordinates of an $m \times n$ area in image can be estimated from the disparity image D obtained from the left and right cameras.

Figure 3-2: Schematic diagram of stereo image processing

The relation between the disparity image D and the orthogonal displacement Z would be:

$$Z = \frac{f \cdot B}{d} \quad 3.6$$

where Z is the distance along the camera Z axis, f is the focal length (in pixels), B is the baseline (in meters) and d is the disparity (in pixels). Using the value of Z the X and Y coordinates can be calculated using the camera projection equations 3.7 and 3.8. The terms u and v are the pixel location in the 2D image.

$$X = \frac{u \cdot Z}{f} \quad 3.7$$

$$Y = \frac{v \cdot Z}{f} \quad 3.8$$

The third step is to analyze the movement patterns of the three markers using PCA (Principal Component Analysis). The marker positions are normalized to obtain zero mean data. The normalized marker positions are represented by vectors M_1 to M_3 . The covariances of these vectors are arranged in the covariance matrix C :

$$C = \begin{bmatrix} cov(M_1, M_1) & cov(M_2, M_1) & cov(M_3, M_1) \\ cov(M_2, M_1) & cov(M_2, M_1) & cov(M_3, M_1) \\ cov(M_2, M_1) & cov(M_2, M_1) & cov(M_3, M_1) \end{bmatrix} \quad 3.9$$

The eigenvectors of matrix C are combined to create the feature vector matrix F , where e_1 to e_3 are the eigenvectors of the covariance matrix C . Finally the marker pattern is transformed using the feature matrix to obtain a new movement data set M' :

$$F = [e_1 \quad e_2 \quad e_3] \quad 3.10$$

$$M' = F \times [M_1 \quad M_2 \quad M_3] \quad 3.11$$

The remaining part of the methodology deals with modeling and predicting the organ movement pattern and approximating the correlation between the organ movement pattern and the skin-marker movement.

3.2 Empirical Modeling Of Kidney Movement

The estimated movement pattern of the kidney can be empirically modeled using a new approach. An overview of the modeling problem is given in Figure 3-3. The position of the organ at time t_1 is known prior to the ablation. The system is registered to this frame/position prior to the surgery. The objective here is to predict the organ position in frame $k + p$ given the organ position in frame k . In this approach, the system is approximated by a non-linear empirical model. This is trained using the signal history, S . As a preprocessing step, the movement pattern is filtered using low pass filters to reduce the noise.

The three dimensional movement of any organ (or tumor) can be modeled based on the respiratory time period T . The position $p(t) = [x(t), y(t), z(t)]$ can be modeled using a simplistic sinusoidal model as shown in equation 3.12

$$p(\varphi, t) = c + a \cos(2\pi ft - \psi) \quad 3.12$$

A more realistic estimation can be done using the Fourier series expansion as given in equation 3.13. The model closely fits the movement pattern for higher values of n .

$$p(\varphi, t) = c + \sum_{n=1}^{\infty} \cos\left(\frac{2\pi nt}{T} - \psi_n\right) \quad 3.13$$

However, the accuracy of the model would be insufficient as it does not explicitly account for the variations in the extent and time period of the renal mobility pattern. The above models also completely ignore the inherent asymmetry of the breathing cycle. Models presented in [97] use sinusoid based shape functions to model the renal movement.

Figure 3-3: Overview of movement prediction

In this project, an adaptive, asymmetric, shape-function based model for the renal mobility is developed. Although the model is explained for one dimensional motion it can be readily extended to two or three dimensions assuming the movements in each axis are independent of each other. The organ position $p(\varphi, t)$ at an instant of time t and phase angle φ can be expressed as:

$$p(\varphi, t) = c_1 S(\varphi, t) + c_2 A(\varphi, t) \quad 3.14$$

The model uses two non-linear functions $S(\varphi, t)$ and $A(\varphi, t)$. $S(\varphi, t)$ is a non-linear shape function while $A(\varphi, t)$ is an asymmetric shape function used to model the asymmetry in the movement. The constants c_1 and c_2 are weighting constants. The model can be trained over a set of M measurements $[p_1, p_2, \dots, p_M]$ which constitute the signal history S_M . The root mean square (RMS) error over each signal period T is evaluated and if it is greater than a preset threshold ϵ , the functions $S(\varphi, t)$ and $A(\varphi, t)$ are modified according to equation 3.15 and 3.16.

$$S'_k(\varphi_k(t)) = \lambda \omega(t) S_k(\varphi_k(t)) + (1 - \lambda \omega(t)) y[t] \quad 3.15$$

$$A'(\varphi, t) = \lambda \omega(t) A(\varphi, t) + (1 - \lambda \omega(t)) y[t] \quad 3.16$$

where, the term λ is a weighting factor such that $\lambda > 0.5$ gives greater weight to the model compared to the measurement. The exponential function, $\omega(t)$, gives more weight to the recent measurements. This model can be used to predict the tumor position for the next p measurements along with non-linear predictors such as the EKF, UKF and ANFIS as explained in the following subsections.

3.2.1 Organ movement prediction using Kalman filter

The underlying model for the Kalman filter is a linear approximation of the kidney movement pattern. The Kalman filter update equation for predicting the respiratory induced movement can be described by:

$$u(k) = Fu(k-1) + Gv(k-1) \quad 3.17$$

and the measurement update equation would be:

$$z(k) = Hu(k) + w(k) \quad 3.18$$

where $u = \begin{bmatrix} u_1 \\ u_2 \end{bmatrix}$, $F = \begin{bmatrix} 1 & \Delta t \\ 0 & 1 \end{bmatrix}$, $H = [1 \ 0]$ and $G = \begin{bmatrix} \Delta t \\ 1 \end{bmatrix}$

The current state of the organ is denoted by u , which comprises of the organ position u_1 and velocity u_2 . The state is updated by equation 3.18 for each sampling instant Δt using the linear movement model F . The system noise, v , is added to the state equation during iteration. The predicted measurement, z , is updated using equation 3.19 and the noise in measurement is accounted for by w .

The best estimate for the next state of the system is now computed using the following equations:

$$r(k) = z(k) - H\hat{u}(k/k-1) \quad 3.19$$

$$S(k) = HP(k/k-1)H^T + R_w \quad 3.20$$

$$K(k) = P(k/k-1)H^T S^{-1} \quad 3.21$$

$$\hat{u}(k/k) = \hat{u}(k/k-1) - K(k)r(k) \quad 3.22$$

$$P(k/k) = P(k/k-1) - K(k)S(k)K(k)^T \quad 3.23$$

where, K represents the Kalman gain and r stands for the innovation which is the difference between the predicted and actual values. The conventional Kalman filter prediction is meant for a prediction horizon of one sample. However in the practical context the prediction horizon must be extended to a finite number of samples as expressed in equations 3.24-3.26 below. The Kalman filter cycle is shown in Figure 3-4.

$$\hat{u}(k+j/k) = F^j \hat{u}(k/k) \quad 3.24$$

$$\hat{z}(k+j/k) = H \hat{u}(k+j/k) \quad 3.25$$

$$P(k+1/k) = F^j P(k/k) F^{jT} \quad 3.26$$

3.2.2 Organ movement prediction using EKF

It is known that respiration induced quasi-periodic movement patterns, such as the movement of abdominal organs, can be well approximated by non-linear sinusoidal functions [71]. EKF is a generalization of the Kalman filter that accommodates such non-linear system models. The non-linear system model described in section 3.2 can be used with EKF as shown in equations 3.27-3.28.

$$u(k) = fu(k-1) + gv(k-1) \quad 3.27$$

$$z(k) = hu(k) + w(k) \quad 3.28$$

$$F_{k-1} = \frac{\partial f}{\partial x} |_{x_{k-1}|x_{k-1},u_{k-1}} \quad 3.29$$

$$H_{k-1} = \frac{\partial h}{\partial x} |_{x_k|x_{k-1}} \quad 3.30$$

The non-linear function, f , is defined by the equation 3.14. The Kalman cycle is then implemented by equations 3.19-3.23. The prediction matrix F and the observation matrix H are defined by equations 3.29-3.30. The algorithm for the EKF is shown in Figure 3-4.

3.2.3 Organ movement prediction using UKF

Although the EKF can accommodate non-linear behavior, it still uses an underlying linear model. Hence, for systems with higher degrees of non-linearity the EKF tends to show poor prediction accuracy. In this work, the Unscented Kalman Filter (UKF) is used which is a more efficient technique for prediction in non-linear systems. UKF uses the unscented transform which chooses sigma points along which the covariance of the non-linear function is propagated. The UKF formulation does not involve laborious computation of the Jacobian matrices (equations 3.30 and 3.31), which makes it computationally more efficient compared to the EKF. The UKF formulation for this problem is identical to that of the EKF as expressed in equations 3.27 - 3.28. The algorithm was adapted from the formulation given in [70]. Prediction using UKF comprises of the following steps:

- i. Augment the state and covariance matrix with the mean and covariance of the process noise.

$$u^a = [\hat{u}^T + E[w^T]^T] \quad 3.31$$

$$P^a = \begin{bmatrix} P & 0 \\ 0 & Q \end{bmatrix} \quad 3.32$$

- ii. Derive sigma points from the augmented state and covariance matrix using the following equations:

$$\chi^0 = x^a \quad 3.33$$

$$\chi^i = x^a + \psi_i \quad 3.34$$

$$\chi^i = x^a - \psi_i \quad 3.35$$

Where ψ_i is the matrix square root of $(L + \lambda)P$ and can be calculated using methods such as Cholesky decomposition.

- iii. Propagate the sigma points using the non-linear function, f , as:

$$\chi_{k/k-1}^i = f(\chi_{k-1/k-1}^i) \quad 3.36$$

- iv. Recombine the weighted sigma points to predict the next state and covariance matrices.

During the update phase the sigma points are calculated as in the prediction phase and are projected through the observation function h .

$$\gamma_k^i = h(\chi_k^i) \quad 3.37$$

The weighted sigma points are recombined to produce the predicted measurement and predicted measurement covariance. The Kalman gain is now computed using the system covariance matrix P_k as shown in equation 3.32. The remaining part of the UKF update phase is identical to the conventional Kalman filter.

$$\hat{z}_k = \sum W_s^i \gamma_k^i$$

3.38

$$P = \sum_{i=0}^{2L} W_c^i [\gamma - z_k][\gamma - z_k]^T \quad 3.39$$

$$K_k = P_{xk} P_{xk}^{-1} \quad 3.40$$

The equations 3.39 - 3.40 can be used for the UKF iteration as shown in Figure 3-4. A more detailed treatment of UKF can be found in [70].

Figure 3-4: Kalman filtering algorithm for organ movement prediction

3.3.4 Organ movement prediction using ANFIS

The goal of ANFIS is to find a model or mapping that will correctly associate the input, which in this case is the position of the organ at previous instants of time, with the target, which is the predicted position, as shown in Figure 3-5. Fuzzy inference based systems such as ANFIS are used in place of conventional mathematical modeling for ill-defined and uncertain systems [98]. The ANFIS architecture is obtained by incorporating fuzzy inference into an adaptive network. A fuzzy inference system comprises of the following functional blocks:

Figure 3-5: ANFIS structure

- Knowledge base* which comprises of a *rule base* containing the *if-then* rules and the *database* which contains the membership functions for the fuzzy sets;
- Decision making unit* that acts upon the data using the rule base;
- Fuzzifier* that converts the crisp data into fuzzy values based on the membership function;
- Defuzzifier* that regenerates the crisp (physical) values from the fuzzified output.

ANFIS is a Sugeno type fuzzy inference system in which membership functions are modified automatically according to the training set [98][98][97][96]. ANFIS is a five layered Sugeno type

network as shown in Figure 3-5, in which each layer can have both fixed and adaptive nodes. The five layers are explained below:

- i. **Layer 1** - This layer is entirely made up of adaptive nodes. The parameters used in this layer are often called *premise parameters*;
- ii. **Layer 2** - This layer implements the MIN criteria or the logical product of all inputs using fixed nodes;
- iii. **Layer 3** - This layer calculates the normalized firing strength of each rule using the MAX criteria;
- iv. **Layer 4** - This layer is made of entirely adaptive nodes. The parameters used in this layer are often called *consequent parameters*;
- v. **Layer 5** - The final layer can be seen as single fixed output function which implements a logical summation of all the consequents.

Any given input element has a degree of membership associated with it based on the membership function (MF). So a fuzzy set A for n input set X can be defined as:

$$A = \{(x, \mu_A(x) \mid x \in X\} \quad 3.41$$

where $\mu_A(x)$ is the membership function. Various functions such as the Gaussian, bell shaped and trapezoidal functions can be used as input or output membership functions. The commonly used membership functions used for ANFIS are summarized in Table 3-1. There is no general rule to determine the optimal MF for a particular application.

The variables $x(k)$ to $x(k-L*p)$ represent the signal history, which is the position of the organ at previous instances of time. The membership functions $A_1, A_2 \dots A_M$ associate a degree of membership for each input. A bias term is sometimes included in layer two. The firing strength of layers two and three are denoted by w_1 and w_M . The output layer sums-up the firing strengths $f_1 - f_M$ of the nodes and presents a crisp or defuzzified value at the output.

ANFIS uses a hybrid learning rule which in turn uses a combination of gradient descent and the least-squares method. This is a dual pass mechanism in which the node outputs, until the fourth layer, are calculated and consequent parameters are identified in the forward pass. The error signals are propagated backwards recursively updating the premise parameters in the backward pass. The main benefit of the hybrid approach is that it converges much faster when compared to pure back propagation.

Table 3-1: Membership functions used for ANFIS

Membership Function	Description
Bell function	$f(x; a, b, c) = \frac{1}{1 + \left \frac{x-c}{a} \right ^{2b}}$
Gaussian	$f(x; \sigma, c) = e^{-\frac{(x-c)^2}{2\sigma^2}}$
Sigmoid	$f(x, a, c) = \frac{1}{1 + e^{-a(x-c)}}$
Trapezoidal	$f(x; a, b, c, d) = \begin{cases} 0, & x \leq a \\ \frac{x-a}{b-a}, & a \leq x \leq b \\ 1, & a \leq x \leq c \\ \frac{c-b}{c-d}, & b \leq x \leq c \\ \frac{x-b}{x-c}, & b \leq x \leq c \\ 0, & x \geq c \end{cases}$
Triangular	$f(x; a, b, c) = \begin{cases} 0, & x \leq a \\ \frac{x-a}{b-a}, & a \leq x \leq b \\ \frac{c-b}{c-a}, & b \leq x \leq c \\ 0, & d \leq x \end{cases}$

The KF and ANFIS based techniques discussed thus far are used for the prediction module. The next section discusses the skin marker correlation module.

3.3 Correlation Model To Map Skin Marker Position

The predictor module is integrated to a correlation module which estimates the organ position based on the movement of the external markers. A schematic representation of the technique developed for the proposed application is shown in Figure 3-6.

Figure 3-6: Schematic representation of the prediction-correlation model

The objective of the correlation model is to find the optimal mapping $f(s(t))$ that maps the tumor target $p(t)$ to a marker position $s(t)$. The initial estimate of f is a linear mapping as given by equation 3.42. The error in prediction $e(t)$ is calculated after k samples based on equation 3.43. This is different from the conventional linear correlation approach in which the function is updated only once during a respiratory period. The parameter k affects the accuracy of the model; a larger value of k indicates prediction over a longer horizon.

$$f(s(t)) = C_1 s(t) + C_2 \quad 3.42$$

$$e_k(t) = z_k(t) - f_k(s(t)) \quad 3.43$$

The parameters C_1 and C_2 are tuned to fit individual subjects. The model is updated for the next k samples if the mean error is greater than the error threshold e_t . This ensures that the model is not over-fitted to the data. The model is updated using the equation 3.44. The extent of change in the model is controlled by the exponential weighting function α given in equation 3.45. The function $\alpha(t)$ also works as a forgetting-factor as the impact of earlier samples is significantly reduced by the exponential weighting.

$$y_{k+1}(t) = y_k(t) + \alpha(t)e_k(t) \quad 3.44$$

$$\alpha(t) = 1 - e^{(-c_3 t)} \quad 3.45$$

The process is repeated over a set of $N * k$ samples. The mapping is then fine-tuned using ANFIS to achieve a non-linear mapping. The algorithm for training the model is shown in Figure 3-7.

Figure 3-7: Flowchart for updating the movement correlation model

Fine-tuning using ANFIS

The objective of ANFIS is to fine tune the predictions provided from the correlation function f . The network is trained using input-output pairs. The inputs to this network are the organ position and velocity as predicted from the mapping function and desired output is the optimized organ position. A schematic representation of the network is given in Figure 3-8.

Figure 3-8: Organ/tumor position correlation using ANFIS

The basic function of the five layers is as follows:

The ANFIS input variables are fuzzified and assigned a specific degree of membership using the membership functions A_1 to A_M in the first layer. The membership functions (MF) are tuned during the training phase. A bias term is also included in the second layer. The firing strength of layers two and three are denoted by w_1 - w_M . The output of layer five is a summation of outputs from layer four denoted by f_1 - f_M . Layer five performs a max operation of the outputs at layer four to give the final weighted expression $pa(k)$.

3.4 Summary

The methodology used to measure and model the movement of the kidney as well as the respiratory markers was explained in this chapter. The measurement of kidney movement consists of in-plane and out-of-plane movement estimation. The in-plane movement was estimated using template matching while the out-of-plane movement was estimated by speckle correlation. The measurement of marker movement was also using template matching followed by stereo image processing to obtain the three-dimensional coordinates. The significance of information from the markers was compared using PCA. The modeling techniques discussed in this chapter comprise of two distinct modules which are used for prediction and correlation. The prediction module consists of a new shape function based model and predictor algorithms such

as UKF, EKF and ANFIS. The correlation module comprises of a new mapping function that gives a gross estimate of the kidney position which can be further fine tuned using ANFIS. The next chapter presents the results obtained from these techniques. The movement compensation strategy that can be used with these modeling techniques is presented in Chapter 5.

CHAPTER 4 : PRE-OPERATIVE MOVEMENT MODELING OF THE KIDNEY - EXPERIMENTAL SET-UP, RESULTS AND DISCUSSION

The methodology for movement estimation and modeling during the pre-operative phase was discussed in the previous chapter. This chapter discusses the experimental set-up and the results obtained. Firstly, an experimental set-up was designed to study the kidney movement in relation with the respiratory movement. The pilot study was conducted on twenty healthy volunteers of different ethnicity, age and physical attributes. The study was then repeated in a clinical environment in collaboration with Singapore General Hospital (SGH) on a sample of eighty four patients. The image sequences collected were quantified using the movement estimation techniques explained in section 3.1 so as to obtain movement data sets. Apart from the statistical normalization, the movement data was also normalized w.r.t the BMI in order to generalize the results. These data sets were used to test the accuracy of the prediction and correlation modules developed in Chapter 3.

An overview of this chapter is as follows. Section 4.1 explains the experimental set-up. Section 4.2 discusses the results of movement estimation using the image sequence obtained from the experimental set-up. The results obtained from the predictor module are discussed in section 4.3 and the results from the correlation module are explained in section 4.4.

4.1 Experimental Set-up To Study Kidney Movement

The objective of the experimental set-up was to simultaneously capture the kidney movement patterns and the respiratory movement. A schematic diagram of the set-up is shown in Figure 4-1. The set-up comprises of a medical ultrasound imaging system to capture the internal movement and a stereo vision camera system to capture the external movement. The ultrasound system used in this study was Aloka SSD-900 with a 3.5 MHz phased array probe (marked as (1) in Figure 4-1). The ultrasound images were grabbed using the Matrox image grabber card

(Matrox Meteor 2). The stereo vision system used was Bumblebee 2X (marked as (2) in Figure 4-1). A Microsoft Foundation Classes (MFC) application developed in-house was used for simultaneous grabbing of ultrasound and camera images.

Figure 4-1: Experimental set-up for capturing renal movement

During the experiment medical grade ECG holders were placed over the abdomen and chest to act as skin markers. These were placed at locations where maximal respiratory movement was observed. The physical coordinates of the center of mass of these markers were tracked using stereo images by observing the disparity information from the right and left cameras. The origin of the stereo camera system was chosen as the global origin. The ultrasound probe position is registered to the global coordinate frame using a reference placed on the probe harness. During the experiment the probe position was controlled using a two dimensional movement platform. The experimental set-up including the probe harness is shown in Figure 4-2a. The probe harness is shown separately in Figure 4-2b for clarity.

The various coordinate systems involved are also indicated in the Figure 4-2a. The origin of the global coordinate system G is set at the midpoint of the right and left cameras. The position of the marker R placed on the probe harness is used as reference for all measurements. The position

of the ultrasound probe from the marker R is measured. The probe position can be tracked using the marker projected on the ultrasound image. Since the probe is assumed to be symmetrical, rotation about the longitudinal axis can be neglected. The orientation of the probe can be calculated with respect to the reference R . The tilt of the probe is measured along the lines AOB and COD marked on the image. The position of the markers $m_1(x, y, z)$ – $m_3(x, y, z)$ is also measured with respect to the same reference R for convenience.

Figure 4-2: Pilot study a) Experimental setup b) Probe harness

The experimental protocol is as follows

- i. Skin markers are placed on the abdomen and chest at positions where maximum displacement is observed. These are tracked by the stereo camera;
- ii. The ultrasound image of the right kidney is located through the intra-costal window from the supine position;
- iii. In order to have sufficient number of samples, images of the moving kidney are captured for 80 ± 5 seconds, under normal respiration. During the process the ultrasound probe is held in position using a custom made probe harness. The procedure is then repeated with respiratory coaching;
- iv. After the right kidney movement is captured the experiment is repeated for the left kidney.

The ribs can be seen as a clear dark shadow next to the kidney. Hence, during our experiments the 12th and 13th ribs were used as anatomical references to measure the extent of organ mobility. The experimental study was conducted in clinical set-up at Singapore General Hospital. A picture of the clinical set-up is shown in Figure 4-3. The next section describes how the movement pattern was estimated and statically analyzed from the image sequences.

Figure 4-3: Clinical set-up to study the kidney movement

4.2 Movement Estimation From Ultrasound Images

The kidney image sequences obtained from the experimental study were tracked using the movement estimation approach as mentioned in section 3.1. The movement comprises of in-plane and out-of-plane movements.

In-plane Movement

The template T and the ROI were obtained from the initial image (Frame 1) as shown in Figure 4-4. The template is tracked over the entire image sequence comprising of 1800 – 2000 frames grabbed at 25fps. The size of the template varies according to the coarse boundary of the kidney.

Figure 4-4: Template based tracking of kidney movement

Out-of-plane Movement

The speckle de-correlation technique was used to estimate the orthogonal displacement. Initially, the target region of interest (ROI) was divided into 25 patches of equal area in order to obtain the speckle correlation curves. The B-mode scans of the kidney were obtained at various depths at a resolution of 4 mm along the orthogonal axis. The speckle correlation curves obtained are shown in Figure 4-5. This indicates the variation of the speckle correlation coefficient as a function of the orthogonal displacement. Each curve represents the variations in the correlation coefficient in successive frames for the pixels in a particular patch. The mean value of the correlation of 25 patches was used for estimating the displacement. The value of σ used was in the range of 0.66 - 0.87.

Figure 4-5: Speckle correlation curves for individual patches where each curve corresponds to patch

Quantification of Movement

The scenarios of coached and natural (un-coached) respiration were treated separately during the movement quantification. During respiratory coaching the subjects are instructed to time the inhale and exhale cycles as prompted by the clinician. The analyses of the data from clinical and non-clinical study were also analyzed independently. A representative kidney movement pattern of the right kidney is shown in Figure 4-6a. It was observed that the right kidney generally exhibited more movement than the left for coached and un-coached respiration in both data sets. The cross-correlation between the movement of the right and left kidneys was poor. The extent of movement was more in the case of coached respiration compared to un-coached respiration for both kidneys. The movement pattern was quasi-periodic with vast variations in amplitude and time period among the subjects.

Figure 4-6: (a) Renal movement pattern (Raw data) (b) Filtered movement pattern

The maximum extent of movement was found to be approximately 38 mm in superior-inferior direction. The extent of movement varied with subject and showed poor repeatability within

subjects in both data sets. The time period varied from 3.6 – 5.6 seconds in the pilot data set and 3.2 – 6.4 seconds in the clinical data set.

Figure 4-7: Frequency analysis of the movement pattern

Frequency analysis of the movement patterns showed a very sharp peak at 0.2 – 0.4 Hz as shown in Figure 4-6 indicating a dominant frequency coinciding with the respiratory frequency. As a pre-processing step, a tenth order Butterworth low-pass filter with cut-off frequency of 2 Hz was used to smooth the data. The higher order filter ensures a steep slope in the frequency response beyond the respiratory frequency of 0.2 - 0.5 Hz. The filtered data, on which further statistical analysis was performed, is shown in Figure 4-6b. The movement of the kidney was studied in the cranio-caudal and transverse directions. The mean values of the extent and period of movement in the cranio-caudal and transverse direction are summarized in Table 4-1 (un-coached respiration) and Table 4-2 (coached respiration) for the pilot study. Multiple samples were acquired from the same subjects to study the repeatability of movement. Repeatability in movement pattern was calculated as dimensionless quantity based on the cross-correlation between the same samples of identical duration and phase. The repeatability was less than 0.45 for un-coached respiration and it was improved in the case of coached respiration to 0.71 for the

cranio-caudal movement. The mean cross-correlation obtained for the kidneys was 0.22 and 0.28 for un-coached and coached respiration respectively.

Table 4-1: Renal mobility statistics for 20 subjects (un-coached respiration)

Un-coached Respiration	Right Kidney		Left Kidney	
	Cranio-caudal	Transverse	Cranio-caudal	Transverse
Extent of movement (mm)	21.50 $\pm$ 2.30	9.40 $\pm$ 1.80	9.66 $\pm$ 3.80	6.24 $\pm$ 2.22
Time period (sec)	3.50 $\pm$ 1.00	3.38 $\pm$ 1.12	3.20 $\pm$ 0.98	3.12 $\pm$ 0.80
Repeatability	0.42 $\pm$ 0.24	0.26 $\pm$ 0.18	0.32 $\pm$ 0.22	0.24 $\pm$ 0.12
Cross Correlation	0.22 $\pm$ 0.26			

Table 4-2: Renal mobility statistics for 20 subjects (coached respiration)

Coached Respiration	Right Kidney		Left Kidney	
	Cranio-caudal	Transverse	Cranio-caudal	Transverse
Extent of movement (mm)	29.50 $\pm$ 3.30	12.40 $\pm$ 2.62	17.42 $\pm$ 0.80	10.4 $\pm$ 2.42
Time period (sec)	3.60 $\pm$ 1.20	3.60 $\pm$ 0.90	3.40 $\pm$ 0.82	3.24 $\pm$ 0.88
Repeatability	0.67 $\pm$ 0.04	0.42 $\pm$ 0.08	0.62 $\pm$ 0.08	0.34 $\pm$ 0.12
Cross Correlation	0.28 $\pm$ 0.12			

The out-of-plane movement calculated for both kidneys followed complex patterns. The movement estimated from speckle correlation was more significant for the right kidney compared to the left. The maximum extent of movement was 14 mm. The variance in the movement pattern was also more for the right kidney. The repeatability of the out-of-plane

movement was less than 0.2 for 18 subjects while the remaining 2 subjects showed a marginal improvement with 0.35 repeatability.

The results of the clinical study are summarized in Table 4-3 (un-coached respiration) and Table 4-4 (coached respiration). During measurement, the vertical direction in the ultrasound image is denoted as X and horizontal direction is denoted as Y. It must be noted that the Y direction roughly corresponds to the cranio-caudal direction. The maximum movement obtained during natural respiration was 37.80 mm in the Y direction for the right kidney. The movement patterns were similar in nature to the patterns obtained in the pilot study. The average movement of the right kidney was 23.32 mm and that of the left kidney was 16.78 mm. The average movement in the Y direction was more than the movement in the X direction.

The cross-correlation between the right kidney and left kidney was 0.4 which indicates that the movement patterns cannot be predicted based on the position of the opposite kidney. The average movement of both kidneys increased under respiratory coaching. Average movements of 27.20 mm and 19.19 mm were observed for right and left kidneys respectively in the Y direction for coached respiration.

Table 4-3: Renal mobility statistics for 84 subjects (un-coached respiration) – clinical study

Un-coached Respiration	Right Kidney		Left Kidney	
	Y	X	Y	X
Extent of movement (mm)	23.32 ± 5.06	13.44 ± 2.90	16.78 ± 3.59	10.15 ± 1.55
Time Period (sec)	3.80 ± 2.4		3.68 ± 3.50	
Cross-correlation	0.26 ± 0.14			

Table 4-4: Renal mobility statistics for 84 subjects (coached respiration) clinical study

Coached Respiration	Right Kidney		Left Kidney	
	Y	X	Y	X
Extent of movement (mm)	27.20 ± 5.00	14.68 ± 2.72	19.19 ± 4.03	11.12 ± 1.81
Time Period (sec)	4.28 ± 1.4		3.90 ± 1.5	
Cross-correlation	0.26 ± 0.16			

Study on subjects with kidney pathology

The sample size of cases with renal pathology was 48. As mentioned earlier the subjects were of different age, gender and physical nature. Pregnant women and subjects with chronic respiratory diseases were excluded from this study as there could be difficulties in executing the study protocol. There is also chance of observing abnormal movement patterns in such subjects. The average extents of movement of the right and left kidney were 22.62 mm and 15.40 mm respectively for natural respiration. Movement histograms for right and left kidney movement are shown in Figure 4-8.

Figure 4-8: Movement histogram (a) Right kidney (b) Left kidney

The movement patterns were classified based on the pathology. The distribution of pathologies observed in this study is shown by a pie-chart in Figure 4-9. Out of the 48 subjects with pathologies, 37 had calcified cysts of sizes ranging from 3 mm to 40 mm. In two subjects multiple cysts were observed in the kidney. These were classified as polycystic kidneys. The second most significant pathology was Angiomyolipoma (AML) which is very common benign kidney tumor. AML was found in 6 subjects. The sizes of AML varied from 7 mm to 42 mm. Renal Cell Carcinoma (RCC) was found in 3 subjects. The RCC observed varied in size, the smallest was 20 mm while the largest was 90 mm. All tumors were found on the surface of the kidney. In most cases the boundary of the tumors could be clearly identified.

Figure 4-9: Distribution of Pathologies

The ultrasound image of various pathologies seen in the kidney is shown in Figure 4-10. A polycystic kidney with three cysts is shown in Figure 4-10a. Figure 4-10b shows a single calcified cyst in the left kidney measuring 26 x 25 x 40 mm. Figure 4-10c shows kidney affected with Renal Cell Carcinoma (RCC). Figure 4-10d shows an Angiomyolipoma in the left kidney seen as a white mass measuring 42 x 36 x 34 mm.

Figure 4-10: Various pathologies of kidney observed in ultrasound images a) Polycystic kidney (c) Renal cyst (c) Renal Cell Carcinoma (RCC) (d) Angiomyolipoma (AML)

The movement patterns of affected kidneys were further analyzed to understand the influence of individual pathologies. The average movement of the affected kidneys was 22.62 mm in Y direction and 13.62 mm in the X direction. This was lesser than the average of movement of normal kidneys in the X and Y direction. The average movement in the Y direction classified according to pathology is shown in Figure 4-11. The lowest average movement was observed in

kidney affected with AML followed by RCC. The average movement of polycystic kidneys is close to that of RCC.

Figure 4-11: Kidney displacements measured for various pathologies

The size of the pathologies varied from 3 mm to 90 mm. The frequency of pathologies of various sizes is shown in Figure 4-12. The average size of the pathology was 17.35 mm. The effect of size of pathology on the movement patterns was also studied.

Figure 4-12: Pathology size histogram

The samples with pathology were grouped into three categories based on the size of pathology as shown in Table 4-5. Category A comprises of small cysts measuring less than 10 mm. Category B comprises of pathologies measuring between 11 mm and 20 mm. The pathologies in this category comprise of mostly calcified cysts and 3 cases of AML. All pathologies measuring more than 20 mm were grouped in category C.

Table 4-5 : Classification of pathologies based on size

Category	Size of pathology	Number of subjects
A	0-10 mm	20
B	11-20 mm	17
C	Greater than 20 mm	11

The movement patterns in the three categories were compared based on the average extent of movement. The average right kidney movement in the Y direction categories A , B and C were 23.8 mm, 22.4 mm and 21.8 mm respectively. The average movements of the left kidney in the Y direction were 18.2 mm, 14.32 mm and 12.84 mm. Similarly the average movement in X direction was 15.42 mm 13.82 and 13.46 mm for the right kidney and 13.66 mm, 9.82 and 9.40 mm for the left kidney. The extents of movement for the three categories can be compared using the box plots shown in Figure 4-13.

Figure 4-13: Kidney displacements for different size of pathology

It can be seen from the Figure 4-13 that the maximum movement is observed in category A followed by category B and C. It can hence be inferred that the sub-centimeter cysts grouped in category A did not have any significant influence on the kidney movement pattern. However, for masses greater than 10 mm there was a noticeable change in the extent and time duration of kidney movement.

Next, the effect of age on the kidney movement patterns was studied. The age of the subjects taking part in this study varied from 20 -80 years. The age wise distribution of subjects with pathology is shown by the histogram in Figure 4-14. The mean age of the subjects was 56 years with a standard deviation of 14.

Figure 4-14 : Age of subjects - histogram

The correlation between age and kidney movement is shown by the scatter plot shown in Figure 4-15. The Pearson coefficient for age and kidney movement was 0.4 for the right kidney and 0.35 for the left kidney. These indicate that the correlation between age of subjects and average kidney movement was weak.

Figure 4-15 : Average kidney movement vs age of subjects

Gender based classification for both right and left kidney movement pattern is shown in Figure 4-16. It was noticed that the average movement of both right and left kidney was more in case of male subjects. The difference in average extent of movement for right and left kidneys were 3.8 mm and 2.4 mm respectively.

Figure 4-16 : Gender based variation in kidney movement

The scenarios of coached and un-coached or natural respiration have been treated separately. A comparison of movements of the left and right kidneys under coached respiration is shown in Figure 4-17. As in the case of natural respiration once again the average extent of movement was more for the right kidney. However compared to natural respiration the extent of movement was more during respiratory coaching for both right and left kidneys. Coaching also improved the periodicity of movement as indicated by the lower variation in time period.

Figure 4-17 : Histogram of kidney movement under respiratory coaching (a) Right kidney (b) Left kidney

The cross correlation between coached and natural kidney movement is shown by the scatter plot in Figure 4-18. It can be seen that mean values of the movement patterns during natural respiration and coached respiration are strongly correlated.

Figure 4-18 : Correlation of average movement under coached and natural respiration

Hysteresis

The movement patterns were split into discrete respiratory cycles. The movement trajectory of the kidney over different respiratory cycles is shown in Figure 4-19. It can be seen that the movement of the kidney does not exactly retrace its path over a respiratory cycle. This phenomenon is called hysteresis. Such hysteresis was observed for both in-plane and out-of-plane movements. This can be seen as a direct consequence of the asymmetry in the breathing pattern. The extent of hysteresis was calculated as the maximum distance between any two points on the hysteresis curve. The maximum hysteresis was found to be 9 mm in the pilot study and 12 mm in the clinical study.

Figure 4-19: Relative movement in transverse and cranio-caudal directions for different respiratory cycles

Next, the relationship between the breathing pattern and the kidney movement was analyzed. The breathing pattern can be understood from the displacement of the skin markers.

Study of the respiratory pattern using skin marker position

The skin marker position was estimated using template tracking techniques. Two to three markers were placed on the subject depending upon the nature of respiration. For subjects with minimal respiratory movement, two markers were sufficient but for subjects with deep breathing patterns three skin markers were used. The markers tracked in the stereo vision image are shown in Figure 4-20.

Figure 4-20: Skin markers placed on the subject

The displacement of the markers was calculated from the central reference point on the camera considered to be the global origin. The movement of the three markers was calculated separately from the image sequences. The marker movement patterns were analyzed using Principal Component Analysis (PCA) to understand the impact of individual markers. The relative amount of information contained in the markers is summarized in the Table 4-6.

Table 4-6: Relative information from skin markers

Number of Markers	Non-clinical Data	Clinical Data
	Information Percentage	Information Percentage
1	98.80	99.20
2	99.40	99.60
3	100	100

From Table 4-6, it can be seen that the difference in information while using one skin marker as opposed to three, is minimal in both data sets. So it is sufficient to use the skin marker with maximal extent of movement. The movement of the skin marker and corresponding kidney movement over one respiratory cycle is shown in Figure 4-21a. The kidney showed poor linear correlation with the respiratory movement for natural or un-coached respiration. However, when the test was conducted under respiratory coaching, most subjects showed better and more consistent correlation with the respiratory movement.

Statistical analysis was performed on the data to study the extent and duration of the respiratory movement. It was found that the maximum movement was 29.45 mm along the sagittal plane and the minimum movement was 4.23 mm along the transverse plane. The statistics derived from the datasets are shown in Table 4-7. The maximum, minimum and mean deviation of the markers were calculated for all subjects. Data obtained from Georgetown University Hospital respiratory database [99] was also used for initial data analysis. The respiratory movement statistics were similar to the data collected in this pilot study and clinical data.

Table 4-7: Statistical analysis of respiratory movement data

Data from Georgetown University Database									
	Marker 1			Marker 2			Marker 1		
	Max	Mean	Min	Max	Mean	Min	Max	Mean	Min
Time Period(sec)	7.20	4.71	2.80	7.50	4.69	3.05	7.50	4.76	3.215
Deviation(mm)	23.53	6.69	1.22	29.45	6.39	1.56	21.41	5.26	2.80
Data from pilot study									
	Marker 1			Marker 2			Marker 3		
	Max	Mean	Min	Max	Mean	Min	Max	Mean	Min
Period (sec)	6.40	5.20	3.80	7.60	4.80	3.40	6.60	4.42	3.21
Deviation(mm)	28.23	10.86	6.22	30.40	15.60	10.72	18.42	8.84	4.70
Data from clinical study									
	Marker 1			Marker 2			Marker 3		
	Max	Mean	Min	Max	Mean	Min	Max	Mean	Min
Period (sec)	7.20	5.80	3.40	7.80	5.40	3.60	-	-	-
Deviation(mm)	24.80	12.28	4.46	26.40	16.30	6.40	-	-	-

There was a wide disparity in the relative extent of movement of markers among subjects. The extent of movement also varied considerably for samples from the same subject. The trends found in the skin marker movement pattern were compared with the kidney movement patterns.

The movement patterns of the kidney and skin markers were similar during the respiratory phase. The phenomenon of hysteresis observed earlier for kidney movement patterns was also found in relation with the respiratory pattern. Figure 4-21a shows the kidney movement in relation with the respiratory movement. The non-linearity between the movement patterns was generally more significant in the exhale phase than the inhale phase.

Figure 4-21: a) Skin marker movement vs kidney movement b) Frequency analysis

The movement data was also analyzed in the frequency domain. The power spectrums of the signals are given in Figure 4-21b. The FFT had dominant peaks in the range of 0.42 - 0.64 Hz for kidney patterns and 0.40 - 0.62 Hz for the respiratory pattern for all three data sets. This gives sufficient confidence that the time period of kidney movement and skin marker movement are very close. More importantly, the movement of the kidney can be predicted from the skin movement pattern. The frequency analysis was also used to determine the cut off frequency of output low pass filters. The analysis till this point was on the raw data. As mentioned earlier, the subjects were of different height, weight, age and ethnicity. In this study, the next step was to normalize the data with respect to the body mass index (BMI), so that the results obtained could be applied to any general population.

Normalization to limit the variation due to height and weight

In order to understand the relation between the sizes of the subject and movement pattern, a grouping was performed. The 20 subjects were divided into three categories based on their normalized BMI as shown in Table 4-8.

Table 4-8: Categorization of subjects

Category	Normalized BMI(Kg/m ²)
A	11-18
B	18-26
C	26-35

The BMI is calculated using equation 4.1

$$BMI = \frac{W}{H^2} \quad 4.1$$

where W is the weight in kilograms and H is the height in meters. According to this grouping, 10/20 subjects belonged to category A, 6/20 belonged to category B and 4/20 to category C in the pilot study. The mean values of the kidney movement in the cranio-caudal and transverse direction are shown by box plots in Figure 4-22 for the three different categories.

Figure 4-22: Mean kidney displacement in cranio-caudal and transverse directions for different categories

Among the three groups, maximum movement was observed in category A for both right and left kidneys. The movement was more in cranio-caudal direction for both categories A and B. But for category C, the difference in movement in both directions was small. The movement in the transverse direction was more than the cranio-caudal direction for one of the subjects in category C. It was found that subjects in category A and category B exhibited significant diaphragmatic respiration while the subjects in category C exhibited abdominal respiration. This could be a possible reason for the change in the kidney movement patterns of the subjects.

The raw data patterns were then normalized to minimize the effect of the height and weight of subjects. The data was divided by a normalization factor K given by equation 4.2, where σ_{BMI} is the variance of the statistically normalized BMI.

$$K = 1 + \sigma_{BMI}^2 \quad 4.2$$

The mean displacements and time periods of the normalized movement patterns of the kidney and the skin markers are compared with the raw data values in Figure 4-23.

Figure 4-23: Comparison of normalized and raw data

The normalized values of respiratory displacements and time periods of the right and left kidney along with the skin marker movement are summarized in Table 4-9.

Table 4-9: Measured movement of the kidney in the cranio-caudal (CC) and transverse (TR) directions

	Natural Respiration			Coached Respiration		
	Right Kidney CC,TR	Left Kidney CC,TR	Skin Marker	Right Kidney CC,TR	Left Kidney CC,TR	Skin Marker
Displacement (mm)	21.40 ± 4.38, 16.46 ± 2.38	17.24 ± 3.78 14.46 ± 3.32	3.32 ± 2.69	24.30 ± 4.60 18.86 ± 3.23	21.24 ± 2.86 16.46 ± 1.98	10.28 ± 1.45
Time period (sec)	3.86 ± 0.86	2.86 ± 0.98	3.48 ± 0.68	4.48 ± 0.26	3.96 ± 0.28	4.68 ± 0.34

4.3 Predictive Modeling

The model developed in section 3.1 was used to model the kidney and skin marker movement patterns. The model is partly repeated here for convenience:

$$p(\varphi, t) = C_1 S(\varphi, t) + C_2 A(\varphi, t) \quad 4.3$$

The dimensionless constants C_1 and C_2 were tuned for individual subjects using an iterative code. In every iteration, the code attempts to minimize the difference between the predicted position and the actual organ position by varying C_1 and C_2 . Tuning was stopped when the change in error was less than a threshold of 0.02 mm. The range of values for C_1 and C_2 were 0.6 – 0.8 for the kidney movement and 0.5 – 0.7 for the skin marker movement as summarized in the Table 4-10. The maximum errors in prediction of the normalized movement were 2.4 mm for the kidney and 1.2 mm for the skin marker pattern for 20 samples collected in the pilot study. The error reduced to 2.2 mm for normal subjects in the clinical data set. However, the maximum

prediction error increased to 3.2 mm for kidney movements in affected subjects. This model was then used as the basis for further prediction using non-linear predictors.

Table 4-10: Tuned values for non-linear prediction module

Movement pattern	C₁	C₂	Pilot study	Clinical study (Normal)	Clinical study (Affected)
Right kidney	1-1.3	0.5-0.75	92%	94%	89%
Left kidney	1-1.3	0.6-0.9	89%	91%	86%
Skin marker	1-1.1	0.5-0.65	98%	98%	96%

Prediction Accuracy of Kalman filter using a linear movement model

A conventional Kalman filter was used to predict the movement patterns. The predictor used a linear model for the movement pattern. The results of the Kalman filter prediction for a prediction horizon of 200 ms (corresponding to 10 samples) compared with the actual values after normalization are shown in Figure 4-24. It was found that the error pattern generally followed the amplitude of movement. The settling time depends on the initial estimate of marker position and velocity. The results were compared for prediction horizons of 5, 10 and 20 data points over 20 samples. It was found that the RMS error increased with increase in the prediction horizon. The maximum RMS error percentage obtained was 18.8 % for a prediction horizon of 15 samples or 600 millisecond. This can be seen as a consequence of the underlying linear model approximation which tends to be inaccurate for longer prediction horizons. The non-linear model developed in section 3.1 cannot be used with the Kalman filter. Hence the model was used for non-linear formulations such as the EKF and UKF. The results obtained from the KF are compared with the EKF and UKF.

Figure 4-24: Predicted position vs measured position using Kalman filter (KF)

Prediction Accuracy of non-linear models with EKF and UKF

The non-linear model developed in section 3.1 was used as the system model for the EKF and UKF formulation. The predictions using EKF and UKF are compared with actual organ position as shown in Figure 4-25 and Figure 4-26. The prediction of the EKF and UKF did not deviate from the actual position by more than 4.4 mm while using the non-linear model. The error patterns (indicated by the green line) indicated that the average and maximum error was lesser in case of the UKF when compared to the EKF. However, both the filters performed better than the KF for all data sets and prediction horizons.

Figure 4-25: Predicted position vs measured position using EKF

Figure 4-26: Predicted position vs measured position using UKF

The linear model and the non-linear shape function based model were used as inputs to the UKF. The results are compared in Figure 4-27. It can be seen that the non-linear shape function based model (green line) was able to predict the pattern more accurately as compared to linear models (blue line). The actual position of the kidney measured from the ultrasound image is indicated using the red line.

Figure 4-27: Actual and predicted values of linear model and non-linear shape function based model

Prediction Accuracy of non-linear models with ANFIS

The next approach to predict the movement was by using ANFIS. For this, the data was divided into training and testing sets. A portion of the samples was also assigned as a checking set which prevents over fitting of data while training. The training data comprises of tuples or samples from the signal history S . A tuple of order k in the training set can be represented as:

$$[s(n-k*p), s(n-(k-1)*p), \dots, s(n-p), s(n)] ; s \in S$$

where k is the number of sample points and p is the prediction horizon. The data is arranged as an $(n \times k)$ matrix. Similar matrices were obtained for the checking and testing data. It was tested with kidney movement data sets. A sample of predicted and actual data for a prediction horizon of 200 ms is shown in Figure 4-28a. The error pattern is shown in Figure 4-28c. Further, the non-linear model was used as an additional input to ANFIS. The model works as an error envelope over the ANFIS network. This reduces the error for datasets with gross shifts in position. The ANFIS prediction and actual organ positions for a single respiratory cycle over a prediction horizon of 5 samples (or 200 ms) is shown in Figure 4-28b.

Figure 4-28: Movement prediction using ANFIS a) Predicted vs measured position b) Error in prediction c) Error pattern

The variation of the RMS error over 20 samples from the pilot study is shown by a histogram in Figure 4-29. It was observed that the error was high for three data sets which had large shifts between the trained and tested data patterns. These were found to be outliers due to rapid changes in position. The average RMS error for the 20 data sets was 12.45%.

Figure 4-29: Root-mean-square error of samples in the pilot study

Similarly the average RMS error for 84 data sets in the clinical study was found to be less than 7%. The variation in the RMS error is shown by a histogram in Figure 4-30. It was also found that the RMS error of the ANFIS based network did not increase significantly with increase in the prediction horizon for all the data sets.

Figure 4-30: Root-mean-square error of samples in the clinical study

The maximum error in prediction while using the non-linear system model was lower compared to the linear Kalman filter based predictor and model free approach using ANFIS. The combination of ANFIS and the non-linear system model effectively reduced the maximum error to 9.85%. The model free approach was better than the linear KF predictor when the number of samples was more than 1000. The next section discusses the results obtained from the correlation module.

4.4 Correlation Of The Skin Marker Movement With Kidney Movement

The correlation model developed in section 3.2 was tested using the data sets collected from the pilot study (20 samples) as well as the clinical data (84 samples). The parameter C_1 , C_2 and C_3 were tuned for individual subjects based on their BMI. Generally, the error was within 10% of the measured value after 400 samples. This technique updates the model over a smaller time

interval k as opposed to the conventional linear model which is updated once in every respiratory cycle. The tuned values are given in Table 4-11.

Table 4-11: Tuned values for corelation module

Movement Pattern	C1	C2	C3	Pilot Study	Clinical Study (Normal)	Clinical Study (Affected)
Right Kidney	1.3-1.6	0.6-0.85	0.2-0.35	96.6	94.4	86.6
Left Kidney	1.3-1.6	0.75-0.95	0.2-0.35	94.8	93.5	84.5

The error in prediction increased when the parameter k was varied from 10 – 25 samples. A predicted movement pattern with measured values is shown in Figure 4-16. The maximum error obtained was 9.8% for a prediction horizon of 25 samples, which corresponds to 1000 ms. The accuracy of the model in comparison with the conventional linear model is shown in

Figure 4-31. The error in the prediction showed a clear pattern with maximum error corresponding to the maximum non-linearity. These variations were effectively accommodated while fine tuning the ANFIS network.

Figure 4-31: Modeled movement pattern vs measured value

ANFIS was used to refine the correlation model. The data was divided into training, checking and testing sets which were arranged into tuples of the form:

$$\begin{array}{lll} [p(1) & p'(1) & z(1)] \\ [p(2) & p'(2) & z(2)] \\ \dots & \dots & \dots \\ [p(n) & p'(n) & z(n)] \end{array}$$

where p indicates the predicted position from the model and z indicates the measured organ position. The checking data was meant to prevent over-fitting and was limited to 10% of the samples. The optimal training set size was determined from the experiment. The approximate relation between the sample size and the training error is shown in Figure 4-32. The optimal value of sample size was found to be 1200 samples.

Figure 4-32: Relation between sample size and error

Another factor that had a significant effect on the accuracy of the prediction was the type of membership function. The most commonly used membership functions such as the bell, gaussian, trapezoidal and triangular were tested. The error was lowest in case of the triangular MF for all sets of data. Although ANFIS has provisions to use a different membership function for the input and output layers, in practice it was found that the accuracy was reduced while using dissimilar functions. The accuracy of various membership functions is summarized in Figure 4-33.

Figure 4-33: Relation between type of membership function and error

The input variables considered for the system were the correlated position $p(t)$, instantaneous organ velocity $p'(t)$, marker position $s(t)$, marker velocity $s'(t)$ and the measured position $z(t - T)$ where T is the average respiratory time period. From the experiment, it was found that the model gave lowest error for the two input network comprising of $p(t)$ and $p'(t)$. The optimal parameters for ANFIS used for this problem are summarized in Table 4-12.

Table 4-12: ANFIS parameters used for training

Parameter	Value
Membership function Type	Triangular
Number of Membership functions	16
Number of nodes	294
Number of training data pairs	820
Number of checking data pairs	100
Number of fuzzy rules	128

The maximum error in the ANFIS tuned model was observed to be 7.2 % for a prediction horizon of 400 ms. Figure 4-34a and Figure 4-34b compare the accuracies of the ANFIS tuned correlation model, correlation model, ANFIS correlator and linear correlator. In both data sets the error increased marginally for larger prediction horizons, as shown in Figure 4-34. The maximum error from the ANFIS tuned model was 7% for data collected from the pilot study and 9.8 % for the data collected from the clinical study. These were lower than the corresponding errors of 12% and 10% from the linear model. This approach was also better than using ANFIS directly to correlate organ positions.

Figure 4-34: Comparison of mean error for various prediction horizons (a) Pilot study (b) Clinical study

The marker correlation model was integrated with a prediction model developed in section 3.1. The variations in error percentage for various prediction horizons are summarized in Table 4-13. The combined accuracy of the ANFIS tuned model with an ANFIS predictor was less than 11.40%, while the accuracy with a UKF based predictor was 11.20% for prediction intervals of 400 ms. However, ANFIS requires a minimum of 1000 training samples in order to provide accurate predictions.

Table 4-13: Accuracy of organ position prediction in percentage using the ANFIS tuned correlation model

Prediction Horizon (Milliseconds)	Pilot Study (20 Subjects)			Clinical study (37 Normal subjects)			Clinical study (48 Affected subjects)		
	Model + ANFIS	Model + KF	Model + UKF	Model + ANFIS	Model + KF	Model + UKF	Model + ANFIS	Model + KF	Model + UKF
400	10.24	11.46	10.28	11.22	12.4	13.2	13.6	14.4	14.5
600	13.46	15.60	13.86	12.88	13.46	14.60	15.32	15.9	16.4
800	15.60	17.80	16.38	14.4	16.2	17.3	15.8	18.8	18.2
1000	16.24	18.46	17.30	16.1	17.1	18.2	18.3	19.4	20.5

The combined average accuracies of the model when used with ANFIS,KF and UKF for the three data sets in compared in Figure 4-35. The combined accuracy of the model and ANFIS was greatest followed by UKF for all datasets. Out of the three data sets highest accuracy was obtained for movement patterns obtained from the clinical study in normal subjects. The accuracy was reduced by approximately 5.4% for affected subjects. The results from the pilot study was less accurate compared to the clinical study in normal subjects. However the accuracies were more than that in affected subjects.

Figure 4-35: Average error of combined prediction and correlation

Real-time applicability

To study the real-time applicability of the system, tests were conducted on a 2.26GHz Core 2 Duo processor with the process running at maximum priority. The processing time and segmentation time is shown in Figure 4-36. The delay in segmentation and actuation contributes to the total system latency. The latencies of image tracking, marker correlation and prediction were 100 ms, 40-60 ms and 100-120 ms respectively. These values could be further reduced by using systems with higher computing power, as this would reduce the system latency. However, these tests prove the feasibility of the model in real-time applications.

Figure 4-36: Latencies for various prediction horizons in milliseconds

4.5 Summary

In this chapter, some of the results obtained for measurement and modeling of kidney movement were discussed. An experimental set-up to simultaneously capture the kidney movement and the respiratory movement was discussed. The data collected was divided into kidney movement pattern and skin marker movement patterns which were tracked separately. The kidney movement comprised of in-plane and out-of-plane movement which were quantified using template matching and speckle de-correlation based techniques respectively. The movement patterns were further analyzed to understand the effect of pathologies such as calcified cysts, Angiomyolipoma and RCC. The extent of movement of both kidneys were affected by the presence of pathologies larger than 10 mm.

The movement patterns were then modeled using a two step approach comprising of prediction and correlation. The prediction module was tuned for specific kidney movement patterns as well as respiratory data. This was used as the basis for non-linear predictors such as UKF, EKF and ANFIS. These methods gave an average accuracy of 92% with a maximum error of 2.8 mm. This was more accurate when compared to the conventional linear predictors which gave an accuracy of 85% and a maximum error of 4.2 mm. The next part of modeling comprised of correlation. Here, a new mapping function was used to estimate the organ position from the skin marker position. The mapping gave 94% accuracy when fine tuned using ANFIS. This was better than the conventional linear correlator. Finally, the real-time applicability of this technique in noninvasive surgery was studied. It was concluded that the technique provides sufficient accuracy for surgical planning for systems with latency less than 1000 ms. A surgical protocol and validation set-up for these models, along with an appropriate HIFU applicator, shall be presented in the next chapter.

CHAPTER 5 : REAL-TIME MOVEMENT COMPENSATION - METHODOLOGY

In this chapter, a movement adaptive surgical protocol that uses the movement model is proposed. A real-time compensation strategy is developed based on the reference trajectory provided from the model. The compensation strategy deals with three main aspects. Firstly, there must be a means to update the pre-operative plan using real-time images. Secondly, an appropriate controller must be derived for this system and thirdly, an applicator design suitable for kidney ablation must be chosen from acoustic field simulation.

The overview of this chapter is as follows. Section 5.1 describes a surgical protocol which can be implemented on a robotic FUS system. Individual modules of the proposed robotic system are discussed in subsequent sections. Section 5.2 describes an image registration based technique to update the pre-operative plan. Section 5.3 derives a controller strategy that can be used for this system. Finally, in section 5.4, a HIFU applicator suitable for kidney ablation is modeled.

5.1 Proposed Surgical Protocol For FUS

The most crucial issue that has to be addressed in robotic FUS is to ensure synchronous movement of the applicator with target. In this work, a motion adaptive protocol is proposed as applicable to an image guided surgical robot. The surgical procedure is divided into three phases- the pre-operative planning, synchronization and treatment as shown in Figure 5-1. Pre-operative planning can be done a few days prior to operation. The first step in pre-operative planning is identifying a set of target points for ablation. The points are distributed such that they cover the entire tumor. The patient-specific prediction and correlation modules are trained during this phase using ultrasound sequences and respiratory movements captured in the surgical position. This is followed by the synchronization phase, just prior to the surgery. During synchronization, the FUS robot traces a reference trajectory estimated from the movement prediction and correlation modules. The process continues with the HIFU applicator turned off, until the movements of the end effector and target are synchronized. The model is updated every time the

error goes beyond the predefined error threshold ϵ_T . The HIFU ablation at the first target point starts after the synchronization time t_s . During exposure, the real-time ultrasound feedback is lost, so the robot follows the moving target based on the respiratory signal. The exposure time t_e is usually 2-3 seconds for the kidney. Deformation in the target tissue, caused due to FUS, can be captured in the ultrasound scans after the exposure. This information is used to update the pre-operative plan and move the applicator to the next treatment point. Now, the system re-enters the synchronization phase to ensure proper tracking of the target. This allows the tissue to cool down to normal temperature, thereby avoiding cavitation effects. Once the applicator movement is synchronized within the error threshold, the next treatment site is ablated.

Figure 5-1: Proposed surgical protocol

A block diagram of a FUS system that can implement this protocol is shown in Figure 5-2. The main modules in this system are the movement prediction model, the image registration module, the controller and the HIFU applicator. The inputs to the system comprise of the real-time ultrasound images and stereo images of external skin marker movement. The movement prediction model consists of prediction and correlation modules. These are trained separately during the pre-operative planning phase and fine-tuned during the synchronization phase. The correlator module uses skin marker positions to estimate the position of the kidney. This ensures that the model captures the breathing pattern of the subject. The prediction module then extrapolates the estimated position over a prediction horizon. This step compensates for the total system latency comprising of robotic actuation latency and imaging latency. The output of the prediction module forms one of the inputs of the controller. The second input of the controller is

obtained from the pre-operative plan. During surgery the pre-operative plan is updated using the intraoperative ultrasound image. The image registration module registers the intraoperative image to the pre-operative ultrasound image.

Figure 5-2: Schematic representation of proposed HIFU surgery system for movement compensation

The registered US image along with output of movement model enables the controller to maintain a constant distance between the HIFU applicator and tumor target. In this project, a multiple probe design is proposed for the applicator to minimize healthy tissue damage [33, 37]. The methodology for the proposed FUS system comprises of the following three tasks – updating the pre-operative plan using image registration, deriving a movement adaptive control strategy based on the movement model and adopting an optimal HIFU applicator design for kidney tumor ablation.

5.2 Pre-operative Plan Update

The initial step in executing the surgical protocol is to update the pre-operative plan based real-time images. This can be done by image registration. The objective of image registration is to find the optimal transformation that maps points on the real-time image to the corresponding

points on the pre-operative image. The transformation in most cases involves both rigid and non rigid components. In this application, two ultrasound image frames, taken at different points of time, have to be registered based on selected features.

The Weighted Geometrical Feature (WGF) approach [29] was adapted to register the images. The pre-operative image of the kidney, P , is considered as the model image while the real-time image, R , is considered to be the data. The algorithm finds the optimal transformation $T(R)$ which maps the data feature set $\{R_i\}$ to a model feature set $\{P_i\}$. A kidney image offers features such as the renal apex, the gross organ boundary and boundary of the tumor which can be used as the basis of registration. The selected features on the data and model can be represented as point sets $\{r_{ij}\}$ and $\{p_{ij}\}$ respectively. The optimal transformation T is determined by iteratively minimizing a distance based cost function written as:

$$d(T) = \sqrt{\sum_{i=1}^{N_s} \sum_{j=1}^{N_p} w_{ij} \|y_{ij} - T(p_{ij})\|^2} \quad 5.1$$

where

$$y_{ij} = C_i[T(p_{ij}), X_i] \quad 5.2$$

The function C is defined as the closest point operator which finds the point y_{ij} closest to the point $T(p_{ij})$. N_p is the number of points in the data set p and N_r is the number of points in the data set r . The iterations are initialized by setting $k=1$ and assuming an initial transformation T_0 .

Iteration comprises of the following steps:

- i. For each shape P_i , compute the closest points $y_{ijk} = C_i(T(p_{ijk}), X_i)$
- ii. Compute the transformation T_k between the points $\{p_{ij0}\}$ and $\{y_{ijk}\}$ using the weights w_{ij}
- iii. Apply the transformation to produce the points $p_{ij,(k+1)} = T_k(p_{ij0})$
- iv. Calculate the change in the transformation $d(T_k) - d(T_{k-1})$

The iteration is terminated when the change is lesser than the tolerance τ . It can be proved that the WGF algorithm monotonically converges to a minimum [81]. The final transformation matrix T will be of the form:

$$T(R) = Rot(R) + Tr \quad 5.3$$

Where Rot is the rotational matrix and Tr is the translation of the kidney. The updated pre-operative plan is used along with the movement model as an input to the control strategy.

5.3 Movement Adaptive Control Strategy

The movement control strategy for this system must be able to effectively coordinate two kinds of movements. Firstly, the applicator must be moved according to the pre-operative plan to cover all potential treatment sites. Secondly, the applicator movement must be synchronized with the respiration induced movement of the organ. Apart from this, the controller must be resilient to common kinds of noise that are encountered in the surgical room. These include the noise from movement of the treatment Table, changes in patient position and noise due to errors in image based tracking. According to the treatment protocol, the pre-operative plan is executed prior to the treatment phase while the synchronized motion is executed during the synchronization and treatment phases. This makes it possible to use separate control strategies for the two motions. Hence a hybrid control strategy is proposed comprising of a PID controller to execute the pre-operative plan and a model predictive controller (MPC) that can control the synchronous motion. The proposed control strategy is shown in Figure 5-3.

Figure 5-3: Proposed movement compensation scheme

Movement according to pre-operative plan using PID controller

The movement reference signal for the PID controller is directly obtained from the pre-operative plan as shown in Figure 5-4. The three linear gains K_P , K_I and K_D are tuned based on the system load. The proportional gain is used to model the system stiffness, while the derivative gain K_D determines the system response time and stability. The integral gain K_I reduces the steady state error of the system. The error signal is generated based on the feedback from the stereo vision system.

Figure 5-4: PID controller for executing the pre-operative plan

Synchronous movement control using MPC controller

The MPC controller is suited for systems with periodic disturbance. In this application, the respiration induced movement can be effectively modeled as a periodic disturbance. This makes the MPC controller highly suitable for this application. MPC requires three components - a

reference signal, a system model and a cost function. The reference signal is the output obtained from the prediction-correlation module. From the control perspective, the system can be modeled as an ARIMAX system as defined by equation:

$$A(q^{-1})y(t) = B(q^{-1})u(t-1) + \frac{C(q^{-1})}{\Delta(q^{-1})}\xi \quad 5.4$$

The matrices A and B model the system dynamics. The operator q^{-1} is the backward operator which is modified as:

$$\Delta(q^{-1}) = \delta(q^{-1})\Delta_R(q^{-1}) \quad 5.5$$

$$\Delta_R(q^{-1}) = 1 - \alpha q^{-T} \quad 5.6$$

This modification is suited for systems which have periodic disturbance such as in this case. This makes the perturbation model $\frac{C(q^{-1})}{\Delta(q^{-1})}\xi$ periodic with a time period T . The variable α assigns a higher weight to more recent measurements and hence can be seen as a forgetting factor. The output y can be separated into two components as:

$$y(t) = y_{th}(t) + \epsilon(t) \quad 5.7$$

$$Ay_{th}(t) = Bu_1(t-1) \quad 5.8$$

$$A\epsilon(t) = Bu_2(t-1) + \frac{C}{\Delta}\xi(t) \quad 5.9$$

$$u(t) = u_1(t) + u_2(t) \quad 5.10$$

The cost function for this application must minimize the error with respect to the reference trajectory r . From equations 5.7 and 5.8 the cost function for the MPC can be derived as:

$$\begin{aligned} \Psi(u,k) = & \sum_{j=N_1}^{N_2} \|\hat{y}(k+j) - r(k+j)\|^2 + \sum_{j=N_1}^{N_2} \|\hat{\epsilon}(k+j)\|^2 + \lambda \sum_{j=N_1}^{N_3} \|\delta u_1(k+j-1)\|^2 + \\ & \mu \sum_{j=N_1}^{N_3} \|\delta u_2(k+j-1)\|^2 \end{aligned} \quad 5.11$$

where N_1 and N_2 are the upper and lower bounds of the cost horizon, while N_3 is the control cost horizon. The terms λ and μ are used as weighting factors. The increment in u is calculated for the control horizon over N_3 samples. A block diagram of the MPC controller consisting of the ultrasound image based feedback loop is shown in Figure 5-5. The control system uses a generalized predictive control algorithm (GPC) to calculate the optimal system input U over unit prediction horizon. The output of the controller is delayed by a delay unit which is indicated by Z^{-1} . The robotic system is denoted by G_R . The error signal for the GPC is calculated as the difference between the system output Y and target point Q predicted from the movement model.

Figure 5-5: MPC controller block diagram

The movement control strategy described in this section aims to orientate a HIFU applicator. In order to establish the feasibility of the concept a HIFU applicator was modeled.

5.4 Modeling The HIFU Applicator Profile

The HIFU applicators can be modeled using direct techniques as shown by O'Neil [100]. An approach similar to that of O'Neil is used in this work for simulation of the acoustic profile from a single focused transducer. Most direct simulation approaches of the ultrasound field can be traced back to the Rayleigh integral [100]. The Rayleigh integral is a special case of the more general Poisson integral which is a steady state solution of the pressure wave equation. It assumes the following boundary conditions:

- i. $-\nabla p = 0$ at the surface of the transducer
- ii. $p = 0$ at a distance $r = \infty$

The Rayleigh integral based model proposed by O'Neil [100] is widely adopted and extended for acoustic field simulation. The schematic representation of this model is shown in Figure 5-6a and Figure 5-6b .

Figure 5-6: Geometric explanation of model – O'Neill *et al* [100]

The terms used in the model are explained below:

A -Focal length of the focal bowl

S - Curved surface of the focal bowl

α - Half angle of the focused transducer

s - Euclidian distance from the surface to the point Q

h - Depth of the focal bowl

φ - Angular coordinate of a point on the surface, perpendicular to the plane

φ_1 - Angular coordinate of a field point, perpendicular to the plane

R - Radial distance to a point Q in the acoustic field

R_1 - Radial distance of a point on the surface of the probe

The velocity potential $\psi(R, \theta)$ at a distance R from the origin and at an angle θ can be represented as equation 5.4.1. Velocity potential does not have a direct physical interpretation; the negative gradient of the velocity potential is the particle velocity $u(r, t)$. The term b is the distance from the center of the transducer to any point on the circumference. R_1 is a vector pointing in the direction of b . The surface element for integration $dS = R_1 dR_1 d\beta$ where β is defined such that $\beta = \phi_1 - \phi$. The Euclidian distance from a point Q_1 on the surface to a field point is written as:

$$\psi(R, \theta) = \frac{u}{2\pi} \int_0^{2\pi} \int_0^b s^{-1} e^{-iks} R_1 dR_1 d\beta \quad 5.12$$

$$s = \sqrt{[(x - x_1)^2 + (r \cos \phi - r_1 \cos \phi_1)^2 + (r \sin \phi - r_1 \sin \phi_1)^2]} \quad 5.13$$

The distances in 5.13 can be written in terms of R_1 and β as in equation 5.14. The term q is defined in equation 5.15. The distance r_1 can be written in terms of R_1 as in equation 5.16.

$$s = \sqrt{(R^2 - 2Rr_1 \sin \theta \cos \beta + qR_1^2)} \quad 5.14$$

$$q = 1 - x/A = 1 - 2hx/b^2 \quad 5.15$$

$$r_1 = R_1 \sin \theta_1 = R_1 \sqrt{(1 - R_1^2/4A^2)} \quad 5.16$$

In this model it is assumed that the depth and wavelength must be small compared to aperture. A similar model is also presented by Kino *et al* [91]. In this model the Rayleigh integral for planar sources is modified to accommodate for a slightly curved surface. The curvature of the focused transducer can be accounted as a phase delay in the beam emitted from various points on the surface.

Figure 5-7: Geometric explanation of model – Kino *et al* [91]

In order to find out the acoustic velocity potential at any point $\Phi(r, z)$, the contributions from all the Hygen sources across the surface of the transducer have to be considered. To find out the contribution of the beam emitted from a point r', z_1, ψ' , the distance from this point to any point in the domain i.e. R_1 needs to be calculated. The corresponding phase delay of this component can be represented as $\exp(-jkR_1)$. The radial displacement at the transducer is represented as $u_0(\theta)$. Hence, the displacement in the z direction in the plane of the baffle is given by equation 5.17.

$$u_z(\theta) = u_0(\theta) \cos \theta \left(\frac{z_0}{z_0 - R_1} \right) \quad 5.17$$

From Figure 5-7 it can be seen that:

$$(z_0 - R_1) = \left(\frac{z_0 - R_1}{\cos \theta} \right) \quad 5.18$$

The aperture angle of the transducer can be related to the distance as:

$$z_0 - z_1 = z_0 \cos \theta_0 \quad 5.19$$

From equations 5.17-5.19 $u_z(\theta)$ can be determined as

$$u_z(\theta) = u_0(\theta) \frac{\cos^2 \theta}{\cos \theta_0} \quad 5.20$$

The expression for the velocity potential at a point $\Phi(r, z, 0)$, in the axial plane of the transducer can now be formulated. This formulation is a Poisson solution of the partial differential equation (PDE) for pressure/potential. Due to the axial symmetry of the source this can be extended to other planes in the field. The potential at a point $(r, z, 0)$ is given by the equation 5.21

$$\Phi(r, \theta, 0) \approx -\frac{u_0}{2\pi} \int \int \frac{e^{(-jk(R+R_1))} \cos^2 \theta}{R \cos \theta_0} r' dr' d\psi' \quad 5.21$$

$$R = \sqrt{r'^2 + r^2 - 2rr' \cos \psi' + (z - z_1)^2} \quad 5.22$$

Using the paraxial or Fresnel approximation which is valid when the aperture of the transducer is large compared to the wavelength of ultrasound, the distance R_1 can be approximated as:

$$R_1 \approx z_1 - r'^2 / 2z_0 \quad 5.23$$

$$R_1 + R = z + \frac{r'^2 + r^2 - 2rr' \cos \psi'}{2z} - \frac{r'^2}{2z_0} \quad 5.24$$

Upon using the Fresnel approximation the angles can be approximated as

$$\cos^2 \theta \approx 1$$

$$\cos \theta_0 \approx 1$$

The final expression for the potential variation in the field is obtained by substituting these values in equation 5.25. This can be further simplified upon integration with respect to ψ , which gives rise to a Bessel function in the solution as given by equation 5.26

$$\Psi(r, z) = -e^{-jk(z+r^2/2z)} \frac{u_0}{2\pi z} \int_0^a \int_0^{2\pi} e^{-(jkr'^2/2)(1/z-1/z_0)} e^{(jkr'r'/z) \cos \psi'} r' dr' d\psi' \quad 5.25$$

$$\Psi(r, z) = -e^{-jk(z+r^2/2z)} \frac{u_0}{2\pi z} \int_0^a J_0\left(\frac{kr'r'}{z}\right) e^{-(jkr'^2/2)(1/z-1/z_0)} r' dr' \quad 5.26$$

The velocity potential ψ given by both models is related to the pressure by equation 5.27, where ω is the angular velocity of the acoustic wave, k is the wave number and ρ is the density of the medium.

$$P(r, z) = i\omega\rho\psi(r, z) \quad 5.27$$

The integrals in 5.4.1 and 5.4.1 are solved numerically using recursive adaptive Simpson quadrature [101]. Simpson's rule or Simpson quadrature is a Newton-Cotes formula for approximating the integral of a function 'f' using quadratic polynomials [101]. It uses parabolic arcs for the approximation. Simpson's rule is derived by integrating a third-order Lagrange interpolating polynomial fit to the function at three equally spaced points. Since it uses quadratic polynomials to approximate functions, Simpson's rule can give exact results till cubic degree [101]. According to composite Simpson's quadrature, as expressed in equation 5.4.7, any function to be integrated over the interval a to b can be numerically approximated as a weighted sum of its values over n subintervals. Using 5.28, the pressure was calculated with subinterval duration of 0.2.

$$\int_a^b f(x)dx \approx \frac{h}{3} \left[f(x_0) + 2 \sum_{j=1}^{n/2-1} f(x_{2j}) + 4 \sum_{j=1}^{n/2} f(x_{2j-1}) + f(x_n) \right] \quad 5.28$$

The original model was modified for modeling the acoustic profile during renal tumor ablation. For this, the acoustic path was divided into intermediate layers of skin, abdominal muscle and kidney with water coupling. The attenuation coefficients for media α_{water} , α_{skin} , α_{muscle} and α_{kidney} were incorporated into the calculation of velocity potential given by equation 5.12. The distance from the transducer to the skin, abdominal muscle and kidney are represented as d_{skin} , d_{muscle} and d_{kidney} . This gives rise to equations 5.29 - 5.31.

For $R_1 \leq d_{\text{skin}}$:

$$\Psi(R, \theta) = \frac{u}{2\pi} \int_0^{2\pi} \int_0^b s^{-1} e^{-(ik + \alpha_{\text{water}})s} R_1 dR_1 d\beta \quad 5.29$$

For $d_{\text{skin}} < R_1 < d_{\text{muscle}}$:

$$\Psi(R, \theta) = \frac{u}{2\pi} \int_0^{2\pi} \int_0^b s^{-1} e^{-i\alpha_{\text{water}} d_{\text{skin}}} e^{-i\alpha_{\text{skin}}(s-d_{\text{skin}})} R_1 dR_1 d\beta \quad 5.30$$

For $d_{\text{muscle}} < R_1 < d_{\text{kidney}}$:

$$\Psi(R, \theta) = \frac{u}{2\pi} \int_0^{2\pi} \int_0^b s^{-1} e^{-i\alpha_{\text{water}} d_{\text{skin}}} e^{-i\alpha_{\text{skin}}(d_{\text{muscle}}-d_{\text{skin}})} e^{-i\alpha_{\text{skin}}(s-d_{\text{muscle}})} R_1 dR_1 d\beta \quad 5.31$$

The model assumes water to be a lossless medium. The change in focal length due to refraction of the layers was not modeled in this simulation. The single probe simulation was then extended for multiple probe simulation using bicubic interpolation. The position vector $[i, j]$ is rotated as shown in equation 5.32 to obtain the transformed coordinates $[i_R, j_R]$. A_{rot} is a rotational matrix defined in equation 5.33 for an angle of inclination φ degrees. The point (i_R, j_R) need not necessarily fall on any of the grid points corresponding to the acoustic field. In such a scenario the velocity potential $\psi(i_R, j_R)$ can be calculated using bi-cubic interpolation as given in equation 5.34. The terms $\psi(i, j)$ indicate the velocity potential at the surrounding grid points. The effective velocity potential $\psi'(i_R, j_R)$ is calculated as the vector sum of the individual velocity potentials ψ_k (i_R, j_R) in equation 5.35, where k denotes the number of the probes.

$$[i_R, j_R] = A_{\text{rot}} \times [i, j] \quad 5.32$$

$$A_{\text{rot}} = \begin{bmatrix} \cos \varphi & \sin \varphi \\ -\sin \varphi & \cos \varphi \end{bmatrix} \quad 5.33$$

$$\psi(i_R, j_R) = \sum_{i=0}^3 \sum_{j=0}^3 a_{ij} \psi(i, j) \quad 5.34$$

$$\psi'(i_R, j_R) = \sum_{k=1}^3 \psi_k(i_R, j_R) \quad 5.35$$

5.4 Summary

This chapter describes image guided surgical protocol as applicable to real-time robotic FUS. The three components involved in a movement adaptive system, namely, image registration,

trajectory control and applicator modeling were discussed in individual subsections. The real-time images were registered to the pre-operative image using a WGF based algorithm. The updated treatment plan, along with the movement model, forms the input to a hybrid controller. The proposed hybrid control scheme comprises of two independent controllers. Firstly, a PID controller to execute the treatment plan and secondly, an MPC controller that provides movement synchronization with the organ. Finally, a multiple probe HIFU applicator was modeled to study its feasibility for kidney tumor ablation. The experimental set-up for testing the methodology along with the initial results obtained are discussed in chapter 6.

CHAPTER 6 : REAL-TIME MOVEMENT COMPENSATION– EXPERIMENTAL TESTBED, RESULTS AND DISCUSSION

This chapter discusses an experimental testbed designed to test and validate the image guided robotic control proposed in chapter 5. The image registration technique was tested on kidney images obtained from volunteers. The movement patterns similar to the kidney movement were generated using a mechatronic jig. A robotic arm was used to implement the control strategy discussed in section 5.3. The HIFU applicator model described in section 5.2 was validated using a separate experimental set-up.

The overview of this chapter is as follows. Section 6.1 describes the experimental testbed to validate the movement adaptive protocol. Section 6.2 discusses the results obtained for ex-vivo kidney movement replication and movement compensation. Section 6.3 describes the experimental set-up used to validate the HIFU applicator field simulation model. Section 6.4 discusses the results obtained from HIFU modeling.

6.1 Laboratory Testbed To Validate The Movement Compensation Scheme

The testbed consists of three components - movement replicating jig, a robotic arm and a real-time imaging system. The movement jig is designed to generate movement patterns similar to the kidney. The movements are tracked using an ultrasound imaging probe mounted on the jig. The operation of the jig is explained in section 6.1.1. The movement control strategy is validated using a detached limb of the kidney tumor ablation robot FUSBOT-US. The simulation and inverse kinematic modeling of the robotic arm and the movement jig is described in section 6.1.2 along with the results obtained from image registration. A picture of the laboratory testbed is as shown in Figure 6-1.

6.1.1 Operation of the movement replicating jig

The operation of the mechatronic jig can be divided into three phases. The first phase corresponds to pre-operative planning, where a three dimensional model of the organ is created, the second phase is real-time replication of the kidney movement tracked under ultrasound and the third phase is validation of the real-time movement compensation scheme. The three phases are discussed in more detail below:

i) Pre-operative modeling

The objective of this phase is to capture a series of images of a gel based phantom made of agar-agar. The phantom is prepared by mixing 300 mg of gel to 500 ml of boiling water and allowing the mixture to set at room temperature. The acoustic properties of the gel are similar to human tissue. The images captured in this phase are used to render three-dimensional images of the target. Hence, the phantom is kept stationary during imaging.

Longitudinal slices of the gel phantom are captured for every 3 mm along the shorter dimension of the phantom by moving the probe. Increasing the resolution beyond 3 mm limit produces overlapping redundant images. The thickness of the kidney is approximately 30 mm [38, 39]. Hence a maximum of 10 scans can be captured in this dimension. A three dimensional image reconstructed from these slices is considered as the template/target image for image registration. Transverse slices are also obtained by moving the probe along the longer dimension of the kidney.

Figure 6-2: Mechatronic test jig

ii) *Real-time tracking of the kidney phantom movement*

The second phase of operation recreates the movement of the kidney using the anthropomorphic phantom. The phantom is moved using the motorized stage in all three dimensions according to organ movement trajectories obtained from the movement study. In this phase the diagnostic probe remains stationary. The images procured are used as the source images for image registration. The images of the moving phantom are also procured in the transverse plane by placing the imaging probe in different positions along the longer axis of the kidney. The maximum displacement from the mean position was assumed to be 40 mm [28]. This was used to derive the maximum velocity that may be necessary for the sliders. The detailed design of the mechatronic jig is explained in APPENDIX A.

iii) *Validation of the real-time movement compensation technique*

The third phase of operation replicates the *synchronization phase* in the surgical protocol. In this phase, kidney movement patterns are replicated using the mechatronic jig while the image robotic arm is controlled by the hybrid controller. The mechatronic jig moves a phantom in all three dimensions based on the kidney movement pattern gathered from subjects during the

ultrasound based study mentioned in Chapter 4. The schematic diagram of the PC based control of the mechatronic jig using a motor controller card is shown in Figure 6-2. The mechatronic jig is connected to three interfaces - the image grabber card, motor controller and the software. The image grabber card streams real-time images from the ultrasound system and the motor controller generates control signals for to the stepper motors. Both these modules are initialized and triggered using the software - Mechatronic Jig V2 developed in-house.

Figure 6-3: Schematic diagram of the mechatronic jig using PC based control

The software was developed using the MFC (Microsoft foundation classes) frame work. The MFC classes communicate with the Matrox 9.0 image grabber card using the MIL 9.0 API. The movement of the motor is controlled using the USB based motor controller card. Control signals are issued from the MFC classes to the motor controller using a virtual serial port. The multilayered command flow diagram of the mechatronic jig is shown in Figure 6-3.

Figure 6-4: Command flow diagram of mechatronic jig software

A screen shot of the Graphic User Interface (GUI) is shown in Figure 6-4. The GUI has options to choose the phase of operation. Manual intervention is necessary for the system in phase 1. After scanning along the longer dimension, the software prompts the user to turn the imaging probe by 90^0 in order to capture images along the shorter dimension. The GUI also provides provision for independent control of the motors. In the second phase, movement of the phantom is based on a predefined pattern read from a text file. Simultaneous movement in the x, y and z dimensions is achieved by multithreading in the software. The image grabbing thread is separated from the motor controller thread in order to minimize latencies.

Figure 6-5: Software to control the mechatronic jig - GUI

6.1.2 Results of movement compensation and control

The first step in movement compensation was to register the pre-operative images to the intraoperative /real-time images using the WGF algorithm. After this, the movement of the kidney was replicated on the jig can, tracked using the robotic arm. The results obtained from these stages are described in this section:

Image registration

The WGF based image registration algorithm was tested on pairs of kidney images acquired during the survey. The images chosen were different frames of the same image sequence as shown in Figure 6-5. The first image, i.e., frame 1, was considered to be the *model* image and the subsequent frame was considered the *data* image. The entire boundary of the organ was considered to be a single feature for registration as shown in Figure 6-5. The contours can be represented as point sets P and R corresponding to the model and the data image. The number points in the model and data point sets were equalized using bi-cubic interpolation. The images registered using this algorithm had an overlapping area of at least 93.40%. Further, the processing time of the algorithm was found to be less than 2 seconds. The clinically accepted time delay for image registration is 40 seconds. These results gave sufficient confidence to use the algorithm in real-time ultrasound tracking of the kidney. After the robot is registered to the current position of the kidney, the movement replication and control was tested.

Figure 6-6: Pre-operative and real-time ultrasound images

Kidney movement replication, real-time compensation and control

The mechanical model of the jig was simulated in Matlab Simulink as shown in Figure 6-6. The three motors in the jig were modeled using the commonly used second order approximation. The three links were simulated body elements. The positions of the body elements were obtained using body sensors. The positions of the three prismatic joints were obtained using joint sensors. Further, the unit impulse response of the system was simulated. From the impulse response, it was seen that the system is expected to give a stable response.

Next, the accuracy of the jig was tested for various movements along the three axes. Individual axes gave a maximum error of less than 0.45 mm for independent execution, while the accuracy was 0.80 mm during parallel execution.

Figure 6-7: Simulation of the movement replicating jig

The movement pattern of the kidney was recreated on the jig. During the experiment, a 4 axis *Galil* controller was used to control the movement. The movement of the jig was tracked using a Bumble-bee stereo camera system. The resolution of the stereo camera system was 1.4 pixels/mm. The movement patterns extracted from the camera image sequences were compared with corresponding kidney movement patterns. The jig was able to recreate the movement pattern with an error not exceeding 1.4 mm (corresponding to 3.6%) for all the normalized movement sequences. The error in movement replication for various patterns is tabulated in Table 6-1.

Table 6-1: Average error for movement replication for various movement patterns

Category	Movement pattern			
	Coached respiration		Natural respiration	
	Right kidney	Left kidney	Right kidney	Left kidney
Category A	0.48 mm	0.44 mm	0.86 mm	0.92 mm
Category B	0.66 mm	0.58 mm	0.73 mm	0.76 mm
Category C	0.47 mm	0.53 mm	0.79 mm	0.85 mm

Figure 6-8 : Control of FUSBOT-US detached limb a) schematic diagram b) line diagram of detached limb

The movement compensation was validated on single detached limb of FUSBOT-US. Since the other limbs of the robot are identical, results on a single limb can be used to prove the feasibility. A line diagram of the detached limb is shown in Figure 6-7b. The detached limb has 2 degrees of freedom (DOF) and it consists of three links denoted L_1 - L_3 and two joints J_R and J_P . Joint J_R is revolute joint and J_P is a prismatic joint actuated using servo motors. A schematic diagram depicting the PC based control of the detached limb is shown in Figure 6-7a. The movement of the detached limb was controlled using a Galil controller card. The signals from the controller are amplified using bidirectional servo amplifiers before being sent to the servo motors. The position of the motor is fed back to controller using encoders.

Prior to the experiment, the detached limb was modeled using Simulink as shown in Figure 6-8. In the model the three links were modeled as body elements. The positions of the links are obtained using body sensors attached to the respective elements. Actuation was provided using joint actuator modules connected to the prismatic and revolute joints. The positions of joints are obtained using joint sensors. The stability and response time of the system was analyzed using the model. The real-time response of the robotic arm was also estimated.

Figure 6-9: Simulation of the detached limb FUSBOT-US

The inverse kinematic model of the detached limb can be derived from Figure 6-7b using basic geometry. The target position (x,y) can be represented in terms of the angular rotation φ and radial displacement r . The inverse kinematic equations then become:

$$x = (L + r) \cos \varphi \quad 6.1$$

$$y = (L + r) \sin \varphi \quad 6.2$$

The corresponding linear velocities can be directly obtained by differentiating equation 6.1 and 6.2 w.r.t time. Hence, the velocities in the x and y direction would be:

$$x' = -(L + r) \sin \varphi \quad 6.3$$

$$y' = (L + r) \cos \varphi \quad 6.4$$

The detached limb has two inputs, u_1 and u_2 , which are the desired values of radial displacement r and angular rotation φ . The system outputs are x and y displacement of the probe from the target. The system latency was studied using servo vision based tracking. The tracked position of the robot for a series of inputs is shown in Figure 6-9.

Figure 6-10 : Movement of the robotic arm tracked by stereo camera

From the vision based tracking, it was concluded that system latency was approximately 200 milliseconds and the error in position was less than 0.6 mm (corresponds to less than 1%). The next section deals with the results obtained from modeling the acoustic profile of the HIFU applicator.

6.2 Validation Results And Extension Of HIFU Applicator Modeling

Acoustic profile simulations of single probe and multi-probe applicators were done using the Rayleigh integral based simulation model described in section 5.2.3. The accuracy of the model was validated using the pulse echo technique. The experimental set-up for validation is given below:

Experimental Set-up for validation of HIFU profile simulation

Acoustic field measurement can be done using a transmitter-receiver based approach [34, 102]. The schematic representation of this system is given in [24, 102]. The test jig for the experimental set-up was developed by the Bio-Mechatronic research group, NTU. The experimental set-up comprises of a pulser-receiver unit, the transducer under test (TUT) which acts as the transmitter and 1.5 mm transducer which acts as the receiver. The pulser-receiver unit

is used for the excitation of the transmitter. The transducer is pulsed at a rate of 400 Hz which was chosen based on the operating frequency of the probe. The acoustic signal generated by the transmitter is captured using the 1.5 mm transducer. Before excitation of the transducer, the receiver and the source are spatially aligned using conical alignment caps placed over the transducers. The alignment process is done with help of the motorized sliders. The receiver cap is placed such that it touches the tip of the transmitter cap. Afterwards the receiver is moved backward by distance equal to the focal length. Once the receiver is moved to the focus the alignment caps are removed. After the probes are aligned, the receiver is moved in the X, Y and Z axis to produce scans of the profiles in the axial and radial planes. A schematic representation of the experimental set-up is shown in Figure 6-10.

Figure 6-11: Ultrasound profile measurement jig [99]

The signal captured at the receiver is transmitted to the ADC along with a synchronization pulse from the pulser/receiver unit. An intermediate buffer amplifier module is used to amplify the signals. The amplifier circuit also acts as an input buffer for the ADC card. The digitized data is then processed by the acoustic profile measurement software, USoundScan V5.1, which was developed in house in NTU [102]. USoundScan V5.1 is used for processing the received data so as to generate the acoustic profiles in the XY and YZ planes. Since acoustic pressure is converted into a voltage signal at the receiver probe, the image generated by the software is based on voltage values. The software can be used to perform scans in the axial (XY) and radial (XZ) planes. The position and velocity of the three sliders of the measurement jig can be

controlled independently using the software. The scanning resolution can be varied from 1 mm to 0.02 mm.

Results of acoustic profile validation

The validation was performed using a 2 MHz focused transducer of diameter 25.4mm and focal length 80mm, which was available at the Bio-Mechatronics group, NTU. Since the solution of the acoustic pressure wave equation used for simulation is valid for any transducer diameter and frequency, the results can be extended to transducers of other dimensions as well. The testing consists of radial and axial profile scans. To scan the radial profile, the receiver is scanned perpendicular to the longitudinal axis of the probe. The result of the XZ scan (radial profile) was used to calculate the RHM (Radial Half Maximum) of the probe. The radial profile obtained is compared with the results from the simulation of the same probe. The profile was generated for the region -5 mm to +5 mm along the radial dimension, this is shown in Figure 6-11a. The ‘trace mouse’ [102] feature of USoundScan software was used to obtain the values at various points along the radial axis. These values have been plotted in Figure 6-11b.

Figure 6-12: Validation results a) Single probe radial profile b) Radial definition

Figure 6-13: Acoustic profile $R = 80$ mm, $\text{dia} = 25.4$ mm and $f = 2$ MHz a) Radial profile b) Axial profile

Similarly, the axial profile of the transducer was measured by moving the receiver probe in the XY plane. The LHM was calculated from the values obtained using the ‘trace mouse’ feature of USoundScan V5.1. These values can be compared with the axial and radial profiles shown in Figure 6-12a. The axial profile obtained from experimentation (Figure 6-13a) and from simulation (Figure 6-13b) can be compared based on the LHM. The values obtained from the above mentioned scheme are voltage signals. Since voltage corresponds to acoustic pressure, the value at 0.707 times the maximum is used to find the radial and axial half intensity. The results of the validation are given in Table 6-2.

Figure 6-14: a) Axial profile from experiment b) Axial profile from simulation

Table 6-2: Comparison of predicted values and experimental results

Parameter	Predicted Value	Measured Value	Absolute Error	Error Percentage
RHM	22 mm	21 mm	1 mm	4.76
LHM	40.2 mm	40.4 mm	2 mm	0.5

It can be observed from Table 6-2 that the difference between the predicted and measured values for the ellipsoidal focus was 0.01 cm in the radial direction and 0.02 cm in the axial direction. This validation was done using a HIFU probe designed for neurological applications. Although, the diameter of probes in the proposed applicator are larger than the available brain tumor ablation probe, these validation results can be used to judge the accuracy of the single probe field simulation. Based on experimental results presented, it can be concluded that the model simulates the acoustic field of the single probe with an accuracy of 95%. The validation results gave sufficient confidence to use the model to determine the suitable parameters for kidney tumor ablation and extend the simulation for the multiple probe approach.

HIFU applicator parameters for renal ablation

While choosing the input parameters, trade-offs are necessary between frequency, penetration depth and aperture size. Factors such as the depth of the kidney from the body surface, dimensions of the tumor and the spacing between the ribs were considered while determining the desirable dimensions for the transducer. The tumors of the kidney are 5cm –7cm in length and are usually located on the surface [30, 40]. The temperature necessary for coagulative necrosis

in renal tissue [23] is 80°C - 100°C . This corresponds to focal intensities of $2000\text{W}/\text{cm}^2$ - $6000\text{W}/\text{cm}^2$ [35]. The depth of the kidney from the body surface can be estimated using empirical formulae [38, 39, 103] which consider factors such as the height and weight of the subject. The depth of the kidney is approximately 18-20 mm for trans-abdominal treatment [35]. This assumes a 1 mm skin thickness and 19 mm thickness for the abdominal wall.

Figure 6-14 is a schematic diagram indicating the maximum depth of penetration necessary to reach deep seated tumors in the kidney. The probe is positioned such that the tip of the ellipsoidal focal region coincides with the extremity of the tumor in the direction of the source. From the schematic diagram, it can be seen that a focal length of 120 mm would be appropriate for the application. When the tumor is in the anterior portion of the kidney i.e. closer to the transducer, the applicator must be retracted by approximately 50 mm. A water chamber of length 100 mm is used to couple the HIFU beam to the tissue. A minimum coupling of 50 mm is provided to ensure that heat dissipation remains below the skin burn threshold without any external cooling.

Figure 6-15: Schematic representation of HIFU ablation of the kidney

The frequency used is partly determined by the depth of penetration required. The attenuation α increases at a rate of $1\text{dB}/\text{MHz}/\text{cm}$ for soft tissue [25]. In order to minimize off-focal heating, a trade-off between the frequency and penetration depth is necessary. In urology, frequencies

between 1 – 1.7 MHz are used for trans-abdominal HIFU. In fact, any frequency in the range specified above may be used for trans- abdominal HIFU, since it has been reported that the change in lesioning capability in this frequency range is minimal [35]. In the proposed system, a frequency of 1.5 MHz was chosen as the operating frequency.

The presence of rib bones in the path of the acoustic beam causes scattering. This results in heating of the surrounding tissue. Hence, a rib sparing window is highly desirable for HIFU dose delivery. Approximately 25 percent of the volume of the kidney [38] is in close proximity with the 11th and 12th floating ribs. The separation between the bones is approximately 20 mm [39]. So the acoustic profile of the probe must be such that the beam width near the rib cage is less than 20 mm. The acoustic power required is determined based on the free space field intensity I_{sp} . The intensity threshold I_{lesion} to ensure lesioning in the kidney tissue at a frequency of 1.5 MHz was reported to be 2128 W/cm² [35].

The acoustic profile of a probe was simulated using the simulation model explained in section 3.1. MATLAB 7.1 was used to develop the software for simulation. It was assumed that the acoustic wave passed through four parallel layers; water, skin, abdominal wall and kidney. In the simulation, the effect of tissue attenuation was considered but the effect of refraction at the boundaries has not been considered. The tissue attenuation was found to be $\alpha_{water} = 0.0022$, $\alpha_{skin} = 2.35$, $\alpha_{abdominal\ wall} = 0.59$, $\alpha_{kidney} = 0.41$ from references [25, 34]. $P_{skin/muscle}$ is the power absorbed in the intermediate layer of skin or muscular tissue. The total attenuation coefficient of the medium was calculated as the weighted average of the individual attenuation coefficients based on the distance. Probe diameters in the range of 60 -100 mm were simulated.

The frequency, focal length and wavelength were 1.5 MHz, 120 mm and 1 mm respectively. The acoustic pressure was simulated over a rectangular region of length 240 mm i.e. twice the focal length. The simulation results for probe diameters 60 -100 mm are summarized in Table 6-3. The acoustic intensity at the focus was calculated in terms of free space intensity I_{sp} . Free space intensity is the power per unit area at the focus for an acoustic output of 1W at the surface of the transducer. $P_{absorbed}$ is the power absorbed by the target tissue [35] and P_{skin} is power absorbed by the skin from the side lobe. The shape of the lesion is defined by the LHM (axial half

maximum radius) and RHM (radial half maximum radius). The suitability of a probe for tumor ablation is determined by the lesioning capability and the degree of off-focal heating. Lesioning capability is a measure of how much of the tissue can be heated to a given temperature at a given time [90]. This measure assumes that the heat is applied just long enough for the lesioning to fill the region till the half maximum intensities [90]. It was found that both lesioning capability and off-focal heating increases with increase in probe diameter.

Table 6-3: Critical parameters of focussed transducers of different diameters

Diameter (mm)	I_{sp} (W/cm²)	$P_{absorbed}$ (W/cm³)	$P_{skin/muscle}$ (W/cm³)	RHM (mm)	LHM (mm)
60	801	129	20.2	1.2	20
70	1473	292	69	0.8	14.6
80	2513	614	104	0.7	10.2
90	3396	1206	107	0.6	8.6
100	5068	2227	159	0.55	7.2

It can be seen from Table 6-3 that the 60 mm probe gives a focal intensity of 801W/cm² which is less than the lesioning threshold (2128W/cm²) for kidney tumor ablation [35]. The lesioning capability of the probe can be increased by increasing the diameter as shown in Table 6-4 but this increases the power absorbed in the skin. The power absorbed by the skin is more than the skin threshold, 50W/cm³ in the case of the 100 mm probe. Hence there is a need to use an applicator configuration that can provide sufficient focal intensity while maintaining the off-focal heating below the skin burn threshold. As mentioned earlier the multiple probe configuration attempts to reduce the off-focal heating by spatially aligning the confocal HIFU probes of smaller dimension. In this project we examine the feasibility of this approach for kidney ablation. Therefore, the extended model was used to simulate multiple transducers.

Results of Multiple Probe acoustic profile simulation

The multiple probe applicators use multiple transducers to create a high intensity at the target due to constructive interference of the con-focal beams [33]. It was hypothesized that a multi-probe applicator [33] with three probes of 60mm could deliver the necessary power without significant skin burns. The three probe configuration was chosen over a two probe applicator

since the latter requires probes larger than 60 mm which can cause off-focal heating. The four probe configuration is not explored as destructive interference might predominate in this case. The acoustic field generated from the multiple probe arrangement is simulated by combining the results obtained from a single probe applicator. The orientations of two probes are changed with respect to a middle probe whose centre point is assumed to be the origin of the coordinate system. The intensity at different points in the acoustic field is calculated by using bi-cubic interpolation.

The output intensity value at any point in the acoustic field of the multi-probe transducer can be obtained from vector addition. In order to offer a rib sparing window, the minimum separation required between the probes is close to 30° . The minimum angular separation is determined by the aperture of the probe and the minimum necessary spatial separation. At 30° angular separation the probes are spatially 4 mm apart. A schematic representation of the multiple probe arrangement is shown in Figure 6-15.

Figure 6-16: Schematic representation of a multi-probe arrangement – side view

Acoustic profile simulation was performed for angles starting from 30° . The power content in the side lobe was more than the skin burn threshold from 35° onwards. The results for angles from 30° to 37° are shown in Figure 6-16a. Since an increasing trend is seen in the side lobe strength, the simulation results are plotted only till 37° . From Figure 6-16b, it can be seen that the separation of approximately 29 mm at the plane of the applicator is given by an orientation of 34° . The free space field intensity I_{sp} for this configuration was $2232\text{W}/\text{cm}^2$.

Figure 6-17: Critical values of acoustic profile for multiple probe arrangement

The peak intensity remains almost constant for the various orientations while the size of the lesion changes. The ratio of the lessioning capability and the side lobe length can be considered a measure of merit for a transducer. The transverse beam plot and radial definition of the acoustic profile for an angle of 34° are shown in Figure 6-17.

Figure 6-18: Multiple probe arrangement 34° a) Transverse Plot b) Radial profile

Based on the simulation results, it was found that the multi-probe approach using three probes of 60 mm diameter at an angular separation of 34° reduces the off-focal heating and provides a ribs acoustic window as opposed to a single transducer. This makes the three probe approach suitable

for this application. A comparison of single probe and multiple probe transducers is summarized in Table 6-5. The total active area of the multi-probe applicator with three 60 mm probes is, $A_M = 2700 \pi$. This is close to the active area, $A_S = 2500\pi$, of a single focused probe of 100 mm diameter. So, the acoustic profiles for these applicators are compared. The focal length was maintained at 120 mm for both arrangements. The radial and axial beam profile of the single probe with the 100 mm diameter is shown in Figure 6-18.

Figure 6-19: Axial and radial profiles 1.5 MHz, 120 mm focus, diameter 100 mm

A comparison of the single probe and multiple probe approaches is summarized in Table 6-4. It was found from this study, that the multi-probe arrangement was able to suppress the side lobe strength by 72.5%. The power absorbed by the skin was less than the skin burn threshold of 50 W/cm^3 . The acoustic intensity delivered at the focus was sufficiently above the ablation threshold of 2128 W/cm^2 . Hence, it was concluded that the multiple probe arrangement was vastly superior to the single probe applicator and was suitable for ablation of tumors in the kidney.

Table 6-4: Comparison of single probe and multiple probe applicators

	Diameter (mm)	Active Area (mm²)	Number of probes	Intensity at target	Power absorbed by skin	Acoustic Window
Single Probe	100	2700π	1	$2227\text{W}/\text{cm}^2$	$159\text{W}/\text{cm}^3$	No
Multiple Probe	60	2500π	3	$2232\text{W}/\text{cm}^2$	$43\text{W}/\text{cm}^3$	28 mm

6.3 Summary

The results obtained from validation of the treatment protocol explained in chapter 5 were discussed in this chapter. A laboratory testbed was developed to implement the movement compensation scheme. Prior to replicating the synchronization phase, the pre-operative images were registered to real-time images. The WGF algorithm was tested on moving kidney images. It was concluded that the registration algorithm gives an accuracy of less than 1 mm. The processing time was 1-2 seconds which makes it appropriate for this application. Once the images were registered, the movement control strategy was tested on a robotic arm of FUSBOT-US. Simultaneously, the movement of the kidney was simulated on a test jig. The movement was recreated with error of less than 1 mm. The movement of the robot was tracked using a stereo camera based scheme which had an accuracy of 1.4 pixels/mm. The accuracy of the robot was also within 1mm and the system latency was less than 100 milliseconds. Hence, this robotic compensation scheme effectively integrates the movement models, developed in chapter 3, into an image guided system. The final step in the validation was to study the feasibility of a multiple probe applicator for this application.

It was observed from the simulation of the single probe applicator that the side lobe power increased significantly for larger probe sizes. The simulation was then validated using the pulse echo technique. This yielded an accuracy of more than 95% which provided sufficient confidence to extend the model for the multiple probe applicator. The single probe structure was compared with the multiple probe applicator for renal ablation. It was found from simulations that the multiple-probe approach provided the necessary focal intensity while considerably

reducing off-focal heating by 72%. The three transducer approach provided a succinct acoustic window of 28 mm for an optimal angular separation of 34 degree, sufficient for renal tumor ablation.

CHAPTER 7 : CONCLUSION AND FUTURE WORK

This research project focuses on providing a movement compensation strategy for noninvasive surgery. This concludes the works presented in chapters 3-6. In this research, a new movement adaptive surgical protocol is proposed. The protocol can be divided into two phases; the pre-operative planning phase and the intraoperative or real-time phase. In the proposed pre-operative phase, the movement pattern of the kidney was studied and modeled. In the intraoperative phase, a movement compensation strategy is developed as applicable to an image guided robot. Finally, the feasibility of using a multiple probe applicator for kidney tumor ablation is also established from simulations. The conclusions from the movement modeling and compensation are presented in section 7.1. The future directions of research in this project are presented in section 7.2. The major contributions and research outcomes from this project are summarized in section 7.3.

7.1 Conclusions

Intra-operational movement of the kidney, caused due to physiological processes such as respiration, can cause significant inaccuracies in dose delivery during noninvasive surgery. The extent of movement of the kidney is significant and subject specific. Hence, it is necessary to incorporate a movement compensation strategy in the surgical protocol. In this project a surgical protocol comprising of the following phases – pre-operative planning, synchronization and treatment is proposed. The target locations in the tumor are identified during pre-operative planning. Along with this, a movement model must be trained to predict the position of the moving kidney. In the synchronization phase and treatment phase, the robotic system is controlled using a hybrid controller which uses the movement model as a reference trajectory. The start point of this research is the quantification of renal mobility.

Study of kidney movement from ultrasound images

An experimental set-up was designed to track the kidney movement using ultrasound image sequences. The collection of statistical data for the respiratory movement of the kidney was done

using a 3.5 MHz ultrasound imaging probe. The respiratory pattern was also simultaneously tracked using markers placed on the body at locations which exhibited maximum movement. The experiment was conducted as a pilot study on 20 volunteers followed by a clinical study in 84 subjects. The kidney movement is visible and can be tracked using ultrasound slices. The movement could be tracked using template based techniques. The movement in the orthogonal dimension was also estimated using a speckle de-correlation based technique. The images were grabbed at a rate of 25 fps which was sufficient to provide a continuous movement pattern. The following were noted regarding the movement pattern:

- i. The maximum extent of movement of the kidney in the pilot study was 28 mm in the superior-inferior direction and 15 mm in the transverse direction for un-coached respiration. The range of movement for coached respiration was from 20 -30 mm.
- ii. The movement of the right kidney was more than the left.
- iii. The movement of the left and right kidneys showed poor cross-correlation, this could be due to dissimilar anatomy of the organs.
- iv. The movement of the kidney does not retrace its path during a respiratory cycle. This can be seen as a direct consequence of the asymmetry in the respiratory cycle.
- v. The movement of the kidney is subject-specific. It is also possible that the kidney movement patterns from the same subject are vastly different at different times. Due to subject specific nature of the movement, it is not possible to use generic models.

Next, the relationship between the kidney movement and skin marker movement was studied. The movement patterns of the skin marker were tracked using the same template matching technique used for kidney movement tracking. The movement of the marker in all three dimensions was estimated from the stereo image sequence images. It was found that the period of respiratory movement was almost equal to the time period of kidney movement. This was reaffirmed by coincidental peaks in the frequency response. This makes it possible to use the skin markers as surrogate kidney movement markers.

The skin marker and kidney movement patterns show considerable variations based on the height and weight of the subject. Based on the body mass index (BMI), the subjects were divided into three categories A, B and C. The following points were noted from the category wise analysis:

- i. The kidney movement was maximum in category A (22.5 mm) followed by category B (21.2 mm) and category C (21.0 mm) for both right and left kidneys.
- ii. The ratio of movements in the cranio-caudal direction to the movement in the transverse direction was lowest in category C. This could be due to the strong influence of abdominal respiration.
- iii. The variance in movement pattern within the three categories was significantly lesser than the overall variance. This indicates that the BMI has a significant impact on the respiratory pattern and consequently, the kidney movement pattern.

The influence of height and weight was then removed from the movement patterns by normalization. This makes it possible to generalize the movement modeling and compensation results obtained from the data. The kidney movement patterns were then modeled using a prediction-correlation model.

Pre-operative Movement Modeling

The prediction-correlation model consists of independent prediction and correlation modules. As part of the prediction module, a new empirical model of the kidney movement was developed. The model was based on sinusoidal shape functions which are ideally suited to model quasi-periodic data such as the kidney movement pattern. The model was able to fit the kidney movement patterns with appropriate tuning for one respiratory cycle. This model was then used as the basic system model for predictors such as the EKF, UKF and ANFIS. The inclusion of the empirical model improved the prediction accuracy of all the predictors. The accuracy of the shape function based model integrated with all the predictors was better than the conventional linear model.

All three non-linear predictors gave low prediction errors while used for the same prediction horizons typically less than 200 milliseconds. The EKF was computationally more intensive compared to UKF and ANIFIS. However, the prediction accuracy was always slightly less than

UKF. These make UKF and ANIFS more suitable for these applications. While comparing ANFIS and UKF, it was found that the predictor error of ANFIS was unaffected by changes in prediction horizon up to 1000 milliseconds. On the other hand, the prediction accuracy of UKF steadily decreased for longer prediction horizons. Since the system latency of most commercially available robotic systems is less than 1000 milliseconds, the empirical model along with ANIFS can be effectively used for movement adaptive trajectory planning. However, the prediction accuracy of ANFIS is affected by two factors:

- i. The sample size of the training set affects the prediction accuracy. From the experiment, it was found that a minimum of 1000 samples were necessary for accurate prediction from ANFIS.
- ii. The choice of the membership function also affects the accuracy of ANIFS. Based on the error percentage triangular MF was found to be most appropriate for this application. Unfortunately, there is no well established means to estimate the most appropriate membership function for a particular application.

So, it was concluded that the ANFIS based predictor is ideally suited for applications in which sufficient training samples are available prior to surgery. For applications that require lower system latency, typically less than 400 milliseconds, the UKF based prediction is more appropriate. The next part of the model was the correlation module.

The correlation module is based on a new mapping function trained for smaller subintervals. This deviates from the conventional techniques of updating the movement model once in every respiratory cycle. The model was able to map the skin marker movement to the organ position with 89% accuracy. The accuracy was calculated as a ratio of the error in position to the maximum displacement. The prediction was further fine tuned using ANFIS which accounts for the non-linear nature of the movement. The model was more accurate when compared to conventional linear correlation networks. Finally, the prediction and correlation modules were integrated to form a unified kidney movement model. This model provides the reference trajectory for real-time compensation.

Real-time movement compensation

The three aspects were addressed in the real-time movement compensation scheme, namely; an image registration technique to update the pre-operative plan using real-time images, a movement control strategy to synchronize the movement of the therapeutic system and modeling scheme to establish the feasibility of a multiple probe HIFU applicator for tumor ablation. A feature based image registration scheme was used to register real-time images to pre-operative images. The error in registration was less than 0.84 mm while using the WGF based registration algorithm. The algorithm completes the registration within 2 seconds which is well within the allowable latency. However, this algorithm is limited to rigid transformations comprising of rotation and translation. The algorithm gives gross estimate of the position of the organ. The next aspect to be considered was a movement control scheme.

The movements during the *treatment* phase comprise of ‘point to point’ movement according to the pre-operative plan and synchronous quasi-periodic movement according to the movement model. A hybrid movement controller was proposed for this application. It comprises of a MPC controller for the repetitive synchronous movement and a simple PID controller for the point to point movement. In order to validate the movement compensation scheme, a laboratory testbed was developed comprising of a movement replicating mechatronic test jig and a detached robotic arm. The mechatronic jig recreates the complicated movement pattern of the kidney. Apart from moving the phantom, the test jig also has provision to hold an ultrasound imaging probe. The accuracy of the jig was found to be 0.5 mm for speeds in the range of 20 mm/s to 100 mm/s. This is within the acceptable error limit of 1 mm. The movement controller was implemented on the robotic arm, which was a detached arm of the kidney ablation robot FUBOT-US developed in the mechatronic research group, RRC. The PID controller was able to provide an accuracy of less than 1 mm in the point to point movement, regardless of the movement pattern. The controller provides an accuracy of less than 1.4 mm while tracking kidney movement patterns obtained from the volunteers. This proved that the movement model could be integrated into an image guided movement compensation scheme. Finally, as a feasibility study, the HIFU applicator suitable for this application was modeled.

Limitations and scope of work presented

Some of the limitations and scope of the methods proposed and implemented in the thesis are mentioned in this section. The approach used for kidney movement quantification is based on the assumption that the kidney can be imaged by placing the ultrasound transducer in the lower costal margin. Although, this would be fair assumption to make in most cases the possibility ectopic kidneys cannot be ruled out. In such a scenario, imaging the kidney using ultrasound would be difficult and such cases are not considered in the scope of this work. However, the measurement and modeling techniques would be relevant as long as some part of the kidney is visible though the intra-costal margin.

The kidney movements in the X and Y direction are measured relative to the first ultrasound frame. The 11th and 12th ribs are used as anatomical references to measure the extent of displacement. The use of anatomical references is prevalent diagnostic imaging as it obviates the need for implanted markers or fiducials. This method gives sufficiently accurate results for calculation of relative movement. However, the absolute position of the kidney cannot be captured with respect to a global frame of reference. Since the objective of this study was to understand the nature of kidney movement and the relationship with skin markers, it would suffice to calculate the relative displacement from the first ultrasound frame.

This study focuses on quasi-periodic movements of the kidney caused predominantly due to respiration. However, there could be gross unpredictable changes in the organ position due to involuntary movements such as coughing and sneezing. Such scenarios cannot be accounted in the prediction–correlation model and hence a ‘fail-safe’ approached is proposed. In such cases the treatment would be stopped and the surgical protocol would be repeated form the synchronization phase. The movement adaptive protocol and movement model are applicable to trajectory planning in any image guided treatment modality. However certain specific issues caused due to the application of HIFU such as volumetric changes or non-rigid deformations in the target tissue are not included in the scope of this project. The registration technique explained in this thesis is limited translational and rotational movements. However this provides a coarse estimate of the transformation which could fine tuned using non-rigid image registration techniques. It must also be noted that non-linear phenomenon such as cavitation caused due to

HIFU ablation have not been investigated in this work. The future areas of research in this project are described in the next section.

7.2 Future Work

In this section, a few areas of research that can be taken up as immediate future work are identified. They include:

Study of movement in affected subjects

The study of movement can be extended to incorporate data from subjects with various pathologies. It was concluded from this study that the respiration induced movement reduces in magnitude due to pathologies. However, the exact impact of individual pathologies is not clear. Extending the study to more affected subjects would also be useful in understanding the relative accuracy of the movement models to various kinds of pathologies.

Implementing advanced controllers

The movement compensation scheme described in this thesis uses a MPC controller. The MPC was chosen due to its ability to compensate repetitive disturbances such as the respiratory movement. However, other advanced control alternatives such as fuzzy controllers and adaptive controllers could also be used as options for synchronous control. Such approaches can be compared with the MPC controller proposed in this work. However, a robust control scheme is not suggested due to the large number of unpredictable factors in the surgical set-up such as dynamics of the couple water bowel, voluntary or involuntary changes in patient position, mechanical vibrations and changes in tissue properties due to HIFU.

Validation of the model using an anthropomorphic phantom

The movement pattern of the kidney can be recreated using the mechatronic jig explained in chapter 6. However appropriate phantoms for the human kidney are not common. Developing an anthropomorphic ultrasound phantom for the kidney can be taken up as a future work in this project. The proposed anthropomorphic phantom comprises of a porcine kidney non-rigidly connected to the walls of a semi open box using silicon tubes. The silicon tubes simulate the

major blood vessels of the kidney which are connected to the hilum [39]. This non-rigid connection allows changes in orientation of the kidney during the movement of the phantom. Such changes in the orientation are present during the respiration induced movement of the kidneys, as it has to move through a considerable amount of extra-peritoneal viscera [39].

The kidney movement can be best understood based on its displacement from the ribs. This makes the ribs an attractive option to be used as an anatomical marker. Hence, an anthropomorphic model of the last two floating ribs shall be used. This is similar to the surgical scenario in the sense that the available acoustic window is limited by the rib interstitial. The phantom ribs are attached to the walls of a semi open box. The box shall be made of three strips, with openings on two sides. This would ensure minimal change in temperature and pressure of water inside and outside the box. The proposed dimensions of the phantom are presented in Table 7-1.

Table 7-1: Specifications of the anthropomorphic phantom

Component	Mass (g)	Dimensions (mm)
Rib phantom	500	20 x 70
Porcine kidney	300	130 x 35 x 60
Silicon tubes	100	5 (radius)
Box	300	150 x 50 x 70

Validation of proposed multiple probe applicator configuration for kidney

The multiple probe approach proposed for the HIFU applicator has not been validated. The actual HIFU power generated at the focus can be measured using RFB techniques. The measurement jig, used for the single probe validation, can be used for the multi-probe approach to validate the acoustic profile. Finally, the concept can be validated in *ex-vivo* kidney tissues such as porcine kidney which is similar to a human kidney.

Modeling other applicator configurations

The multiple probe approach used in this project can be compared to other applicator configurations such as the phased array and segmented probe configurations. The model adapted in this thesis is based on the Raleigh integral, which assumes circular boundaries. Hence, the

model was not extended for the complicated geometry of the segmented probe. These probes can be modeled using approaches such as FEM and BEM.

7.3 Major Contributions

Respiration induced movement of upper abdominal organs is a major cause of inaccuracy in noninvasive surgery. Currently techniques such as voluntary breath suppression or general anesthesia (GA) are being employed to prevent such movement. Voluntary breath suppression is often ineffective in cases where the organ movements are large. This approach also has the disadvantage that it increases the treatment time. GA is effective in suppressing organ movement, but often leads to anesthesia related complications. This study explores the possibility of accommodating the movement as part of the treatment protocol. The study can be segregated into three phases - movement measurement, movement modeling and movement compensation. The major contributions from each phase are described in this section.

Movement measurement was specific to kidney movement patterns in relation to skin marker movement. An experimental set-up was developed to accurately measure the kidney movement from two dimensional B-mode scans. This set-up can be used for similar studies for other abdominal organs such as the liver. The study established the nature of relationship between the respiratory signal and the kidney position. Phenomena such as respiratory hysteresis which are more profound in kidney movement were analyzed in depth. The study also analyzes the impact of pathologies on the kidney movement patterns. In this respect the outcomes are vastly different from earlier studies carried out for gross movement quantization on upper abdominal organs.

The next task undertaken was to develop an accurate movement model of the target organ from the data obtained. Currently such models are limited to simplistic movement patterns such as that of the liver. In this project a general prediction-correlation model capable of predicting complex movement patterns has been developed. The model was tested on kidney movement pattern which are much more complex compared to other abdominal organs such as the liver. The model

has two major advantages firstly it can be customized for individual subjects based on their breathing pattern and secondly it models the asymmetric nature of respiration.

Attempts have been made to integrate the non-linear techniques such as Kalman filters for respiratory signal prediction. However, Kalman filters are not ideally suited for systems with high degrees of non-linearity. In this project, two new approaches namely ANFIS and UKF have been used to fine tune the prediction-correlation model. ANFIS is a neural fuzzy inference system based on hybrid learning. This provides the optimal non-linear mapping between respiratory pattern and the kidney position. It must be noted that this approach is different from few other techniques which use non-linear techniques for time series prediction. The second approach integrated to the new non-linear model was UKF. The UKF circumvents the limitation of Kalman filters for systems with high degrees of non-linearity. The UKF was found to be computationally more efficient than the conventionally used EKF. In this work it was found that UKF can be used as for accurate prediction over small prediction horizons. It can also be used in scenarios where sufficient samples are not available to train the fuzzy inference system.

Finally, a new movement adaptive surgical protocol was proposed. Although the protocol has been explained in (chapter 5) the context of FUS, it can be extended to other image guided noninvasive treatment modalities. The protocol was implemented on a laboratory testbed comprising of an ultrasound imaging system and a robotic arm. The experiments conducted on the laboratory testbed prove the feasibility of the concept in a real-time scenario. The testbed developed in this work can be used to implement similar control and compensation techniques. The major contributions can hence be summarized as:

- Quantification of kidney movement patterns using two dimensional ultrasound
- Establishing the relation between kidney movement and respiration from statistical data
- Studying the impact of pathologies such as RCC and Angeliomyomas on kidney movement patterns
- Development of a new predictive movement model for the kidney

- Development of a new correlation model to map internal organ movements such as the kidney to the respiratory signal
- Implementing a control scheme suitable for movement compensation based on the new prediction-correlation model
- Development of a movement adaptive protocol for noninvasive surgery and proving the feasibility of the concept on a laboratory testbed.

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APPENDIX A MECHATRONIC JIG

A summary of the design of the mechatronic jig used for movement validation is provided in this section. The test jig requires three linear slides to provide three degrees of freedom for the phantom. The slide consists of a carriage with a supporting railing; the movement shall be imparted to the slider by using a lead screw a schematic diagram of this arrangement is shown in Figure A-1. The main factors considered for designing the slide are the load carrying capacity of the arrangement and the maximum speed of movement of the lead screw. The movement of the three axes are coupled using a plate attached to a bracket.

Figure A-1: Schematic diagram of the mechatronic jig - single axis

The load on X and Y axis would be radial. It would comprise of the load on the Z axis and the mass of the slides coupled below it along with the motors, connecting plates and brackets. The components proposed to be used in the mechatronic jig are summarized in Table A-1.

Table A-1: List of components

Component	Mass(Kg)	Dimension (mm)
Slide X	0.6	262 x 73 x 29
Slide Y, Z	0.6	212 x 73 x 29
Motors	0.4	65 x 62 x 45
Connecting Plate	0.2	100 x 60
Adaptors	0.1	16 mm (dia) x 15
Diagnostic Probe 3.5Mz	0.90	70(dia) x 172
HIFU Probes 2 MHz	0.16	25.4(dia) x 50
Multiple Probe Holder	0.44	180 x 50 x 50
Phantom	1.20	100 x 35 x 70

A stepper motor SAS4004-102 of torque 0.38 Nm and 400 rpm is chosen for all 3 axis. This was chosen such that the operation of the motor is in the advisable range. The desirable specifications for the motors are summarized in Table A-2

Table A-2: Motor specification for three axes

Component	Torque Required (Nm)	Motor Suggested	Motor Type	Max Torque(Nm)
X Axis Motor	0.180	SAS4004-102	Stepper	0.38
Y Axis Motor	0.075	SAS4004-102	Stepper	0.38
Z Axis Motor	0.090	SAS4004-102	Stepper	0.38