Needle Navigation for Image Guided Brachytherapy of Gynecologic Cancer

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Navigering av Nål vid Bildstyrd Brachyterapi av Gynekologisk Cancer

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Abstract

In the past twenty years, the combination of the advances in medical imaging technologies and therapeutic methods had a great impact in developing minimally invasive interventional procedures. Although the use of medical imaging for the surgery and therapy guidance dates back to the early days of x-ray discovery, there is an increasing evidence in using the new imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound in the operating rooms. The focus of this thesis is on developing image-guided interventional methods and techniques to support the radiation therapy treatment of gynecologic cancers. Gynecologic cancers which involves malignancies of the uterus, cervix, vagina and the ovaries are one of the top causes of mortality and morbidity among the women in U.S. and worldwide. The common treatment plan for radiation therapy of gynecologic cancers is chemotherapy and external beam radiation therapy followed by brachytherapy. Gynecological brachytherapy involves placement of interstitial catheters in and around the tumor area, often with the aid of an applicator. The goal is to create an optimal brachytherapy treatment plan that leads to maximal radiation dose to the cancerous tissue and minimal destructive radiation to the organs at risk. The accuracy of the catheter placement has a leading effect in the success of the treatment. However there are several techniques are developed for navigation of catheters and needles for procedures such as prostate biopsy, brain biopsy, and cardiac ablation, it is obviously lacking for gynecologic brachytherapy procedures.

This thesis proposes a technique which aims to increase the accuracy and efficiency of catheter placements in gynecologic brachytherapy by guiding the catheters with an electromagnetic tracking system. To increase the accuracy of needle placement a navigation system has been set up and the appropriate software tools were developed and released for the public use as a module in the open-source 3D Slicer software. The developed technology can be translated from benchmark to the bedside to offer the potential benefit of maximizing tumor coverage during catheter placement while avoiding damage to the
adjacent organs including bladder, rectum and bowel. To test the designed system two independent experiments were designed and performed on a phantom model in order to evaluate the targeting accuracy of the tracking system and the mean targeting error over all experiments was less than 2.9 mm, which can be compared to the targeting errors in the available commercial clinical navigation systems.
List of Abbreviations

CT  Computed Tomography
EM  Electromagnetic
HDR High Dose Rate
ICP Iterative Closest Point
IGI Image Guided Interventions
IGT Image Guided Therapy
MRI Magnetic Resonance Imaging
OAR Organs at Risk
OR  Operating Room
PET Positron Emission Tomography
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Chapter 1

Introduction

According to the 2013 cancer facts & figures [1], the gynecologic malignancies, which include cancers of the uterine cervix, uterine corpus, ovary, vulva, vagina and other genital organs are the fourth most frequent type of cancer estimated in women in the United States. Typical radiotherapy-based treatment for most of the primary and recurrent gynecologic cancers involves chemo-radiation external beam radiotherapy followed by brachytherapy [2]. In this thesis, technical solutions have been proposed for improving the delivery of brachytherapy radiation treatment to the patients with gynecologic cancer.

1.1 Advanced Multimodality Image Guided Operating Suite

In 2011 Brigham and Women’s Hospital, a teaching hospital of the Harvard Medical School, launched a multimodal operating suite, AMIGO (Advanced Multimodality Image Guided Operating suite) with the goal of making all possible imaging modalities available to the physician during surgical or interventional procedures. AMIGO (Figure 1.1) is a 5700 square foot space sophisticated interventional and surgical area which comprises three rooms. In AMIGO a multidisciplinary team consisting of surgery team, interventional radiologists, radiation oncologist, imaging physicists and computer scien-
tists work together to treat the patients by using the various imaging modalities available in the suit.

Figure 1.2 shows a side view of the three main rooms of the AMIGO suite. The left room is the magnetic resonance imaging (MRI) room in which a high field 3 Tesla, 70 cm wide bore Siemens MRI scanner is mounted on the ceiling which makes it possible to move it out into the operating room at the center. The room is equipped with MRI compatible anesthesia machine and vital signs monitor equipments. The ability to move the MRI enables flexibility in different surgical procedures and makes it possible to do the MR imaging in the operating room. The middle room is an operating room (OR) which is the heart of the AMIGO suite. The OR is equipped with an electronically controlled surgical table with the ability to change the table top to fit different surgery and angiography needs. The surgical table is surrounded by various state-of-the-art image-guided therapy devices such as a surgical navigation system (BrainLAB) and mobile imaging modalities such as two ultrasound devices (BK Medical, Siemens) a C-Arm x-Ray and a near-infrared imaging system. There are several large monitor displays mounted on movable arms in the room which shows the selected images and other relevant patient information which have been collected and displayed by a video integration system. A PET-CT room is located
at the right side of the OR room. In this room the metabolic activity and the function of a particular region of the body is imaged through the molecular imaging modality using the positron emission tomography (PET). In the procedures of the thermal ablation or resection of the tumors the surgeons can use the integration of the metabolic function information from PET with anatomical information from CT and MRI to localize and target the cancerous tissue and use the valuable information in the treatment procedure.

From the first operation on September 2011 until October 2013, 274 procedures have been performed in the AMIGO operating suite. The breadth of clinical activity in AMIGO is considerable, as illustrated by the variety of cases performed there: 37 craniotomies, 3 brain laser ablations, 3 brain biopsies, 15 transsphenoidal, 5 breast lumpectomies, 7 EP cardiac ablations, 6 prostate brachytherapy case, 75 cryoablutions (liver, kidney), 18 soft tissue biopsies (liver, kidney), 5 cryo/biopsy combo, 8 PET/CT cryoablutions, 47 prostate biopsies, 44 gynecologic brachytherapy procedures, and 1 parathyroidectomy.

The technical solutions proposed in this thesis were motivated by the unmet needs of the gynecologic brachytherapy procedures that have been performed in AMIGO suite. A brief introduction to the problems this thesis seeks to address, and the solution is provided next, while details follow in the subsequent chapters.

1.2 Image-guided Gynecologic Brachytherapy

Brachytherapy involves delivery of radiation directly to the cancerous tissue, and the type of gynecologic brachytherapy used for AMIGO patients involves placement of plastic
catheters into and around the tumor. Finally, through these catheters, radiation seeds are implanted. The catheters are implanted under imaging guidance provided by ultrasound and MRI. Once the catheters are implanted in the patient’s perineum, a treatment plan is created using commercial treatment planning software. The patient is transferred to a radiation therapy vault where an afterloading machine is connected to the catheters and radiation is delivered to the tissue. This is an in-patient procedure in which twice a day treatment is provided in prescribed fractions over next days after the surgery [3], during which catheters stay inserted in patient’s perineum.

1.3 Thesis contributions

The contributions of this thesis are in two different steps of the AMIGO gynecologic brachytherapy procedure. First, it provides a navigation system based on electromagnetic tracking devices to aid the placement of the catheters under MRI guidance. And
second, it provides a solution to measure displacements in the catheter positions between the different treatment fractions. The solution for the placement of the catheters is an integration of a commercial electromagnetic tracker (NDI Aurora, Northern Digital Inc.) and custom algorithms for registration and calibration of images and three dimensional models of surgical tools and brachytherapy applicator, and implementation in the 3D Slicer software, a multi-platform, free and open source software package. The displacement measurement tool uses the same electromagnetically tracked sensors to record the catheter geometry at each fraction, and then reports the detected deviation. If this reported displacement is greater than a prescribed threshold, the treatment team is alerted, and evaluate if a imaging and planning needs to be repeated.

1.4 Roadmap

Chapter 2 begins with an overview of gynecologic cancer and the state of the art radiation therapy based treatments especially image-guided based procedures. Next, chapter 3 provides the technical background of the key elements including surgical navigation and image registration that constitute the contributions of this thesis. Then chapter 4 provides details of the methods proposed in this thesis and the developed system. Chapter 5 provides experimental setup and their results, and finally chapter 6 provides a discussion of these results as well as recommendations for promising areas of future work.
Chapter 2

Background: Gynecologic Interstitial Brachytherapy

Malignant neoplasm, also known as cancer consists of a wide group of diseases caused by uncontrolled growth of cells. Unregulated cell divisions can create malignant tumors, which have the potential to invade the nearby organs. However, it should be noted that not all tumors are cancerous. Unlike malignant tumors, non-cancerous (benign) tumors do not have the ability to invade neighboring cells.

Cancer is one of the world’s major public health concerns. According to the 2012 cancer statistics [4], one fourth of all deaths in the United States are because of cancer. Diagnosis of cancer can be done in several ways including identification of specific signs and symptoms in the patient, performing cancer screening tests, and taking medical images of the inner organs. A histology test is usually performed on a tissue sample (biopsy) that the physician believes is potentially cancerous. The standard treatments for cancer include chemotherapy, radiation therapy, and surgery.

Gynecologic cancers are one of the leading causes of mortality in women worldwide. Gynecologic cancers, which affect the female genital tract, include uterine corpus and cervix, ovary, vulva, vagina, and other genital organs. External beam radiotherapy followed by brachytherapy is the standard treatment of gynecologic malignancies [2]. The
focus of this thesis is on the brachytherapy part of the treatment. Brachytherapy \footnote{Brachytherapy originates from the Greek word brachys meaning short distance.} is a type of radiation therapy in which the radioactive sources that deliver the radiation dose are placed inside and next to the tumor tissue. The placement of radioactive seeds close to the cancerous tissue makes it possible to expose the tumor to a conformal dose escalation following the external beam radiotherapy. Interstitial brachytherapy is the type of brachytherapy procedure in which catheters or hollow needles are inserted inside the tumor tissue within which radioactive sources will be introduced later. Interstitial brachytherapy is widely used to treat the large advanced cervix cancers which invade the para-uterine tissue, the lower third of vagina, the bladder or rectum, and also different cancers of vagina \cite{3}.

Following the surgical procedure of catheter placement, a remote afterloading device inserts the seeds of radiation sources (usually Iridium 192) inside the catheters. Depending on the plan of radiotherapy, the radiation type can be either high-dose rate (HDR) or low-dose rate (LDR).

### 2.1 Image-guided Brachytherapy Procedure

The patient will be informed about the interstitial brachytherapy procedure during the external beam radiotherapy period and will sign the consent forms before undergoing the operation \cite{3}. In the brachytherapy operating suite, the patient will be under general endotracheal anesthesia; an anesthesiologist will stay in the suite throughout the case. When the patient is under general anesthesia, a pair of stirrups will be used to raise the patients legs to a lithotomy position.

The appropriate use of pre-operative and intra-operative image guidance helps the radiation oncologists carefully estimate and plan radiation dose for the tumor and normal tissue. Using 3D imaging techniques during the catheter placement can guide the physician in measuring the insertion depth and the correct placement of needles into the
cancerous tissue. With the aid of intraoperative volumetric imaging, misplaced catheters can be removed and repositioned, thus limiting toxicity to surrounding organs at risk, such as the bladder and the rectum. In situations where the intraoperative 3D imaging modalities are not an available option or are very costly, ultrasound guidance can be used to place intrauterine tandem. Physician can take advantage of an abdominal ultrasound probe to visualize the tandem and place the catheters into the uterus and cervix while preventing needle insertion into the bladder and rectum.

One of the important steps in brachytherapy treatment is selecting the appropriate applicator to cover the tumor tissue in the most efficient way. The physician decides on the type of the applicator based on the vaginal residual thickness of the tumor. A vaginal cylinder would be appropriate for vaginal lesions with residues less than 5 mm while for the bigger tumors using interstitial brachytherapy is often necessary \[\text{3}\]. Interstitial brachytherapy can be performed freehand or with the aid of a template. Template is a device which is used to guide the needles to desired locations and facilitate providing a homogenous dose distribution. The Syed-Neblett interstitial template (Figure 2.1) is a gynecological applicator to place the catheters in vaginal or cervical cancers with extensions in vaginal tissue \[\text{3}\]. The material for the Syed-Neblett template is plastic and the template needs to be fixed to perineal skin by suturing the corners. Freehand insertion is only recommended in cases where the tumor is in the lower part of vagina and can be examined visually or by palpation \[\text{3}\]. There is always a risk of needle insertion into bladder or rectum and intraoperative or postoperative 3D imaging is an invaluable tool to check and correct the needle misplacement.

The applicators, needles, and catheters that are going to be used in image-guided procedures need to be MRI or CT compatible. Figure 2.2 shows the required MR-compatible set up for an interstitial gynecologic brachytherapy procedure.

After sterilization, but prior to insertion of the needles, a Foley catheter is inserted into the bladder, the obturator is then inserted into the vagina, and the template corners are sutured to the perineal skin \[\text{3}\]. The first group of needles (covered with catheters)
Figure 2.1: A 3D graphic model of an interstitial applicator which is used in BWH interstitial brachytherapy cases: a Syed-Neblett template attached to a vaginal obturator (photo from [5]).

Figure 2.2: Syed-Neblett gynecologic template, vaginal obturator, metal trocars (needles) and flexible plastic catheters. The trocars are inserted into catheters to make them rigid enough for tissue insertion. All of the materials are MR compatible which is necessary in the case of MR guided brachytherapy. (From Gynecologic Radiation Therapy [3])
are inserted into the obturator tracks then other needles are inserted into the template holes. During the insertion procedure, imaging is performed to check whether any needles have been inserted into the rectum or bladder. If intra-operative imaging is not a choice, postoperative imaging should be done after all needles have been inserted. By checking tumor coverage, placement adjustments or insertion of new needles is performed until the results become satisfactory. After the final imaging and possible repositioning of the needles, the catheters are labeled with numbers and are glued to the template (Figure 2.3). Treatment planning requires contouring of the tumor and organs at risk (OAR). For contouring, appropriate scanning of the volume of interest is needed. The physician benefits from the pre-operative scans to find the exact location of tumor in the post-operative images. Usually the whole vagina, the sigmoid, the rectum, and the bladder are contoured (Figure 2.4). After the contouring, the prescription, which consists of the computed dose and the fractions, is applied to the patient.

2.2 Interstitial Brachytherapy at AMIGO

At Brigham and Womens Hospital (BWH) image-guided interstitial brachytherapy used to be performed at a 0.5 Tesla Signa SP (GE Healthcare) image guided therapy unit during the period 2002 – 2006. Since September 2011, all the image-guided gynecological brachytherapy cases undergo the procedure at AMIGO suite.

Prior to the procedure the physician performs a number of clinical examinations both at the diagnosis step and later at external beam radiation therapy period to assess the tumor size and its extensions. The physical examinations include a rectovaginal test to find out the tumor size and assess whether it extends to other surrounding tissues or not. Based on this examinations the physician decides on the applicator type: tandem coupled with ovid (T&O), with ring (T&R) or interstitial (Syed-Neblett template) (Figure 2.5).
2.2.1 Preoperative Imaging

All the patients undergo diagnostic MR imaging before the start of external beam radiotherapy. The preoperative imaging protocol consists of the following MRI sequences: T2-weighted TSE (turbo spin echo), T1-weighted TSE with and without contrast media injections, HASTE (single-shot half-Fourier fast spin echo), VIBE (fat-suppressed 3D gradient echo), diffusion-weighted echo planar imaging and GRE (RF-spoiled gradient echo) [6]. The treatment starts with external beam radiation therapy and continues with an Image-guided brachytherapy at AMIGO suite.

2.2.2 Needle Placement

At AMIGO OR room the patient is placed in a lithotomy position using padded stirrups. A visual examination of the vagina and cervix is performed using a sterile speculum.
Figure 2.4: An axial view of a CT scan of the region of interest. Contrast agent is used to improve the bladder and rectum visibility. The tumor and OAR (bladder and rectum in this case) are contoured. (From Gynecologic Radiation Therapy [3])

Figure 2.5: Different types of gynecologic brachytherapy applicators: left: Syed-Neblett template(violet) with central obturator(white), middle: tandem and ring (T&R) and left: tandem and ovoids (T&O).
following by a uterine sound and in some cases ultrasound examination. After the examinations the cylindrical obturator is inserted into the vagina and the templates holes are filled with sterile surgical lubricant for better contrast and then it is fixed over the obturator. After placing the template and obturator the template is sutured in four points to the skin. The patient while kept in lithotomy position is moved to the MR room. The patients arms are fixed to her chest and if needed her legs are adjusted to fit into MR bore. The wide 70 cm MRI wide bore facilitates the procedure. While the patient is in the scanner all her vital signs are monitored on a screen outside the MRI room by an anesthesiologist. The first scan is usually a T2-weighted MR localizer. The needle placement process starts by inserting the ProGuide (Nucletron Co) plastic catheters with metal trocars through the template holes (Figure 2.6).

A bSSFP \(^2\) sagittal scanning is acquired for checking the state of the most superior placed needles. The needles are checked for probable bowel invasion and adjustments are made if necessary. Following the checking scan, other groups of catheters are inserted and quick checking T2-weighted scans (scan time around 1 minute) are acquired after insertion of each set until the tumor is completely covered. Final confirmation scans consists of a T2-weighted MRI (slice thickness 1.6 mm) and a diffusion weighted echo-planar scan.

### 2.2.3 Radiotherapy Planning

For treatment planning purpose the patient is moved to the PET/CT room at AMIGO and a final validating CT scan is acquired. The preoperative MR, the final MR and the CT scans are transformed to the treatment planning station with dedicated software (Plato or OncentraGYN from Nucletron or BrachyVision from Varian) and the OAR are contoured. The patient is moved from AMIGO to the radiation oncology treatment clinics in an appropriately shielded room. Based on the treatment planning results, high-dose-rate (HDR) brachytherapy seeds are delivered to the tumor area through the catheters using an afterloading machine \([6]\). The interstitial brachytherapy treatment continues for 5-
Figure 2.6: At BWH AMIGO suite the patient is in lithotomy position inside the MR scanner bore while the surgeon inserts the needles.

6 days and the patient receives HDR brachytherapy fractions twice a day during this period [6].
Chapter 3

Background: Surgical Navigation Systems

In its broadest definition navigation can be thought as a study which leads to finding out the position and direction of a moving object, hence a navigation system is considered as a system which aids this goal. Ship navigators use the navigation system besides the map to find the ship’s position on sea and find the desired direction to reach the port while avoid colliding the rocks. The very same concept applies to surgical navigation systems in which surgeon aims to reach a target point while trying to avoid injuries to critical organs using diagnostic radiology images (as maps) and tracking systems (as compass and global positioning system). Surgical navigation system is the heart of computer-aided surgery and therapy systems which enables surgeon to know the exact position and orientation of surgical tools in relation to patient anatomy and surgical workspace. In image-guided surgery, navigation system leads surgeon to navigate through the pre-operative and intra-operative images of patient by moving the instruments to reach the organs of interest. The basic components of a surgical navigation system is depicted in the Figure 3.1.

Surgical navigation system consists of scanners and imaging devices, tracking system, computer workstation with surgical navigation software and finally a communication
network on which different devices can talk to each other. Setting up a surgical navigation system can be summarized in these steps:

1. Establishing a connection between different devices through a network protocol.

2. Registration of different 3D images of patient with 3D models of anatomical organs.


4. Registration of the imaging coordinate system with surgical workspace coordinate system using the tracking device stylus.

5. Visualization of surgical device models along with the 3D images.

6. Overlaying real-time images of intraoperative imaging modalities such as ultrasound to the visualization scene.

In this chapter the main components of a typical surgical navigation system is discussed. First the different types of tracking systems which are electromagnetic and optical
trackers are discussed. These systems are used for measuring the position and orientation of interventional tools in 3D surgical workstation. Next the rigid point-based registration problem is explained which is the de facto standard solution for the current surgical navigation registration problem. Finally the tracked ultrasound imaging is presented which has been recently adopted as a useful technology in image-guided procedures.

3.1 Tracking Systems

The position and in some cases the orientation of the surgical instruments relative to the patient is measured by tracking devices. Historically, the first successful use of tracking systems was reported in the computer aided neurosurgery procedures by using the frameless stereotaxy systems in the 1980s. The first generation of the trackers used in frameless stereotaxy systems were mechanical localizers which were robotic articulated arms equipped with position encoders in all the joints and linkages. The drawbacks for mechanical localizers were limitation in tracking of only one instrument at a time, sterilization problems and size issue in the operating rooms. These drawbacks motivated the researchers to pursue for other tracking solutions which led to the two main category of the currently available trackers: optical and electromagnetic tracking systems. The feasibility of using optical trackers besides the acceptable range of accuracy made optical tracking systems an adapting surgery tool in many operating theaters. Some of the successful commercial optical trackers which were adapted well include Optotrack 3020 and Polaris by Northern Digital and Flashpoint 5000 by Boulder Innovation group. The dependence of the optical tracking on the need for the line of sight is however a considerable drawback which limits the use of these category of trackers in many surgical situations and procedures. Electromagnetic tracking systems with no dependence on the line of sight has to potential to be a useful replica of the optical systems, however the accuracy and the reliability of the sensors output is a big issue and is not comparable with the optical trackers especially in surgery conditions in the presence of ferromagnetic materials.
The main principles of optical and electromagnetic tracking systems are discussed in the following sections.

### 3.1.1 Optical Tracking Systems

The principal idea behind measuring the position in optical tracking systems is triangulation. In geometry and trigonometry, triangulation is defined as the process of finding the position of a point by measuring the angles from three edges of a triangle in a fixed baseline. In optical tracking systems usually a pair of video cameras or CCD sensors detect the markers. The markers can be optically recognizable printed patterns, energy emitting or reflecting objects. In order to calculate the three-dimensional position of a marker the sensor should detect the marker in at least three sensor axes to find the three dimensional orthogonal planes. The technique of triangulation calculates the 3D coordinates and angular orientation of the markers on a stylus or pen to determine six degrees of freedom. Optical tracking systems fall into the two following categories: video-based tracking systems and Infrared-based tracking systems. In video-based optical tracking systems two or multiple calibrated cameras produce video sequences and an image processing algorithm recognizes the patterns of the markers and hence locate them in the three dimensional space. The markers which are used in video-based systems resemble the ones that are used in crash test simulations in automobile manufacturing industry. Claron Tracking (Figure 3.2) is a commercially available system using video-based tracking.

Multiple CCD units are used in IR-based tracking systems to detect the infrared energy which is emitted or reflected by markers. The ambient light of the room is eliminated by an optical filter mounted on the CCD unit. The common IR-based trackers can be either active optical trackers or passive optical trackers. In active type like Optotrak Cetrus (Northern Digital Inc) near IR-range LEDs are used as markers. Based on the prior information about the geometry of the object(for example distance between mark-
ers) and the fixed distance between the CCD units, the processing unit of the tracker uses triangulation to find out the position of markers and objects. In order to determine the six degrees of freedom (6 DOF) information of an object (position and orientation, AKA pose), at least three non-collinear LEDs are required. In the passive IR-base trackers such as Polaris Spectra and Vicra (Northern Digital Inc), retro-reflective markers (usually with sphere shapes) reflect the illumination of the camera unit in the form of a near infrared range waves.

Optical trackers are widely used in clinical and surgical procedures which require tracking and navigation. High precision and reliability of these kinds of trackers made them an ideal tracking solution in many procedure such as cranial neurosurgery interventions, however the need for line of sight is still a great limitation which is a main issue in many surgical work flows [7].

3.1.2 Electromagnetic Tracking Systems

Electromagnetic tracking systems have been used in many virtual reality applications before their use in image-guided surgery applications. Although the optical trackers dominate the image guided surgery applications, the fact that electromagnetic trackers do not require the line of sight and can track flexible instruments inside the body has
brought the researchers focus to these category of trackers. There are several commercially available EM-based tracking systems in medical equipments market such as NDI Aurora, Ascension driveBAY, Ascension trakSTAR2, GE ENTrak Plus and Medronic AXIEM. The main disadvantage of EM trackers is the sensors susceptibility to the magnetic field distortions which can affect the final measurement, lower the accuracy and stability of the sensors output. Generally all the EM tracking systems consist of three main parts (Figure 3.4):

1. **Field Generator**: produces the magnetic field and consists of multiple coils placed in different orientations in a specific configuration.

2. **The EM Sensor**: consists of one or multiple arranged coils that generates an electric current in the presence of the magnetic field and is usually combined with a signal amplifier.
Figure 3.4: A typical EM tracker consists of a field generator, an electromagnetic sensor and a processing unit. (Image courtesy of Northern Digital Inc.)

3. **The Processing Unit**: synchronizes the induced current and converts it to position and orientation data using the model of the magnetic field and then sends the data to the surgical navigation computer.

Based on the type of magnetic field there are mainly two types of EM trackers, AC-driven and DC-driven. AC-driven tracking systems are the first generation of these type which first developed by Polhemus Inc. The AC-driven trackers classically consist of three coils for each axis of the Cartesian coordinate system in three dimensional space for a non-medical application. AC-driven systems are not affected by earths magnetic field which is a great benefit compared to the drawback that they will induce eddy currents in the nearly conductive materials which produce an unwanted magnetic field and hence distort the sensors measurement. The NDI (Northern Digital Inc) Aurora system is one of the currently used AC-driven tracking systems which uses a field generator with six tetrahedral coils.
Direct current (DC) trackers overcome the eddy current induction problem by utilizing a pulsed DC field generator but still the earth’s magnetic field and any other DC magnetic field must be canceled out to get the correct sensor measurement. Ascension Technology Inc driveBAY and trakSTAR2 are two commercially available DC-based tackers currently available.

The development of miniature five and six degrees of freedom sensors made these technology a useful solution for image-guided interventional procedures. These sensors have the ability to track flexible instruments inside the body without dependence to line of sight. Several applications need catheter, needle or endoscopic tracking which are not feasible with optical tracking systems but miniature EM tracking sensors can be used successfully.

Optical tracking systems still have much better accuracy comparing with the electromagnetic type. However there is an increasing improvement on the EM tracking technologies to increase their measurement accuracy and stability.

3.2 Rigid Point-based Registration

Registration is an important part of any surgical navigation system. By registration pre-operative scans, intra-operative image data sets are aligned with the patient anatomy and models of surgical devices in a three dimensional coordinate system. One of the most clinically adopted alignment techniques which is widely used in commercially available surgical navigation systems is the point-based rigid registration. In image processing and computer vision context, registration is the problem of finding the unknown transformation which transfer all the features appear in coordinate system A to the corresponding features in the coordinate system B in a way that the data sets in both coordinates are aligned with each other [9]. Point-based rigid registration which is also known as absolute orientation problem is a special kind of the general registration task. In this case the problem is to find the rigid transformation between two Cartesian coordinate systems
by two given point sets. Based on the knowledge about the correspondence (pairing) between the two data sets, there are mainly two approaches to address the registration problem: If the correspondence is known the closed form analytic solution based on least-square solution is the most common approach. In the case of unknown pairing between the points the solution is usually ICP (iterative closest point).

### 3.2.1 Point Acquisition and Pivot Calibration

A stylus is a pointing device which is equipped with a tracking sensor (optical or electromagenetic) and is used in surgical navigation systems to collect points by touching certain predefined points as inputs to the registration algorithm. The tracking unit, measures the position and orientation of the stylus in tracking system coordinate system. Usually there is a difference between the position of stylus tip and the position of mounted sensor. Therefore it is a vital task to first calibrate the stylus, so that the measured position would refer to the stylus tip position. The process is known as pivot calibration and performed by pivoting stylus tip around a fixed point.

A method is presented here to solve the pivot calibration problem. It is possible to calculate the 3D coordinates of the object by knowing the translation between the sensor coordinate system and the stylus tip. For each of the sensor transformations

$$\mathbf{F}(\text{sensor})_i = [\mathbf{R}_i, \mathbf{t}_i]$$

six unknown variables needs to be determined from the following three equations:

$$\mathbf{R}_i\mathbf{t}_{\text{tip}} + \mathbf{t}_i = \mathbf{t}_{\text{post}}$$

By pivoting the stylus around a point we record several transformations and find the unknowns by solving the following least squares problem:
3.2.2 Solution for the Rigid Registration Problem

The rigid registration problem is formulated here based on [10]. Given the moving (m) and fixed (f) points and imaging spaces:

\[
\begin{bmatrix}
R_0 - I \\
\vdots \\
R_n - I
\end{bmatrix}
\begin{bmatrix}
t_{\text{tip}} \\
t_{\text{post}}
\end{bmatrix}
= 
\begin{bmatrix}
t_0 \\
\vdots \\
t_n - I
\end{bmatrix}
\]

where:

\[\Omega_f \subset \mathbb{R}^3, \Omega_m \subset \mathbb{R}^3\]

The rigid registration problem can be formulated as finding the rigid transformation that satisfies:

\[\tau: x_f \mapsto x_m \iff \tau(x_f) = x_m\]

in which:

To solve the problem and reach a unique result at least three non collinear point sets must be collected. In an ideal case where the precision our tracking device is infinity we can propose the following solution for three point registration problem. To find the transformation between the two different coordinate systems we first assign one of the coordinate systems as the origin (fixed coordinate system and the other as moving coordinate system) considering the given points are \(p_{1f}, p_{2f}, p_{3f}\) and \(p_{1m}, p_{2m}, p_{3m}\) the transformation can be calculated using the following steps [9]:
1. Building the three coordinate $x$, $y$ and $z$ axes:

\[
x = \frac{p_2 - p_1}{|p_2 - p_1|}
\]

\[
y = (p_3 - p_1) - [(p_3 - p_1).x]x
\]

\[
y = y/|y|
\]

\[
z = x \times y
\]

2. Constructing the rotation matrices for individual point sets and the rotation between the moving point sets to the fixed point sets:

\[
R_f = [x_f, y_f, z_f]R_m = [x_m, y_m, z_m]
\]

\[
R = R_f R_m^t
\]

3. And finally calculating the translation between the moving coordinate system and the fixed coordinate system:

\[
t = p_{f1} - R p_{m1}
\]
Chapter 4

Needle Navigation System

In this chapter the hardware and software components of the navigation system are presented. In order to test the navigation system a synthetic phantom was also prepared which is discussed in this chapter.

4.1 Navigation Hardware

The hardware components of the designed navigation system (Figure 4.1) consist of a navigation computer, an Aurora tracking system (Northern Digital Inc, Waterloo, ON, Canada) which is equipped with an EM field generator. For convenience the EM field generator was placed beneath the surgical table during the setup. To detect the catheter tip position a 1.3mm diameter, 6 DOF sensor (Northern Digital Inc) was used in the setup. A navigation screen mounted in the operating room in order to guide the process of catheter placement.

4.2 Navigation Software

The processing and display of appropriate information which is available in pre- or intra-operative medical images is a principle in navigation systems which is used to aid in the accurate placement of instruments in the patients body and also to monitor trajectory of
Numerous existing modules using the free and open-source software platform 3D Slicer \[12\] \[13\], as well as custom developed functionality, were used to create the user interface for navigation. The main role of software in this system is to visualize the tracked catheters in the context of cross-sectional images as well as the 3D model of the segmented structures. Besides using the software tools from the 3D Slicer software package, the PlusServer application from the PLUS open source library \[14\] is also used to transmit the 6 DOF position and orientation of the tracked catheter to 3D Slicer using the OpenIGTLink communication protocol \[15\]. The following are the four key software methods and functions employed in the navigation system.

**Registration of MR and CT Images**

MR and CT images of the phantom are co-registered in 3D Slicer. First, a set of corresponding landmarks is manually selected by the operator in each volume. A rigid transformation is then calculated by minimizing the distances between point-pairs by a
least squares algorithm (Fiducial Registration Module of 3D Slicer). The results of this registration are then fine-tuned using a second method (Transforms Module in 3D Slicer) in which interactive sliders allow the operator to translate and rotate one image relative to the other while visually checking the alignment of the overlaid volumes in three orthogonal cross-sections. Visual inspection by the operator is used to determine when the registration is adequate. For enhancing the scene visualization, a 3D CAD model of the obturator and template are also rendered.

**Segmentation**

In image-guided therapy, segmentation of the tumor and the OAR is a necessary step in radiation therapy dose planning and facilitates targeting by providing 3D dimensional visualization to the operator. A number of segmentation methods are available in 3D Slicer, including: painting brushes with thresholding and wand effects, competitive region growing, watershed methods, fast marching, and probabilistic segmentation using the Expectation-Maximization algorithm \cite{16,17}. Subsequent to segmentation, 3D surface models of the binary label maps can be generated using the marching cube algorithm \cite{18} that is implemented in the Model Maker module of 3D Slicer.

**EM Coordinate System to Image Coordinate System Registration**

Rigid landmark-based registration was used for aligning the EM tracker coordinate system to the CT/MR coordinate system: 1) a sequence of landmarks was selected manually on the image volume; 2) a stylus, instrumented with the electromagnetic tracking sensor, was used to touch the corresponding points on the phantom, and the software recorded the 3D positions of these points; 3) the rigid transformation for mapping the two coordinate spaces was calculated.
Target Selection and Visualization of Tracked Catheter

The navigation system provides real-time visualization of catheter positions and orientations with respect to the MR and CT images and surface rendered models of the applicator and targets. Using this visualization, strategies can be devised to reach the target(s).

4.3 Phantom

A commercial, synthetic gel-based phantom (CIRS, Norfolk, VA) was modified and used to evaluate the targeting accuracy of the designed navigation system in the designed experiments. A vaginal obturator was placed in the phantom and attached to a gynecologic Syed-Neblett template, which is CT- and MR-compatible (illustrated in Figures 4.2-a and 4.2-b). Four registration catheters were placed in the phantom – their distal tips served as fiducial points for the registration of the EM tracker coordinate system to the CT/MR coordinate system. The accuracy with which landmarks can be localized in both the image and on the phantom impacts the overall targeting accuracy of the navigation system. The distal ends of brachytherapy catheters, which have a distinct appearance in CT scans and are reproducibly localizable using the EM sensor, were employed as registration landmarks in this study.

4.4 Image-guided brachytherapy setup

Different imaging modalities can be used in gynecologic image-guided brachytherapy. MRI of the pelvic area reveals useful structural and anatomic information whereas CT images can display the details of catheters and the applicator. Pre-procedural CT and MR images of the phantom were acquired after applicator placement but before further placement of catheters. In addition, before each insertion experiment, a CT scan was taken with the fiducial catheters in place. In order to identify fiducial points in the CT scan, copper radiopaque wires (Figure 4.2-c) were inserted in the fiducial catheters. The

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fiducial point (catheter tip) is depicted in the CT. These radiopaque wires are designed to localize the tip position accessible to an HDR brachytherapy source inside the catheter. Figure 4.2.d shows two structures (labeled as A and B), which are considered organs of interest and added to the navigation scene during the procedure; they are visible in the MR image but not in the CT (Figure 4.2.e). In clinical cases, these structures can play the same role as tumors and OAR in navigational approaches. Figure 4.2.f shows the results of MR and CT registration.

The navigation scene (Figure 4.3) was created by aligning the MR, CT, and 3D models of template and obturator. Structure A was segmented using the threshold painter, structure B was delineated with the grow-cut segmentation tool [19], and the resulting 3D models were created and added to the scene. The EM tracker coordinate system was then registered to the image, and the real-time position of the catheter with respect to the phantom was added to the scene.
Figure 4.2: Setup of the proposed navigation system for experiments (a) The gynecologic brachytherapy applicator comprised of a Syed-Neblett template and a vaginal obturator (b) The phantom (transparent) with placed applicator and four fiducial catheters. (c) The visibility of the catheter tips in the CT is enhanced by placing copper markers inside them. (d) Sagittal slice through the MR scan of the phantom shows two structures (A and B) that are not visible in CT scan (e) Sagittal slice through the CT scan of the phantom shows the applicator but the structures are not visible (f) Sagittal slice of MR overlaid on CT scan after registration shows the structures as well as the applicator.
Figure 4.3: A navigation screen from 3D Slicer during catheter insertion experiment. (a) Axial slice through the phantom MRI that shows the catheter tip, structure A, and the obturator. (b) 3D rendering of the brachytherapy applicator CAD model, the catheter (cyan), structures A and B, and target (red sphere). (c) Coronal slice through the phantom MRI during the placement procedure; when the red trajectory of the moving catheter aligns well with target, the operator assumes the catheter placement is correct. (d) Sagittal slice through the phantom MRI showing the catheter, applicator, structures A and B, and the target.
Chapter 5

Experimental Setup & Results

5.1 Accuracy Evaluation Experiments

Two independent sets of experiments were performed to evaluate the accuracy of image-guided catheter placement using the proposed navigation system.

5.1.1 Experiment 1: Using 12 Catheter Tips as Targets

In this experiment, one operator created targets by placing twelve commercially available 6F (French gauge) brachytherapy catheters (Nucletron Inc., Netherlands) in the phantom such that their tips covered structure A. The same operator also placed four additional catheters, two on the surface of the template and two on the distal end of the obturator, so that their distal tips would serve as fiducial points for the EM tracker to image registration. After the insertion of all 16 catheters (12 targets, 4 fiducials), a CT scan of the phantom was acquired and the target catheters were removed. This CT scan was used as a navigation map for the subsequent targeting evaluation procedures. Three different operators performed four navigated insertion procedures with the goal of reaching the twelve distal catheter tip targets with the help of the navigation map. The fiducial catheters remained in the same positions during the entire experiment. A total of 48 catheters were inserted with the guidance of the navigation system. The transparent
phantom was covered with opaque material during the experiments so that the operators could not inadvertently gain additional visual information about the actual trajectory of their needles. Following each set of 12-catheter insertions, a confirmatory CT scan was acquired and the results were compared with the planning CT scan to calculate the targeting error.

5.1.2 Experiment 2: Using Three Gold Seeds as Targets

In this experiment, one operator placed gold seeds and fiducial catheters inside the phantom. The operator then covered it with an opaque material and provided it to the second operator, who acquired a CT scan and performed the remainder of the experiment. The second operator located the three targets in the CT scan and planned the insertion by finding the specific template hole and depth of insertion. The navigation system was used to guide three catheters to hit the gold targets. After the insertion, a confirmatory CT scan was taken in order to calculate the distance between the gold seeds and the catheter tips so as to determine the targeting accuracy of the placement system.

5.2 Results

5.2.1 Experiment 1: Using 12 Catheter Tips as Targets

The targeting accuracy was evaluated based on 48 catheter insertions from four procedures. After each procedure, a CT scan of the phantom with the placed catheters was acquired and registered to the planning CT scan. Distances between corresponding catheter tip positions were used to calculate targeting errors. Figure 4 shows the appearance of the target catheters in the planning CT scan and the 3D models of the placed catheters that are extracted using the 3D Slicer iGyne module from the post-insertion CT scan. The mean and standard deviation of the targeting error from each of the four procedures is shown in Table 5.1.
The targeting error for each of the catheters, across the four placement procedures, is illustrated in Figure 5a. The distances for different catheter insertion in the X-Y plane (mediolateral plane (X) and anteroposterior plane (Y)) was also calculated and is depicted in Figure 5b.

Table 5.1: Targeting error in Experiment 1. Values for mean and standard deviation of the targeting errors in four procedures, each performed by a different operator and consisting of the placement of 12 catheters using navigation.

<table>
<thead>
<tr>
<th>Procedure #</th>
<th>Targeting error (mean ± standard deviation in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.49 ± 1.45</td>
</tr>
<tr>
<td>2</td>
<td>3.55 ± 3.08</td>
</tr>
<tr>
<td>3</td>
<td>3.10 ± 1.46</td>
</tr>
<tr>
<td>4</td>
<td>2.41 ± 1.09</td>
</tr>
<tr>
<td>Combined 4 procedures</td>
<td>2.89 ± 1.93</td>
</tr>
</tbody>
</table>

5.2.2 Experiment 2: Using 3 Gold Seeds as Targets

In this experiment, the targeting error was computed as the Euclidean distance between the tip position of the placed catheters and the corresponding center of the gold seeds. Figure 5.3 illustrates the catheter tips and the gold targets in the confirmatory CT scan. Table 5.2 shows the mean and standard deviation of the targeting error averaged over three catheter placements by a single operator.

Table 5.2: Targeting error in Experiment 2. Values for mean and standard deviation averaged over 3 catheter placements with the goal of reaching the gold seed with the catheter tip. Delta X, delta Y and delta Z are right-left, anterior-posterior and superior-inferior directions in the CT scanner coordinate system.

<table>
<thead>
<tr>
<th></th>
<th>delta X (mm)</th>
<th>delta Y (mm)</th>
<th>delta Z (mm)</th>
<th>targeting error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment #2</td>
<td>1.22 ± 0.89</td>
<td>1.54 ± 0.91</td>
<td>1.54 ± 1.67</td>
<td>2.95 ± 0.83</td>
</tr>
</tbody>
</table>
Figure 5.1: The planning CT scan and 3D models of the inserted and fiducial catheters in Experiment 1. (a) Axial slice through the CT of the phantom shows the planning catheter tip as a white dot and the placed catheter tip as a black circle. (b) 3D models of the fiducial catheters and the placed catheters. (c) Sagittal slice through the phantom: alignment of fiducial catheter model (extracted from post-placement CT) with the white line (the same catheter in planning CT) ensures the registration accuracy. (d) Coronal slice through the post-placement CT of the phantom. The targeting error is visible as the displacement between the placed and the planned catheters.
Figure 5.2: Targeting errors for 48 catheters placements, performed in 4 procedures. (a) The distance between each planned and placed tip. (b) Displacement error in the X-Y plane (the plane parallel to the guiding template).
Figure 5.3: Catheter tips and gold seeds in the post-insertion CT for Experiment 2. (a) Axial slice through the phantom CT shows gold seeds and catheter tips clearly. (b) 3D models of placed catheters whose tips are indicated as red balls and centers of gold seeds indicated by green balls through the axial slice of phantom CT. (c) Sagittal slice through the phantom CT and a single placed catheter relative to the corresponding gold seed. (d) Coronal slice through the phantom CT showing a second catheter and corresponding gold seed.
Chapter 6

Conclusion and Future Works

A navigation system for guiding the gynecology brachytherapy catheter placement was designed and a method was deployed for evaluating of this system. The accuracy of the procedure of image-guided catheter placement was evaluated with a mean targeting error of 2.89 mm over 48 catheter placements by 3 different operators in a benchtop experiment that closely mimics interstitial gynecologic brachytherapy. Similarly, in another experiment a user aimed at targeting implanted fiducials in a phantom and a targeting error of brachytherapy interstitial catheters <3 mm was acquired. It is worth mentioning that a basic difference between this study and the similar studies are in the process of assessing targeting error. In measuring the targetting accuracy for the tests in this thesis brachytherapy markers were used in order to estimate the distance between target and catheter tip. It is clinically relevant that the catheter tip measured using this methodology corresponds to the tip dwell location of an HDR brachytherapy source. A distance exists between the tip dwell location and the physical tip of the catheter to allow for clearance of the source. Therefore, in our set of experiments, a perfect position may not correspond to a targeting error of 0 mm. Exact evaluation of this effect and of possible misalignment between the location of the EM tracking probe and the tip dwell location will be performed in the future. Although it is not possible to extrapolate these results to in vivo experiments, the accuracy observed in this study is consistent with the clinical
need for precisely positioning interstitial catheters in a tumor without piercing adjacent critical structures. Furthermore, given a particular selection of template insertion hole, the visualization of catheters and extrapolation of possible catheter paths may prove useful for real-time planning of the catheter configuration. The next steps will include fabrication of catheters with embedded EM sensors followed by an evaluation of targeting accuracy and placement time with and without navigation. Future validation of these results using patient data will allow for the estimate of potential benefits of using EM technology in brachytherapy: reduction in implantation time, reduction of frequency of OAR perforation, and increased tumor coverage resulting from optimal positioning of the catheters.
Bibliography


